Clavicular fracture treatment: choices and challenges

Woltz, S.

Author: Woltz, S.
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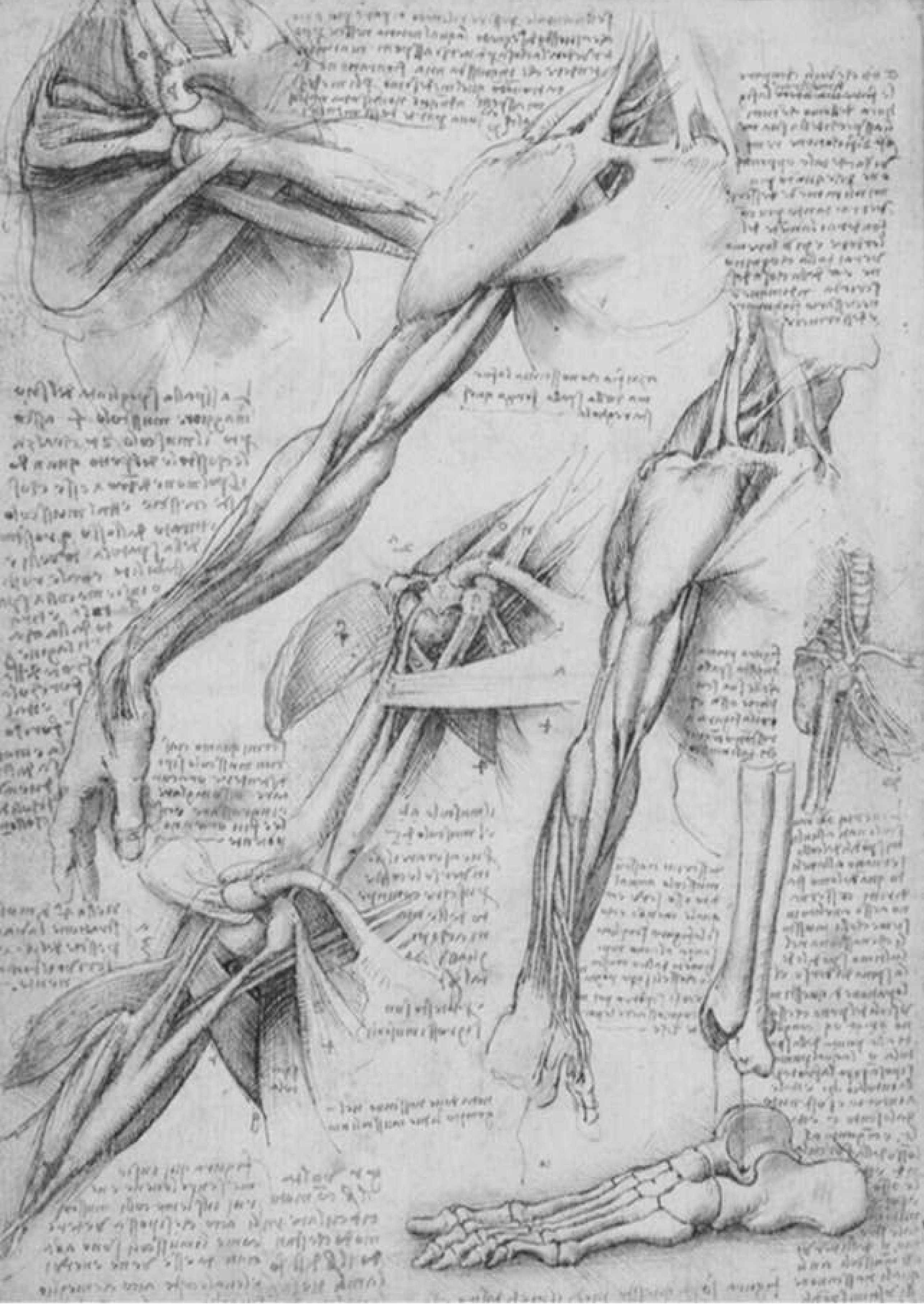

CHAPTER 5

Plate fixation versus nonoperative treatment for displaced midshaft clavicular fractures: A meta-analysis of randomized controlled trials

Sarah Woltz
Pieta Krijnen
Inger B. Schipper

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ABSTRACT

Background

The aim was to analyse whether patients with a displaced midshaft clavicular fracture are best managed with plate fixation or nonoperative treatment with respect to nonunion, secondary operations, and functional outcome, by evaluating all available randomized controlled trials (RCTs) on this subject.

Patients and methods

A systematic search of electronic databases (PubMed, MEDLINE, Embase, and Web of Science) was performed to identify RCTs comparing nonoperative treatment with plate fixation for displaced midshaft clavicular fractures. Risk of bias of the studies was assessed. Outcomes evaluated were nonunion, shoulder function (Constant score and Disabilities of the Arm, Shoulder and Hand [DASH] score), and secondary operations.

Results

Six RCTs (614 patients) were included. The risk of nonunion was lower in the operatively treated patients (relative risk [RR] = 0.14, 95% confidence interval [CI] = 0.06 to 0.32). One-third of the patients with a nonunion did not receive further treatment. Secondary operations for adverse events were performed less often in the operatively treated patients (RR = 0.42, 95% CI = 0.25 to 0.71). When plate removal operations were also included, a secondary operation was performed in 17.6% in the operative group and 16.6% in the nonoperative group (RR = 1.01, 95% CI = 0.64 to 1.59). Constant and DASH scores after 1 year were somewhat better after plate fixation, with mean differences of 4.4 points (95% CI, 0.9 to 7.9 points) and 5.1 points (95% CI, 0.1 to 10.1 points), respectively.

Conclusion

Plate fixation significantly reduces the risk of nonunion, but does not have a clinically relevant advantage regarding final functional outcome. Secondary operations are common after both treatments. Overall, there is not enough evidence to support routine operative treatment for all patients with a displaced midshaft clavicular fracture.

INTRODUCTION

Clavicular fractures are common and occur typically in younger patients, posing a burden for this active population. Nonunion of nonoperatively treated, fully displaced midshaft clavicular fractures occurs much more frequently than was thought for centuries[1-3]. As a result, operative treatment has substantially gained in popularity in the past decade, even though complications following surgery are substantial and not all studies have shown that operative treatment results in better shoulder function[4-7].

Remarkably, more meta-analyses than randomized controlled trials (RCTs) have been published on this subject[8-13]. Unfortunately, all have limitations that reduce their value for daily practice and evidence-based treatment guidelines. Most of the available meta-analyses compare nonoperative with operative treatment, but include 2 essentially different operative techniques (plate and pin fixation), each of which is known to have specific characteristics and complications, and thus cannot be regarded as a single treatment modality[9,10,12,13]. Also, some meta-analyses include nonrandomized trials, which may introduce bias[11,14], or include only a few studies[8].

In the current meta-analysis, we chose to compare nonoperative treatment with open reduction and plate fixation, as the latter is the most widely used operative technique for clavicular fixation.

Compared with previous meta-analyses, we include 2 recent RCTs that substantially add to the number of patients analysed. Furthermore, not only nonunion and function but also secondary operations were studied. To our knowledge, the only previous meta-analysis that explicitly evaluated secondary operation rates incorrectly performed the calculation using the number of patients randomized, instead of the number of patients who completed follow-up[14].

The aim of this meta-analysis was to analyse all RCTs that compared nonoperative treatment with plate fixation in patients with a displaced midshaft clavicular fracture and to provide high-quality evidence for treatment of displaced midshaft clavicular fractures in daily clinical practice.

MATERIALS AND METHODS

This meta-analysis was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement[15,16].

We selected RCTs comparing plate fixation with nonoperative treatment in patients with a displaced midshaft clavicular fracture and reporting data for ≥1 of the following outcome measures: nonunion, shoulder function, complications, and secondary operations. Studies were excluded if they concerned children (<16 years), if they had a follow-up of <12 months, or if the full-text article was not available in English, Dutch, French, or German.

With the help of a trained medical librarian, we searched PubMed, MEDLINE, Embase, and the Web of Science in April 2016, using a combination of different terms and synonyms for "clavicle," "fracture," and "randomized controlled trial" (see Appendix 2, p166, for the full search strategy). In addition, the reference lists of previously published randomized trials, review articles, and meta-analyses were manually searched for additional eligible studies. Duplicates were removed. The titles and abstracts of the search results were independently screened by 2 reviewers (S.W. and P.K.). In case of presumed eligibility, the full-text article was reviewed using the same inclusion and exclusion criteria. In case of disagreement, consensus was reached by discussion and by consulting a third reviewer (I.B.S.) if necessary.

The 2 reviewers independently extracted data on study characteristics (year of publication, randomization method, patient and treatment characteristics). Data on the following outcome measures were documented: nonunion, secondary operations due to adverse events (e.g., nonunion, wound infection, plate failure), implant removal operations at the request of the patient due to plate irritation or cosmetic considerations, and function measured with the Constant score or the Disabilities of the Arm, Shoulder and Hand (DASH) score. If mean outcomes were reported with a 95% confidence interval (CI), the corresponding standard deviation (SD) was calculated.

Seven aspects of the studies related to the risk of bias were assessed, following the instructions in the Cochrane Handbook for Systematic Reviews of Interventions[17].

RevMan software (version 5.3; The Cochrane Collaboration)[18] was used for the analysis. Treatment effects were estimated by calculating the relative risk (RR) with 95% CI for dichotomous variables, and the mean difference with 95% CI for continuous variables.

Studies were weighted by the inverse of the variance (IV) of the outcome. A random-effects model was used for all analyses, as clinical heterogeneity was assumed to exist because of differences in study methods (e.g., plate type) and outcome definitions (e.g., nonunion) across studies.

RESULTS

The search terms described above identified 301 references (Figure 1). A manual search of reference lists yielded 4 additional references. After removal of duplicates, 131 articles were screened for relevance on the basis of the title and abstract. Of the 11 articles that were possibly eligible for inclusion, 5 were excluded because no full text was available (n = 1), the article was in Portuguese (n = 1), the study was not an RCT (n = 2), and medial and lateral fractures were included (n = 1). The remaining 6 studies were included in this meta-analysis.

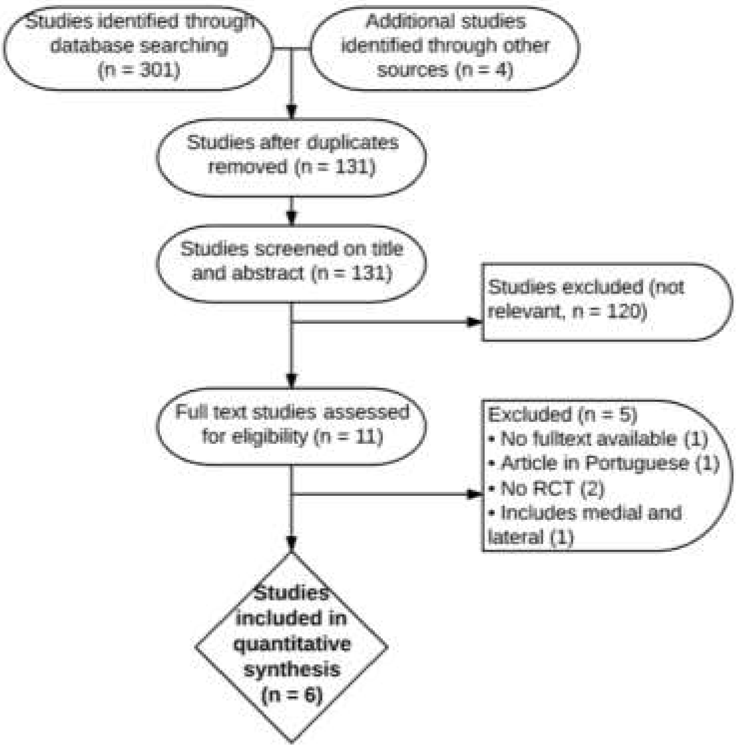

Figure 1*. Flowchart of study selection.*

Study Characteristics and Quality

Five of the included studies were published between 2007 and 2015[6,7,19-21]; the remaining RCT on 160 patients had been accepted for publication[22] at the time, and data were available to the authors prior to its publication (Table 1). The 6 studies included a total of 614 patients (317 treated with plate fixation and 297 treated nonoperatively). One study only included comminuted fractures and did not exclude open fractures[20], and 1 studied a working population who had had labor-related accidents[21]. The primary outcome was nonunion in 2 studies[19,22] and the Constant and/or DASH scores in 2 other studies[6,7]. In the remaining 2 studies, the primary outcome was not explicitly defined.

Table 1. Characteristics of the included studies

Study	No of patients randomized (O/N)	No of patients analysed[a] (O/N)	Age criteria (yr)	% Male (O/N)	Operative intervention: plate type[b] (n)	Nonop. Intervention
COTS, 2007[7]	132 (67/65)	111 (62/49)	16-60	78 (85/69)	LCDCP (44), REC (15), precontoured (4), other (4)	Sling
Melean, 2015[21]	76 (34/42)	76 (34/42)	>18	Not stated	3.5mm LCP / locking REC	Sling 6 wks
Mirzatolooei, 2011[20]	60 (29/31)	50 (26/24)	18-65	82 (77/88)	3.5mm REC	Sling and elastic cotton band
Robinson, 2013[19]	200 (95/105)	178 (86/92)	16-60	88 (87/88)	Locking Clavicle Plate (Acumed)	Collar and cuff
Virtanen, 2012[6]	60 (28/32)	51 (26/25)	18-70	87 (86/88)	2.8mm REC	Sling
Woltz, 2017[22]	160 (86/74)	148 (83/65)	18-60	91 (93/89)	Precontoured (68), REC (2), LCDCP (2), unknown (11)	Sling 2 wks

[a] Number of patients analysed for the primary outcome measure (operative/nonoperative).
[b] LCDCP=limited contact dynamic compression plate, REC=reconstruction, and LCP=locking compression plate.

An overview of the estimated risk of bias for each study is presented in Figure 2. The researchers were blinded when assessing functional outcomes in only 1 study (by letting the patient wear a t-shirt)[19], and the primary outcome measurements could not be blinded in any of the studies. In 2 studies, the numbers on which sample size calculations were based were unclear[20,21]. Risk of "other" types of bias was judged to be present in 1 study because the exact rate of follow-up was not reported[21], and in 1 study because all patients who were not included or declined participation in the study were treated nonoperatively, which could have led to a selection bias[19].

Nonunion

Nonunion was defined as absence of cortical bridging of the bone on computed tomography imaging in 2 studies[19,21] and on radiographs in the other 4, after a period ranging from 4 to 12 months. Six (1.9%) of 317 operatively treated patients developed a

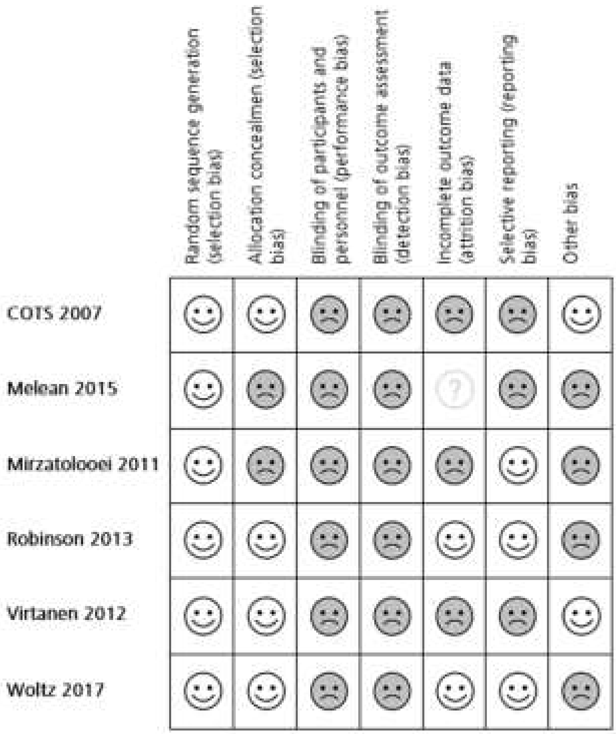

Figure 2. *Risk of bias summary for included studies. "Happy face"= risk of bias not present, "unhappy face" = risk of bias present, and "?" = insufficient information to judge risk of bias.*

nonunion, compared with 49 (16.5%) of 297 nonoperatively treated patients (RR = 0.14, 95% CI = 0.06 to 0.32, p < 0.0001) (Figure 3).

The method for dealing with patients with a nonunion differed among the studies. Overall, nonunion was treated with secondary plate fixation in 67% of the patients (n = 37), whereas the remaining one-third of patients with a nonunion did not receive further treatment. Robinson et al. offered secondary plate fixation to all patients with fracture nonunion after 6 months, and 13 of 16 consented[19]. In the Canadian Orthopaedic Trauma Society (COTS) study, all patients who had a nonunion after 1 year of follow-up underwent a secondary operation[23]. In the study by Melean et al., all 4 patients with a nonunion received secondary plate fixation, but the timing was not reported[21]. In the study by Woltz et al., 5 patients with a nonunion were operated on within the study follow-up period of 1 year, 5 others received surgery after >1 year, and 7 were asymptomatic and chose to receive no further treatment[22]. In 2 studies, none of the patients with a nonunion elected to receive the offered secondary surgical treatment, and therefore could not be included in the analysis of this outcome[6,20]. Overall, secondary operations for nonunion occurred more often after nonoperative treatment than after plate fixation (10.9% versus 1.3%, RR = 0.14, 95% CI = 0.05 to 0.36, p < 0.0001).

Secondary Operations

Reports on whether secondary operations were performed, and on their details, varied among studies. Mirzatolooei[20] described 19 patients with a malunion, but did not state if these patients underwent secondary operative treatment; it was noted that at least 1 patient did not. Indications for all secondary operations are presented per study in Table 2, p81. Secondary operations for adverse events occurred less frequently in the plate fixation group than in the nonoperative treatment group (6.9% versus 16.2%, RR = 0.42, 95% CI = 0.25 to 0.71, p = 0.001) (Figure 4). This would have been true even if all patients with a malunion in the study by Mirzatolooei had received a secondary operation. The overall rate of secondary operations (i.e., operations due to adverse events and implant removal operations) did not differ significantly between the treatment groups (17.6% for plate fixation versus 16.6% for nonoperative treatment, RR = 1.01, 95% CI = 0.64 to 1.59, p = 0.97). Implant removal was performed frequently in four studies[7,19,21,22]. Mirzatolooei[20] reported that some plates were removed, but did not state how many. Virtanen et al.[6] did not mention elective plate removal operations.

Study or Subgroup	Plate fixation Events	Plate fixation Total	Nonoperative treatment Events	Nonoperative treatment Total	Weight	Risk Ratio IV, Random, 95% CI
COTS 2007	2	62	7	49	27.8%	0.23 [0.05, 1.04]
Melean 2015	0	34	4	42	7.8%	0.14 [0.01, 2.45]
Mirzatolooei 2011	1	26	1	24	8.8%	0.92 [0.06, 13.95]
Robinson 2013	1	86	16	92	16.2%	0.07 [0.01, 0.49]
Virtanen 2012	0	26	6	25	8.1%	0.07 [0.00, 1.25]
Woltz 2017	2	83	15	65	31.3%	0.10 [0.02, 0.44]
Total (95% CI)		**317**		**297**	**100.0%**	**0.14 [0.06, 0.32]**
Total events	6		49			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.10$, $df = 5$ ($P = 0.68$); $I^2 = 0\%$
Test for overall effect: $Z = 4.71$ ($P < 0.00001$)

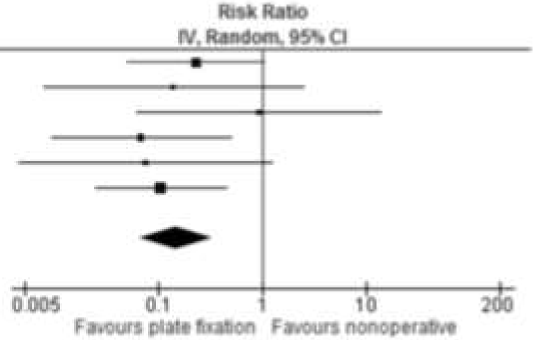

***Figure** 3. Nonunion after plate fixation versus nonoperative treatment. IV = inverse variance, and df = degrees of freedom.*

Study or Subgroup	Plate fixation Events	Plate fixation Total	Nonoperative treatment Events	Nonoperative treatment Total	Weight	Risk Ratio IV, Random, 95% CI
COTS 2007	6	62	16	49	31.2%	0.30 [0.13, 0.70]
Melean 2015	0	34	4	42	3.2%	0.14 [0.01, 2.45]
Mirzatolooei 2011	2	26	0	24	3.0%	4.63 [0.23, 91.81]
Robinson 2013	5	86	17	92	26.2%	0.31 [0.12, 0.82]
Virtanen 2012	0	26	1	25	2.7%	0.32 [0.01, 7.53]
Woltz 2017	9	84	11	70	33.7%	0.68 [0.30, 1.55]
Total (95% CI)		**318**		**302**	**100.0%**	**0.42 [0.25, 0.71]**
Total events	22		49			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 5.41$, $df = 5$ ($P = 0.37$); $I^2 = 8\%$
Test for overall effect: $Z = 3.23$ ($P = 0.001$)

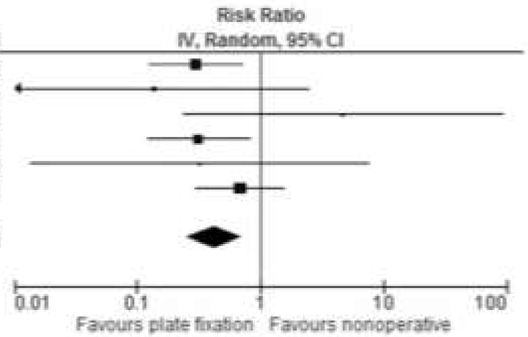

***Figure 4**. Secondary operations for adverse events after plate fixation versus nonoperative treatment. IV = inverse variance, and df = degrees of freedom.*

	Plate fixation			Nonoperative treatment				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
COTS 2007	96	5	62	90	20	49	13.3%	6.00 [0.26, 11.74]
Melean 2015	93	1	34	87	4	42	20.3%	6.00 [4.74, 7.26]
Mirzatolooei 2011	89.8	6	26	78.8	8	24	16.4%	11.00 [7.06, 14.94]
Robinson 2013	92	9.5	86	87.8	12.5	92	17.6%	4.20 [0.95, 7.45]
Virtanen 2012	86.5	11.5	26	86.1	8.9	25	13.5%	0.40 [-5.23, 6.03]
Woltz 2017	95.4	7.8	75	96.6	6.3	58	18.9%	-1.20 [-3.60, 1.20]
Total (95% CI)			**309**			**290**	**100.0%**	**4.39 [0.90, 7.87]**

Heterogeneity: $Tau^2 = 15.20$; $Chi^2 = 39.71$, $df = 5$ ($P < 0.00001$); $I^2 = 87\%$
Test for overall effect: $Z = 2.47$ ($P = 0.01$)

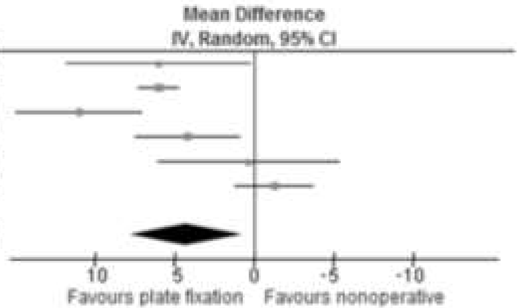

Figure 5. *Constant score 1 year after plate fixation versus nonoperative treatment. IV = inverse variance, and df = degrees of freedom.*

	Plate fixation			Nonoperative treatment				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
COTS 2007	5	2.5	62	13	6.25	49	21.1%	-8.00 [-9.86, -6.14]
Mirzatolooei 2011	8.6	2	26	21.3	6	24	20.6%	-12.70 [-15.22, -10.18]
Robinson 2013	3.4	7.1	86	6.1	9.8	92	20.7%	-2.70 [-5.20, -0.20]
Virtanen 2012	4.3	6.1	26	7.1	13.5	25	16.9%	-2.80 [-8.59, 2.99]
Woltz 2017	4.5	7.6	80	3.2	7.4	64	20.7%	1.30 [-1.16, 3.76]
Total (95% CI)			**280**			**254**	**100.0%**	**-5.07 [-10.08, -0.06]**

Heterogeneity: $Tau^2 = 30.00$; $Chi^2 = 73.05$, $df = 4$ ($P < 0.00001$); $I^2 = 95\%$
Test for overall effect: $Z = 1.99$ ($P = 0.05$)

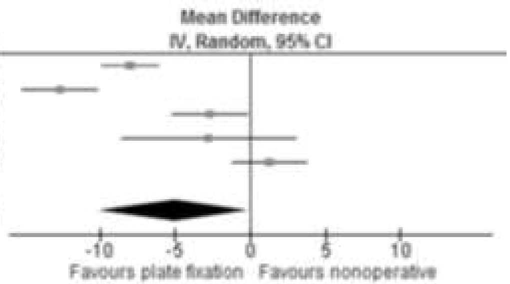

Figure 6. *DASH score 1 year after plate fixation versus nonoperative treatment. IV = inverse variance, and df = degrees of freedom.*

Table 2. Numbers and reasons for secondary operations

Study	Plate fixation	Nonoperative treatment
COTS, 2007[7]	2 nonunion 1 implant failure 3 infection 5 plate removal	7 nonunion 9 malunion
Melean, 2015[21]	4 plate removal	4 nonunion
Mirzatolooei, 2011[20]	1 implant failure 1 infection	-
Robinson, 2013[19]	1 nonunion 1 implant failure 1 refracture 1 neurologic complication 2 fracture lateral to plate 10 plate removal	13 nonunion 4 malunion
Virtanen, 2012[6]	-	1 neurologic complication
Woltz, 2017[22]	1 nonunion 6 implant failure 2 infection 14 plate removal	9 nonunion 1 neurologic complication 1 malunion 1 plate removal[a]
Total	56	50

[a] One nonoperatively treated patient developed a nonunion and was treated with secondary plate fixation after four months. At one year, plate removal was scheduled. This patient was analysed in the nonoperative group following the intention to treat principle.

Functional Outcomes

Constant scores were measured after 1 year in all 6 studies, and DASH scores were reported in 5 studies. One study only graphically presented Constant and DASH scores and SDs, and we measured values by hand on the graphs[7]. The mean scores reported in the 6 studies, however, may not reflect the final shoulder function for all patients, as some studies also included the patients with a nonunion who were yet to receive surgery[7,22] or those who had received secondary plate fixation only a few months prior to analysis[19,22]. Melean et al.[21] did not state whether secondary plate fixation was performed before or after the 1-year follow-up time point. When ignoring this information and including all patients in the meta-analysis, the mean Constant score of the operatively treated patients was 4.4 points (95% CI = 0.9 to 7.9 points, $p = 0.01$) higher than that of the nonoperatively treated patients (Figure 5). The mean difference in DASH scores at 1 year after trauma was 5.1 points (95% CI = 0.1 to 10.1 points, $p = 0.05$) in favour of plate fixation (Figure 6, p80). Robinson et al.[19] reported that the difference in functional scores between groups ceased to be significant when considering the united fractures only: mean Constant scores for plate fixation and nonoperative treatment were 89.4 and 82.5, and mean DASH scores were 4.8 and 3.2, respectively (SDs not reported). Woltz et al.[22] reported that the patients with a nonunion who were yet to receive surgery had a lower functional score than the patients with a united fracture: mean Constant scores were 86.2 (SD = 11.7) and 96.3 (SD = 6.7) ($p = 0.01$), and mean DASH scores were 14.7 (SD = 14.6) and 3.3 (SD = 6.1) ($p = 0.005$), respectively.

DISCUSSION

This meta-analysis of 6 RCTs that evaluated a total of 614 patients shows that plate fixation significantly reduced the rate of nonunion of displaced midshaft clavicular fractures to 2% compared with 16% for nonoperative treatment. Plate fixation resulted in somewhat better DASH and Constant scores, but the clinical relevance of this difference is unclear. Also, approximately 17% of the patients in each group had a secondary operation after the initial treatment.

Overall, approximately two-thirds of the patients with nonunion elected to undergo secondary fixation, whereas one-third did not receive any further treatment. In the 2 studies in which all patients with a nonunion received secondary fixation, it was not stated whether all of these patients had symptoms and deliberately opted for surgery, or whether this was the physicians' standard treatment choice[7,21]. In light of the current trend toward shared decision-making, it is important to thoroughly explain the treatment options and inquire about the patient's preferences in case of nonunion, as it is clear that not all nonunions require operative treatment. Also, secondary surgery for nonunion should be considered earlier than after 9 to 12 months, to minimize delay in recovery for those patients.

Secondary operations were performed in approximately 17% of patients in each group. However, in the majority of patients in the operative group (33 of 56), this was a plate removal operation, which generally is technically simpler, imposes less risk of complications, and has a shorter rehabilitation time than other operations such as secondary plate fixation with bone-grafting. Excluding these plate removal operations, secondary operations occurred more often in the nonoperative group (16.2%) than in the operative group (6.9%, p = 0.001). It is conspicuous, however, that the 3 largest studies[7,19,22] reported much higher percentages of patients with secondary operations than the 3 smaller studies[6,20,21], in which, for instance, only 1 infection and 1 implant failure requiring a secondary operation appeared to have occurred. This discrepancy may be the result of either underreporting or coincidence due to the small study samples.

After 1 year, Constant and DASH scores were significantly better after plate fixation than after nonoperative treatment. However, the mean differences were only 4.4 (95% CI = 0.9 to 7.9) and 5.1 (95% CI = 0.1 to 10.1) points, respectively, which are less than the 10 to 15 points generally regarded as the minimal difference to be clinically relevant[24-26]. The implications of the difference in scores for daily practice are therefore limited. Also, patients with a symptomatic nonunion who were yet to receive a secondary operation were included in these mean scores, which probably influenced the results to the detriment of the nonoperative group. When analyzing united fractures only, as Robinson et al.[19] did, there was no longer a functional difference between the groups after 1 year. This implies that nonoperative treatment itself is not associated with functional impairment, but symptomatic nonunion is.

An early functional benefit is generally regarded as a well-established advantage of operative treatment. Three of the 5 studies that evaluated early functional outcomes reported such a difference[7,19,21], but it was measured in various ways (e.g., time to return to work, functional scores) and at different time points (6 weeks and 3 months), so no pooled analysis could be performed. However, short-term differences should be discussed with the patient when choosing the best treatment.

Limitations of this meta-analysis are partly inherent to the design: the quality of our conclusions can only be as good as that of the included studies, and although only Level-I RCTs were included to optimize the quality of the data, there was a considerable risk of bias in all studies.

In addition, the included studies used different plate types and plate positions, which could have influenced implant failure and removal rates and may have been a source of clinical heterogeneity. Unfortunately, plate location and plate type could not be related to complications on the basis of the information provided in the articles. The way in which patients with a nonunion were identified and treated also differed among the studies, as did the timing of secondary operations.

We did not evaluate other operative techniques such as pin fixation in this meta-analysis. This was a deliberate choice for reasons previously discussed. A Bayesian network meta-analysis showed lower nonunion rates after pin fixation than after nonoperative treatment, and lower infection rates after pin fixation than after plate fixation, but that study did not address arm function or secondary operations[11]. A recent meta-analysis comparing plate and pin fixation, found no differences regarding nonunions, infections, and reoperations[27]. Another surgical alternative is minimally invasive plate fixation, which is thought to reduce both the interference with the blood supply to the bone that promotes healing and the infection risk by minimizing skin incision. Both pin fixation and minimally invasive plate fixation are good treatment alternatives, provided that the surgeon is experienced in these techniques[5].

Overall, plate fixation offers clear advantages but also has considerable drawbacks. It is a good option for patients who demand quick recovery and optimal arm function, and for patients with risk factors for nonunion such as large displacement, comminution, and smoking[28,29]. For less active patients and in case of relatively favourable fracture characteristics, however, the risks and benefits must be weighed differently and nonoperative treatment appears to be the better option.

In conclusion, this meta-analysis shows that plate fixation dramatically reduces nonunion rates but does not appear to offer a clinically relevant advantage in terms of final functional outcome. Secondary operations are common, regardless of the initial treatment. One-third of the patients with a nonunion did not opt for further treatment. For daily clinical practice, we do not advocate routine plate fixation for all patients, but rather an individualized treatment based on shared decision-making, guided by the presence of risk factors for nonunion and patients' values and preferences.

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