

Surgical Treatment of Proximal Humerus Fractures. A systematic review and meta-analysis

Running Title: Meta-Analysis Surgical Treatment Proximal Humerus Fractures

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The authors declare that they have no conflict of interest

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EH, KT and VG substantially contributed to acquisition, analysis and interpretation of data and drafted the article. Statistical analyses were made by EH. All authors contributed substantially to conception and design and revised it critically for important intellectual content and provided final approval of the version to be published. They agreed to act as guarantor of the work ensuring that questions related to any part of the work are appropriately investigated and resolved.

Availability of data and materials

Not applicable

Compliance with ethical standards**Conflict of interest**

The authors declare no conflict of interest with the presented body of research.

Ethical Approval

Not applicable

Informed Consent

For this type of study informed consent is not required.

Abstract

Introduction:

The purpose of this study was to perform a systematic review and meta-analysis of both randomized controlled and observational studies comparing surgical interventions for proximal humerus fractures.

Methods:

Systematic review of Medline, Embase, Scopus, and Google Scholar, including all level 1-3 studies from 2000 to 2022 comparing surgical treatment with ORIF, IM nailing, hemiarthroplasty, total and reverse shoulder arthroplasty (RTS) was conducted. Clinical outcome scores, range of motion (ROM), and complications were included. Risk of bias was assessed using the Cochrane Collaboration's ROB2 tool and ROBINS-I tool. The GRADE system was used to assess the overall quality of the body of evidence. Heterogeneity was assessed using χ^2 and I^2 statistics.

Results:

Thirty-five studies were included in the analysis. Twenty-five studies had a high risk of bias and were of low and very low quality. Comparisons between ORIF and hemiarthroplasty favored ORIF for clinical outcomes ($p=0.0001$), abduction ($p=0.002$), flexion ($p=0.001$), and external rotation ($p=0.007$). Comparisons between ORIF and IM nailing were not significant for clinical outcomes ($p=0.0001$) or ROM. Comparisons

between ORIF and RTS were not significant for clinical outcomes ($p=0.0001$) but favored RTS for flexion ($p=0.02$) and external rotation ($p=0.02$). Comparisons between hemiarthroplasty and RTS favored RTS for clinical outcomes ($p=0.0001$), abduction ($p=0.0001$) and flexion ($p=0.0001$). Complication rates between groups were not significant for all comparisons.

Conclusions:

This meta-analysis for surgical treatment of proximal humerus fractures demonstrated that ORIF is superior to hemiarthroplasty, ORIF is comparable to IM nailing, reverse shoulder arthroplasty is superior to hemiarthroplasty but comparable to ORIF with similar clinical outcomes, ROM and complication rates. However, the study validity is compromised by high risk of bias and low level of certainty. The results should therefore be interpreted with caution. Ultimately, shared decision making should reflect the fracture characteristics, bone quality, individual surgeon's experience, the patient's functional demands, and patient expectations.

Keywords:

Proximal humerus fractures; surgical treatment; displaced fractures; Neer proximal humerus; clinical outcomes; meta-analysis

Level of evidence

Level III; systematic review and meta-analysis

Introduction

Proximal humerus fractures comprise approximately five percent of all fractures [1]. These fractures are more commonly observed in elderly patients and are often associated with osteoporosis [2]. As demographics in the developed world are changing and the aging population increases, one can expect an increase in the prevalence of these fractures [1,2]. Between 1970 and 1998 an annual increase of 15% of proximal humerus fractures has been observed and further increases can be expected [3]. Most proximal humerus fractures can be treated conservatively with good functional outcomes, and generally only 25% of fractures require operative intervention [4]. Furthermore, surgical intervention often reflects multiple factors including patient age, physical activity, bone quality, fracture patterns, and displacement [5].

The treatment of displaced fractures is still controversial and often depends on the surgeons' experience and personal preferences [6]. For example, shoulder surgeons were more likely to consider arthroplasty and trauma surgeons were more likely to use ORIF or suggest conservative treatment [6]. The current evidence does not seem very helpful and is often limited by study heterogeneity, risk of bias, and low samples sizes [7].

A Cochrane review from 2015 concluded that there is moderate evidence that non-surgical treatment with displaced two-part fractures of the surgical neck is comparable to surgical treatment [8]. However, displaced 3-part and 4-part fractures more likely benefit from surgical treatment, which seems to result in superior outcomes but is also associated with higher rates of reoperations [9]. A broad spectrum of operative interventions have been described and include open reduction and internal fixation

(ORIF) with plates or locking plates, intramedullary nailing, hemiarthroplasty, total shoulder arthroplasty, to reverse shoulder replacement [9,10]. A recent network meta-analysis suggested that reverse shoulder arthroplasty has the best clinical outcomes whilst ORIF had the highest reoperation rates with poor clinical outcomes [10]. However, risk of bias, study heterogeneity, low methodological quality, and omission of randomized but also observational studies substantially reduces the validity of these conclusions [7,11].

The inclusion of observational studies into systematic reviews and meta-analysis is a feasible concept and potentially has several advantages [5]. Inclusion of these studies increases sample size for meta-analysis, and can also increase the generalizability of the pooled results [5]. The inclusion of observational studies into meta-analysis does not result in differences in the risk estimate of treatment effects of an intervention derived from meta-analysis of randomized controlled trials or observational studies [12,13]. The purpose of this study was therefore to perform a systematic review and meta-analysis of both randomized controlled and observational studies comparing surgical interventions for proximal humerus fractures.

Methods

The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [14], and the updated guidelines described in the Cochrane Handbook [15].

Eligibility criteria

All randomized level of evidence (LOE) grade 1 and 2 and observational LOE 3 studies that compared surgical treatment of proximal humerus fractures were included, if they fulfilled the following inclusion and exclusion criteria. Studies were included if they were published between January 2000 and May 2022. This timeframe was selected to include studies which describe more contemporary techniques. Studies were included if they compared any of the following surgical interventions: ORIF with proximal humerus locking plates, proximal humeral intramedullary nails, hemiarthroplasty, total and reverse shoulder arthroplasty. Further inclusion criteria included: minimum follow-up of 6 months; inclusion of at least one functional validated outcome score such as Constant, ASES, DASH, VAS, OSS, UCLA, or SANE, and preferably the inclusion of range of motion and complications; and minimum mean age of 50 years. Clinical case LOE IV studies and case series were excluded as well as abstracts and conference proceedings. It is accepted that the omission of “grey” data sources could potentially result in publication bias. However, it was considered unlikely that these publications would have fulfilled the eligibility criteria.

Literature search

A systematic review of the literature was performed to identify all publications in English and German, screening the databases Medline, Embase, Scopus, and Google Scholar. These databases were screened using the following terms and Boolean operators: “proximal humerus” AND/OR “fracture” AND/OR “Neer proximal humerus fracture” AND/OR “3-part”; AND/OR “4-part” AND/OR “2-part” AND/OR surgical treatment” AND/OR “operative treatment”. For the Medline search the following MeSH terms were used in addition to the above search strategy: “fracture, proximal

humerus”, “fractures, proximal humerus”, “proximal humerus fracture”, “humerus surgical neck fracture”, “humeral surgical neck fracture” and “proximal humerus fractures”. Two reviewers conducted independent title and abstract screening. Disagreements between reviewers were resolved by consensus, and if no consensus was reached, they were carried forward to the full text review. All eligible articles were manually cross-referenced to ensure that other potential studies were included.

Data extraction and quality assessment

An electronic data extraction form was used to obtain the following data from each article: level of evidence, country, age, gender, length of follow-up, sample size, clinical outcome scores, range of motion and complications. Risk of bias for LOE I and II studies was assessed using the Cochrane Collaboration’s Risk of Bias Tool [15]. For LOE III studies the ROBINS-I tool was used. The Methodological Index for Non-Randomized Studies (MINORS) was used to assess study quality for non-randomized studies, and the Modified Coleman Methodology Score (CMS) was used as a validated instrument to assess the quality of both randomized and non-randomized studies. The MINORS score was categorized into the following categories: <6 very low quality, <10 poor quality, <14 fair quality, and >16 good quality. The CMS was categorized as follows: 85-100 excellent quality; 70-84 good quality; 55-69 fair quality; <55 poor quality. Any disagreement between reviewers was resolved by consensus and/or by arbitration between the two senior authors.

The GRADE system was used by two reviewers to assess the certainty of evidence for each outcome measure [15]. The recommendations from the Cochrane Handbook were followed, and an initial level of certainty assigned. Outcomes were downgraded if there

was a high risk of bias, inconsistency and imprecision of the results, and indirectness of evidence. Studies were upgraded if there were large treatment effects, a dose-response, or reasons to oppose plausible residual bias and confounding effects. Any disagreement between reviewers was resolved by consensus and/or by arbitration between the two senior authors.

Statistical analysis

Inter-observer differences for study eligibility and risk of bias were measured using Cohen's kappa coefficient. Heterogeneity of the data was assessed using χ^2 and I^2 statistics. Outcomes were pooled using a random effects model if the I^2 statistic was >25%, and a fixed model was used if the statistic was <25%. Pooling of data for clinical outcomes, stability measures, and functional testing was only performed if a minimum of three studies were available. The prevalence of osteoarthritis between groups was pooled as a binary yes/no variable, and analyzed by calculating the odds ratios. If standard deviations were not reported, the standard deviation was calculated using the following formula: $SD = \max - \min / 4$ [15,16]. All tests of significance were two-tailed, and an α of less than 0.05 was considered significant. Publication bias was assessed using funnel plots and Egger's test. Funnel and forest plots, and all statistical analyses, were performed using STATA SE (Version 13.0; StataCorp, College Station, Texas, USA) for Windows, and the comprehensive meta-analysis software package (CMA), version 3 (Biostat Inc, Englewood, NJ, USA).

Results

Study selection and characteristics

The initial literature search identified 3,694 studies for consideration. Of those, 2,225 studies were excluded for duplication, and the titles of the remaining 1,469 publications were checked for eligibility. Another 842 studies were excluded, and following abstract review of 627 studies, the full text manuscripts of 82 studies were examined. Thirty-five studies met all of the eligibility criteria and were included in the analysis [16-50] (Figure 1). Five studies were considered level I evidence [20,28,32,38,50], four were level II evidence [17,24,41,48] and twenty-six studies were level III evidence [16,18,19,21-23,25-27,29-31,33-37,39,40,42-47,49]. All 35 studies were published in English between 2008 and 2022 with a cumulative total of 2672 cases. Of these patients 1061 underwent surgical reconstruction with locked plates, 787 had hemiarthroplasty surgery, 446 were treated with locked intramedullary nailing and 377 underwent reverse total shoulder arthroplasty. The study characteristics are summarized in Tables 1 to 4. Overall agreement between the two reviewers for final eligibility was excellent (kappa value 0.89, 95% CI 0.85-0.92).

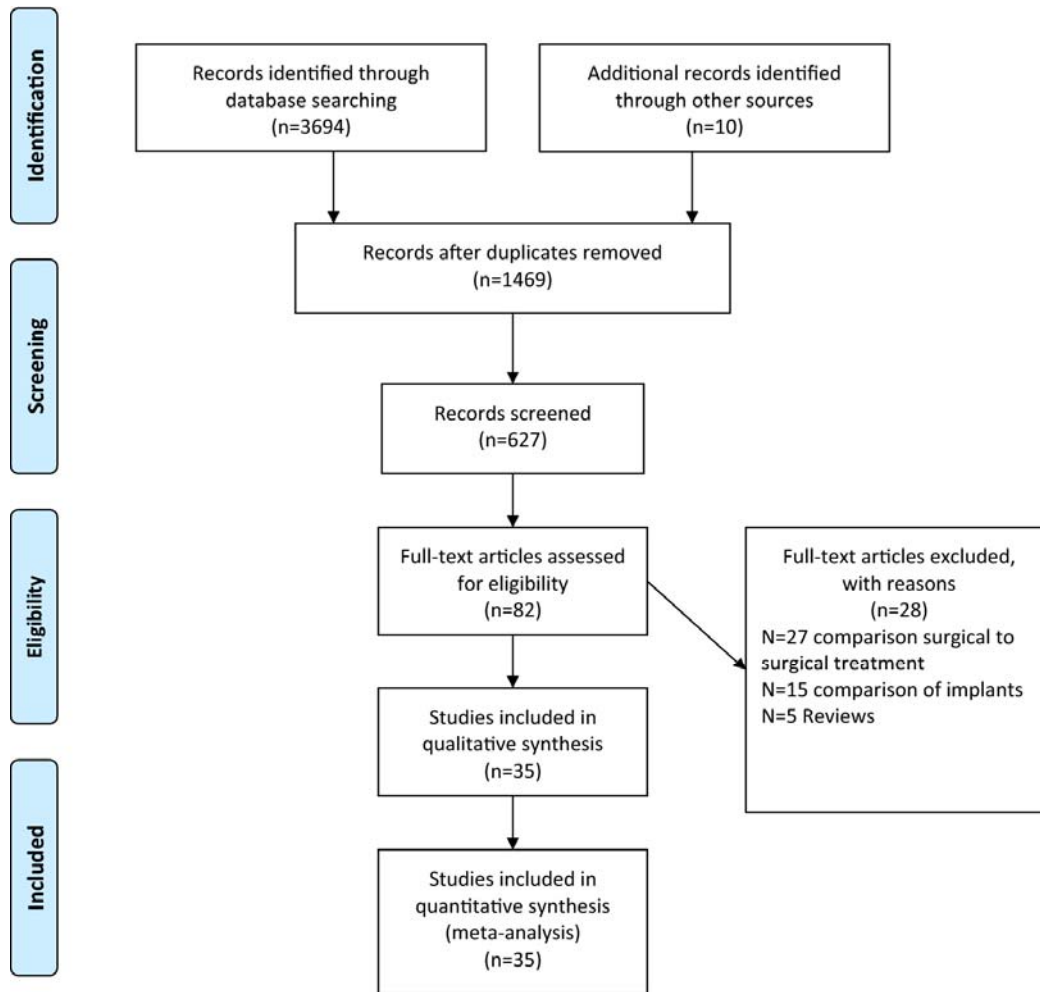


Figure 1. PRISMA flow diagram. From the initial 3704 records, 35 studies were included in the quantitative synthesis

Table 1: ORIF versus Hemiarthroplasty

Authors	LOE	Country	Patients (n) Hemi-ORIF	Age (years)	Gender	Neer Classification	Follow-Up (months)	Outcomes
Dietrich 2008	III	Germany	59 52	80 (70-92) 82 (71-92)	M=7 F=52 M=10 F=42	3 part 19-11 4 part 40-40	Not mentioned	Constant 41 (17-77) – 71 (31-92) OSS: 29 (14-41) – 20 (12-51) Complications: not mentioned
Bastian 2009	II	Switzerland	51 49	66 (38-87) 54 (21-88)	M=45 F=55	2 part 0-6 3 part 19-29 4 part 30-6	60 (39-85)	Constant 70 (39-84) 77 (37-98) SSV 90 (40-100) – 92 (40-100) Complications 16% - 37%
Solberg 2009	III	USA	48 38	67.4+6.3 66.5+8.6	M=14 F=34 M=12 F=26	3 part: 25-23 4 part: 15-23 Dislocation: 8:10	35.3+8.9 36.1+10	Constant 68.6+9.5-60.6+5.9 Complications: 21% - 39%
Kim 2011	III	Korea	26 38	67+14.8 63.5+9.2	M=10 F=16 M=19 F=19	3 part: 11 – 24 4 part: 15-14	24	Constant 70+7.4 – 75+6.5 Complications: not mentioned
Cai 2012	I	China	19 15	71.1 (67-85) 72.4 (71-86)	M=3 F=16 M=4 F=11	4 part 19-15	24	Constant: 72.9-60.1 DASH 9.2-15.3 Complications 16%-23%
Spross 2012	III	Switzerland	22 22	76 (55-92) 75 (42-93)	M=3 F=19 M=4 F=18	3 part: 0-3 4 part: 6-10 Dislocation: 2-1 Head impression 7-7 Head split 7-1	36 (12-83) 21 (12-60)	Constant 54.5 (38-86) – 65.2 (41-100) Complications: 4.5%-64%
Chalmers 2014	III	USA	9 9	72+7 71+7	M=2 F=7 M=2 F=7	3+4 part	35+14 36+18	VAS 3+3 – 1+1 ASES 66+31 – 75+15 ROM Flexion 106+29 -108+40 ROM Ext Rotation 28+19 – 46+21 Complications: 11% -11%
Repetto 2017	III	Italy	24 19	67.5+10.2 65.3+12.4			42.2+18.7 36.5+17.9	Constant 48.4+27.3 – 61.8+14.7 DASH 33.8+28.7 – 33.8+28.7 SST 5.6+3.9 – 11.7+3.1 ROM Flexion 103+58 – 131+50 ROM Ext Rotation 16.5+16 – 23.2+8.8 ROM Abduction 90.5+24.7 – 104.4+21.3
Thorsness 2017	III	USA	15 15	73 73	Not mentioned	Dislocation: 3-9 Head Spilt: 8-2 Both: 4-4	60	Constant: 53.6+19.2 – 69.1+15.7 DASH: 29.2+17.6 – 13.8+18.2 ASES 66.2+22.1 – 86.5+13.5
Spross 2019	II	Switzerland	4 36	66	M=58 F=134	3+4 part	12	Constant 44-63 Complications 50% - 44%
Erpala 2021	III	Turkey	15 18	68.5+11.3 69.5+11.5	M=5 F=10 M=6 F=12	3 part 10-12 4 part 5-6	42.3 (21-54) 24.2 (20-38)	DASH 23.3 (14.6-36.2) – 12.1 (5.2-24.2) Constant 49.7+11.8 – 71.6+16.2 ASES 54.9 (42-78) – 77.5 (51-97)

								ROM Flexion 61+23 – 106+34 ROM Abduction 55+18-102-38 ROM External Rotation 30 (10-60) – 52 (30-60)
Gurnani 2022	III	India	10 10	72.8 67.2	M=5 F=5 M=5 F=5	3 and 4 part		Constant 62.6 – 71.3 ROM Flexion 89-109 ROM Abduction 85-98 ROM External Rotation 54-64
Peker 2022	III	Turkey	18 30	67.3+10.1 60+9.4	M=7 F=11 M=16 F=30	3 part 5-18 4 part 6-5 Dislocation 7-7	18.7+16.4 – 18.3+10.2	Constant 59.1+17.8 – 66.8+17.6 UCLA 24.9+4.1 – 26.1+4.4 VAS 1.9+1.9 – 2.5+1.8 ROM Flexion 63.9+45.4 – 88.3+41.1 ROM Abduction 65.6+39 – 80.2+33.1 Complications 44% - 30%

Table 2: ORIF versus Intramedullary Nailing

Authors	LOE	Country	Patients (n) ORIF-Nail	Age (years)	Gender	Neer Classification	Follow-Up (months)	Outcome
Gradl 2009	III	Germany	76 76	63+16	M=24F=52 M=24 F=52	2 part: 26-26 3 part: 30 – 30 4 part: 16- 16 Dislocation: 8 - 8	12.8+0.4	Constant 77+19 – 80+19 Complications: 28% - 22%
Matziolis 2010	III	Germany	11 11	54.8+16.9 55.6+16.5	M=4 F=7 M=4 F=7	Displaced 2 part	36	Constant 83+29-78+17 Complications 36% - 36%
Zhu 2011	I	China	25-25	50.5+19.9 54.8+17.1	M=8 F=18 M=6 F=16	2 part: 25-25	36	VAS: 0.5+1.8 – 1+1 ASES: 94+6.3 – 90+8.1 Constant: 94.5+5.8 – 93.3+6.7 ROM Flexion : 157.3+15.1 – 160.8+11.9 ROM External Rotation: 40.4+17.4 – 47.8+17.3 Complications: 31% - 4% Infection 0 – 0 Screw Penetration 5 – 0
Konrad 2012	III	Germany	153 58	65.5+15.6 64.8+13	M=40 F=113 M=11 F=47	3 part: 153-58	12	Pain: n= 54 – 9 Constant: 87+14 – 89+11 Complications: 31% - 21% Intra-operative: 27-5 Post-operative: 28-12
Lekic 2012	III	USA	12 12	58.8+17.3 60.2+17.7	M=3 F=9 M=2 F=10	2 part: 12-12	14.7+5.8 12.9+9.5	ROM Flexion : 157.3+15.1 – 160.8+11.9 ROM External Rotation: 141.2+30.2 – 120.8+34.5 Complications: 33% - 42% Painful hardware 0-2 Heterotopic ossification 0-3 Screw Penetration 3-0 Osteonecrosis 1-0
Trepat 2012	III	Spain	11 13	68.3+17.3 64.5+20.7	M=3 F=8 M=6 F=7	AO Type A31, A 32, A33	6	Constant 64-63.8 OSS 19-19.8 ROM Flexion: 130-131 ROM Abduction 126-121 ROM Ext Rotation: 35-39 Complications 45%-77%
Urda 2012	III	Spain	14 24	71+13.5 70.9+11.4	M=3 F=11 M=6 F=18	2 part	40.7+18	Constant 82.45+17.7 – 72.7+15.9 ROM Abduction 134.7+35 – 115.8+33.5 ROM Flexion 153+28 – 128+49

								ROM Ext Rotation 40+17 – 31+15.4 Complications 33% - 31%
Tamimi 2015	III	Canada	44 19	65.3+15.2	M=15 F=29 M=9 F=10	2 part 8-13 3+4 part 36-6	25.9+15 22.5+9	Constant 62.9+16.8 – 63.9+23.6 DASH 38.4+19.2 – 34.9+26.5 Complications: 18% - 7%
Gracitelli 2016	I	Brazil	36 36	66.4+8.1 64.5+9.6	M=9 F=27 M=10 F=25	2 part: 16-16 3 part: 17-16	12	Constant 71.5+12.8 – 70.3+15.8 DASH: 14.3+13 – 18.1+18.8 VAS: 1.3+2.1 – 1.7+2.3 Complications: 30% - 87%
Lee 2017	I	Korea	31 38	58.6+12.3 59.7+12	M=11 F=20 M=12 F=26	2 part: 31-38	24	VAS 0.9+1.1 – 1.3+1.3 ASES 91.9+6.8 – 90.2+7.1 UCLA 31.8+2.7 – 30.7+3.1
Ge 2017	III	China	69 72	75.1+8.5 76.9+8.1	M=24 F=45 M=22 F=50	2 part: 38 – 36 3 part: 31 - 36	24	Constant 82.3+9 – 65.4+10.6 ASES 80.1+9.0 – 81.5+8.9 VAS: 0.81+0.6 – 0.83+0.66 ROM Flexion: 164+9 – 161+12.7 ROM External Rotation: 48.3+6.9 – 45.9+8.5
Plath 2019	II	Germany	27 28	77.1 (60-92) 71.1 (60-87)	M=7 F=25 M=10 F=26	2 part: 4-5 3 part: 24-25 4 part: 4-6	12.8	Constant 64+20-67+20.2 DASH 42+1934+17.8 VAS 1+1.6-0+1.8 ROM Flexion 130+43.5-124.1+45.4 ROM Abduction: 123.3+52-120.9+49.1 Complications: 34.3% - 33.3%
Bu 2021	III	China	48 34	66.3+7 67.2+6.3	M=17 F=31 M=11 F=2326	2 part: 28-19 3 part: 13-10 4 part: 7-5	15.6 (12-24)	Constant 78.7+.1 – 81.9+9.7 ASES 82.8+7.1 – 85.4+9.2 VAS 0.52+0.51 – 0.38+0.55 Complications 54% - 9%

Table 3: ORIF versus Reverse Total Shoulder Arthroplasty

Authors	LOE	Country	Patients (n) Reverse-ORIF	Age (years)	Gender	Neer Classification	Follow-Up (months)	Outcome
Chalmers 2014	III	USA	9 9	77+6 71+7	M=2 F=7 M=2 F=7	3+4 part	14+6 36+18	VAS 1+1 – 1+1 ASES 80+11 – 75+15 ROM Flexion 133+20 -108+40 ROM Ext Rotation 41+19 – 46+21 Complications: 11% - 11%
Repetto 2017	III	Italy	27 19	71.2+7.5 65.3+12.4			41.7+17.1 36.5+17.9	Constant 58.5+8.5 – 61.8+14.7 DASH 28.6+12.3 – 33.8+28.7 SST 6.7+2.1 – 11.7+3.1 ROM Flexion 125+45 – 131+50 ROM Ext Rotation 20.3+10.6 – 23.2+8.8 ROM Abduction 110+32 – 104.4+21.3
Spross 2019	II	Switzerland	20 36					Constant 69 – 63 Complications 0% - 44%
Fraser 2020	I		64 60	75.7+6.1 74.7+6.5	M=5 F=59 M=8 F=52	AO B2 26-29 C2: 38-31	24	Constant 68 (64-72) – 54.6 (48.5-60.7) OSS 40.8 (38.8-42.7) – 36.5 (34-39) Complications 11%-20%
Klug 2020	III	Germany	30 30	73.9+6.7 72.5+6.3	M=5 F=25 M=5 F=25	3-part 1:10 4-part: 17-18 head splitting 12/2	49 (12-83) 38 (12-50)	ASES 74.6+21.6 – 83.4+17.2 OSS 37.7+10.3-42.8+5.7 Constant 69.9+26-81.4+17.2 DASH 25.3+20—14.3+14.7 ROM External Rotation 39+25-52+23 Complications 10% - 30%

Table 4: Hemiarthroplasty versus Reverse Total Shoulder Arthroplasty

Authors	LOE	Country	Patients (n) Reverse- Hemi	Age (years)	Gender	Neer Classification	Follow-Up (months)	Outcome
Gallinet 2009	III	France	16 17	74 (58-84) 74 (49-80.5)	M=3 F=13 M=2 F=15	3 and 4 part	12.4 (4-18) 16.5 (6-55)	Constant 53 (34-76) – 39 (19-61) DASH 37.4 (11.7-65) – 41.2 (18.3-60.7) ROM Flexion 97 (10-150) – 53 (30-100) ROM Abduction 91 (10-150) – 60 (30-90) ROM Ext Rot 9 (0-80) – 13.5 (0-30) Complications: 19% - 18%
Garrigues 2009	III	USA	10 9	80.5 (67-97) 69.3 (57-87)	Not mentioned	3 and 4 part	42	ASES 81.1 (75-88) – 47.4 (30-81) SANE 85 (70-95) – 38.5 (0-90) ROM Flexion 121 (90-145) – 91 (30-140) ROM Ext Rotation: 34 (10-45) – 31 (5-60) Complications: 10% - 44%
Young 2009	III	New Zealand	10 10	77.2 75.5	M=0 F=10 M=2 F=8	3 part 2-2 4 part: 8-8	77.2 75.5	ASES 65 (40-88) – 67 (26-100) OSS 28.7 (15-56) – 22.4 (12-34) ROM Flexion 115 (45-140) – 108 (50-180) ROM Ext Rot 49 (5-105) – 48 (10-90) Complications: 0% - 20%
Boyle 2012	III	New Zealand	55 313	79.6 (57-90) 71.9 (27-96)	M=4 F=51 M=69 F=244	3 and 4 part	60	OSS 41.5+2.3-32.3+1.2 Complications: 3.6-.3.5
Cuff 2013	II	USA	24 23	74.4	Not mentioned	4 part	33 (24-48)	ASES 77 (67-82) – 62 (28-84) SST 7.4 (6-9) – 5.8 (1-9) ROM Flexion 139 (102-172) – 100 (30-170) ROM Ext Rotation: 24 (8-42) – 25 (0-48) Complications: 8% - 9%
Baudi 2014	III	Italy	25 28	77 70			26	Constant 56.2+14.9 – 42.3+16.6 DASH 40.4+25 – 46.1+27.9 ASES: 59.8+22.9 – 43.5+26.5 ROM Flexion 131+36 – 89+44 ROM Abduction 128+36-82+40 ROM Ext rotation: 15+11-23+15 Complications 4% - 24%
Chalmers 2014	III	USA	9 9	77+6 72+7	M=2 F=7 M=2 F=7	3+4 part	14+6 59+14	VAS 1+1 – 3+3 ASES 80+11 – 66+31 ROM Flexion 133+20 -106+29 ROM Ext Rotation 41+19 – 28+19 Complications: 11% - 11%

Sebastia-Forcada 2014	I	Spain	31 30	74.7 (70-85) 73.3 (70-83)	M=4 F=27 M=5 F=25	3 part: 5-4 4 part: 21-20 4 part dislocation: 5-6	24	Constant 56.1 (24-80) – 40 (8-74) UCLA: 29.1 (16-34) – 21.1 (6-34) DASH: 17.5 (12-30) – 24.4 (13-41) ROM Flexion: 120 (40-180) – 80 (20-180) ROM Abduction: 113 (50-170) – 79 (30-150) ROM External Rotation: 5 (0-10)- 3 (0-10) Complications: 6.5% - 26%
Repetto 2017	III	Italy	27 24	71.2+7.5 67.5+10.2			41.7+17.1 42.2+18.7	Constant 58.5+8.5 – 48.4+27.3 DASH 28.6+12.3 – 33.8+28.7 SST 6.7+2.1 – 5.6+3.9 ROM Flexion 125+45 – 91+25 ROM Ext Rotation 20.3+10.6 – 16.5+16 ROM Abduction 110+32 – 90.5+24.7
Spross 2019	II	Switzerland	20 4					Constant 69 – 44 Complications 0% - 50%

Risk of bias and quality assessment

The findings of the risk of bias assessment are summarized in Tables 5 and 6.

Risk of bias Cochrane Assessment Tool Version 2

Three of the five level I evidence studies [20,28,38] were assessed as having a high risk of bias. Two studies had used an intention to treat protocol [28,38] and one study [20] did not include any information on the randomization process and how bias due to missing outcome data was handled. All four level II evidence studies [17,24,41,48] were assessed as having a high risk of bias. This assessment was based on the high risk of bias introduced by bias from the randomization process. In addition, two studies [17,47] had a loss to follow-up rate exceeding 20%.

Risk of bias ROBINS-I Assessment Tool

The ROBINS-I tool was used to assess the risk of bias for observational studies. Sixteen studies [18,19,25,26,29,30,31,34,39,42,43,44,45,46,47,49] had a moderate risk of bias. The main reason for this assessment was based on bias in the selection of participants for all 16 studies. Seven studies [22,23,27,35,36,37,40] overall risk of bias was serious. The main reason for this assessment was based on bias due to confounding for all seven. Three studies [16,21,33] had a critical risk of bias based on bias due to deviations from the intended interventions. Publication bias was not detected. The funnel plot was symmetric and Egger's regression intercept (Intercept -1.66, t-value 0.42, p-level 0.65) was not significant (Figure 2).

Table 5 Risk of Bias Cochrane Risk of Bias Assessment Tool Version 2 for Randomized Controlled Trials

Authors	LOE	Bias from Randomization	Bias from Deviations from Intended Interventions	Bias due to Missing Outcome Data	Bias in Measurement of the Outcome	Bias in Selection of the Reported Results	Overall Risk of Bias
Zhu 2011	I	Low	Low	Low	Low	Low	Low
Cai 2012	I	High	Low	High	Low	Low	High
Sebastia-Forcada 2014	I	Low	Low	Low	Low	Low	Low
Gracitelli 2016	I	Low	High	Low	Low	Low	High
Fraser 2020	I	Low	High	Low	Low	Low	High
Bastian 2009	II	High	Low	High	Low	Low	High
Cuff 2013	II	High	Low	Low	Low	Some	High
Plath 2019	II	High	Low	Low	Low	Low	High
Spross 2019	II	High	High	High	Low	High	High

Bias from Randomization	Green		Green		Red		Red	
Bias Deviations	Green		Green		Red		Red	
Bias Missing Outcome Data	Green		Green		Red		Red	
Bias Measurement Outcome	Green		Green		Green		Green	
Selection Reported Results	Green		Green		Green		Yellow	
Total Bias	Yellow		Red		Red		Red	
	25%		50%		75%		100%	

Table 6 Risk of Bias Assessment for Non-Randomized Studies with the ROBINS-I tool

Authors	LOE	Bias due to Confounding	Bias in Selection of Participants	Bias in Classification of Interventions	Bias due to Deviations from Intended Interventions	Bias due to Missing Data	Bias in Measurement of Outcomes	Bias in Selection of the Reported Results	Overall Bias
Dietrich 2008	III	Critical	Moderate	Moderate	Critical	Moderate	Low	Low	Critical
Gallinet 2009	III	Low	Moderate	Low	Low	Low	Low	Moderate	Moderate
Gradl 2009	III	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Solberg 2009	III	Low	Moderate	Low	Low	Low	Low	Moderate	Moderate
Matziolis 2010	III	Moderate	Moderate	Moderate	Moderate	Low	Low	Moderate	Moderate
Young 2010	III	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Kim 2011	III	Serious	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Boyle 2012	III	Low	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Garrigues 2012	III	Low	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Konrad 2012	III	Critical	Moderate	Moderate	Critical	Moderate	Low	Moderate	Critical
Lekic 2012	III	Moderate	Moderate	Moderate	Moderate	Low	Low	Moderate	Moderate
Spross 2012	III	Moderate	Moderate	Moderate	Moderate	Moderate	Low	Low	Moderate
Trepap 2012	III	Serious	Moderate	Moderate	Moderate	Moderate	Low	Moderate	Serious
Urda 2012	III	Serious	Moderate	Moderate	Serious	Low	Low	Low	Serious
Baudi 2014	III	Moderate	Moderate	Moderate	Moderate	Moderate	Low	Moderate	Moderate
Chalmers 2014	III	Serious	Moderate	Serious	Critical	High	Low	Low	Critical
Ge 2017	III	Serious	Moderate	Serious	Critical	Low	Low	Low	Serious
Lee 2017	III	Low	Moderate	Low	Low	Moderate	Low	Low	Moderate
Tamimi 2015	III	Serious	Moderate	Serious	Critical	Serious	Low	Low	Serious
Repetto 2017	III	Serious	Moderate	Moderate	Serious	Low	Low	Low	Serious
Thorsness 2017	III	Serious	Moderate	Moderate	Moderate	Serious	Low	Moderate	Serious
Klug 2020	III	Moderate	Moderate	Moderate	Moderate	Moderate	Low	Moderate	Moderate
Bu 2021	III	Moderate	Moderate	Moderate	Moderate	Moderate	Low	Low	Moderate
Erpala 2021	III	Critical	Moderate	Moderate	Moderate	Moderate	Low	Low	Moderate
Gurnani 2022	III	Moderate	Moderate	Moderate	Moderate	Moderate	Low	Moderate	Moderate
Peker 2022	III	Serious	Moderate	Moderate	Serious	Serious	Low	Low	Serious

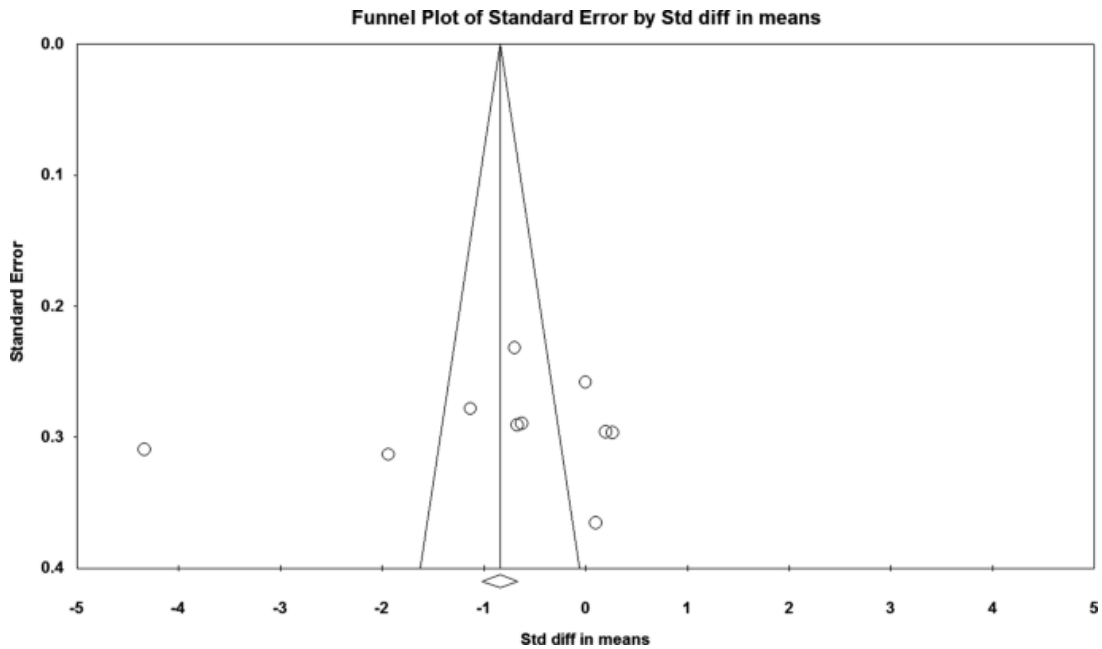


Figure 2. Publication bias: Publication bias was not detected. The funnel plot was symmetric and Egger’s regression intercept (Intercept = 1.66, t -value 0.42, p -level 0.65) was not significant

Quality Assessment

The CMS score (Table 7) revealed that all five level I evidence studies were of good quality, with a mean score of 75 (range 71-78). All level II evidence studies were assessed as having fair quality, with a mean score of 65 (range 59-67). Five of the twenty-six LOE III studies [18,23,33,40,42] were assessed as having fair quality, and the other twenty-one studies had poor quality. The MINORS score (Table 8) for non-randomized studies assessed one study [40] as having good quality, twenty studies [16,18,21-23,25-27,29-31,33,35,37,39,42,43,46,47,49] as having fair quality, and five studies [19,34,36,44,45] as low quality.

There were obvious differences with regards to quality assessment between CMS and MINORS. These differences are explained by a slightly different focus of these quality scores. MINORS has a focus on an adequate and contemporary control group and

Table 7: Modified Coleman Methodology Score

Authors	Total Points	Study Size	Mean Follow-Up	Percent of patients with follow-up	Number of Interventions	Type of Study	Diagnostic Certainty	Description Surgical Technique	Description Post Op Rehabilitation	Outcome Criteria	Procedures for Assessing Outcomes	Description of Subject Selection
Zhu 2011	78	4	3	3	10	15	5	5	5	10	8	10
Cai 2012	71	0	0	3	10	15	5	5	5	10	8	10
Sebastia-Forcada 2014	75	4	0	3	10	15	5	5	5	10	8	10
Gracitelli 2016	75	4	0	3	10	15	5	5	5	10	8	10
Fraser 2020	75	7	0	0	10	15	5	5	5	10	8	10
Mean Score	75											
Bastian 2009	67	7	0	0	10	15	5	5	5	10	5	5
Cuff 2013	59	4	0	0	10	15	5	5	0	10	5	5
Plath 2019	67	4	0	0	10	15	5	5	3	10	5	10
Spross 2019	68	10	0	0	10	15	5	5	0	10	3	10
Mean Score	65											
Dietrich 2008	52	7	0	0	10	0	5	5	5	10	5	5
Gallinet 2009	33	0	0	3	10	0	5	5	0	10	0	0
Gradl 2009	50	10	0	0	10	0	5	5	5	10	5	0
Solberg 2009	60	7	0	3	10	0	5	5	5	10	5	10
Matziolis 2010	38	0	3	0	10	0	5	5	5	10	0	0
Young 2010	35	0	0	0	10	0	5	5	5	10	0	0
Kim 2011	39	4	0	0	10	0	5	5	5	10	0	0
Boyle 2012	50	4	3	0	10	0	5	5	0	10	8	5
Garrigues 2012	35	0	0	0	10	0	5	5	5	10	0	0
Konrad 2012	58	10	0	0	10	10	5	5	0	10	3	5
Lekic 2012	40	0	0	0	10	0	5	5	5	10	0	5
Spross 2012	45	0	0	0	10	0	5	5	5	10	5	5
Trepat 2012	41	0	0	3	10	0	5	5	5	10	3	0
Urda 2012	47	4	0	3	10	0	5	5	5	10	0	5
Baudi 2014	44	4	0	0	10	0	5	5	5	10	5	0
Chalmers 2014	51	0	3	5	10	0	5	5	5	10	8	0
Tamimi 2015	53	10	0	0	10	0	5	5	5	10	3	5
Ge 2017	63	10	0	0	10	0	5	5	5	10	8	10
Lee 2017	44	4	0	0	10	0	5	5	5	10	0	5

Repetto 2017	47	4	0	0	10	0	5	5	5	10	3	5
Thorsness 2017	56	0	3	0	10	0	5	5	5	10	8	10
Klug 2020	50	4	3	0	10	0	5	5	5	10	3	5
Bu 2021	57	4	0	5	10	0	5	5	5	10	8	5
Erpala 2021	42	4	0	0	10	0	5	5	5	10	3	0
Gurnani 2022	42	0	0	0	10	10	5	5	0	7	5	0
Peker 2022	47	4	0	0	10	0	5	5	5	10	8	0
	47											

Table 8: MINORS Quality Assessment for Non-Randomized LOE III Studies

Authors	Total Points	Clearly Stated Aim	Inclusion of Consecutive Patients	Prospective Collection of Data	Appropriate Endpoints	Unbiased Assessment	Follow-up Appropriate	Loss of Follow-up <5%	Sample Size Calculation	Control Group	Contemporary Groups	Baseline Group Equivalence	Adequate Statistical Analysis
Dietrich 2008	12	2	2	0	2	0	0	0	0	1	1	2	2
Gallinet 2009	11	1	0	0	2	0	1	1	0	1	2	1	2
Gradl 2009	14	2	2	0	2	0	1	1	0	0	2	2	2
Solberg 2009	15	2	2	0	2	0	2	1	0	0	2	2	2
Matziolis 2010	11	1	2	0	2	0	2	0	0	0	2	0	2
Young 2010	10	1	1	0	2	0	1	0	0	0	1	2	2
Kim 2011	11	1	0	0	2	0	2	0	0	0	2	2	2
Boyle 2012	13	1	2	0	2	0	2	0	0	0	2	2	2
Garrigues 2012	10	1	2	0	2	0	1	0	0	0	2	0	2
Konrad 2012	15	2	2	2	2	0	1	0	0	0	2	2	2
Lecic 2012	9	1	1	0	2	0	0	0	0	0	2	2	1
Spross 2012	13	2	2	0	2	0	1	0	0	0	2	2	2
Trepat 2012	14	2	2	0	2	1	1	0	0	0	2	2	2
Urda 2012	10	2	2	0	2	0	0	0	0	0	2	0	2
Baudi 2014	11	1	2	0	2	0	0	0	0	0	2	2	2
Chalmers 2014	12	1	1	0	2	0	2	2	0	0	0	2	2
Tamimi 2015	14	1	2	0	2	0	2	0	0	0	2	1	2
Ge 2017	16	2	2	0	2	0	2	0	0	2	2	2	2
Lee 2017	15	2	2	0	2	0	2	1	0	0	2	2	2
Repetto 2017	15	1	2	0	2	0	2	0	0	2	2	2	2
Thorsness 2017	14	2	2	0	2	0	2	0	0	0	2	2	2
Klug 2020	13	1	2	0	2	0	2	0	0	0	2	2	2
Bu 2021	14	1	2	0	2	1	2	0	0	0	2	2	2
Erpala 2021	13	1	2	0	2	0	2	0	0	0	2	2	2
Gurnani 2022	11	1	2	2	2	0	0	0	0	0	2	1	1
Peker 2022	12	1	2	0	2	1	0	0	0	0	2	2	2

baseline characteristics, whereas CMS has a focus on study size, description of surgical technique, rehabilitation, outcome criteria and their assessment. Despite the subtle differences in quality assessment between the two scores, the outcome of quality assessment for the included studies were relatively similar with no obvious outliers.

Applying the Grade criteria to the individual studies, all randomized controlled trials (RCT) were categorized with initial high quality of evidence and observational comparative studies were categorized with low quality of evidence (Table 9). All RCTs were downgraded. Seven studies had a moderate final level of certainty [17,28,32,38,41,48,50] and two studies [20,47] were downgraded to a low final level of certainty. All comparative observational studies were downgraded to a very low level of certainty. The overall Grade domains were assessed as follows: Limitations in study design was downgraded to moderate as most studies had either some or high risk of bias and these limitations are likely to lower the confidence in the estimate of the effect. The domain inconsistency of results was downgraded to low quality as the heterogeneity as the I^2 statistic for the majority (64%) of pooled estimates was above 70% and only four pooled estimates (28%) had an I^2 statistic of 0%. The indirectness of evidence domain was downgraded to low quality as it could not be established whether the comparative observational studies sufficiently accounted for potential demographic differences in patient population. The imprecision of results domain was downgraded to low quality as all included studies did not report the 95% confidence intervals. None of the studies included any factors that increased the quality of the evidence. The final GRADE quality assessment was downgraded to low level of certainty as all four domains were downgraded.

Table 9: Quality Assessment using the Cochrane GRADE system

Authors	LOE	Initial Level of Certainty	Final Level of Certainty	Limitations in Study Design - Risk of Bias	Inconsistency of Results	Indirectness of evidence	Imprecision of Results	Increase Quality of Evidence	Opposing Plausible Residual Bias and Confounding (Upgrading)
Cai 2012	I	High	Low	High	N/A		95% CI missing		
Zhu 2011	I	High	Moderate	Low	N/A		95% CI missing		
Sebastia-Forcada 2014	I	High	Moderate	Low	N/A		95% CI missing		
Gracitelli 2016	I	High	Moderate	Low	N/A		95% CI missing		
Fraser 2020	I	High	Moderate	Low	N/A		95% CI missing		
					N/A		95% CI missing		
Bastian 2009	II	High	Moderate	Low	N/A		95% CI missing		
Cuff 2013	II	High	Moderate	Low	N/A		95% CI missing		
Plath 2019	II	High	Moderate	Low	N/A		95% CI missing		
Spross 2019	II	High	Low	High	N/A		95% CI missing		
					N/A		95% CI missing		
Dietrich 2008	III	Low	Very Low	High	N/A		95% CI missing		
Gallinet 2009	III	Low	Very Low	Low	N/A		95% CI missing		
Gradl 2009	III	Low	Very Low	Low	N/A		95% CI missing		
Solberg 2009	III	Low	Very Low	Low	N/A		95% CI missing		
Matziolis 2010	III	Low	Very Low	Some	N/A		95% CI missing		
Young 2010	III	Low	Very Low	Some	N/A		95% CI missing		
Kim 2011	III	Low	Very Low	High	N/A		95% CI missing		
Boyle 2012	III	Low	Very Low	Low	N/A		95% CI missing		
Garrigues 2012	III	Low	Very Low	Low	N/A		95% CI missing		
Konrad 2012	III	Low	Very Low	High	N/A		95% CI missing		
Lekic 2012	III	Low	Very Low	Some	N/A		95% CI missing		
Spross 2012	III	Low	Very Low	Some	N/A		95% CI missing		
Trepas 2012	III	Low	Very Low	Some	N/A		95% CI missing		
Urda 2012	III	Low	Very Low	High	N/A		95% CI missing		
Baudi 2014	III	Low	Very Low	Some	N/A		95% CI missing		
Chalmers 2014	III	Low	Very Low	High	N/A		95% CI missing		
Ge 2017	III	Low	Very Low	High	N/A		95% CI missing		

Lee 2017	III	Low	Very Low	Low	N/A		95% CI missing		
Tamimi 2015	III	Low	Very Low	High	N/A		95% CI missing		
Repetto 2017	III	Low	Very Low	High	N/A		95% CI missing		
Thorsness 2017	III	Low	Very Low	Some	N/A		95% CI missing		
Klug 2020	III	Low	Very Low	Some	N/A		95% CI missing		
Bu 2021	III	Low	Very Low	Some	N/A		95% CI missing		
Erpala 2021	III	Low	Very Low	Some	N/A		95% CI missing		
Gurnani 2022	III	Low	Very Low	Some	N/A		95% CI missing		
Peker 2022	III	Low	Very Low	High	N/A		95% CI missing		

Clinical outcomes and between implant comparisons

The clinical outcomes for all studies are summarized in Tables 1-4. Thirty-three studies [16-33, 35-43,45-50] reported Constant and ASES scores and were included in the analysis. When comparing ORIF to hemiarthroplasty, the pooled estimate for these studies demonstrated significant differences between the two groups in favor of ORIF (SMD -0.556, 95% CI: 0.721 to -0.391, $p=0.0001$, $I^2= 88\%$; Figure 3). According to Cohen, the magnitude effect is medium, suggesting that the SMD represents true differences between groups and that 69% of the hemiarthroplasty group outcomes are below the mean of the ORIF group [51]. When comparing ORIF to IM Nailing, the pooled estimate for these studies demonstrated no significant differences between the two groups. (SMD 0.167, 95% CI: -2.08 to 0.541, $p=0.383$, $I^2= 89\%$; Figure 4). According to Cohen the magnitude effect is small, suggesting that the differences between groups are negligible. [51]. When comparing ORIF to Reverse Shoulder Arthroplasty (RTS) and RTS to hemiarthroplasty, the pooled estimate for both these groups demonstrated non-significant differences between the two groups, and with both comparisons in favor of RTS (SMD 1.037, 95% CI: -0.865 to 2.939, $p=0.285$, $I^2= 98\%$; Figure 5; SMD 1.160, 95% CI: 0.696 to 1.625, $p=0.0001$, $I^2= 70\%$; Figure 6). According to Cohen the magnitude effect is large in the ORIF vs RTS group, suggesting that the SMD represents true differences between groups [51]. However, the lack of statistical significance and overlapping 95% confidence intervals suggest that these differences are not relevant. Regarding the RTS vs hemiarthroplasty, again according to Cohen the magnitude effect is large, strongly suggesting that the SMD represents true differences between groups. In this case, specifically, 79% of the hemiarthroplasty group outcomes are below the mean of the RTS group [51].

ORIF vs Hemi

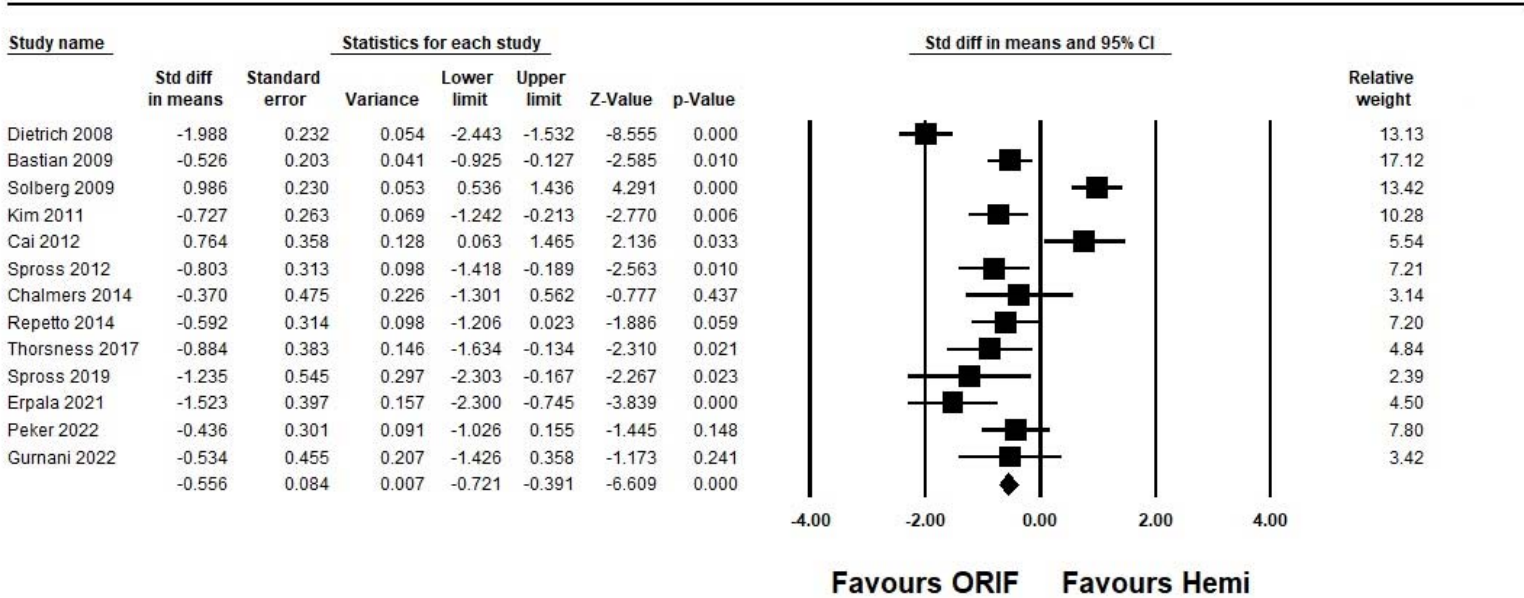


Figure 3. Forest plot comparing clinical outcomes of ORIF to hemiarthroplasty. The pooled estimate for all studies demonstrated significant differences in favor of ORIF ($p = 0.0001$)

ORIF vs IM Nailing

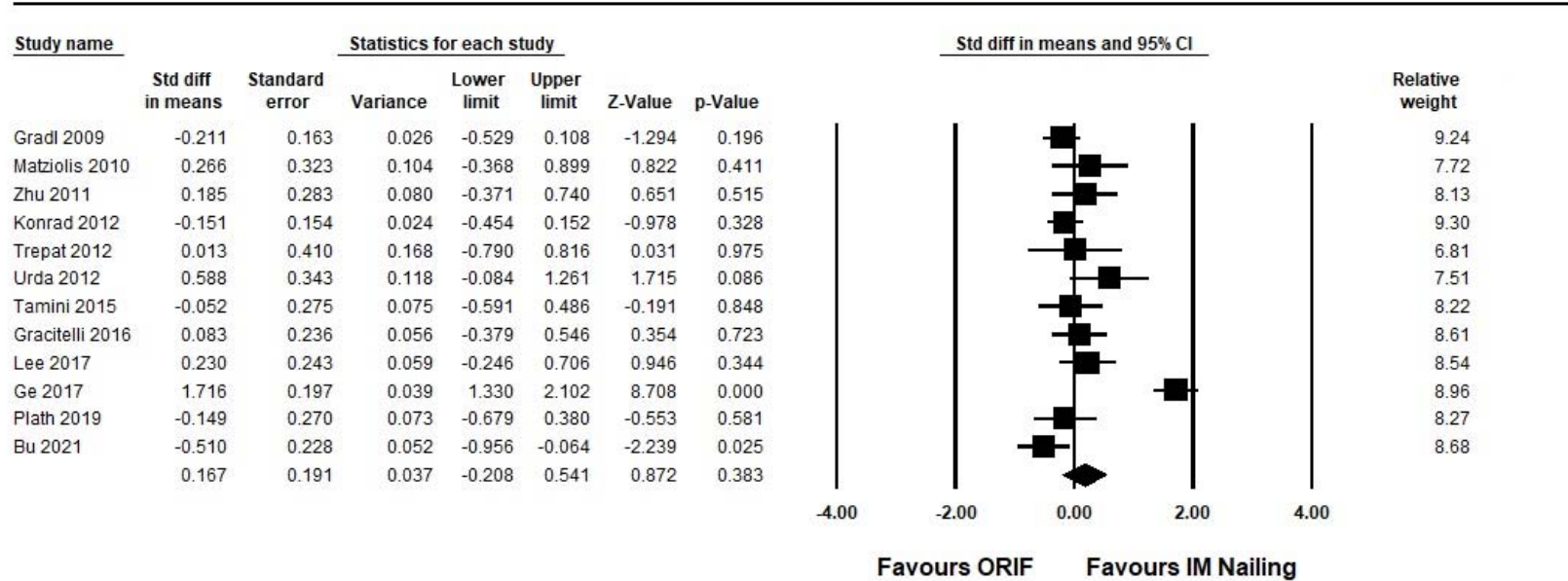


Figure 4. Forest plot comparing clinical outcomes of ORIF to intramedullary nailing. The pooled estimate for all studies demonstrated no between-group differences ($p = 0.383$)

ORIF vs Reverse

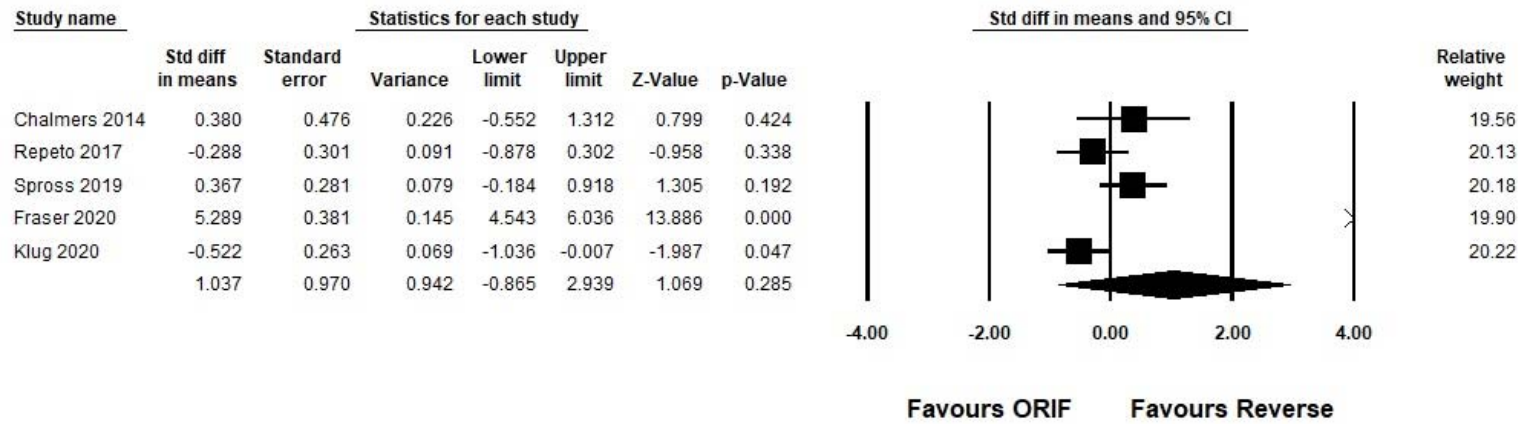


Figure 5. Forest plot comparing clinical outcomes of ORIF to reverse shoulder arthroplasty (RTS). The pooled estimate for all studies demonstrated no between-group differences ($p = 0.285$), but a large magnitude effect was observed in favor of RTS

Hemi vs Reverse

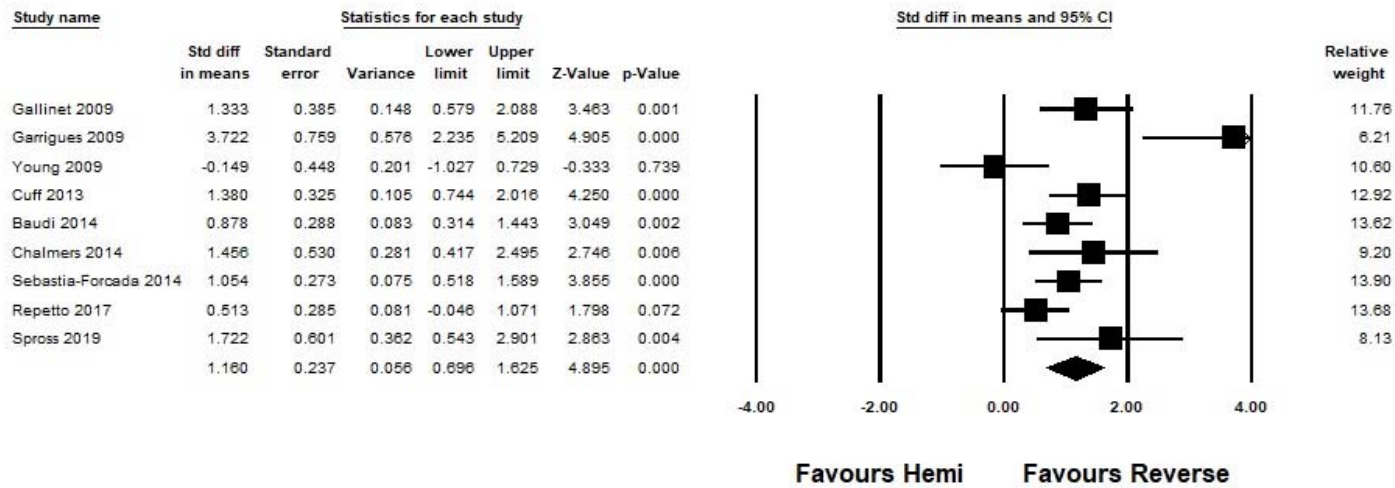


Figure 6. Forest plot comparing clinical outcomes of reverse shoulder arthroplasty (RTS) to hemiarthroplasty. The pooled estimate for all studies demonstrated significant ($p = 0.0001$) between-group differences in favor of RTS

Range of motion

Eighteen studies [21,22,25-29,32,34-36,40,41,43-45,48-50] included range of motion assessments and were included in the analysis.

Abduction

When comparing ORIF to hemiarthroplasty and reverse shoulder arthroplasty (RTS) to hemiarthroplasty, the pooled estimate for these studies demonstrated significant differences within each comparative group in favor of ORIF (SMD -1.002, 95% CI: -1.874 to -0.130, $p=0.0024$, $I^2= 82\%$; Figure 7) and RTS (SMD 1.030, 95% CI: 0.023 to 1.328, $p=0.0001$, $I^2= 0\%$; Figure 9), respectively. According to Cohen the magnitude effect is large, strongly suggesting that the SMD represents true differences between groups, and that 79% of the hemiarthroplasty group outcomes are below the mean of the ORIF and the RTS group [51]. When comparing ORIF to IM Nailing, the pooled estimate for these studies demonstrated no significant differences between the two groups. (SMD 0.256, 95% CI: -0.095 to 0.606, $p=0.153$, $I^2= 0\%$; Figure 8). According to Cohen the magnitude effect is small, suggesting that the differences between groups are negligible. [51]. When comparing Reverse Shoulder Arthroplasty (RTS) to hemiarthroplasty, the pooled estimate for these studies demonstrated significant differences between the two groups in favor of RTS (SMD 1.030, 95% CI: 0.023 to 1.328, $p=0.0001$, $I^2= 0\%$; Figure 9). According to Cohen the magnitude effect is large, strongly suggesting that the SMD represents true differences between groups and that 79% of the hemiarthroplasty group outcomes are below the mean of the RTS group [51]. Only one study [22] compared abduction between ORIF and Reverse Shoulder Arthroplasty (RTS); pooled estimates were, therefore, not calculated.

ORIF vs Hemi

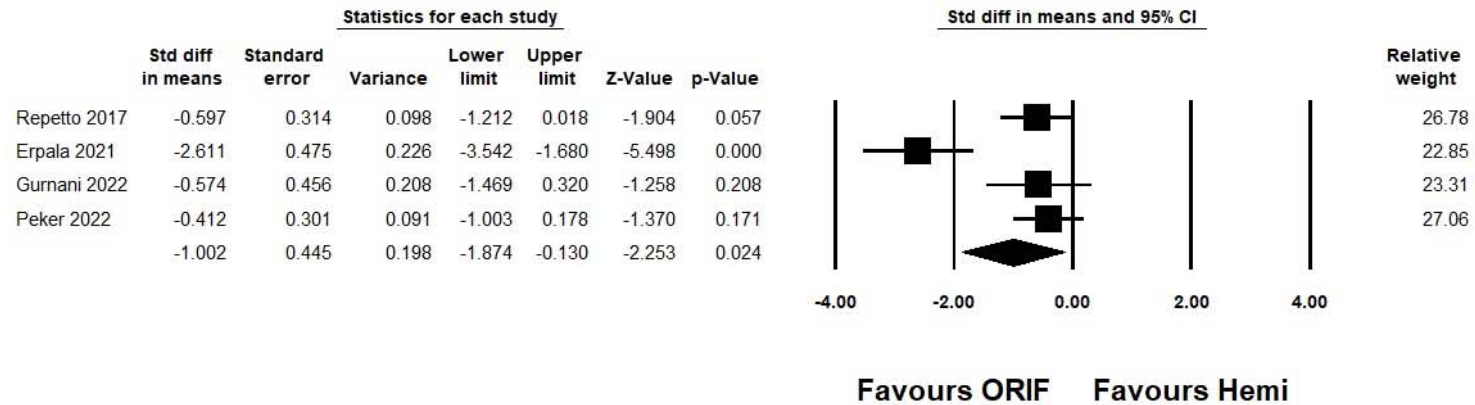


Figure 7. Forest plot comparing abduction of ORIF to hemiarthroplasty. The pooled estimate for all studies demonstrated significant differences in favor of ORIF ($p = 0.0024$)

IM Nailing vs ORIF

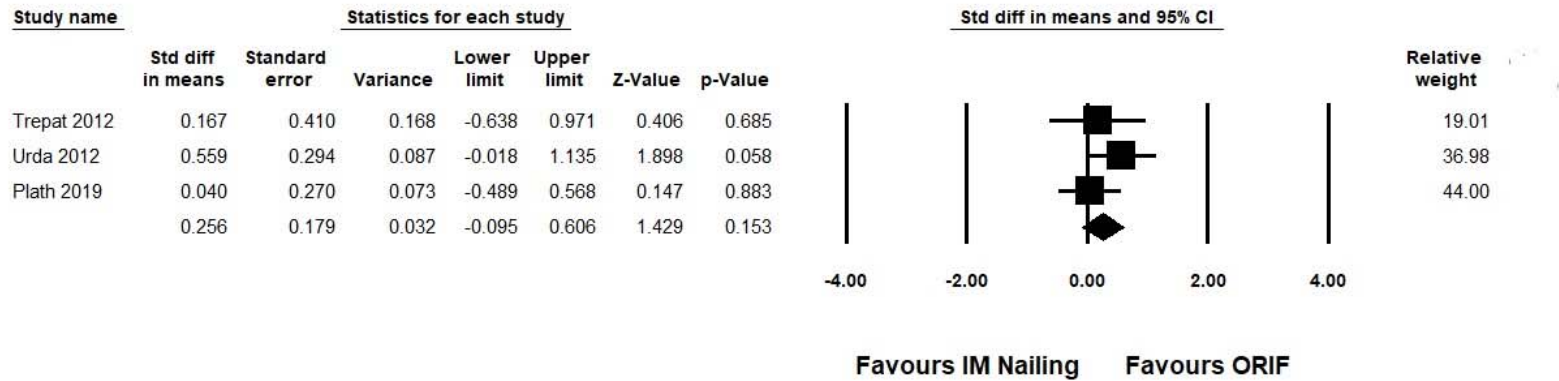


Figure 8. Forest plot comparing abduction of reverse shoulder arthroplasty (RTS) to hemiarthroplasty. The pooled estimate for all studies demonstrated significant between-group differences ($p = 0.0001$) in favor of RTS

Hemi vs Reverse

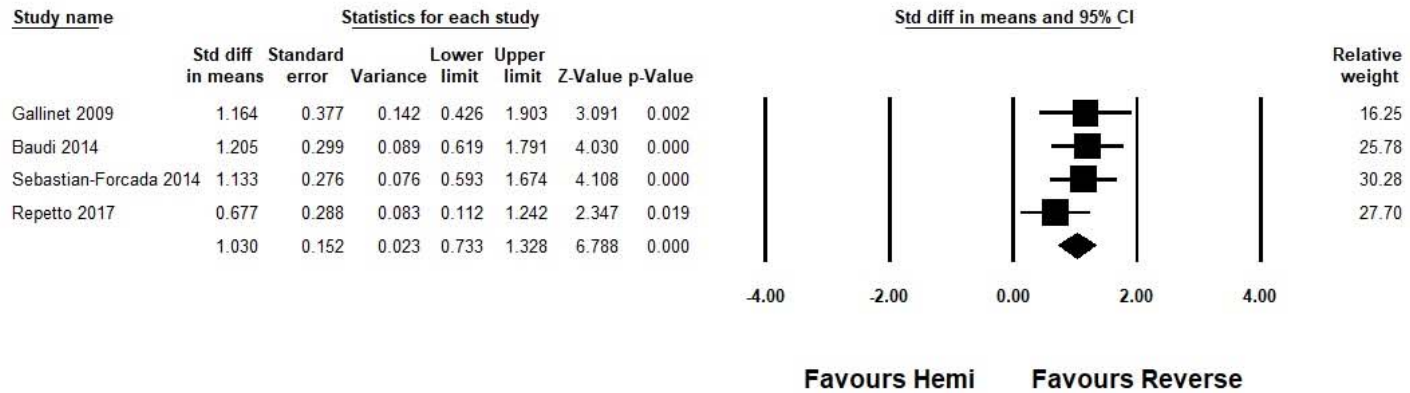


Figure 9. Forest plot comparing abduction of ORIF to intramedullary nailing. The pooled estimate for all studies demonstrated no between-group differences ($p = 0.153$)

Forward Flexion

When comparing ORIF to hemiarthroplasty and reverse shoulder arthroplasty (RTS) to hemiarthroplasty, the pooled estimate for both these studies demonstrated significant differences within each comparative group in favor of ORIF (SMD -0.708, 95% CI: -1.143 to -0.272, $p=0.001$, $I^2=92\%$; Figure 10) and RTS (SMD 1.118, 95% CI: 0.873 to 1.362, $p=0.0001$, $I^2=0\%$; Figure 12), respectively. According to Cohen the magnitude effect is medium for the ORIF vs hemiarthroplasty comparison, and large for the RTS vs hemiarthroplasty comparison, suggesting that the SMD represents true differences between groups and that 69% and 79% of the hemiarthroplasty group outcomes are below the mean of the ORIF group and RTS group, respectively [51]. When comparing ORIF to IM Nailing, the pooled estimate for these studies demonstrated no significant differences between the two groups. (SMD 0.530, 95% CI: -0.090 to 1.150, $p=0.094$, $I^2=88\%$; Figure 11). According to Cohen the magnitude effect is large, suggesting that the SMD represents true differences between groups [51]. However, the lack of statistical significance and overlapping 95% confidence intervals suggests that these differences are not relevant. Only two studies [21,22] compared forward flexion between ORIF and Reverse Shoulder Arthroplasty (RTS); pooled estimates were, therefore, not calculated.

ORIF vs Hemi

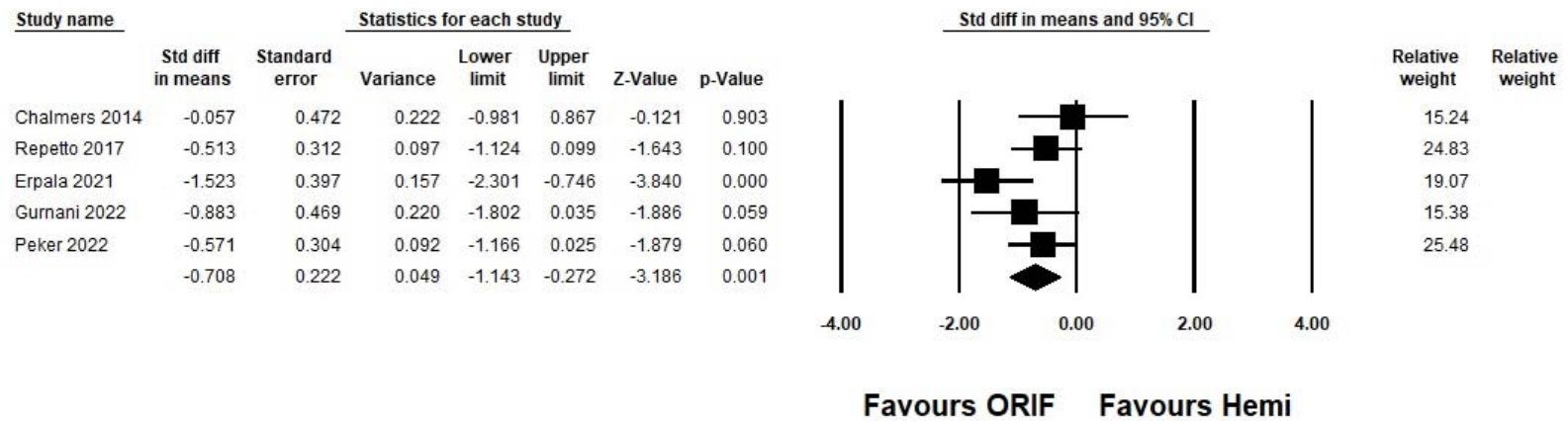


Figure 10. Forest plot comparing forward flexion of ORIF to hemiarthroplasty. The pooled estimate for all studies demonstrated significant differences in favor of ORIF ($p = 0.001$)

IM Nailing vs ORIF

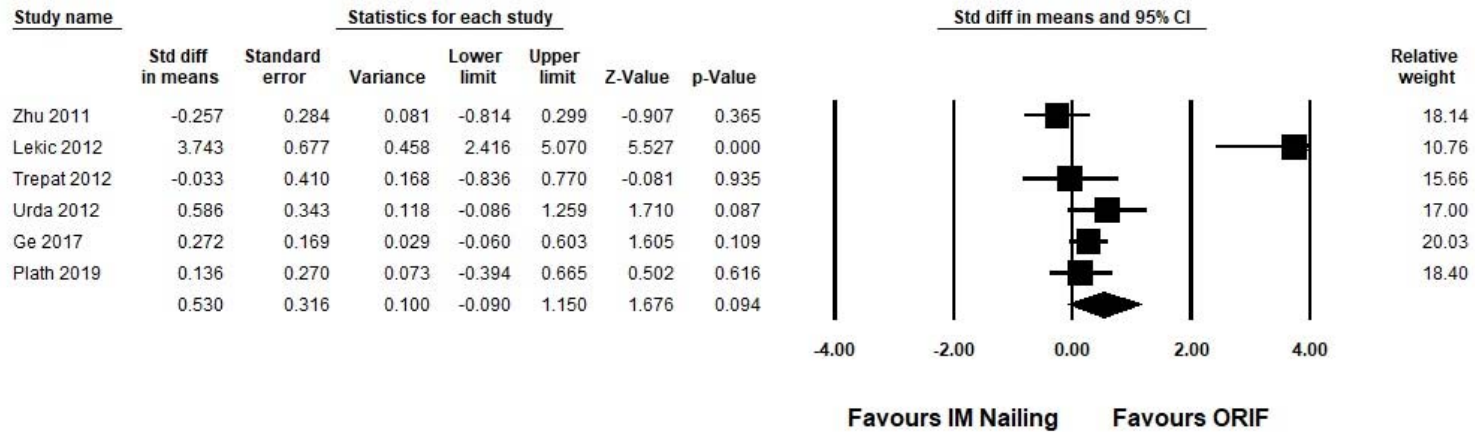


Figure 11. Forest plot comparing forward flexion of reverse shoulder arthroplasty (RTS) to hemiarthroplasty. The pooled estimate for all studies demonstrated significant between-group differences ($p = 0.0001$) in favor of RTS

Hemi vs Reverse

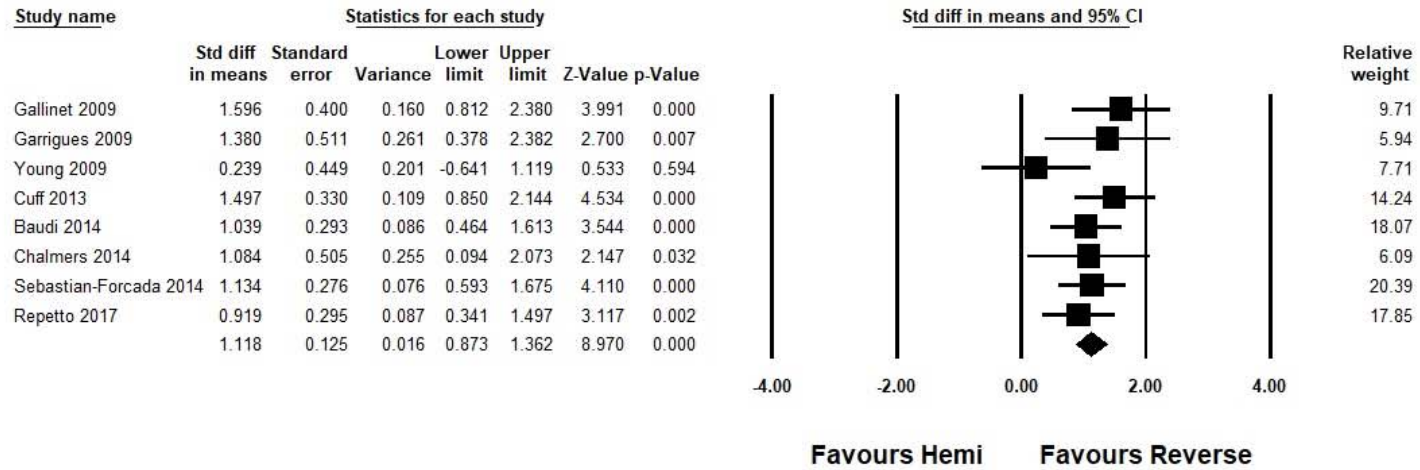


Figure 12. Forest plot comparing forward flexion of ORIF to intramedullary nailing. The pooled estimate for all studies demonstrated no between-group differences ($p = 0.094$)

External rotation

When comparing ORIF to hemiarthroplasty and ORIF to Reverse Shoulder Arthroplasty (RTS), the pooled estimate for these studies demonstrated significant differences within each comparative group in favor of ORIF (SMD -1.048, 95% CI: -1.809 to -0.287, $p=0.007$, $I^2= 71\%$; Figure 13) and RTS (SMD -0.406, 95% CI: -0.764 to -0.048, $p=0.026$, $I^2= 0\%$; Figure 15), respectively. According to Cohen the magnitude effect for the ORIF vs hemiarthroplasty comparison is large, and medium for the ORIF vs RTS comparison, suggesting that the SMD represents true differences between groups; 79% of the hemiarthroplasty group outcomes are below the mean of the ORIF group, and 69% of the ORIF group outcomes are below the mean of the RTS group [51]. When comparing ORIF to IM Nailing and Reverse Shoulder Arthroplasty (RTS) to hemiarthroplasty, the pooled estimate for these studies demonstrated no significant differences within each comparative group (ORIF vs IM Nailing: SMD 0.122, 95% CI: -0.82 to 0.525, $p=0.554$, $I^2= 56\%$; Figure 14; RTS vs hemiarthroplasty: SMD -0.278, 95% CI: -1.079 to 0.522, $p=0.495$, $I^2= 89\%$; Figure 16). According to Cohen the magnitude effect within each comparative group is small, suggesting that the differences between groups are negligible. [51]. When comparing ORIF to Reverse Shoulder Arthroplasty (RTS), the pooled estimate for these studies demonstrated significant differences between the two groups in favor of RTS (SMD -0.406, 95% CI: -0.764 to -0.048, $p=0.026$, $I^2= 0\%$; Figure 15). According to Cohen the magnitude effect is medium, suggesting that the SMD represent true differences between groups; 69% of the ORIF group outcomes are below the mean of the RTS group [51]. When comparing Reverse Shoulder Arthroplasty (RTS) to hemiarthroplasty, the pooled estimate for these studies demonstrated no significant differences between the two groups. (SMD -0.278, 95% CI: -1.079 to 0.522, $p=0.495$, $I^2= 89\%$; Figure 16).

ORIF vs Hemi

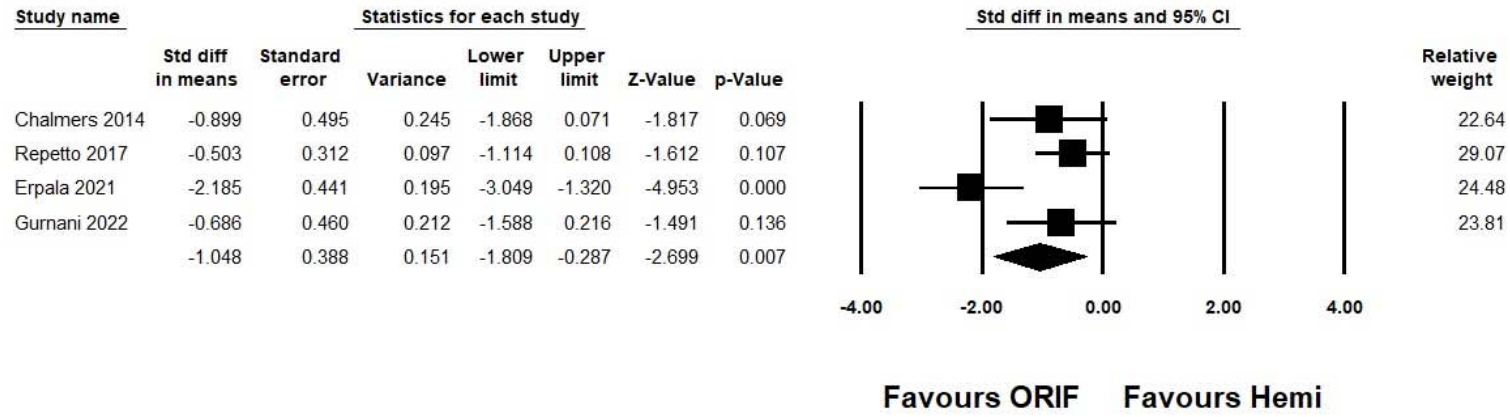


Figure 13. Forest plot comparing external rotation of ORIF to hemiarthroplasty. The pooled estimate for all studies demonstrated significant differences in favor of ORIF ($p = 0.007$)

ORIF vs IM Nailing

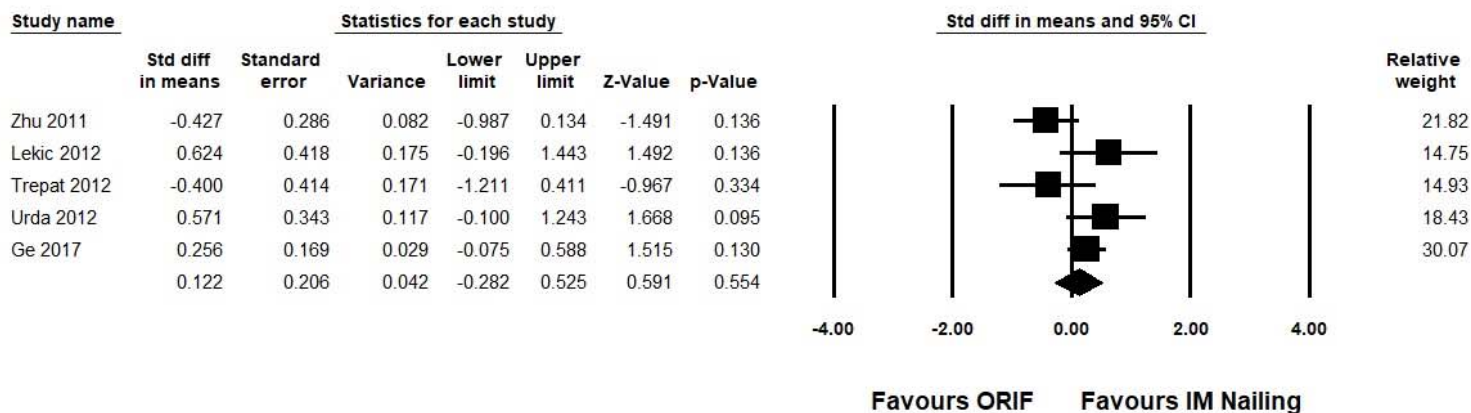


Figure 14. Forest plot external rotation of ORIF to reverse shoulder arthroplasty (RTS). The pooled estimate for all studies demonstrated significant between-group differences ($p = 0.026$) in favor of RTS

Reverse vs ORIF

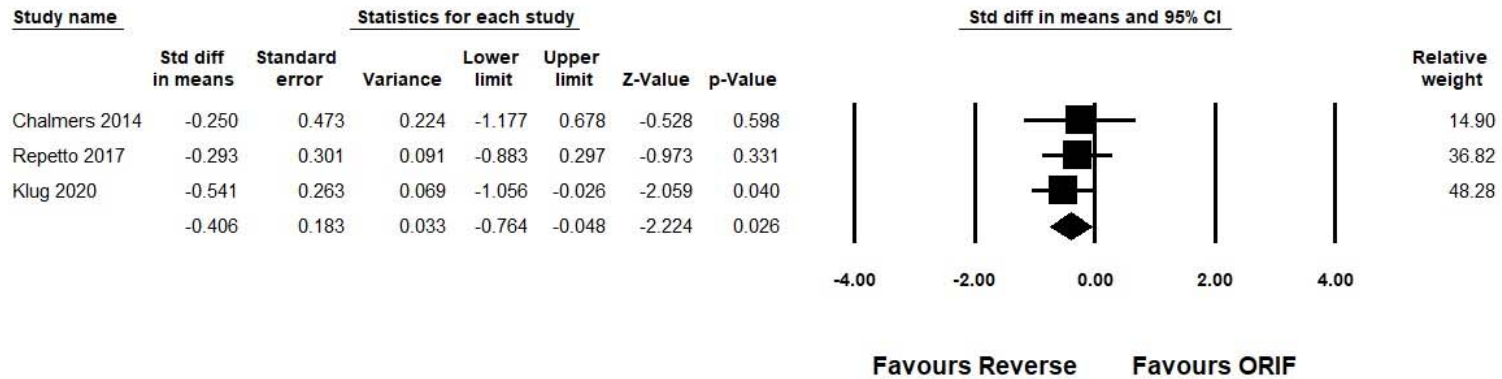


Figure 15. Forest plot comparing external rotation of ORIF to intramedullary nailing. The pooled estimate for all studies demonstrated no between-group differences ($p = 0.554$)

Hemi v Reverse

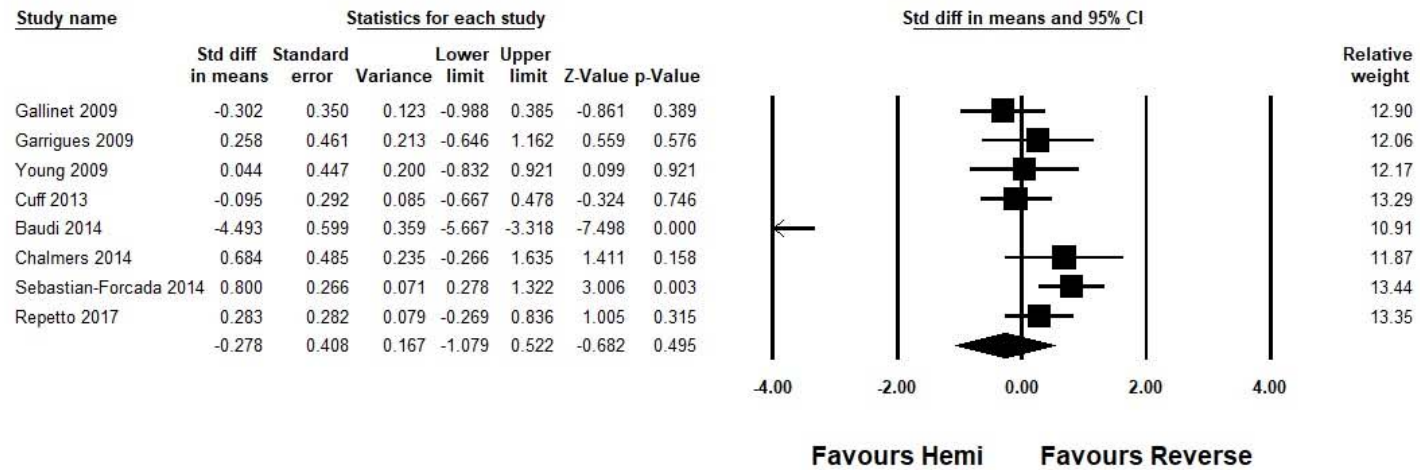


Figure 16. Forest plot comparing external rotation of reverse shoulder arthroplasty (RTS) to hemiarthroplasty. The pooled estimate for all studies demonstrated no between-group differences ($p = 0.522$)

According to Cohen the magnitude effect is small, suggesting that the differences between groups are negligible. [51].

Complications

When comparing ORIF to hemiarthroplasty, IM Nailing, and Reverse Shoulder Arthroplasty (RTS), the pooled estimates in all cases demonstrated overall lower complication rates in the hemiarthroplasty group (Odds ratio 0.508, 95% confidence intervals 0.215-1.202, $p=0.123$; (Figure 17), the IM Nailing group (Odds ratio 1.215, 95% confidence intervals 0.849-1.738, $p=0.287$; Figure 18), and the RTS group (Odds ratio 0.424, 95% confidence intervals 0.192-0.937, $p=0.034$) (Figure 19), respectively. In the ORIF vs hemiarthroplasty and the ORIF vs IM Nailing groups these differences were not statistically significant, with overlapping 95% confidence intervals and small to medium odds ratios, and the between group differences are considered negligible. [52]. However, in the ORIF vs RTS group, these differences were statistically significant but overlapping 95% confidence intervals were observed, which indicates that the between group differences are negligible. When comparing Reverse Shoulder Arthroplasty (RTS) to hemiarthroplasty, the pooled estimates demonstrated overall lower complication rates in the RTS group (Odds ratio 0.383, 95% confidence intervals 0.190-0.770, $p=0.007$) (Figure 20). These differences were statistically significant, but overlapping 95% confidence intervals were observed indicating that the between group differences are negligible.

Hemi vs ORIF

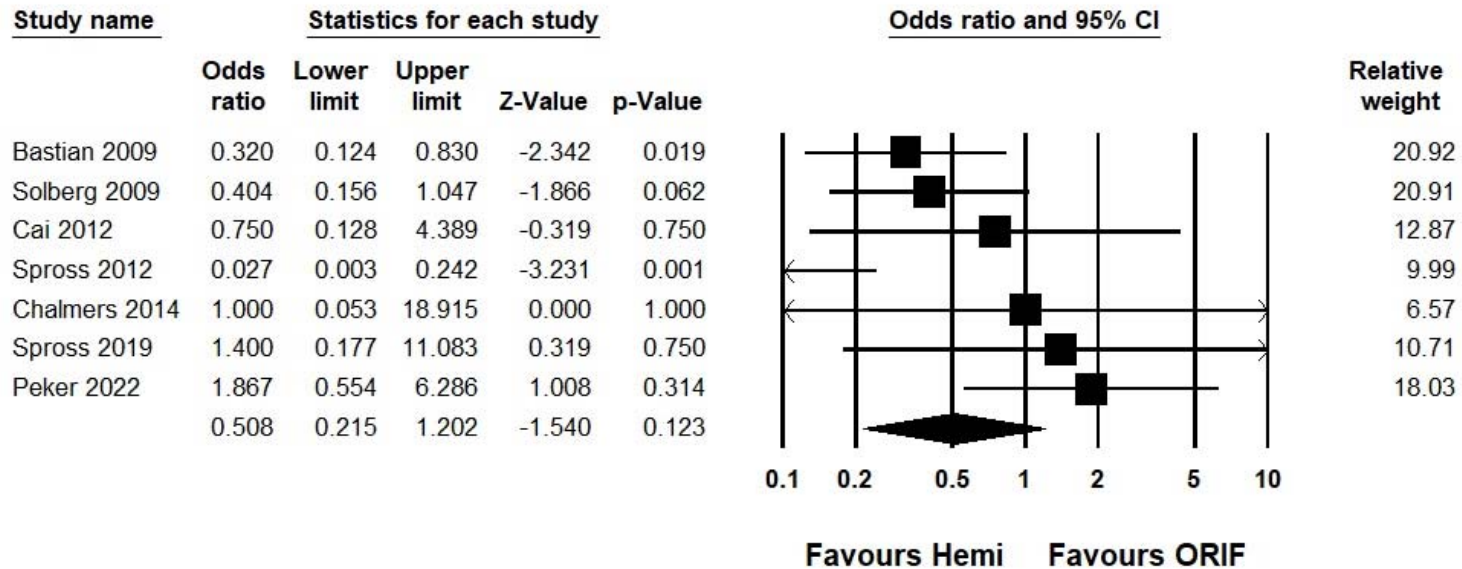


Figure 17. Forest plot comparing complication rates of ORIF to hemiarthroplasty. The pooled estimate for all studies demonstrated no between-group differences ($p = 0.123$) but demonstrated overall lower complication rates in the hemiarthroplasty group

ORIF vs IM Nailing

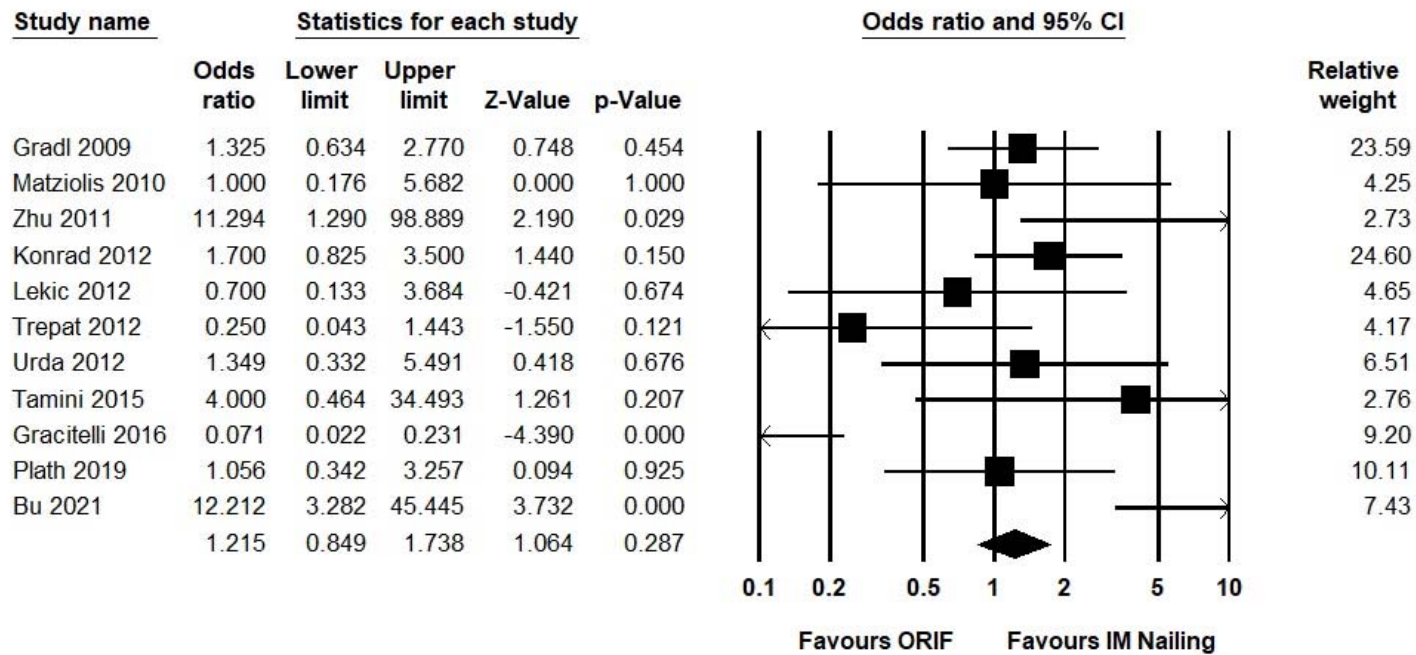


Figure 18. Forest plot comparing complication rates of ORIF to intramedullary nailing. The pooled estimate for all studies demonstrated no between-group differences ($p = 0.287$) but demonstrated overall lower complication rates in the IM nail group

Reverse vs ORIF

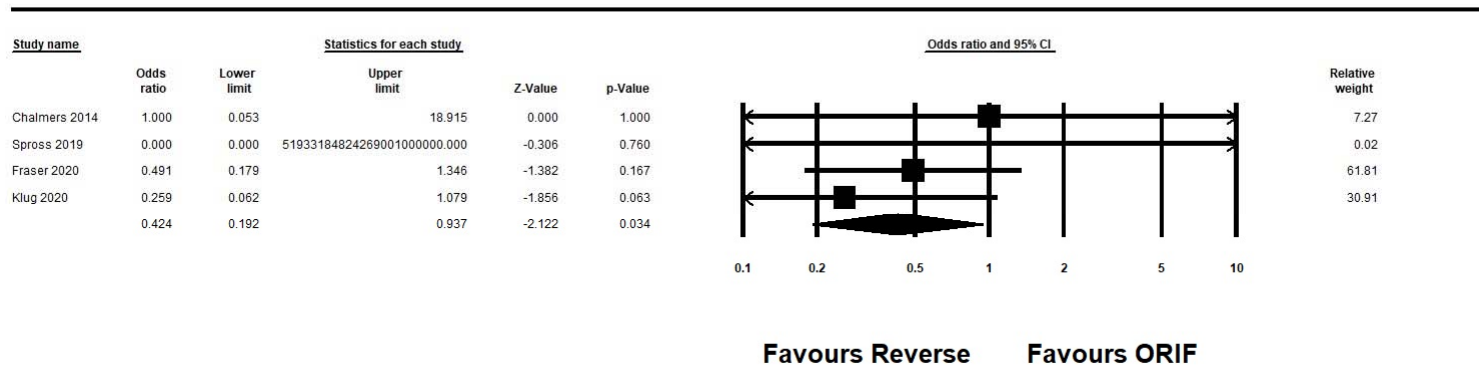


Figure 19. Forest plot comparing clinical outcomes of ORIF to reverse shoulder arthroplasty (RTS). The pooled estimate for all studies demonstrated significant between-group differences ($p = 0.034$) in favor of RTS, but overlapping 95% confidence intervals indicate that these differences were not relevant

Reverse vs ORIF

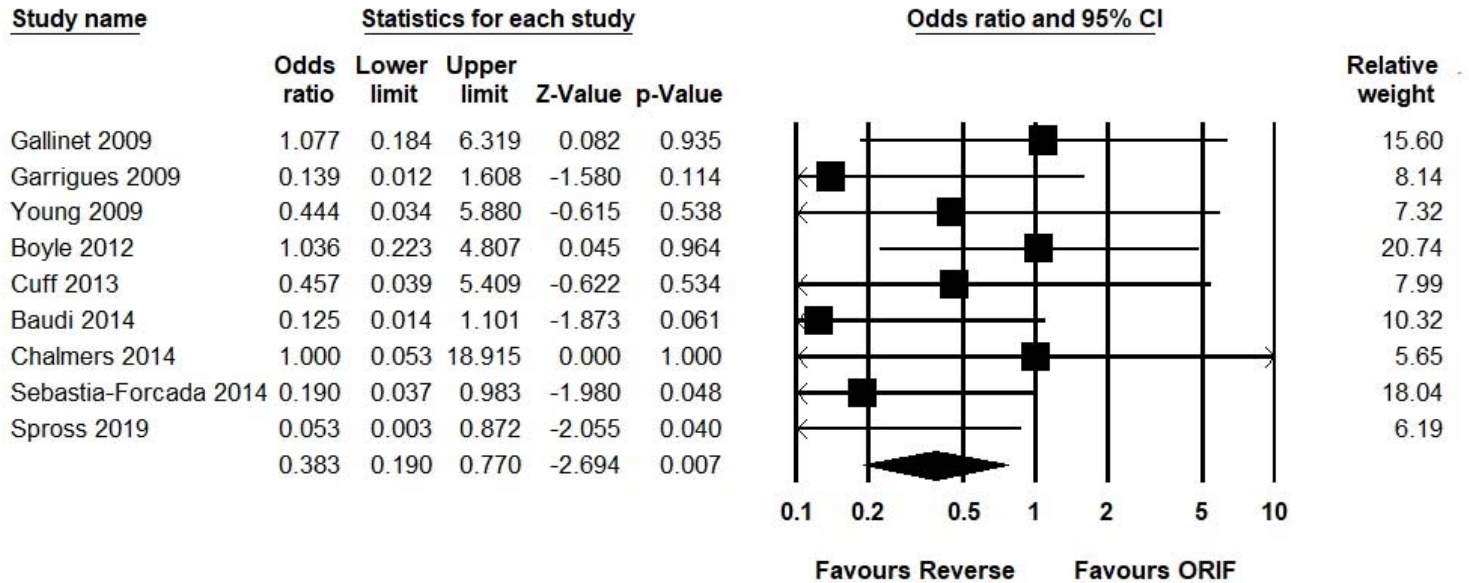


Figure 20. Forest plot comparing clinical outcomes of reverse shoulder arthroplasty (RTS) to hemiarthroplasty. The pooled estimate for all studies demonstrated significant ($p = 0.007$) between-group differences in favor of RTS, but overlapping 95% confidence intervals indicate that these differences were not relevant

Discussion

The results of this meta-analysis had interesting and unexpected results. For three- and four-part fractures ORIF was clearly superior to hemiarthroplasty and resulted in better clinical outcomes and range of motion with similar complication rates. There were no available studies that also included two-part fractures and there is currently no accepted indication to treat two-part fractures with hemiarthroplasty. The data convincingly showed that 69-79% of hemiarthroplasty outcomes were below the mean results reported following ORIF. Although the complication rates were lower in the hemiarthroplasty group this difference was non-significant, with overlapping 95% confidence intervals suggesting that these between group differences were negligible. The meta data therefore advocates ORIF as a better option for 3- and 4-part fractures of the proximal humerus when compared to hemiarthroplasty. This confirms the results of a meta-analysis by Deng et al. [52], who included studies published until 2014 and concluded that patients treated with locked plating had better clinical outcomes with similar complication and reoperation rates compared to patients treated with hemiarthroplasty. Our meta-analysis included five additional studies and increased the sample size by 22%, further strengthening the conclusions of Deng et al. Surgeons should therefore carefully weigh their options, and when deciding whether to use hemiarthroplasty or locked plating for a specific patient they should strongly consider selecting locked plating as the better option.

Comparisons between ORIF and IM nailing did not reveal any significant between group differences. Meta-analysis demonstrated that clinical outcomes, range of motion, and complication rates were very similar for both surgical techniques indicating that either technique is a feasible option. Studies included for meta-analysis covered mainly

treatment for 2- and 3-part fractures. Theoretically, locking plates have the advantage of better bending and torsion resistance [53]. In contrast, central fixation with IM nailing can resist greater varus loads [34] and possibly result in higher stability for eversion, flexion, and extension movements [54]. An earlier meta-analysis concluded that IM nailing is superior to locked plating in terms of blood loss, operative time, rates of fracture healing, and complications, but could not establish any differences for clinical outcomes, range of motion, and pain symptoms as these were not analyzed [55]. The study was also limited due to a narrow population group, comprising mainly Chinese studies. Although forest plots for intra-operative blood loss, operation time, fracture healing time, and overall complication rates were constructed, the above-mentioned flaws limit both the internal and external validity of their analysis. In 2017, Sun et al. performed a similar meta-analysis which included 10 studies. Their results were comparable to those of the current meta-analysis, in that they demonstrated that both locking plates and IM nails are comparably effective options for proximal humerus fractures [56]. For this reason, surgeons who consider either of the two options can choose between nailing or plating with equal confidence, and make the selection based on personal preference, available equipment, skills, and personal experience.

When comparing ORIF to reverse shoulder arthroplasty (RTS) there were no between group differences for clinical outcomes or complication rates. Although the meta data suggests that clinical outcomes and complication rates for 3- and 4-part fractures favored RTS with a large magnitude effect, the results were statistically non-significant and overlapping 95% confidence intervals were observed. This is somewhat surprising as there is a current trend towards the use of RTS as the preferred treatment for 3-part, 4-part, and head-splitting fractures [57]. Similar to studies comparing ORIF to

hemiarthroplasty, there were no available studies that also included two-part fractures and there is currently no accepted indication to treat two-part fractures with RTS. Orman et al reported that RTS resulted in fewer adverse effects and better clinical outcomes when compared to hemiarthroplasty, although this was comparable to non-surgical treatment [58]. Unbehau et al. performed a survival analysis for arthroplasty following proximal humerus fractures, deriving data from the Nordic Arthroplasty Register, and reported a 10-year survival rate of 86% with a median time to revision of 18 months [59]. In their opinion these figures constitute low survival rates and concluded that surgeons should be critical when it comes to initial fracture management [59]. However, the meta-data from the current study does not support RTS over ORIF, and surgeons should therefore carefully consider their options. Nevertheless, the large magnitude effect supports RTS, and future studies are required to increase sample sizes and provide further evidence. Certainly, non-operative treatment can also be considered, and Shu et al. reported the results of the members of the science of variation group meeting who suggested that surgeons should consider initial nonoperative treatment with an option for future conversion to reverse arthroplasty [60].

Comparisons between hemiarthroplasty and reverse shoulder arthroplasty (RTS) revealed significant between group differences in favor of RTS. For clinical outcomes, abduction, and flexion range, 79% of the mean outcomes for hemiarthroplasty are below the mean results of RTS for 3- and 4-part fractures. A significantly lower complication rate was also observed in the RTS group. However, despite an odds ratio of 0.38 in favor of the RTS group, overlapping 95% confidence intervals indicate that these results are not clinically relevant. As seen with the comparison between hemiarthroplasty and ORIF, treatment with hemiarthroplasty is clearly inferior and one

could argue that hemiarthroplasty for the treatment of proximal humerus fractures should no longer be considered a feasible or reliable option.

The results of this meta-analysis will be helpful in decision-making for all surgeons who treat proximal humerus fractures. The recommendations based on the meta data of this analysis are that ORIF is clearly preferred over hemiarthroplasty, that ORIF and IM nailing produce comparable outcomes. While reverse shoulder arthroplasty is superior to hemiarthroplasty for 3- and 4-part fractures, it provides no obvious advantages over ORIF. However, many other factors should be taken into consideration when planning treatment including patient age, head trauma, concomitant femoral neck fractures, congestive heart failure, chronic alcoholism, obesity, dementia, pneumonia, and anemia, all of which may adversely affect outcomes [61]. Decision-making for these complex and controversial topics is inherently difficult. Internal fixation appears to be the preferred treatment for many surgeons, but there is still no current agreement on the main factors that influence their decisions [62]. Interestingly, 51% of surgeons consider patient-based factors, 51% fracture morphology, 42% surgeon factors, and 11% bone quality [62]. These difficulties in decision-making are also reflected by low agreement rates between surgeons. Experienced shoulder surgeons only agree in 63% of cases on the treatment that should be performed, and these uncertainties may also contribute to the potential for inferior outcomes [64].

Limitations

The limitations of this meta-analysis are inherently related to the limitations of the included studies. The Cochrane Handbook indicates that high risk of bias within and across trials may seriously alter the results, and is sufficient to affect the interpretation

of results [15]. In this meta-analysis the across trial high risk of bias was 68%, and this is possibly sufficient to conclude that the results should be interpreted with caution. Unfortunately, 30 of the 35 studies had a very low final level of certainty, one study had a low final level of certainty, and only four studies had a moderate final level of certainty. According to the Cochrane Handbook [15], this reduces the confidence in the effect estimate and is sufficient to affect the interpretation of results with the true effect being different. The Grade Recommendations for clinicians are therefore considered to be weak [15]. For this reason, surgeons must recognize that different choices will be appropriate for different patients, and that surgeons must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may well be useful in helping individuals making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working towards a shared decision [15]. An individual surgeons' experience and patient expectations will almost certainly continue to be the most important factors to be considered.

Conclusions

This meta-analysis for surgical treatment of proximal humerus fractures demonstrated that ORIF is superior to hemiarthroplasty, ORIF is comparable to intramedullary nailing, and reverse shoulder arthroplasty is superior to hemiarthroplasty but comparable to ORIF with similar clinical outcomes, range of motion, and complication rates. However, the study validity remains compromised by high risk of bias and low level of certainty, and these results should therefore be interpreted with caution. At this time, shared decision-making should confidently reflect the treating surgeon's skills

and experience balanced against patient demands and expectations, tempered by their comorbidities while respecting the realities of bone quality and injury severity.

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