J Shoulder Elbow Surg (2020) 29, 2495–2504

ELSEVIER

Journal of Shoulder and Elbow Surgery

www.elsevier.com/locate/ymse

Operative versus nonoperative treatment of humeral shaft fractures: a systematic review and meta-analysis

Ingunn Lode, MD[a,*], Vegard Nordviste, MD[a], Julie Ladeby Erichsen, MD[b], Hagen Schmal, DMSc[b], Bjarke Viberg, PhD[a]

[a]*Department of Orthopaedic Surgery and Traumatology, Kolding Hospital—Part of Hospital Lillebaelt, Kolding, Denmark*
[b]*Department of Orthopaedic Surgery and Traumatology, Odense University Hospital, Odense, Denmark*

Background: The humeral shaft fracture accounts for 1%-3% of all fractures and occurs in both the young and old population. However, the optimal treatment is still a matter of debate. Even though nonoperative treatment is commonly considered the gold standard, advantages have been described using operative stabilization. This systematic review aims to compare operative and nonoperative treatment in adult patients with humeral shaft fractures.
Method: We used the following databases: PubMed, Embase, Cochrane, and CINAHL on October 1, 2018, searching for randomized controlled trials (RCTs) and cohort studies. Two reviewers screened the studies using Covidence, followed by systematic data extraction. The primary outcome was defined as posttreatment complications such as nonunion, radial nerve palsy, malunion, and infections. The secondary outcomes were functional scores and patient-reported outcome measures (PROMs). To assess study quality, the risk of bias in nonrandomized studies of interventions and the Cochrane risk of bias tool were used.
Results: Twelve studies were included: 1 RCT, 1 prospective cohort, and 10 retrospective cohorts with a total of 1406 patients, of whom 835 were treated operatively and 571 nonoperatively. Mean age ranged from 35 to 64, and 54% of the patients were male. The cohort studies had, in general, moderate bias, whereas the RCT had a low bias. There were statistically significant fewer nonunions in the operative treated group with a risk ratio of 0.49 (0.35-0.67), yielding a number needed to treat = 12. There were more deep infections in the operative group with a risk ratio of 2.76 (1.01-7.53) but otherwise no statistical differences concerning malunion or nerve damage. Only 1 study included PROM data.
Conclusion: There were fewer nonunions in the operative group but more deep infections. Because of the lack of studies reporting PROMs, the potential positive effect of operative therapy in early aftercare could not be evaluated. Therefore, PROMs should be mandatory in future comparative studies.
Level of evidence: Level III; Systematic Review

Keywords: Humeral shaft fracture; operative treatment; nonoperative treatment; complication; nonunion; malunion; surgery

The nonoperative approach has historically been the most used treatment for humeral shaft fractures, whereas functional bracing is the preferred method for many orthopedic surgeons.[24] However, some studies suggest an increase in the amount of operatively treated cases with plate fixation being the gold standard of operative

Institutional review board approval was not required for this systematic review.

*Reprint requests: Ingunn Lode, MD, Lillebalt Kolding Sygehus, Sygehusvej 24, Kolding 6000, Denmark.

E-mail address: inglode@gmail.com (I. Lode).

1058-2746/$ - see front matter
https://doi.org/10.1016/j.jse.2020.05.030

methods.[3] What is the evidence for choosing between operative and nonoperative treatment for humeral shaft fractures?

Fewer iatrogenic complications such as infections and nerve damage are the benefits of nonoperative treatment, but the approach has a higher risk for nonunion with a reported range between 2% and 20%.[2,22] The potential benefits of operative treatment could include low frequency of both nonunion and postoperative malunion, allowing earlier mobilization.[6,19] However, there might be a higher risk of infection, fixation failure, and secondary nerve damage.[6,19] Both methods report advantages and disadvantages; however, the optimal method of treating a diaphyseal humeral fracture is yet to be determined. Currently, a systematic review combining the existing data of treatment outcome is missing, rendering the choice of optimal treatment to the surgeons' personal preference.

This study aimed, therefore, to conduct a systematic review and meta-analysis comparing nonoperative and operative treatment for humeral shaft fractures in adults.

Method

Protocol and registration

The systematic review and meta-analysis were planned, performed, and reported according to the preferred reporting items for systematic reviews and meta-analysis guideline statement.[17] Before the data extraction and analysis, a study protocol was registered with the PROSPERO register of systematic reviews with the registration number 116733.

Eligibility criteria

Our research question was based on a population, intervention, comparison, outcome (PICO) model that consisted of a patient population older than 16 years with a humeral shaft fracture receiving either operative (external or internal fixation) or nonoperative (braces, sling, collar 'n' cuff, or similar) treatment. The primary outcome was defined as post-treatment complications and the secondary outcome as physical function and patient-reported outcome measure (PROM). The aim was to find randomized controlled trials (RCTs) and cohort studies that investigate the differences and perform a meta-analysis. Articles that were not in English, French, or German were excluded. The time limitation was set to articles written after 1990 due to the introduction of the low contact dynamic compression plate, in an attempt to exclude obsolete fixation methods.

Information sources

In cooperation with a scientific librarian, 2 of the authors (IL and VN) searched the following databases: PubMed, Embase (Classic + Embase 1947 to 2018 week 20), Cochrane, and CINAHL. The search was performed on October 1, 2018. Searches in gray literature gave no results.

Search

All 4 databases were searched with the same search strategy. No limitations were applied. The following search string was used in PubMed:

((((((((((((humerus[MeSH Terms]) OR humeral) OR humerus) OR humeri) OR diaphysis) OR diaphyseal) :OR "upper limb") OR "upper extremity") OR "upper arm)) AND ((((((fracture[MeSH Terms]) OR humeral shaft fracture[MeSH Terms]) OR humeral fracture[MeSH Terms]) OR fracture) OR fractured) OR fractures)) AND ((((((((((((fracture fixation[MeSH Terms]) OR fracture healing[MeSH Terms]) OR orthopedic surgery[MeSH Terms]) OR surgery) OR surgical) OR operation) OR operative) OR operational) OR operate) OR orthopedic) OR orthopaedic)) AND ((((((((((physical therapy modalities[MeSH Terms]) OR conservative) OR conventional) OR non surgical) OR nonsurgical) OR non operative) OR nonoperative) OR collar) OR cuff) OR sling

Study selection

The search results were managed in Covidence, where the list of an initial 10,036 articles was reduced to 8071 after duplicates were removed (Fig. 1). Two authors (IL and VN) screened the articles independently by title and abstracts; disagreements were resolved by discussion. The full text was read for final article inclusion, and the whole author group discussed any disagreements.

Data collection process

Two authors (IL and VN) created a data extraction table and filled in all data independently. After completion, all entries were cross-checked. Disagreements were resolved by discussion between the 2 authors, and the whole author group discussed any unresolved issues.

Data items

The following data were extracted: first author, country, number of patients, study design, male/female ratio, age, patient type, fracture type (Arbeitsgemeinschaft für Osteosynthesefragen [AO] classification), mechanism of injury, study period (start to end of study), time to follow-up (time from surgery to outcomes was registered), loss to follow-up, treatment technique, nonunion, malunion, infection, postoperative nerve damage, mean time to union, PROM, and functional outcome. PROM and functional outcomes such as elbow and shoulder range of motion

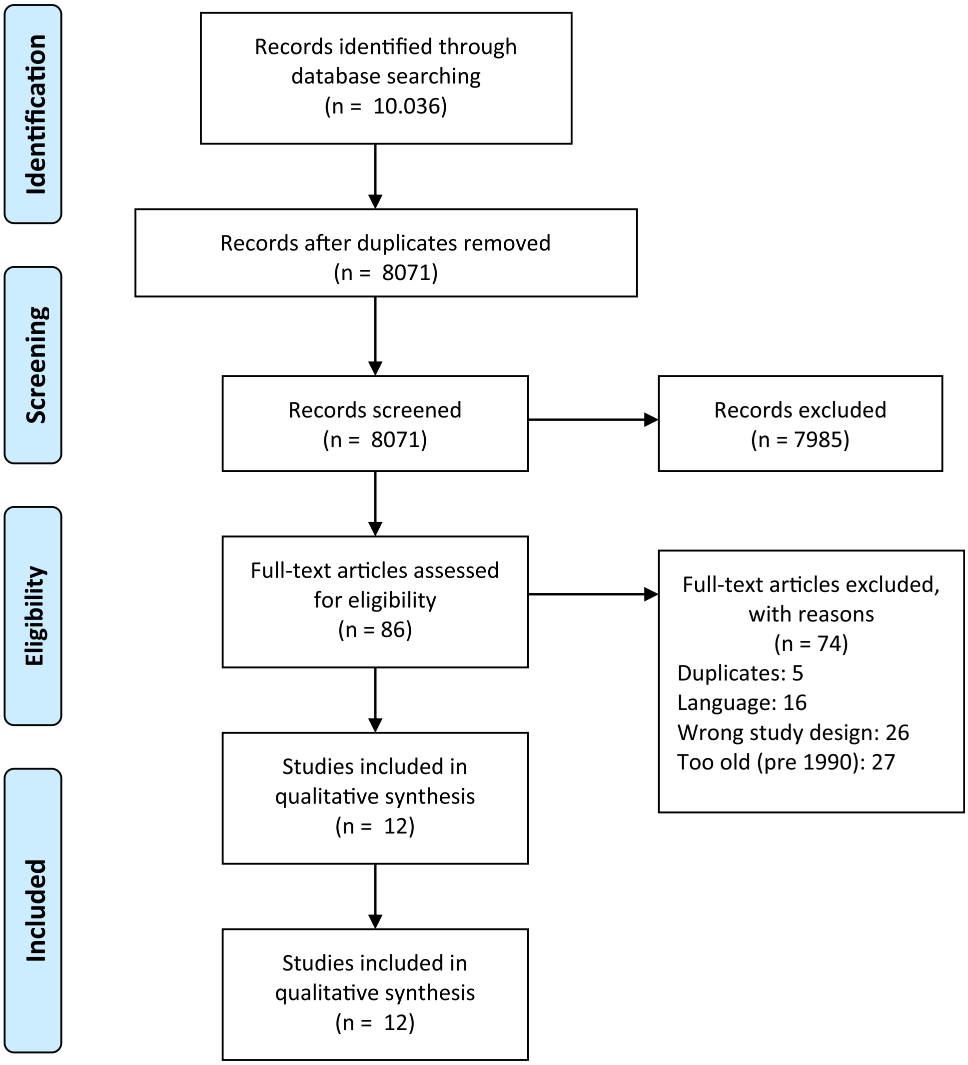

Figure 1 PRISMA flow diagram of the screening process. *PRISMA*, preferred reporting items for systematic reviews and meta-analysis.

(ROM) were reported in a variety of ways making any combined comparison difficult.

Nonunion was defined in this review as a fracture's inability to heal within 26 weeks, as union after this is less than likely, and many patients are reoperated at this point.[4] This was in accordance with the definition used in the reviewed articles. Malunion was defined as radiographic angulation >5° or sagittal angulation >10° as seen on postoperative radiographs.[9] This review considered only deep infections, defining them as infections that needed any surgical débridement and/or intravenous antibiotics.

Risk of bias in individual studies

The methodology used in the 12 articles was quality assessed using the risk of bias in nonrandomized studies of interventions,[23] and the RCT was measured by the Cochrane risk of bias tool (RoB 2.0).[10] These tools assess the quality in the following domains: confounding, selection of participants, intervention classification, deviations from intent, missing data, outcome measurement, selection of results, and overall quality of the study. All articles were judged to be low, moderate, serious, or critical.

Summary measures

Outcomes were reported across studies and were quantitatively analyzed using forest plots (statistical software: RevMan 5.3, Copenhagen, Denmark). The intervention effect was expressed as a risk ratio (RR). Statistical significance was defined as $P \leq .05$. Pooled data were assessed for heterogeneity using the χ^2 and I^2 tests. Heterogeneity was defined as "absent" (0%-25%), "low" (26%-50%), "moderate" (51%-75%), or "high" (76%-100%). Fixed-effect meta-analysis was carried out when the I^2 was less than 50%; otherwise, a random-effects model was used.[11]

Table I Demographics of the included studies

Study	LoE	Period of inclusion	Patients (n)	Male sex (%)		Treatment (n)	Percentage	Age, mean (±SD)	A (%)	AO 12 B (%)	C (%)	Follow-up (weeks)
Denard et al (2010)[5]	III	2001-2006	213	54	OP	150	70	35 (±16)	–	–	–	34
USA					Non-OP	63	30	36 (±17)	–	–	–	
Dielwart et al (2017)[6]	III	2006-2011	71	58	OP	40	56	38	23	8	9	43
USA					Non-OP	31	44	39	16	7	8	
Harkin and Large (2017)[8]	III	2008-2015	126	33	OP	30	23	64	49	14	17	26
Australia					Non-OP	96	77		16	8	3	
Jawa et al (2006)[12]	III	2000-2004	40	50	OP	19	48	50	–	–	–	–
USA					Non-OP	21	52	41	–	–	–	
Klestil et al (1997)[13]	III	1993-1994	63	54	OP	27	43	45	48	10	5	–
Austria					Non-OP	36	57	44				
Mahabier et al (2013)[14]	III	2002-2008	186	43	OP	95	51	61	14	17	22	–
The Netherlands					Non-OP	91	49	61	13	14	0	
Matsunaga et al (2017)[15]	I	2012-2015	110	66	OP	58	53	37 (±15)	38	15	3	52
Brazil					Non-OP	52	47	40 (±17)	28	17	6	
Middendorp et al (2011)[16]	II	2000-2004	47	51	OP	33	70	53 (±19)	11	3	0	52
Switzerland					Non-OP	14	30	51 (±24)	23	10	0	
Osman et al (1998)[18]	III	1994-1997	104	58	OP	72	69	48	–	–	–	18
France					Non-OP	32	31		–	–	–	
Ristic et al (2011)[21]	III	2004-2010	61	57	OP	39	64	29	13	14	12	52
Serbia					Non-OP	22	36	61	14	5	3	
Wallny et al (1997)[25]	III	1990-1994	89	56	OP	45	51	56	–	–	–	27
Germany					Non-OP	44	49	59	–	–	–	
Westrick et al (2017)[26]	III	2000-2012	296	63	OP	227	77	31	13	14	18	52
USA					Non-OP	69	23	42	17	16	22	

LoE, level of evidence; *OP*, operative; *Non-OP*, nonoperative; *SD*, standard deviation.

Table II Outcome measures

Study	PROM	Comparison	Functional	Comparison
Denard et al (2010)[5]	–	–	Elbow ROM	No difference
Dielwart et al (2017)[6]	–	–	–	–
Harkin and Large (2017)[8]	–	–	–	–
Jawa et al (2006)[12]	–	–	Shoulder ROM	No difference
			Elbow ROM	No difference
Klestil et al (1997)[13]	–	–	–	–
Mahabier et al (2013)[14]	–	–	–	–
Matsunaga et al (2017)[15]	DASH	OP 6 point better after 6 mo	Constant score	No difference
	SF-36	No difference		
	VAS	No difference		
Middendorp et al (2011)[16]	VAS	No difference	Shoulder ROM	No difference
			Elbow ROM	No difference
Osman et al (1998)[18]	–	–	Stewart & Hundley score	No difference
			Shoulder ROM	No difference
			Elbow ROM	No difference
Ristic et al (2011)[21]	–	–	Constant score	No difference
			Mayo elbow score	OP 17-31 point better
Wallny et al (1997)[25]	–	–	Shoulder ROM	OP 49% free mobility, non-OP 86%
			Elbow ROM	No difference
Westrick et al (2017)[26]	–	–	–	–

PROM, patient-reported outcome measure; *DASH*, Disabilities of the Arm, Shoulder and Hand score; *SF-36*, 36-Item Short Form; *VAS*, visual analog scale; *OP*, operative; *ROM*, range of motion; *Non-OP*, nonoperative.

Results

Study selection

The screening in Covidence resulted in 86 articles eligible for full-text assessment. Twenty-seven predated 1990, 26 had the wrong study design, 16 were removed due to the language exclusion criteria, and 5 were duplicates. Twelve articles were included, of which 1 was an RCT, 1 was a prospective cohort, and 10 were retrospective cohorts.[6,5,8,12-16,18,21,25,26] They were all included in the meta-analysis (Fig. 1).

Study characteristics

The articles contained 1406 patients, of whom 835 received operative treatment, whereas 571 were treated nonoperatively (Table I). The mean age ranged from 35 to 64, and 54% of the patients were male. The results of nonunion were reported in 10 articles, malunion in 5 articles, infection frequency in 9 articles of which 7 were defined as deep, nerve damage in 11 articles, and mean time to union in 5 articles. Only 2 articles had included PROM, whereas 7 had included functional outcome (Table II). There were no differences in shoulder or elbow ROM, but otherwise, there was no consistency in the use of functional scores for comparison.

Risk of bias within studies

The studies were dominated by Level II and III evidence cohort studies and were considered to be generally at moderate risk of bias (Table III), whereas the RCT had a low risk of bias across all domains (Table IV). In the cohort studies, we inevitably found confounding biases as the choice of procedure was based on the AO classification of the fractures, the prefracture health status of patients, and the preference of the surgeons. Also, no articles had stratified their results based on age, gender, BMI, cause of fracture, or other potentially confounding biases. However, some articles advocated that there was no significant difference between the demographic groups.[5,15] Most articles had extensive explanations of their selection of participants and method of analysis. The degree of deviation from intended intervention and missing data was relatively low.

Results of individual studies

All articles reported a higher nonunion frequency in the nonoperative group[12] except 1, which reported no incidents in either the operative or nonoperative group (Table V). Higher malunion frequencies were reported in nonoperative groups in all studies except for 1.[12] Frequencies of infection and nerve damage were generally low, ranging around 5% in both groups. Denard et al[5] reported both infection and nerve damage in the nonoperative group because some open fractures were treated nonoperatively. Four articles

Table III Assessment of risk of bias using the risk of bias in nonrandomized studies of interventions-I

Study	1. Confounding	2. Selection of participants	3. Intervention classification	4. Deviations from intent	5. Missing data	6. Outcome measurement	7. Selection of results
Denard et al (2010)[5]	Serious	Moderate	Moderate	Low	Low	Low	Moderate
Dielwart et al (2017)[6]	Moderate	Serious	Moderate	Low	Low	Low	Moderate
Harkin and Large (2017)[8]	Serious	Serious	Low	Low	Low	Moderate	Moderate
Jawa et al (2006)[12]	Serious	Moderate	Moderate	Low	Moderate	Low	Moderate
Klestil et al (1997)[13]	Moderate	Low	Low	Low	Moderate	Moderate	Moderate
Mahabier et al (2013)[14]	Serious	Low	Moderate	Low	Low	Moderate	Moderate
Middendorp et al (2011)[16]	Moderate	Low	Moderate	Low	Moderate	Low	Moderate
Osman et al (1998)[18]	Moderate	Low	Moderate	Low	Moderate	Moderate	Moderate
Ristic et al (2011)[21]	Serious	Low	Moderate	Low	Low	Moderate	Moderate
Wallny et al (1997)[25]	Serious	Low	Low	Low	Moderate	Low	Moderate
Westrick et al (2017)[26]	Serious	Moderate	Moderate	Low	Serious	Moderate	Moderate

Table IV Assessment of risk of bias using RoB 2.0

Study	1. Randomization process	2. Deviations from the intended interventions	3. Missing outcome data	4. Measurement of the outcome	5. Selection of the reported result
Matsunaga et al (2017)[15]	Low	Low/some concern	Low	Low	Low

reported longer healing periods in the operatively treated group and 1 article in the nonoperative group. There was only 1 study that included the results of a PROM questionnaire.[15] Therein, no difference was found. The only clinically relevant item was the ROM, which was not different in the other studies (Table II).

Synthesis of results

Nonunion

Ten studies reported on nonunion, and all were included in the meta-analysis. In the operative group (n = 751), 61 fractures developed nonunion vs. 84 fractures in the nonoperative group (n = 505), resulting in a number needed to treat of 12 patients. The meta-analysis (Fig. 2) showed a significant lower occurrence of nonunion in the operative group with an RR of 0.49 (95% confidence interval [CI]: 0.35-0.67, P = .0001) with no significant heterogeneity (χ^2: 10.13; P =.26; I^2: 21%).

Malunion

Five studies reported on malunion, and all were included in the meta-analysis. There were 14 cases in the operative group (n = 226) and 26 cases in the nonoperative group (n = 203). Meta-analysis (Fig. 3) showed no significant difference between the operative and nonoperative groups with an RR of 0.52 (95% CI: 0.15-1.80, P = .31). The heterogeneity measured by I2 was reported as moderate (53%) and might be related to the results of the study by Jawa et al.[12] However, the χ^2 test results in a nonsignificant P value (P = .07), and, therefore, the heterogeneity was not considered significant (χ^2: 8.52; P = .07; I^2: 53%).

Infection

Nine studies reported on infection, and all were included in the meta-analysis. In the operative group, 22 cases (n = 599) developed an infection, compared with 2 in the nonoperative group (n = 330) both of which were open fractures caused by low-energy gunshot wounds.[5] Meta-analysis (Fig. 4) showed a statistically significant lower occurrence of infection in the nonoperative group with an RR of 2.76 (95% CI: 1.01-7.53) with no significant heterogeneity (χ^2: 1.18; P = .95; I^2: 0%).

The weight of the individual studies was reported as high as 50.7% for Denard et al,[5] and therefore, we excluded this trial to clarify whether this had any influence on the calculations of the meta-analysis. Again, the findings were statistically significant, resulting in an RR of 3.42 (95% CI: 1.08-10.88; P = .05).

Nerve damage

Eleven studies reported on nerve damage, and all were included in the meta-analysis. Nerve damage occurred in 32 patients after surgery, whereas only 8 suffered from nerve damage in the nonoperative group. The meta-analysis (Fig. 5) showed no statistically significant difference between the 2 groups with an RR of 2.69 (95% CI: 0.92-7.87). Moderate heterogeneity was seen (χ^2: 16.83; P = .05; I^2: 47%).

Discussion

Our meta-analysis shows a significantly lower occurrence of nonunions in operatively treated humeral shaft fractures.

Table V Treatment, fracture union, and complications

Study		Treatment	Nonunion n (%)	Malunion n (%)	Infection n (%)	Nerve damage n (%)	Mean time to union (weeks)
Denard et al (2010)[5]	OP	Plate	13 (9)	2 (1)	7 (5)	4 (3)	19.7
	Non-OP	Brace, sling	13 (21)	8 (13)	2 (3)	6 (10)	19.1
Dielwart et al (2017)[6]	OP	Plate, IMN	2 (5)	0 (0)	1 (3)	2 (5)	17
	Non-OP	Brace, sling	2 (7)	4 (13)	0 (0)	0 (0)	15
Harkin and Large (2017)[8]	OP	Plate, IMN	1 (4)	–	–	3 (10)	15
	Non-OP	Brace, sling	22 (27)	–	–	0 (0)	14.4
Jawa et al (2006)[12]	OP	Plate	0 (0)	3 (16)	1 (5)	3 (16)	–
	Non-OP	Brace	0 (0)	0 (0)	0 (0)	0 (0)	–
Klestil et al (1997)[13]	OP	Plate, IMN	1 (4)	9 (33)	2 (8)	1 (4)	–
	Non-OP	Brace	3 (8)	13 (36)	0 (0)	0 (0)	–
Mahabier et al (2013)[14]	OP	Plate, IMN, EF, wire	18* (19)	–	–	4 (4)	15.5
	Non-OP	Brace	18* (20)	–	–	0 (0)	13.5
Matsunaga et al (2017)[15]	OP	Plate (bridging)	0 (0)	0 (0)	0 (0)	2 (4)	–
	Non-OP	Brace	8 (15)	1 (2)	0 (0)	0 (0)	–
Middendorp et al (2011)[16]	OP	IMN (retrograde)	1 (3)	–	0 (0)	0 (0)	–
	Non-OP	Brace	3 (21)	–	0 (0)	0 (0)	–
Osman et al (1998)[18]	OP	Plate, IMN, wire	3 (4)	–	0 (0)	5 (6)	7.4
	Non-OP	Brace	2 (6)	–	0 (0)	5 (6)	8
Ristic et al (2011)[21]	OP	Plate, IMN, EF	–	–	–	–	–
	Non-OP	Hanging cast	–	–	–	–	–
Wallny et al (1997)[25]	OP	IMN	–	–	1 (2)	1 (2)	–
	Non-OP	Sling (Gilcrest)	–	–	0 (0)	0 (0)	–
Westrick et al (2017)[26]	OP	Plate, IMN, EF	22 (10)	–	8 (4)	5 (2)	–
	Non-OP	Brace	16 (23)	–	0 (0)	0 (0)	–

OP, operative; *Non-OP*, nonoperative; *IMN*, intramedullary nail; *EF*, external fixation; *Nerve damage*, postoperative/treatment.
* Defined in the study as delayed union.

Study or Subgroup	Operative Events	Operative Total	Nonoperative Events	Nonoperative Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Denard 2010	13	150	13	63	20.6%	0.42 [0.21, 0.85]
Dielwart 2017	2	40	2	31	2.5%	0.78 [0.12, 5.20]
Harkin 2017	1	30	22	96	11.8%	0.15 [0.02, 1.03]
Jawa 2006	0	19	0	21		Not estimable
Klestil 1997	1	27	3	36	2.9%	0.44 [0.05, 4.04]
Mahabier 2013	18	95	18	91	20.7%	0.96 [0.53, 1.72]
Matsunaga 2017	0	58	8	52	10.1%	0.05 [0.00, 0.89]
Middendorp 2011	1	33	0	14	0.8%	1.32 [0.06, 30.65]
Osman 1998	3	72	2	32	3.1%	0.67 [0.12, 3.80]
Westrick 2017	22	227	16	69	27.6%	0.42 [0.23, 0.75]
Total (95% CI)		**751**		**505**	**100.0%**	**0.49 [0.35, 0.67]**
Total events	61		84			

Heterogeneity: Chi^2 = 10.13, df = 8 (P = 0.26); I^2 = 21%
Test for overall effect: Z = 4.31 (P < 0.0001)

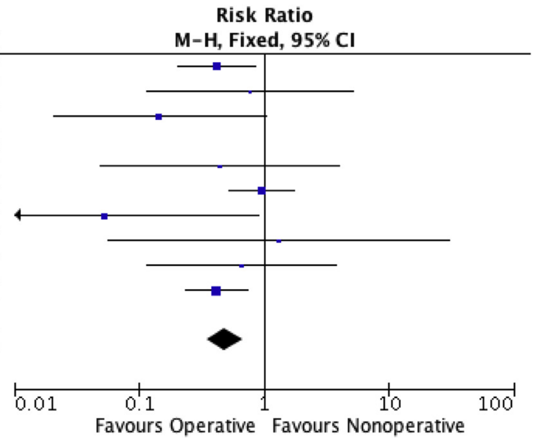

Figure 2 Comparison of nonunion between the operation and cast group of humeral shaft fractures. *CI*, confidence interval; *M-H*, Mantel-Haenszel.

Nonunions occurred in 0%-27% of the nonoperatively treated patients compared with 0%-19% of the operative group. Mahabier et al[14] report the highest frequency of operative nonunion with 19% after 24 weeks. Unfortunately, the authors do not describe any reason for this high occurrence, nor whether any patients subsequently gained union or were reoperated within 1 year. When looking at the remaining studies, the highest frequency of nonunions after operative stabilization is 10%. The variations between the reported nonunion frequencies could be attributed to elements not explained in detail by the authors, such as compliance or follow-up procedures. Not surprisingly, deep

Study or Subgroup	Operative Events	Operative Total	Nonoperative Events	Nonoperative Total	Weight	Risk Ratio M-H, Random, 95% CI
Denard 2010	2	82	8	63	25.9%	0.19 [0.04, 0.87]
Dielwart 2017	0	40	4	31	12.8%	0.09 [0.00, 1.55]
Jawa 2006	3	19	0	21	12.7%	7.70 [0.42, 140.03]
Klestil 1997	9	27	13	36	37.5%	0.92 [0.46, 1.84]
Matsunaga 2017	0	58	1	52	11.1%	0.30 [0.01, 7.19]
Total (95% CI)		**226**		**203**	**100.0%**	**0.52 [0.15, 1.80]**
Total events	14		26			

Heterogeneity: Tau² = 0.93; Chi² = 8.52, df = 4 (P = 0.07); I² = 53%
Test for overall effect: Z = 1.02 (P = 0.31)

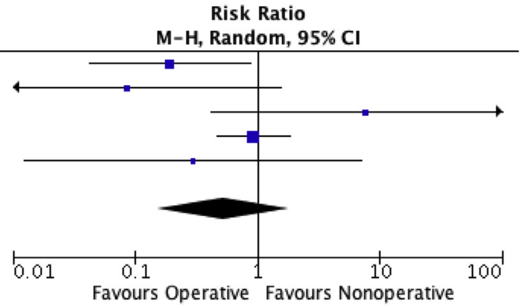

Figure 3 Comparison of malunion between the operation and cast group of humeral shaft fractures. *CI*, confidence interval; *M-H*, Mantel-Haenszel.

Study or Subgroup	Operative Events	Operative Total	Nonoperative Events	Nonoperative Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Denard 2010	7	150	2	63	50.7%	1.47 [0.31, 6.88]
Dielwart 2017	1	40	0	31	10.1%	2.34 [0.10, 55.58]
Jawa 2006	1	19	0	21	8.6%	3.30 [0.14, 76.46]
Klestil 1997	2	27	0	36	7.8%	6.61 [0.33, 132.23]
Matsunaga 2017	0	58	0	52		Not estimable
Middendorp 2011	0	33	0	14		Not estimable
Wallny 1997	1	45	0	44	9.1%	2.93 [0.12, 70.16]
Westrick 2017	8	227	0	69	13.8%	5.22 [0.31, 89.29]
Total (95% CI)		**599**		**330**	**100.0%**	**2.76 [1.01, 7.53]**
Total events	20		2			

Heterogeneity: Chi² = 1.18, df = 5 (P = 0.95); I² = 0%
Test for overall effect: Z = 1.99 (P = 0.05)

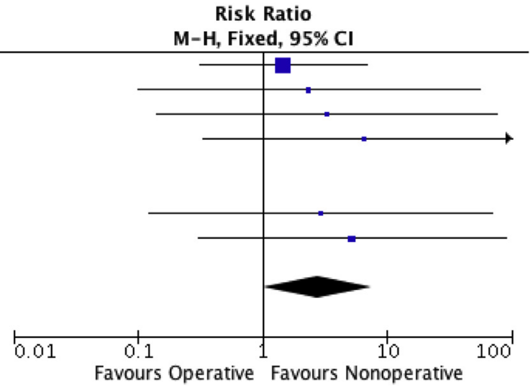

Figure 4 Comparison of infection between the operation and cast group of humeral shaft fractures. *CI*, confidence interval; *M-H*, Mantel-Haenszel.

infections occurred more often in the operative group. No significant results related to the occurrence of malunions or nerve damages were found.

To lower the risk of nonunion in nonoperatively treated patients, Driesman et al[7] described in 2017 a method for early prediction of nonunion. By performing a simple examination for gross motion at the fracture site 6 weeks after treatment, they could identify who would develop a fracture nonunion with a high sensitivity and specificity. This could provide an early indicator of how the fracture is healing and a tool in the shared decision-making of the ongoing fracture treatment.

A meta-analysis on PROMs was not performed because only 2 studies included PROMs. Middendorp et al[16] showed a considerable significance of operative treatment after 6 weeks in the Constant score combining ROM and strength, and they were able to demonstrate that operatively treated patients were reintroduced to their work earlier compared with nonoperatively treated patients. This would be an expected finding if we compare humeral shaft fractures with the literature of clavicle fractures where there is a faster recovery in the operative group, as seen in 2 RCTs evaluating clavicle fractures.[1,20] However, the RCT on humeral shaft fractures[15] reported no significant difference between the operative and nonoperative group regarding any domains of the 36-Item Short Form questionnaire, Constant-Murley, or visual analog scale pain score. One possible explanation is that their postoperative rehabilitation protocol stated that both groups were not allowed any rotation or ROM higher than 90° during the first 6 weeks. The potential advantages from operative treatment might, therefore, be lost, as the 2 groups receive the same postoperative rehabilitation. Future studies should not only include PROMs but also allow early mobilization after surgery when compared with nonoperative treatment.

Limitations

There are several limitations in this study. All except 2 of the included studies are retrospective cohorts with moderate and severe risk of bias, rendering our results unable to obtain the highest value of validity. Cohort studies inevitably have a risk of selection bias because the participants and the treatment personnel were not blinded. We were able to find only 1 RCT study comparing operative and nonoperative treatment.

A confounding factor is the patients lost to follow-up. In all, 313 patients were lost to follow-up across all studies.

Study or Subgroup	Operative Events	Operative Total	Nonoperative Events	Nonoperative Total	Weight	Risk Ratio M-H, Random, 95% CI
Denard 2010	4	150	6	63	17.9%	0.28 [0.08, 0.96]
Dielwart 2017	5	40	0	31	8.8%	8.59 [0.49, 149.60]
Harkin 2017	3	30	0	96	8.5%	21.90 [1.16, 412.44]
Jawa 2006	3	19	0	21	8.7%	7.70 [0.42, 140.03]
Klestil 1997	1	27	0	36	7.7%	3.96 [0.17, 93.70]
Mahabier 2013	4	95	0	91	8.6%	8.63 [0.47, 157.97]
Matsunaga 2017	2	58	0	52	8.2%	4.49 [0.22, 91.45]
Middendorp 2011	0	33	0	14		Not estimable
Osman 1998	4	72	2	32	15.1%	0.89 [0.17, 4.61]
Wallny 1997	1	45	0	44	7.7%	2.93 [0.12, 70.16]
Westrick 2017	5	227	0	69	8.7%	3.38 [0.19, 60.32]
Total (95% CI)		**796**		**549**	**100.0%**	**2.69 [0.92, 7.87]**
Total events	32		8			

Heterogeneity: $Tau^2 = 1.29$; $Chi^2 = 16.83$, df = 9 (P = 0.05); $I^2 = 47\%$
Test for overall effect: Z = 1.80 (P = 0.07)

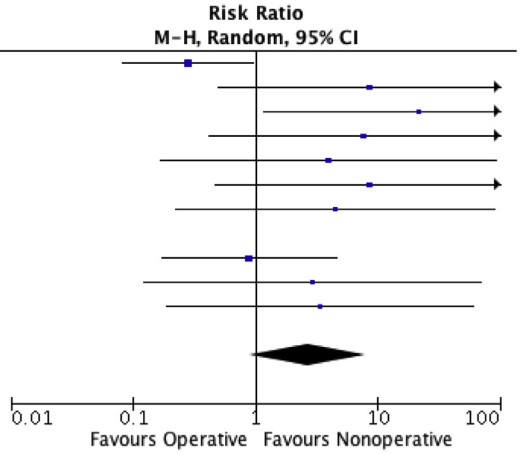

Figure 5 Comparison of nerve damage between the operation and cast group of humeral shaft fractures. *CI*, confidence interval; *M-H*, Mantel-Haenszel.

Westrick et al[26] described a potential skewing of data toward elderly patients sustaining low-energy trauma as the patients lost were likely younger.

A meta-analysis could not be performed on PROM or ROM, as the included studies had different ways of reporting it. These measurements are important and would have provided interesting results as they report the patients' physical function and ability to regain normal motion and strength after treatment. For future studies, measurements such as time and capacity to return to normal physical function would create a more holistic measurement.

Conclusion

This systematic review and meta-analysis report fewer nonunions but more deep infections in the operative group compared with the nonoperative group when evaluating the treatment of humeral shaft fractures. Generally, there was moderate bias across studies. Because of the lack of studies reporting PROMs, the potential positive effect of operative therapy in early aftercare could not be evaluated. Therefore, PROMs should be mandatory in future comparative studies.

Disclaimer

The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

References

1. Ahrens PM, Garlick NI, Barber J, Tims EM, Clavicle Trial Collaborative Group. The clavicle trial: a multicenter randomized controlled trial comparing operative with nonoperative treatment of displaced midshaft clavicle fractures. J Bone Joint Surg Am 2017;99:1345-54. https://doi.org/10.2106/JBJS.16.01112
2. Ali E, Griffiths D, Obi N, Tytherleigh-Strong G, Van Rensburg L. Nonoperative treatment of humeral shaft fractures revisited. J Shoulder Elbow Surg 2015;24:210-4. https://doi.org/10.1016/j.jse.2014.05.009
3. Bhandari M, Devereaux PJ, McKee MD, Schemitsch EH. Compression plating versus intramedullary nailing of humeral shaft fractures—a meta-analysis. Acta Orthop 2006;77:279-84. https://doi.org/10.1080/17453670610046037
4. Cleveland KB. Delayed union and nonunion of fractures. In: Canale ST, Beaty JH, editors. Campbell's operative orthopaedics. 12th ed. Maryland Heights, MO: Mosby; 2013. p. 2981-2.
5. Denard A, Richards JE, Obremskey WT, Tucker MC, Floyd M, Herzog GA. Outcome of nonoperative vs operative treatment of humeral shaft fractures: a retrospective study of 213 patients. Orthopedics 2010;33. https://doi.org/10.3928/01477447-20100625-16
6. Dielwart C, Harmer L, Thompson J, Seymour RB, Karunakar MA. Management of closed diaphyseal humerus fractures in patients with injury severity score ≥17. J Orthop Trauma 2017;31:220-4. https://doi.org/10.1097/BOT.0000000000000768
7. Driesman AS, Fisher N, Karia R, Konda S, Egol KA. Fracture site mobility at 6 weeks after humeral shaft fracture predicts nonunion without surgery. J Orthop Trauma 2017;31:657-62. https://doi.org/10.1097/BOT.0000000000000960
8. Harkin FE, Large RJ. Humeral shaft fractures: union outcomes in a large cohort. J Shoulder Elbow Surg 2017;26:1881-8. https://doi.org/10.1016/j.jse.2017.07.001
9. Harris AM, Patterson BM, Sontich JK, Vallier HA. Results and outcomes after operative treatment of high-energy tibial plafond fractures. Foot Ankle Int 2006;27:256-65. https://doi.org/10.1177/107110070602700406
10. Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, et al. A revised tool for assessing risk of bias in randomized trials. Cochrane Database Syst Rev 2016;10(Suppl. 1):29-31. https://doi.org/10.1002/14651858.CD201601
11. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557-60. https://doi.org/10.1136/bmj.327.7414.557

12. Jawa A, McCarty P, Doornberg J, Harris M, Ring D. Extra-articular distal-third diaphyseal fractures of the humerus. A comparison of functional bracing and plate fixation. J Bone Joint Surg Am 2006;88: 2343-7. https://doi.org/10.2106/JBJS.F.00334
13. Klestil TH, Rangger CH, Kathrein A, Brenner E, Beck E. The conservative and surgical therapy of traumatic humeral shaft fractures. Chirurg 1997;68:1132-6 [in German].
14. Mahabier KC, Vogels LMM, Punt BJ, Roukema GR, Patka P, Van Lieshout EMM. Humeral shaft fractures: retrospective results of non-operative and operative treatment of 186 patients. Injury 2013;44:427-30. https://doi.org/10.1016/j.injury.2012.08.003
15. Matsunaga FT, Tamaoki MJS, Matsumoto MH, Netto NA, Faloppa F, Belloti JC. Minimally invasive osteosynthesis with a bridge plate versus a functional brace for humeral shaft fractures: a randomized controlled trial. J Bone Joint Surg Am 2017;99:583-92. https://doi.org/10.2106/JBJS.16.00628
16. Middendorp JJV, Kazacsay F, Lichtenhahn P, Renner N, Babst R, Melcher G. Outcomes following operative and non-operative management of humeral midshaft fractures: a prospective, observational cohort study of 47 patients. Eur J Trauma Emerg Surg 2011;37:287-96. https://doi.org/10.1007/s00068-011-0099-0
17. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097. https://doi.org/10.1371/journal.pmed.1000097
18. Osman N, Touam C, Masmejean E, Asfazadourian H, Alnot JY. Results of non-operative and operative treatment of humeral shaft fractures a series of 104 cases. Chir Main 1998;17:195-206.
19. Pidhorz L. Acute and chronic humeral shaft fractures in adults. Orthop Traumatol Surg Res 2015;101(Suppl. 1):S41-9. https://doi.org/10.1016/j.otsr.2014.07.034
20. Qvist AH, Væsel MT, Jensen CM, Jensen SL. Plate fixation compared with nonoperative treatment of displaced midshaft clavicular fractures: a randomized clinical trial. Bone Joint J 2018;100-B:1385-91. https://doi.org/10.1302/0301-620X.100B10.BJJ-2017-1137.R3
21. Ristic V, Maljanovic M, Arsic M, Matijevic R, Milankov M. Comparison of the results of treatment of humeral shaft fractures by different methods. Med Pregl 2011;64:490-6. https://doi.org/10.2298/MPNS1110490R
22. Spiguel AR, Steffner RJ. Humeral shaft fractures. Curr Rev Musculoskelet Med 2012;5:177-83. https://doi.org/10.1007/s12178-012-9125-z
23. Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919. https://doi.org/10.1136/bmj.i4919
24. Walker M, Palumbo B, Badman B, Brooks J, Van Gelderen J, Mighell M. Humeral shaft fractures: a review. J Shoulder Elbow Surg 2011;20:833-44. https://doi.org/10.1016/j.jse.2010.11.030
25. Wallny T, Sagebiel C, Westerman K, Wagner UA, Reimer M. Comparative results of bracing and interlocking nailing in the treatment of humeral shaft fractures. Int Orthop 1997;21:374-9.
26. Westrick E, Hamilton B, Toogood P, Henley B, Firoozabadi R. Humeral shaft fractures: results of operative and non-operative treatment. Int Orthop 2017;41:385-95. https://doi.org/10.1007/s00264-016-3210-7