Review Article The effect of percutaneous reduction during intramedullary nailing for femoral and tibial fractures: a meta-analysis

Tao Zhu¹, Shaodong Qiu¹, Nan Li², Haibo Yang¹, Jianping Zheng¹, Yong Yang¹

¹Department of Orthopedic Trauma, General Hospital of Ningxia Medical University, Yinchuan 750004, Ningxia, China; ²Academic Affairs Office, Ningxia Medical University, Yinchuan 750004, Ningxia, China

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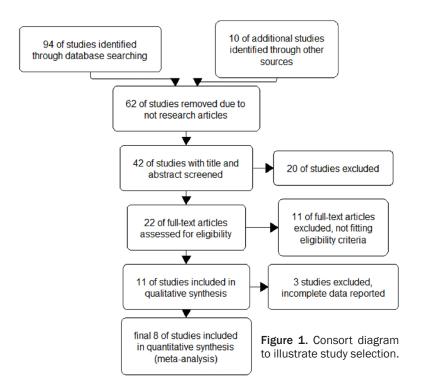
Abstract: The aim of this meta-analysis was to compare the outcomes of percutaneous reduction and other reductions during intramedullary nailing (IN) in the treatment of femoral and tibial fractures. Relevant clinical studies using percutaneous reduction aimed at inspecting the clinical effects of percutaneous reduction during IN for femoral and tibial fractures were searched in MEDLINE, EMBASE, and Cochrane library. Eight studies with 479 patients were included. Meta-analysis was performed on potential extractable clinical outcomes such as operation time, time to recovery, and incidents of complications. The results show that percutaneous reduction could significantly reduce the proportion of complications (Percutaneous: 0.11, 95% CI: 0.07-0.15; other: 0.3, 95% CI: 0.22-0.40) and result in significantly less operation time (standardized mean difference: -0.45, 95% CI: -0.83-0.06) compared to other reduction techniques. No significant heterogeneity or publication bias was observed in the proportion of complications of patients treated with the percutaneous reduction technique. In conclusion, the current evidence indicates that percutaneous reduction may be a better choice than other reduction techniques for treatment of femoral and tibial fractures.

Keywords: Percutaneous reduction, intramedullary nailing (IN), fractures, meta-analysis

Introduction

Reamed, locked IN is a commonly-used treatment for isolated fractures in the femoral shaft. Both antegrade and retrograde femoral nailing provide reliable healing and allow for immediate postoperative weight-bearing [1, 2]. However, for proximal and distal femoral fractures, challenges arise since fractures are highly comminuted and have significantly bone loss which may lead to an extension of proximal or distal segments if no reduction technique is employed before reaming and nail placement [3]. When the correct technique and reduction maneuvers are utilized, a large incision and significant stripping of the soft tissue are created, which may influence fracture healing. Thus, percutaneous/minimally invasive techniques are in great need. Mastery of these techniques and appropriate reduction are thought to reduce damage to soft tissue, reduce iatrogenic muscle injury, and adhesion formation.

Several percutaneous reduction methods are available for dealing with the fragments in the femoral fractures. For instance, Georgiadis and Burgar proposed to use percutaneous skeletal joysticks to guide the nail into an appropriate trajectory and correct angular deformity by forming an artificial cortex [4]. Pettett et al. employed a temporary placement of a drill bit and placed it on the concave side of the deformity, which offered a minimally invasive option for improving sagittal and coronal plane alignment in the setting of a comminuted femoral shaft fracture treated with a retrograde femoral intramedullary nail [5]. Given the recent increase in the number of published randomized trials evaluating the effect of percutaneous strategies for hip fracture care, we conducted a meta-analysis of randomized trials or other clinical studies to evaluate the relative clinical results of femoral fractures after the treatment of extracapsular hip fractures. We hypothesized that employing percutaneous reduction tech-



Inclusion/exclusion criteria

We identified English written literature that satisfied the following criteria: (1) Published random clinical trials, casecontrol studies, and cohort studies. (2) Study population targets on the adult patients with femoral fractures. (3) The intervention contains the use of percutaneous reduction techniques. (4) Study was published after 2010. (5) Clinical measures included recovery time, procedure-related complications, and measures for activity level. Duplicates or multiple publications of the same study, case reports, and animal studies were excluded from the study selection process.

niques would improve the outcome of femoral fracture. In this systematic review, we sought to answer the following questions by combining multiple pieces of clinical evidence: (1) Whether percutaneous reduction confers any significant advantage; (2) Whether a heterogeneity was found among different reduction techniques during the treatment of femoral and tibial fractures.

Material and methods

Literature search

We conducted a literature search on the database of Medline, Cochrane library, and Embase by using the keywords "percutaneous reduction", "intramedullary nailing", "internal fixation", "femoral fractures", "hip screw", and "clinical trial" and their combinations. The search strategy used was broad in order to encompass all potentially relevant articles. We examined the bibliographies of retrieved studies. One of the authors reviewed the titles, and if the title suggested any possibility that the article might meet eligibility criteria, it was retrieved. Two authors reviewed the abstracts and chose potentially eligible studies for retrieval. Review of the complete articles for eligibility included only the Methods section and was thus blind to author, institution, journal, and results.

Data extraction

Data were extracted for eligible studies that met the inclusion criteria. For each study, information such as first author, published year, study characteristics, clinical characteristics of patients, interventions, clinical outcome that were measured, and the results of comparison of the effect of two intervention groups. Two authors independently extracted data and all disagreements were resolved by discussion with the third author. 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.

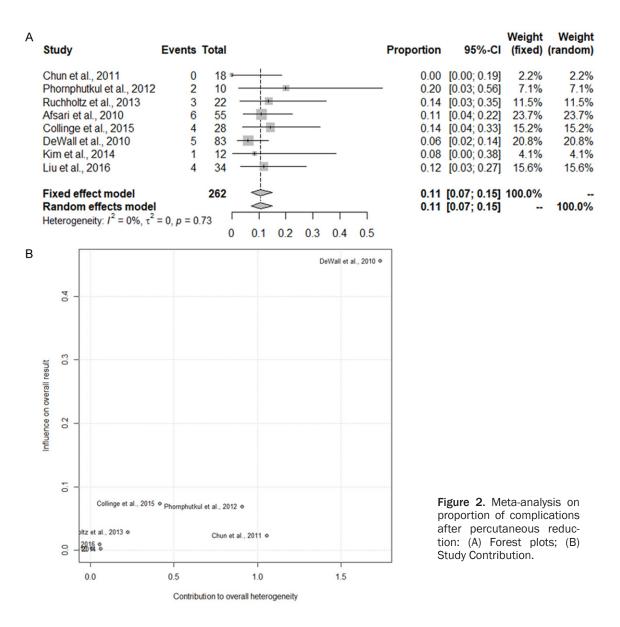
Statistical analyses

All statistical analyses were conducted in R version 3.4.1 with functional packages "meta", "rmeta", and "metafor". Study characteristics were summarized by extracting descriptive statistics from the selected articles. When the incidence of a certain outcome was provided, the proportion and 95% confidence interval were calculated. When the outcome measure was continuous, standardized mean difference (SMD) or the mean difference (MD) was used, 95% confidence intervals were determined for all effect sizes. Heterogeneity of all eligible

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 Table 1. Patient Characteristics of selected studies

Author	Country of study	Study Design	Patient Enroll- ment	Follow-up	Total Sample Size	Mean Age	Percutaneous Reduction Technique	Fracture Type	Clinical Measures
Chun et al., 2011	South Korea	Retrospective cohort	2007.06-2008.12	> 1 year	119	77	Steinman pin	Sagittally Unstable Intertrochateric Fractures	Anesthetic time, activity level, degree of recovery
Phornphutkul et al., 2012	Canada	Prospective	2007.05-2008.12	13.2 months	10	74	Percutaneous cerclage wir- ing and minimally invasive plate osteosynthesis (MIPO)	Periprosthetic femoral fractures	The reduction time, fixation time, operative time, activity level
Ruchholtz et al., 2013	Germany	Prospective	2008.02-2011.02	12 months	41	79.8	Polyaxial locking plate	Periprosthetic and peri- implant fractures	Operation time, complications, perioperative needs
Afsari et al., 2010	US	Prospective	2003.12-2007.01	> 6 months	55	55	Percutaneous clamp	High subtrochanteric femoral Fractures	Fracture union
Collinge et al., 2015	US	Retrospective cohort	2001-2010	1 year	54	/	Percutaneous clamp	Spiral and oblique fractures of the tibial shaft	Fracture union, time to recovery
DeWall et al., 2010	US	Retrospective cohort	2000.01-2007.05	2 year	125	40	Indirect manipulation or screws	Intra-articular calca- neus fractures	SF-36 mental score, wound complication
Kim et al., 2014	South Korea	Prospective	2009.05-2012.04	> 12 months	12	48.3	Percutaneous cerclage	Subtrochanteric femoral fractures	Merle d'Aubigne score, activity level, mean time to recovery
Liu et al., 2016	China	Retrospective cohort	/	20 months	63	6.4	Percutaneous joystick	Femoral shaft fractures	Complications, operative time



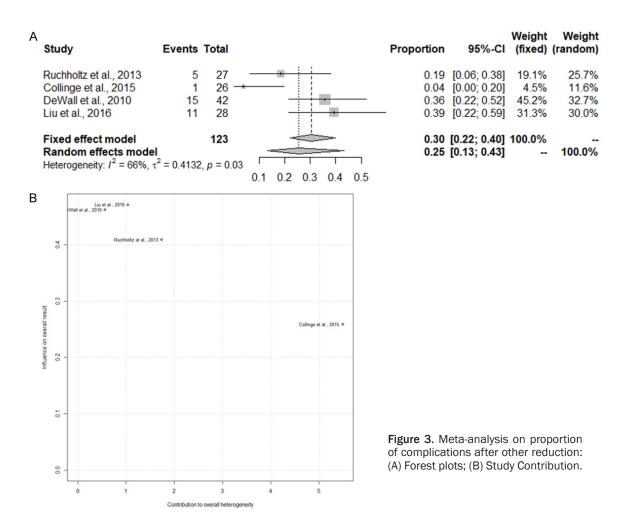
studies was analyzed using Chi-square tests or I² statistics before meta-analysis. If there was no significant heterogeneity (P \geq 0.05, I² < 50%), a fixed effect model was used, otherwise (P < 0.05) a random effect model was used. Sensitivity analysis was carried out by creating a Baujat plot to explore heterogeneity and describes the influence of each study on the overall treatment effect in meta-analysis. Publication bias was visualized as a funnel plot. Egger's test and inverted funnel plots with Trimand-Hill correction were utilized to provide diagnosis of potential publication bias and assess funnel asymmetry. Fail-safe N was used to determine the number of NULL studies that have to be added to reduce the significance of the meta-analysis to 0.05. For all the analyses,

a *P* value of less than 0.05 (two-tailed) was considered statistically significant.

Results

Study selection

A total 94 articles employed percutaneous reduction techniques followed by IN for femoral and tibial fractures: 83 were from MEDLINE, 3 were from Cochrane Library, and 8 were from Embase. An additional 10 articles were identified from Google Scholar. After removing duplicates, case study, clinical notes, and reviews, 42 studies with titles and abstracts were retrieved for screening. Eleven studies were used for qualitative synthesis after checking



inclusion/exclusion criteria. Three studies were removed for inability of retrieving data. Eight studies were included in our final meta-analysis [6-13] (Figure 1).

Study characteristics

The selected studies were conducted in South Korea, China, United States, Canada, and Germany with a total of 479 patients with tibial and femoral fractures. Four studies were retrospective cohort studies and 4 studies were prospective studies. The patients were enrolled from 2000-2012 with diagnosis of intertrochateric femoral fractures, femoral shaft fractures, periprosthetic femoral fractures, tibial shaft fracture, and subtrochanteric femur fractures. Most studies had patients aged above 40 years old except one study focused on children. The follow-up time was more than 3 months or to full recovery for all studies. The percutaneous reduction techniques include: Steinman pin, cerclage wiring, joystick, clamp, hooks, and polyaxial locking plate. Union rate, operation time, activity level, time to recovery, or incidents of complications were measured as primary clinical outcomes (**Table 1**).

Primary analyses

Our primary analyses were to compare the clinical outcomes, such as operation time, incident of cutout, complications, and time to recovery, of percutaneous reduction with other reduction techniques such as open reduction during IN for treating femoral and tibial fractures if the data were available.

Complications

Complications such as infections, skin irritation, and incision pain after employing percutaneous reduction techniques were reported in the majority of our selected studies. However, not all studies had a control group to illustrate the advantage of percutaneous reduction com-

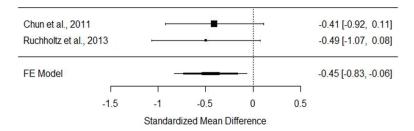
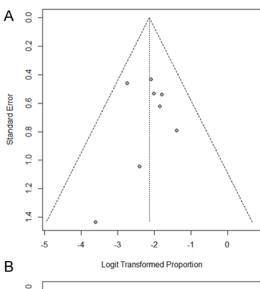


Figure 4. Forest plot to compare the operation time between percutaneous and other reduction techniques.



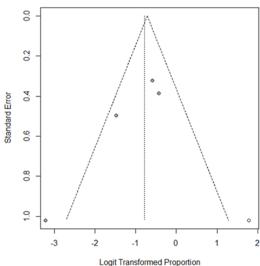


Figure 5. Publication Bias visualized by funnel plots: (A) Percutaneous reduction; (B) Other reduction.

pared to other reduction techniques. Thus, to fully use the information we extracted, we applied the inverse variance method to calculate an overall single proportion of complications for percutaneous reduction and others.

As indicated by the results, no significant heterogeneity was found among the percutaneous reduction group (p = 0.73). The overall proportion of complications after using a fixedeffect model was 0.11 (95% CI: 0.07-0.15). The study published by DeWall et al. was the most influential on the pooled results (**Figure 2A**, **2B**). A large heterogeneity was

found among the studies using the other reduction techniques ($I^2 = 66\%$, p < 0.05). The overall proportion of complications after using a fixed-effect model was 0.3 (95% CI: 0.22-0.40) and a random-effect model was 0.25 (95% CI: 0.13-0.43). Studies conducted by DeWall et al. and Liu et al. were the most influential and the study conducted by Collinage contributed most to the overall heterogeneity (**Figure 3A, 3B**). By comparing the incident proportion of complications between percutaneous reduction and other reduction techniques, we could conclude that percutaneous reduction technique reduced the risk of complications.

Operation time

Four studies and 2 studies reported the operation time for percutaneous and other reduction techniques, respectively. We pooled the data from the studies that reported the both operation time. Heterogeneity tests indicated no statistical evidence of heterogeneity (p = 0.824). Data pooled by a fixed-effects model and the meta-analysis indicated an insignificantly shorter operation time in the percutaneous reduction group (mean difference: -0.45, 95% CI: -0.83--0.06, P < 0.01; Figure 4).

Publication bias

Publication bias for the pooled proportion of complications was visualized as a funnel plot with trim-and-fill method to adjust the bias in meta-analysis (**Figure 5**). No study was added in the group using percutaneous reduction technique and 1 study was added in the group using other reduction technique. Through regression test for funnel plot asymmetry, we observed no significant publication bias in the group using percutaneous reduction techniques (z = -0.2177, p = 0.8277) but there was significant publication bias in the group using other reduction techniques (z = -2.7763, p = 0.0055).

Discussion

Mal-union and non-union are common complications after IN of femoral and tibial fracture due to issues in stabilization of fractures. Excessive dissection and muscle-stripping to place multiple fixation tools that can result in delayed union or nonunion due to osseous devascularization. Thus, minimally invasive reduction techniques are in great need. Percutaneous reduction, inserted by means of a minimally invasive procedure, allows surgeons to minimize soft tissue dissection, thereby reducing surgical trauma and blood loss. It is a useful technique that may aid in improving bone growth and alignment, as well as decreasing the fracture gap during IN in the treatment of femoral and tibial fractures. Several early studies reported that it's a safe and effective technique that leads to earlier, more predictable, and better bone healing than other techniques [14, 15]. To our knowledge, there are few systematic reviews that summarize the evidence for comparing percutaneous reduction technique with other techniques during IN. In this systematic review, we extracted clinical evidence published after 2010 and employed meta-analysis to answer the question that whether percutaneous reduction technique improves clinical outcomes of femoral and tibial fractures.

The results of this meta-analysis demonstrate that operation time, and proportion of complications after surgery in the percutaneous reduction group are significantly less than in the group using other reduction techniques. Therefore, because of its minimal invasiveness, we recommend percutaneous reduction as a safe and effective choice especially in the treatment of elderly patients with femoral and tibial fracture.

There are several limitations in our meta-analysis: (1) Most of the selected studies were with a small sample size (< 50). (2) No clinical trial was identified and included in our meta-analysis due to limited relevant studies. Thus, the quality of included studies is relatively low, which may might weaken the strength of the findings and make the results less convincing. (3) Several studies only inspected outcomes after using the percutaneous reduction technique. To efficiently use the extracted data, we calculate the incident proportion of complications for

percutaneous and other reduction technique in a separate manner. Thus, the results are indirect compared to using relative risks or risk ratio as summarized metrics. (4) Only two studies were included to calculate mean difference in operation time, whose sample size of patients was quite limited, which might weaken the strength of the findings. (5) We did not consider the heterogeneity of different fracture subtypes and percutaneous reduction tools. (6) There was one study focused on children, which is significantly different from other studies which targeted patients in middle to older age groups. Thus, in the future, more randomized clinical trials with higher study quality will be needed to illustrate the superiority of percutaneous reduction technique over other reductions techniques during IN for treating femoral and tibial fractures.

Disclosure of conflict of interest

None.

Address correspondence to: Tao Zhu, Department of Orthopedic Trauma, General Hospital of Ningxia Medical University, No. 804 South Shengli Street, Xingqing District, Yinchuan 750004, Ningxia Province, China. Tel: +86-18695127188; Fax: +86-951-6744457; E-mail: loopy_zt@163.com

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