Intramedullary versus extramedullary fixation in the treatment of subtrochanteric femur fractures: A comprehensive systematic review and meta-analysis

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ABSTRACT

Objective: This meta-analysis aimed to compare the clinical outcomes of intramedullary fixation with the extramedullary fixation in the surgical management of subtrochanteric fractures by analyzing relevant randomized controlled trials (RCTs) and retrospective cohort studies (RCSs).

Methods: The PubMed, Embase, Cochrane Library, Wanfang database, and Chinese National Knowledge Infrastructure (CNKI) were searched from their inception till June 29, 2020. Two reviewers extracted the data, including operation time, intraoperative blood loss, fluoroscopy time, length of stay, union time, nonunion rate, infection rate, implant failure rate, reoperation rate, Harris hip score, and mortality rate. The Cochrane risk-of-bias tool and the Newcastle-Ottawa quality assessment scale were used to evaluate the methodological quality of RCTs and RCSs, respectively. Statistical heterogeneity was quantitatively evaluated with the I2 statistic.

Results: There were no significant differences in operation time, intraoperative blood loss, average length of stay in hospital, infection rate, implant failure rate, Harris hip scores, and mortality rate. Intramedullary nail could achieve shorter union time (MD=-1.77, 95% CI -3.40 to -0.14, p=0.03), lower nonunion rate (RR=0.36, 95%CI 0.14 to 0.97, p=0.04), and reoperation rate (RR=0.46, 95% CI 0.24 to 0.89, p=0.02) than extramedullary fixations. The subgroup analysis indicated that intramedullary nail was superior than extramedullary fixations in operation time, reoperation rate, and Harris hip scores in the ≥60-year subgroup. However, the intraoperative blood loss in intramedullary nail group was significantly higher than that of extramedullary fixation group in the <60-year subgroup.

Conclusion: The results of this study have revealed that intramedullary fixation can confer shorter union time, lower nonunion, and reoperation rates compared with extramedullary fixations. Therefore, intramedullary fixation should be considered as the first selection for the treatment of patients with subtrochanteric fractures.

Level of Evidence: Level II, Therapeutic study

Introduction

Subtrochanteric fractures are defined as the fractures that take place between the less trochanter and 5 cm distally in the shaft of the femur, which account for 10%-34% of hip fractures (1, 2). The incidence of subtrochanteric fractures has a bimodal age distribution, affecting young patients following high-energy trauma and older patients after low-velocity trauma secondary to osteoporosis or metastatic pathological lesions (3).

The characteristics of the subtrochanteric region have determined the complexity of the treatment for this fracture. The joint reaction force and hip muscle contraction forces lead to a great stress state in the subtrochanteric region. One biomechanical study showed that there was 6.3 MPa pressure on the medial side and 6.2 MPa on the lateral side within 2.5-7.5 cm below the lesser trochanter in an 89 kg adult (4). This area is predominantly cortical bone with poor vascularity that accounts for longer healing time after a fracture. Thus, any internal fixation device is subject to significant concentrated bending stress, leading to implant fatigue and fixation failure if the fracture does not unite on time. Furthermore, the deforming forces of flexion and external rotation from the iliopectos, abduction from the gluteus medius, adduction and shortening of the shaft from the hamstrings and adductors, as well as the degree of the comminution of the medial cortical buttress at the subtrochanteric region constitute a surgical challenge for the orthopedic surgeon (5, 6). The literature reported that the complication rate of the surgery of subtrochanteric fractures was ranging from 19% to 32% (7).

Open or closed reduction and internal fixation surgery is the critical method for the treatment of the subtrochanteric fractures. Intramedullary and extramedullary fixations are two types of implants for the fixation of subtrochanteric fractures. Many studies advocated the use of the intramedullary nailing as the first choice for the treatment of the subtrochanteric fractures because of the central fixation and small incision, which can minimize the soft tissue dissection and preserve vascularity at the fracture site (8, 9). However, studies have reported that extramedullary fixation, such as plating, could achieve satisfactory outcomes because of the minimally invasive percutaneous plate osteosynthesis (MIPO) technique (10, 11). This technique also avoids extensive soft tissue dissection in the long bone fracture, which could reduce the surgical damage and complications common in patients treated by conventional plating (12). Although orthopedic surgeons should consider many factors to select the fixation method, whether intramedul-
lary or extramedullary fixation is more appropriate for the treatment of subtrochanteric fractures is still controversial. A total of 3 meta-analyses (9, 13, 14) have been published. Xie’s meta-analysis indicated that intramedullary fixation had shorter operation time, less intraoperative blood loss, shorter length of incision, shorter length of stay, better functional outcomes, and a lower rate of fixation failure and reoperation compared with the extramedullary fixation (13). Liu’s meta-analysis showed that there was no significant difference in any outcomes between intramedullary and extramedullary fixations, except for the fixation complications (14). Kuzyk’s meta-analysis demonstrated that intramedullary fixation could reduce the operative time and fixation failure (9). However, most of the patients in some included studies in these meta-analyses (9, 13, 14) did not suffer the subtrochanteric fractures. Most of the included studies in Kuzyk’s meta-analysis did not have control groups (9). Therefore, this meta-analysis was conducted to evaluate the outcomes of intramedullary fixation versus extramedullary fixation in the surgical management of subtrochanteric fractures by analyzing the current randomized controlled trials (RCTs) and retrospective cohort studies (RCSs) that compared intramedullary and extramedullary fixations for subtrochanteric fractures.

Materials and Methods

This meta-analysis was carried out according to the guidelines of the Cochrane Collaboration but was not a formal Cochrane review (15). The findings are reported as recommended by the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (16).

Search strategy

We searched PubMed, Embase, the Cochrane Library, Wanfang database, and Chinese National Knowledge Infrastructure (CNKI) from their inception till June 29, 2020. The following search strategy was used in the English database: (extramedullary OR intramedullary) AND subtrochanteric. The limit in searching was title and abstract. We also searched the references of previously published randomized trials, reviews, and meta-analysis for additional eligible studies. No language restrictions were used.

Inclusion and exclusion criteria

Studies were included in the meta-analysis if they met the following criteria: they were RCTs or RCSs; they compared intramedullary and extramedullary fixations for patients with subtrochanteric fractures; the patients included in the trials were older than 18 years. Studies were excluded if they were experimental trials; data were incomplete or unavaiilable; they were non-original articles, such as reviews, or letters and comments; not all the patients have the subtrochanteric fractures.

Evaluated outcomes

Operation time, intraoperative blood loss, fluoroscopy time, length of stay, union time, nonunion rate, infection rate, implant failure rate, reoperation rate, Harris hip score, and mortality rate.

HIGHLIGHTS

- The intramedullary nail could achieve shorter union time, lower nonunion rate and reoperation rate compared with the extramedullary fixations for the treatment of Subtrochanteric fractures.
- Subgroup analysis indicated that intramedullary nail was superior to extramedullarily fixation in operation time, reoperation rate and Harris hip scores in <60 years subgroup.
- The intraoperative blood loss in intramedullary group was significantly more than extramedullary group in <60 years subgroup.

Study selection

Two independent reviewers performed the selection of studies and consensus was used to resolve any disagreement. Duplicates were initially excluded. The titles and abstracts were screened to exclude the irrelevant articles or those that do not meet the inclusion criteria. Subsequently, the remaining studies were assessed through full-text reading and carefully selected according to the inclusion and exclusion criteria.

Data extraction

Data from the included studies were extracted by two independent reviewers using a standard data-collection form. The data extracted from the studies included last name of the first author, publication year, country, study design, sample size, age of subjects, sex distribution, the type of fracture, the type of interventions, follow-up term, operation time, intraoperative blood loss, the average length of stay in the hospital, union time, nonunion rate, infection rate, implant failure rate, reoperation rate, Harris hip score, mortality rate. Samples sizes, means and standard deviations were extracted for continuous outcomes, and the number of cases were extracted for dichotomous outcomes. If trials reported incomplete data, authors were contacted for further information.

Methodological quality assessment

Two reviewers independently assessed the methodological quality and the risk of bias of the included RCTs using the Cochrane risk-of-bias tool (17). Disagreements were resolved by consulting a third reviewer. The following aspects were assessed: randomization, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Each item was scored as high, low, or unclear risk of bias. The quality of RCSs was assessed using the Newcastle-Ottawa quality assessment scale (NOS) (18) for non-randomized case-controlled studies and cohort studies. Three items were assessed: selection, comparability, and exposure. The NOS uses a scoring system that ranges from zero to nine points. The score more than 6 points was considered to be high-quality.

Data synthesis and analysis

The RevMan 5.3 software (the Nordic Cochrane Center, the Cochrane Collaboration, Copenhagen, Denmark) was used to conduct this meta-analysis. The I² statistic was used to assess heterogeneity between trials, and value higher than 50% were defined as high heterogeneity (19). When the I²<50%, a fixed-effect model was used to calculate mean differences (MD) and 95% confidence intervals (CI) for continuous measures and risk ratio (RR) and 95% CI was used for dichotomous measures. When the I²>50%, the random effect model was used to calculate these parameters. Because the bone quality decreased with age and osteoporosis was more common in the elderly, the subgroup analysis was stratified by the age >60 years or <60 years. When three studies were included in the comparisons, a sensitivity analysis was done by omitting one or more studies that might increase the heterogeneity of each outcome to see whether specified factors could influence the overall effects of each outcome (20).

Results

Literature search and study characteristics

Figure 1 illustrates the selection flow of studies in our meta-analysis. We retrieved a total of 2,162 potential studies. In total, 21 studies were needed to be full-text assessment after the title and abstract scanning. A total of 4 RCTs (21-24) were excluded because most of the patients in these trials did not suffer a subtrochanteric fracture. A total of 2 studies.
A total of 924 subjects with subtrochanteric fracture were reported, in including 486 with intramedullary fixation and 438 with extramedullary fixation. The average age of 8 trials (28, 30, 32, 33, 35, 36, 38, 39) was less than 60 years, and of 5 trials (8, 29, 31, 34, 37) was more than 60 years. The intramedullary fixation evolved in trials included proximal femoral nail (PFN), Russel-Taylor reconstruction nail (RTNR), Gamma nail, and InterTan nail and proximal femoral nail antitrotation (PFNA). The extramedullary fixation evolved in trials included a 95° blade plate (BP), dynamic condylar screw (DCS), locking compression plate-distal femur (LCP-DF), compression hip screw (CHS), reverse less invasive stabilization system-distal femur (LISS-DF), proximal femoral locking plate (PFLP), and dynamic hip screw (DHS). The follow-up periods of the included trials were all more than 3 months. Table 1 illustrates the characteristics of included studies.

### Table 1. The characteristics of included studies

| Study design                  | Included study | Country    | Sample size (IM/EM) | Fracture type     | Age (IM/EM) | Female (IM/EM) | Intramedullary fixation | Extramedullary fixation | Outcomes                                                                 | Follow-up period (months) |
|------------------------------|----------------|------------|---------------------|-------------------|-------------|----------------|-------------------------|------------------------|---------------------------------------------------------------------------|--------------------------|
| Randomized controlled trial  | Rahme 2007     | Australia  | 29/29               | Seinsheimer I-IV  | 73 ± 67     | 18/17          |PFN                       | 95° blade plate          | operation time, length of stay, blood transfusion, complication rate, SF-36 score | 12                       |
| Lee 2007                     | China          | 34/32      | Seinsheimer III-V   | 35.4 (7.9)/36.8 (9.2) | 9/6         | RTRN           | DCS                     | operation time, fluoroscopy time, length of incision, blood loss, blood transfusion, length of stay, fracture union time, union rate, pain in thigh and hip, hip movements | >24                      |
| Goldhagen 1994               | USA            | 34/36      | NR                  | 78                | 22          | Gamma nail     | CHS                     | operation time, fluoroscopy time, blood loss, blood transfusion, complications | >6                       |
| Retrospective cohort study    | Shin 2017      | Korea      | 50/31               | AO/OTA 32-A, B or C | 51.0±16.0/55.2±14.5 | 18/11 | PFNA           | LCP-DF                  | operation time, fluoroscopy time, blood transfusion, fracture union time, full weight bearing time, Harris scores, complications | >12                      |
| Imerci 2015                  | Turkey         | 16/15      | AO/OTA 32-A, B or C | 43(19-81)/48(21-86) | 5/7         | PFNA           | Reverse LISS-DF         | operation time, fluoroscopy time, blood transfusion, length of stay, fracture union time, full weight bearing time, Harris scores, complications | >11                      |
| Mirbolook 2015               | Iran           | 43/71      | Russell-Taylor Ia   | 47.28±15.94       | 51          | PFN            | PFLP                    | Harris scores, full weight bearing time, complications                      | 6                        |
| Yadav 2014                   | India          | 15/15      | Russell-Taylor Ia-Ia | 37.5              | 7           | PFN            | DCS                     | operation time, fluoroscopy time, blood transfusion, length of stay, blood loss, complications | 12                       |
| Burnei 2011                  | Romania        | 37/31      | Seinsheimer I-IV    | 64                | 27          | Gamma nail     | DHS, DCS                | operation time, length of stay, complications                              | 3                        |
| Saarenpää 2007               | Finland        | 43/15      | Seinsheimer I-V     | 76.8±74.1         | 30/12       | Gamma nail     | DHS                     | operation time, length of stay, 4 complications, functional parameters    |                          |
| Brien 1991                   | USA            | 33/25      | Winquist-Hansen I-IV| 26/39             | 4/8         | Interlocking   | 95° blade plate        | operation time, blood loss, fracture union time, complications            | >9                       |
| Han 2019                     | China          | 35/23      | Seinsheimer I-V     | 66.5±23.5/63.4±22.4 | 17/15       | Long Gamma nail | PFLP                    | operation time, blood loss, length of stay, fracture union time, Harris scores | >14                      |
| Dou 2015                     | China          | 47/48      | Seinsheimer I-V     | 57                | 50          | PFNA           | Reverse LISS, PFLP      | Operation time, blood loss, fracture union time, Harris scores             | >3                       |
| Li 2013                      | China          | 34/31      | Russell-Taylor II   | 52.5±12.1/54.4±15.9 | 11/14       | PFNA, LCP, DHS  | DHS                     | Operation time, blood loss, length of stay, fracture union time, Harris scores | >12                      |
| Xie 2017                     | China          | 36/34      | Seinsheimer I-V     | 57.97±20.97/60.85±18.63 | 12/11       | InterTan nail  | PFLP                    | Operation time, blood loss, length of stay, fracture union time, Harris scores, VAS, full weight bearing time | >12                      |

IM: intramedullary; EM: extramedullary, PFN: proximal femoral nail; RTNR: Russell-Taylor reconstruction nail; DCS: dynamic condylar screw; CHS: compression hip screw; PFNA: proximal femoral nail antitrotation; LISS-DF: less invasive synthesis system-distal femur; PFLP: proximal femoral locking plate; DHS: dynamic hip screw; VAS: visual analogue scale/score

### Study quality assessment

All the included RCTs (8, 28, 29) had conducted the proper randomization but none of them conducted the allocation concealment and blinding of patients and outcome assessor. The outcome data of 2 of the RCTs (8, 29) was incomplete. All the included RCTs (8, 28, 29) did not have selective reporting and other bias. (Table 2)

A total of 3 RCSs (37, 39, 40) achieved 7 scores, 4 (32-35) achieved 6 scores, 2 (30, 38) achieved 5 scores, 1 (36) achieved 4 scores and 1 (31) achieved 3 scores. The quality of all RCSs was moderate to high, except Burnei’s study (31). (Table 3)
Operation time
In total, 1 RCT (28) and 5 RCSs (33, 37-40) were identified for the operation time. High heterogeneity ($I^2=83\%$, $p<0.0001$) was detected, so the random effect model was used for analysis. The pooled results showed that no significant difference was detected between the two groups (MD=−6.82, 95%CI -16.63 to 2.99, $p=0.17$). The sensitivity analysis showed that the overall effect could not be influenced by omitting any single study for each comparison.

Intraoperative blood loss
In total, 1 RCT (28) and 5 RCSs (33, 37-40) were identified for the intraoperative blood loss. High heterogeneity ($I^2=98\%$, $p<0.00001$) was detected, so the random effect model was used for analysis. The pooled results showed that no significant difference was detected between the two groups (MD=31.73, 95%CI -68.84 to 132.30, $p=0.54$). The sensitivity analysis showed that the overall effect could not be influenced by omitting any single study for each comparison.

Fluoroscopy time
In total, 2 RCTs (28, 29) and 2 RCSs (32, 36) reported the fluoroscopy time. However, data from the included studies could not be used for meta-analysis. One RCT (28) and 1 RCS (32) reported that the fluoroscopy time of intramedullary nail was significantly longer than extramedullary fixation. One RCT and 1 RCS showed no significant difference between these groups on fluoroscopy time. Over the included studies, the average fluoroscopy time of intramedullary nail

| Included studies | Randomized adequately | Allocation concealed | Patient blinded | Outcome assessor blinded | Incomplete outcome data | Selective reporting | Other bias |
|------------------|-----------------------|----------------------|----------------|-------------------------|------------------------|-------------------|-----------|
| Rahme 2007       | Low risk              | High risk            | High risk      | High risk               | Low risk               | Low risk          | Low risk  |
| Lee 2007         | Low risk              | High risk            | High risk      | High risk               | High risk              | Low risk          | Low risk  |
| Goldhagen 1994   | Low risk              | High risk            | High risk      | High risk               | Low risk               | Low risk          | Low risk  |

Table 2. The methodological quality assessment of RCTs

Figure 1. The study selection flow of this meta-analysis
and extramedullary fixation was 160.9 seconds and 111.6 seconds, respectively.

**Length of stay**

One RCT (28) and 3 RCSs (37, 39, 40) reported length of stay. No significant heterogeneity ($I^2=0\%$, $p=0.98$) was found in the pooled outcome, so a fixed-effect model was utilized. The pooled results showed that no significant difference was detected between the intramedullary nail and extramedullary fixations (MD=-0.77, 95%CI -1.92 - 0.38, $p=0.19$). The sensitivity analysis showed that the overall effect could not be influenced by omitting any single study for each comparison.

**Union time**

One RCT (28) and 5 RCSs (35, 37-40) were identified for the union time. High heterogeneity ($I^2=72\%$, $p=0.003$) was detected, so the random effect model was used for this outcome. The available evidence demonstrated that the fracture union time in intramedullary nail group was significantly shorter than that in extramedullary fixation group (MD=-1.77, 95%CI -3.40 - -0.14, $p=0.03$). However, sensitivity analysis showed that the overall effect could be influenced by omitting any single study for each comparison (Figure 2).

**Nonunion rate**

Two RCTs (8, 28) and 3 RCSs (33, 35, 39) reported the nonunion rate. No heterogeneity ($I^2=0\%$, $p=0.04$) was found, so the fixed-effect model was used in this analysis. The pooled results showed that the nonunion rate in intramedullary nail group was significantly less compared with that in extramedullary fixation group (RR=0.36, 95%CI 0.14 - 0.97, $p=0.04$). However, sensitivity analysis showed that the overall effect could be influenced by omitting any single study for each comparison (Figure 3).

**Infection rate**

Two RCTs (8, 28) and 7 RCSs (30-34, 36, 40) reported infection rate. No heterogeneity ($I^2=0\%$, $p=0.55$) was found in this outcome, so the fixed-effect model was used. The pooled results showed that no significant difference was detected between the two groups (RR=0.95, 95%CI 0.55 - 1.65, $p=0.86$). The sensitivity analysis showed that the overall effect could not be influenced by omitting any single study for each comparison.

**Implant failure rate**

Three RCTs (8, 28, 29) and 5 RCSs (30, 31, 33, 34, 40) reported the implant failure rate. No heterogeneity ($I^2=0\%$, $p=0.54$) was found in this outcome, so the fixed-effect model was used. The pooled results showed that no significant difference was detected between the two groups (RR=0.74, 95%CI 0.35 - 1.55, $p=0.42$). The sensitivity analysis showed that the overall effect could not be influenced by omitting any single study for each comparison.

**Reoperation rate**

There were 3 RCTs (8, 28, 29) and 3 RCSs (31, 34, 39) reporting the reoperation rate. Low heterogeneity ($I^2=34\%$, $p=0.03$) was found, so the fixed-effect model was used in this analysis. The pooled results showed that the overall effect could be influenced by omitting any single study for each comparison (Figure 3).

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### Table 3. The methodological quality assessment of RCSs

| Included studies | Selection | Comparability | Exposure | Total score |
|------------------|-----------|---------------|----------|-------------|
| Shin 2017        | 2         | 2             | 2        | 6           |
| Imerci 2015      | 2         | 2             | 2        | 6           |
| Mirbolook 2015   | 2         | 2             | 2        | 6           |
| Yadav 2014       | 2         | 0             | 2        | 4           |
| Burnei 2011      | 2         | 0             | 1        | 3           |
| Saarenpää 2007   | 2         | 2             | 2        | 6           |
| Brien 1991       | 2         | 0             | 3        | 5           |
| Han 2019         | 2         | 2             | 3        | 7           |
| Dou 2015         | 2         | 2             | 3        | 7           |
| Li 2013          | 2         | 2             | 3        | 7           |
| Xie 2017         | 2         | 2             | 3        | 7           |

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Figure 2. The forest plot to illustrate the mean difference in the union time of subtrochanteric fracture between intramedullary and extramedullary fixations.

Figure 3. The forest plot to illustrate the risk ratio in the nonunion rate of subtrochanteric fracture between intramedullary and extramedullary fixations.
showed that the reoperation rate in intramedullary nail group was significantly less compared with that in extramedullary fixation group (RR=0.46, 95%CI 0.24 ~ 0.89, p=0.02). However, sensitivity analysis showed that the overall effect could be influenced by omitting any single study for each comparison (Figure 4).

### Harris hip score

Three RCSs reported the Harris hip scores (37-39). High heterogeneity (I²=61%) was detected, and the random effect model was used for analysis. The pooled results showed that no significant difference was detected between the two groups (MD=2.00, 95%CI -1.34 ~ 5.35, p=0.24). However, sensitivity analysis showed that the overall effect could be influenced by omitting any single study for each comparison (Figure 4).

### Mortality rate

One RCT and one RCS reported the mortality rate (8, 34). No heterogeneity (I²=0%, p=0.47) was detected, so the fixed-effect model was used for analysis. The pooled results showed that no significant difference was detected between the two groups (RR=2.04, 95%CI 0.73 ~ 5.68, p=0.17). Sensitivity analysis was not used in this comparison as there were only two studies in this comparison.

### Subgroup analysis

All the comparisons were conducted the subgroup analysis, except for the mortality rate. In≥60 years subgroup, the operation time, reoperation rate and Harris hip scores in intramedullary nail group were significantly superior to that in extramedullary fixation group. In<60 years subgroup, the intraoperative blood loss in the intramedullary nail group was significantly more compared with that in extramedullary fixation group. There were no significant differences between the two groups in the subgroup analysis for the other comparisons.

### Discussion

Due to the anatomical peculiarity, the treatment of subtrochanteric fractures is still a great challenge to the orthopedic surgeons not only because of the osteosynthesis difficulties but also for the still frequent complications. The optimal device for stabilization of subtrochanteric fractures would be an implant that resists the tendency for shaft medialization, as well as rotation and Varus angulation of the proximal fragment. There has been considerable controversy in the literature regarding the best type of implant (41). Both intramedullary and extramedullary fixation have been championed for the management of subtrochanteric fractures (42). This meta-analysis has demonstrated that intramedullary nail could achieve shorter union time, lower nonunion rate and reoperation rate compared with the extramedullary fixations for the treatment of the subtrochanteric fractures. Subgroup analysis indicated that intramedullary nail was superior to extramedullary fixations in operation time, reoperation rate and Harris hip scores in ≥60 years subgroup. However, the in-

### Table 4. The results of subgroup analysis of the comparisons

| Comparisons          | Subgroups | No. of studies | Patients (IM/EM) | I² | Heterogeneity [p] | MD/RR | 95% CI | Z test [p] |
|----------------------|-----------|----------------|-----------------|----|------------------|-------|--------|------------|
| Operation time       | ≥60       | 3              | 115/82          | 0% | 0.49             | -7.67 | -14.98 to -0.36 | 0.04 |
|                      | <60       | 2              | 81/80           | 25%| 0.25             | 2.97  | -1.57 to 7.52   | 0.20 |
| Intraoperative blood loss | ≥60 | 3              | 115/82          | 98%| -0.00001         | 23.77 | -163.90 to 211.43 | 0.60 |
|                      | <60       | 2              | 81/80           | 70%| 0.07             | 97.96 | 7.51 to 188.45  | 0.03 |
| Length of stay       | ≥60       | 2              | 65/51           | 0% | 1                | -1.00 | -2.56 to 0.56   | 0.21 |
|                      | <60       | 1              | 34/32           | NA | NA               | -0.70 | -4.75 to 3.35   | 0.74 |
| Union time           | ≥60       | 3              | 115/82          | 79%| 0.009            | -2.67 | -7.45 to 2.10   | 0.27 |
|                      | <60       | 2              | 81/80           | 80%| 0.03             | -1.95 | 0.00 to 0.90    | 0.18 |
| Nonunion rate        | ≥60       | 3              | 113/91          | 41%| 0.18             | 0.32  | 0.10 to 0.99    | 0.05 |
|                      | <60       | 2              | 77/103          | 0% | 0.61             | 0.54  | 0.08 to 3.91    | 0.54 |
| Infection rate       | ≥60       | 3              | 109/75          | 56%| 0.10             | 0.82  | 0.08 to 8.28    | 0.87 |
|                      | <60       | 5              | 141/158         | 0% | 0.66             | 1.09  | 0.51 to 2.33    | 0.82 |
| Implant failure rate | ≥60       | 4              | 143/113         | 41%| 0.17             | 0.56  | 0.22 to 1.47    | 0.24 |
|                      | <60       | 3              | 110/128         | 0% | 0.79             | 1.13  | 0.25 to 5.05    | 0.68 |
| Reoperation rate     | ≥60       | 5              | 173/138         | 34%| 0.19             | 0.40  | 0.20 to 0.81    | 0.01 |
|                      | <60       | 1              | 34/32           | NA | NA               | 1.68  | 0.18 to 19.77   | 0.60 |
| Harris hip scores    | ≥60       | 2              | 65/51           | 0% | 0.92             | 4.10  | 0.84 to 7.36    | 0.01 |
|                      | <60       | 1              | 47/48           | NA | NA               | -0.13 | -1.85 to 1.59   | 0.88 |

IM: intramedullary; EM: extramedullary; No.: number; MD: mean difference; RR: risk ratio; CI: confidence intervals.

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Figure 4. The forest plot to illustrate the risk ratio in the reoperative rate of subtrochanteric fracture between intramedullary and extramedullary fixations.
traoperative blood loss in the intramedullary nail group was significantly more compared with that in extramedullary fixation group in <60 years subgroup.

For the extramedullary fixation, high-stress shielding effect was detected on the bone beneath the plate, which caused the lack of stress stimulation at the fracture site and made the union of the fracture slower [43-45]. While the central fixation of intramedullary nail made the stress shielding effect less than that of extramedullary fixation and the role of loading sharing play the main effect [46, 47]. The union of the fracture was facilitated under loading sharing effect.

Although our meta-analysis could not synthesize the data about fluoroscopy time, the average fluoroscopy time of intramedullary nail was longer than extramedullary fixation based on the four included studies [28, 29, 32, 36]. The intramedullary nail always needed more fluoroscopy time to guide and correct the direction of the nail or screws (28), especially the long intramedullary nail (48). However, the difficulties caused by the insertion of a guidewire and distal screws could be reduced by new technique (49) or C-Arm with better mobility and imaging quality (50).

The reasons for reoperation were nonunion, implant failure, refracture and so on (34, 47). It has been reported that there is a high failure rate of extramedullary fixation, especially locking plate (51, 52), which might be the reason for the high reoperation rate of extramedullary fixation.

Our meta-analysis conducted the age-based subgroup analysis of the included trials because the incidence of subtrochanteric fractures has a bimodal age distribution: young and old people (3). The results of Ekstrom et al.’s study was similar to our meta-analysis (22). The average age of the patients included in Ekstrom et al.’s study was 83 years old, and the results showed that the operation time of intramedullary nail was shorter than that of extramedullary fixation (22). Sadowski et al.’s study included the patients with an average age at 77 years old, and the operation time was similar to this meta-analysis (24). Liu’s meta-analysis recommended intramedullary nail for the treatment of elderly patients with subtrochanteric fractures because a significant decrease was found in the complication rate for patients who were treated with an intramedullary nail (14). Our meta-analysis found that intramedullary nail could achieve shorter operation time, lower reoperation rate and higher Harris scores compared with extra-medullary fixations. The systematic review of Kuzyk et al., evaluated 3 level I trials and 9 level IV trials and indicated that the operation time and reoperation rate of the intramedullary nail were superior to that of extramedullary fixations for the treatment of the subtrochanteric fractures [9].

The intraoperative blood loss in the intramedullary nail group was significantly more compared with that in extramedullary fixation group in <60 years subgroup. In the two trials included in this comparison, the extramedullary fixations were all inserted by the MIPO technique [53]. Because of the locking screw design, it is not necessary to strip the periosteum during plate insertion. This prevents blood circulation to the injured part and enhances healing of the fracture, and minimal invasive internal fixation techniques disrupt the femoral blood supply less than the traditional open method (54). Hence, the intraoperative blood loss was reduced than traditional technique and intramedullary nail.

The results of this meta-analysis should be interpreted with caution because of the following limitations. First, only three RCTs were included in this study. However, the RCSs could also give us some evidence, although the level of evidence was lower. Second, the length of the follow-up period was variable. We could only extract the data at the end of the follow-up period. Third, the types of intramedullary and extramedullary fixations were variable, and the types of subtrochanteric fracture were also variable. Because of the limited number of included studies, we could not conduct the subgroup analysis based on the type of implant or the type of subtrochanteric fracture and evaluate the publication bias. Therefore, additional well-design RCTs with more participants, long-term follow-up, and data on patient-reported outcomes are needed to confirm whether the intramedullary fixation is superior to the extramedullary fixation for the treatment of subtrochanteric fractures.

In conclusion, pooled results from this meta-analysis found that intramedullary nail could achieve shorter union time, lower nonunion rate and reoperation rate compared with the extramedullary fixations for the treatment of the subtrochanteric fractures. Subgroup analysis indicated that intramedullary nail was superior to extramedullary fixations in operation time, reoperation rate and Harris hip scores in >60 years subgroup. However, the intraoperative blood loss in the intramedullary nail group was significantly more compared with that in extramedullary fixation group in <60 years subgroup. The intramedullary nail should be considered as the first selection for the treatment of patients with subtrochanteric fractures. However, the surgeons also should pay attention to the intraoperative blood loss in patients younger than 60 years after choosing the intramedullary nail.

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