

Network Meta-Analysis of Open Reduction Internal Fixation, Intramedullary Nail Fixation, and Distal Femoral Replacement for Periprosthetic Distal Femur Fractures

Yao Lu[†], Yibo Xu[†], Cheng Ren[†], Qian Wang, Liang Sun, Chengcheng Zhang, Qiang Huang, Hanzhong Xue, Zhong Li, Kun Zhang, Yang Zhao* and Teng Ma*

Department of Orthopaedic Surgery, Honghui Hospital, Xi'an Jiaotong University, Xi'an, China

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*Correspondence:

Yang Zhao zy881027@126.com Teng Ma gukemt@163.com [†]These authors share first authorship

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Lu Y, Xu Y, Ren C, Wang Q, Sun L, Zhang C, Huang Q, Xue H, Li Z, Zhang K, Zhao Y and Ma T (2022) Network Meta-Analysis of Open Reduction Internal Fixation, Intramedullary Nail Fixation, and Distal Femoral Replacement for Periprosthetic Distal Femur Fractures. Front. Mater. 9:862698. doi: 10.3389/fmats.2022.862698 **Background:** Although open reduction internal fixation (ORIF) with periarticular locking plates, retrograde intramedullary nail (IMN) fixation, and distal femoral replacement (DFR) have been widely used for the treatment of periprosthetic distal femur fractures (PPDFF), it remains unclear which one may be an optimal surgical strategy.

Objective: This network meta-analysis aimed to determine the optimal surgical strategy for PPDFF from ORIF, IMN, and DFR by evaluating major complication rates and revision rates.

Patients and Methods: We identified eligible studies by performing an updated literature search in PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) and checking published meta-analyses. The methodological index for non-randomized studies (MINORS) was used to assess the methodological quality of eligible studies. Major complications and revision rates were defined as outcomes of interest. All statistical analyses were performed by ADDIS 1.4 software.

Results: We included 17 eligible studies in the final analysis. Statistical analyses did not reveal significant differences when ORIF was compared with IMN and ORIF compared with DFR, and IMN compared with DFR in terms of two clinical outcomes. However, DFR achieved a beneficial trend in major complications [odds ratio (OR) = 1.34; 95% CrI = 0.48-3.80] and revision (OR = 1.64; 95% CrI = 0.68-4.38) rates compared with IMN. Ranking probabilities indicate that DFR has the highest probability of being the optimal option, followed by ORIF and IMN.

Conclusion: There was no difference in major complications or reoperations between the three treatments. However, ORIF with periarticular locking plates may be a preferred alternative option because DFR is limited by the high cost. Moreover, our study highlights the need for future prospective trials evaluating the outcomes of these three surgical strategies.

Keywords: periprosthetic distal femur fracture, distal femoral replacement, periarticular locked plate, retrograde intramedullary nail, network meta-analysis

INTRODUCTION

As the prevalence of total knee arthroplasty (TKA) increases among the aging population, periprosthetic distal femur fracture (PPDFF) is becoming increasingly common with an incidence ranging from 0.3–2.5% (Agarwal et al., 2014; Konan et al., 2016). Meanwhile, the literature also reported a higher incidence of revision arthroplasties, ranging from 1.6% to 38.0% (Gracia-Ochoa et al., 2016). Studies revealed that the 1-year mortality of this injury has been increasing up to 15%, and the overall incidence of postoperative complications was as high as 37% (Ebraheim et al., 2014; Myers et al., 2018). More importantly, the morbidity rate of PPDFF is as high as 25% in the geriatric population (Lotzien et al., 2019).

Therapeutic strategies for PPDFF include nonoperative and surgical management; however, previous studies have reported poor outcomes in patients treated with nonoperative management (Darrith et al., 2020). In contrast, surgical management was identified as the preferred therapeutic option (Su et al., 2004; Kinney and Engh, 2018). Although several surgical approaches have been widely used for treating PPDFF (Darrith et al., 2020), advancements in implant technology have greatly increased the focus on three primary surgical strategies, including open reduction internal fixation (ORIF) with periarticular locking plates, or intramedullary nail fixation (IMN), and distal femoral replacement (DFR) (Quinzi et al., 2021). Currently, several pairwise meta-analyses (Ebraheim et al., 2015; Shin et al., 2017; Liu et al., 2019; Shah et al., 2020) have compared the clinical efficacy and safety of these three surgical strategies; however, a definitive conclusion about which one should be preferentially selected for the treatment of PPDFF remains unclear.

It is noted that the most recent systematic review and metaanalysis (Quinzi et al., 2021) separately investigated the comparative efficacy and safety of ORIF, IMN, and DFR in patients with PPDFF. Unfortunately, the preferred therapeutic option was still not determined due to the shortage of pair-wise meta-analysis (Lu and Ades, 2004). Additionally, all previously published meta-analyses did not include all eligible studies in the final analysis, and additional studies have also been published recently. Therefore, we conducted this network meta-analysis to determine the optimal surgical strategy by providing an up-todate synthesis of the early complication rates and revision rates of three options including ORIF with periarticular locking plates, retrograde IMN, and DFR for PPDFF.

METHODS

Study Design

The current network meta-analysis was performed following the Cochrane handbook for reviewers of systematic reviews (Higgins and Green, 2011), and the pooled results were reported according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) for network meta-analysis (PRISMA-NMA) (Hutton et al., 2015; Page et al., 2021). This network meta-analysis was exempted from ethical approval and informed

consent because it was undertaken with previously published data.

Eligibility Criteria

We defined inclusion criteria following previous meta-analyses (Shah et al., 2020; Quinzi et al., 2021; Wadhwa et al., 2021): 1) patients were confirmed with PPDFF based on recognized criteria, 2) comparison of at least two of ORIF with periarticular locked plates, retrograde IMN, and DFR was available, 3) reported at least one of the data on major complications and revision rate, 4) randomized controlled trials (RCTs), or retrospective or prospective study designs, and 5) full text published in English.

The following exclusion criteria were also defined: 1) adequate sample size (<5 patients), 2) did not report outcomes of interest, 3) duplicate studies with inadequate information or poor methodological quality, and 4) animal study, review, correspondence, letter to the editor, and conference abstract.

Information Sources

We obtained six meta-analyses (Ebraheim et al., 2015; Shin et al., 2017; Liu et al., 2019; Shah et al., 2020; Quinzi et al., 2021; Wadhwa et al., 2021) through searching PubMed by two reviewers using periprosthetic distal femoral fracture and synonyms, and two (Quinzi et al., 2021; Wadhwa et al., 2021) out of the six meta-analyses published in 2021. Then we conducted an updated literature search in PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) from January 2020 until July 2021 in order to identify additional potential studies. We also manually checked references of all published meta-analyses and included studies to identify additional studies. Details of the literature search strategies are documented in **Supplementary Table S1**. A third senior reviewer was invited to solve any disagreements during the literature retrieval.

Study Selection

Two independent reviewers conducted the study selection. First, all identified potentially eligible records were imported into EndNote for literature database development. Second, all duplicate records were labeled and then removed into the trash file. Third, ineligible records were removed after screening titles and abstracts for eligibility. Fourth, full-text was checked for evaluating eligibility. Fifth, full-texts of all studies included in previous meta-analyses were downloaded and then verified for eligibility. A third senior reviewer was invited to solve any disagreements. The details of identifying and selecting eligible studies are displayed in **Figure 1**.

Outcomes of Interest

In this network meta-analysis, we evaluated two outcomes including major complication rates over the follow-up period and all-cause revision rates. Major complication rates were defined as the incidence of deep infection, nonunion, symptomatic malunion, hardware failure, aseptic loosening of arthroplasty, periprosthetic fracture, and extensor mechanism complications (Quinzi et al., 2021).



Data Extraction

Two independent reviewers utilized the standard data extraction sheet to extract the following information: basic characteristics of the study (the first author's name, publication year, country of the first author, study design, comparison, and methodological information), essential characteristics of patients [sample size (%male), mean age (years), mean Charlson Comorbidity Index (CCI) score, mean American Society of Anesthesiologists (ASA) score, and mean time of follow-up], and outcomes. A third senior reviewer was asked to solve any disagreements.

Geometry of the Network

We used Stata 14.0 (Stata Corp LP, College Station, Texas, United States) to create an evidence structure of three surgical treatments on the basis of accumulated sample size and the number of eligible studies. The accumulated sample size was used to weigh the size of the circle representing treatment, and the accumulated numbers of eligible studies were used to weigh the width of the line representing the number of studies.

METHODOLOGICAL QUALITY ASSESSMENT

All included studies in this network meta-analysis were retrospective cohort or case series; we, therefore, utilized the non-randomized cohort studies using the methodological index for non-randomized studies (MINORS) (Slim et al., 2003) to assess the methodological quality of the evidence.

Statistical Analysis

We simultaneously performed direct and network meta-analysis, which was conducted with the aggregate data drug information system (ADDIS) software (Groningen, the Netherlands, www. drugis.org). For the direct meta-analysis, a random-effects model which considers the variations across studies in the real world was used. Estimates were reported in the odds ratio (OR) with a 95% confidence interval (CI) because two outcomes were categorical variables. Statistical heterogeneity was evaluated by using the chi-square test (Cochrane Q) (Bowden et al., 2011) and an I² statistical heterogeneity was considered if the *p*-value was less than 0.1 and the I² value was equal to or more than 50.0% (Higgins et al., 2003).

Network meta-analysis was performed using the Markov Chain Monte Carlo (MCMC) simulation which is graphically displayed in Supplementary Figure S1. Estimates were reported in OR with a 95% credible interval (CrI). For major complications rates, parameters including four chains, 20,000 tunings and 50,000 simulation iterations, the thinning interval of 10, 10,000 inference samples, and variance scaling factor of 2.5 (Cipriani et al., 2013) were defined to achieve a good convergence. However, for the revision rate, four chains, 20,000 tuning, and 100,000 simulation iterations, the thinning interval of 10, 20,000 inference samples, and variance scaling factor of 2.5 (Cipriani et al., 2013) were defined to achieve a good convergence. The convergence of data was evaluated using the Brooks Gelman-Rubin statistical method, and a good convergence was suggested when a potential proportional reduction factor (PRF) was close to 1 (Brooks and Gelman, 1998; Burger and Schall, 2015). Moreover, a PRF of 1.2 also indicated an acceptable convergence (Brooks and Gelman, 1998; Burger and Schall, 2015).

Inconsistency Test

In this network meta-analysis, a closed loop was available for three surgical treatments, and we, therefore, conducted the split node method to investigate whether the presence of inconsistency or not between direct and indirect effects (Dias et al., 2010; Albert and Makowski, 2019). This test was performed by using Stata 14.0 (Stata Corp LP, College Station, Texas, United States).

Ranking Probabilities

We estimated the ranking probabilities of being a certain rank for these three surgical treatments and utilized surface under the cumulative ranking curve (SUCRA) values to generate a ranking hierarchy of surgical treatments (Singh et al., 2015).

Publication Bias Test

We created the comparison-adjusted funnel plot to qualitatively examine the publication bias and small study effects because the accumulated number of eligible studies was more than 10 (Palma Perez and Delgado Rodriguez, 2006). The publication bias test was performed by using Stata 14.0 (Stata Corp LP, College Station, Texas, United States).

RESULTS

Retrieval and Selection of Study

A total of 119 records were initially identified after conducting an updated search, and then 28 duplicate records were removed. A total of 90 ineligible studies were excluded after screening titles, abstracts, and full-texts for eligibility due to meta-analysis, unrelated to the topic, and duplicate records, so one study (Gausden et al., 2021) was considered to meet our selection criteria. Moreover, we obtained 16 eligible studies (Platzer et al., 2010; Hou et al., 2012; Aldrian et al., 2013; Horneff et al., 2013; Kiluçoğlu et al., 2013; Gondalia et al., 2014; Meneghini et al., 2014; Leino et al., 2015; Park and Lee, 2016; Matlovich et al., 2017; Ruder et al., 2017; Gan et al., 2018; Hoellwarth et al., 2018; Darrith et al., 2020; García Guirao et al., 2020; Jennison and Yarlagadda, 2020) from published meta-analyses and references. Finally, we included 17 studies (Platzer et al., 2010; Hou et al., 2012; Aldrian et al., 2013; Horneff et al., 2013; Kiluçoğlu et al., 2013; Gondalia et al., 2014; Meneghini et al., 2014; Leino et al., 2015; Park and Lee, 2016; Matlovich et al., 2017; Ruder et al., 2017; Gan et al., 2018; Hoellwarth et al., 2018; Darrith et al., 2020; García Guirao et al., 2020; Jennison and Yarlagadda, 2020; Gausden et al., 2021) in this network meta-analysis. Details of study retrieval and selection are shown in Figure 1.

Basic Characteristics of Eligible Studies and Participants

A total of 14 retrospective cohort studies (Platzer et al., 2010; Hou et al., 2012; Horneff et al., 2013; Kiluçoğlu et al., 2013; Gondalia et al., 2014; Meneghini et al., 2014; Leino et al., 2015; Park and Lee, 2016; Matlovich et al., 2017; Ruder et al., 2017; Gan et al., 2018; Hoellwarth et al., 2018; Darrith et al., 2020; Gausden et al., 2021) and 3 case series (Aldrian et al., 2013; García Guirao et al., 2020; Jennison and Yarlagadda, 2020) were included. Three studies were 3-arm designs (Platzer et al., 2010; Darrith et al., 2020; García Guirao et al., 2020), and the remaining 14 studies were 2-arm designs (Hou et al., 2012; Aldrian et al., 2013; Horneff et al., 2013; Kiluçoğlu et al., 2013; Gondalia et al., 2014; Meneghini et al., 2014; Leino et al., 2015; Park and Lee, 2016; Matlovich et al., 2017; Ruder et al., 2017; Gan et al., 2018; Hoellwarth et al., 2018; Jennison and Yarlagadda, 2020; Gausden et al., 2021). The accumulated sample size was 655, 250, and 159 in ORIF,



IMN, and DFR groups, respectively. Comparison of ORIF and IMN, ORIF, and DFR, as well as IMN and DFR was available in 12 (Platzer et al., 2010; Hou et al., 2012; Aldrian et al., 2013; Horneff et al., 2013; Kiluçoğlu et al., 2013; Gondalia et al., 2014; Meneghini et al., 2014; Park and Lee, 2016; Matlovich et al., 2017; Darrith et al., 2020; García Guirao et al., 2020; Gausden et al., 2021), 8 (Platzer et al., 2010; Leino et al., 2015; Ruder et al., 2017; Gan et al., 2018; Hoellwarth et al., 2018; Darrith et al., 2020; García Guirao et al., 2020; Jennison and Yarlagadda, 2020), and three studies (Platzer et al., 2010; Darrith et al., 2020; García Guirao et al., 2020), respectively. The evidence structure of the three surgical techniques is shown in **Figure 2**. The MINORS score of individual study ranged from 14 to 17, with a moderate level for overall methodological quality. The basic characteristics of included studies and patients are summarized in **Tables 1**, 2.

Inconsistency Test

Node split generated an inconsistency factor (IF) of 1.01 with a *p*-value of 0.303 for the closed loop of major complications rates and an IF of 1.02 with a *p*-value of 0.264 for the closed loop of revision rates (**Supplementary Figure S2**), suggesting consistency between direct and indirect effects.

Meta-Analysis of Major Complication Rates

Direct meta-analyses did not reveal significant difference for comparison between ORIF and IMN (12 studies, OR = 0.74; 95% CI = 0.38 to 1.45; $I^2 = 37.7\%$), comparison between ORIF and DFR (eight studies, OR = 1.08; 95% CI = 0.59 to 1.99; $I^2 = 0.00\%$), and comparison between INM and DFR (three studies, OR = 0.61, 95% CI = 0.12 to 3.18, $I^2 = 0.00\%$). Meanwhile, these results were not significantly changed in the network meta-analysis of comparison between ORIF and INM (OR = 0.78; 95% CrI = 0.39–1.49), comparison between ORIF and DFR (OR = 1.04; 95% CrI = 0.44–2.44), and comparison between INM and DFR (OR = 1.34; 95% CrI = 0.48–3.80). However, the trend between INM and DFR was inversely benefitted to DFR because OR was changed from 0.61 to 1.37. All statistical results are shown in **Figure 3**.

TABLE 1 | Characteristics of included studies (n = 16).

Study	Country	Study design	Comparison	MINORS score
Gondalia (2014)	United States	Retrospective cohort study	ORIF vs. IMN	17
Hornef (2013)	Oregon	Retrospective cohort study	ORIF vs. IMN	17
Hou (2012)	China	Retrospective cohort study	ORIF vs. IMN	17
Kilucoglu (2013)	Turkey	Retrospective cohort study	ORIF vs. IMN	15
Meneghini (2014)	Indiana	Retrospective cohort study	ORIF vs. IMN	15
Park (2016)	Korea	Retrospective cohort study	ORIF vs. IMN	17
Gausden (2021)	United States	Retrospective cohort study	ORIF vs. IMN	17
Aldrian (2013)	Austria	Retrospective case series	ORIF vs. IMN	17
Matlovich (2017)	Canada	Retrospective cohort study	ORIF vs. IMN	17
Hoellwarth (2018)	United States	Retrospective cohort study	ORIF vs. DFR	17
Gan (2018)	Singapore	Retrospective cohort study	ORIF vs. DFR	16
Jennison (2020)	United Kingdom	Retrospective case series	ORIF vs. DFR	17
Leino (2015)	Finland	Retrospective cohort study	ORIF vs. DFR	17
Ruder (2017)	United States	Retrospective cohort study	ORIF vs. DFR	15
Platzer (2010)	Austria	Retrospective cohort study	ORIF vs. IMN vs. DFR	14
Darrith (2020)	United States	Retrospective cohort study	ORIF vs. IMN vs. DFR	17
Guirao (2020)	Spain	Retrospective case series	ORIF vs. IMN vs. DFR	17

ORIF, open reduction internal fixation; IMN, intramedullary nail; DFR, distal femoral replacement; MINORS, the Methodological index for non-randomized studies.

The Meta-Analysis of Revision Rates

Direct meta-analyses revealed a marginally favorable result in patients who received ORIF compared with IMN (12 studies, OR = 0.60; 95% CI = 0.35 to 1.03; $I^2 = 0.00\%$). However, this result received the support of network meta-analysis (OR = 0.60; 95% CrI = 0.31–1.10). For remaining comparisons including the comparison between ORIF and DFR (eight studies, OR = 0.96; 95% CI = 0.32 to 1.10; $I^2 = 0.00\%$) and comparison between IMN and DFR (three studies, OR = 0.73; 95% CI = 0.15 to 3.53; $I^2 = 0.00\%$) did not achieve statistically significant level in direct meta-analyses. Similarly, the network meta-analyses of these two comparisons did possess unchanged results. However, the trend between INM and DFR was inversely benefitted to DFR because OR was changed from 0.73 to 1.64 in network meta-analysis. All statistical results are shown in **Figure 4**.

Ranking of Probabilities

We generated ranking probabilities of these three surgical treatments in terms of major complication rates and revision rates. According to the results of ranking probabilities, DFR had the highest probability of becoming the best option, ORIF had the probability of ranking at a second option, and IMN at the third option for two outcomes. The plot of rankings of three surgical treatments is shown in **Figure 5**.

Publication Bias

We generated a comparison-adjusted funnel plot for major complications and revision rates, and a symmetric outline indicates the absence of publication bias and small sample size effects (**Supplementary Figure S3**).

DISCUSSION

Although the surgical strategy has been the preferred therapeutic option for PPDFF (Su et al., 2004; Kinney and Engh, 2018) and has been widely used in clinical practice (Darrith et al., 2020), it

remains debatable regarding the optimal surgical procedure of choice (Quinzi et al., 2021) because several surgical regimes including ORIF, IMN, and DFR were available. In this network meta-analysis, we aimed to determine which regimes should be preferentially selected by evaluating major complication rates and revision rates following ORIF, IMN, and DFR. Pooled results suggest that these three surgical regimes have no statistical difference in the treatment of PPDFF. However, we still find that DFR should be preferentially selected to treat PPDFF, according to the rank probabilities of three regimes when objective resources are allowed.

Compared to conventional plating, ORIF with periarticular locking plates has the ability to improve rates of union and then decrease rates of revision because plating may facilitate a more anatomic reduction and allow for more predictable restoration of joint alignment (Christ et al., 2018). Meanwhile, IMN fixation has been proved to have the ability to avoid soft-tissue stripping and provide biomechanical advantages compared with ORIF with periarticular locking plates (Bong et al., 2002). Although several studies have investigated the comparative efficacy and safety of the two techniques (Horneff et al., 2013; Gondalia et al., 2014; Meneghini et al., 2014), there remains no consensus on the optimal treatment. Meanwhile, published meta-analyses (Shin et al., 2017; Liu et al., 2019; Shah et al., 2020) did not also reveal a significant difference between these two techniques in terms of clinical outcomes. More importantly, IMN fixation has significant dependence on the types of TKA prosthetic design, indirect reduction techniques, and previous hip implants (Shah et al., 2020). In this network meta-analysis, we also suggested that ORIF with periarticular locking plates should be preferentially selected according to the ranking probabilities compared with IMN fixation, although no difference is detected in major complications rates and revision rates between ORIF with periarticular locking plates and IMN fixation.

With the rapid improvements in prosthetic design, distal femoral replacement (DFR) has also been proposed to treat

TABLE 2 | Characteristics of patients in eligible studies (n = 16).

Study	Surgery information	Sample size (%male)	Mean age, years	Mean CCI score	ASA score	Follow-up, months
Gondalia (2014)	ORIF	24	68.5	n.r	n.r	34.6
	IMN	18				
Hornef (2013)	ORIF	28 (36%)	68.9	n.r	n.r	n.r
	IMN	35 (26%)				
Hou (2012)	ORIF	34 (29%)	76.0	n.r	2.95	29
	IMN	18 (33%)				
Kilucoglu (2013)	ORIF	9	72.5	n.r	n.r	4.3
	IMN	7				
Meneghini (2014)	ORIF	62 (15%)	74.0	n.r	n.r	31.8
	IMN	19 (26%)				
Park (2016)	ORIF	21 (5%)	74.5	n.r	n.r	n.r
	IMN	20 (15%)				
Gausden (2021)	ORIF	74 (28%)	75.5	n.r	n.r	n.r
	IMN	23 (61%)				
Aldrian (2013)	ORIF	48	75.6	n.r	n.r	n.r
	IMN	38				
Matlovich (2017)	ORIF	36 (25%)	75.6	n.r	n.r	14.8
	IMN	19 (16%)				
Hoellwarth (2018)	ORIF	87	70.1	5.4	n.r	n.r
. ,	DFR	53				
Gan (2018)	ORIF	8 (0)	72.3	n.r	2.5	n.r
	DFR	7 (0)				
Jennison (2020)	ORIF	42 (19%)	79.9	4.67	2.5	n.r
	DFR	13 (0)				
Leino (2015)	ORIF	39 (13%)	79.0	n.r	3.05	29.9
	DFR	29 (17%)				
Ruder (2017)	ORIF	35 (23%)	80.5	1.85	n.r	29.5
	DFR	23 (17%)				
Platzer (2010)	ORIF	15	78.6	n.r	n.r	n.r
	DFR	8				
	IMN	3				
Darrith (2020)	ORIF	45	73.8	4.5	3.05	5.6
	DFR	5			0.00	5.0
	IMN	22				
Guirao (2020)	ORIF	48	75.1	4.38	n.r	61.3
	DFR	40				5.10
	IMN	9				

ORIF, open reduction internal fixation; IMN, intramedullary nail; DFR, distal femoral replacement; CCI, Charlson Comorbidity Index; ASA, American Society of Anesthesiologists Score, n.r., not reported.

PPDFF in geriatric patients (Meluzio et al., 2020). Unfortunately, primary studies (Platzer et al., 2010; Darrith et al., 2020) and subsequent meta-analyses (Wadhwa et al., 2021) did not reveal the difference between the two techniques in a series of clinical outcomes. It is noted that deep infection is a major concern faced by the DFR technique (Mortazavi et al., 2010; Rahman et al., 2016); however, our network meta-analysis indicates beneficial trends for DFR related to ORIF with periarticular locking plates and IMN fixation although the statistical difference was not obtained. DFR is suggested as an optimal treatment option for PPDFF compared to other two surgical treatments; however, it should be rationally selected because this surgical technique is characterized by high cost (Quinzi et al., 2021).

Several meta-analyses have been published to compare two of these three surgical treatments; however, our study has more advantages. First and foremost, we utilized network meta-analysis to rank these three surgical treatments and, therefore, provide definitive evidence for making a decision in clinical practice. Second, more eligible studies appear in this network metaanalysis to generate more reliable and robust results. Third, both direct and indirect evidence were simultaneously incorporated to estimate the overall results, and thus the limitation resulting from an insufficient number of eligible studies directly comparing two out of three treatments is partially overcome.

Certainly, we must also recognize some limitations in this network meta-analysis. First, the accumulated sample size is relatively inadequate although 17 eligible studies are included, and thus, our findings should be cautiously interpreted, and future studies with a larger sample size should be designed. Second, some eligible studies did not report specific follow-up time; we cannot, therefore, calculate adjusted estimates according to follow-up time. Third, subgroup analysis cannot be conducted according to types of fractures, CCI score, and ASA score due to limited data.

	Direct meta-analysis			Network meta-analysis			
Comparison	Study	OR (95% CI)	Heterogeneity (I2)		OR (95% Crl)		
	Aldrian 2013	1.45 (0.38, 5.48)	_				
	Darrith 2020	0.62 (0.06, 6.88)					
	Gausden 2021	1.27 (0.25, 6.60)					
	Gondalia 2014	2.06 (0.43, 9.87)					
		5.57 (0.61, 49.89)	· · · · ·				
	Hornef 2013	0.25 (0.07, 0.90)	—	_			
ORIF vs IMN	Hou 2012	0.22 (0.03, 1.40)					
	Kilucoglu 2013	0.31 (0.02, 5.66)					
	Matlovich 2017	0.08 (0.01, 0.79)					
	Meneghini 2014	2.04 (0.41, 0.31)					
	Park 2016	0.28 (0.02, 3.22)					
	Platzer 2010	1.08 (0.07, 16.47)	-				
	Overall	0.74 (0.38, 1.45)	⊢ ♦	37.7%	0.78 (0.39, 1.49)	⊢ ♦	-
	Darrith 2020	1.54 (0.28, 8.60)					
	Gan 2018	2.00 (0.11, 37.27)					
	Guirao 2020	1.14 (0.11, 11.38)					
ORIF vs DFR	Hoellwarth 2018	1.92 (0.49, 7.54)					
	Jennison 2019	0.53 (0.13, 2.23)		4			
	Leino 2015	1.58 (0.35, 7.10)		—			
	Platzer 2010	0.31 (0.01, 6.53)					
	Ruder 2017	0.62 (0.11, 3.53)		-			
	Overall	1.08 (0.59, 1.99)		0.00%	1.04 (0.44, 2.44)	· · · •	
	Darrith 2020		_				
IMN vs DFR	Guirao 2020	0.21 (0.01, 3.92)					
l	Platzer 2010	0.29 (0.01, 11.3)			1 24 /0 49 2 90		
	Overall	0.61 (0.12, 3.18)		0.00%	1.34 (0.48, 3.80)		
		0.005	0.05 0.5	5 50 500	0	.1 1	10

Comparison	5. Georgeo.	OR (95% CI)		Direct meta-analysis Study OR (95% CI) Heterogeneity (12			Network meta-analysis OR (95% CrI)			
				Hete	erogeneity (12)	OK (95% CII)				
	Aldrian 2013	0.77 (0.18, 3.39)	I							
	Darrith 2020	0.62 (0.06, 6.88)								
	Gausden 2021	1.64 (0.33, 8.26)								
	Gondalia 2014	0.50 (0.09, 2.72)	⊢							
	Guirao 2020	2.71 (0.51, 4.61)	H							
ORIF vs IMN	Hornef 2013	0.25 (0.07, 0.90)								
JRIF VS IIVIIN	Hou 2012	0.50 (0.06, 4.09)								
	Kilucoglu 2013	0.10 (0.02, 5.66)	-							
Ν	Aatlovich 2017	0.08 (0.01, 0.79)								
M	1eneghini 2014	1.24 (0.13, 12.25)	H							
	Park 2016	0.28 (0.02, 3.22)								
	Platzer 2010	1.08 (0.07, 16.47)								
	Overall	0.60 (0.35, 1.03)	⊢+-		0.00%	0.60 (0.31, 1.10)		4		
	Darrith 2020	1.54 (0.28, 8.60)								
	Gan 2018	6.99 (0.37, 97.59)		-						
	Guirao 2020	1.14 (0.11, 11.38)	H							
ORIF vs DFR	oellwarth 2018	1.92 (0.49 <i>,</i> 7.54)								
JRIE VS DER	Jennison 2019	0.53 (0.13, 2.23)		-						
	Leino 2015	0.67 (0.22, 2.01)		-						
	Platzer 2010	0.31 (0.01, 6.53)								
	Ruder 2017	0.64 (0.08, 5.09)								
	Overall	0.96 (0.54, 1.72)		-	0.00%	0.99 (0.32, 1.10)		— —		
	Darrith 2020	2.50 (0.16, 39.62)		-	-					
IMN vs DFR	Guirao 2020	0.42 (0.03, 5.5)9								
	Platzer 2010	0.29 (0.01, 11.3)								
	Overall	0.73 (0.15, 3.53)	· •		0.00%	1.64 (0.68, 4.38)	H 1	•	-	
		0.005	0.5		50	0.1		1	10	
					1					



CONCLUSION

Based on the best available evidence, ORIF with periarticular locking plates, IMN fixation, and DFR are comparable in major complication rates and revision rates. However, DFR should be preferentially selected under the full consideration of cost. Otherwise, ORIF with periarticular locking plates maybe a preferred alternative option. Moreover, our network metaanalysis emphasizes the need for future prospective randomized controlled trials evaluating the outcomes of these three surgical strategies.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**; further inquiries can be directed to the corresponding authors.

AUTHOR CONTRIBUTIONS

Substantially contributed to conception or design: YL, YZ, and TM. Contributed to the acquisition, analysis, or interpretation of

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data: QW, LS, CZ, and QH. Drafted the manuscript for important content: YX and CR. Critically revised the manuscript for important intellectual content: HX, ZL, and KZ. Gave final approval: all authors.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmats.2022.862698/full#supplementary-material

Supplementary Figure S1 | Schematic figure for Monte Carlo simulation.

Supplementary Figure S2 | Node split plot of major complications and revision rates.

Supplementary Figure S3 | Comparison-adjusted funnel plot of major complications (A) and revision (B) rates.

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