Interventions for Treating Displaced Midshaft Clavicular Fractures
A Bayesian Network Meta-Analysis of Randomized Controlled Trials

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Abstract: Displaced midshaft clavicle fractures are frequent injuries. There are 3 treatment methods including conservative treatment, plate fixation, and intramedullary pin fixation. However, which is the best treatment remains a topic of debate.

To establish the optimum treatment for displaced midshaft clavicular fractures, we did a network meta-analysis to compare 3 treatments in terms of postoperative nonunion and infection.

We searched PubMed, the Cochrane Library, and Embase for relevant randomized controlled trials (RCTs) until the end of October 2014. Two investigators independently reviewed the abstract and full text of eligible studies and extracted information. We used WinBUGS 1.4 (Imperial College School of Medicine at St Mary’s, London) to perform our Bayesian network meta-analysis. We used the graphical tools in STATA 12 (StataCorp, Texas) to present the results of statistical analyses of WinBUGS 14. Nonunion and infection were presented as odd ratios (ORs) with 95% confidence intervals (CIs). We also presented the results using surface under the cumulative ranking curve (SUCRA). A higher SUCRA value suggests better results for respective treatment method.

Thirteen RCTs were included in our network meta-analysis, with a total of 894 patients randomized to receive 1 of 3 treatments. Nonunion rates were 0.9%, 2.4%, and 11.4% for intramedullary pin fixation, plate fixation, and conservative method, respectively. Nonunion occurred more commonly in patients treated with conservative method than in patients treated with either plate fixation (OR, 0.18; 95% CI, 0.05–0.46) or intramedullary pin fixation (OR, 0.12; 95% CI, 0.01–0.50). There was no significant difference between plate and intramedullary pin fixation in nonunion (OR, 3.64; 95% CI, 0.31–17.27). Furthermore, SUCRA probabilities were 87.8%, 62.0%, and 0.2% for intramedullary pin fixation, plate fixation, and conservative method, respectively. Infection rates were 3.6% and 3.9% for intramedullary pin fixation and plate fixation, respectively. There was no significant difference between plate and intramedullary pin fixation in infection (OR, 3.64; 95% CI, 0.31–17.27). SUCRA probabilities were 46.5% and 8.5% for intramedullary pin and plate fixation, respectively.

Our network meta-analysis suggested that intramedullary pin fixation is the optimum treatment method for displaced midshaft clavicle fracture because of the low probabilities of nonunion and infection.

INTRODUCTION
Clavicle fractures are frequent injuries, accounting for 2.6% to 4% of all fracture in adults. The most common type of clavicle fracture is the midshaft fracture. It frequently results in short-term disability and pain, eventually causing longer-term deformity and disability. Conservative interventions are widely used and are recommended for treating midshaft clavicle fractures. Traditionally, displaced clavicle fractures are treated conservatively with a figure-of-eight bandage or a sling. Recently, surgery treatment methods have been increasingly used for displaced midshaft fracture of the clavicle, mainly involving plate or intramedullary pin fixation.

Some randomized controlled trials (RCTs) have been published regarding surgical treatment versus conservative treatment and comparison of different operation methods. Individual RCTs may be underpowered to show subtle clinical differences because of the smaller patient number. Several meta-analyses or systematic reviews comparing surgical versus conservative interventions for the treatment of midshaft clavicle fracture have also been published. In addition, 2 systematic reviews also compared the difference between plate and intramedullary pin fixation. However, traditional meta-analysis methods only directly compare 2 different methods. When comparing ≥3 treatments, it is impossible. Bayesian network meta-analysis is known as mixed treatment comparison and it could combine direct and indirect comparisons to resolve this problem.

To establish the optimum treatment for displaced midshaft clavicular fractures, we did a network meta-analysis to compare 3 treatments including conservative treatment, plate fixation, and intramedullary pin fixation in terms of postoperative nonunion and infection.

METHOD
We did our systematic review in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Ethical approval and informed patient consent was not required as this study was a literature review and had no direct patient contact or influence on patient care.
Search Strategy

We searched PubMed, the Cochrane Library, and Embase for relevant RCTs until the end of October 2014. The following keywords were used: "clavicle" or "clavicular," "fracture," and "random." No language or publication restrictions were applied. Articles in languages other than English were translated with the help of medically knowledgeable speakers.

Selection Criteria

We systematically reviewed the literature according to the following criteria: a target population of displaced midshaft clavicular fractures in adults; RCTs evaluating 2 or 3 of the 3 treatments including plate fixation, intramedullary pin fixation, and conservative treatment; and a minimum of 12-month follow-up. We excluded studies if they contained only 1 or none of the 3 treatments. Two authors independently scanned records to exclude irrelevant studies and identify trials that met the eligibility criteria. Differences in opinion between authors were resolved by discussion and consultation with a third author.

Data Extraction

Two investigators independently reviewed the abstract and full text of eligible studies and extracted information into an electronic database, including publication year, patients characteristics, random methods, inclusion and exclusion criteria, treatment methods, and outcomes (nonunion and infection). The primary outcome was the incidence of nonunion. Nonunion was defined as an unsuccessful healing of the bone after 6 months. We also compared the incidence of infection between plate fixation and intramedullary pin fixation.

Assessment of Methodological Quality

The risk of bias was assessed independently by 2 investigators with the Detsky scale. Disagreement was resolved through discussing. The Detsky score was used because it has been used previously to determine the methodological quality of published orthopedic RCTs and has shown good consistency and reliability. A quality score of >75% (≥16 scores) was considered to indicate high quality, scores >50% and <75% (11–15 scores) indicated moderate quality, and scores <50% (≤10 scores) indicated low quality, which is consistent with the previous research.

Data Analysis

We used WinBUGS1.4 (Imperial College School of Medicine at St Mary’s, London) to perform our Bayesian network meta-analysis using the statistic method described by Chaimani et al. Furthermore, we used the graphical tools in STATA12 (StataCorp, Texas) to present the results of statistical analyses of WinBUGS1.4. Funnel plot was used to assess the presence of small-study effects in our meta-analysis. A funnel plot is a scatterplot of study effect size versus some measure of its precision. Inconsistency refers to differences between direct and various indirect effect estimates for the same comparison. To assess inconsistency, we estimated the inconsistency factors in closed loop based on the method described by Chaimani et al. Nonunion and infection were presented as odd ratios (ORs) with 95% confidence intervals (CIs). This network meta-analysis could provide information about ranking of all evaluated interventions for the outcome. We also presented the results using surface under the cumulative ranking curve (SUCRA). A higher SUCRA value suggests better results for respective treatment method.

RESULTS

Search Results

We identified 171 potentially relevant references from database searches after screening out repeated literature (Figure 1). Of these references, we excluded 140 at the initial
| Study (Year)        | Design           | Number of Patients | Comparison                                      | Included/Excluded Criteria                                                                 | Mean Age, y | Female Patients (%) | Follow-Up, mo |
|-------------------|------------------|--------------------|-------------------------------------------------|-------------------------------------------------------------------------------------------|-------------|---------------------|---------------|
| COTS6,24 (2007)   | Multicenter RCT  | 111                | Plate (including LCDCP, reconstruction plate, and precontoured plate) VS sling | Incl: isolated displaced midshaft fracture, age between 16 and 60 y                         | 34          | 24 (21%)            | 12            |
| Lee et al23 (2007)| Single RCT       | 62                 | Knowles pin VS plate*                           | Excl: pathological fracture, open fracture, associated neurovascular injury                | 58          | 36 (58%)            | 30            |
| Figueiredo et al25 (2008) | Single RCT | 40                 | Plate* VS sling                                 | Incl: ages >18 y, isolated acute, closed, displaced midshaft fracture                      | 30          | 9 (22%)             | 12            |
| Koch et al26 (2008) | Single RCT      | 68                 | Intramedullary titan pin VS figure-of-eight     | Incl: athletes with an isolated fracture of middle third of the clavicle                  | 35          | 23 (34%)            | 19            |
| Judd et al27 (2009) | Single RCT      | 57                 | Modified Hagie pin VS sling                     | Excl: open fractures, neurologic compromise                                                | 26          | 5 (9%)              | 12            |
| Ferran et al29 (2010) | Single RCT      | 32                 | Rockwood pin VS LCDCP                          | Incl: isolated midshaft clavicle fracture with displacement                                | 29          | 5 (16%)             | 12            |
| Assobhi30 (2011)  | Single RCT       | 38                 | RTEN VS reconstruction plate                    | Incl: ages between 16 and 60 y, displaced midshaft clavicle fracture                      | 31          | 5 (13%)             | 12            |
| Mirzatolooe31 (2011) | Single RCT      | 50                 | Reconstruction plate VS sling                   | Excl: ipsilateral injuries, pathological fractures, open fractures                       | 35          | 9 (18%)             | 12            |
| Smekal et al28,32 (2011) | Single RCT | 112                | Elastic stable intramedullary nailing VS sling | Incl: isolated, unilateral, displaced midshaft clavicle fracture, age between 18 and 65 y | 37          | 14 (13%)            | 24            |
| Virtanen et al7 (2012) | Single RCT     | 51                 | Reconstruction plate VS sling                   | Excl: multiply injured patient, associated neurovascular injury, pathological fracture, open fracture, concomitant upper-extremity fracture | 36          | 8 (15%)             | 12            |
screening through reviewing title and abstract. We retrieved the full text of potential articles. Fifteen eligible publications, reporting 13 RCTs were included in our network meta-analysis, with a total of 894 patients randomized to receive one of three treatments. We summarized all included studies in Table 1. Figure 2 shows all comparisons within the network.

Methodological Quality
The median Detsky scores for the included trials were 15.8. The overall methodological quality was moderate. The detailed Detsky quality scores of the included studies are listed in Table 2.

Inconsistency Test
In Figure 3, the funnel plot is symmetrical to the line and it implies that there are no small-study effects in our network meta-analysis. Figure 4 shows that there is no significant inconsistency as its CIs are compatible with zero.

Nonunion
The nonunion was reported in all 13 included trials. Nonunion rates were 0.9%, 2.4%, and 11.4% for intramedullary pin fixation, plate fixation, and conservative method, respectively. Nonunion occurred more commonly in patients treated with conservative method than in patients treated with either plate fixation (OR, 0.18; 95% CI, 0.05–0.46) or intramedullary pin fixation (OR, 0.12; 95% CI, 0.01–0.50) (Figure 5). There was no significant difference between plate and intramedullary pin fixation in nonunion rate (OR, 3.64; 95% CI, 0.31–17.27). Furthermore, SUCRA probabilities were 87.8%, 62.0%, and 0.2% for intramedullary pin fixation, plate fixation, and conservative method, respectively (Figure 6). In Figure 7, we summarized the ranking of the three treatment methods in terms of the probability of nonunion.

Infection
Infection rates were 3.6% and 3.9% for intramedullary pin fixation and plate fixation, respectively. The direct and indirect result of the meta-analysis showed that there was no significant difference between plate and intramedullary pin fixation in infection rate (OR, 3.64; 95% CI, 0.31–17.27) (Figure 5). Furthermore, SUCRA probabilities were 46.5% and 8.5% for

![Image of network diagram](https://example.com/network_diagram.png)

**FIGURE 2.** Network of the comparisons for the Bayesian network meta-analysis. RCT = randomized controlled trial.
| Scale Item Scale | COTS<sup>6,24</sup> (2007) | Lee et al<sup>23</sup> (2007) | Figueired et al<sup>25</sup> (2008) | Koch et al<sup>26</sup> (2008) | Judd et al<sup>27</sup> (2009) | Ferran et al<sup>29</sup> (2010) | Assobhi<sup>30</sup> (2011) | Mirzatolooei<sup>31</sup> (2011) | Smekal et al<sup>28,32</sup> (2011) | Virtanen et al<sup>7</sup> (2012) | Dugar et al<sup>33</sup> (2013) | Robinson et al<sup>8</sup> (2013) | Narsaria et al<sup>34</sup> (2014) |
|------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Randomization    | Were the patients assigned randomly? | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | | | | | | | | | | | | |
|                  | Description of randomization | 2 0 2 0 2 2 0 2 2 2 0 1 0 1 0 | | | | | | | | | | | | |
|                  | Do you believe there could have been bias in treatment assignment? | 1 0 1 0 1 1 0 1 1 1 1 1 1 1 0 | | | | | | | | | | | | |
| Outcome          | Was there a description of the criteria for measuring outcomes? | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | | | | | | | | | | | | |
|                  | Were the criteria objective? | 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 | | | | | | | | | | | | |
|                  | Were outcome assessors blind to treatment received? | 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | | | | | | | | | | | | |
| Eligibility      | Were inclusion/exclusion criteria clearly defined? | 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 | | | | | | | | | | | | |
|                  | Do you know how many patients were excluded from the trial? | 2 0 2 0 1 2 0 0 0 0 2 0 0 0 0 | | | | | | | | | | | | |
| Therapy          | Was the therapeutic regimen fully described for the treatment group? | 2 2 2 2 1 2 2 2 2 2 2 1 2 2 2 | | | | | | | | | | | | |
|                  | Was the therapeutic regimen fully described for the control group? | 2 1 2 0 0 2 2 2 2 2 2 1 2 2 2 | | | | | | | | | | | | |
| Statistical analysis | Was there a statistical analysis? (Test stated and P values given.) | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | | | | | | | | | | | | |
|                  | Was the statistical analysis appropriate? | 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 | | | | | | | | | | | | |
|                  | If the trial was negative, were confidence intervals or post hoc power calculations performed? | 1 1 1 0 1 1 1 0 1 1 0 1 0 1 1 | | | | | | | | | | | | |
| Sample size      | Was there a sample size justification before the study? | 1 0 0 0 0 0 1 1 0 0 1 0 1 0 1 0 | | | | | | | | | | | | |
| Total score      | | 20 13 19 10 16 20 15 16 17 20 9 17 14 | | | | | | | | | | | | |

COTS = Canadian Orthopaedic Trauma Society.
intramedullary pin fixation and plate fixation, respectively (Figure 8). In Figure 7, we summarized the ranking of the 2 treatment methods in terms of the probability of infection.

**DISCUSSION**

The best treatment for displaced midshaft clavicle fractures remains a topic of debate. Many studies showed a high risk for nonunion after conservative treatment. Operative treatment is playing a more and more important role. Plate fixation and intramedullary pin fixation are main operation methods. Recently, several meta-analyses regarding the management of displaced midshaft clavicle fracture have been published. Most of them focused on the comparison between operative and nonoperative treatments. However, synthesis of present evidence using traditional meta-analysis methods is a challenging task because there are 3 major treatment methods. No network meta-analysis concerning this topic was published.

This is the first network meta-analysis that assesses the treatments of displaced midshaft clavicle fracture. Network meta-analysis is a well-established research by comparing different treatments. Thirteen RCTs were included in our network meta-analysis, and 4 of them directly compared plate fixation with intramedullary pin. When comparing with conservative treatment, either plate or intramedullary pin significantly decreased the postoperative nonunion rate. Although there was no significant difference between pin and plate based on OR value, the results of SUCRA ranking suggested that intramedullary pin fixation had the lower probability of nonunion than plate fixation (Figures 6 and 7). SUCRA results also

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**FIGURE 3.** Funnel plot of this network meta-analysis. C = conservative treatment, I = intramedullary pin fixation, P = plate fixation.

**FIGURE 4.** Inconsistency plot of this network meta-analysis. C = conservative treatment, I = intramedullary pin fixation, IFs = inconsistency factors, P = plate fixation.

**FIGURE 5.** Odd ratios with 95% confidence intervals for nonunion and infection.

**FIGURE 6.** Surface under the cumulative ranking curves for nonunion.

**FIGURE 7.** Ranking of treatments in terms of nonunion and infection.
suggested that intramedullary pin fixation had a lower probability of infection than plate fixation (Figures 7 and 8). Hence, we concluded that intramedullary pin fixation is the preferred choice for treating displaced midshaft clavicular fractures.

Intramedullary pin fixation had a lower rate of nonunion and infection than plate fixation, which can be explained by less damaged blood supply during the operation. Favorable soft tissue and adequate blood supply are the critical factors for the fracture consolidation. Although plate fixation is better to resist bending and torsional forces than intramedullary pin fixation regarding biomechanics, it needs greater exposure and more extensive soft tissue stripping that may affect fracture healing and increase the risk of infection. Intramedullary pin fixation is a minimally invasive alternative that avoids those problems encountered with plating. Furthermore, the removal of plates necessitated new admissions, general anesthesia, and another large-sized incision, whereas nail removal was performed under local anesthesia with minimal sedation and a tiny incision over the tip of the nail. On the other hand, plate fixation has absolute stability, whereas intramedullary pin fixation provides elastic fixation that is an advantage to fracture healing.

We did not compare the incidence of malunion and shoulder scores due to the lack of unified evaluation criteria. Some studies reported symptomatic malunion, but radiologic malunion was assessed in other studies. Similarly, although all RCTs reported the shoulder scores in their studies, there were multiple shoulder scores among them including the American Shoulder and Elbow Surgeons score, Constant score, Disabilities of the Arm, Shoulder, and Hand score, and Oxford Shoulder score. Furthermore, some studies did not report the detailed data of mean and standard deviation. Therefore, we did not pool these data to ensure the rationality and validity of this meta-analysis.

The present analysis included more RCTs through an extensive search. The enlarged sample size provided more accurate estimates of effects. The main limitation of the study was that we could not compare the specific fixators. For example, there were several types of intramedullary pins in the included studies such as the elastic intramedullary pin, Rockwood pin, and Knowles pin. It is noteworthy that there were neither small-study effects nor was there significant inconsistency in our network meta-analysis.

In conclusion, our network meta-analysis suggested that intramedullary pin fixation is the optimum treatment method for displaced midshaft clavicle fracture because of the low probabilities of nonunion and infection.

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