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Comparison between Operative and Nonoperative Treatment of Humeral Diaphysis Fracture: Systematic Review and Meta-Analysis

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Abstract

Introduction: Humeral diaphysis fractures have traditionally been treated non-operatively using casts or functional bracing. Although non-operative treatment has demonstrated successful outcomes, operative treatment continues to increase. However, there is a lack of high-quality evidence to show that the operative treatment is superior to non-operative treatment. The aim of the study is to evaluate evidence on the effectiveness of operative *vs*. non-operative interventions for non-malignant closed fractures of the humeral shaft in adults.

Material and Methods: Qualitative and quantitative analysis of randomized controlled trials systematically gathered from Pubmed (Medline), EMBASE, CINAHL, Cochrane Central and Scopus – databases in May 2020. The methodological quality of articles was assessed according to the Cochrane Collaboration's domain-based framework. Random effects meta-analysis was employed.

Results: Of 354 records, 176 were screened based on their titles and abstracts and four based on their full texts. Three RCTs were included in this meta-analysis. The average age of the patients varied from 37 to 50 years and the duration of follow-up was one year. The risk of systematic bias was low for two RCTs and high for one. The pooled between-groups difference was measured using the Disabilities of the Arm, Shoulder and Hand (DASH) score, the Constant-Murray score, and the pain severity level. The proportion of nonunion, differences were 1.9 (95% CI 0.1 to 3.6), 1.8 (95% CI - 1.6 to 5.1, 0.3 (95% CI - 0.2 to 0.8) and 0.1 (95% CI 0.0 to 0.4), respectively. The heterogeneity was low and all the I^2 were 0%.

Conclusion: No evidence was found to support any clinically significant superiority of operative over non-operative treatment in closed extra-articular humeral shaft fractures. In these situations, non-operative treatment should remain the treatment of choice being less prone to adverse effects than surgery.

Keywords: Humeral fractures; Shoulder fractures; Arm/surgery

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Introduction

Humeral shaft fractures account for up to 3% of all fractures in adults, and have an annual incidence of 13/100,000 [1-4]. These fractures are typically associated either with falls amongst the elderly or with high-energy traumas amongst younger persons [2].

Non-operative treatment is a conservative method which uses functional bracings, casts or splints. Traditionally, it is the primary treatment for humeral diaphyseal shaft fractures. As a conservative treatment, non-operative methods have received high satisfaction rates [5-8]. Despite this, the effectiveness of non-operative treatment has been questioned due to the high rates of delayed healing or non-union for up to 50% of some subgroups, e.g. in proximal or transverse shaft fractures [2,7,9,10].

In cases where acceptable bony alignment cannot be achieved by non-operative (conservative) treatment, operative treatment is indicated, for example, when there are skin problems preventing bracing, or when there are soft tissue problems caused by high-energy traumas. In addition, female sex, smoking and mental disorders have also been thought to associate with higher non-union rates [11].

Operative treatment is generally associated with lower non-union rates compared to non-

operative treatment, and the risk of iatrogenic radial nerve palsy during surgery has been reported to be up to 7% and the rate of postoperative infection up to 6% [12,13]. The common options for surgical treatment in humeral shaft fractures are Open Reduction and Plate Fixation (ORIF); Intramedullary Nailing (IMN) and Minimally Invasive Percutaneous Osteosynthesis (MIPO) [14]. A recent network meta-analysis of different operative treatment options has reported similar results with the exception of the more frequent incidence of shoulder impingement amongst patients treated with ORIF or MIPO [15].

An older review of randomized controlled trials RCTs has failed to identify any RCTs comparing non-operative treatment with operative treatment [16]. A recent meta-analysis and systematic review of two RCTs and observational studies found no differences between both treatment methods [17]. Respectively, no evidence has suggested the superiority of operative over conservative treatment [18]. Despite this lack of evidence, surgical treatment for humeral shaft fractures has continued to grow substantially due to recommendations from experts [19-21].

The objective of this review is to evaluate the current evidence on the effectiveness of non-operative and operative approaches to treating closed humeral shaft fractures.

Material and Methods

The review was registered at the Prospero database – registration number CRD42019119035.

Search criteria

Criteria for considering studies for this review were based on PICOS framework (Population, Intervention, Comparison, Outcome, and Studies) as follows:

- **Population:** Over 17-year-old adults with a closed mid-third humeral shaft fracture. Patients with malignant or intra-articular fractures, with concurrent fractures in other bones or with previous mid-third fracture of the same humerus were excluded.
- **Intervention:** Any operative treatment during bone healing.
- **Comparison:** Any conservative treatment without intended operation.
- **Outcome:** Any (>1 year) outcome including perceived, clinical and radiological outcome measures.
- **Studies:** Randomized controlled studies published in English with abstract available without restriction on the time of publication.

Search strategy

The Cochrane Controlled Trails Register (CENTRAL), PubMed, EMBASE, CINAHL and Scopus databases were searched in May 2020. The search clause for PubMed was:

"Humeral fractures"[Mesh] OR "shoulder fractures"[Mesh] OR (humer*[TIAB] AND fractur*[TIAB]) NOT (proximal[TI] OR *arthroplast*[TI] OR child[Mesh] OR child*[TI] OR "Review Literature as Topic"[Mesh] OR "Review" [Publication Type] OR review[TI] OR meta*[TI] OR protocol[TI]).

AND (Randomized Controlled Trial[ptyp] OR randomi*[TI]) AND has abstract[text] AND English[lang].

The clause was adopted when searching at the other databases. Additionally, the reference lists of the identified articles were checked for relevancy.

Study selection and methodological quality assessment

After saving all the identified records in a citation manager (Endnote® X7.2, Thomson Reuters, New York, NY, USA), duplicates, conference proceedings, theses, reviews, study protocols and experts opinions were excluded using a built-in function of Endnote® (Figure 1). Additionally, using the same function, papers on pediatrics, proximal humeral fractures, and arthroplasty were excluded as well. Two independent reviewers screened the retained records based on their titles and abstracts, and then based on their full articles. Disagreements were resolved by consensus or by a third reviewer. Two independent reviewers rated the risk of systematic bias in the included RCTs according to the Cochrane Collaboration's domain-based evaluation framework [22]. The domains were assessed in following sequence: 1) Selection bias (randomized sequence generation and allocation concealment); 2) performance bias (blinding of participants and personnel); 3) detection bias (blinding of outcome assessment); 4) attrition bias (incomplete outcome data e.g. due to dropouts); 5) reporting bias (selective reporting); and 6) other sources of bias. The risk of systematic bias was graded as low, high or unclear.

The data needed for meta-analysis were extracted using a standardized form based on the recommendations by the Cochrane Handbook for Systematic Reviewers of Interventions Version 5.1.0. The form included study name, year, country, sample size, gender and age distribution, intervention methods and conservative treatment type, and main results.

Statistical analysis

A random-effects model was used to quantify the pooled effect size of the included studies, which was a more fitting choice than a fixed-effect model considering the context of medical decisions making and generalizing the results beyond the selected samples. The results were presented as raw mean differences and accompanied by 95% Confidence Intervals (95% CIs). When pooling the incidence of adverse effects, Risk Ratios (RRs) were used. The heterogeneity was tested using the Q test and I^2 statistic. Heterogeneity was deemed present if Q was greater than the degree of freedom (number of studies – 1). The I^2 statistic described the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance). When the number of pooled studies was 10 or more, the potential publication bias was assessed using the Egger's test (two-tailed p-value considered significant if =<0.05), and trim-and-fill correction was applied if needed. All calculations were performed using the Comprehensive Meta-Analysis CMA software, Version 3.0, available from www.meta-analysis.com.

Results

Basic characteristics

The search resulted in 354 records (Figure 1). Of them, 176 were screened based on their titles and abstracts and four based on their full texts. One RCT was excluded due to a follow-up that was shorter than defined by the inclusion criteria [23]. Finally, three RCTs were considered relevant and included in the further analysis [24-26]. The sample sizes varied from 30 to 58 patients and they were predominated by men (53% to 77%). The average age of the patients varied from 37 to 50 years – around 40 years in two studies [24,25]

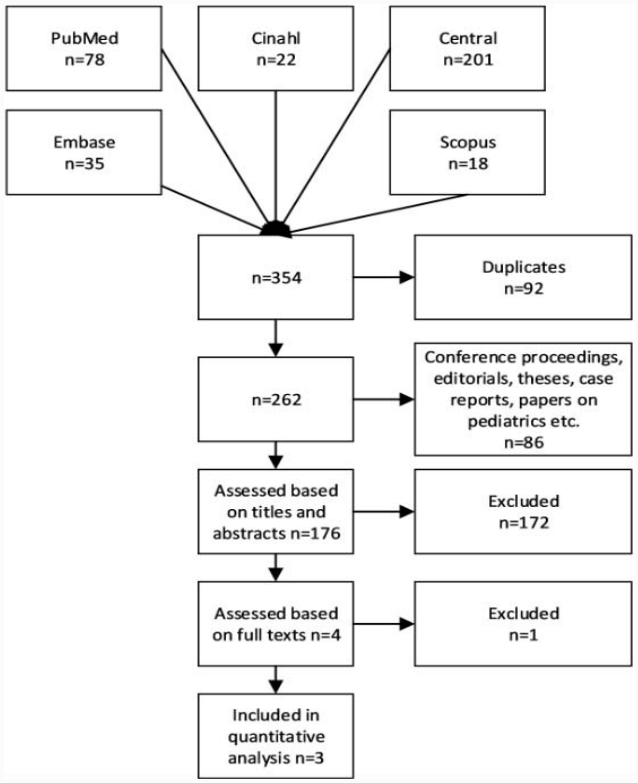

Figure 1: Flow chart.

and 10 years older in third study [26]. All three studies had a one year follow-up time. There were no significant differences between groups in health-related quality of life measured by the Short Form (36) Health Survey (SF-36) or by the 15D the health-related life-quality questionnaire [24,26]). One study has compared patients' willingness to redo the same treatment: Surgery group 97% *vs.* bracing group 71%.

Surgical techniques

Minimally invasive surgical technique with two small anterior approaches and a bridge plate was used by one study [24]. Other RCTs have employed standard open reduction and internal osteosynthesis [25,26].

Conservative treatment

In two RCTs, after closed reduction, arm was immobilized using a U-splint for two weeks; splint was replaced after two weeks by a functional brace that allowed movement of shoulder and elbow; brace was worn for six weeks or until fracture consolidation [24,25]. In one study, a trained plaster technician has applied a functional brace covering the arm from shoulder to elbow allowing freely motion in both joints; the patients were instructed on how to cope and tighten the brace until fracture union [26].

Inclusion and exclusion criteria

One study has defined humeral shaft as an area between four cm distal to a surgical neck and four cm proximal to the upper border of olecranon fossa [24]. Another RCT has defined humeral shaft as a zone between superior border of pectoralis major tendon attachment and five cm from the upper border of olecranon fossa [26]. Third RCT has defined humeral shaft as an area between the proximal and distal metaphysis without extension to proximal and distal articular surfaces [25]. The inclusion and exclusion criteria were similar in all three RCTs: Adults with closed extra-articular fractures excluding pathological fractures, multiple traumas, and neurovascular injuries.

Conclusions of the RCTs

One RCT found statistically significant advantage of surgery over functional bracing measured by DASH up to six months (but not longer than that), lower nonunion rate, and less residual deformity, suggesting that only nonunion rate was likely to have clinical relevance [24]. Another RCT stated that union was faster in a surgical group and conservative treatment was associated with a higher risk of nonunion [25]. Third RCT (with substantial crossover from conservative to surgical group) did not observe any superiority of one approach over another [26].

Risk of systematic bias

The risk of systematic bias was low for two RCTs [24,26] and high for one [25]. The most frequent source of potential bias was related to unblinded design.

Meta-analysis

Four outcome measures were appearing in the RCTs more than

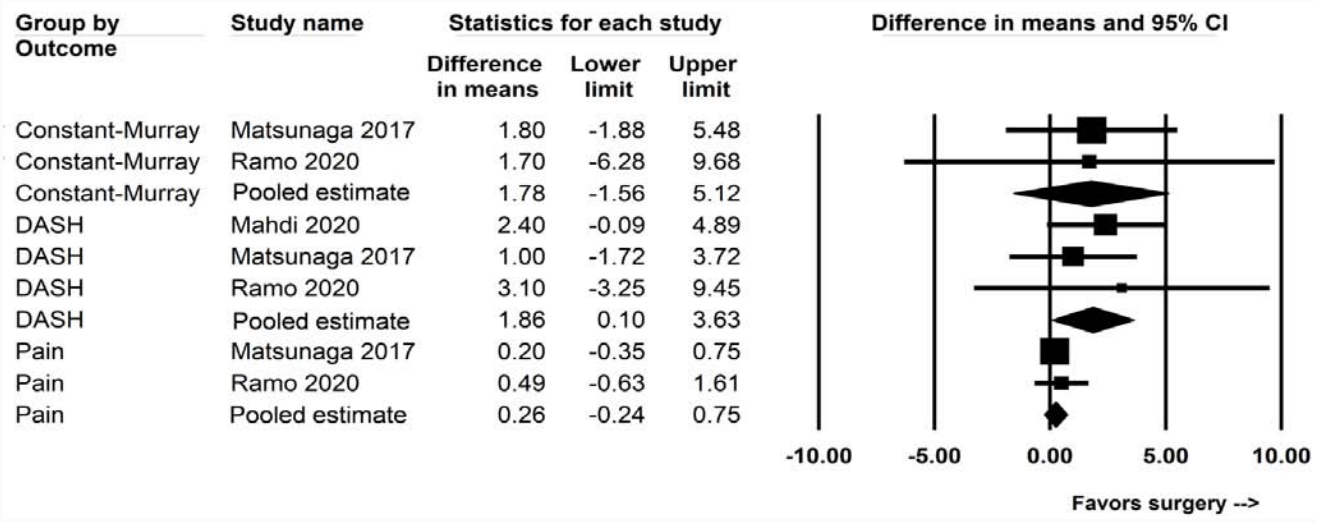

Figure 2: The pooled between-groups difference in the DASH score was borderline significant.

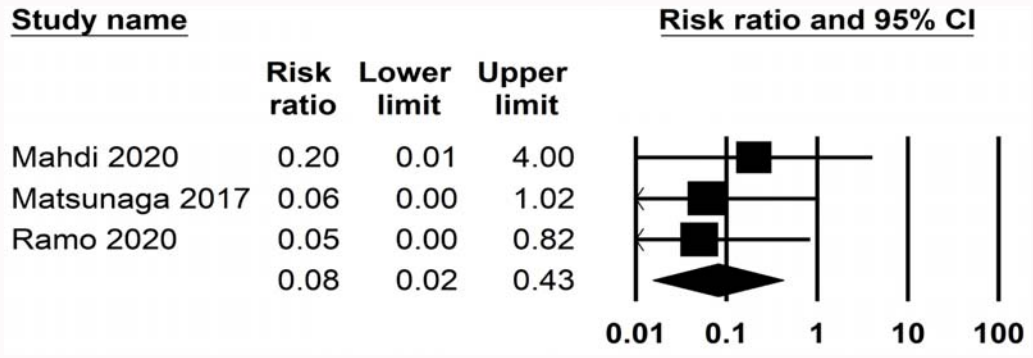

Figure 3: The pooled RR of nonunion was significant.

once: the DASH score, the Constant-Murray score, pain severity level, and proportion of nonunion. These four were employed in the meta-analysis. The pooled between-groups difference in the DASH score was borderline significant 1.86 (95% CI 0.10 to 3.63) points in favor of surgery (Figure 2). The pooled difference in the Constant-Murray scores was insignificant 1.78 (95% CI - 1.56 to 5.12) points. The pooled difference in the level of pain severity was insignificant as well 0.26 (95% CI - 0.24 to 0.75) points. The pooled RR of nonunion was significant 0.08 (95% CI 0.02 to 0.43) in favor of surgery (Figure 3). The heterogeneity was low – all Q-statistics were below the degrees of freedom and all the I^2 were 0%.

Discussion

This systematic review and meta-analysis of three RCTs found no significant evidence on the clinical superiority of operative over non-operative treatment in closed extra-articular humeral shaft fractures measured by the DASH score, the Constant-Murray score, pain severity level, and the proportion of nonunion. The pooled between-groups difference in the DASH score was borderline statistically significant in favor of surgery with a lower 95% confidence limit close to zero.

Two systematic reviews and meta-analyses on the topic have been published recently [27]. De Wall et al. [17] have searched for data in March 2019 and found two RCT studies. One of them – study by Kumar et al. [28] was rejected in our analyses because of too short follow-up (6 months). The systematic review and meta-analysis by Sargeant et al. [27] has been conducted before September 2018. That review has found a single RCT by Matsunagas et al. [24] including additionally seven retrospective cohort studies. The conclusions of that two reviews have been similar to ours regarding the reduced risk of nonunion in surgery compared to non-operative treatment. Also, that reviews have not observed any significant difference in functional outcomes between two approaches reporting satisfactory results achieved by both methods.

This is the first meta-analysis employed three RCTs. In the present meta-analysis, both treatment options in humeral shaft fractures seemed to be similarly effective in uncomplicated cases. However, the complication profiles of these two approached were different – surgery was associated with greater risk of temporary radial nerve palsy and infection while conservative approach was associated with greater risk of non-union or malunion. While the included RCTs have reported faster healing with less pain in operative group, the differences between groups have been small and clinically unimportant [29]. The situation is similar with the research investigating treatment of several other fractures of upper limb – multiple RCTs have not observed the clinically important differences between operative and non-operative treatment [31,32].

Meta-analysis is always approximation. The number of studies on the topic was limited, which could be attributed to the rareness of these fractures, which might make organizing an RCT difficult. Indeed, one previous trial, initially designed as an international multicenter RCT, has been converted into an observational study due to the difficulties in enrolment [30]. This difficulty might also explain modest sample sizes of the included studies, which has resulted into wide confidence intervals of the included RCTs. On the other hand, the confidence intervals of pooled effects were substantially narrower indicating similarity in the direction of effects.

The present findings emphasize the importance of thorough individual selection of treatment approach in different patients. For example, physically active patients of working age might more greatly benefit from operative treatment those results in early mobilization allowing an earlier active motion in the fractured arm and a shorter sick leave.

Further research conducted as large-sample RCTs may improve the preciseness of the observed findings. Cost-effectiveness analysis might clarify possible differences between two approaches amongst different patient groups. Also, subgroup analyses of patient-related risk factors for delayed union or non-union are needed. The right time for conversion from conservative treatment to surgery in cases of non-union is needed to be defined.

Conclusion

No evidence was found to support a clinically significant superiority of operative over non-operative treatment in closed extra-articular humeral shaft fractures. Therefore, until additional evidence is found, a non-operative treatment approach may remain the first choice as a more safe intervention.

Authors' Contribution

All the authors (KL, EE, AL, and MS) made substantial contributions to the conception and design of the work, the acquisition, analysis, and interpretation of data, revising the work critically for important intellectual content, and made a final approval of the version to be published. KL was responsible for the drafting the work. MS was responsible for the statistical analysis of the data. All the authors (KL, EE, AL, and MS) agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy

or integrity of any part of the work are appropriately investigated and resolved.

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