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# Intramedullary Nail Versus Plate Fixation for Humeral Shaft Fractures: A Systematic Review of Overlapping Meta-analyses

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**Abstract:** Multiple meta-analyses have been published to compare intramedullary nail and plate for treating humeral shaft fractures; however, results are discordant.

The purposes of current study were to perform a systematic review of overlapping meta-analyses comparing intramedullary nail and plate fixation for the treatment of humeral shaft fractures, to appraise the methodological quality and the quality of reporting of meta-analyses, and to propose a guide through the currently discordant available evidence.

This systematic review was performed according to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analysis. The literature was systematically reviewed to identify meta-analyses comparing intramedullary nail and plate fixation for the treatment of humeral shaft fractures. Only meta-analyses exclusively including randomized clinical trials (RCTs) met eligibility criteria in this systematic review. Methodological quality for each included study was assessed using the Oxford Levels of Evidence and the Assessment of Multiple Systematic Reviews Instrument. We extracted all variables from the included studies and listed the results reported by them. Heterogeneity information of each variable was extracted for the included studies. An $I^2$ of $<60\%$ is accepted in this systematic review. The Jadad algorithm was then applied to determine which meta-analyses provided the best evidence.

Seven studies met the inclusion criteria in this study. All studies included RCTs or quasi-RCT and were Level II of evidence. Assessment of Multiple Systematic Reviews scores varied from 6 to 10 with a median of 7.86. Heterogeneity of each outcome was acceptable in those meta-analyses pooled results. The Jadad algorithm suggested that the meta-analyses can be selected based on the search strategies and application of selection. As a result, 2 meta-analyses with more RCTs were selected in this systematic review. The best available evidence suggested that the differences between intramedullary nail and plate fixation were not significant in fracture union, radial nerve injury, and infection. But intramedullary nail significantly increased the risk of shoulder complications (shoulder impingement and restriction of shoulder movement) and reoperation.

We concluded that plate fixation is superior to intramedullary nail for the treatment of humeral shaft fractures.

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**Abbreviations**: AMSTAR = Assessment of Multiple Systematic Reviews, RCT = randomized clinical trial.

## INTRODUCTION

Humeral shaft fracture is one of the most common fractures in adults, accounting for approximately 3% of all fracture types.[1,2] Although it is generally agreed that the majority of humeral shaft fractures are best treated conservatively, there are indications for primary or secondary operative treatment in some situations.[3,4] In the past few decades, development in implant design and internal fixation technique has occurred, which leads to widely expanding the indications for operation and generating new debate on procedure choice.[5]

Intramedullary nail and plate are the 2 most commonly used surgical treatments. Both procedures have certain biomechanical and physiologic advantages and disadvantages. Intramedullary nailing of humeral shaft fractures is load-sharing implant that allows preservation of periosteal blood supply and minimizes disruption of fracture biology. Plate fixation allows direct visualization, anatomic reduction, and rigid fracture fixation of the fracture and facilitates identification, exploration, and protection of the radial nerve. There is no consensus as to whether intramedullary nail or plate is the optimal treatment method.

Randomized clinical trials (RCTs) comparing intramedullary nail and plate are conflicted as to which fixation procedure is better than the other one.[6–9] Although several meta-analyses have been published to compare the 2 fixation methods for the treatment of humeral shaft fractures, they also showed different results in their articles.[10–13] Such conflicting studies have led to uncertainty among decision-makers and practitioners regarding the operative approach for humeral shaft fractures.

The purposes of current study were to perform a systematic review of overlapping meta-analyses comparing intramedullary nail and plate fixation for the treatment of humeral shaft fractures, to appraise the methodological quality and the quality of reporting of meta-analyses, and to propose a guide through the currently discordant available evidence.

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## MATERIALS AND METHODS

This systematic review was performed according to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analysis, which was recommended to ensure high-quality reporting of systematic reviews and meta-analyses.[14] Ethical approval and informed patient consent were not required, as this study was a literature review and had no direct patient contact or influence on patient care.

### Study Search

We searched the Cochrane Central Register of Controlled Trials, PubMed, and EMBASE. The following keywords were used for the searches: humeral or humerus; shaft, diaphysial, or diaphysis; fracture; and meta-analysis or systematic review. We checked the reference lists of published studies to identify additional systematic reviews or meta-analyses. The search was performed on September 6, 2014, and was limited to articles written in English.

### Eligibility Criteria

The study inclusion criteria were: meta-analysis exclusively including RCTs; meta-analysis comparing intramedullary nail with plate fixation for the treatment of humeral shaft fractures; meta-analysis reported at least 1 variable (eg, fracture union, shoulder score, and complication). The exclusion criteria were: narrative review; meta-analysis including non-RCTs; systematic review did not pool data or perform a meta-analysis; and meetings abstract or correspondence was excluded because most of them did not provide enough detailed data and important methodological information.

### Selection of Meta-analyses

Two authors independently checked titles and abstracts from the searches to identify potentially eligible studies. The authors were not blinded to the names of original researchers, journals, or institutions. They independently retrieved and reviewed full-text articles for the purpose of applying eligibility criteria. When there were discrepancies between authors, a consensus was reached through discussion or a third author was consulted.

### Data Extraction

Two authors independently extracted the information of each study using standardized extraction forms, including lead author, publication year, search database, primary trial design, participants, number of included RCTs, level of evidence, conflicts of interest, and variables. Each author independently extracted all information. When there were discrepancies between authors, a third author was consulted.

### Quality Assessment

Methodological quality for each included meta-analysis was assessed using the Oxford Levels of Evidence[15] and the Assessment of Multiple Systematic Reviews (AMSTAR) Instrument.[16] AMSTAR is currently reported as a measurement tool with extensive application to assess the methodological quality of systematic review/meta-analysis.[16,17] It has good reliability, validity, and responsibility.[18] Both authors independently assessed methodological quality. They then met and reviewed every item for agreement.

### Assessment of Heterogeneity

Heterogeneity information of each variable was extracted for the included studies. We explored whether the studies evaluated possible sources of heterogeneity across studies and whether the investigators formally performed a sensitivity analysis. According to the Cochrane Handbook, heterogeneity is considered not important between 0% and 40%; moderate between 30% and 60%; substantial between 50% and 90%, and

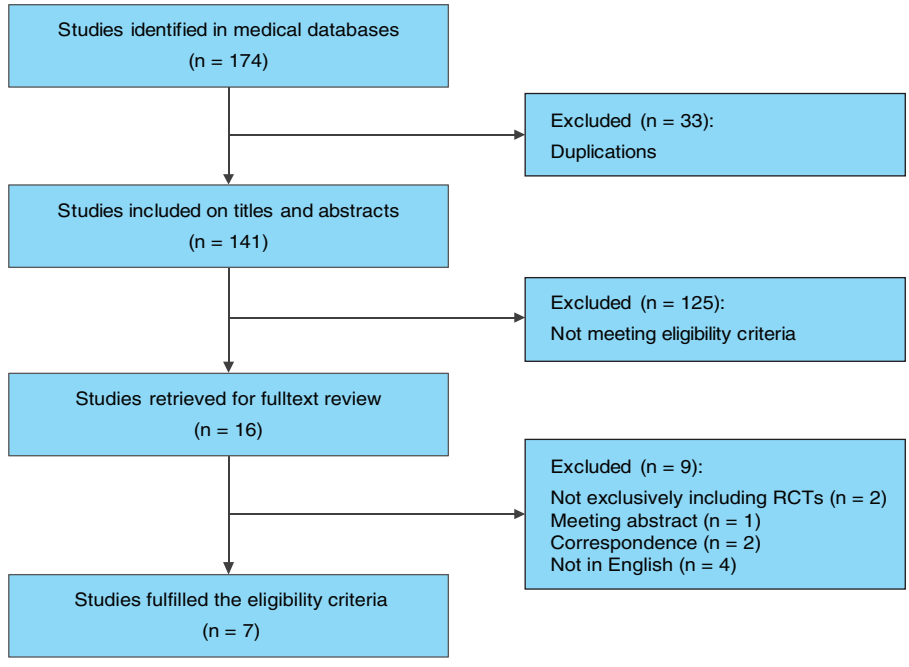


**FIGURE 1.** Flow diagram summarizing the selection process of meta-analyses.

**TABLE 1.** General Description of the Characteristics of Each Meta-analysis

| Authors | Journal | Date of Last Literature Search | Date of Publication | No. of Included RCTs |
|---|---|---|---|---|
| Bhandari et al 2006[13] | Acta Orthopaedica | January, 2004 | April, 2006 | 3 |
| Heineman et al 2010[19] | Acta Orthopaedica | November, 2007 | April, 2010 | 4 |
| Kurup et al 2011[21] | Cochrane Database of Syst Rev | February, 2011 | June, 2011 | 5 |
| Zheng et al 2012[22] | Eur J Orthop Surg Traumatol | February, 2011 | August, 2012 | 4 |
| Ouyang et al 2013[23] | J Shoulder Elbow Surg | July, 2011 | March, 2013 | 10 |
| Wang et al 2013[24] | J Orthop Sci | December, 2011 | May, 2013 | 9 |
| Ma et al 2013[10] | PLoS One | December, 2012 | December, 2013 | 10 |

**TABLE 2.** Primary Studies Included in Meta-analyses

| Authors | Bolano (1995)[31] | Chapman et al (2000)[25] | McCormack et al (2000)[6] | Kesemenli et al (2003)[26] | Benegas et al (2007)[27] | Changulani et al (2007)[7] | Daglar et al (2007)[28] | Raghavendra et al (2007)[29] | Huang et al (2008)[30] | Putti et al (2009)[8] | Singisetti et al (2010)[9] | Li et al (2011)[32] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bhandari et al 2006[13] | + | + | + | | | | | | | | | |
| Heineman et al 2010[19] | + | + | + | | | + | | | | | | |
| Kurup et al 2011[21] | + | + | + | + | | + | + | | | | | |
| Zheng et al 2012[22] | | + | | | | + | | | | + | + | |
| Ouyang et al 2013[23] | + | + | + | + | + | + | + | + | | + | + | |
| Wang et al 2013[24] | + | + | + | + | | + | | | + | + | + | + |
| Ma et al 2013[10] | + | + | + | + | + | + | | + | | + | + | + |

**TABLE 3.** Databases used by each study in their literature searches

| Authors | PubMed | Medline | Embase | Cochrane Library | OVID | Google scholar | Others |
|---|---|---|---|---|---|---|---|
| Bhandari et al (2006)[13] | | + | | + | | | + |
| Heineman et al (2010)[19] | + | + | + | + | | | + |
| Kurup et al (2011)[21] | | + | + | + | | | + |
| Zheng et al (2012)[22] | | + | + | + | | | + |
| Ouyang et al (2013)[23] | | + | + | + | + | + | + |
| Wang et al (2013)[24] | + | | + | + | | | + |
| Ma et al (2013)[10] | | + | + | + | + | + | + |

considerable between 75% and 100%. Therefore, an $I^2$ of less than 60% is accepted in this systematic review.

## Application of Jadad Decision Algorithm

The Jadad decision algorithm[19] was used to provide treatment recommendations. This methodology determines the source of discordance between systematic reviews, including differences in clinical question, inclusion and exclusion criteria, data extraction, quality assessment, data pooling, and statistical analysis.[19] Three authors independently applied the algorithm and arrived at a consensus as to which of the meta-analyses provided the best currently available evidence.

# RESULTS

## Search Results

A flow diagram that depicts the search process can be found in Figure 1. One hundred and seventy-four titles were found initially. Seven studies met the inclusion criteria and were selected as appropriate for inclusion in this systematic review.[10,13,20–24] Two studies were excluded because they did not exclusively included RCTs.[11,12] A general description of the characteristics of each meta-analysis is provided in Table 1.[10,13,19,21–24] The number of primary studies varied widely from 3 in those studies published in 2006 to 10 for 2 studies published in 2013 (Table 2).[6–9,25–32] All studies performed meta-analyses and pooled data.

## Search Methodology

Most studies comprehensively searched databases. All of the included studies searched Cochrane Library and Medline (PubMed). There was heterogeneity as to whether studies also included searches of Embase, OVID, and Google scholar. Table 3 gives details regarding search methodology used by each included study.[10,13,19,21–24]

## Methodological Quality

All studies included RCTs or quasi-RCTs and were Level II of evidence (Table 4).[10,13,19,21–24] Only one study reported that the GRADE was used in their research.[10] AMSTAR results for each question from each meta-analysis are shown in Table 5.[10,13,19,21–24] AMSTAR scores varied from 6 to 10 with a median of 7.86. One Cochrane review by Kurup et al[21] was the most highest quality study, with 10 of the 11 (91%) of the AMSTAR criteria.

## Heterogeneity Assessment

The $I^2$ statistic value was calculated to assess study heterogeneity as a measure for determining the interstudy variability in all meta-analyses. Heterogeneity of each outcome was acceptable (<60%) in those meta-analyses pooled results (Table 6).[10,13,19,21–24] Of the 7 meta-analyses, 3 meta-analyses conducted sensitivity analyses based on publication status or methodological quality (Table 4).[13,20,23]

## Results of Jadad Decision Algorithm

The results of all included meta-analyses were summarized in Figure 2. Given that all of the meta-analyses addressed the same study question, the included meta-analyses did not include the same primary trials, and the selection criteria were similar among included meta-analyses, the Jadad algorithm suggested that the meta-analyses can be selected based on the search strategies and application of selection. As a result, 2 meta-analyses[10,23] with more RCTs were selected (Figure 3). Both of them suggested that the differences between intramedullary nail and plate fixation were not significant in fracture union, radial nerve injury, and infection. But intramedullary nail significantly increased the risk of shoulder complications (shoulder impingement, restriction of shoulder movement) and reoperation (Figure 2).

**TABLE 4.** Methodological Information for Each Included Study

| Authors | Included Study Design | Level of Evidence | Software | GRADE Use | Sensitivity Analysis |
|---|---|---|---|---|---|
| Bhandari et al (2006)[13] | RCT or quasi-RCT | Level II | NA | No | Yes |
| Heineman et al (2010)[19] | RCT or quasi-RCT | Level II | Revman | No | Yes |
| Kurup et al (2011)[21] | RCT or quasi-RCT | Level II | Revman | No | No |
| Zheng et al (2012)[22] | RCT or quasi-RCT | Level II | Revman | No | No |
| Ouyang et al (2013)[23] | RCT or quasi-RCT | Level II | Revman | No | Yes |
| Wang et al (2013)[24] | RCT or quasi-RCT | Level II; | Revman | No | No |
| Ma et al (2013)[10] | RCT or quasi-RCT | Level II | Revman | Yes | No |

RCT = randomized controlled trials.

**TABLE 5.** AMSTAR Criteria for Each Included Study

| Items | Bhandari et al 2006[13] | Heineman et al 2010[19] | Kurup et al 2011[21] | Zheng et al 2012[22] | Ouyang et al 2013[23] | Wang et al 2013[24] | Ma et al 2013[10] |
|---|---|---|---|---|---|---|---|
| Was an a priori design provided? | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Was there duplicate study selection and data extraction? | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| Was a comprehensive literature search performed? | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Was the status of publication (ie, grey literature) used as an inclusion criterion? | 1 | 1 | 1 | 0 | 1 | 1 | 1 |
| Was a list of studies (included and excluded) provided? | 0 | 0 | 1 | 0 | 0 | 1 | 0 |
| Were the characteristics of the included studies provided? | 1 | 1 | 1 | 0 | 1 | 1 | 1 |
| Was the scientific quality of the included studies assessed and documented? | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Was the scientific quality of the included studies used appropriately in formulating conclusions? | 1 | 1 | 1 | 1 | 1 | 0 | 1 |
| Were the methods used to combine the findings of studies appropriate? | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| Was the likelihood of publication bias assessed? | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| Was the conflict of interest stated? | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Total scores | 6 | 7 | 10 | 6 | 8 | 9 | 9 |

**TABLE 6.** $I^2$ Statistic Value of Each Variable in Each Meta-analysis

| Outcomes | Bhandari et al 2006[13] | Heineman et al 2010[19] | Kurup et al 2011[21] | Zheng et al 2012[22] | Ouyang et al 2013[23] | Wang et al 2013[24] | Ma et al 2013[10] |
|---|---|---|---|---|---|---|---|
| ASES score | | | — | | | | 5% |
| Rodríguez-Merchán criteria | | | | | | 0% | |
| Steward and Huntley criteria | | | — | | | | |
| Fracture nonunion | 25% | 0% | | 0% | 0% | NA | |
| Fracture delayed union | | | | | 0% | 0% | |
| Fracture malunion | | | | | | NA | |
| Fracture union | | | 0% | | | | 0% |
| Total complications | | 53% | | 1% | | 33% | |
| Radial nerve injury | 10% | 0% | 31% | 0% | 11% | NA | 15% |
| Intraoperative fracture comminution | | | 0% | | 0% | 0% | 0% |
| Infection | 0% | 0% | 20% | 0% | 0% | NA | 0% |
| Shoulder pain | | | | | | 0% | |
| Shoulder impingement | 0% | | 0% | 0% | 0% | | 0% |
| Restriction and impingement of shoulder | | | | | | 0% | |
| Restriction of shoulder range of movement | | | 0% | | 0% | | 0% |
| Elbow pain | | | | | | 0% | |
| Elbow impingement | | | — | | | | |
| Restriction of elbow range of movement | | | — | | | | |
| Implant failure | | | | | 0% | NA | 0% |
| Reoperation | 10% | 58% | | | 29% | | 21% |
| Need for removal of metalwork | | | 20% | | | 11% | |
| Return to pre-injury occupation | | | — | | | | |
| Operating time | | | — | | | | |
| Blood loss | | | — | | | | |


**FIGURE 2.** Results of each included meta-analysis. Red means favoring plate; green means no difference; yellow means not reporting; and blue means favoring nail. Arabic numerals means the number of included randomized clinical trials.

## DISCUSSION

Systematic reviews or meta-analyses are considered the highest level of scientific evidence.[33] They are performed with use of meta-analytic methods and can help clinicians to make informed clinical decisions. Multiple meta-analyses focusing on the same topic have been written on how best to appraise some treatment methods, but have led to conflicting conclusions.[19] These discordances complicate surgeons, patients, and policy-makers. Several published meta-analyses have demonstrated that both intramedullary nail and plate fixation improve the preoperative clinical status, but it is not clear which of the 2 interventions provides better outcomes. For example, recently, a meta-analysis by Dai et al[12] showed intramedullary nail may lead to a lower risk of infection and postoperative nerve palsy. However, Ma et al[10] and Liu et al[11] concluded that both intramedullary nail and plate can achieve a similar incidence of radial nerve injury and infection.

Although 3 meta-analyses[10,23,24] comprehensively searched databases within similar period, they still included different RCTs and reached different conclusions for the treatment of humeral shaft fractures. How is it possible that meta-analyses on the same topic reach such different conclusions?

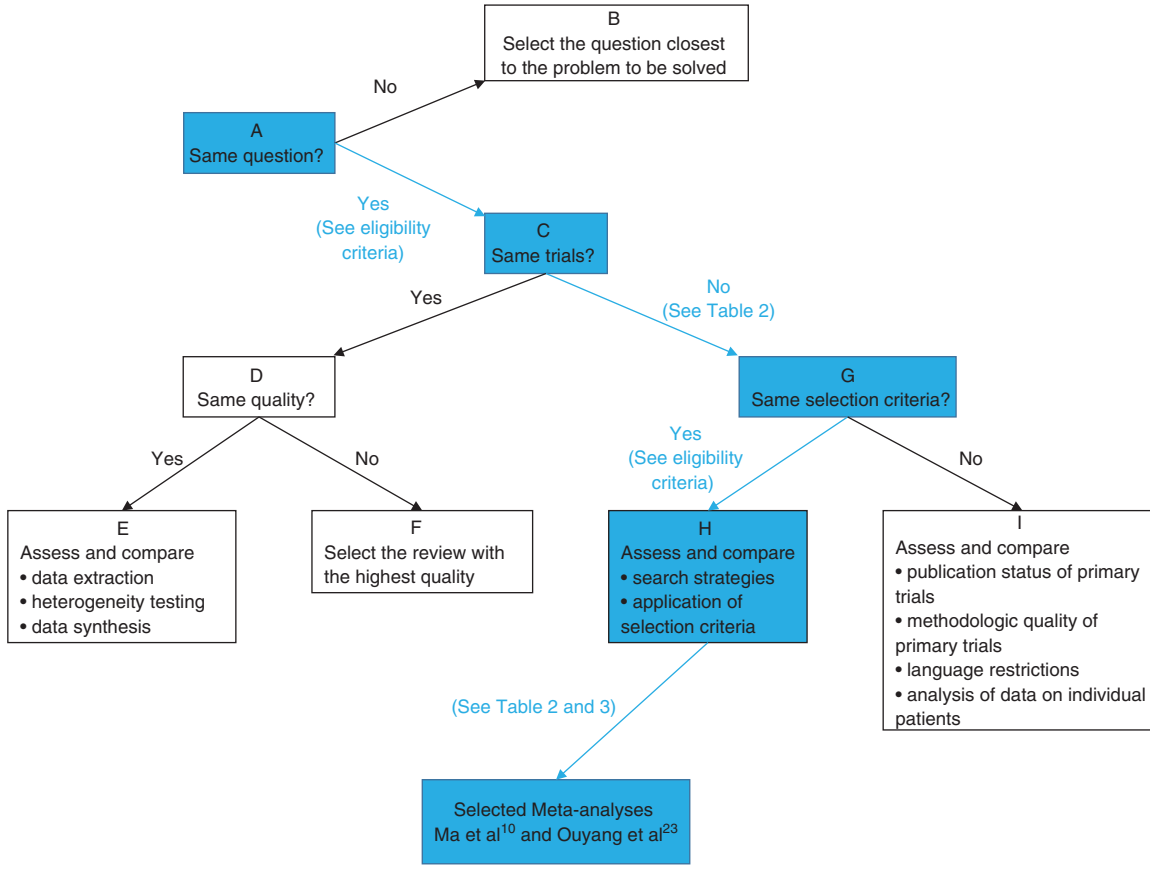


**FIGURE 3.** Flow diagram of Jadad decision algorithm.

Jadad et al[19] summarized the potential sources of discordance among meta-analyses including the clinical question (population of patients, interventions, outcome measures, and setting), study selection and inclusion (selection criteria, application of selection criteria, strategies used to search the literature), data extraction (methods used to measure outcomes, end points, human error), assessment of study quality (methods used to assess quality, interpretations of quality assessments, methods used to incorporate quality assessments in review), assessment of the ability to combine studies (statistical methods, clinical criteria used to judge the ability to combine studies), and statistical methods for data synthesis. Jadad et al[19] also provided a decision tool (decision algorithm) to help decision-makers select from among discordant reviews. It is a useful tool for differentiating between overlapping reviews and was widely used, as shown in the present study.

According to the Jadad model, the meta-analyses by Ouyang et al[23] and Ma et al[10] were selected in this systematic review. Ouyang et al[23] found that plate fixation reduced the risk of shoulder impingement and shoulder restriction in comparison with intramedullary nail. Sensitivity analysis showed intramedullary nail was associated with an increased risk of reoperation. No significant differences were found in iatrogenic fracture comminution, postoperative infection, radial nerve palsy, nonunion, delayed union, and implant failure between the 2 groups. Ma et al[10] found that the differences between intramedullary nail and plate fixation were not significant in fracture union, radial nerve injury, and infection. Intramedullary nail was associated with an increased risk of intraoperative fracture comminution, an increased risk of shoulder impingement, more restriction of shoulder movement, a higher incidence of implant failure, and an increased risk of reoperation. Thus, both the meta-analyses by Ouyang et al[23] and Ma et al[10] showed that intramedullary nail may increase the occurrence of shoulder problems, although intramedullary nail and plate fixation can achieve similar fracture union. So we concluded that plate fixation is superior to intramedullary nail for the treatment of humeral shaft fractures.

There are limitations to our study. First, our search strategy was limited by the exclusion of non-English literature that might have met our inclusion criteria, although we searched for as many meta-analyses as possible. Second, although only the meta-analyses exclusively including RCT design were assessed to ensure the high quality of this systematic review, all meta-analyses were Level II evidence. And none of them was Level I evidence.

## CONCLUSION

In this systematic review of overlapping meta-analyses comparing intramedullary nail and plate fixation for the treatment of humeral shaft fractures, the best available evidence suggested that the differences between intramedullary nail and plate fixation were not significant in fracture union, radial nerve injury, and infection. But intramedullary nail significantly increased the risk of shoulder complications (shoulder

impingement and restriction of shoulder movement) and reoperation. Thus, we concluded that plate fixation is superior to intramedullary nail for the treatment of humeral shaft fractures.

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