Surgical Versus Nonsurgical Treatment for Midshaft Clavicle Fractures in Patients Aged 16 Years and Older

A Systematic Review, Meta-analysis, and Comparison of Randomized Controlled Trials and Observational Studies

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Background: There is no consensus on the choice of treatment of midshaft clavicle fractures (MCFs).

Purpose: The aims of this systematic review and meta-analysis were (1) to compare fracture healing disorders and functional outcomes of surgical versus nonsurgical treatment of MCFs and (2) to compare effect estimates obtained from randomized controlled trials (RCTs) and observational studies.

Study Design: Systematic review and meta-analysis.

Methods: The PubMed/MEDLINE, Embase, CENTRAL, and CINAHL databases were searched for both RCTs and observational studies. Using the MINORS instrument, all included studies were assessed on their methodological quality. The primary outcome was a nonunion. Effects of surgical versus nonsurgical treatment were estimated using random-effects meta-analysis models.

Results: A total of 20 studies were included, of which 8 were RCTs and 12 were observational studies including 1760 patients. Results were similar across the different study designs. A meta-analysis of 19 studies revealed that nonunions were significantly less common after surgical treatment than after nonsurgical treatment (odds ratio [OR], 0.18 [95% CI, 0.10-0.33]). The risk of malunions did not differ between surgical and nonsurgical treatment (OR, 0.38 [95% CI, 0.12-1.19]). Both the long-term Disabilities of the Arm, Shoulder and Hand (DASH) and Constant-Murley scores favored surgical treatment (DASH: mean difference [MD], −2.04 [95% CI, −3.56 to −0.52]; Constant-Murley: MD, 3.23 [95% CI, 1.52 to 4.95]). No differences were observed regarding revision surgery (OR, 0.85 [95% CI, 0.42-1.73]). Including only high-quality studies, both the number of malunions and days to return to work show significant differences in favor of surgical treatment (malunions: OR, 0.26 [95% CI, 0.07 to 0.92]; return to work: MD, −8.64 [95% CI, −16.22 to −1.05]).

Conclusion: This meta-analysis of high-quality studies showed that surgical treatment of MCFs results in fewer nonunions, fewer malunions, and an accelerated return to work compared with nonsurgical treatment. A meta-analysis of surgical treatments need not be restricted to randomized trials, provided that the included observational studies are of high quality.

Keywords: clavicle fracture; nonoperative; surgical; quality assessment; systematic review; meta-analysis

Clavicle fractures represent 2.6% to 4% of all fractures and 35% to 44% of those in the shoulder girdle.[37,41] Midshaft clavicle fractures (MCFs) are among the most common upper extremity injuries managed by orthopaedic trauma surgeons. Midshaft fractures account for 69% of all clavicle fractures, of which half are displaced.[44] Most clavicle fractures occur in young men and are caused by falls, sports, and road-traffic accidents.[44]

Open fractures, compromised overlying skin, and the presence of neurovascular damage require surgical treatment.[23] However, there is no consensus about the choice of treatment of closed MCFs without these factors.[38,49,50] In the past decades, indications for surgical treatment seem to have broadened, and surgical treatment is increasingly favored, especially by shoulder specialists.[7,8,51] However, still half of the surgeons treat their patients nonsurgically.[50]

Several systematic reviews and meta-analyses have previously been published, with contradicting results.[4,13,30] All

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of these studies only included randomized controlled trials (RCTs).[28,30,42,58] Yet, the holy grail of RCTs has recently been debated.[3] Observational studies can be included in meta-analyses to increase the sample size and generalizability of findings, provided the quality (ie, validity) of the observational studies is of the same level as that of the RCTs. Observational studies are very suitable to identify relatively rare outcomes such as infrequent complications. The recent literature shows no differences in effect estimates between RCTs and observational studies.[20] Therefore, meta-analyses including high-quality observational studies in surgery may be considered complementary to those including RCTs only.[1,3,20]

The aim of this systematic review and meta-analysis was (1) to compare fracture healing disorders and functional outcomes of surgical versus nonsurgical treatment of MCFs and (2) to compare effect estimates obtained from RCTs and observational studies.

METHODS

A published protocol for this review does not exist. No ethical committee approval was necessary for this literature review.

Search Strategy and Selection Criteria

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Quality of Reporting of Meta-analyses (QUOROM) standards.[35,36] Published RCTs and observational studies concerning the comparison of surgical and nonsurgical treatment for acute MCFs in patients aged 16 years and older were included. Two reviewers (D.P.J.S. and D.J.C.V.) independently conducted an electronic systematic search in PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and CINAHL for articles published up to December 1, 2015. The search syntax is provided in Appendix 1 (available online). Duplicate articles were removed. Titles and abstracts of retrieved citations were screened, and potentially suitable studies were read in full by both reviewers. Articles were included if written in the English, Dutch, German, or French language. Only published data have been included. A minimum follow-up time was not required for inclusion. Letters, comments, abstracts for conferences, case reports, study protocols, reviews, biomechanical studies, animal studies, studies that included patients with (only) floating shoulders, studies describing a surgical technique, and noncomparative studies were excluded. In addition, studies were excluded if only a comparison of delayed surgery versus nonsurgical treatment was made. No further restrictions or filters were applied in the search. Citation tracking and reference screening of the selected studies were performed. Disagreements in the search were resolved by discussion with a third independent reviewer (R.M.H.).

Quality Assessment

The methodological quality of all included studies was independently assessed by 2 reviewers (D.P.J.S. and D.J.C.V.) using the Methodological Index for Non-Randomized Studies (MINORS).[46] The MINORS is a validated instrument designed to assess the methodological quality and clear reporting of observational surgical studies.[46] The MINORS is externally validated using RCTs and, therefore, also appropriate to assess the quality of RCTs.[46] Three other reviewers (T.K.T., O.A.J.M., and R.M.H.) independently assessed the quality of 7 of 20 articles to improve unity on the use of the MINORS. An included study published by 2 of the authors (D.J.C.V. and T.K.T.) was assessed by 2 other reviewers (D.P.J.S. and R.M.H.).[53] Disagreements were resolved by discussion with a third independent reviewer (R.M.H.). Details on the quality scoring system are given in Appendix 2 (available online).

Data Extraction

The following data were extracted: first author, year of publication, study design, country in which the study was performed, fracture displacement, type of fractures, mean follow-up, treatment groups, type of plate or intramedullary fixation material used in surgical groups, nonsurgical treatment method, number of patients per group, and outcomes including CIs and/or *P* values. Definitions of displacement were used according to the methods section of the included studies.

Outcome Measures

Fracture healing disorders in this study were nonunions and malunions. Definitions of nonunion and malunion were used according to the methods section of the included studies. The primary outcome was a nonunion. The effectiveness of both the nonsurgical and surgical treatment was evaluated using the following secondary outcome measures: functional scores (Disabilities of the Arm, Shoulder and Hand [DASH] and Constant-Murley scores) in both the short term ($<$1 year)

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and long term ($\geq$1 year), return to work in days, revision surgery, and implant removal.[11,22]

Revision surgery was defined as a second operative fixation procedure in the surgical treatment group and as an operative fixation procedure after initial treatment in the nonsurgical treatment group. Return to work was defined as the number of days needed until work, duty, or daily activities could be resumed. For studies that used both plate and intramedullary fixation, the results of the combination of plate and intramedullary fixation were used. If these results of the whole surgical treatment group were not available, the results of plate fixation were used, which is the most common surgical treatment.[13]

Statistical Analysis

Data management, statistical analyses, and graphical representation were performed using Review Manager software (RevMan v 5.3.5) provided by the Cochrane Collaboration.[43] When means or SDs were not reported in an article, these were calculated if possible using the available information. If the range was available for outcome variables, the SD was estimated as range divided by 4.[21] The SD was estimated from the standard error (SE) using the formula $SE = SD/\sqrt{n}$, where n is the sample size. The SE was estimated from the 95% CI by dividing the width of the CI by $2 \times 1.96 = 3.92$. Data were converted into the same units if needed.

Outcomes reported by 2 or more studies were pooled in a meta-analysis. Short-term and long-term results were analyzed separately. The assessment of statistical heterogeneity was performed by visual inspection of the forest plots and estimating statistical measures of heterogeneity: Cochran Q (chi-square test), I^2, and τ^2 (tau-square test). The random-effects model was used for meta-analyses. The overall-effect Z test was used to determine significance. A 2-sided P value of $<.05$ was considered statistically significant. All analyses were stratified by study design, that is, cohort studies and RCTs separately. All analyses were then repeated by including all studies (ie, irrespective of study design).

For continuous outcomes, a weighted mean difference (MD) was estimated. The inverse variance statistical method was used to construct a 95% CI. A pooled odds ratio (OR) was estimated for dichotomous outcomes. The Mantel-Haenszel statistical method was used to construct a 95% CI. Zero-event data were handled using different methods.[6] In the crude method, data of all studies were pooled and analyzed without taking clustering of data within studies into account. In the inverse variance method, the log(OR) of each study was weighted by the inverse of the within-study variance (also known as the fixed-effects model). When the inverse variance method was applied with correction, 0.5 was added to each cell of the 2×2 table of that study if one (or both) of the treatment arms experienced no events. The same correction was made for the DerSimonian-Laird method (also referred to as the random-effects model), but in contrast to the inverse variance method, the weighting was based on the inverse of the sum of the within-study variance and the between-study variance.[6] If a study had missing data, available case analysis was performed.

After the primary analyses, sensitivity analyses on the effect of study quality were performed for the primary outcome. In the sensitivity analysis on high quality, only studies with a MINORS score above 16 (of a maximum score of 24) were included. Another sensitivity analysis was performed using only low-quality studies (MINORS score of $\leq$16).[46] Potential publication (or reporting) bias was assessed using a funnel plot, showing intervention effect estimates on the primary outcome from individual studies against their SE.[14]

RESULTS

Search

The electronic searches detected 1080 articles. After removing duplicates, 563 articles were screened on title and abstract. A total of 22 possible relevant studies from the initial search were assessed on full text for eligibility, and references were checked for suitable related citations. The study of Vander Have et al[54] was excluded because it was performed on adolescents. The study of Smekal et al[48] was excluded because of overlap in the patient population with another study from their group.[47] A total of 132 studies were excluded because these articles did not describe acute MCFs or included patients under the age of 16 years. In total, 20 studies could be included for analysis.[‡‡] Of all included studies, 8 were RCTs, and 12 were observational, of which 5 were prospective studies and 7 were retrospective studies. The search results, reasons for exclusion, and selection process are summarized in the flowchart in Figure 1.

Two studies were excluded because of language and the inclusion of medial and lateral fractures. The search string can be found in Appendix 1.

Quality Assessment

Appendix 3 (available online) shows the distribution of study quality across the studies. The mean ($\pm$SD) MINORS score was 17.2 $\pm$ 3.0 (range, 11-22). For the RCTs, the mean score was 18.6 $\pm$ 3.5 (range, 11-22), and for the observational studies, it was 16.2 $\pm$ 2.3 (range, 11-19).

Baseline Characteristics

The characteristics of all included studies, their treatment groups, and included types of fractures are described in Appendix 4 (available online). Studies did not apply different inclusion or exclusion criteria for their treatment groups. Plate fixation was compared with nonsurgical treatment in 10 (50%) studies, intramedullary fixation was compared with nonsurgical treatment in 6 (30%) studies, and both plate and intramedullary fixation were compared with nonsurgical treatment in 4 (20%) studies.

‡‡References 2, 5, 9, 10, 12, 16, 17, 24-27, 29, 33, 34, 45, 47, 52, 53, 55, 57.

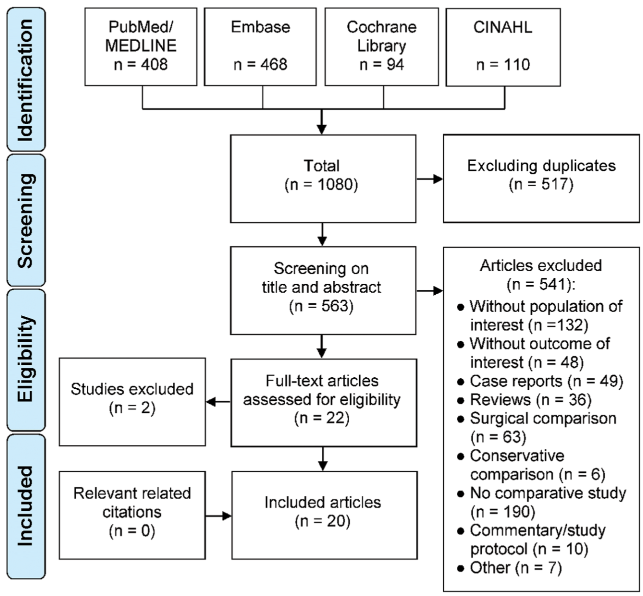

Figure 1. Flowchart of the articles included in a systematic review of midshaft clavicle fractures comparing nonsurgical versus surgical treatment.

A total of 620 patients were treated using plate fixation, 284 patients were treated using intramedullary fixation, and 856 patients were nonsurgically treated. The studies included a total of 1760 participants (80.2% male) with a mean age of 35.5 years (range, 25-46 years). The number of patients included in a study ranged between 40 and 200. In total, more patients were included in the observational studies (studies, n = 12; patients, n = 1068; mean age, 36.3 years; age range, 27-46 years) compared with the RCTs (studies, n = 8; patients, n = 692; mean age, 34.0 years; age range, 25-41 years). The mean age and male/female ratio did not appear to be different across the different study designs.

Fracture Healing Disorders

Nineteen (95%) of the 20 included studies reported the number of nonunions (see Appendix 5, available online).[§§] The study of George et al[16] was excluded because the number of nonunions was not reported. In the study by Witzel,[57] no events occurred in both treatment arms. Nonunions occurred significantly less after surgical treatment than after nonsurgical treatment, with an OR of 0.18 (95% CI, 0.10-0.33; $P <$ .01) (Figure 2). Surgical treatment resulted in a nonunion in 1.4% and nonsurgical treatment in 10.5%. The different methods to handle studies in which no event occurred in either (or both) of the treatment arms yielded similar results (data shown in Appendix 6, available online).

Thirteen studies (65%) reported the risk of malunions, which showed comparable results between surgical and nonsurgical treatment, with an OR of 0.38 (95% CI, 0.12-1.19; P = .10) (see Appendix 7, available online).[‖‖] Surgical treatment resulted in a malunion in 6.4% and nonsurgical treatment in 13.6%.

Functional Scores and Return to Work

Both the short-term DASH scores and Constant-Murley scores showed comparable results between surgical and nonsurgical treatment (Table 1). The long-term DASH scores and Constant-Murley scores showed significant differences in favor of surgical treatment compared with nonsurgical treatment (DASH: MD, −2.04 [95% CI, −3.56 to −0.52], P = .01; Constant-Murley: MD, 3.23 [95% CI, 1.52 to 4.95], $P <$ .01) (see Appendices 8 and 9, available online).

Seven studies (35%) reported the return to work or daily activities, of which in 5 studies, an SD was documented or could be estimated.[2,5,17,27,33,45,53] Analysis showed comparable results between surgical and nonsurgical treatment (MD, −2.80 [95% CI, −15.03 to 9.42]; P = .65).

Revision Surgery and Implant Removal

Eighteen studies (90%) reported the number of revision surgeries.[¶¶] Analysis showed no significant differences between surgical and nonsurgical treatment (OR, 0.85 [95% CI, 0.42-1.73]; P = .65) (see Appendix 10, available online). Surgical treatment resulted in revision surgery in 8.2%, and 9.8% required operative fixation after initial nonsurgical treatment. Implant removal was reported in 10 studies (50%).[##] The mean percentage of implant removal was 35% (range, 3.7%-100%).

Study Design Analyses

Results were similar across all included studies when analyses were stratified by study design as shown in the forest plots (Figure 2 and Appendices 7-10). The subgroups did differ in the significance of the results in 3 secondary outcomes: malunions, long-term DASH scores, and long-term Constant-Murley scores. In these outcomes, the RCTs showed a significant result compared with the insignificant results of the observational studies. Nevertheless, in all of these studies, the outcomes did remain in favor of the surgical treatment group.

Sensitivity Analyses on Quality

Sensitivity analysis using high-quality studies on the primary outcome, nonunions, resulted in an overall OR of 0.18 (95% CI, 0.09-0.37; $P <$ .01) (Table 1). There were no outcomes that changed direction; however, the number of malunions and days to return to work became significant outcome parameters in favor of the surgical treatment group (Table 1).

§§References 2, 5, 9, 10, 12, 17, 24-27, 29, 33, 34, 45, 47, 52, 53, 55, 57.

‖‖References 9, 10, 17, 26, 27, 29, 34, 45, 47, 52, 53, 55, 57.

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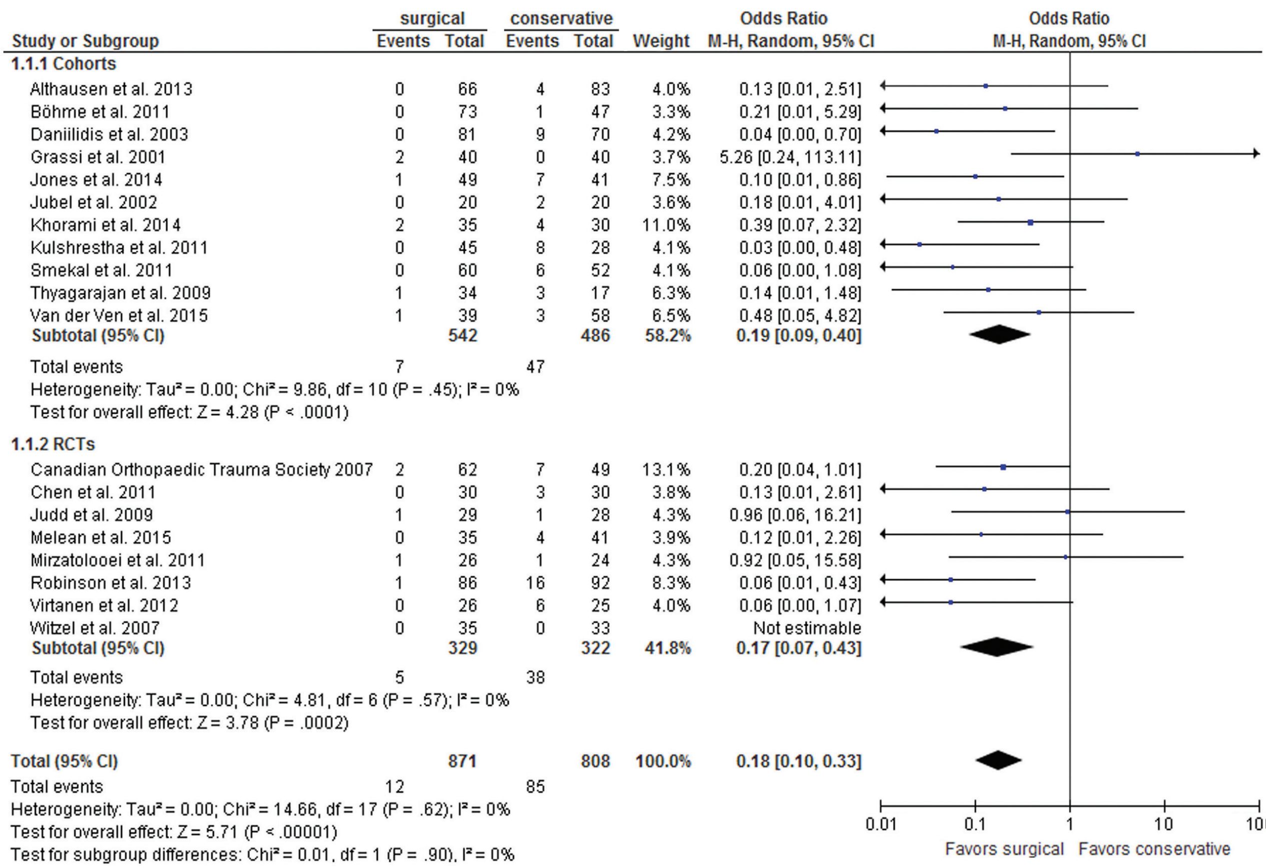

Figure 2. Nonunions in a systematic review of midshaft clavicle fractures comparing nonsurgical versus surgical treatment.

Sensitivity analysis using low-quality studies on the primary outcome resulted in an OR of 0.18 (95% CI, 0.06-0.50; $P < .01$). The other outcomes changed in insignificant results or were not estimatable because no studies could be included. The days to return to work changed to favorable results for nonsurgical treatment including only 1 study.

Assessment of Publication Bias

A funnel plot with the ORs and SEs of the studies including nonunions is shown in Figure 3. The funnel plot asymmetry analysis showed relative symmetry, indicating no evidence or a very low risk of existing publication bias in this systematic review and meta-analysis. When excluding outliers with an OR of 5.26, the appearance of the figure structure stays intact.[17]

DISCUSSION

Results of this systematic review and meta-analysis including both RCTs and observational studies showed fewer nonunions for surgical treatment of MCFs compared with nonsurgical treatment. Functional outcomes were statistically significant in favor of surgical treatment, but these differences seem of little clinical importance.[4,15,18] The subgroup analysis of only RCTs and observational studies displayed similar results. In high-quality studies, fewer malunions and a faster return to work in favor of the surgical treatment group were observed.

Functional outcomes might be statistically significant; nevertheless, an MD of 2 points on the DASH score and 3 points on the Constant-Murley score are clinically irrelevant.[4,15,18] For each of these scores, a 10-point difference is deemed clinically relevant.[4,18]

More nonunions were observed after nonsurgical treatment in this study for all groups. These numbers are in accordance with other systematic reviews and meta-analyses about this topic.[28,31,32] The earlier return to daily activities after surgical treatment also corresponds with results of another review.[19] However, in that study, Hill[19] only included 3 studies, whereas our meta-analysis included 20 studies.[26,47,48] In a previous review and meta-analysis, plate and intramedullary fixation were compared. No differences were found in terms of function and number of nonunions. Major reinterventions and refractures after implant removal occurred more frequently after plate fixation.[20]

One of the most important observations of this study is that high-quality observational studies and RCTs provided similar results for this topic (Table 1). By excluding low-quality observational studies, malunions and return to work became significant in favor of surgical treatment.

TABLE 1
Results of Sensitivity Analyses in a Systematic Review of MCFs Comparing Nonsurgical Versus Surgical Treatment[a]

				Sensitivity Analyses	
Outcome	Results	Subgroup Cohorts	Subgroup RCTs	High-Quality Studies	Low-Quality Studies
Nonunions[b]	0.18 (0.10 to 0.33)	0.19 (0.09 to 0.40)	0.17 (0.07 to 0.43)	0.18 (0.09 to 0.37)	0.18 (0.06 to 0.50)
Malunions[b]	0.38 (0.12 to 1.19)	0.73 (0.15 to 3.61)	0.18 (0.04 to 0.79)	0.26 (0.07 to 0.92)	3.06 (0.44 to 21.26)
DASH score[c]					
Short term	−3.09 (−10.04 to 3.85)	−4.38 (−15.05 to 6.29)	−0.10 (−7.74 to 7.54)[d]	−3.09 (−10.04 to 3.85)	NE
Long term	−2.04 (−3.56 to −0.52)	−0.68 (−3.69 to 2.32)	−2.70 (−2.88 to −2.53)	−2.04 (−3.78 to −0.30)	−1.70 (−6.00 to 2.60)[d]
Constant-Murley score[c]					
Short term	3.07 (−2.19 to 8.34)	6.00 (−5.51 to 17.51)	0.25 (−3.97 to 4.47)	3.07 (−2.19 to 8.34)	NE
Long term	3.23 (1.52 to 4.95)	3.82 (−0.47 to 8.11)	4.18 (3.96 to 4.41)	4.08 (3.62 to 4.54)	5.44 (−2.37 to 13.24)
Return to work[c]	−2.80 (−15.03 to 9.42)	2.96 (−19.83 to 25.75)	−12.26 (−33.83 to 9.31)	−8.64 (−16.22 to −1.05)	24.00 (18.86 to 29.14)[d]
Revision surgery[b]	0.85 (0.42 to 1.73)	1.16 (0.50 to 2.67)	0.52 (0.16 to 1.74)	0.69 (0.27 to 1.78)	1.20 (0.43 to 3.30)

[a]DASH, Disabilities of the Arm, Shoulder and Hand; MCF, midshaft clavicle fracture; NE, not estimable because no studies could be included; RCT, randomized controlled trial.
[b]Results are presented as odds ratio (95% CI).
[c]Results are presented as mean difference (95% CI).
[d]Only 1 study with SD available or calculable could be included.

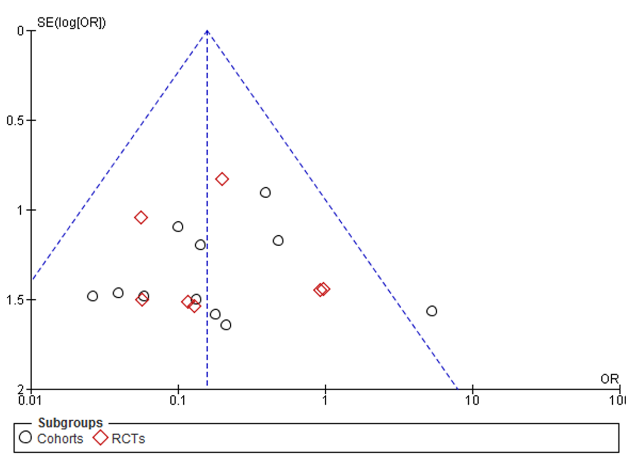

Figure 3. Funnel plot of included studies using the number of nonunions in a systematic review of midshaft clavicle fractures comparing nonsurgical versus surgical treatment.

Therefore, low-quality observational studies had enough effect to possibly influence recommendations from this meta-analysis. Obviously, recommendations based on a meta-analysis should be made on the quality of the included studies, not only on their study design.

This is the first review that shows an accelerated return to work after surgical treatment of MCFs. As patients with MCFs are generally in the working population, with a peak incidence in male patients younger than 30 years old, this might be an important consideration.[44] On the other hand, surgical treatment of all MCFs would substantially increase the cost for society of treating this common injury. Three recent studies about the cost-effectiveness of surgical treatment emphasize this dilemma.[2,39,56] Walton et al[56] described the financial effect for society. They found that nonsurgical treatment followed by delayed surgery resulted in approximately US$11,500 cost savings from the perspective of a single health insurance payer. However, costs to the patients were not accounted for in their analysis.[56] Althausen et al[2] calculated that surgical treatment resulted in approximately US$5000 cost savings from the perspective of the patient, although the initial hospital bill was higher because of surgical charges. Furthermore, operatively treated patients missed fewer days from work (8 vs 35 days, respectively) and returned to full duty 25 days sooner than nonoperatively treated patients. Pearson et al[39] concluded that the cost-effectiveness of surgical treatment depended on the durability of functional advantage compared with nonsurgical treatment. When functional benefits persisted for more than 9 years, surgical treatment had favorable value compared with many accepted health interventions.[39] However, no comparative studies have yet described the long-term outcomes of surgical versus nonsurgical treatment of MCFs.

Previously published meta-analyses on this topic only included RCTs for analysis.[31,42,58] Currently, the value of the different study designs is being discussed.[1,3] This is the first meta-analysis comparing surgical and nonsurgical treatment of MCFs in which data on RCTs and observational studies were combined. Therefore, information on 1760 patients were included, resulting in the largest sample size in a meta-analysis on this topic, which consequently led to an increase in power. Because of this increased power, effects may have been detected that would have gone unnoticed if only including RCTs. In addition, combining information from both RCTs and observational studies can provide a broader view of the available evidence, possibly leading to results that have better generalizability, which might improve the applicability of recommendations based on systematic reviews.[40] Because of the often stringent inclusion and exclusion criteria of RCTs, the generalizability of trial results may be hampered, and finding similar effect estimates in observational studies may support the relevance of study results for clinical practice. We note, however, that the baseline characteristics of patients enrolled in the studies included in our meta-analysis did not materially differ across study designs, suggesting that results of randomized trials on MCFs already have wide applicability.

Observational studies inherently have a greater risk of bias because of the nonrandom allocation of treatment. Therefore, pooling results of studies with a different design is counterintuitive. However, we consider this approach appropriate because RCTs and observational studies showed similar results and the potential for unmeasured confounding in the observational studies was considered small. This corresponds to an earlier meta-analysis including observational studies in which the primary outcome, that is, reinterventions, showed comparable results between RCTs and observational studies when comparing plate and intramedullary fixation of clavicle fractures.[20] The potential for bias in the observational studies included in our meta-analysis appeared to be small (given the comparability of measured patient characteristics between treatment arms).

Despite a low risk of publication bias in this systematic review and meta-analysis, several factors possibly influencing our results should be mentioned. For example, definitions varied according to the included studies, such as displacement, nonunion, and malunion. Also, time to return to work could be affected by the type of occupation. In the current analysis, no distinction could be made between laborers and physically demanding occupations from sedentary occupations. Finally, both plate and intramedullary fixation have been included for the analysis of surgical treatment. As a recently published meta-analysis comparing plate and intramedullary fixation found no significant differences regarding functional outcomes and the number of nonunions, combining the results of functional outcomes and nonunions of both techniques was justified in our opinion.[20] Furthermore, results were homogeneous across studies.

CONCLUSION

This systematic review and meta-analysis shows that surgical treatment of MCFs resulted in fewer nonunions, fewer malunions, and an accelerated return to work. Functional outcomes were comparable between the groups. RCTs and observational studies showed similar results. Observational studies provide relevant data for meta-analyses as long as the quality of the included studies is taken into account and the results are interpreted in the right clinical context. The results of this meta-analysis favor surgical treatment of MCFs. However, it should always be kept in mind that patient-specific factors should be taken into account. The final decision for surgical or nonsurgical treatment should be based on shared decision making.

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