swiss medical board

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Scope Protocol

Efficacy and safety of surgical interventions for full-thickness rotator cuff tears: a systematic review protocol

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Introduction

Will be included at a later stage (review stage).

Objectives

The aim of this systematic review is to evaluate the efficacy and safety of any surgical intervention in comparison to no or conservative treatment in patients with full-thickness rotator cuff tears. The following PICO will be addressed: Is a surgical intervention compared with no treatment or conservative treatment in patients with full-thickness rotator cuff tears associated with better patient-relevant outcomes?

Methods

This systematic review will be registered in the international prospective register of systematic reviews (PROSPERO; https://www.crd.york.ac.uk/prospero/) and conducted after following the transparent reporting of systematic reviews and meta-Analyses statement (PRISMA; http://prisma-statement.org/PRISMAStatement/).

Population

Inclusion criteria: Eligible patients are children and adults with traumatic or degenerative full-thickness rotator cuff tears, defined as the complete discontinuation of the tendon(s) of any (one [or more)]) of the rotator cuff muscles (supraspinatus, infraspinatus, teres minor,

subscapularis), irrespective of the etiology of the tear (degenerative or traumatic), time of diagnosis, patient age and comorbidities. The full-thickness tear, however, must have been confirmed by an appropriate diagnostic imaging modality such as magnetic resonance imaging (MRI), magnetic resonance arthrography (MRA) or ultrasonography (US). Studies including a mixed patient population (i.e., patients with a variety of rotator cuff diseases) will only be considered *(i)* if the proportion of patients with a full-thickness rotator cuff tear exceeds 80% or *(ii)* if the study includes subgroup results for patients with full-thickness rotator cuff tears.

Exclusion criteria: Studies focusing on populations of patients with rotator cuff tendinopathy, partial-thickness rotator cuff tears or calcific tendinitis in the absence of a full-thickness tear will be excluded. We will further exclude studies in which the full-thickness tear has not been confirmed by diagnostic imaging.

Intervention

Inclusion criteria: Any surgical technique (i.e., arthroscopic cuff repair, open or mini-open surgery) using any repair method (e.g. suture, reconstruction [by tendon transfer and/or capsular reconstruction], reinsertion or refixation with or without augmentation and/or acromioplasty) will be considered (provided the intervention is applied in the patient population defined above).

Exclusion criteria: Studies, in which the surgical intervention is supplemented by a biological intervention (e.g. platelet-rich plasma, growth factors, stem cell or other cell-based therapies) will be excluded. Shoulder joint replacements will also not be considered as intervention.

Comparison treatment

Inclusion criteria: Comparison treatments include placebo, sham, no treatment, “watchful waiting” or any conservative treatment such as physiotherapy or pharmacological treatment including injection therapies.

Exclusion criteria: Studies comparing different surgical interventions will not be considered, as well as studies in which the surgical intervention is compared with extracorporeal shockwave therapy (ESWT), magnetic field therapy, biological interventions (e.g. platelet-rich plasma, growth factors, stem cell or other cell-based therapies), laser treatment, thermotherapy (heat or cold) or hyperbaric oxygen therapy (HBOT).

Outcome measures

The following patient-relevant outcome measures will be considered:

- Shoulder function, measured by a standardized assessment, e.g. Constant Shoulder Score (CSS), Oxford Shoulder Score (OSS), American Shoulder and Elbow Surgeons (ASES) score, University of California at Los Angeles (UCLA) score or Simple Shoulder Test (SST)
- Shoulder pain, e.g. pain intensity, measured by a standardized instrument such as a visual analogue scale (VAS) or a numerical rating scale (NRScale)
- Shoulder range of motion (ROM)
- Shoulder muscle strength
- Health-related Quality of Life (QOL), measured by a standardized instrument, e.g. 36-Item Short Form Health Survey (SF-36) or Euro-QOL (EQ5D)
- Occupational impairment defined as (i) length of time until re-entry into working life and/or (ii) rates of individuals who changed their occupation because of their shoulder problem
- Length of hospital stay

  - Any treatment-related adverse events (except for surgical complications, see below) according to the definition of the study authors[1-3]
  - Any surgical complication, e.g. peripheral neurologic injuries, infections, wound healing disorders
  - Failed surgery (i.e., re-rupture of the repaired tendon(s),as defined by study authors)
  - Re-operation rates

- Further outcome measure considered (as suggested by the stakeholders):
  - Structural findings, e.g. muscle atrophy, measured by an appropriate imaging modality

In studies in which outcomes are measured at multiple times points, we intend to capture the time-dependent 'variability' of outcomes by extracting all numerical data reported for each time point considered. Additionally, if the available data permits, results will be presented for short-term follow-up (e.g. four weeks following the intervention) and for long-term follow-up (e.g. more than four weeks following the intervention).

Study types

(i) Randomized controlled trials (RCTs) and *(ii)* non-randomised studies (NRSs) including prospective and retrospective controlled cohort studies, case-control studies and controlled before after studies (CBAs) fulfilling the above mentioned inclusion criteria will be considered for this systematic review.

For RCTs, we will consider study results reported in full-text publications, study registers or in abstract form (provided sufficient data are available). For NRSs, we will consider study results only reported in full-text publications and study registers. We will not consider study results of NRSs exclusively reported in an abstract form. The reason for this restriction is that the limited information on study methods precludes a thorough risk of bias assessment which is particularly important for this study type (NRSs).

Literature search

Bibliographic database searches

Systematic literature searches for relevant published studies will be conducted by an information specialist in the following electronic databases:

- Medline, Medline Daily Update, Medline In Process & Other Non-Indexed Citations, Medline Epub Ahead of Print (via Ovid)
- Science Citation Index Expanded, Conference Proceedings Citation Index- Science Conference Proceedings Citation Index- Science, BIOSIS Citation Index (via Web of Science)
- Cochrane Library (via Wiley)
- Embase (via Embase.com/Elsevier)
- Sportdiscus (via Ebsco)

Searches in study registers

Searches for ongoing trials or unpublished completed trials will be conducted in ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (http://www.who.int/ictrp/search/en).

Supplementary searches

We will use relevant studies and/or reviews to search for additional references via the Pubmed similar articles function (https://www.nlm.nih.gov/bsd/disted/pubmedtutorial/020_190.html) and forward citation tracking using the Web of Science Core Collection. Reference lists of

relevant studies and reviews will be searched and experts in the field will be contacted to enquire about any further relevant studies that may not have been retrieved by the electronic searches.

We will not use any date or language restrictions in the electronic searches for trials. Furthermore, search strategies for all databases will be adapted from our Medline strategy (Appendix A). This search strategy was peer-reviewed by a second information specialist and validated by checking whether the strategy identified studies already known, including those cited in the systematic reviews by Ryösä et al.[4] and Coghlan et al.[5] For each database, the date of the search, the search strategy as well as the number of search results will be documented.

Identification of relevant studies

Titles and abstracts of the citations identified by the searches will be independently screened by two reviewers (title and abstract screening), and full texts of all potentially relevant articles will be obtained. Full texts will also be independently checked for eligibility by two reviewers, and reasons for exclusions will be documented (full-text screening). Any disagreement will be resolved by consensus, moderated by a third reviewer. To standardize the screening process, two purpose-designed forms will be used: an ‘abstract screening form‘ and a ‘full text screening form’ . Both will include the inclusion and exclusion criteria for the review. The ‘abstract screening’ form will be used as a guidance document to assist the title and abstract screening. The ‘full text screening form’ form will be used to extract and document the key criteria that are relevant for the ultimate decision of whether a study will be included or excluded as well as the key justification for the decision by each reviewer. The title and abstract screening will be

piloted in abstrackr (http://abstrackr.cebm.brown.edu/) on a random subset of 50 search results. The 'full text screening form' will be piloted on three exemplary RCTs. The complete screening process will be conducted in Covidence (https://www.covidence.org/home).

Data extraction

Two review authors will extract the following data:

Study characteristics, i.e., year of publication, study type, setting, start and end of study, sample size (total and for each treatment arm), follow-up time, and inclusion and exclusion criteria.

Patient characteristics, i.e., definition of the included patient population, etiology of the full-thickness rotator cuff tear (traumatic, degenerative), extent of the full-thickness rotator cuff tear (e.g. minor, major, single tendon or combined rupture), extent of shoulder-related functional disability, the diagnostic imaging modality used to establish the diagnosis (e.g. MRI, US), patient age, number of patients with re-operations, number of patients with co-morbidities, numbers of females and males.

Characteristics of the intervention, i.e., definition of the surgical technique (arthroscopic cuff repair, open or mini-open surgery) including the repair method (e.g. suture, reinsertion or refixation with or without augmentation and/or acromioplasty), experience of the surgeon, time between the diagnosis and surgical intervention.

Characteristics of the comparator treatment, e.g. placebo, sham, no treatment ("watchful waiting"), or type of conservative treatment (i.e., duration and type of physiotherapy or duration, agent, dose and route of delivery of pharmacological treatment).

Withdrawals and drop-outs, i.e., numbers and reasons for withdrawals/drop-outs for each study arm.

Outcome measures, i.e., description of assessment tools used, data for continuous/dichotomous/categorical efficacy variables, unit of measurement, upper and lower scale limits, collected and reported time points of measurement. Where adjusted analyses are available in primary studies, these adjusted estimates of treatment effects will be used. Where adjusted analyses are not available, we will extract the unadjusted data as reported in the study.

All data will be entered into the Review Manager (RevMan 5.3) by one reviewer and checked by a second.

Risk of bias assessment

Risk of bias of RCTs will be assessed according to the methodology described in the Cochrane Handbook for Systematic Reviews of Interventions.[6] The following domains will be addressed: (i) randomisation sequence generation, (ii) allocation concealment, (iii) masking (blinding) of participants, trial personal, and outcome assessors, (iv) incomplete outcome data, (v) selective outcome reporting (for example, absence of data for outcomes measured), and (vi) other sources of bias (bias due to problems not covered elsewhere). These items will be judged with 'low', 'high' or 'unclear' risk of bias.

Bias in NRSs will be evaluated separately according to the 'Risk of Bias in Non-randomised Studies of Interventions' (ROBINS-I) tool[7], addressing the following domains: (i) bias due to confounding (e.g. etiology or extent of the full-thickness rotator cuff tear, age, gender, co-morbidity, patients with re-operations, co-intervention), (ii) bias in selection of participants into the study (e.g. inception bias), (iii) bias in measurement of the intervention, (iv) bias due to departures from intended

interventions, (v) bias due to missing data, (vi) bias in measurement of outcomes, (vii) bias in selection of the reported result and (viii) overall bias. These items will be judged as 'low', 'moderate', 'serious', 'critical' or 'unclear' risk of bias.

The ratings for the individual domains for each RCT and NRS will be presented in a 'risk of bias' table, separately.

GRADE assessment

The certainty of evidence of the patient-relevant outcomes (i.e., shoulder pain, function integrity ROM, QoL, surgical complications, other complications, adverse events and re-operation rate) will be assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.[8 9] In brief, this assessment will address study limitations (risk of bias), imprecision (when 95% confidence intervals are wide and/or are close to null effect around the point estimate), inconsistency (that ist, differences in estimates of effect across studies that assessed the same comparison), indirectness (that is, differences in patient characteristics, differing (co-) intervention, differing extent to which intervention of interest is optimally conducted, differing comparator, and differences in measurement of outcome), dissemination bias and potential criteria (e.g. large effect estimates) that can increase certainty. Based on these criteria, the certainty of the evidence for each comparison and outcome can be categorized as either high, moderate, low, or very low. The results will be presented in a Summary of Findings (SoF) Table as suggested by the GRADE Working Group.

Risk of bias assessment and the GRADE assessment will be conducted independently by two reviewers. Any disagreements will be resolved by discussion and consensus involving, when needed a third person.

Assessment of dissemination bias

We plan to minimise the impact of dissemination bias by ensuring a comprehensive search for eligible studies including searches of trial registries (see above 'Literature search'). A funnel plot and appropriate statistical tests for small study effects will be performed if ≥10 studies are available for an outcome.[10]

Data synthesis and analysis

Data from different study types

Data from RCTs and NRSs will be analysed—due to different mechanisms of bias—separately.[11]

Measures of treatment effect

Continuous outcomes: We will analyse outcomes measured with a scale as continuous outcomes (e.g. patient-reported shoulder function, shoulder pain). If more than one scale is used to measure an outcome in the very same study, only the measurement that has been obtained using a validated scale will be considered (for validated scales see scales reported under 'outcome measures' above). In the case when more than one validated or more than one but only scales that are not validated are reported for one outcome, we will use the results provided by the scale that is most commonly used in the other included studies. The treatment effect for each continuous outcome will be expressed as the weighted mean difference (WMD)

with its 95% confidence interval (CI), considering the change between baseline and follow-up measurement of each treatment arm. Where continuous outcomes are measured using different scales, the treatment effect will be expressed as the standardised mean difference (SMD) with its 95% CI. As recommended by Guyatt et al., and where possible, treatment effects will additionally be expressed by the ratio of means (RoM) with their 95 % CIs to facilitate interpretation.[12]

Dichotomous outcomes: The treatment effect for dichotomous outcomes (e.g. complications, re-operation rate) will be expressed as a risk ratio (RR) or odds ratio (OR) (in case case-control studies) with 95 % confidence intervals.

Meta-analyses

We intend to conduct meta-analyses of all outcomes depending on the availability of sufficient data from sufficiently homogenous studies. Meta-analysis of data from NRSs will only be considered among studies with similar design (e.g. prospective cohort studies will only be combined with other prospective cohort studies).

Meta-analyses will be conducted using Review Manager (RevMan) Version 5.3[13] and treatment effects will be calculated based on a random effects model.[14]

Assessment of heterogeneity

Heterogeneity will be evaluated and quantified based on I^2 and the statistical test chi square. Thereby, a chi-square p value <0.10 or an $I^2 \geq 75$ % will be considered as “significant” heterogeneity.[15]

Sensitivity and subgroup analyses will be performed irrespective of the presence of “significant” heterogeneity (see below).

Subgroup analyses

Subgroup analyses will be performed to examine whether estimates of MD/SMD or RR (or OR) will be affected by participants’ age, the etiology and/or extent of the complete rotator cuff tear; extent of shoulder-related functional disability (shoulder function); surgical intervention; surgeon’s experience with the intervention; and type of conservative treatment. Differences in effect estimates will be assessed by interaction tests available within RevMan Version 5.3.[13]

Sensitivity analyses

Sensitivity analyses will be conducted to determine the impact of bias through the exclusion of studies with high risk of bias. In case of any differences between these estimates, these will be considered in the results and discussion.

Unit of analysis

The unit of analysis will be the individual participant.

Dealing with missing data

Data will be analysed—if possible—on intention-to-treat (ITT) basis or according to recently developed recommendations for systematic reviewers for addressing missing data in clinical trials.[16 17] We will also check trial register records or attempt to contact study authors to obtain information on missing data. If results are only reported in graphs, we will estimate the values based on these graphs.

Results

Will be completed at a later stage (review stage).

Discussion

Will be completed at a later stage (review stage).

References

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Appendix A. Search strategy in Medline.

Ovid MEDLINE(R) 1946 to May Week 3 2018, Ovid MEDLINE(R) Epub Ahead of Print May 25, 2018, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations May 25, 2018, Ovid MEDLINE(R) Daily Update May 25, 2018			
	#	**Searches**	**Results**
A. Rotator cuff tear	1	Rotator Cuff Injuries/	4586
	2	Shoulder Impingement Syndrome/	1592
	3	((rotator cuff* or supraspinatus or infraspinatus or teres minor or subscapularis) adj3 (tear? or rupture* or injur* or disease or impingement)).ti,ab.	5864
	4	((shoulder or subacromial) adj impingement).ti,ab.	1105
	5	or/1-4	8711
B. Surgery	6	Rotator Cuff/su [Surgery]	3134
	7	Rotator Cuff Injuries/su	384
	8	Arthroscopy/	20721
	9	(arthroscop* or acrom?oplast*).ti,ab.	26810
	10	((rotator cuff* or supraspinatus or infraspinatus or teres minor or subscapularis or tendon?) adj3 (surg* or repair or fixation or refixation or suture? or reconstruct* or reinsertion or open)).ti,ab.	10824
	11	or/6-10	40277
A+B	12	5 and 11	4758
Humans only	13	exp animals/ not exp humans/	4464699
	14	12 not 13	4519
Exclude Editorials	15	editorial/	458893
	16	**14 not 15**	**4468**