Interventions for proximal humeral fractures: key messages from a Cochrane review

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Background

Fractures of the proximal humerus are common injuries, especially in older people. Patients are managed on a daily basis in most emergency departments and orthopedic clinics. Definitive treatment is either non-surgical or surgical where options include open reduction and internal fixation with locking plates, intramedullary nailing, hemiarthroplasty (HA) and, most recently, reverse total shoulder arthroplasty (RTSA) (1). Preferred treatment approaches, including the use of surgery for displaced fractures, vary geographically and between hospitals.

The evidence base for treatment of proximal humeral fractures has expanded substantially within the last decade and several high-quality randomized trials are now available. To assist clinical decision-makers and help inform patients, our Cochrane review aimed to provide critical summaries of the available best quality evidence for treatment options.

We present the key messages from an enlarged and updated Cochrane review (2) based on 47 randomized trials with 3,179 participants.

Methods

For a systematic review and meta-analysis we included the randomized trials identified in our search of multiple databases up to September 2020. We updated our search in November 2021, and assessed the suitability of newly identified trials for inclusion: no newly published trials were available or otherwise suitable for immediate inclusion for our 4 main comparisons. Pairs of review authors independently selected studies, assessed risk of bias, and extracted data. We pooled data where appropriate and used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for assessing the certainty of evidence for each outcome (see Table 1 for interpretation). The review does not

Table 1. Grades of evidence

High certainty:	we are very confident that the true effect lies
	close to that of the estimate of the effect
Moderate certainty	: we are moderately confident in the effect esti-
	mate. The true effect is likely to be close to the
	estimate of the effect, but there is a possibility
	that it is substantially different
Low certainty:	our confidence in the effect estimate is limited.
	The true effect may be substantially different
	from the estimate of the effect
Very low certainty:	we have very little confidence in the effect esti-
	mate. The true effect is likely to be substantially
	different from the estimate of the effect

cover 2-part tuberosity fractures, fracture-dislocations, articular surface fractures and fractures in young people.

Results

Of the 47 included trials, 12 evaluated non-surgical treatments, 10 compared surgical with non-surgical treatments, 23 compared 2 methods of surgery, and 2 tested timing of mobilization after surgery. Only 6 of the 26 comparisons presented in the review were tested by 2 or more trials. 4 of the 6 multi-trial comparisons were prioritized a priori for presentation. These are summarized below.

Surgical versus non-surgical treatment

This key comparison was based on 10 trials with 717, predominantly older (aged 60 years or over), participants suffering a displaced 2-, 3-, or 4-part fracture involving the humeral neck. The findings for 3 key outcomes are shown in Table 2. We found high-certainty evidence of no clinically important difference between surgical and non-surgical treatment in patient-reported shoulder function at 1 year (Figure 1) or at 2 years (423 partici-

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Table 2. Modified summary of findings for comparison of surgical versus non-surgical treatment

Patients: older patients with displaced (Neer) proximal humeral fractures treated at hospital (10 trials, 717 participants) Intervention: surgical treatment: usually locking plate or hemiarthroplasty; reverse shoulder arthroplasty used in 1 trial Comparison: non-surgical treatment: sling 'immobilisation'; closed reduction in 2 trials Outcome: functional score and quality of life at 1 year, additional surgery at 2 years

Outcomes	Illustrative com Assumed risk Non-surgical treatment	nparative risks ^a (95% CI) Corresponding risk Surgical treatment	Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
Functional scores ^a (higher = better outcome) Follow-up: 1 year		The overall mean difference in function was 0.10 SD higher (0.07 lower to 0.27 higher)	SMD 0.10 ^b (-0.07 to 0.27)	552 participants (7 studies)	s ⊕⊕⊕⊕ High	All estimates of between- group differences were smaller than the predefined MCID for individual scores
Quality of life: EQ-5D (1: best quality of life) Follow-up: 1 year	Mean score ranged from 0.65 to 0.90	The mean EQ-5D score in the surgery groups was 0.01 higher (0.02 lower to 0.04 higher)	MD 0.01 (-0.02 to 0.04)	502 participants (6 studies)	s ⊕⊕⊕⊕ High	The MCID of 0.12 was outside the 95% CI at this time period.
Additional surgery (re-operation or secondary surgery) Follow-up: up to 2 years	35 per 1,000	73 per 1,000 (43–129)	RR 2.06 (1.21–3.51)	667 participants (9 studies)	s ⊕⊕⊝⊝ Low	Additional surgery was reported for 54 participants in total.

CI: confidence interval; EQ-5D: European Quality of Life-5 Dimensions; MCID: minimal clinically important difference; MD: mean difference; RR: risk ratio; SMD: standardised mean difference

^a American Shoulder and Elbow Surgeons score (ASES; 1 trial), Disability of the Arm, Shoulder and Hand questionnaire (DASH; 4 trials), Oxford Shoulder Score (OSS; 1 trial); Simple Shoulder Test (SST; 1 trial)

^b SMD 0.2: small difference, 0.5: moderate difference, 0.8 large difference

	Surgery			Non-surgical		Std. Mean Difference		Std. Mean Difference	Risk of Bias			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	ABCDEFG		
6.1.1 Disability of the Arm, Shoulder, and Hand (0 to 100: worst disability) (reversed)												
Launonen 2019a	-18	18.5	35	-17.5	17	39	13.4%	-0.03 [-0.48, 0.43]		$\bullet \bullet \circ \circ \circ \bullet \bullet \bullet \bullet$		
Lopiz 2019	-20.7	13.9	29	-28.8	19.6	30	10.4%	0.47 [-0.05, 0.99]		? • • • ? • •		
Olerud 2011a	-29.1	23.3	27	-35.1	24.2	27	9.8%	0.25 [-0.29, 0.78]		$\bullet \bullet $		
Olerud 2011b Subtotal (95% CI)	-32	22.6	26 117	-35	23.8	25 121	9.3% 42.9%	0.13 [-0.42, 0.68] 0.19 [-0.07, 0.44]	-	••••?•?		
Heterogeneity: Chi ² =	2.09, df=	= 3 (P =	0.55);	² = 0%								
Test for overall effect:	Z=1.45	(P = 0.1)	5)									
6.1.2 American Shou	der and	Elbow S	Surgeo	ons (0 to	24: be	st)						
Fjalestad 2010a (1) Subtotal (95% Cl)	14.8	6.6	23 23	15.5	6.9	25 25	8.7% 8.7%	-0.10 [-0.67, 0.46] - 0.10 [-0.67, 0.46]		•••		
Heterogeneity: Not ap	plicable											
Test for overall effect:	Z = 0.35	(P = 0.7)	2)									
6.1.3 Simple Shoulde	r Test (0	to 12: k	pest)									
Boons 2012	7.17	2.95	23	6.83	2.88	24	8.5%	0.11 [-0.46, 0.69]		•••••		
Subtotal (95% CI)			23			24	8.5%	0.11 [-0.46, 0.69]				
Heterogeneity: Not ap	plicable											
Test for overall effect:	Z = 0.39	(P = 0.6	i9)									
6 1 4 Oxford Shouldo	r Scoro	0 to 49	hoet)									
DroEUED 2015 (2)	20.22	0 616	100	20.0	0 471	110	20.0%	0.0410.02.0241				
Subtotal (95% Cl)	39.23	9.015	109	30.0	9.471	110	39.9%	0.04 [-0.22, 0.31]	-			
Heterogeneity: Not an	nlicable		105			110	55.570	0.04[-0.22, 0.01]				
Test for overall effect:	7 = 0.33	(P = 0.7)	(4)									
restion overall ellett.	2 - 0.00	(i = 0.1	-7/									
Total (95% CI)			272			280	100.0%	0.10 [-0.07, 0.27]	◆			
Heterogeneity: Chi ² =	3.22. df=	= 6 (P =	0.78);	I [≈] = 0%						-		
Test for overall effect:	Z=1.17	(P = 0.2)	(4)						-1 -U.5 U U.5 1			
Test for subgroup diffe	erences:	Chi ² = 1	1.13, d	f= 3 (P=	= 0.77),	² = 0%			ravours non-surgical ravours surgery			
Footnotes									Risk of bias legend			
(1) Values made negative to reverse order of effect									(A) Random sequence generation (selection bias)			
(2) Adjusted scores									(B) Allocation concealment (selection bi	as)		
									(C) Blinding (performance bias and dete	ection bias): Functional		
									(D) Incomplete outcome data (attrition b	ias): Functional		
									(E) Selective reporting (reporting bias)			
									(F) Balance in baseline characteristics?			
									(G) Free from performance bias?			

Figure 1. Surgical versus non-surgical treatment: functional scores at 12 months

	Surge	ery	Non-sur	gical		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	ABCDEFG
6.19.1 at 6 to 12 mont	hs							
Boons 2012	1	25	0	25	2.6%	3.00 [0.13, 70.30]		
Kristiansen 1988	1	15	2	16	10.2%	0.53 [0.05, 5.29]		?? • • ? • ?
Lopiz 2019	0	30	1	32	7.7%	0.35 [0.02, 8.39]	· · · · · ·	? • • • ? • •
Stableforth 1984	1	16	0	16	2.6%	3.00 [0.13, 68.57]		?? • • ? ? ?
Subtotal (95% CI)		86		89	23.2%	1.04 [0.29, 3.74]	-	
Total events	3		3					
Heterogeneity: Chi ² = 1	1.64, df =	3 (P =	0.65); l ² =	0%				
Test for overall effect: 2	Z = 0.05 ((P = 0.9	36)					
6.19.2 at 2 years								
Fialestad 2010a	8	25	1	25	5.3%	8.00 [1.08, 59,32]		$\bullet \bullet \bullet ? ? ? \bullet$
Launonen 2019a	3	40	0	42	2.6%	7.34 [0.39, 137,78]		
Olerud 2011a	9	29	1	29	5.3%	9.00 [1.22, 66,56]		
Olerud 2011b	3	27	1	25	5.5%	2.78 [0.31, 24.99]		$\bullet \bullet \bullet \bullet \circ \circ \circ \circ \circ$
ProFHER 2015	11	125	11	125	58.2%	1.00 [0.45, 2.22]		
Subtotal (95% CI)		246		246	76.8%	2.37 [1.31, 4.28]	•	
Total events	34		14					
Heterogeneity: Chi ² = 8	3.21, df=	4 (P =	0.08); 2 =	51%				
Test for overall effect: 2	Z = 2.87 ((P = 0.0	004)					
Total (95% CI)		332		335	100.0%	2.06 [1.21, 3.51]	•	
Total events	37		17					
Heterogeneity: Chi ² = 1	0.43, df	= 8 (P :	= 0.24); l ²	= 23%				
Test for overall effect: 2	Z = 2.68 ((P = 0.0)	007)				Eavours surgery Eavours non-surgica	I.
Test for subgroup diffe	rences:	Chi ² =	1.32, df =	1 (P = 0)	.25), I ² = 2	24.4%	ratears surgery ratears non surgica	
Risk of bias legend								
(A) Random sequence	e genera	tion (se	election bi	as)				
(B) Allocation conceal	ment (se	lection	bias)					
(C) Blinding (performa	nce bias	and de	etection b	ias): Fu	nctional o	utcomes, pain, clinic	al outcomes, complications	
(D) Incomplete outcome data (attrition bias): Functional outcomes, pain, clinical outcomes, complications								
(E) Selective reporting (reporting bias)								
(F) Balance in baseline	e charact	teristics	s?					
(G) Free from performa	ance bias	s?						

Figure 2. Surgical versus non-surgical treatment: additional surgery (re-operation or secondary surgery)

pants). We found moderate-certainty evidence of no clinically important difference in patient-reported shoulder function at 6 months (347 participants). We found high-certainty evidence of no clinically important difference in quality of life at 1 year. We found low-certainty evidence of a higher risk of additional surgery in the surgery group (Figure 2). Surgical treatments in the 10 trials included locking plates, HA, or RTSA.

Early versus delayed mobilization for non-surgically treated fractures

5 trials compared early versus delayed mobilization (350 participants). Very-low certainty evidence from single study trials means that we are uncertain in the finding of better shoulder function at 1 year in the early mobilization group (82 participants), or in the findings of no or little between-group difference in function at 3 months (50 participants) or at 2 years (74 participants). We found very low-certainty evidence of no important between-group difference in quality of life at 1 year. 5 serious shoulder complications, spread between the 2 groups, were reported.

Locking plate versus locking nail

4 trials compared these 2 methods (270 participants, mainly 2-part fractures). We found low-certainty evidence of no clinically important between-group difference in shoulder function at 1 year (227 participants), at 6 months (174 participants), or at 2 years (101 participants). We found very low-certainty evidence of no between-group difference in quality of life (53 participants), and of little between-group differences in adverse events (250 participants) and additional surgery (193 participants).

Reverse total shoulder arthroplasty versus hemiarthroplasty There was very low-certainty evidence from 2 trials (161 participants, 3- or 4-part fractures, some fracture-dislocations) of no or minimal between-group differences in self-reported shoulder function or quality of life at 1 or at a minimum of 2 years' follow-up. There was very low-certainty evidence of a lower risk of complications after RTSA (160 participants). 10 people (6 %) underwent reoperation; all 8 cases in the HA group received an RTSA (very low-certainty evidence).

CONCLUSIONS

- Surgery does not result in a better outcome compared with non-surgical treatment in displaced 2-, 3-, and 4-part fractures.
- Surgery may increase the need for subsequent surgery.
- There is insufficient evidence to inform the choices between
- different non-surgical, surgical, or rehabilitation interventions.

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