



# Open versus arthroscopic acromioclavicular joint resection: a systematic review and meta-analysis

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## Abstract

**Introduction** The purpose of this study was to perform a meta-analysis comparing open and arthroscopic surgical techniques for distal clavicle resection.

**Methods** A systematic review of Medline, Embase, Scopus, and Google Scholar identified relevant publications in the English and German literature between 1997 and 2017. All included studies were levels I–IV, describing both treatments, with a minimum of 12 month follow-up, had at least one validated outcome score and documented patient recruitment, study design, demographic details, and surgical technique. Studies were excluded if they were only abstracts or conference proceedings, involved revision procedures, or the loss to follow-up exceeded 20%. Publication bias and risk of bias were assessed using the Cochrane Collaboration tools, and heterogeneity was assessed using the  $I^2$  statistic.

**Results** Four studies ( $n=319$  patients) met the criteria for inclusion. The pooled estimate for clinical outcomes (Constant, ASES) demonstrated no significant differences (SMD 0.323,  $I^2=0\%$ ,  $p=0.065$ ) between open and arthroscopic resection, although the analysis favored open resection. The pooled estimate for clinical outcomes (SST) also demonstrated no significant differences (SMD 0.744,  $I^2=49.82\%$ ,  $p=0.144$ ) between open and arthroscopic resection, but the analysis again favored open resection. The pooled estimate for VAS assessment of pain demonstrated no differences (SMD 0.217,  $I^2=58.96\%$ ;  $p=0.404$ ) between open and arthroscopic resection.

**Conclusion** The results of this study suggest that similar functional and clinical outcomes can be achieved with either open or arthroscopic distal clavicle resection. The observed trend that open resection may have a more favorable outcome warrants further investigation.

**Level of evidence** Level 3; systematic review and meta-analysis.

**Keywords** Acromioclavicular joint · Open resection · Mumford procedure · Arthroscopic resection · Meta-analysis · Systematic review · Distal clavicle resection

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## Introduction

Disorders of the acromioclavicular joint (ACJ) are common, and initial treatment is usually non-operative [1]. Surgical resection of the lateral clavicle is only considered following failure of conservative treatment, and is the procedure of choice for osteoarthritis, osteolysis, and symptomatic posttraumatic changes [2–4]. ACJ disorders can be treated surgically using either open or arthroscopic resection. Open resection was first described by Mumford [5], and was originally used to treat chronic acromioclavicular instability. Arthroscopic surgery is now a popular alternative [2], and modern arthroscopic techniques have been shown to minimize trauma to the surrounding tissues [3]. This transition was perhaps motivated by the potential for open resection to

result in acromioclavicular instability due to damage caused to the superior capsule and adjacent ligamentous structures [6]. Arthroscopic resection can either be performed via a bursal/subacromial approach or via a direct approach [3]. In a systematic review, Pensak et al. suggested that patients treated by the direct approach had a faster return to activity [3]. In contrast, Levine et al. have compared the direct versus the bursal approach and were unable to demonstrate any difference in return to activity [7]. One of the concerns with the direct approach is the potential for damage to the superior capsule, resulting in distal clavicle instability [3, 7].

Several studies have demonstrated both surgical techniques obtain excellent functional results and pain relief [1, 3, 8, 9]. Robertson et al. reported significantly less pain in patients undergoing arthroscopic surgery, but could not demonstrate any differences for functional or patient perceived outcomes [4]. In contrast, other authors were unable to identify any differences in outcomes between open and arthroscopic resection [3, 8, 10]. Given these conflicting reports, it is difficult to determine the preferred technique [3]. Furthermore, other factors such as cost, patient preference, and availability of equipment must also be considered. However, previously published comparative studies have unequal numbers of patients, and may not be powered sufficiently to definitively establish the superiority of either technique, resulting in a type II error. Pooling these studies, and using the statistical tools of meta-analysis, might have an added benefit to further investigate whether differences exist between arthroscopic and open ACJ resection.

Therefore, the purpose of this study was to perform a meta-analysis between open and arthroscopic surgical techniques for lateral clavicle resection. We hypothesized that there would be no significant differences in clinical outcomes and pain relief following either procedure.

## Methods

The methods described in the Cochrane Handbook were used to conduct this systematic review and meta-analysis [11]. The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines and checklist were used to evaluate and report the results of interventions and outcomes [12].

### Eligibility criteria

All studies that compared arthroscopic to open acromioclavicular joint/lateral clavicle resection in patients between 18 and 60 years of age from 1997 to 2017 were identified and considered for inclusion if the following criteria were met: level I–IV studies describing both treatments; utilization of at least one validated outcome score (ASES, Constant,

Rowe, SANE, DASH, WORC, WOOS, SPADI, UCLA Shoulder Score, SST); a minimum of 12 months follow-up; complete documentation of patient recruitment, study design, demographic details, and surgical technique.

Studies were excluded if they were abstracts or conference proceedings, if patients had revision procedures, or the loss to follow-up exceeded 20%. The omission of these “grey” data could potentially result in publication bias. However, publication bias was routinely assessed with meta-analysis tools. Studies were not specifically excluded if the lateral clavicle resection was part of rotator cuff surgery, involved treatment of long head biceps lesions, or was associated with subacromial decompression in either treatment group. It is acknowledged that the inclusion of these additional procedures may have resulted in selection bias. However, isolated acromioclavicular joint surgery is not commonly performed, and symmetric distribution of these confounders most likely will not influence this analysis.

### Literature research

A systematic review of the literature was performed to identify all publications over the last 20 years in the English and German literature describing lateral clavicle resection. Medline, Embase, Scopus, and Google Scholar were systematically searched using the following terms and Boolean operators: “acromioclavicular”, “lateral clavicle”, “distal clavicle”, AND/OR “resection”; “open” AND/OR “arthroscopic” AND/OR “clavicle resection” OR “acromioclavicular joint resection”. The references of all relevant published studies were manually cross-referenced and considered if they met the inclusion criteria. Two reviewers then conducted independent title and abstract screenings. Disagreements between reviewers were resolved by consensus, and if no consensus was reached, they were carried forward to the full-text review.

### Data extraction and quality assessment

Age, sample size, level of evidence, length of follow-up, potential confounders, and clinical outcome data were extracted from each article using an electronic data form. The senior author independently completed the data extraction, and the second reviewer verified the data.

Risk of bias was assessed using the Cochrane Collaboration Risk of Bias Tool [11]. The GRADE system was used by the senior author to assess the quality of the body of evidence for each outcome measure; the second reviewer verified the assessments [11]. The Cochrane Handbook recommends downgrading study quality if there were limitations in the design, indirectness of evidence, unexplained heterogeneity, imprecision of results, or the high probability of publication bias [11, 13]. To reduce reviewer bias, all

institutional and author information were concealed to the second reviewer. Any disagreement between reviewers was again 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 the  $I^2$  statistic. Outcomes were pooled using a random effects model if the  $I^2$  statistic was  $> 10\%$ ; a fixed effect model was used if the  $I^2$  statistic was  $< 10\%$ . This particular limit was selected, because several authors have demonstrated that the conclusions of homogeneity in meta-analyses of small number studies are often unjustified [14, 15]. If standard deviations were not reported, then the standard deviation was calculated using the following formula:  $SD = \max - \min (\text{range})/4$ . Hozo, et al. have confirmed that this formula provides a satisfactory estimate of standard deviation [16]. All tests of significance were two-tailed, and an  $\alpha$  of less than 0.05 was considered significant. Publication bias was assessed using funnel plots and Eggers test for intercept. Funnel and forest plots, as well

as all statistical analyses, were performed using STATA SE (Version 12.0; StataCorp, College Station, TX, USA) for Windows, and the Comprehensive Meta-analysis software package (CMA), version 3 (Biostat Inc, Englewood, NJ, USA).

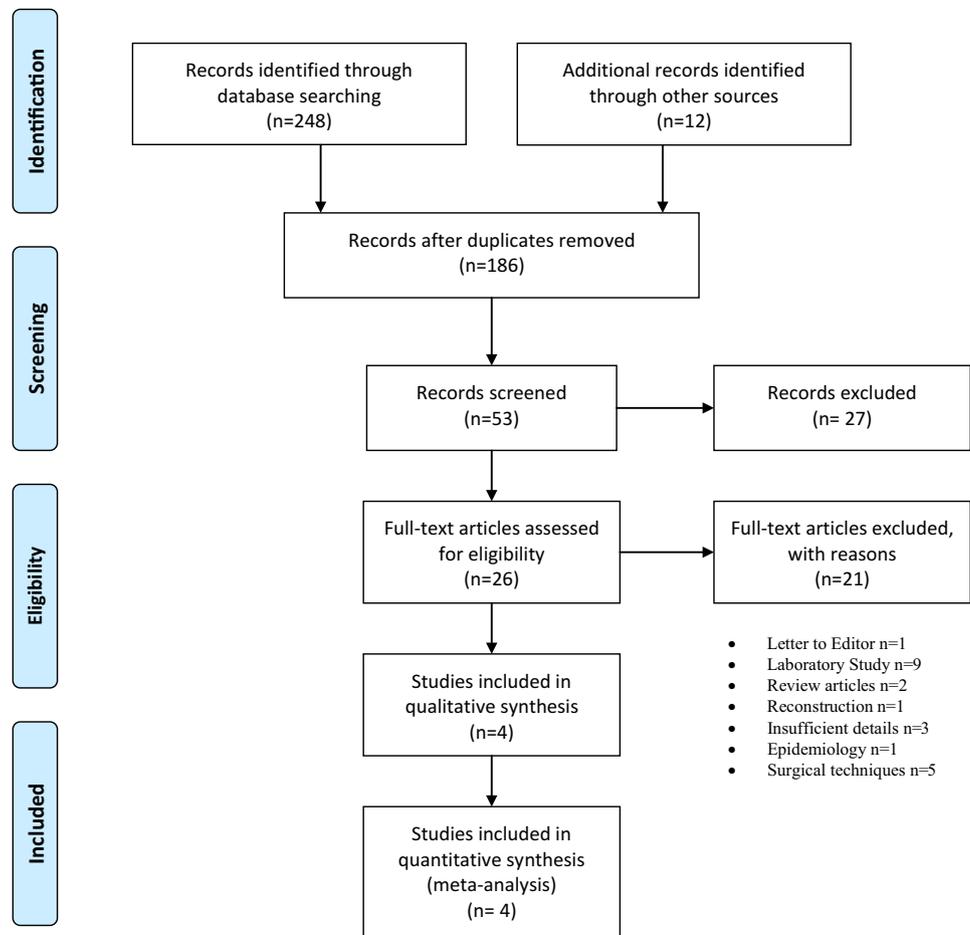
## Results

### Study selection and characteristics

The literature search identified 260 studies for consideration. Following removal of duplicates and a screening of abstracts, only 26 studies were eligible for inclusion. An examination of these full-text manuscripts was conducted, and only four studies met all of the eligibility criteria to be included in the analysis (Fig. 1) [2, 4, 8, 9].

The  $\kappa$  values for overall agreement between the two reviewers for the final eligibility was excellent ( $\kappa$  value 0.96, 95% CI 0.92–0.98). The four included studies were all published in English between 2007 and 2014. The cumulative total number of cases was 319; of those, 229 cases were treated arthroscopically, and the remaining 90 cases

**Fig. 1** PRISMA flow diagram. From the initial 260 records, 4 studies were included for analysis here



were treated with open resection. The study characteristics, demographics, and extracted outcomes are summarized in Tables 1 and 2.

### Risk of bias

The findings of the bias risk assessment are summarized in Table 3. Of the four studies, only one used a prospective randomized design [9]. The authors performed randomization based on stratifying according to etiology and pre-operative pain score [9]. This approach was assessed as high for random sequence generation, allocation concealment, blinding of personnel, and outcome assessment. The other three studies were level III comparative studies and the risk of bias assessment for randomization was, therefore, not applicable [2, 4, 8]. However, given the recommendations in the Cochrane Handbook, those three studies were assessed as high risk for these items (Table 3). For the other three items outlined in the Cochrane Handbook for Systematic Reviews of Interventions [11], attrition bias (incomplete outcome data), reporting bias (selective reporting), and other biases were assessed as low risk for all four studies. There were no missing outcome data, all expected outcomes were reported, and a funnel plot suggested that the studies all appeared to be free of other sources of bias (Fig. 2). Eggers intercept value was  $-3.754$  (95% CI  $-10.497$  to  $3.365$ ) with a  $p$  value of  $0.13$ , confirming that publication bias was not present.

Using the GRADE quality assessment criteria, three studies [2, 4, 8] were automatically downgraded as recommended by the GRADE handbook for limitations in design, specifically for their non-randomized nature. Freedman et al. were the only prospective randomized study, but was also downgraded because of the limitations and high risk of bias assessment with their randomization protocol [9]. All four studies were further downgraded by one level for indirectness of evidence. Differences in treatment and management, including patients who underwent other surgical procedures, were interpreted as differences in interventions based on the recommendation of the GRADE handbook [13]. In summary, all studies were double-downgraded and were considered to be of lower quality.

### Clinical outcome and pain scores

Clinical outcome scores were reported by all studies (Table 2). However, Duindam et al. have utilized the DASH score, and consequently, this study could not be used for pooling. Two studies [4, 9] have used the American Shoulder and Elbow Surgeons Score (ASES), and one study [8] has used the Constant score. These latter three studies were pooled as the two outcome scores are similar [1], and it has been shown that the ASES provides equivalent results to more objective evaluations such as the Constant score [17]. The  $I^2$  statistic for these three included

**Table 1** Characteristics of the included studies

References	Study details	LOE <sup>a</sup>	Sample size	Group allocation	Outcome measures	Confounders
Duindam et al. [2]	Retrospective chart review Time: 2008–2011 Open or arthroscopic subacromial	3	ASC: $n = 108$ Open: $n = 41$	Unknown	Dash, VAS Radiographic resection Complications, operative time, costs	Subacromial decompressions included
Robertson et al. [4]	Retrospective chart review Time: 1999–2006 Open or arthroscopic subacromial	3	ASC: $n = 32$ Open: $n = 17$	Patient decided approach	ASES, VAS Radiographic resection Operative time	RC repairs, biceps, labrum, subacromial decompressions included Underpowered: for ASES (8 point difference required)
Elhassan et al. [8]	Retrospective chart review Time: 2000–2005 Open or arthroscopic direct superior	3	ASC: $n = 81$ Open: $n = 23$	Unknown	Constant, VAS Subjective satisfaction	Subacromial decompressions, biceps and labral lesions, RC repairs included
Freedman et al. [9]	Prospective randomized Time: 2003–2004 Open or arthroscopic subacromial	2	ASC: $n = 8$ Open: $n = 9$	Randomization stratified according to etiology and pre-operative VAS score	ASES, VAS, SF36 Subjective satisfaction	Questionnaires mailed when military personnel Underpowered: post-hoc power showed that 14 pts per group were needed

<sup>a</sup>Level of evidence

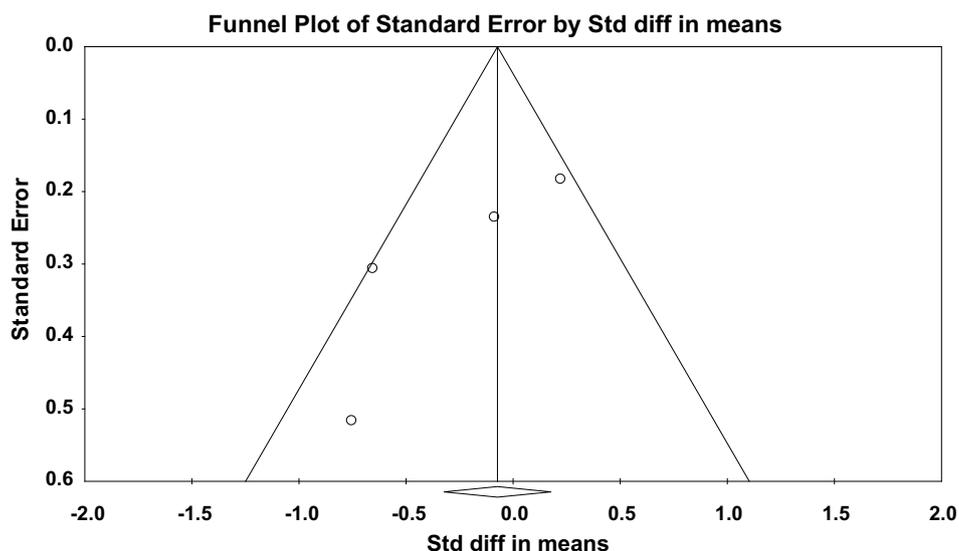
**Table 2** Outcomes of the included studies

References	Sample size	Age	Follow-up	Clinical outcome	Other outcomes
Duindam et al. [2]	ASC: <i>n</i> = 108 Open: <i>n</i> = 41	ASC: 53.8 ± 9.8 years Open: 53.1: ±9.2 years	ASC: 2.8 ± 1 years Open: 3.6 ± 1 years	Dash Arthroscopic: 22 ± 41; open: 21 ± 33 VAS Arthroscopic: 20 ± 50; open: 10 ± 23	Complications Arthroscopic: 11; open: 3 Radiographic resection Arthroscopic: 5.4 ± 3.25 mm; open: 10.1 ± 5.3 mm Operative time Arthroscopic: 38 + 15 min; open: 24 + 12 min Costs Arthroscopic: \$992 USD; open: \$393 USD
Robertson et al. [4]	ASC: <i>n</i> = 32 Open: <i>n</i> = 17	ASC: 47 years (range 19–69) Open: 51 years (range 35–76)	ASC: 5.3 years Open: 4.2 years	ASES Arthroscopic: 94.6 ± 8.6; open: 87.5 ± 17.6 VAS Arthroscopic: 0.61 ± 1.02; open: 1.59 ± 2.15 Subjective shoulder satisfaction Arthroscopic: 92.9 ± 8.6; open: 89.7 ± 12.5	Radiographic resection Arthroscopic: 9.5 ± 2.9 mm; open: 12.8 ± 2.1 mm Operative time Arthroscopic: 48 ± 10.7 min; open: 53.1 ± 15 min
Elhassan et al. [8]	ASC: <i>n</i> = 81 Open: <i>n</i> = 23	Mean: 45 years (range 23–73) ASC: 45 years (range 23–71) Open: 50 years (range 30–73)	Mean: 51 m (range 15–91) ASC: 49 m (16–83) Open: 53 m (15–91)	Constant Arthroscopic: 89 (39–100); open: 87 (43–100) VAS Arthroscopic: 1.6 (0–5); open: 1.7 (0–4) Subjective shoulder satisfaction Arthroscopic: 82 (40–100); open: 81 (40–100)	Radiographic resection Arthroscopic: 9.5 (3.8–16.5) mm; open: 13.5 (4.8–23.4) mm
Freedman et al. [9]	ASC: <i>n</i> = 8 Open: <i>n</i> = 9	Mean: 40 years (range 24–56)	Mean; 12 m	ASES Arthroscopic: 85; open: 80 VAS Arthroscopic: 1; open: 1.75 Subjective shoulder satisfaction Arthroscopic: 100 (7/7); open: 75 (6/8)	Radiographic resection Arthroscopic: 10 mm; open: 11 mm

**Table 3** Risk of bias assessment

	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Participants and Personnel (Performance Bias)	Blinding of Outcome Assessment (Detection Bias)	Incomplete Outcome Data (Attrition Bias)	Selective reporting (Reporting Bias)	(Other Bias)
Duindam et al., 2014 <sup>2</sup>	⊖	⊖	⊖	⊖	⊕	⊕	⊕
Robertson et al., 2011 <sup>4</sup>	⊖	⊖	⊖	⊖	⊕	⊕	⊕
Elhassan et al., 2009 <sup>8</sup>	⊖	⊖	⊖	⊖	⊕	⊕	⊕
Freedman et al., 2007 <sup>9</sup>	⊖	⊖	⊖	⊖	⊕	⊕	⊕

**Fig. 2** Distribution of the four included studies is symmetric, and does not suggest publication bias



studies [4, 8, 9] was 0%, and therefore, a fixed effect model was used. The pooled estimate demonstrated no significant differences in clinical outcomes between open and arthroscopic ACJ resection (SMD 0.323, 95% CI –0.020 to 0.665,  $p=0.065$ ,  $I^2=0%$ ; Fig. 3). However, the differences nearly reached significance in favor of open resection, and meta-analysis suggested that all three studies [4, 8, 9] favored open over arthroscopic resection (Fig. 3).

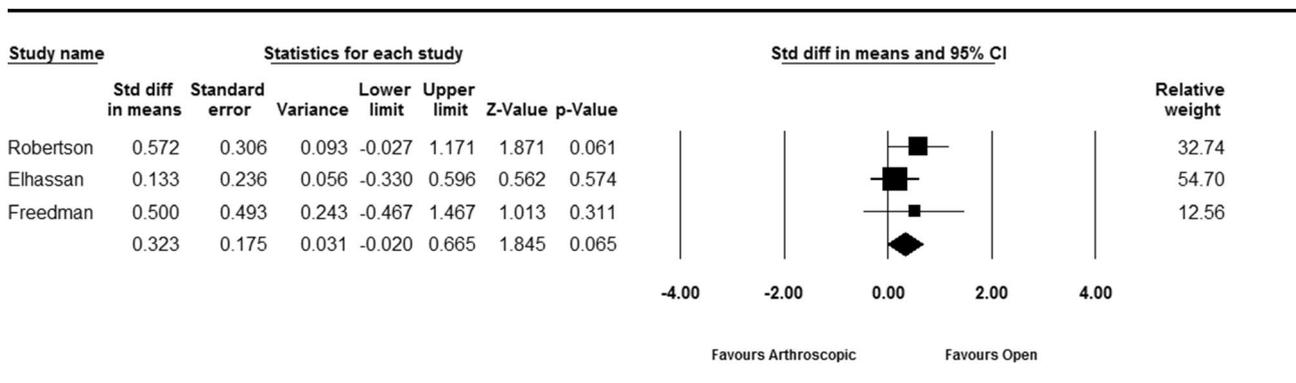
The simple shoulder test (SST) was also reported in these same three publications [4, 8, 9]. The  $I^2$  statistic for the three included studies [4, 8, 9] was 48.82%, and therefore, a random effect model was used. The pooled estimate demonstrated no significant differences in clinical outcomes between open and arthroscopic ACJ resection (SMD 0.744, 95% CI –0.259 to 1.742,  $p=0.144$ ,  $I^2=49.82%$ ; Fig. 4). However, meta-analysis suggested that all three studies [4, 8, 9] favored open over arthroscopic resection (Fig. 4).

The Visual Analogue Scale (VAS) was used for the assessment of pain, with a simple shoulder test (SST)

reported by all four studies [2, 4, 8, 9]. The  $I^2$  statistic for the four studies [2, 4, 8, 9] was 58.962%, and therefore, a random effect model was used. The pooled estimate demonstrated no significant differences in clinical outcomes between open and arthroscopic acromioclavicular joint resection (SMD –0.181, 95% CI –0.607 to 0.245,  $p=0.404$ ,  $I^2=58.96%$ ; Fig. 5).

**Radiographic resection**

The resection length was reported by all studies (Table 2) [2, 4, 8, 9]. The  $I^2$  statistic for the four studies was 0%, and therefore, a fixed effect model was used. The pooled estimate demonstrated significant differences in distal clavicle resection between open and arthroscopic ACJ resection (SMD 1.158, 95% CI 0.895–1.421,  $p < 0.0001$ ,  $I^2=0%$ ; Fig. 6). The results demonstrated that significantly more bone was removed from the distal clavicle when performing an open resection.



**Fig. 3** Pooled estimate for clinical outcomes demonstrated no significant differences ( $p=0.065$ ), but favored open resection

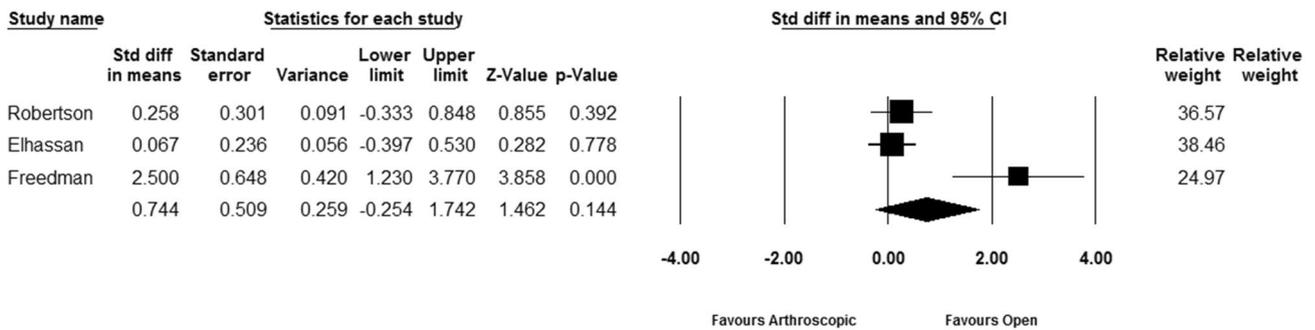


Fig. 4 Pooled estimated for the simple shoulder test demonstrated no significant differences ( $p=0.144$ ), but favored open resection

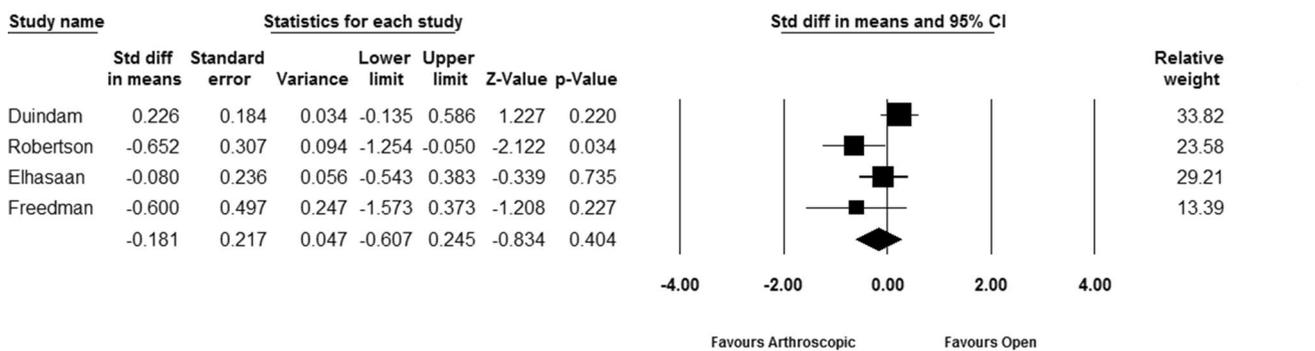


Fig. 5 Pooled estimated for VAS demonstrated no significant differences ( $p=0.404$ ) in clinical outcomes

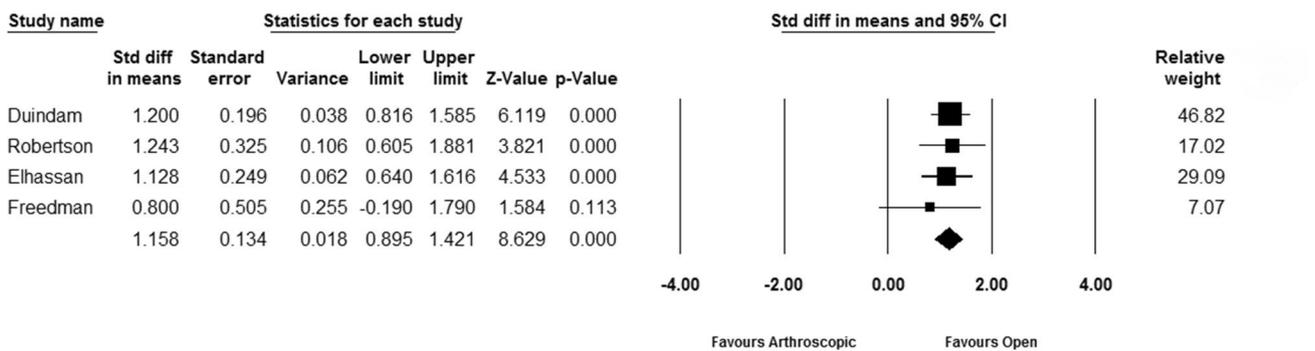


Fig. 6 Pooled estimate for demonstrated significant differences ( $p < 0.0001$ ) in distal clavicle resection, but open resection removed significantly more bone

## Discussion

The results of this meta-analysis of open versus arthroscopic ACJ resection have demonstrated that there were no significant differences in outcomes following either procedure. However, it has suggested that open resection was slightly more favored, resulting in non-significantly better clinical outcomes, with no difference in pain relief at 12–60 months after surgery.

Flatow et al. were the first group to compare open versus arthroscopic resection, and reported comparable clinical outcomes with return to all activities, full range of motion, and recovery of strength with no pain [18]. However, pain relief and return to normal activities occurred 3.4 months earlier in the arthroscopic group. In that study, the mean resection for both open and arthroscopic groups was 18 and 17 mm, respectively. In the four included studies in this meta-analysis [2, 4, 8, 9], the length of resection was substantially shorter, ranging from 5.4 to 10 mm in the arthroscopic group, and 10–13 mm in the open group. A study by Duindam et al. suggested that the length of resection might significantly influence clinical outcomes [2]. They reported that, provided the amount of the excised distal clavicle was large enough to prevent bone contact between the medial acromion and resected clavicle, the clinical outcome would most likely not be different whether an open or arthroscopic approach was used. It is important to recognize that if the resection is excessive, the resulting ACJ instability may be associated with more pain and an inferior outcome. Eskola et al. also demonstrated that patients who had a resection of less than 10 mm had significantly better outcomes and less pain than patients with a resection in excess of 10 mm [19]. However, these findings were obtained in patients with traumatic acromioclavicular dislocations and might not be applicable to patients with degenerative diseases.

The absence of differences in clinical outcomes is somewhat surprising, as the minimally invasive arthroscopic approach should theoretically cause less tissue disruption and preserve the superior capsule and ligamentous structures. A possible and provocative explanation may be that the apparent benefits of arthroscopic surgery may reflect the subjective perceptions of both surgeons and patients [20]. Sperling et al. demonstrated that patients expected functional outcomes would be superior with an arthroscopic approach [20]. Patients also strongly believed that there would be less pain, a faster recovery, better range of motion, and less time away from activities following arthroscopic resection [20]. One could argue that this potential confounder may have resulted in positive bias towards better outcomes following arthroscopic surgery.

Pensak et al. have previously performed a similar systematic review, and concluded that patients undergoing

arthroscopic resection, especially using a direct approach, exhibited a faster return to activities with similar long-term outcomes when compared to open resection [3]. However, this analysis only incorporated one of the studies included here [9], and the results may have been significantly different with the inclusion of additional studies [2, 4, 8, 9]. The conclusions drawn by Pensak et al. are unlikely to be valid, as they were based on only two comparative studies [3, 9, 21]. On closer inspection, the study by Charron et al. compared a direct versus an indirect arthroscopic approach, and this obviously does not allow any comparison between open and arthroscopic outcomes [21]. The study by Freedman et al. had a very low sample size of only 17 patients, yet the authors concluded that there was no difference in outcomes between arthroscopic and open surgery [9]. Pensak et al. have used level IV evidence, including six studies reporting on arthroscopic surgery and nine studies reporting on open surgery outcomes to conclude that a direct arthroscopic approach results in faster return to activity [3]. This approach is not based on sound scientific principles, and these conclusions must, therefore, be viewed with extreme caution.

Two of the reports [2, 8] not included in Pensak et al. [3] simultaneously performed routine arthroscopies in patients undergoing open acromioclavicular resection, and in both studies, the authors demonstrated no differences between open and arthroscopic resection [2, 8]. Although Duindam et al. did not specifically report whether routine diagnostic arthroscopic evaluation was performed in the open resection group, they did report that 24% of patients underwent arthroscopic subacromial decompression [2].

Of the four included studies, only Duindam et al. [2] reported complication rates, and the arthroscopic group showed a higher complication rate. Eight percent experienced symptoms of frozen shoulder arthroscopically, compared to 2.4% in the open group; 3.7% underwent revision surgery compared to 2.4% in the open group. Elhassan et al. reported 3.7% recurrence of bone in the arthroscopic group requiring revision surgery [8]. The current study did not specifically analyze between group complication rates as only one of the included publications reported their complications [2]. Although there was a trend towards higher revision rates and complications in the arthroscopic group, the available data are currently insufficient to conclude that arthroscopic surgery has a higher complication rate.

The heterogeneity of the included studies was assessed using the  $I^2$  statistic. The results revealed that heterogeneity was very low for the clinical outcomes (ASES, Constant) and the radiographic measures, and were moderate for the simple shoulder test and VAS. As there was no considerable variation in results between studies and consistency in the direction or estimates of effect, the results of this meta-analysis provide reliable evidence that arthroscopic distal

clavicle resection is not clinically superior to an open procedure, negating the often-presumed potential advantages of arthroscopic surgery for this condition.

The GRADE assessment of the included studies reveals that all of the studies were considered low quality. All four of the studies were downgraded because of the presence of indirectness of evidence. Downgrading was performed, because the included studies were designed as comparative observational level III studies. Furthermore, differences in treatment and management, including patients who underwent other simultaneous surgical procedures, were interpreted as differences in interventions according to the GRADE handbook [13]. Attrition, reporting, transfer, and performance bias was not observed. Meta-analysis is a quantitative tool that uses statistical methods to investigate measures of central tendencies, and is currently widely regarded as the highest level of evidence [22]. However, the inclusion of lower level studies possibly results in conclusions beyond those of the actual results reported [22]. Harris suggested that, as a minimum, level III studies with two treatment arms should be included to reduce systematic error [23]. In concordance with the GRADE handbook, we are moderately confident that the true effect is likely to be close to the estimate of the effect. Furthermore, additional high-quality studies and research may likely have an impact, and could conceivably change the estimate in either direction. While the implications for clinical practice remain uncertain, the results of this meta-analysis clearly suggest that both open and arthroscopic distal clavicle resection produce reliable and reproducible results with comparable clinical outcomes. Arthroscopic surgical techniques have no obvious clinical advantage when utilized for this condition.

The limitations of the included studies are also the principal limitations of this meta-analysis. The retrospective nature of three studies [2, 4, 8], the unequal numbers between the two groups, and the simultaneous treatment of other pathology all potentially reduce the external validity of this analysis. The low quality of the selected studies, mainly based on the high risk of bias and the lack of randomized level I and II studies, further decreases the external validity of both the included studies and this meta-analysis.

## Conclusions

The results of this systematic review and meta-analysis suggest that similar functional and clinical outcomes can be achieved with either open or arthroscopic lateral clavicle resection. The observed trend that open ACJ resection may have a more favorable outcome warrants further investigation.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

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