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Analyzing outcomes after proximal humerus fractures in patients <65 years: a systematic review and meta-analysis

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Background: There has been an increasing amount of interest and research examining best practices for the treatment of proximal humerus fractures (PHF). Recent, high-level randomized control trials and many retrospective cohort studies have failed to demonstrate clear benefit of surgical management for these injuries especially in the elderly (generally defined as ≥65 years old). There is a paucity of research available on outcomes after surgical and nonsurgical treatment of proximal humerus fractures in adults younger than 65 years, and comparative data are almost nonexistent. The purpose of our study was to perform a systematic review and meta-analysis on the available data to determine if the literature supports surgical management over conservative treatment for PHFs in adults younger than 65 years.

Materials and methods: Adhering to PRISMA guidelines, a systematic review of proximal humerus fractures was performed using MEDLINE and Google Scholar databases. Studies were included if they reported useable data such as outcome measures for adult patients younger than 65 years. Quality of nonrandomized studies was assessed utilizing the MINORs criteria. Extracted data were analyzed using statistical software with *P*-value set at 0.05.

Results: Six studies were included in the study for data extraction and statistical analysis. When comparing Constant Scores (CS) and Oxford Shoulder Scores (OSS) of operatively and nonoperatively treated adult patients aged less than 65 years, no statistical differences were found. Furthermore, no statistical differences in CS or OSS were found comparing elderly patients (defined as ≥65 years) and adult patients (defined as 18 to <65 years). Analysis of DASH outcome data did show statistical differences of the three cohorts (nonoperative <65, operative <65, and operative ≥65). Thus, only the limb-specific (not joint specific) outcome score (DASH) was found to be significantly different upon data analysis. Differences in shoulder-specific outcome scores (OSS and CS) failed to meet significance.

Conclusion: The available literature does not demonstrate a clear clinical benefit of operative treatment over nonoperative management of proximal humeral fractures in adult patients younger than 65 years. These results challenge the widely accepted practice of choosing surgical treatment in adult patients younger than 65 years with PHFs.

Proximal humerus fractures (PHF) continue to be a significant burden on the healthcare system. The vast majority of PHFs occur later in life with an exponential increase after the fifth to sixth decades.[1,2] They are the third most common osteoporotic fracture and have been proven to be independent risk factors for subsequent hip fracture.[5,6] Despite the morbidity and societal burden associated with these fractures, research on the treatment and outcomes for these injuries has been inconclusive.

Treatment for proximal humerus fractures range from nonoperative management to arthroplasty. There is an expanding body of literature analyzing outcomes of operative procedures, yet there is a disparity in reported data for conservative treatments. Due to the improvements seen in the literature with surgery, operative

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

According to the Department of Clinical Investigations Institutional Review Board at Tripler Army Medical Center, systematic reviews and meta-analysis are IRB exempt.

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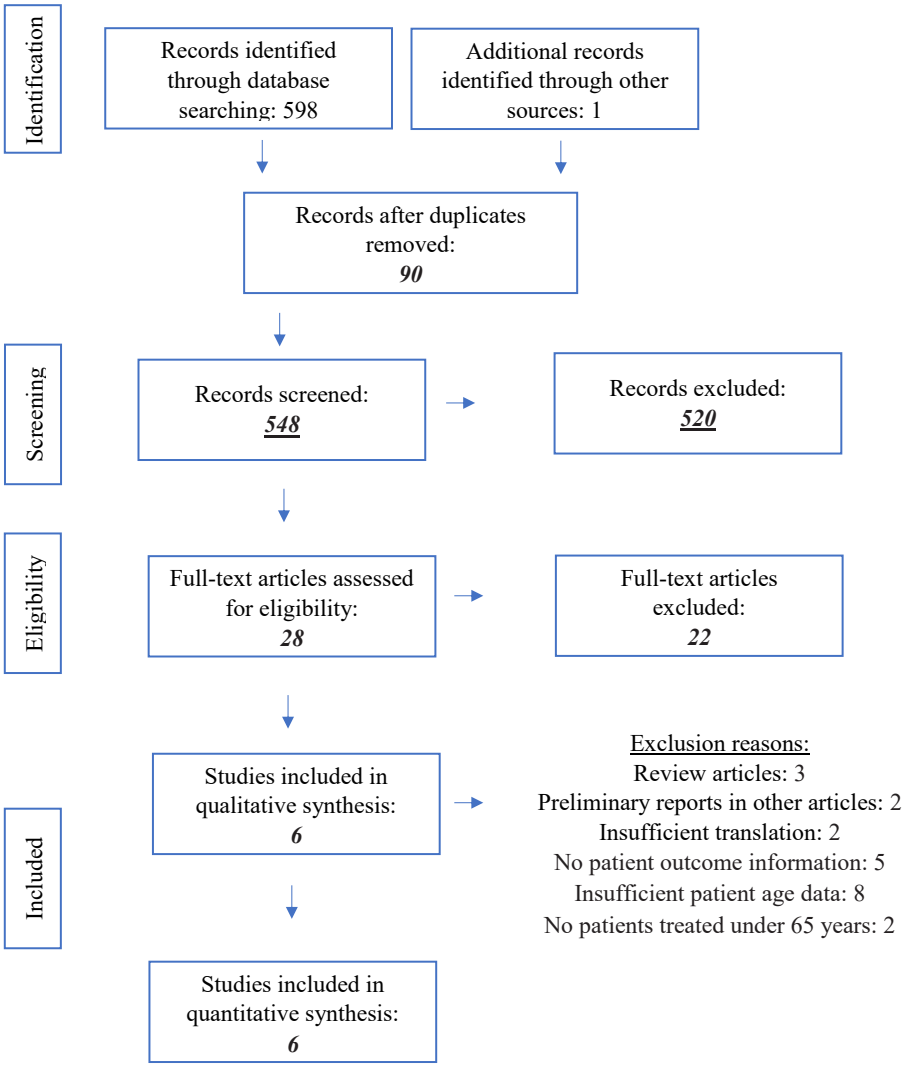

Figure 1 PRISMA (Preferred Reporting Items for Systemic Meta-Analyses) flow diagram.

management is widely pursued. Studies from around the world report up to 40% of PHFs being treated surgically and 100-400% increases over time in the use of operative management for proximal humerus fractures.[8,22,24] Despite this drastic trend, the highest- level evidence available reports no benefit of surgery over conservative therapy across all age groups.[17-19]

Outcome data for PHFs is lacking in a few critical areas. The available outcome data mostly focuses on the elderly (defined as ≥65); there are limited studies analyzing outcomes of PHFs in adult patients (defined as 18 to <65 years). Citing patient characteristics such as better bone quality and increased physical demand, many surgeons advocate for operative management for adult patients.[10] Although logical, the use of surgery over conservative therapy in the adult population is unproven in the literature with a paucity of comparative and even observational studies. Thus, a systematic review and meta-analysis was performed to compare operative treatment versus nonoperative management for proximal humerus fractures in adult patients (18 to <65 years). We hypothesized there would be a statistically significant difference between operative treatment and nonoperative management of proximal humerus fractures in adult patients younger than 65 years.

Materials and methods

Search strategy

In accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, a systematic review of the literature was completed using a search performed on MEDLINE and Google Scholar on July 5, 2020. The Boolean statement utilized in the MEDLINE search was: (((proximal humerus fracture[Title/Abstract]) OR proximal humeral fracture [Title/Abstract])) AND (((operative[Title/Abstract]) OR surgical[Title/Abstract]) OR surgery[Title/Abstract]). Search statement utilized in Google Scholar was: allintitle: proximal fracture surgery OR operative humeral OR humerus.

For each of the searches, the titles and abstracts were screened and the full text versions of articles that met criteria were downloaded. Full texts were reviewed and any relevant referenced articles that were not already obtained were ordered and obtained. "Related citations" were also reviewed during the searches, and the "cited by" function on Google Scholar was also used to identify any additional studies. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were downloaded

Table I
MINORS criteria scoring for nonrandomized studies.

	Clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss to follow-up less than 5%	Prospective calculation of the study size	An adequate control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analyses	Total/(16 or 24)
Tamimi 2015	2	2	0	2	1	2	1	0	1	2	0	2	15/24
Robinson 2019	2	2	0	2	0	2	1	0	N/A	N/A	N/A	N/A	9/16
Keser 2004	2	1	0	1	0	2	1	0	N/A	N/A	N/A	N/A	7/16

MINORS, methodological index for nonrandomized studies; *N/A*, not applicable.

and followed during this review. In addition to following PRISMA guidelines, identified non-randomized studies were scored using the methodological index for nonrandomized studies (MINORS) criteria to identify risk of bias.[15,16]

Study selection

Criteria for inclusion were peer-reviewed studies (published articles or abstracts) evaluating operative treatment and nonoperative management of proximal humeral fractures in adult patients (18 to < 65 years of age) with clear extractable data and mean follow-up greater than one year. Only studies with author provided translation of the article text to English were included. Throughout the duration of the search, the contents of each article, as well as the reference list, were screened for overlap of patients from other studies.

Data abstraction

Authors G.L. and I.H. independently performed a search of the literature and screened titles and abstracts and downloaded the articles for inclusion. The decision to include articles was made by consensus, and, if necessary, the final decision was made by the senior author K.M.

Data collected included patient age, surgical treatment, type of fracture, complications, and patient-reported outcomes (Disabilities of the Arm, Shoulder and Hand, Oxford Shoulder Survey, Near, Constant).

Statistical analysis

Data were initially collated and analyzed with the Microsoft Excel (Microsoft Corp., Redmond, WA, USA). When available, raw data including mean, standard deviation, and number of patients were collected and used to calculate the sum of terms. Studies with individual raw patient data without means and standard deviations were manually input into Microsoft Excel for inclusion into the final data calculations; or if individual scatter plots of the data were available, the estimated data point values were used to calculate the sum of terms utilizing the means and standard deviations identified using computerized software (Webplotdigitizer by Ankit Rohatgi). The null hypothesis for this study is there is no difference in outcome data between adult patients (18 to <65 years of age) and elderly patients ($\geq$65 years of age). A two-tailed, unpaired t-test was performed for continuous outcomes. The *P* value for statistical significance was set at .05. Review Manage (RevMan) version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for meta-analysis. When pooling the data in studies, the means and standard deviations were calculated by RevMan.

Results

A total of 637 (MEDLINE: 537; Google Scholar 95) studies were screened for relevance. After identification of 23 potentially relevant studies, they were downloaded and the reviews of the reference lists yielded an additional 4 studies, for a total of 27 studies. Twenty-two articles were excluded; 3 were review articles with no new data, 2 were preliminary reports that were contained in another study by the same author, 2 were in a foreign language without author approved translations available, 5 articles had no patient outcome information, 8 articles had insufficient patient age information and 2 articles did not have patients under 65 years.

Six studies met criteria and were included in this review with a mean follow-up of 42.3 months encompassing Neer I-IV fracture

types. Figure 1 of PHF studies summarizes the PRISMA flow diagram of study selection.

The 6 studies included in the data extraction and analyzation were made up of 3 level I randomized controlled trials and 3 comparative cohorts (level IV evidence) reporting outcomes after surgical procedures (mostly proximal humerus plating/shoulder arthroplasty) and nonoperative management (most commonly a sling plus or minus a swathe).[11,17-20,23] Two out of the 3 non-randomized studies had lower MINORs criteria grades, indicating a potential high level of bias (Table I). Two studies reported outcome level data utilizing the Oxford Shoulder Scale (OSS), 2 studies reported Disabilities of the Arm, Shoulder, and Hand scores (DASH), and 2 studies reported Constant Scores (CS). The extracted data means and standard deviations for all cohorts are reported in Table II.

In studies reporting post-surgical OSS outcomes, no statistically significant difference in OSS was calculated when comparing the adult (OSS = 40.9 ± 8.4) versus the elderly (OSS = 37.6 ± 10.6; $P = .106$). No difference was also found when comparing operative (OSS = 39.5 + 10.2) versus nonoperative management in adult patients (40.9 + 8.4; $P = .859$) (Tables II–IV). Analyzation of CS of adult patients also failed to show a statistically significant between operative (65.6 ± 15.6) and nonoperative cohorts (64.7 + 13.07; $P = .859$). Furthermore, a statistical comparison of CS between operatively treated elderly patients versus adult patients did not yield a significant difference between the two differently aged cohorts (Table III).

Only when examining DASH scores was there a statistical difference. Comparison of DASH scores of adults (18.2) versus the elderly (27.8) yielded a statistical significance ($P = .0017$). Finally, data analysis revealed a statistical difference in DASH scores when comparing nonoperative management versus operative treatment in adult patients. Complications were under reported in most studies but tended to be greater in the surgical cohort with 106 reoperations being reported in the study by Robinson et al (mostly for persistent stiffness or symptomatic hardware).[20]

Table II
Extracted outcome data means for all patients.

Outcome scale	Age of cohort (y)	n	Mean	Std. Dev.
Oxford Shoulder Scale (c)	<65	50	40.9	8.4
Oxford Shoulder Scale (s)	<65	213	39.5	10.2
Oxford Shoulder Scale (s)	≥65	101	37.6	10.6
Constant Score (c)	<65	14	64.7	13.07
Constant Score (s)	<65	22	65.6	15.6
Constant Score (s)	≥65	22	60.2	17.7
DASH (c)	<65	7	41.7	22.0
DASH (s)	<65	195	18.1785	20.5878
DASH (s)	≥65	67	27.8269	24.1167

c, conservative; *s*, surgery; *n*, number; *std. dev.*, standard deviation; *DASH*, disabilities of the arm, shoulder, hand score.

Table III
Outcome analysis comparing operatively treated <65 and ≥65 y.

Outcome scale	95% CI: upper limit	95% CI: lower limit	DF	*P* value
OSS*	0.4295	−4.4701	312	.1057
Constant Score†	4.7512	−15.5512	42	.2892
DASH‡	15.6544	3.6424	260	.0017

OSS, Oxford Shoulder Scale; *DASH*, disabilities of the arm, shoulder, and hand; *CI*, confidence interval; *DF*, degrees of freedom.
* OSS for operative <65 (39.5 ± 10.2) versus operative ≥65 (37.6 ± 10.6).
† CS for operative <65 (65.6 ± 15.6) versus operative ≥65 (60.2 ± 17.7).
‡ DASH for operative <65 (18.2 ± 20.6) versus operative ≥65 (27.8 ± 24.1).

Table IV
Outcome analysis comparing operative versus nonoperative in <65 y.

Outcome scale	95% CI: upper limit	95% CI: lower limit	DF	*P* value
OSS*	4.4594	−1.6594	261	.3684
Constant Score†	−9.3024	11.1024	34	.8588
DASH‡	39.1594	7.8406	200	.0035

OSS, Oxford Shoulder Scale; *DASH*, disabilities of the arm, shoulder, and hand; *CI*, confidence interval; *DF*, degrees of freedom.
* OSS for operative <65 (39.5 ± 10.2) versus conservative <65 (40.9 ± 8.4).
† CS for operative <65 (65.6 ± 15.6) versus conservative <65 (64.7 ± 13.1).
‡ DASH for operative <65 (18.2 ± 20.6) versus conservative <65 (41.7 ± 22.0).

Discussion

Management of proximal humerus fractures remains contentious. Studies examining outcomes following surgical management in adults <65 years are scarce, and data for nonoperative management in this age group is almost nonexistent. Despite the lack of research and unknown outcomes, there has been a global trend towards operative management for these injuries, especially in adults younger than 65 years.[22] Ideally, surgical management should yield superior outcomes when compared to nonoperative management in any cohort; however, clear benefit of surgery over nonoperative management for any age group remains elusive and thus controversial. A recent study by Caliskan and Dogan found no benefits of surgery across Neer Type II-IV fracture types in a cohort with a mean age less than 60 years.[3] There was some increased grip strength with surgical intervention in Neer II fractures at the cost of increased pain, and there was a trend toward improved strength of the forearm for type III fractures. Type IV fractures had no benefit.

Multiple meta-analysis and high-level studies have analyzed the outcomes of nonoperative versus operative outcomes with the consensus of operative treatment providing no clear benefit to nonoperative management in the elderly patient.[2] It is now generally accepted that operative management in PHF fractures is not advantageous in the elderly. Despite the focus on the elderly, no study has compared outcomes in adult patients (defined in our study as 18 to <65 years).[9] Thus, we present the first systematic review and meta-analysis analyzing outcomes of operative treatment versus nonoperative management in adult patients with PHFs.

We found that operative treatment of PHFs provides no significant improvements in OSS and CS when compared to nonoperative management therapy, regardless of age. This finding is in agreement with the Proximal Fracture of the Humerus Evaluation by Randomization (PROFHER) study by Rangan et al which concluded surgery did not improve outcomes when compared to conservative management in patients across all age groups. Our analysis further corroborates this as we found no significant differences in surgical outcome when comparing the elderly to the adult cohort. In addition to not finding surgery advantageous when comparing age groups, we also found surgery did not offer any clear benefits over nonoperative methods when only analyzing patients younger than 65 years. These findings challenge the common practice of operating on PHFs in patients younger than 65 years, as it may be exposing patients to intraoperative and postsurgical complications with no added clinical benefit. Furthermore, it has been reported that patients see the greatest improvements in upper extremity function after PHF about a year from injury. This large improvement seen in observation surgical studies may just be normal physiological healing that would have occurred without surgery.

On the other hand, when utilizing data available for the DASH scores, we found a statistically significant difference between the

elderly and adult cohorts in favor of operative treatment for adult patients. The mean difference in DASH score between the two treatment cohorts for adults was 23.5, and the difference in DASH scores between adult and elderly patients was 9.6. When evaluating DASH scores, it is important to note the difference between statistical and clinical benefit. The minimally clinically important difference of the DASH score has been reported to be 10.83-13.[7,25] As a result, the difference of 9.6 between the operatively managed cohorts is statistically significant, but not clinically significant. This finding corroborates recent studies reporting elderly patients fairing about the same as the adults after surgery for PHFs, challenging the rationale of choosing nonoperative management in the elderly due to perceived lack of benefit.[26] Therefore, surgery seems to only offer clear benefit to adults (18 to <65 years) in regard to DASH scores when comparing nonoperative to operative cohorts.

The discrepancies between outcome measures (CS and OSS vs. DASH) may be attributed to the difference in construct validities. Although these three scores are reported to be reliable measures of shoulder function for various pathologies, only the CS and OSS are shoulder specific. Previous research has identified a high correlation exists between the CS and OSS, while a low correlation exists between the CS and DASH, and our data seems to reflect these reported relationships.[1] Regarding the CS, it is considered the gold standard in Europe and criticism includes its time-consuming nature and lack of proper standardization.[21] Criticisms of the DASH score include being limb, not joint, specific and it being susceptible to patient bias due to its subjective nature.[4,14]

There are several limitations in our study. Due to the scarcity of the studies and difficulty identifying useable data within the bodies of the papers, it is likely some available data were missed. Scarcity of data resulted in a small sample of the adult (18 to <65 years) nonoperative arm and the DASH outcome group, which greatly diminished the power of this study. In addition, curated data for nonoperative management utilizing DASH scores was unable to be included because of missing statistical parameters. It is likely that inclusion of this data would have a significant impact on the DASH scores for the younger than 65 years nonoperative cohort.[13] Furthermore, lack of high-level data created a need to include lower-level observational studies for the meta-analysis, lowering the level of evidence of the meta-analysis, and opening the study to limitations and biases associated with retrospective cohort designs. Finally, we hoped to structure the study in a way to be inclusive to all-comers; however, selection bias is likely given the inclusion criteria for the various studies was variable.

Conclusions

Outcome data for patients younger than 65 years with proximal humeral fractures is scarce and difficult to find. There is a need for long-term outcome data in patients younger than 65 years with proximal humeral fractures. A subanalysis performed by the largest randomized control trial to date by Rangan et al indicated no significant difference in primary outcomes between operative and nonoperative management in patients younger than 65 years. Furthermore, it found no statistical difference in outcomes between adult and elderly patients in regards to OSS. This systematic review and meta-analysis demonstrated no significant clinical difference in operative versus nonoperative treatment of proximal humeral fractures in adults younger than 65 years. Currently, the literature does not support surgical treatment over conservative management for proximal humerus fractures, regardless of age.

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