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REVIEW ARTICLE

MIPO versus nailing for humeral shaft fractures: a meta-analysis and systematic review of randomised clinical trials and observational studies

Bryan J. M. van de Wall[1] · Ralf Baumgärtner[1] · R. Marijn Houwert[2] · Björn C. Link[1] · Marilyn Heng[3] · Matthias Knobe[1] · Rolf H. H. Groenwold[4] · Reto Babst[1] · Frank J. P. Beeres[1]

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Abstract

Purpose There is no consensus on the optimal operative technique for humeral shaft fractures. This meta-analysis aims to compare minimal-invasive plate osteosynthesis (MIPO) with nail fixation for humeral shaft fractures regarding healing, complications and functional results.

Methods PubMed/Medline/Embase/CENTRAL/CINAHL were searched for randomized clinical trials (RCT) and observational studies comparing MIPO with nailing for humeral shaft fractures. Effect estimates were pooled across studies using random effects models and presented as weighted odds ratio (OR), risk difference (RD), mean difference (MD) and standardized mean difference (SMD) with corresponding 95% confidence interval (95%CI). Analyses were repeated stratified by study design (RCTs and observational studies).

Results A total of 2 RCTs (87 patients) and 5 observational studies (595 patients) were included. The effects estimated in observational studies and RCTs were similar in direction and magnitude for all outcomes except operation duration. MIPO has a lower risk for non-union (RD 7%; OR 0.2, 95% CI 0.1–0.5) and re-intervention (RD 13%; OR 0.3, 95% CI 0.1–0.8). Functional shoulder (SMD 1.0, 95% CI 0.2–1.8) and elbow scores (SMD 0.4, 95% CI 0–0.8) were better among patients treated with MIPO. The risk for radial nerve palsy following surgery was equal (RD 2%; OR 0.6, 95% CI 0.3–1.2) and nerve function recovered spontaneously in all patients in both groups. No difference was detected with regard to infection, time to union and operation duration.

Conclusion MIPO has a considerable lower risk for non-union and re-intervention, leads to better shoulder function and, to a lesser extent, better elbow function compared to nailing. Although nailing appears to be a viable option, the evidence suggests that MIPO should be the preferred treatment of choice. The learning curve of minimal-invasive plating should, however, be taken into account when interpreting these results.

Keywords Humeral shaft fractures · Minimal-invasive plate fixation · Nailing

Supplementary information The online version of this article (https://doi.org/10.1007/s00068-020-01585-w) contains supplementary material, which is available to authorized users.

✉ Bryan J. M. van de Wall
bryan_vdwall@hotmail.com

[1] Department of Orthopaedic and Trauma Surgery, Lucerne Cantonal Hospital, Spitalstrasse 16, 6000 Luzern, Switzerland

[2] Department of Trauma Surgery, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands

[3] Department of Orthopaedic Surgery, Harvard Medical School Orthopaedic Trauma Initiative, Massachusetts General Hospital Boston, Boston, USA

[4] Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands

Introduction

Humeral shaft fractures are commonly seen in adults, accounting for approximately 3% of all fractures [1, 2]. Various methods are used to surgically treat these fractures. Minimally invasive techniques are of specific interest among orthopaedic trauma surgeons as these techniques have a smaller impact on local vascularity which should lead to improved healing of the fracture site [3]. Currently two minimally invasive techniques exist for treating humeral shaft fractures including minimally invasive plate osteosynthesis (MIPO) and intramedullary nail fixation. While MIPO has an additional risk for radial nerve damage as the nerve is, depending on the plate position, usually not directly visualised during plate positioning, nails, on the other hand, may cause more shoulder or elbow complaints as they are introduced in the vicinity of these joints [4, 5]. To make a fair comparison between the techniques, one must consider all aspects of MIPO and nailing including risk for non-union, re-intervention, radial nerve palsy, infection, time to union, operation duration, general quality of life, shoulder and elbow function.

The aim of the present meta-analysis is to compare MIPO to nailing for patients with humeral shaft fractures with regard to the aforementioned outcomes. In contrast to traditional meta-analysis, the present study included not only results of RCTs but also of observational studies as previous meta-analyses have shown that estimates and study populations of both study designs appear to be quite similar for research on patients with humeral shaft fractures [2]. To test whether this assumption holds, subgroup analyses were performed stratified by study design.

Methods

This systematic review and meta-analysis was performed and reported according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) checklist [6, 7]. A protocol for this review has not been published. No ethical committee approval was necessary for this literature review.

Search strategy and selection criteria

The PubMed/Medline, Embase, CENTRAL, and CINAHL databases were searched on 23 March 2020, for studies comparing MIPO with nailing for humeral shaft fractures. The search syntax is described in supplementary material Table 1. Two reviewers (BJMvdW, RB) independently screened title and abstract for eligibility. Both observational studies and randomised clinical trials were included.

The same two reviewers independently performed the full-text screening. Inclusion criteria were humeral shaft fracture, comparison of MIPO with nailing, age 16 years or older, and reporting on outcomes of interest (non-union, re-intervention, time to union, radial nerve palsy, infection, operation duration, functional outcome). MIPO was defined as obtaining closed reduction under intra-operative fluoroscopy combined with indirect reduction and plate fixation through two separate incisions (irrespective of length) proximal and distal from the fracture focus. Nailing encompassed both antegrade and retrograde nailing. Exclusion criteria were comparison of ORIF to either MIPO or nailing, pathological fractures, treatment for delayed or non-union, studies with an average follow-up less than 6 months, languages other than English, French, German or Dutch, no availability of full-text, letters, meeting proceedings, and case reports. Disagreements on eligibility of full-text articles were resolved by consensus or by discussion with a third reviewer (FJPB). References of all included studies were screened to identify studies not found in the original literature search.

Data extraction

Two reviewers (BJMvdW, RB) independently performed data extraction using a predefined data extraction sheet. The following baseline characteristics were extracted from the included studies; first author, year of publication, study period, country in which study was performed, study design, number of included patients, type of implant, gender, age, open/closed fracture, AO/OTA Fracture and Dislocation classification, low- or high energy trauma, and follow-up duration [8].

Quality assessment

Two reviewers (BJMvdW, RB) independently assessed the methodological quality of included studies using the Methodological Index for Non-randomised Studies (MINORS) [9]. The MINORS is a validated instrument for assessment of methodological quality of cohort studies, resulting in a score between 0 and 24. Disagreements were resolved by consensus. Details on methodological quality assessment are provided in supplementary material Table 2.

Study outcome

Outcome measures included non-union, re-intervention, radial nerve palsy following surgery (secondary radial nerve

palsy), infection, operation duration (minutes), time to union (weeks), general quality of life, shoulder and elbow functional scores between 6 and 12 months after ORIF or MIPO.

Non-union was defined as absence of fracture consolidation 6 months after treatment, with the absence of radiological bridging callus at 3 out of 4 cortices on conventional X-ray in two directions [10]. Re-intervention included all surgical procedures performed during follow-up. Infection encompassed both superficial and deep surgical wound infections [11].

General quality of life scores included the Short-Form 36 (SF-36), EuroQol-5D (EQ-5D) and visual analogue scale (VAS) for generic quality of life. Upper extremity functional scores included Disabilities of Arm, Shoulder and Hand (DASH) score. Shoulder functional scores included University of California at Los Angeles (UCLA) Shoulder Score, Constant score, American Shoulder and Elbow Surgeons (ASES) shoulder score, Oxford Shoulder score and Neer score. Elbow functional scores included Oxford elbow score, Mayo elbow performance score and the Broberg–Morrey score. The functional scores were standardised and pooled for each field (general quality of life, upper extremity function, shoulder function, elbow function) separately.

Statistical analysis

Information about continuous variables was presented as means with standard deviation (SD) or range, or information was converted to mean and SD using the methods described in the Cochrane Handbook for Systematic Reviews of Interventions [12]. Dichotomous variables were presented as counts and percentages. Effects of treatment options on binary outcomes were pooled using the (random effects) Mantel–Haenszel method and presented as odds ratio (OR), risk difference (RD), mean difference (MD) and standardised mean difference (SMD) each with a 95% confidence interval (95% CI). Hereafter the terms weighted OR, weighted RD, weighted MD and weighted SMD are used for brevity. In case of zero-cell counts in one of the two treatment groups, 0.5 was added to all cells of the contingency table of treatment and outcome of those studies in which this occurred. Effects of treatment options on continuous outcomes were pooled using the (random effects) inverse variance weighting method and presented as mean difference (time to union, operation duration) or standardised mean difference (functional scores) with 95% CI. None of the observational studies corrected for confounding. Therefore, the estimated relations between treatment and outcome presented for these studies are unadjusted for possible confounding.

Heterogeneity between studies was assessed for all ORs by visual inspection of forest plots and by the I^2 statistic for heterogeneity. All analyses were stratified according to study design, i.e., randomised clinical trials or observational studies. Differences in effect estimates between the two groups of studies were assessed using the χ^2 test as described in the Cochrane Handbook for Systematic Reviews of Interventions. A p value below 0.05 was considered statistically significant. Publication bias was assessed by visual inspection of funnel plots, which are presented for each outcome separately in the Supplementary materials. Review Manager (RevMan, version 5.3.5) was used for all statistical analysis.

Sensitivity analysis

Sensitivity analysis was performed on the outcome re-intervention. The effect estimate of the primary meta-analysis on re-intervention for all indications (including non-union) was compared to the risk estimates of re-intervention for indications other than non-union.

Additional sensitivity analyses were performed for all other outcomes on high quality studies, studies published after 2015 and studies with a mean age higher than 40 years. High quality studies were defined as studies with a MINORS score of 16 or higher (range 0–24). The cut-point of 2015 was chosen based on the median publication year of included studies. The cut-point for age was based on the overall mean age of the patients in the included studies.

Results

Search

Figure 1 presents the flowchart of the literature search and study selection. A total of seven articles were included; two RCTs and five observational studies [13–19].

Study characteristics

The 7 studies included 682 patients; 325 were treated with MIPO and 357 with nailing. Table 1 shows the baseline characteristics of all studies. The overall weighted mean age was 41.0 (range 16–94) years. Among the studies that reported mean age stratified by surgical intervention group, the mean age was 41.9 years in the MIPO and 40.8 years in nail group; for these studies, the overall weighted mean age was 41.3 years. The studies included 470 (68.9%) males. The mean follow-up per study ranged from 6 to 62 months.

The two RCTs included 87 patients of whom 45 were treated with MIPO. Only one trial reported on type of implant used and included dynamic compression plates (DCP) in the MIPO group and unreamed humeral nail UHN™ (Depuis Synthes, Zuchwil, Switzerland) in the nailing group. The five observational studies included 595 patients, of whom 280 were treated with MIPO. Two studies reported on type of implant used and included DCP and

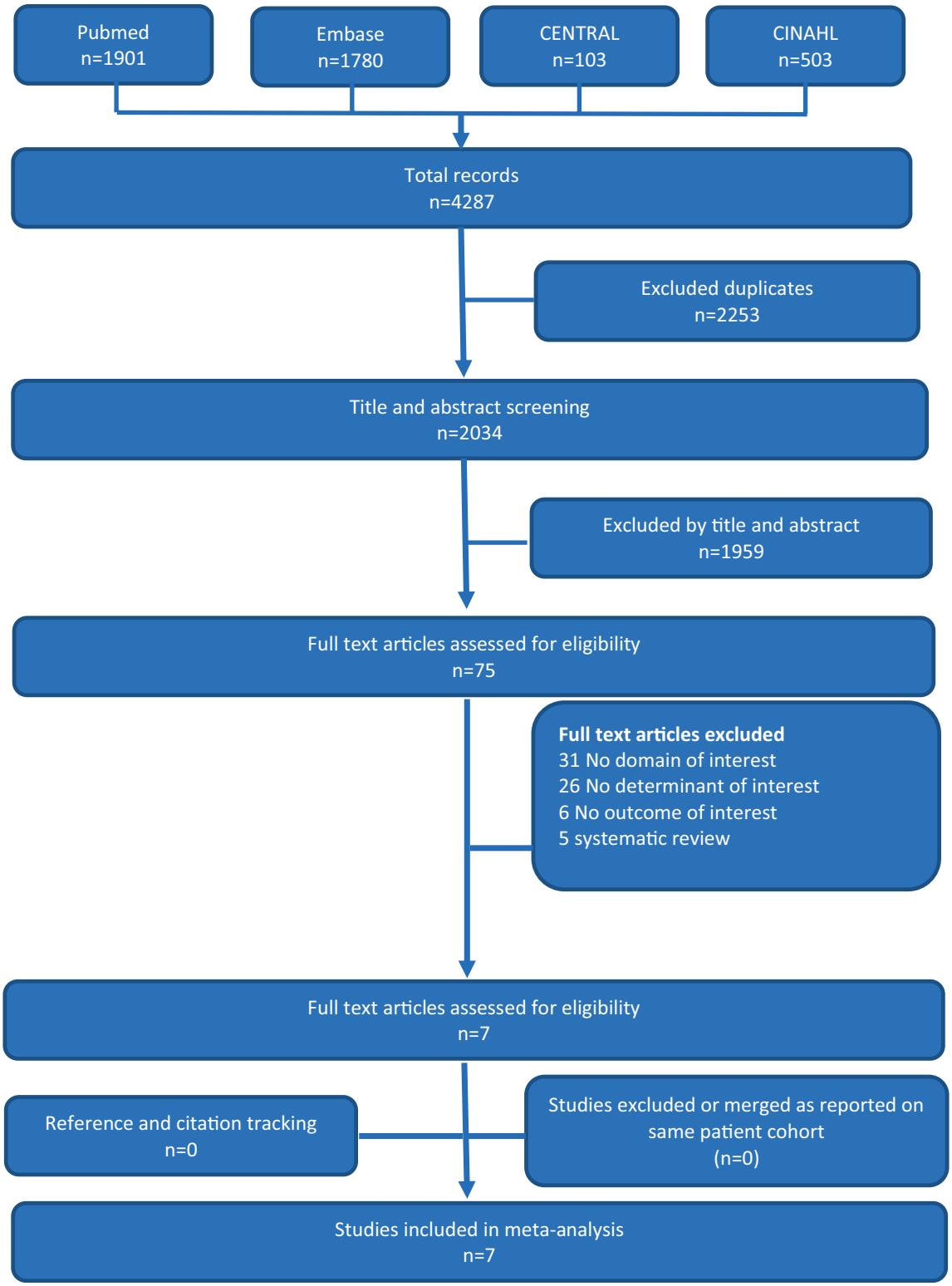

Fig. 1 Flow diagram of search and selection of studies on MIPO versus nailing for humeral shaft fractures

locking compression plates (LCP) in the MIPO group and Fixion™ (Dic-O-Tech, St. Herzliya, Israel) expandable nail for the nailing group.

Table 1 Characteristics of studies included in systematic review of MIPO versus nail for humeral shaft fractures

Author	Year	Country	Design	Study period	Comparison	Implant	Nail	Total number of patients		Gender male/female		Mean age (SD)		Open fracture		AO (A|B|C)		HET		Follow-up (mean and/or range)
						MIPO		MIPO	Nail	MIPO	Nail	MIPO	Nail	MIPO	Nail	MIPO	Nail	MIPO	Nail	
Randomised clinical trials																				
Lian	2013	China	RCT	2007–2010	MIPO|nail (ante/retrograde)	NR	NR	24	23	15|9	16|7	39 (15)	38 (15)	0	0	9|9|5	8|12|2	NR	NR	15 months (range 7–20)
Benegas	2014	Brazil	RCT	2003–2007	MIPO|nail (antegrade)	DCP	UHN	21	19	12|9	14|5	45 (17)	38 (19)	2	1	12|7|2	9|4|6	NR	NR	12 months
Observational studies																				
An	2012	China	Retro	2004–2008	MIPO|nail (antegrade)	DCP	Fixion	15	19	11|4	12|7	34 (8)	40 (14)	0	0	6|7|2	10|8|1	NR	NR	22 months (range 12–62)
Davies	2016	Autralia	Retro	2004–2012	MIPO|nail (antegrade)	NR	NR	15	15	10|5	10|5	48 (20)	47 (17)	NR	NR	6|4|5	6|5|4	NR	NR	> 12 months
Kulkarni	2017	India	Retro	2014–2016	MIPO|nail (antegrade)	NR	NR	34	44	83|29		40 (13)		2	4	18|10|6	31|10|3	NR	NR	> 6 months
Gonçalves	2018	Brazil	Retro	2014–2016	MIPO|nail (NR)	NR	NR	12	5	40|11		35 (14)		NR	NR	34|7|10		35		12 months
Yuan	2019	China	Retro	2010–2016	MIPO|nail (NR)	LCP	NR	204	232	119|84	128|104	42 (15)	41 (13)	NR	NR	115|64|25	127|79|26	NR	NR	26 months (range 16–36)

NR not reported, *Retro* retrospective study, *RCT* randomised clinical trial, *HET* High energy trauma

Quality assessment

The details and distribution of the MINORS scores are described in Table 2. The mean MINORS score was 17 (range 13–23); this was 23 for the 2 RCTs and 15 for the 5 observational studies.

Non-union

Non-union rate was reported in all seven studies [13–19]. Non-union occurred in 1.2% of patients treated with MIPO and 9.0% treated with nailing (weighted RD 7%, 95% CI 1–13%). There was a lower risk of non-union in patients treated with MIPO (weighted OR 0.2 95% CI 0.1–0.5; $I^2 = 0\%$) (Fig. 2). The effect estimates were similar between RCTs (weighted OR 0.4, 95% CI 0.1–2.8; $I^2 = 0\%$) and observational studies (weighted OR 0.1, 95%CI 0–0.5; $I^2 = 0\%$) (test for subgroup difference: p value 0.38; $I^2 = 0\%$).

Re-intervention

Re-intervention was reported in five studies—two RCTs and three observational studies [13, 14, 16, 18, 19]. Re-intervention was required in 7.3% of patients after MIPO and in 22.5% treated with nail fixation (weighted RD 13%, 95% CI 0–28%). MIPO had a lower risk for re-intervention (weighted OR 0.3, 95% CI 0.1–0.8; $I^2 = 16\%$) (Fig. 3). The effect estimates were similar between RCTs (weighted OR 0.6, 95% CI 0–27.8; $I^2 = 76\%$) and observational studies (weighted OR 0.3, 95%CI 0.1–0.7; $I^2 = 0\%$) (test for subgroup difference: p value 0.67; $I^2 = 0\%$).

The most frequent indication for re-intervention among patients treated with MIPO was due to infection ($n = 3$). Other indications included implant removal ($n = 2$), non-union ($n = 2$) and hematoma ($n = 1$) (supplementary material Table 3). The most frequent indication for re-intervention among patients who underwent nailing was non-union ($n = 14$) followed by shoulder impingement complaints ($n = 10$), infection ($n = 2$) and peri-implant fracture ($n = 1$) (supplementary material Table 4).

Time to union

Three studies reported on mean time to union – one RCT and two observational studies [13, 15, 18]. The weighted mean time to union in the MIPO group was 17.6 weeks versus 15.6 weeks in the nailing group. There was no difference in time to union between treatment groups (weighted MD 2.4 weeks, 95% CI − 2.2 to 6.0; $I^2 = 75\%$) (Fig. 4). The effect estimates of RCT (weighted MD 0.3 weeks, 95% CI − 1.0 to 1.6) and observational studies (weighted MD 4.5 weeks, 95%CI − 2.8 to 11.8) were similar (test for subgroup difference: p value 0.27; $I^2 = 18\%$).

Table 2 Quality assessment of studies included in systematic review of MIPO versus nailing for humeral shaft fractures

	Randomised clinical trials	Benegas 2014	Lian 2013	Observational studies	Yuan 2019	Goncalves 2018	Kulkarni 2017	Davies 2016	An 2012
Clearly stated aim		2	2		2	1	2	2	2
Inclusion of consecutive patients		2	2		2	2	2	2	2
Prospective data collection		2	2		0	0	0	0	0
Appropriate endpoints		2	2		1	1	2	2	2
Unbiased assessment endpoints		1	1		0	0	0	0	0
Appropriate follow-up (> 1 year)		2	2		2	1	1	2	2
Loss-to-follow-up < 5%		2	2		1	0	0	0	0
Prospective calculation study size		2	2		0	0	0	0	0
Adequate control group		2	2		2	2	2	2	2
Contemporary groups		2	2		2	2	2	2	2
Baseline quivalence of groups		2	2		2	2	2	2	2
Adequate statistical analysis		2	2		2	2	2	2	2
Total		23	23		16	13	15	16	16

Items based on the MINORS criteria

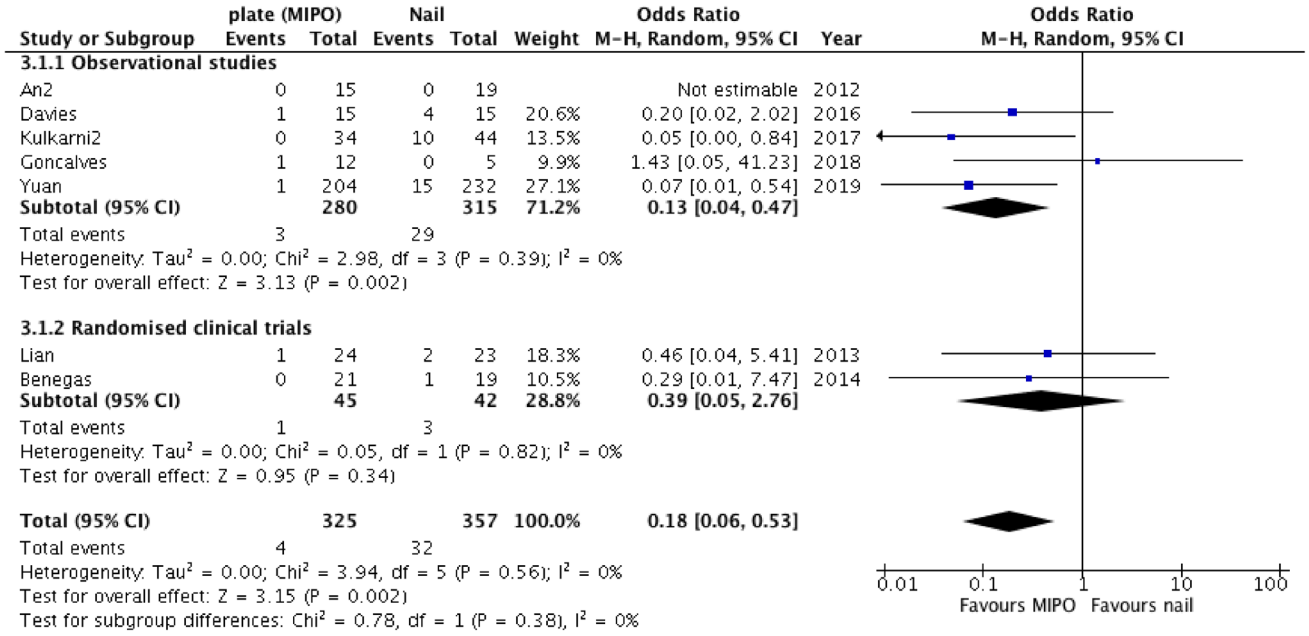

Fig. 2 Forest plot of non-union rate after MIPO versus nailing for humeral shaft fractures

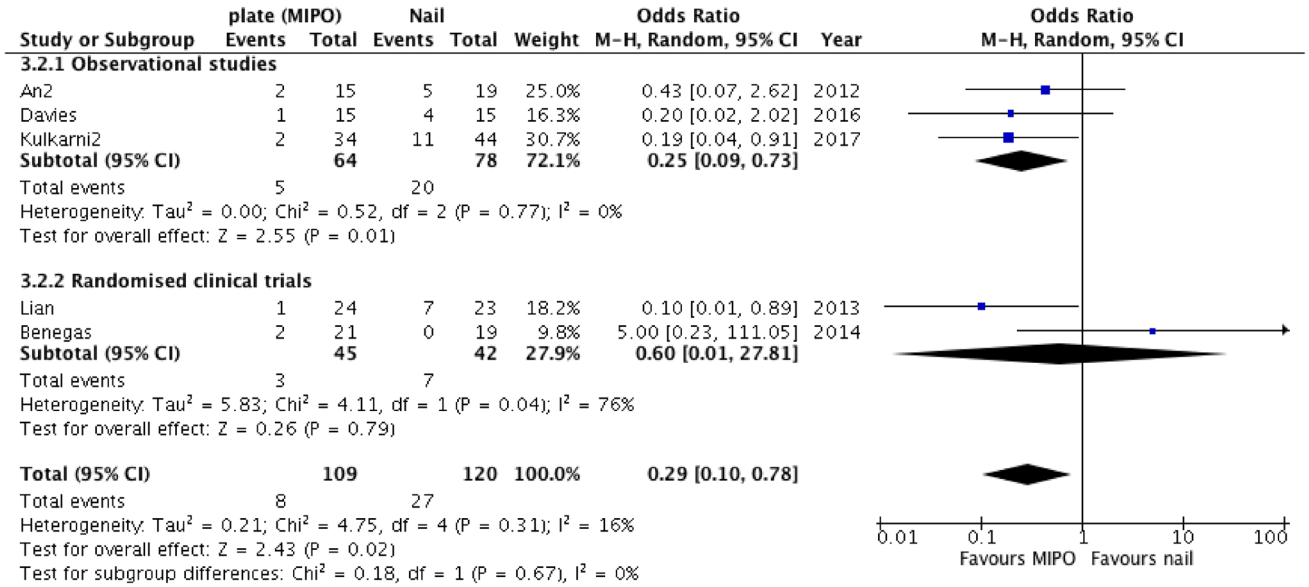

Fig. 3 Forest plot of re-intervention after MIPO versus nailing for humeral shaft fractures

Secondary radial nerve palsy

Secondary radial nerve palsy was reported in all studies. [13–19] Secondary radial nerve palsy occurred in 3.4% of patients treated with MIPO versus 6.4% in the nailing group (weighted RD 2%, 95% CI 0–5%). The risk of radial nerve palsy secondary to operation was equal in both groups (weighted OR 0.6, 95% CI 0.3–1.2; $I^2 = 0\%$) (Fig. 5). The effect estimates in RCTs (weighted OR 0.3, 95% CI 0–3.0; I^2 = not applicable) and observational studies (weighted OR 0.6, 95% CI 0.2–1.9; $I^2 = 18\%$) were similar (test for subgroup difference: p value 0.59; $I^2 = 0\%$). In all patients nerve function recovered spontaneously.

Infection

Infection was reported in six studies—two RCTs and four observational studies [13–16, 18, 19]. Infection occurred in

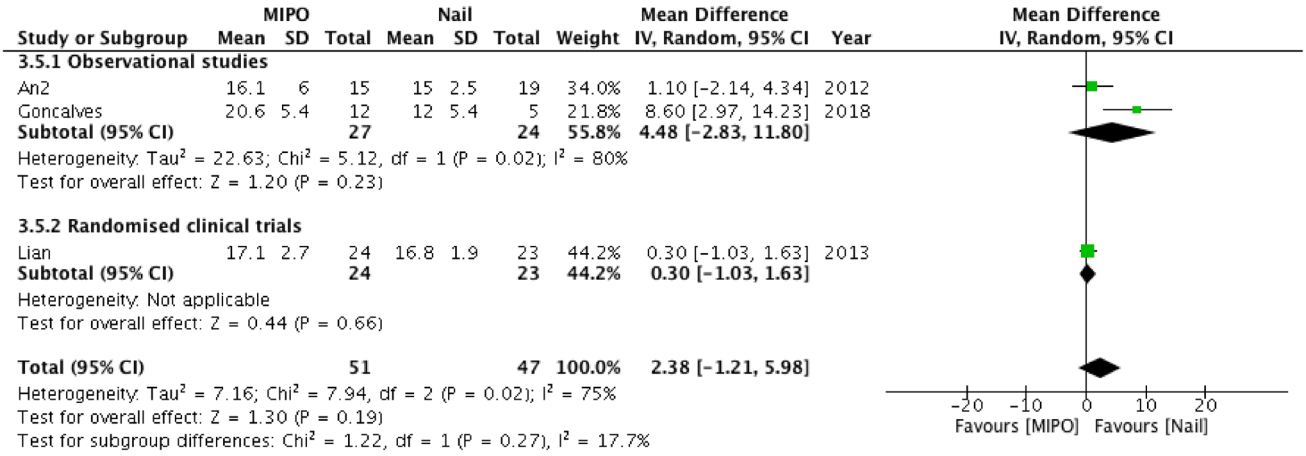

Fig. 4 Forest plot of time to union (weeks) MIPO versus nailing for humeral shaft fractures

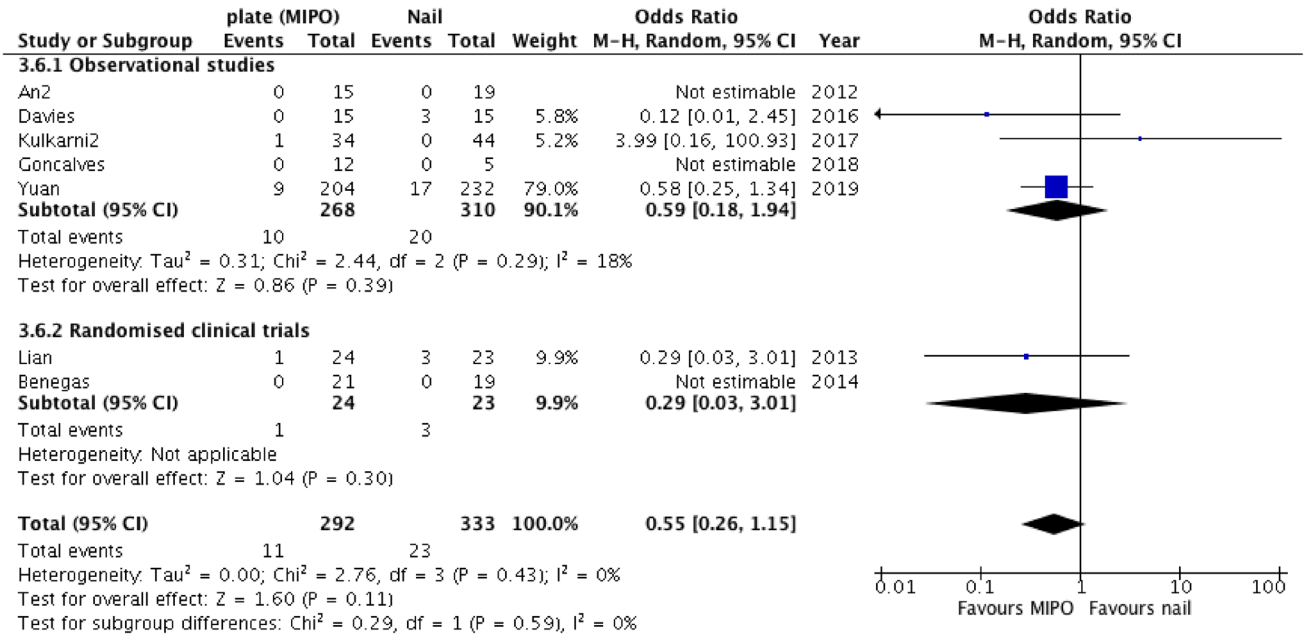

Fig. 5 Forest plot of secondary radial nerve palsy after MIPO versus nailing for humeral shaft fractures

1.7% of patients after MIPO and in 2.3% treated with nailing (weighted RD 0%, 95% CI −5 to −4%). No difference was detected in risk of infection between both treatment groups (weighted OR: 0.9, 95% CI 0.2–3.9; $I^2 = 0\%$) and the effect estimates of RCTs (weighted OR 0.9, 95% CI 0.1–15.5; $I^2 = 0\%$ and observational studies (OR 0.9, 95% CI 0.2–4.9; $I^2 = 0\%$) were similar (test for subgroup difference: p value 0.99; $I^2 = 0\%$) (Fig. 6).

Operation duration

Three studies reported on operation duration—one RCT and two observational studies [13, 17, 18]. The weighted mean operation duration in the MIPO group was 105 min versus 100 min in the nailing group. There was no difference in operation duration between both groups (weighted MD −2 min, 95% CI −30 to 27; I^2=97%) (Fig. 7). The effect estimates of RCTs (weighted MD −31 min, 95% CI −40 to 22; I^2 = not applicable) differed from those of observational studies (weighted MD −2 min, 95% CI −20 to 17; $I^2 = 55\%$) (test for subgroup difference: p value < 0.01; $I^2 = 96\%$).

Functional shoulder scores

Four studies reported on functional shoulder scores—two RCTs and two observational studies [13, 17–19].

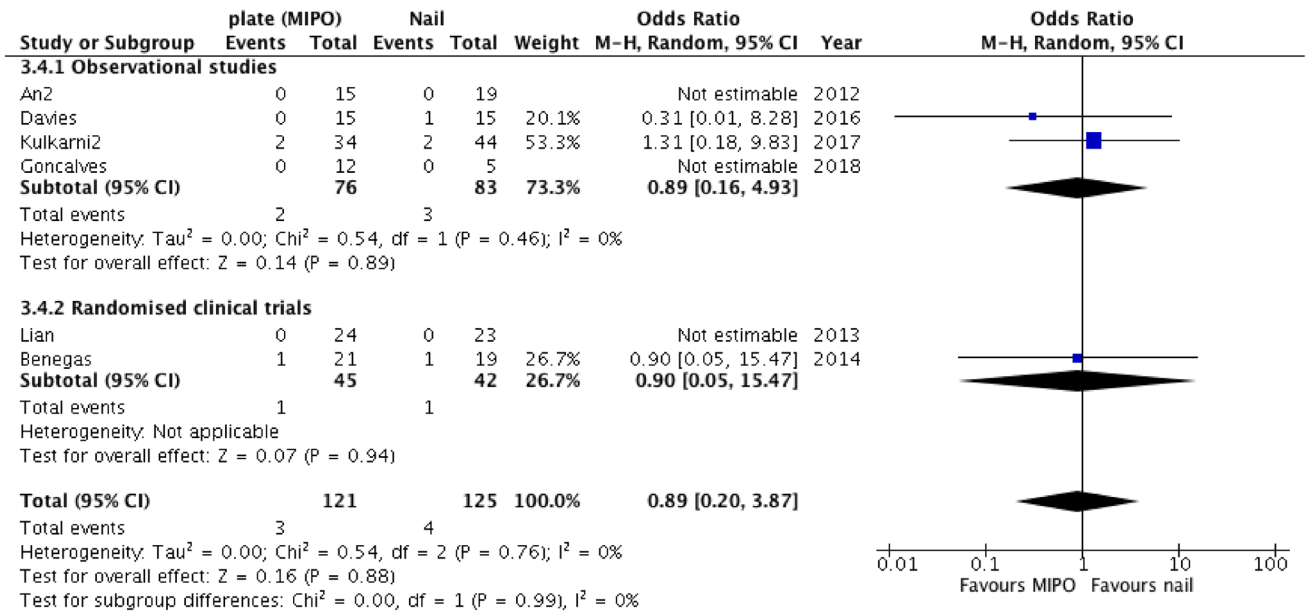

Fig. 6 Forest plot of infection after MIPO versus nailing for humeral shaft fractures

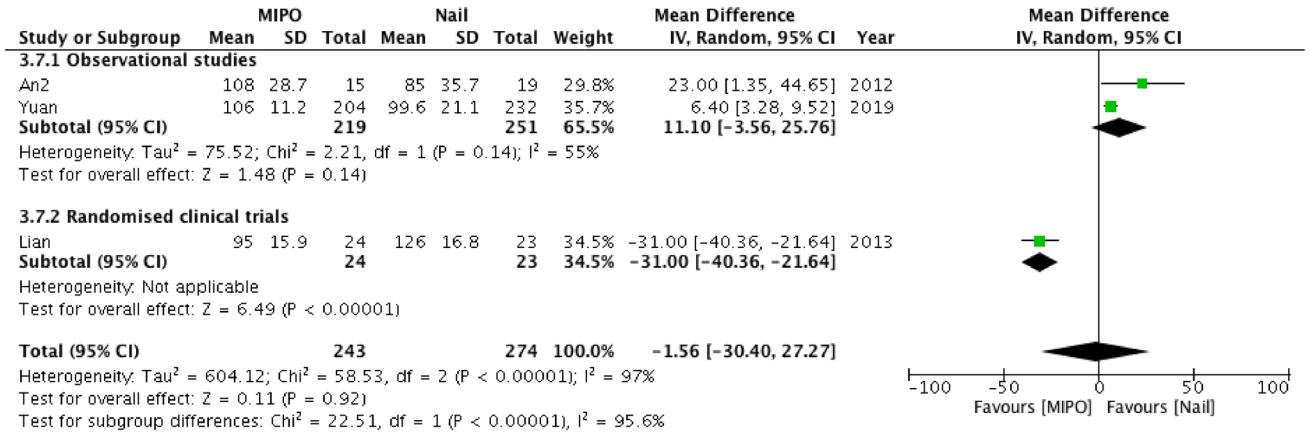

Fig. 7 Forest plot of operation duration (minutes) after MIPO versus nailing for humeral shaft fractures

Functional shoulder scores were better among patients treated with MIPO (weighted SMD 1.0, 95% CI 0.2–1.8; $I^{2=}$90%) (Fig. 8). The estimates of randomised clinical trials (weighted SMD 0.5, 95% CI −0.4 to 1.5; $I^2 = 79\%$) and observational studies (weighted SMD 1.5, 95% CI 1.0–2.1; $I^2 = 61\%$) were similar (test for subgroup difference: p value 0.07; $I^2 = 69\%$).

Functional elbow scores

Four studies reported on functional elbow scores—two RCTs and two observational studies.[13, 17–19] Functional elbow scores were better in patients treated with MIPO (weighted SMD 0.4, 95% CI 0–0.8; $I^2 = 63\%$) (Fig. 9). The estimates of randomised clinical trials (weighted SMD 0.5, 95% CI −0.3 to 1.3; $I^2 = 73\%$) and observational studies (weighted SMD 0.4, 95% CI 0–0.8; $I^2 = 65\%$) were similar (test for subgroup difference: p value 0.83; $I^2 = 0\%$).

Other outcomes

No studies reported on either general quality of life and functional scores of the total upper extremity.

Sensitivity analysis

Re-intervention for indications other than non-union were reported in five studies—two RCTs and three observational

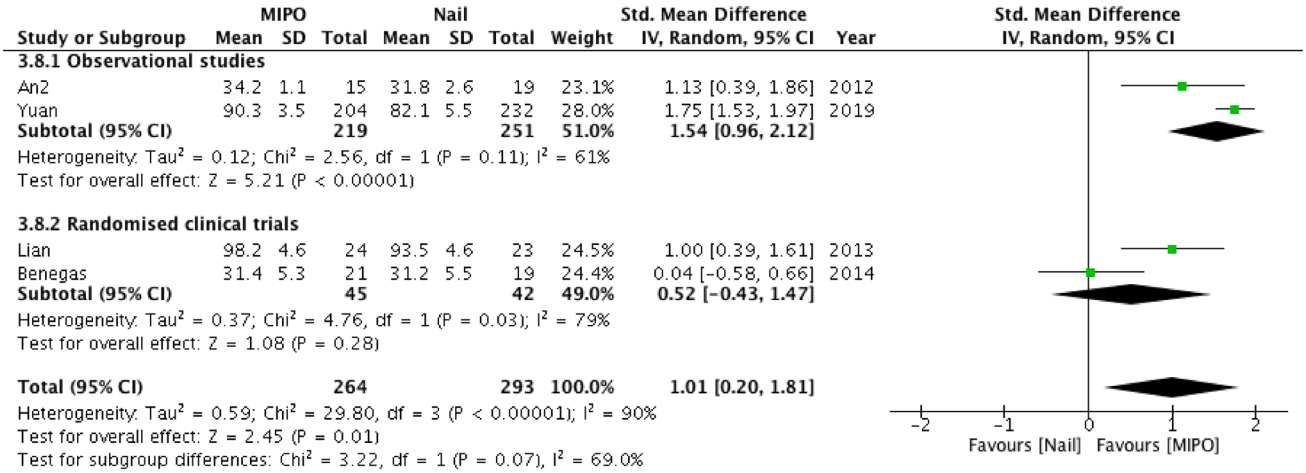

Fig. 8 Forest plot of standardised mean difference in functional shoulder scores after MIPO versus nailing for humeral shaft fractures

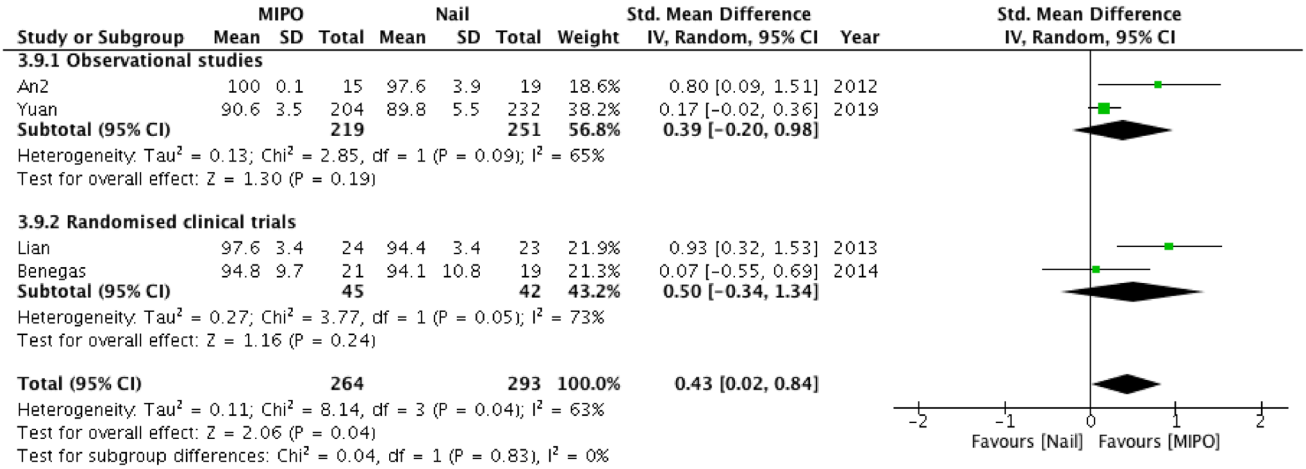

Fig. 9 Forest plot of standardised mean difference in functional elbow scores after MIPO versus nailing for humeral shaft fractures

studies [13, 14, 16, 18, 19]. Re-intervention for indications other than non-union occurred in 3.3% of patients after ORIF and in 6.6% treated with MIPO (weighted RD 0%, 95% CI 0–3%). The pooled analysis showed no significant difference between treatment groups (weighted OR 0.6, 95% CI 0.2–2.9; $I^2 = 0\%$) and the effect estimates of randomised clinical trials and observational studies were similar (test for subgroup difference: p value 0.85; $I^2 = 0\%$) (Fig. 10).

Table 3 shows the results of the sensitivity analysis on all other outcomes with regard to high quality studies, studies published after 2015, and studies with a mean age higher than 40 years. No significant differences were found between the primary analysis and subgroup analysis.

Discussion

This systematic review and meta-analysis of seven studies, including randomised clinical trials and observational studies, compared minimally invasive plate osteosynthesis (MIPO) with nailing in patients with humeral shaft fractures. MIPO carries a lower risk for non-union and re-intervention. Re-intervention in the nailing group was mainly required due to either non-union or shoulder impingement complaints. Functional shoulder and elbow scores were better in patients after MIPO compared to patients treated with nailing. The risk of secondary radial

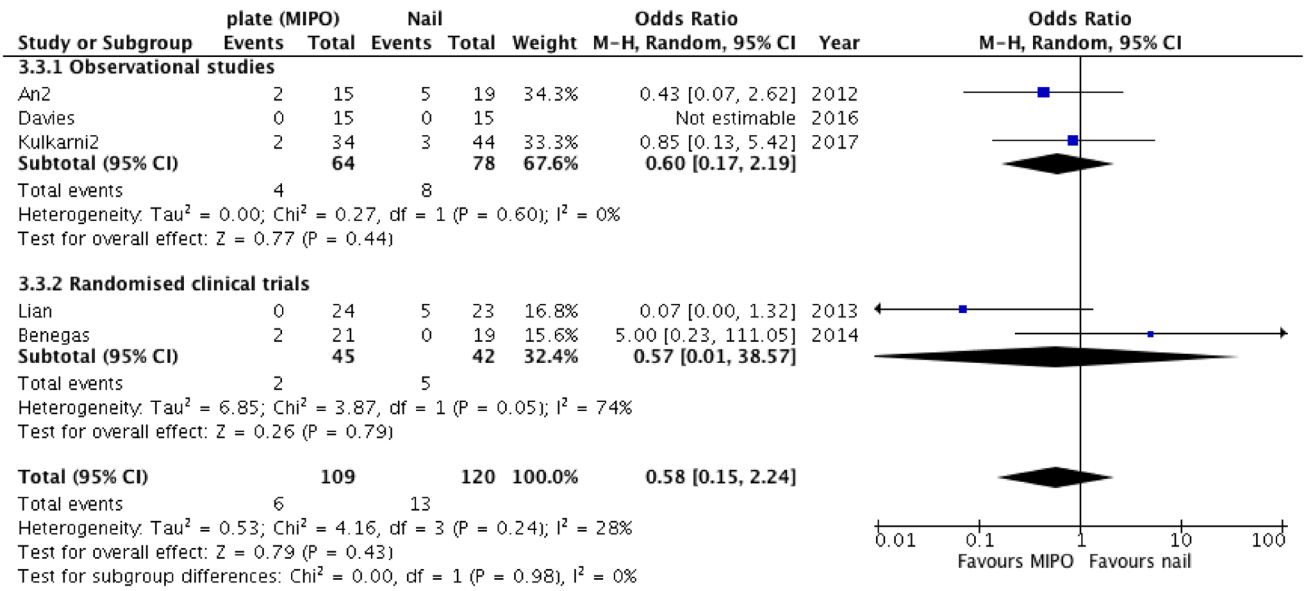

Fig. 10 Forest plot of re-intervention rate (other indications than non-union) after MIPO versus nailing for humeral shaft fractures

Table 3 Results of secondary sensitivity analysis on all outcomes for MIPO versus nail for humeral shaft fractures

	Non-union	Re-intervention	Secondary radial nerve palsy	Time to union (weeks)	Infection	Operation duration (minutes)	Functional shoulder scores	Functional elbow scores
	OR [95% CI]	OR [95% CI]	OR [95% CI]	MD [95% CI]	OR [95% CI]	MD [95% CI]	SMD [95% CI]	SMD [95% CI]
All studies	0.2 [0.1–0.5]	0.3 [0.1–0.8]	0.6 [0.3–1.2]	2.4 [−1.2 to 6.0]	0.9 [0.2–3.9]	−2 [−30 to 27]	1.0 [0.2 to 1.8]	0.4 [0–0.8]
High quality studies	0.2 [0.1–0.6]	0.4 [0.1–1.5]	0.5 [0.2–1.0]	0.4 [−0.8 to 1.7]	0.6 [0.1–4.9]	−2 [−30 to 27]	1.0 [0.2 to 1.8]	0.4 [0–0.8]
Low quality studies	0.2 [0–7.2]	NC	NC	NC	NC	NC	NC	NC
Studies after 2015	0.1 [0–0.5]	0.2 [0.1–0.7]	0.6 [0.2–1.9]	NC	0.9 [0.2–4.9]	NC	NC	NC
Studies before 2015	0.4 [0.1–2.8]	0.5 [0.1–3.1]	NC	0.4 [−0.8 to 1.7]	NC	−5 [−58 to 48]	0.7 [0 to 1.4]	0.6 [0.1–1.1]
Studies age > 40 years	0.1 [0 – 0.4]	0.4 [0.1–2.3]	0.6 [0.2–1.9]	NC	0.9 [0.2–3.9]	NC	0.9 [−0.8 to 2.6]	0.16 [0–0.3]
Studies < 40 years	0.7 [0.1–5.0]	0.2 [0.1–1.0]	NC	2.4 [−1.2 to 6.0]	NC	−5 [−58 to 48]	1.1 [0.6 to 1.5]	0.9 [0.4–1.3]

OR odds ratio, *MD* mean difference, *SMD* standardised mean difference, *95% CI* 95% confidence interval, *NC* not calculable (less than 2 studies available)

nerve palsy after surgery did not differ between treatment groups and nerve function recovered spontaneously in all patients in both groups. No differences were found regarding infection risk, time to union, and operation duration. The effect estimates obtained from RCTs and observational studies were similar for all outcomes except for operation duration.

Comparison with previous findings

To date, five meta-analyses have been published on this subject. Noteworthy, none compared MIPO directly to nailing in a traditional meta-analysis. Hohmann et al. and Zhang et al. published their meta-analyses in 2016 comparing MIPO to a control group consisting of ORIF and nailing combined [20, 21]. They found a shorter operation

duration, better functional results and lower complication rate in favour of MIPO. As the alternative techniques (nailing and ORIF) were grouped together, it is not possible to determine to which one of the two techniques MIPO was superior. Wen et al. published a meta-analysis comparing plating, in general, to nailing in 2019 [4]. In a subgroup analysis of two studies, they found an equal risk of infection and lower risk of non-union for MIPO compared to nailing, as also demonstrated in our study. No differences were observed in functional shoulder and elbow scores, possibly due to limited power compared to the present meta-analysis. Qui et al. and Zhao et al. performed a network analysis in 2016 and 2017, respectively, to overcome the insufficiency of direct evidence at that time [22, 23]. Although MIPO ranked as best treatment in a general sense, no difference were found regarding the individual outcomes non-union, time to union, infection, radial nerve palsy, operation time, and complication rate. Furthermore, functional shoulder and elbow scores were not analysed and they did not take into account that there might be a difference in effect estimates between observational studies and randomised clinical trials. The present traditional meta-analysis could detect differences in several outcomes of interest, most likely because treatment modalities were solely directly compared and due to a larger amount of studies available for analysis.

Interpretation of results

MIPO showed some remarkable and pronounced differences with nailing. There was a fairly large difference in risk of non-union (weighted RD 7%) and re-intervention (weighted RD 13%) in favour of MIPO. Re-intervention in the nailing group was mainly required for non-union (52%) and shoulder impingement (37%), a complication specific for the use of antegrade nails in humeral shaft fractures [4].

The difference in functional shoulder scores was also relatively large as demonstrated by a weighted SMD of 1.0. Half a standard deviation of health-related quality of life scores corresponds with the minimal important clinical difference (MID) [24]. A weighted SMD of 1.0 is twice this MID. Therefore, it may be expected that the difference between MIPO and nailing in shoulder function is highly noticeable in a clinical setting.

To a lesser extent, there was also a difference in functional elbow scores favouring MIPO as demonstrated by a weighted SMD of 0.4. It is difficult to understand what the driving mechanism is behind the negative effect of nailing on elbow function, as almost all studies used antegrade nailing and practically none a retrograde technique, which are known to cause elbow complaints [25]. That being said, the SMD was below the MID threshold making it less relevant for clinical practice.

We observed a difference between effect estimates obtained from RCTs and observational studies on the outcome operation duration. Operation duration is a variable that is highly dependent on experience of the surgeon inevitably leading to large heterogeneity when measured as an outcome, as also found in the present study. This hampers the interpretation of the pooled effect estimate.

Implications for the future

Surgical implants and techniques for fixation of humeral shaft fractures are rapidly developing. On the field of nailing, straight nails are increasingly being used as they are believed to cause less shoulder complaints [26]. Interest in the use of helical plates is growing, as these facilitate minimally invasive plating for more proximal humeral shaft fractures [27]. New MIPO techniques are emerging making it possible to treat fractures in the most distal part of the humeral shaft that would otherwise have been treated with an open posterior approach and conventional plating [28]. It would be interesting to be able to include these subtleties in future research and investigate how these developments affect the results.

Finally, when considering implicating MIPO as standard technique for treating humeral shaft fractures in daily practice, the learning curve should be taken into account. Previous studies have shown higher risks for complications during this period, but in the current study we had no information available to investigate this aspect [29]. The safest way is to see these results in a setting, where there already is an established level of expertise for MIPO.

This meta-analysis a part of a large project aiming to compare all literature on treatment options for humeral shaft fractures directly with one another. The comparison of conservative versus operative treatment, minimally invasive plating versus open plating and nailing versus open plating are addressed other meta-analyses [2, 30].

Limitations

Several limitations have to be considered. Firstly, there was considerable heterogeneity for the outcomes re-intervention, operation duration, and time to union making the effect estimates less accurate. Secondly, a relatively small number of studies was available for pooled analysis of which particularly the number of randomised trials was small. Thirdly, although baseline characteristics were comparable across treatment groups (both in the RCTs and observational studies), any residual confounding among observational studies cannot be ruled out. Specifically, we could not take into account the level of expertise each hospital, where the included studies were performed, had with MIPO and correct for level of training.

Conclusion

MIPO has a considerable lower risk for non-union and re-intervention, leads to better shoulder function and, to a lesser extent, better elbow function compared to nailing. Although secondary radial nerve palsy following surgery occurs in both groups, nerve function recovered spontaneously in all of our patients. Infection is equally rare in both groups and no differences were detected in operation duration and time to union. These results should, however, be seen in the setting, where there is an established level of expertise for MIPO.

In conclusion, the evidence suggests that MIPO should be the preferred treatment in humeral shaft fractures, taking into account the level of training one has with this technique.

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Compliance with ethical standards

Conflict of interest None.

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