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ABOUT COVER

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SYSTEMATIC REVIEWS

Clinical effect of operative *vs* nonoperative treatment on humeral shaft fractures: Systematic review and meta-analysis of clinical trials

Yang Li, Yi Luo, Jing Peng, Jun Fan, Xiao-Tao Long

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Abstract

BACKGROUND

Whether operation is superior to non-operation for humeral shaft fracture remains debatable. We hypothesized that operation could decrease the nonunion and reintervention rates and increase the functional outcomes.

AIM

To compare the clinical efficacy between operative and nonoperative approaches for humeral shaft fractures.

METHODS

We searched the PubMed, Web of Science, ScienceDirect, and Cochrane databases from 1990 to December 2023 for clinical trials and cohort studies comparing the effects of operative and conservative methods on humeral shaft fractures. Two investigators independently extracted data from the eligible studies, and the other two assessed the methodological quality of each study. The quality of the included studies was assessed using the Cochrane risk bias or Newcastle-Ottawa Scale. The nonunion, reintervention and the overall complications and functional scores were pooled and analyzed using Review Manager software (version 5.3).

RESULTS

A total of four randomized control trials and 13 cohort studies were included, with 1285 and 1346 patients in the operative and nonoperative groups, respectively. Patients in the operative group were treated with a plate or nail, whereas those in the conservative group were managed with splint or functional bracing. Four studies were assessed as having a high risk of bias, and the other 13 were of a low risk of bias according to the Newcastle-Ottawa Scale or Cochrane risk bias tool. The operative group had a significantly decreased rate of nonunion [odds ratio (OR) 0.30; 95%CI: 0.23 to 0.40), reintervention (OR: 0.33; 95%CI: 0.24 to 0.47), and overall complications (OR: 0.62; 95%CI: 0.49 to 0.78)]. The pooled effect of the Disabilities of Arm, Shoulder, and Hand score showed a significant difference at 3 [mean difference (MD) -8.26; 95%CI: -13.60 to -2.92], 6 (MD: -6.72; 95%CI: -11.34 to -2.10), and 12 months (MD: -2.55; 95%CI: -4.36 to -0.74). The pooled effect of Visual Analog Scale scores and the Constant-Murley score did not significantly differ between the two groups.

CONCLUSION

This systematic review and meta-analysis revealed a trend of rapid functional recovery and decreased rates of nonunion and reintervention after operation for humeral shaft fracture compared to conservative treatment.

Key Words: Humeral shaft fracture; Operation; Nonoperation; Brace; Systematic review

Core Tip: Whether operation is superior to non-operation for humeral shaft fracture remains debatable. This systematic review was conducted to investigate the effect of the two methods in terms of nonunion, reintervention, overall complications, and functional scores. The results revealed that lower rates of nonunion, reintervention, overall complications, and faster functional recovery could be achieved with operative treatment. This approach is significantly useful for clinicians in therapy decision-making.

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INTRODUCTION

Humeral shaft fracture is common in adults, accounting for approximately 3% of all extremity fractures, with an incidence of approximately 13 per 100000 persons per year[1,2]. Treatment options mainly include surgical and conservative methods. Conservative treatment involves the use of a splint or brace to stabilize the fracture, which is non-traumatic and helps avoid surgical complications. However, there are still disadvantages, such as nonunion, delayed union, and malalignment. Surgical management typically involves osteosynthesis using a plate or nail, which can lead to early functional recovery. Patients may experience complications, such as infection, iatrogenic radial nerve palsy, and implant failure because of surgery[2,3].

Conventional nonoperative treatment was once regarded by many surgeons as the standard treatment, with a satisfactory union rate and ideal functional recovery. There are considerable differences in reports about union rates for conservative treatment. Sarmiento *et al*[4] reported a nonunion rate as low as 2% for closed humeral fractures, and the residual deformities were acceptable. Kapil Mani *et al*[5] also confirmed a 97.2% union rate in a series of 108 humeral shaft fractures with 90.9% patient angulation ≤ 15°. A review of clinical trials revealed that the union rate was 94.5% and not so promising functional scores[6]. Serrano *et al*[7] retrospectively reviewed 1182 humeral shaft fractures managed nonoperatively and found that the nonunion rate was 17%, and 29% of patients ultimately underwent operation. Moreover, nonoperation with functional bracing has also been approved as a cost-effective strategy[8]. However, with the demand for early mobilization, fast functional recovery, and the development of implants and new techniques, an increasing number of surgeons advocate operative treatment for this fracture, and operative management has become prevalent recently. Plate or intramedullary nailing fixation were the most popular operative method by which high union rate, perfect alignment, and upper limb function can be restored[9,10]. A prospective cohort study verified that operative management can result in an earlier functional recovery and return to activities[11]. The complications of operation, such as infection and iatrogenic radial nerve injuries, have led to other concerns about the operation[12-14].

In recent decades, a series of studies have compared the conservative and surgical management of humeral shaft fracture. The results of the trials were contradictory. Some studies have reported comparable union rate, function recovery and complications[11,15,16]. Other cohort trials revealed fast functional recovery in the operation group, and nonunion occurred more often in conservative management group[17-19]. Recent meta-analyses or systematic reviews have also confused us with the different results of functional recovery and complications[20-22].

At present, there is still controversy and lack of high-quality evidence to provide a reference for clinicians and patients, and the optimal treatment method is still under debate in clinical research. We hypothesized that surgical treatment would result in superior function, a low nonunion rate, and comparable overall complications. Thus, we conducted the systematic review aimed to clarify whether the operative method decreases the nonunion rate and promotes functional recovery, and we believed that this review could provide evidence for treatment choice. This systematic review was registered in the International prospective register of systematic reviews, PROSPERO (CRD42022348712).

MATERIALS AND METHODS

Systematic literature search

We searched PubMed, Web of Science, ScienceDirect, and the Cochrane Library for randomized control trials (RCT) and cohort studies published in English from 1990 to December 2023. The search strategy was based on the combination of key words "Humeral Fractures (MeSH terms)," "nonoperative," "functional brace," "operative," "osteosynthesis." Two researchers independently evaluated the titles and abstracts of studies comparing the effects of operative and non-operative treatment for adult humeral shaft fracture. The full text was then screened for eligibility. The references of the included articles were also reviewed to identify relevant studies that may have been missed during the initial search process.

Inclusion and exclusion criteria

Studies meeting the following inclusion criteria were included in the study: studies comparing the operative and non-operative methods for humeral shaft fracture in adults; the operative management included plate osteosynthesis or intramedullary nailing; the non-operative method included casting or functional bracing; randomized controlled trials or comparative cohort studies; follow-up more than 6 months; and published in English and the full text can be accessed. Studies including patients with polytrauma, old fractures, and pathological fractures were excluded.

Data extraction and quality assessment

Two investigators independently browsed the abstracts and identified potential studies. Subsequently, the full texts were carefully screened to confirm the inclusion of studies based on the inclusion and exclusion criteria. Two researchers then extracted data from the included studies, and another two assessed the methodological quality of each included study. Any disagreement was resolved by consensus and discussion with a third assessor. If two or more studies reported the same data, only the study with the most complete data was included.

The following data were extracted from the included studies: study design; characteristics of participants; the fixation methods; the length of follow-up; the Disabilities of Arm, Shoulder and Hand (DASH) score; the Constant-Murley score; Visual Analog Scale (VAS) scores; the union time; and the main adverse events, such as nonunion, reintervention, infection, and iatrogenic radial nerve palsy.

The quality of RCTs was assessed using the Cochrane risk bias tool, which comprises six domains: Random sequence generation, allocation concealment, blinding, incomplete outcome data, evidence of selective reporting, and evidence of other biases. Each domain was scored as low, high, or unclear. Studies were considered to have a low risk of bias if all domains were assessed as low risk of bias or only one item was scored as high risk or unclear. If two domains were scored as high or unclear, the study was considered at moderate risk. When more than two domains were scored as high risk, the study was considered to have a high risk of bias. The comparable trials were assessed using the Newcastle-Ottawa Scale, which includes three areas: The selection of the study groups, the comparability of the groups, the ascertainment of either the exposure or outcome of interest, and a total score ≥ 5 represented high quality.

Statistical analysis

Data were analyzed using Review Manager 5.3 software. Mean differences (MD) with 95%CIs were calculated for continuous variable outcomes. Odds ratio (OR) were calculated for dichotomous outcomes. Alpha was set at 0.05, and all tests were 2-tailed. Heterogeneity among studies was assessed using I-squared (I^2) and χ^2 tests. Effects with no statistical heterogeneity ($I^2 < 50\%$ or $P \geq 0.1$) were analyzed using a fixed-effects model. Effects with statistical heterogeneity ($I^2 \geq 50\%$ or $P < 0.1$) were analyzed using a random-effects model. For outcomes that could not be pooled by meta-analysis, the outcomes were reported as descriptive statistics. Publication bias was assessed by visual inspection of the funnel plots.

RESULTS

Characteristics of the studies

In total, 1295 studies were retrieved from the following databases: 323 from PubMed, 447 from Web of Science, 202 from ScienceDirect, and 323 from the Cochrane Library. After excluding 829 duplicate articles, 466 articles remained. After reviewing the titles and abstracts, 427 additional papers were excluded. Finally, after thorough examination of the full texts, 22 studies were excluded. Ultimately, 4 random control trials and 13 comparative cohort studies were included in this research (Figure 1)[11,15-19,23-33]. The pool sample consisted of 1285 patients treated by operative method and 1346 patients who underwent function bracing. The characteristics of the 17 trials are presented in Table 1.

Quality assessment

The four RCTs were assessed using the Cochrane risk bias tool. Two studies did not report the methods of randomization and allocation concealment, which can be regarded as a high risk of selection bias. Because the intervention was operational, the performer of the studies cannot be blinded, and performance bias could exist. In the outcome assessment, the blinding method was used in only one study. In summary, two RCTs were assessed as having a high risk of bias, one was considered to have a moderate risk of bias, and one was considered to have a low risk of bias (Figure 2). The remaining 13 cohort studies were assessed using Newcastle-Ottawa Scale, with 11 studies assessed as high quality and only two studies regarded as low quality (Table 2).

Table 1 Characteristics of the 17 studies included in the meta-analysis

Ref.	Year	Study design	Simple size	Mean/median age (year)		Female/male, *n*		Type of fracture, (AO/OTA: A/B/C), *n*		Treatment		Mean FU (months)
			OP/non-OP	OP	Non-OP	OP	Non-OP	OP	Non-OP	OP	Non-OP	
Rämö *et al*[25]	2020	RCT	38/44	49.6	48.4	18/12	10/24	34/4/0	36/7/1	ORPO	FB	12
Kumar *et al*[26]	2017	RCT	20/20	37.6	32.7	5/15	6/14	20/0/0	19/1/0	ORPO	FB	6
Hosseini *et al*[24]	2019	RCT	30/30	NA	NA	7/23	4/26	18/4/8	21/5/4	ORPO	FB	12
Matsunaga *et al*[23]	2017	RCT	58/52	37.3	40.3	23/35	14/38	38/15/3	28/17/6	MIPO	FB	12
Wallny *et al*[32]	1997	Cohort	45/44	56	59	19/26	20/24	NA	NA	Nail	FB	27
Jawa *et al*[15]	2006	Cohort	19/21	50	41	8/11	12/9	NA	NA	ORPO	FB	21
Oliver *et al*[27]	2021	Cohort	139/523	44.7	58.5	60/79	299/224	82/53/4	169/283/72	ORPO, nail	FB	5
Westrick *et al*[19]	2017	Cohort	227/69	31	42	144/52	35/34	NA	NA	ORPO, nail	FB	12
Mahabier *et al*[16]	2013	Cohort	95/91	61.1	60.6	51/44	55/36	52/35/8	42/42/7	ORPO	FB	NA
Harkin and Large[18]	2017	Cohort	30/96	NA	NA	21/9	64/32	NA	NA	ORPO, nail	FB	NA
Dielwart *et al*[28]	2017	Cohort	40/31	37.5	39.3	22/18	8/23	23/8/9	16/7/8	ORPO, nail	FB	10.6
Osman *et al*[31]	1998	Cohort	72/32	48	48	NA	NA	NA	NA	ORPO, nail	Splint	NA
Ekholm *et al*[30]	2008	Cohort	7/20	47.6	52.6	3/4	15/3	7/0/0	20/0/0	ORPO, nail	FB	74.4
Denard *et al*[29]	2010	Cohort	150/63	34.9	36.4	68/82	29/34	NA	NA	ORPO	FB	NA
Den Hartog *et al*[17]	2022	Cohort	245/145	53	62	94/51	133/112	171/74/0	92/53/0	ORPO, nail	FB	12
van Middendorp *et al*[11]	2011	Cohort	33/14	53	51	14/19	9/5	6/17/10	6/5/3	Nail	FB	12
Cannada *et al*[33]	2021	Cohort	45/57	41	41.5	14/31	25/32	26/17/2	30/20/7	ORPO	FB	6

Because of the follow-up lost, the number of patients may less than that of the primary simple size. NA: Not available; RCT: Randomized clinical trials; ORPO: Open reduction and plate osteosynthesis; FU: Follow up; FB: Functional bracing; AO/OTA: AO Foundation and Orthopaedic Trauma Association; MIPO: Minimally invasive percutaneous plate osteosynthesis; OP: Operation.

Nonunion in the two groups

Nonunion is an important indicator of treatment outcomes. All 17 studies reported nonunion in patients after operative or conservative treatment. Specifically, for 89 out of 1285 patients in the operative group and 257 out of 1346 patients in the conservative group experienced nonunion. There was no significant statistical heterogeneity (χ^2 = 25.05; P < 0.01, I^2 = 36%), and the data were analyzed with a fixed-effects model. The results showed a significant difference in the nonunion rate (6.9% *vs* 19.1%) between the two groups (OR: 0.30; 95%CI: 0.23 to 0.40; Figure 3A); the operative method decreased nonunion rate by 63.9% compared to the non-operative method.

Table 2 Quality assessment of the 13 cohort studies using the Newcastle-Ottawa Scale

Ref.	Selection	Comparability	Outcome	Total	Study quality
Wallny *et al*[32]	++++	+	++	7 +	High
Jawa *et al*[15]	++++		++	5 +	High
Oliver *et al*[27]	++++		++	5 +	High
Westrick *et al*[19]	++++		++	5 +	High
Mahabier *et al*[16]	++++	++	+++	9 +	High
Harkin and Large[18]	+++	+	+	5 +	High
Dielwart *et al*[28]	+++	+	++	6 +	High
Osman *et al*[31]	+++		+	4 +	Low
Ekholm *et al*[30]	+++	+	+++	7 +	High
Denard *et al*[29]	+++	+	+	5 +	High
Den Hartog *et al*[17]	++++	+	+++	8 +	High
van Middendorp *et al*[11]	++++	+	++	7 +	High
Cannada *et al*[33]	++	+	+	4 +	Low

Scale: Zero to 9 +; 5 or more + indicates a higher quality study.

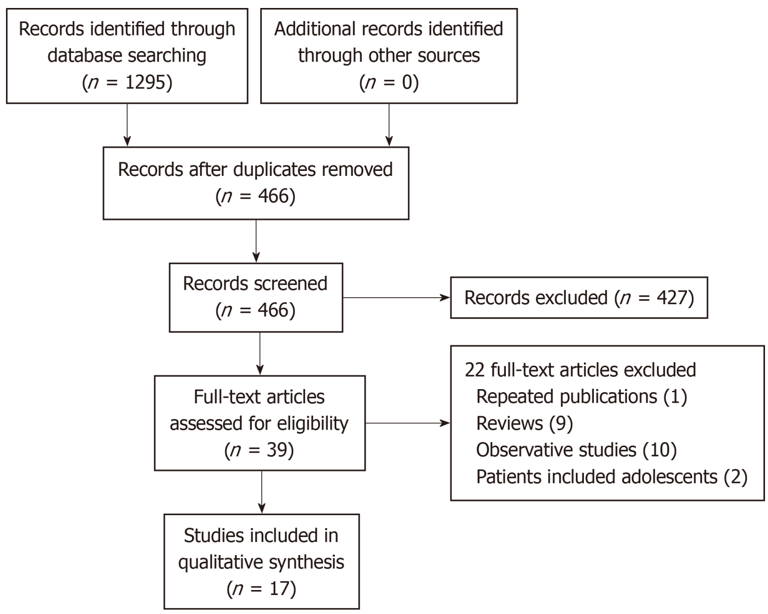


Figure 1 The preferred reporting items for systematic reviews and meta-analyses flow diagram of screening process.

New radial nerve palsy

Postoperative radial nerve palsy was also an important complication that affected patient satisfaction and functional recovery. The incidence could also occur in the non-operative group during close reduction. Of the 14 trials that reported new radial nerve palsy, two RCTs and 12 comparative studies. Thirty-eight of the 1059 available patients in the operative group and 12 of the 722 patients in the conservative group underwent new radial nerve palsy. There was no significant statistical heterogeneity (χ^2 = 15.50; P = 0.16, I^2 = 29%), and the data were analyzed using a fixed-effects model. The results showed significant differences between the two groups (OR: 1.83; 95%CI: 1.04 to 3.22; Figure 3B), with the incidence of new radial nerve palsy tending to increase in the operation group.

Secondary surgical interventions in the two groups

Secondary surgical interventions may result from severe complications or an inability to tolerate bracing, which is an important factor to evaluate the treatment outcome. Of the 12 studies, 12 reported the details of secondary surgical interventions. In the operative group, 67 (8.9%) of 757 patients underwent reoperation due to nonunion, infection,

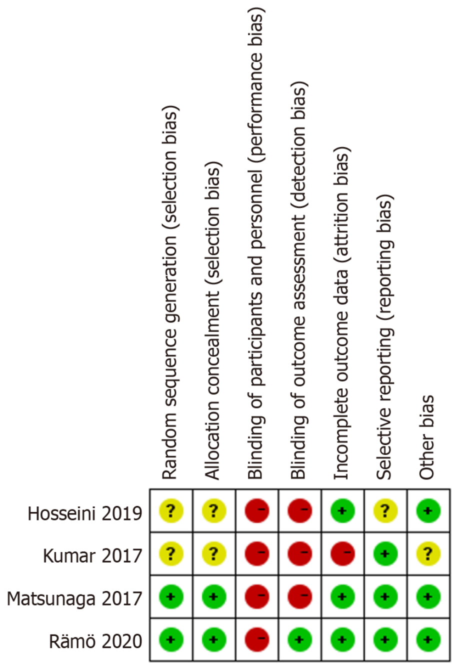


Figure 2 The risk of bias in the 4 randomized control trials assessed with the Cochrane risk bias tool.

impingement, or other reasons. In the conservative group, 103 (19.9%) patients underwent surgical intervention because of nonunion, malunion, loss of reduction, or refracture and did not tolerate the bracing. The pooled effect showed that the rate of secondary surgical intervention was higher in the conservative group (OR: 0.33; 95%CI: 0.24 to 0.47; Figure 3C).

Overall complication rate

The overall complication rate was also a significant factor to be considered in the treatment effect. Thirteen studies detailed the occurrence of all complications in their reports. The pooled effect showed that the rate of overall complications was higher in the conservative group (25.3% *vs* 18.4%) than in the operative group (OR: 0.62; 95%CI: 0.49 to 0.78; Figure 3D).

DASH score recovery at 3, 6, and 12 months between the two groups

Only two trials reported the comparison of DASH score at 3 months; overall, 88 patients in the operative group and 90 patients in the conservative group were assessed. This analysis revealed significant statistical heterogeneity (χ^2 = 2.03; I^2 = 57%), and the data were analyzed using a random-effects model. The results showed a significant difference in DASH score at 3 months postoperatively (MD: -8.26; 95%CI: -13.60 to -2.92; Figure 3E).

Three trials reported the comparison of DASH scores at 6 months; overall, 108 patients in the operative group and 110 patients in the conservative group were assessed. In this analysis, there was significant statistical heterogeneity (χ^2 = 4.39; I^2 = 54%); thus, the data were analyzed using a random-effects model. The results revealed significant differences in DASH score at 6 months postoperatively (MD: -6.72; 95%CI: -11.34 to -2.10; Figure 3E).

Two trials reported the comparison of DASH scores at 12 months; overall, 88 patients in the operative group and 88 patients in the conservative group were assessed. In this analysis, the data were analyzed using a random-effects model. The results revealed significant differences in DASH score at 12 months postoperatively (MD: -2.55; 95%CI: -4.36 to -0.74; Figure 3E).

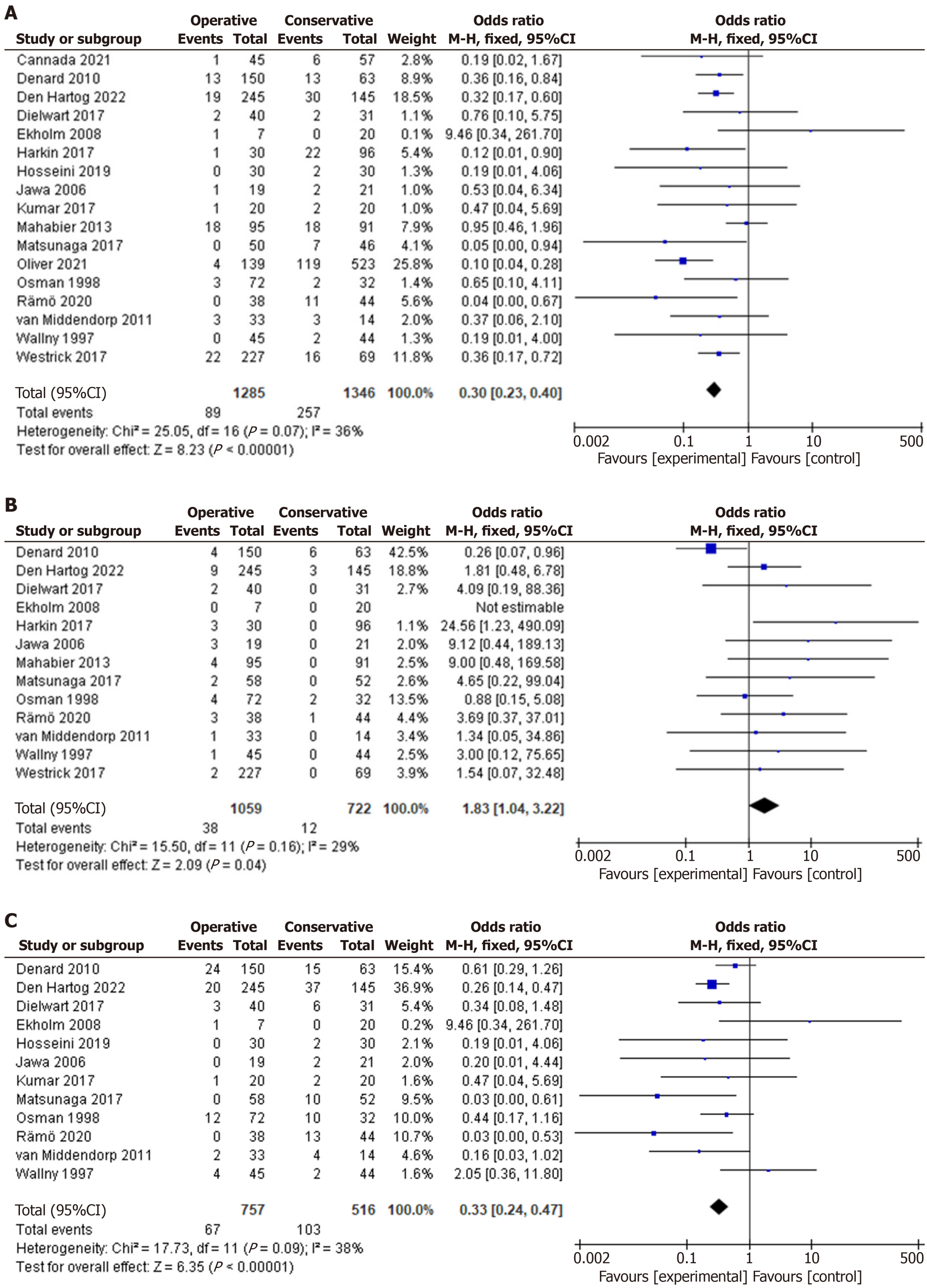
Another prospective cohort study[17] also reported on the DASH score outcome, but the data could not be pooled in the analysis. In this report, the DASH score was lower in the surgical group until three months, indicating earlier functional recovery.

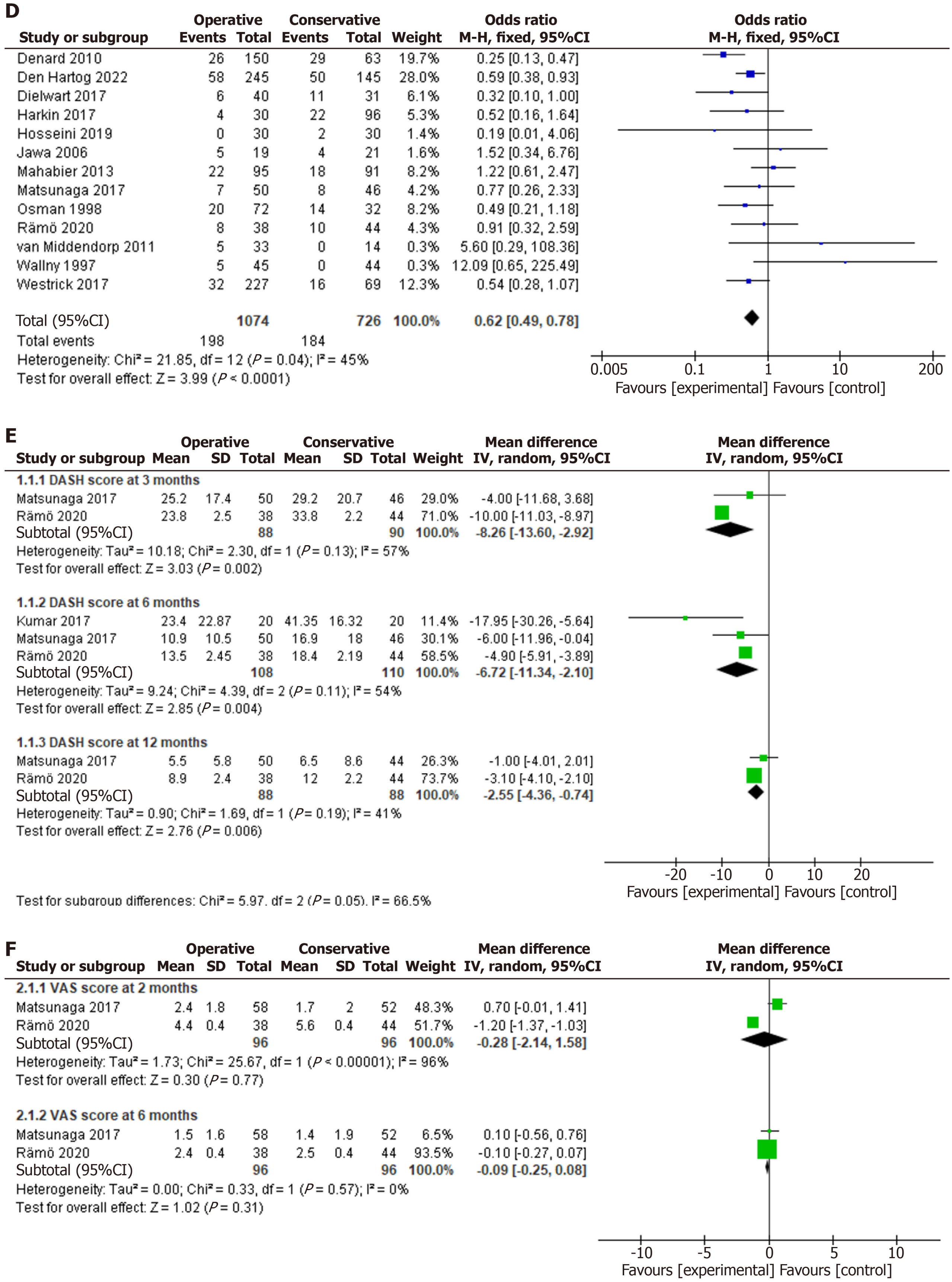
VAS scores, Constant-Murley score, and Short Form-36 scores

Two studies reported VAS scores at 2 and 6 months. Of the 96 patients in the operative and conservative groups, 96 were assessed. In this analysis, the data were analyzed using a random-effects model. The overall pooled VAS score did not differ between the two groups at 2 months (MD: -0.28; 95%CI: -2.14 to 1.58; Figure 3F) and 6 months postoperatively (MD: -0.09; 95%CI: -0.25 to 0.08; Figure 3F).

Two studies reported the Constant-Murley score at 2 and 6 months. The overall pooled effect of Constant-Murley score was not significantly different at 2 months postoperatively (MD: 17.79; 95%CI: -7.59 to 43.55; Figure 3G). The between-group mean difference was 8.75 at 6 months postoperatively, with a significant difference between the two groups (MD: 8.75; 95%CI: 7.51 to 9.99; Figure 3G).

Only two trials reported the Short Form-36 (SF-36) questionnaire after initial management[17,23]. The studies revealed no significant differences between the two groups in terms of the SF-36 at 1, 2, 6, and 12 months postoperatively.


A
Study or subgroup | Operative Events Total | Conservative Events Total | Weight | Odds ratio M-H, fixed, 95%CI | Odds ratio M-H, fixed, 95%CI
Cannada 2021 1 45 6 57 2.8% 0.19 [0.02, 1.67]
Denard 2010 13 150 13 63 8.9% 0.36 [0.16, 0.84]
Den Hartog 2022 19 245 30 145 18.5% 0.32 [0.17, 0.60]
Dielwart 2017 2 40 2 31 1.1% 0.76 [0.10, 5.75]
Ekholm 2008 1 7 0 20 0.1% 9.46 [0.34, 261.70]
Harkin 2017 1 30 22 96 5.4% 0.12 [0.01, 0.90]
Hosseini 2019 0 30 2 30 1.3% 0.19 [0.01, 4.06]
Jawa 2006 1 19 2 21 1.0% 0.53 [0.04, 6.34]
Kumar 2017 1 20 2 20 1.0% 0.47 [0.04, 5.69]
Mahabier 2013 18 95 18 91 7.9% 0.95 [0.46, 1.96]
Matsunaga 2017 0 50 7 46 4.1% 0.05 [0.00, 0.94]
Oliver 2021 4 139 119 523 25.8% 0.10 [0.04, 0.28]
Osman 1998 3 72 2 32 1.4% 0.65 [0.10, 4.11]
Rämö 2020 0 38 11 44 5.6% 0.04 [0.00, 0.67]
van Middendorp 2011 3 33 3 14 2.0% 0.37 [0.06, 2.10]
Wallny 1997 0 45 2 44 1.3% 0.19 [0.01, 4.00]
Westrick 2017 22 227 16 69 11.8% 0.36 [0.17, 0.72]
Total (95%CI) 1285 1346 100.0% 0.30 [0.23, 0.40]
Total events 89 257
Heterogeneity: Chi² = 25.05, df = 16 (P = 0.07); I² = 36%
Test for overall effect: Z = 8.23 (P < 0.00001)
0.002 0.1 1 10 500
Favours [experimental] Favours [control]
B
Study or subgroup | Operative Events Total | Conservative Events Total | Weight | Odds ratio M-H, fixed, 95%CI | Odds ratio M-H, fixed, 95%CI
Denard 2010 4 150 6 63 42.5% 0.26 [0.07, 0.96]
Den Hartog 2022 9 245 3 145 18.8% 1.81 [0.48, 6.78]
Dielwart 2017 2 40 0 31 2.7% 4.09 [0.19, 88.36]
Ekholm 2008 0 7 0 20 Not estimable
Harkin 2017 3 30 0 96 1.1% 24.56 [1.23, 490.09]
Jawa 2006 3 19 0 21 2.0% 9.12 [0.44, 189.13]
Mahabier 2013 4 95 0 91 2.5% 9.00 [0.48, 169.58]
Matsunaga 2017 2 58 0 52 2.6% 4.65 [0.22, 99.04]
Osman 1998 4 72 2 32 13.5% 0.88 [0.15, 5.08]
Rämö 2020 3 38 1 44 4.4% 3.69 [0.37, 37.01]
van Middendorp 2011 1 33 0 14 3.4% 1.34 [0.05, 34.86]
Wallny 1997 1 45 0 44 2.5% 3.00 [0.12, 75.65]
Westrick 2017 2 227 0 69 3.9% 1.54 [0.07, 32.48]
Total (95%CI) 1059 722 100.0% 1.83 [1.04, 3.22]
Total events 38 12
Heterogeneity: Chi² = 15.50, df = 11 (P = 0.16); I² = 29%
Test for overall effect: Z = 2.09 (P = 0.04)
0.002 0.1 1 10 500
Favours [experimental] Favours [control]
C
Study or subgroup | Operative Events Total | Conservative Events Total | Weight | Odds ratio M-H, fixed, 95%CI | Odds ratio M-H, fixed, 95%CI
Denard 2010 24 150 15 63 15.4% 0.61 [0.29, 1.26]
Den Hartog 2022 20 245 37 145 36.9% 0.26 [0.14, 0.47]
Dielwart 2017 3 40 6 31 5.4% 0.34 [0.08, 1.48]
Ekholm 2008 1 7 0 20 0.2% 9.46 [0.34, 261.70]
Hosseini 2019 0 30 2 30 2.1% 0.19 [0.01, 4.06]
Jawa 2006 0 19 2 21 2.0% 0.20 [0.01, 4.44]
Kumar 2017 1 20 2 20 1.6% 0.47 [0.04, 5.69]
Matsunaga 2017 0 58 10 52 9.5% 0.03 [0.00, 0.61]
Osman 1998 12 72 10 32 10.0% 0.44 [0.17, 1.16]
Rämö 2020 0 38 13 44 10.7% 0.03 [0.00, 0.53]
van Middendorp 2011 2 33 4 14 4.6% 0.16 [0.03, 1.02]
Wallny 1997 4 45 2 44 1.6% 2.05 [0.36, 11.80]
Total (95%CI) 757 516 100.0% 0.33 [0.24, 0.47]
Total events 67 103
Heterogeneity: Chi² = 17.73, df = 11 (P = 0.09); I² = 38%
Test for overall effect: Z = 6.35 (P < 0.00001)
0.002 0.1 1 10 500
Favours [experimental] Favours [control]


D
Study or subgroup | Operative Events | Total | Conservative Events | Total | Weight | Odds ratio M-H, fixed, 95%CI
Denard 2010 26 150 29 63 19.7% 0.25 [0.13, 0.47]
Den Hartog 2022 58 245 50 145 28.0% 0.59 [0.38, 0.93]
Dielwart 2017 6 40 11 31 6.1% 0.32 [0.10, 1.00]
Harkin 2017 4 30 22 96 5.3% 0.52 [0.16, 1.64]
Hosseini 2019 0 30 2 30 1.4% 0.19 [0.01, 4.06]
Jawa 2006 5 19 4 21 1.6% 1.52 [0.34, 6.76]
Mahabier 2013 22 95 18 91 8.2% 1.22 [0.61, 2.47]
Matsunaga 2017 7 50 8 46 4.2% 0.77 [0.26, 2.33]
Osman 1998 20 72 14 32 8.2% 0.49 [0.21, 1.18]
Rämö 2020 8 38 10 44 4.3% 0.91 [0.32, 2.59]
van Middendorp 2011 5 33 0 14 0.3% 5.60 [0.29, 108.36]
Wallny 1997 5 45 0 44 0.3% 12.09 [0.65, 225.49]
Westrick 2017 32 227 16 69 12.3% 0.54 [0.28, 1.07]
Total (95%CI) 1074 726 100.0% 0.62 [0.49, 0.78]
Total events 198 184
Heterogeneity: Chi² = 21.85, df = 12 (P = 0.04); I² = 45%
Test for overall effect: Z = 3.99 (P < 0.0001)
Odds ratio M-H, fixed, 95%CI
0.005 0.1 1 10 200
Favours [experimental] Favours [control]
E
Study or subgroup | Operative Mean | SD | Total | Conservative Mean | SD | Total | Weight | Mean difference IV, random, 95%CI
1.1.1 DASH score at 3 months
Matsunaga 2017 25.2 17.4 50 29.2 20.7 46 29.0% -4.00 [-11.68, 3.68]
Rämö 2020 23.8 2.5 38 33.8 2.2 44 71.0% -10.00 [-11.03, -8.97]
Subtotal (95%CI) 88 90 100.0% -8.26 [-13.60, -2.92]
Heterogeneity: Tau² = 10.18; Chi² = 2.30, df = 1 (P = 0.13); I² = 57%
Test for overall effect: Z = 3.03 (P = 0.002)
1.1.2 DASH score at 6 months
Kumar 2017 23.4 22.87 20 41.35 16.32 20 11.4% -17.95 [-30.26, -5.64]
Matsunaga 2017 10.9 10.5 50 16.9 18 46 30.1% -6.00 [-11.96, -0.04]
Rämö 2020 13.5 2.45 38 18.4 2.19 44 58.5% -4.90 [-5.91, -3.89]
Subtotal (95%CI) 108 110 100.0% -6.72 [-11.34, -2.10]
Heterogeneity: Tau² = 9.24; Chi² = 4.39, df = 2 (P = 0.11); I² = 54%
Test for overall effect: Z = 2.85 (P = 0.004)
1.1.3 DASH score at 12 months
Matsunaga 2017 5.5 5.8 50 6.5 8.6 44 26.3% -1.00 [-4.01, 2.01]
Rämö 2020 8.9 2.4 38 12 2.2 44 73.7% -3.10 [-4.10, -2.10]
Subtotal (95%CI) 88 88 100.0% -2.55 [-4.36, -0.74]
Heterogeneity: Tau² = 0.90; Chi² = 1.69, df = 1 (P = 0.19); I² = 41%
Test for overall effect: Z = 2.76 (P = 0.006)
Test for subgroup differences: Chi² = 5.97, df = 2 (P = 0.05), I² = 66.5%
Mean difference IV, random, 95%CI
-20 -10 0 10 20
Favours [experimental] Favours [control]
F
Study or subgroup | Operative Mean | SD | Total | Conservative Mean | SD | Total | Weight | Mean difference IV, random, 95%CI
2.1.1 VAS score at 2 months
Matsunaga 2017 2.4 1.8 58 1.7 2 52 48.3% 0.70 [-0.01, 1.41]
Rämö 2020 4.4 0.4 38 5.6 0.4 44 51.7% -1.20 [-1.37, -1.03]
Subtotal (95%CI) 96 96 100.0% -0.28 [-2.14, 1.58]
Heterogeneity: Tau² = 1.73; Chi² = 25.67, df = 1 (P < 0.00001); I² = 96%
Test for overall effect: Z = 0.30 (P = 0.77)
2.1.2 VAS score at 6 months
Matsunaga 2017 1.5 1.6 58 1.4 1.9 52 6.5% 0.10 [-0.56, 0.76]
Rämö 2020 2.4 0.4 38 2.5 0.4 44 93.5% -0.10 [-0.27, 0.07]
Subtotal (95%CI) 96 96 100.0% -0.09 [-0.25, 0.08]
Heterogeneity: Tau² = 0.00; Chi² = 0.33, df = 1 (P = 0.57); I² = 0%
Test for overall effect: Z = 1.02 (P = 0.31)
Mean difference IV, random, 95%CI
-10 -5 0 5 10
Favours [experimental] Favours [control]

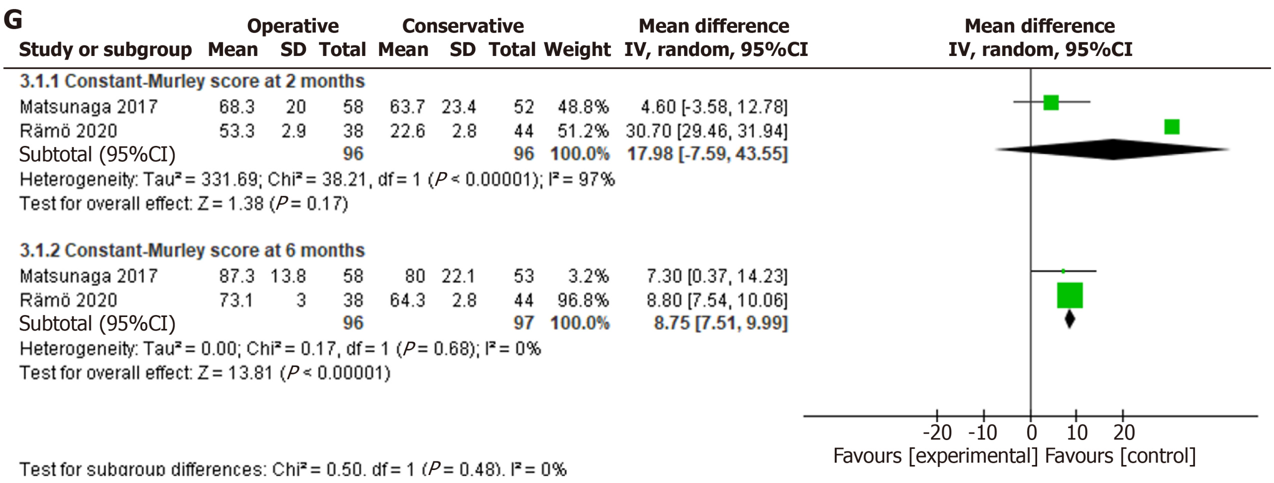


Figure 3 The comparison between the two groups. A: The nonunion comparison between the two groups; B: The new radial nerve palsy comparison between the two groups; C: The secondary surgical intervention between the two groups; D: The overall complication rate between the two groups; E: The Disabilities of Arm, Shoulder and Hand score recovery between the two groups at 3, 6 and 12 months; F: The visual analogue scale score between the two groups at 2, 6 months; G: The Constant-Murley score between the two groups at 2, 6 months. DASH score: Disabilities of Arm, Shoulder and Hand score; VAS: Visual analogue scale.

The union time between the two groups

Two RCTs reported and compared union times between the two groups. Kumar *et al*[26] reported an average union time of 15.36 weeks in the operative group and 11 weeks in the non-operative group. However, Hosseini Khameneh *et al*[24] reported an average union time of 13.9 ± 2.1 weeks in the operative group and 18.7 ± 3.0 weeks in the conservative group. Five cohort studies reported the time to union in the two groups, and all five studies showed no difference between the conservative and operative groups[16,18,19,28,29]. In the conservative group, the union time ranged from a median of 11 to 22 weeks. In the operative group, the time to union was 12-28 weeks. Because the data could not be pooled, it was difficult to estimate the difference in union time between the two groups.

Sensitivity analysis and publication bias

Sensitivity analysis was performed for the outcomes of nonunion and DASH scores. The fixed-effects and random-effect models were switched for sensitivity analysis, and the pooled analysis showed that the results of the meta-analysis were stable. The tendency of the nonunion rate did not reveal a difference when pooled analysis was carried out only for RCTs (OR: 0.33, 95%CI: 0.25-0.44) or cohort studies (OR: 0.10, 95%CI: 0.03-0.36). The funnel plot of the nonunion and overall complications revealed a symmetrical distribution (Figure 4), implying that publication bias was unlikely to influence the main outcomes.

DISCUSSION

Although controversy exists about the optimal treatment of humeral shaft fracture, in this systematic review, conservative treatment with splint or functional braces was associated with high rates of nonunion, reintervention, and overall complications and slow functional recovery, thereby confirming the superiority of surgical treatment.

For the four RCTs, two trials were subjected to selection, performance, and detection bias, which were assessed as high risk factors of bias[24,26]. In the quality assessment of the other two studies, one was assessed as having a low risk of bias, and the other was regarded as having a moderate risk of bias[23,25]. In addition, for the remaining 13 cohort studies, two were low quality. Significant heterogeneity was found in the data on functional outcome, which may result from differences among surgeons and the method of operation. Furthermore, the data from similar follow-up time points (not the same time point) pooled was also the origin of the heterogeneity. Fortunately, the trend of the primary outcome did not change in the sensitivity analysis. For the functional outcome (DASH score, VAS scores, Constant-Murley score), as bias and heterogeneity existed, the evidence for the functional outcome was regarded as medium grade, according to the GRADE standard. Concerning the outcomes of union, radial nerve palsy, secondary surgical intervention, and overall complications, because three studies with high risk of bias were included in the analysis, the evidence for this outcome can be described as moderate level evidence.

A few systematic reviews have compared the conservative treatment with operation for humeral shaft fracture[20,22,34-36]. Without published RCTs, two reviews did not provide evidence to determine which method was superior[34,35]. The other two reviews mainly incorporated observational studies and concluded that the operative method could reduce the rate of nonunion comparing conservative treatment[20,22]. Because the pooled data were mainly from observational studies with imbalanced baseline characteristics, there was a high degree of bias and significant heterogeneity, which could significantly decrease the level of evidence and the reliability of the results. In this systematic review, recently

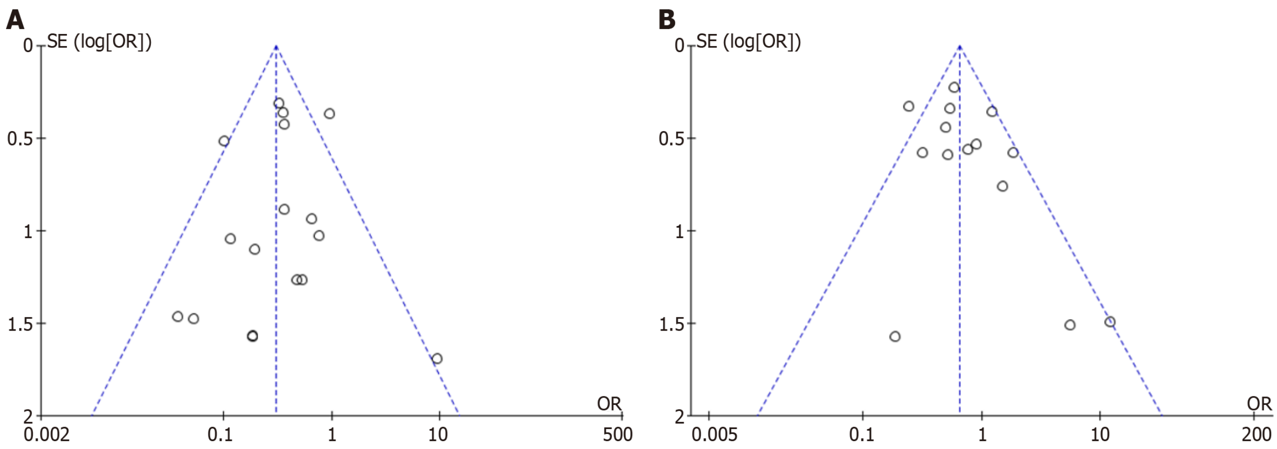


Figure 4 Funnel plot of nonunion and overall complications. A: Funnel plot of nonunion; B: Funnel plot of overall complications. OR: Odds ratio.

published RCTs and cohort studies with a large sample size were included; thus, the results were more reliable. Moreover, our review also emphatically analyzed the functional outcomes, which ultimately implied a trend toward faster functional recovery, such as the DASH score, VAS scores, Constant-Murley score.

Many observational studies have compared the results of conservative treatment with operation for humeral shaft fracture, with contradictory results regarding the nonunion rate[11,16,18,19,27,29]. The highest rate of nonunion in conservative patients reported in these reports can reach to 33%[18], whereas the rate of nonunion in the operative group ranges from 2.9% to 12%. Because of the significantly different baseline characteristics and small sample sizes in these studies, it was difficult to obtain credible results. For example, the site of diaphyseal fracture, significant displacement, and angulation can also affect the results[37]. In the study of Jawa *et al*[15], all patients with distal third diaphyseal fracture healed with functional bracing[15]. However, Harkin and Large[18] and Broadbent *et al*[38] reported the presence of a proximal third fracture was associated with nonunion in conservative patients. In cases of proximal shaft fracture, the immobilization of the functional brace is relatively poor, which may be a factor in nonunion. The recent systematic review included two RCTs and ten observational studies, ultimately confirmed the results that the rate of nonunion was higher in the conservative group (15.3%) than in the operative group (6.4%)[20]. In our review, the nonunion rate was 19.1% in the conservative group and 6.9% in the operative group, which is in line with previous research. Considering the recent RCTs and larger sample cohort trials included in our meta-analysis, the pooled effect was more reliable. The potential reason for the decreased nonunion rate may be the increased mechanical stability after operation, which is an important factor for bone union.

New radial nerve palsy can also occur during operation or close reduction. Fourteen trials reported new radial nerve palsy, and the overall rates of new radial nerve palsy were 3.6% and 1.7% in the operation and conservative groups, respectively, with a significant increase in the operation group. Reintervention and overall complications were also important outcomes in both groups. The rate of secondary surgical intervention was higher in the conservative group (19.9%) than operation group (8.9%), mainly caused by the nonunion. In addition to nonunion, malunion, loss of reduction, refracture, and not tolerance to bracing were the main reasons for reintervention in the conservative group. This also implied that surgical treatment may be superior to conservation. Surgical complications are usually a disadvantage of surgical treatment. The pooled effect of overall complications also revealed a higher rate in the non-operation group, which implied that the operation did not result in more complications.

Functional outcomes were important factors to evaluate fracture recovery. In previous studies, only a few studies reported differences in the DASH scores between the two groups. A recent meta-analysis revealed no difference between the conservative and operative groups in terms of DASH score at 6 months postoperatively[20]. In a recent prospective cohort study with a large number of patients, the DASH score in the operative group was lower than that of the conservative group during the first 3 months, with a mean difference of 7.3 point[17]. In our meta-analysis, the DASH score showed superior results in the operative group at the first 6 months follow-up, with a mean difference of 8.26 point at three and 6.72 point at 6 months. The mean difference was larger than the minimally important change in the DASH score (6.7 points) reported[39], which mean there was not only statistical differences but also clinical significance. Although no significant difference existed between the two groups in the VAS scores and Constant-Murley score, the pooled effect also revealed a superior trend toward operation. These results reflected a faster recovery in the operation group within the first few months. The reason may be that more stable fracture fixation was associated with early functional mobilization. A recent study also supported this result and confirmed that operative treatment of humeral shaft fracture can lead to an earlier return to sport[40].

Several limitations still exist in this meta-analysis. The main limitation was that most of the included studies were cohort studies, and four studies were high risk of bias, which in-creased the bias and ultimately decreased the evidence level. The surgical methods and follow-up intervals included in the study were not completely consistent, which increased the heterogeneity. Finally, only three RCTs and one cohort study reported functional outcomes, and the sample included for analysis was small. Due to these limitations, more high-quality RCTs are needed to improve the evidence level and the reliability of the results.

In this review, because the majority of studies were cohort trials and some were assessed with high risk of bias, the results can be regarded as medium- or low-level evidence, and more high-quality randomized controlled trials should be conducted. Although the pooled analysis showed superior outcomes of surgical treatment, conservative management remains the cornerstone of treatment. Patients should be informed about the merits and shortcomings of the two methods. In particular, when conservative treatment is applied to humeral shaft fracture, the relatively higher rates of complications, such as nonunion and secondary surgical reintervention, should be fully understood.

CONCLUSION

This systematic review and meta-analysis demonstrated that decreased rates of nonunion, reintervention, and overall complication, as well as a trend of rapid functional recovery, could be achieved with operative treatment for humeral shaft fracture compared to conservative treatment. Surgical treatment did not increase the incidence of overall complications.

FOOTNOTES

Author contributions: Li Y and Luo Y contributed to equally; Peng J conceived the design of the study and prepared the manuscript; Li Y and Luo Y finished the literature search and data extraction; Fan J and Long XT assessed the methodological quality; Li Y, and Luo Y contributed to data analysis and wrote the manuscript; All authors have read and approved the final manuscript.

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