Complications in humeral shaft fractures – non-union, iatrogenic radial nerve palsy, and postoperative infection: a systematic review and meta-analysis

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- The aim of this systematic review and meta-analysis was to assess risk for iatrogenic radial nerve palsy (iRNP), non-union, and post-operative infection in humeral shaft fractures.
- A PubMed search including original articles comparing different treatments for humeral shaft fractures published since January 2000 was performed. Random effect models with relative risks (RR) and 95% CIs were calculated for treatment groups and outcomes.
- Of the 841 results, 43 studies were included in the meta-analysis (11 level II, 5 level III, 27 level IV). Twenty-seven compared intramedullary nailing (IM) with ORIF, nine conservative with operative treatment, four ORIF with minimally invasive plate osteosynthesis (MIPO), and three anterior/anterolateral with posterior approach. iRNP risk was higher for ORIF vs IM (18 studies; RR: 1.80; $P=0.047$), ORIF vs MIPO (4 studies; RR: 5.60; $P=0.011$), and posterior vs anterior/anterolateral approach (3 studies; RR: 2.68; $P=0.005$). Non-union risk was lower for operative vs conservative therapy (six studies; RR: 0.37; $P<0.001$), but not significantly different between ORIF and IM (21 studies; RR: 1.00; $P=0.997$), or approaches (two studies; RR: 0.36; $P=0.369$). Post-operative infection risk was higher for ORIF vs IM (14 studies; RR: 1.84; $P=0.004$) but not different between approaches (2 studies; RR: 0.95; $P=0.960$).
- Surgery appears to be the method of choice when aiming to secure bony union, albeit risk for iRNP has to be considered, particularly in case of ORIF vs IM or MIPO, and posterior approach. Due to the limited number of randomised studies, evidence on the best treatment option remains moderate, though.

Keywords

- humeral shaft fracture
- postoperative complications
- treatment

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Introduction

The incidence of humeral shaft fractures is estimated at 13 per 10 000 patients per year (1), amounting to 1.0–3.0% of all fractures (2, 3, 4). Humeral shaft fractures may be treated by conservative or operative modalities, with specific constellations as polytrauma, vascular injury, instability, or open fracture demanding a surgical approach (5, 6). The frequency of surgical therapy has increased over the years (7), including plate osteosynthesis via a conventional open reduction and internal fixation (ORIF) or minimally invasive plate osteosynthesis (MIPO), and retrograde and antegrade intramedullary nailing

(IM) (6, 8, 9). Complications of both conservative and operative treatment approaches are non-union, while post-operative infections and iatrogenic radial nerve palsy (iRNP) do naturally occur following surgical therapy.

As complication profiles are known to differ between conservative and surgical therapy, operative techniques, and implant types, but this evidence is largely based on individual comparative studies, the herein performed systematic review and meta-analysis aim at analysing the outcome for treatment of humeral shaft fractures, focusing on risk for non-union, iRNP, and post-operative infection.

Methods

Search strategy, selection criteria

The current systematic review adhered to the PRISMA guidelines (10). A literature search in PubMed was performed for the current systematic review and meta-analysis, using the following search term: ((humerus) AND (shaft)) AND (fracture). All studies published from 1 January 2020 until 21 December 12 were potentially eligible (Supplementary Table 1 for full search code, see section on [supplementary materials](#) given at the end of this article). Notably, studies identified through other sources were not limited to a specific publication date.

Inclusion criteria

Any English or German original cohort study (either randomised controlled trial (RCT), prospective non-randomised study, or retrospective cohort study) dealing with humeral shaft fractures, comparing two treatment approaches, and assessing at least one of the three outcomes namely iRNP, non-union, or infection were potentially eligible.

Exclusion criteria

All other publications, including (systematic) reviews, meta-analyses, Cochrane reviews, case reports, expert opinions, editorials, study protocols, non-comparative studies, those with insufficient information, pathological fractures, and non-English or -German articles were excluded. Data extraction was performed by one of the co-authors (MAS). In case of discrepant findings, decision towards article inclusion or exclusion was reached after thorough consideration and discussion amongst co-authors (SB, MAS).

Analysis of data

Items assessed from the individual studies included: outcome measure (i.e. iRNP, non-union, infection), comparison group (e.g. conservative vs operative, MIPO vs ORIF, IM vs ORIF), patient number, and those experiencing and non-experiencing the outcome parameter. Furthermore, level of evidence as defined by the Oxford Centre for Evidence-Based Medicine (OCEBM) was ascertained (11).

The Newcastle–Ottawa scale (NOS) for non-randomised case–control and cohort studies was used to assess quality of all publications included (12). Notably, also the quality of those eight studies reporting on randomised cohorts was assessed with the NOS to allow comparability to publications with non-randomised cohorts. The NOS itself is based on the three items selection (maximum 4 points), comparability (maximum 2 points), and outcome

(for cohort studies; maximum 3 points) or exposure (for case-control studies; maximum 3 points). A total score ranging from 0 to 9 results from adding the scores of individual items, with higher values indicating higher study quality (12).

Statistical analysis

All statistical analyses were performed with Stata/SE 16.1 for Mac (StataCorp LLC, College Station, Texas, United States). For each outcome parameter and comparison group, random effect models using restricted maximum likelihood methods were calculated and relative risks (RR) with corresponding 95% CI provided. RCTs, prospective case–control studies, and retrospective case–control studies were pooled, thus increasing the sample size, as previously described (13, 14, 15). Heterogeneity between studies pooled in each model was assessed with Higgins I^2 (16). Small, medium, and large heterogeneity was defined as I^2 amounting to $\leq 25\%$, $>25\text{--}<50\%$, and $>75\%$, respectively (16). Harbord test was used to assess presence of publication bias (17). In case heterogeneity was medium to large, and/or publication bias was present, additional sensitivity analyses to assess the robustness of findings were performed. As recommended by the Cochrane Handbook for Systematic Reviews of Interventions, studies with zero events in both arms were excluded from the meta-analysis itself (18).

Results

Literature search retrieved 841 results. Additional 57 studies were identified through cross-reference checking of literature in previous original articles and (systematic) reviews on humeral shaft fractures, resulting in 898 articles. After removal of 5 duplicates, 893 entries were screened, of whom 641 were subsequently excluded. The remaining 252 full-text articles were assessed for eligibility. After excluding further 193 full-text articles not meeting the inclusion criteria, 59 studies remained. Further 16 studies were excluded as comparing similar approaches or implant types ($n=10$), dealing with outcome following persisting non-union ($n=4$), involving pathological humeral fracture ($n=1$), or analysing outcome between primary and delayed surgery ($n=1$). Thus, 43 studies were included in the final quantitative meta-analysis (Fig. 1).

Study characteristics

Altogether, the 43 studies investigated comprised 7688 patients with humeral shaft fractures. Eleven studies were randomised controlled trials (level II; 25.6%) (19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29), 5 were prospective

Figure 1

Flow chart showing study selection.

non-randomised case-control studies (III; 11.6%) (30, 31, 32, 33, 34), and 27 were retrospective cohort studies (IV; 62.8%) (6, 8, 9, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58). Twenty-seven studies compared IM with ORIF (6, 19, 20, 22, 24, 25, 26, 27, 28, 29, 30, 31, 33, 36, 39, 40, 41, 42, 47, 48, 52, 53, 54, 55, 56, 57, 58) (including two studies with external fixator (39) or MIPO (42) as third comparator that was not considered upon meta-analysis), nine studies compared conservative with operative treatment attempt (23, 34, 35, 38, 43, 45, 49, 50, 51) (including one study on paediatric humeral shaft fractures (43)), four studies compared MIPO with ORIF (21, 32, 37, 46), and three studies compared anterior or anterolateral with posterior approach to the humeral shaft (8, 9, 44). Mean NOS score over all 43 studies included was 6.0 ± 0.8 points (Table 1).

Subsequently, the three outcomes, iRNP, non-union, and post-operative infection, will be outlined for individual comparator groups.

Iatrogenic radial nerve palsy risk

Of 34 studies involving patients treated surgically by different methods, 25 reported outcomes on post-operative radial nerve palsy (8, 9, 19, 20, 21, 22, 24, 25, 26, 29, 30, 31, 32, 33, 36, 37, 40, 44, 46, 47, 48, 52, 54, 55, 57). Eighteen of these studies compared IM with ORIF (19, 20, 22, 24, 25, 26, 29, 30, 31, 33, 36, 40, 47, 48, 52, 54, 55, 57), four MIPO with ORIF (21, 32, 37, 46), and another three anterior/anterolateral with posterior surgical approaches to the humeral shaft (8, 9, 44).

IM vs ORIF

Of the 18 studies reporting on radial nerve palsy risk following IM vs ORIF, 7 were level II (19, 20, 22, 24, 25, 26, 29), 3 level III (30, 31, 33), and 8 level IV (36, 40, 47, 48, 52, 55, 55, 57).

Whilst the subgroup analyses for retrospective (RR: 1.59; 95% CI: 0.76–3.33; $P=0.089$) and prospective studies (RR: 2.19; 95%CI: 0.86–5.57; $P=0.100$) revealed a non-significantly higher iRNP risk for ORIF in comparison to IM, the overall meta-analysis showed a significantly increased iRNP risk for ORIF (RR: 1.80; 95%CI: 1.01–3.21; $P=0.047$; Fig. 2). Between-study heterogeneity was small ($I^2=0.0\%$), and no significant publication bias was present (Harbord's $P=0.927$).

MIPO vs ORIF

According to the meta-analysis of four studies on MIPO vs ORIF (21, 32, 37, 46) (one level II (21), one level III (32), two level IV (37, 46)), risk for iRNP was significantly higher for ORIF in comparison to MIPO (RR for ORIF: 5.60; 95% CI: 1.48–21.18; $P=0.011$; Fig. 3A). Heterogeneity between studies was small ($I^2=0.0\%$). No significant publication bias was found (Harbord's $P=0.839$).

Anterior/anterolateral vs. posterior approach

All three studies comparing anterior or anterolateral with posterior approach to the humeral shaft and reporting on post-operative radial nerve palsy risk were level IV (8, 9, 44). Following a posterior approach, risk of developing iRNP was significantly higher in comparison to an anterior or anterolateral approach (RR: 2.68; 95% CI: 1.34–5.36;

Table 1 Description of studies included together with Newcastle–Ottawa scale (NOS).

Study	Groups	Patients, <i>n</i>	Outcome factors	LOE	Newcastle–Ottawa scale			
					Selection	Comparability [‡]	Outcome	Total
Conservative vs operative treatment								
Westrick <i>et al.</i> (35)	Conservative	69	NU	IV	****		**	6
	Operative	227						
Harkin <i>et al.</i> (38)	Conservative	96	NU	IV	****		*	5
	Operative	30						
Matsunaga <i>et al.</i> (23)	Conservative	46	NU, infection	II	***	*	**	6
	Operative	50						
O’Shaughnessy <i>et al.</i> (43)	Conservative	65	Iatrogenic RNP, NU	IV	***		**	5
	Operative	15						
Jawa <i>et al.</i> (45)	Conservative	21	NU	IV	****		*	5
	Operative	19						
Denard <i>et al.</i> (49)	Conservative	63	NU	IV	***		**	5
	Operative	150						
Broadbent <i>et al.</i> (34)	Conservative	89	NU	III	****		**	6
	Operative	21						
Dielwart <i>et al.</i> (50)	Conservative	31	NU	IV	****		*	5
	Operative	40						
Ekholm <i>et al.</i> (51)	Conservative	20	NU	IV	****		**	6
	Operative	7						
Intramedullary nailing vs ORIF								
Schwab <i>et al.</i> (36)	IM	62	Iatrogenic RNP	IV	***		**	5
	ORIF	89						
Bisaccia <i>et al.</i> (39)	IM	26	NU, infection	IV	****	*	**	7
	ORIF	32						
	(Fixateur Externe [†])	(21 [†])						
Changulani <i>et al.</i> (19)	IM	23	Iatrogenic RNP, NU, infection	II	***		**	5
	ORIF	24						
Li <i>et al.</i> (20)	IM	32	Iatrogenic RNP, NU, infection	II	***	*	***	7
	ORIF	33						
Denies <i>et al.</i> (40)	IM	49	Iatrogenic RNP, NU, infection	IV	****		**	6
	ORIF	42						
Putnam <i>et al.</i> (41)	IM	591	Infection	IV	***		**	5
	ORIF	1418						
Singiseti & Ambedkar (30)	IM	20	Iatrogenic RNP, NU, Infection	III	****		**	6
	ORIF	16						
McCormack <i>et al.</i> (22)	IM	21	Iatrogenic RNP, NU, infection	II	***		**	5
	ORIF	23						
Kulkarni <i>et al.</i> (42)	IM	44	NU, infection	IV	****		*	5
	ORIF	34						
	(MIPO [†])	(34 [†])						
Kumar <i>et al.</i> (31)	IM	15	Iatrogenic RNP, NU, infection	III	****		*	5
	ORIF	15						
Wali <i>et al.</i> (24)	IM	25	Iatrogenic RNP, infection	II	***	*	**	6
	ORIF	25						
Akalin <i>et al.</i> (25)	IM	30	Iatrogenic RNP, NU, infection	II	****	*	***	8
	ORIF	33						
Fan <i>et al.</i> (26)	IM	30	Iatrogenic RNP, NU, infection	II	****		***	7
	ORIF	30						
Khan <i>et al.</i> (47)	IM	30	Iatrogenic RNP, NU, infection	IV	***		**	5
	ORIF	30						
Raghavendra & Bhalodia (33)	IM	18	Iatrogenic RNP, NU, infection	III	***		***	6
	ORIF	18						
Hashmi <i>et al.</i> (48)	IM	22	Iatrogenic RNP, NU, infection	IV	***		***	6
	ORIF	39						
Lian <i>et al.</i> (27)	IM	23	NU	II	****		***	7
	ORIF	24						
Chao <i>et al.</i> (52)	IM	56	Iatrogenic RNP, NU	IV	***		***	6
	ORIF	36						
Chapman <i>et al.</i> (28)	IM	38	NU, infection	II	****		***	7
	ORIF	46						
Goncalves <i>et al.</i> (53)	IM	5	NU	IV	****		**	6
	ORIF	41						
Gottschalk <i>et al.</i> (6)	IM	870	NU, infection	IV	****		**	6
	ORIF	2560						
Kulkarni <i>et al.</i> (54)	IM	31	Iatrogenic RNP, NU	IV	***		**	5
	ORIF	25						
Putti <i>et al.</i> (54)	IM	16	Iatrogenic RNP, NU, infection	IV	***	*	***	7
	ORIF	18						
Radulescu <i>et al.</i> (29)	IM	102	Iatrogenic RNP, NU	II	***	*	***	7
	ORIF	82						
Wang <i>et al.</i> (56)	IM	26	NU	IV	****		***	7
	ORIF	30						

Zhang <i>et al.</i> (57)	IM ORIF	34 46	Iatrogenic RNP, NU	IV	***	*	***	7
Benegas <i>et al.</i> (58)	IM ORIF	11 14	NU	IV	****	*	***	8
MIPO vs ORIF								
Lee and Yoon (37)	MIPO ORIF	24 28	Iatrogenic RNP	IV	****	*	**	7
Kim <i>et al.</i> (21)	MIPO ORIF	36 32	Iatrogenic RNP (infection*)	II	****		***	7
Esmailieh <i>et al.</i> (32)	MIPO ORIF	32 33	Iatrogenic RNP, NU (infection*)	III	****	*	**	7
An <i>et al.</i> (46)	MIPO ORIF	17 16	Iatrogenic RNP (infection*)	IV	****		*	5
Surgical Approaches								
Lotzien <i>et al.</i> (9)	A/AA PA	33 25	Iatrogenic RNP, NU, infection	IV	***		**	5
Streufert <i>et al.</i> (44)	A/AA PA (PS†)	97 94 (68†)	Iatrogenic RNP, infection	IV	****	*	**	7
Li <i>et al.</i> (8)	A/AA PA	50 57	Iatrogenic RNP, NU, infection	IV	***		***	6

†Not included in meta-analysis; *patients with primary nerve injury excluded; *Asterisks depict allocated points per item assessed.

A/AA, anterior/anterolateral approach; IM, intramedullary nailing; LOE, level of evidence; MIPO, minimally invasive plate osteosynthesis; NU, non-union; ORIF, open reduction internal fixation; PA, posterior approach; PS, posterior split; RNP, radial nerve palsy.

$P = 0.005$; Fig. 3B). Heterogeneity was small ($I^2 = 0.0\%$), and no publication bias was found (Harbord's $P = 0.903$).

Non-union risk

Thirty-five studies reported on non-union risk following humeral shaft fractures, with 24 studies comparing IMs with ORIF (6, 19, 20, 22, 25, 26, 27, 28, 29, 30, 31, 33, 39, 40, 42, 47, 48, 52, 53, 54, 55, 56, 57, 58), 9 studies conservative with operative treatment (23, 34, 35, 38, 43, 45, 49, 50, 51), and 2 anterior/anterolateral with posterior approach (8, 9). Of these 35 articles, 9 reported on level II studies (19, 20, 22, 23, 25, 26, 27, 28, 29), 4 on level III studies (30, 31, 33, 34), and 22 on level IV studies (6, 8, 9, 23, 35, 38, 39, 40, 42, 43, 45, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58).

Conservative vs operative treatment

Nine studies (one level II (23), one level III (34), seven level IV (35, 38, 43, 45, 49, 50, 51)) reported on non-union rate following conservative vs operative treatment. Three (43, 45, 51) (one including paediatric patients (43)) reported on no events in either arm, wherefore they were excluded from the final meta-analysis.

According to the meta-analysis of remaining six studies, risk for non-union was significantly lower after operative treatment (RR: 0.37; 95% CI: 0.25–0.56; $P < 0.001$; Fig. 4A). Heterogeneity was small ($I^2 = 0.0\%$). No significant publication bias was present (Harbord's $P = 0.908$).

Anterior/anterolateral vs posterior approach

Meta-analysis of the two studies (both level IV (8, 9)) comparing surgical approaches to the humeral shaft revealed no significantly altered risk to develop non-union (RR for posterior approach: 0.36; 95% CI: 0.04–3.36; $P = 0.369$; Fig. 4B), with small heterogeneity ($I^2 = 0.0\%$). Publication bias could not be assessed.

IM vs ORIF

Twenty-four studies (8 level II (19, 20, 22, 25, 26, 27, 28, 29), 3 level III (30, 31, 33), 13 level IV (6, 39, 40, 42, 47, 48, 52, 53, 54, 55, 56, 57, 58)) reported on non-union risk for IM vs ORIF. In three (47, 48, 58) of these studies, no event was reported in either arm, wherefore these were excluded from the meta-analysis.

Meta-analysis of the remaining 21 studies revealed no significant difference in non-union risk between IM and ORIF (RR for ORIF: 1.00; 95% CI: 0.71–1.41; $P = 0.997$; Fig. 5). Heterogeneity was small ($I^2 = 0.0\%$), and no significant publication bias was encountered (Harbord's $P = 0.882$). Subgroup analysis for retrospective (RR: 1.08; 95% CI: 0.70–1.66; $P = 0.719$) and prospective studies (RR: 0.86; 95% CI: 0.48–1.55; $P = 0.621$) revealed likewise no significantly differing non-union risk for IM vs ORIF.

Post-operative infection risk

Altogether, 24 of 34 studies reporting on surgically treated patients with humeral shaft fractures provided information on post-operative infections. These included 18 studies comparing IM with ORIF (6, 19, 20, 22, 24, 25, 26, 28, 30, 31, 33, 39, 40, 41, 42, 47, 48, 55), 3 comparing anterior/anterolateral with posterior approach (8, 9, 44), and 3 comparing MIPO with ORIF (21, 32, 46). However, the latter group was not analysed as two of the three articles reported on zero-event outcomes (21, 46). Of the remaining 21 studies, 7 were level II (19, 20, 22, 24, 25, 26, 28), 3 level III (30, 31, 33), and 11 level IV (6, 8, 9, 39, 40, 41, 42, 44, 47, 48, 55).

IM vs ORIF

Of the 18 studies reporting on post-operative infection risk following IM vs ORIF, 7 were level II (19, 20, 22, 24, 25, 26, 28), 3 level III (30, 31, 33), and 8 level IV studies

Radial Nerve Palsy (RNP) Risk - IM vs. ORIF

Legend: RNP - Radial Nerve Palsy; IM - Intramedullary Nailing; ORIF - Open Reduction Internal Fixation based on univariate binary outcomes

Figure 2

Forest plot of studies analysing post-operative radial nerve palsy risk depending on intramedullary nailing vs ORIF. Amber diamond depicts effect size for subgroups prospective (top) and retrospective (bottom) studies. Red diamond shows overall effect size, solid red line overall effect size value, and dashed black line the no-effect line.

(6, 39, 40, 41, 42, 47, 48, 55). Four of these (20, 26, 33, 39) reported on zero events in both arms, wherefore they were excluded from the meta-analysis.

The final meta-analysis with 14 studies revealed a significantly higher post-operative infection risk for ORIF in

comparison to IM (RR for ORIF: 1.84; 95% CI: 1.22–2.79; $P=0.004$; Fig. 6A). Heterogeneity was small ($I^2 = 0.0\%$), and no significant publication bias was encountered (Harbord's $P=0.884$). Notably, subgroup analysis of retrospective ($P=0.021$) studies revealed a significantly

A

Radial Nerve Palsy (RNP) Risk - MIPO vs. ORIF

Legend: RNP - Radial Nerve Palsy; MIPO - Minimally Invasive Plate Osteosynthesis; ORIF - Open Reduction Internal Fixation based on univariate binary outcomes

B

Radial Nerve Palsy Risk - Anterior/Anterolateral vs. Posterior Approach

Legend: RNP - Radial Nerve Palsy based on univariate binary outcomes

Figure 3

Forest plot of studies analysing post-operative radial nerve palsy risk depending on MIPO vs ORIF (A) and anterior/anterolateral vs posterior approach (B). Red diamond shows overall effect size, solid red line overall effect size value, and dashed black line the no-effect line.

higher infection risk for ORIF, while the effect was only marginally significant for prospective studies ($P = 0.059$).

Anterior/anterolateral vs posterior approach

Three studies reported on infection risk depending on surgical approach chosen (all level IV (8, 9, 44)). One study (9) reported on zero events in both arms and was thus excluded.

According to the meta-analysis including the remaining two studies, RR for post-operative infection following a posterior approach was 0.95 (95% CI: 0.14–6.66; $P = 0.960$; Fig. 6B) in comparison to anterior/anterolateral approach. Heterogeneity was small ($I^2 = 0.0\%$). Publication bias could not be assessed.

Discussion

According to this systematic review and meta-analysis involving 7688 patients with humeral shaft fractures, there appears to be an elevated risk for iRNP following ORIF in comparison to IM, ORIF in comparison to MIPO, as well as after posterior approach vs anterior or anterolateral approach. Also, ORIF is associated with higher post-operative infection risk as compared with IM. While non-union risk is comparable between ORIF and IM, and between anterior/anterolateral and posterior approach, conservative treatment is associated with a significantly higher non-union risk when compared with any surgical therapy for humeral shaft fractures.

A

Non-Union Risk - Conservative vs. Operative

Legend: NU - Non-Union
based on univariate binary outcomes

B

Non-Union Risk - Anterior/Anterolateral vs. Posterior Approach

Legend: NU - Non-Union
based on univariate binary outcomes

Figure 4

Forest plot of studies analysing non-union risk after humeral shaft fractures depending on conservative vs operative approach (A) and anterior/anterolateral vs posterior approach (B). Red diamond shows overall effect size, solid red line overall effect size value, and dashed black line the no-effect line.

Similar to a large analysis of the American Board of Orthopaedic Surgery (ABOS) database by Gottschalk *et al.*, we observed an overall significantly higher risk for iRNP after ORIF in comparison to IM (6). Furthermore, our results are in line with those made in previous meta-analyses involving 18 (59), 10 (60), 10 (5) and 3 studies (61), respectively.

Additionally, for MIPO vs ORIF, a five-fold increased risk for intraoperative radial nerve injury was found, corroborating the results published by Zhao *et al.* in a network meta-analysis involving two RCTs (62). Of note, the estimated risk – as reflected by the odds ratio

– reported by Zhao *et al.* was relatively higher than the herein observed risk – represented by the RR – which may be due to the different methodological approaches chosen, as well as a potential over-estimation of the OR due to an event rate exceeding 10% (63, 64). However, as in our meta-analysis, 8 of 18 and 2 of 4 studies comparing IM with ORIF as well as MIPO with ORIF, respectively, were non-randomised in their nature, it cannot be ruled out that patients undergoing open reduction had injuries contraindicating any closed reduction (e.g. extensive soft tissue involvement, multi-fragmented fracture (65, 66)) that would by themselves have increased the likelihood

Non-Union Risk - IM vs. ORIF

Legend: NU - Non-Union; IM - Intramedullary Nailing; ORIF - Open Reduction Internal Fixation based on univariate binary outcomes

Figure 5

Forest plot of studies analysing non-union risk after humeral shaft fractures depending intramedullary nailing vs ORIF. Amber diamond depicts effect size for subgroups prospective (top) and retrospective (bottom) studies. Red diamond shows overall effect size value, and dashed black line the no-effect line.

A

Risk for Postoperative Infection - Intramedullary Nailing vs. ORIF

IM - Intramedullary Nailing; ORIF - Open Reduction Internal Fixation
based on univariate binary outcomes

B

Risk for Postoperative Infection - Anterior/Anterolateral vs. Posterior Approach

Random-effects REML model
based on univariate binary outcomes

Figure 6

Forest plot of studies evaluating post-operative infection risk in surgically treated humeral shaft fractures depending on intramedullary nailing vs ORIF (A) and anterior/anterolateral vs posterior approach (B). Amber diamond depicts effect size for subgroups prospective (top) and retrospective (bottom) studies on IM vs ORIF (A). Red diamond shows overall effect size, solid red line overall effect size value, and dashed black line the no-effect line (A and B).

of the radial nerve being in danger. Interestingly, we also observed a significantly higher risk of iRNP in case a posterior rather than anterior or anterolateral surgical approach to the humeral shaft had been chosen, which could as well be caused by a selection bias as surgeons may have attempted to explore an already endangered radial nerve via a direct posterior exposure of the humeral shaft.

Bearing these complications in mind, conservative treatment for humeral shaft fractures is a historically well-established alternative (66, 67). Nevertheless, the rate of operative treatment has steadily increased over the years, with today roughly one-third of patients – based on data from 2011 – still treated by conservative measures (7). Albeit a conservative approach naturally lacks surgery-associated risks, a longer immobilisation period, eventually reduced quality of life, and prolonged return to work can be seen disadvantageous (15).

According to the current meta-analysis, a conservative treatment attempt seems to be associated with a significantly higher risk for non-union. This is in line with a previous meta-analysis by van de Wall *et al.* (15) who, apart from nine observational studies, also pooled results from two RCTs. Of note, effect estimates of observational studies and RCTs in that study were comparable, wherefore the authors considered the potential for confounding due to the retrospective non-randomised studies rather minor (15). Furthermore, taking into account that surgery is often indicated in case of open injuries, multi-fragmentary fractures, and considerable displacement – all of which may increase the risk for non-union – the overall higher risk for non-union in case a conservative treatment is chosen appears even more striking.

Regarding different surgical exposures, the risk for non-union was not significantly different between anterior/ anterolateral and posterior approaches to the humeral shaft. Furthermore, we observed a non-significantly different non-union risk when comparing IM with ORIF, being in line with previous meta-analyses (5, 59, 60, 61). This contradicts common knowledge that open reduction leads to significant exposure of the fracture site, which could potentially – together with required periosteal stripping to allow anatomical reduction – limit blood supply and thus impair fracture healing. For the same reasons, ORIF may be associated with an increased post-operative infection risk in comparison to IM, an assumption supported by the results of the current meta-analysis. In fact, a nearly two-fold increased risk for post-operative infection was observed for ORIF in comparison to IM. Our observations are in line with a recent meta-analysis by Beeres *et al.* (59), albeit contradicting findings in previous ones (5, 60, 61). Notably, the type of surgical exposure was non-significantly associated with altered risk for post-operative infection in our meta-analysis, although

one should bear in mind that the two studies included had been retrospective in nature.

The current systematic review and meta-analysis have some limitations that have to be considered. First, the majority of articles included described retrospective studies, wherefore non-random assignment to one or the other treatment arm has to be assumed. Secondly, several studies had to be excluded as not providing sufficient information on the outcome variables of interest. Thirdly, different surgical exposures chosen for ORIF (when compared with MIPO or IM) were not considered in the analyses as the main goal was to identify differences between surgical techniques exposing and not exposing the fracture itself. Fourthly, we did not perform adjusted meta-analyses for underlying differences between groups due to small sample sizes. Fifthly, time to union and restitution from iRNP were not analysed, as both outcomes depend on frequency of examinations scheduled that may be more prone to bias than steady outcomes as infection, post-operative radial nerve palsy, and non-union.

Conclusions

According to the current meta-analysis involving 43 studies and 7688 patients with humeral shaft fractures reporting on outcomes non-union, post-operative radial nerve palsy, and infection risk, the method of choice when aiming at secure bony union appears to be surgery, albeit risk for radial nerve palsy has to be considered, especially in case a posterior rather than anterior/ anterolateral approach, and ORIF rather than MIPO or IM is chosen. Also, higher infection risk following ORIF in comparison to IM should be considered upon treatment planning. Yet, evidence on best treatment option for humeral shaft fractures remains moderate, taking into account the limited number of randomised studies available, as well as the multiple factors contributing to decision making.

Supplementary materials

This is linked to the online version of the paper at <https://doi.org/10.1530/EOR-21-0097>.

ICMJE Conflict of Interest Statement

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