Safety and Effectiveness of Intra-articular Corticosteroid Injection Following Arthroscopic Shoulder Surgery

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Research article

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Abstract

Background

To evaluate the safety and effectiveness of intra-articular corticosteroid injection following arthroscopic shoulder surgery.

Method

PubMed, Cochrane Library, EMBASE, Web of Science and CNKI were retrieved from the inception of electronic databases to June 2020. All analyses were performed using Stata/SE 15.1 version (StataCorp).

Result

6 papers were included in this meta-analysis. There was no significant difference in tear rate (OR = 0.713, 95% CI: 0.450 to 1.129, P = 0.149), constant score (MD = 6.212, 95% CI: 2.552 to 9.971, P = 0.001), rating scale of the American shoulder and elbow surgeons (ASES) score (MD=-0.116, 95% CI: -1.769 to 1.546) and the university of California at Los Angeles shoulder rating (UCLA) score (MD = -1.461, 95% CI: -3.221 to 0.299). The infection rate of patients who received corticosteroid injection within 1 month after operation was significantly higher ($P < 0.05$), but there was no significant change in the infection rate of patients who received corticosteroid injection within 2–4 months after operation.

Conclusion

The use of corticosteroids after shoulder arthroscopy will not increase the rate of postoperative tears, but the injection of corticosteroid within 1 month will increase the postoperative infection rate.

Introduction

Adhesive shoulder arthritis, calcified supraspinatus tendonitis, shoulder synovitis and shoulder osteoarthritis could cause irreversible shoulder joint damage with the main clinical manifestations of limited mobility and pain[1–4]. Although conservative treatment and open surgery have been the main treatment methods for these diseases, with the popularization of arthroscopy technology, it has become one of the main treatment option[5, 6]. The main application advantages of shoulder arthroscopy are less injury of shoulder joint, sufficient removal of focus, low postoperative pain and fast recovery[7]. It is estimated that more than 270,000 patients underwent rotator cuff repair in 2006 in the United States and more than 250,000 patients completed rotator cuff repair under shoulder arthroscopy[8]. However, despite the replacement of surgical instruments and the increasingly sophisticated technique of the operators, patients often have severe postoperative pain and shoulder stiffness after arthroscopic rotator cuff repair, which is closely related to postoperative rotator cuff tear and poor functional recovery[9, 10].

Local corticosteroid blocking therapy has become one of the vital treatments for inflammatory shoulder pain because of reducing synovial inflammation, accelerating early functional recovery after surgery and is widely accepted by orthopedists[11]. Nicholas [12]compared the effect of two groups with high-grade, partial-thickness rotator cuff tears based on whether they received a subacromial corticosteroid injections or not and showed that the injection subgroup experienced a significant increase in rating scale of the American shoulder and elbow surgeons (ASES) and Constant score. However, there are still concerns about whether corticosteroid use will increase the incidence of infection, early tendon rupture and delayed tendon healing after arthroscopy[13, 14]. It is worth noting that 50,478 shoulder arthroscopy patients, of whom 4115 received injections in the 6-month preoperative period was accompanied with a significant increase in both the overall infection rate and severe infection rate in patients who received corticosteroid injections within 2 weeks. Meanwhile,some researchers believe that timing and dose of injections prior to arthroscopic rotator cuff repair impacts the risk of infection[15]. Therefore, there is still great controversy regarding the safety and clinical efficacy of intra-articular corticosteroid injection after shoulder arthroscopy. The purpose of this research is to explore the safety and clinical efficacy of intra-articular corticosteroid injection after shoulder arthroscopy, with a view to providing clinical guidance.

Materials And Methods

Literature and search strategy

The retrieved object is the research literature on the analysis of safety or effectiveness of corticosteroid injections in patients with arthroscopic shoulder surgery published publicly in the electronic databases including PubMed, Cochrane Library, EMBASE, and Web of Science from the inception of electronic databases to June 2020. We retrieved the following keywords in combination with Boolean logic: “arthroscopy” “shoulder Injuries” “rotator cuff injuries” “shoulder impingement syndrome” “corticosteroids” “steroids” “triamcinolone” “betamethasone” “dexamethasone”. Beyond that, the research of the appraisal reference list was manually checked to determine other potential qualification trials. The process iterates until no more articles could be determined. The meta-analysis was based on acknowledged PRISMA guideline (the prioritized reported items for systematic review and meta-analysis)[16].

Inclusion And Exclusion Criteria

The articles will be incorporated into the present meta-analysis if the literatures meet the following principles in accordance with PICOS. Population: patients with definite diagnosis of shoulder disease such as adhesive shoulder arthritis, calcified supraspinatus tendonitis or rotator cuff tear; Intervention: patients receiving arthroscopic shoulder surgery; Comparison: the safety and effectiveness of patients with or without corticosteroid injection; Outcome measures: one or more adequate data of the outcomes could be conducted statistical analysis; Study design: an official published RCT or RCS. Exclusion criteria:(I) Non-English written literature (II) abstracts, letters, editorials, expert opinions, case reports, review and basic research including animal and cell experiments (III) non-comparative study (IV) inadequate raw data.

Data Extraction And Outcome Measures

Two of the reviewers (Wen-chen Lu, Ting-jiang Wang) respectively extracted data from the included studies. The following essential information was captured: first author names, publication year, samples size, study design, outcomes and other relevant data. The extracted data [median, range, mean difference, 95% confidence interval (CI) and standard deviation (SD)] is input into the designed standardized table. When there are differences of opinion, another authority author has the final decision. The outcome measurements were tear rate, postoperative infection, constant score, ASES score and the university of California at Los Angeles shoulder rating (UCLA) score.

Quality Assessment And Statistical Analysis

Newcastle-Ottawa Scale (NOS) and Risk Bias in Non-randomized intervention studies (ROBINS-I) were respectively conducted to evaluate the methodological quality of the included RCTs and RCS. The literature quality evaluation was conducted separately by two reviewers (Wen-chen Lu, Zhi-hong Tang). Consensus was reached through consultation for divergence. The GRADEpro software was used for evidence quality assessment. We use the Stata 15.1 version (Stata Corporation, College Station, Texas, USA) for statistical analyses. When I^2 50%, the data was considered as obvious heterogeneity. We conduct a meta-analysis using random-effect model according to Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0). Otherwise, fixed-effect model was performed. For continuous outcomes (constant score, ASES score and UCLA score), Weighted Mean Difference (WMD) were expressed for the evaluation. For discontinuous various outcomes (tear rate, infection), Odds Ratio (OR) were applied for the assessment.

Results

Search results

A total of 895 studies were identified as potentially relevant literature reports. There were no additional studies identified through other sources. We got 570 articles when the duplicate was removed. By scanning the title and abstract, 500 studies were excluded according to the eligibility criteria. Another 64 articles were further excluded by reading the full text. Ultimately, 6 articles[17–22] were eligible for data extraction and meta-analysis. The searching process is shown in Fig. 1.

Characteristics Of Included Studies

The characteristics of the 6 included studies are summarized in Table 1. 7682 individuals were incorporated into our trial of whom 4184 patients with corticosteroid injection and 3498 patients with corticosteroid injection. Among them, 5 articles were RCS, and 1 article was a RCT. 4 studies from Korea, 1 study from the USA and 1 study from France.

Study Quality And Risk Of Bias

The quality of the included studies was evaluated by the scale of ROBINS-I. The details were presented in Table 2.

Methodological Quality Assessment

The total qualities of the evidence were low for the tear rate, postoperative infection, constant score, ASES score and UCLA score (Table 3).

Outcomes Of The Meta-analysis

primary outcome indicator

Tear rate

A total of 5 articles reported the last follow-up tearing events. The heterogeneity test of the included articles indicated that there was no heterogeneity among the studies (heterogeneity P = 0.397, I^2 = 1.6%). The result show that there was no significant difference between the two groups in the rate of postoperative tear. (OR = 0.713, 95% CI: 0.450 to 1.129, P = 0.149; Fig. 2).

Post-operation infection

A total of three papers mentioned postoperative complications and two of them claimed that their study had no complications. Only a review of one large database including 3946 patients reported the relevant infection data. Due to the lack of sufficient data, a descriptive analysis of postoperative infection rates will be used. KEW [19]compared the incidence of postoperation infection of patients undergoing shoulder arthroscopy operation between two groups. Finally, they found that the infection rate of patients who received corticosteroid injection within 1 month after operation was significantly higher ($P < 0.05$), but there was no significant change in the infection rate of patients who received corticosteroid injection within 2–4 months after operation ($P > 0.05$).

Secondary Outcome Indicator

Constant score

2 publications focused on the constant score in two groups. The heterogeneity test of the included studies demonstrated significant heterogeneity ($I^2 = 91.5\%$, $P = 0.001$). The result of the random effect model showed that there was no statistical significance. (MD = -0.990, 95% CI: -12.445 to 10.464, $P = 0.865$; Fig. 3).

ASES score

2 articles described the relationship between the corticosteroid injection and the ASES score. The heterogeneity test of the included articles indicated that there was heterogeneity among the studies. The results of random effect model analysis suggested that there was no statistical significance. (heterogeneity $P = 0.277$, $I^2 = 15.4\%$, MD=-0.116, 95% CI: -1.769 to 1.546, $P = 0.893$; Fig. 4).

UCLA score

2 articles described the relationship between the corticosteroid injection and the UCLA score. The heterogeneity test indicated that there was significant heterogeneity ($I^2 = 65.9\%$, $P = 0.087$). The result of random analysis indicated that there was no statistical significance. (MD = -1.461, 95% CI: -3.221 to 0.299, $P = 0.104$; Fig. 5).

Discussion

Oral nonsteroidal anti-inflammatory analgesic drugs, intra-articular corticosteroid injection, physical therapy and joint capsule release are used to treat shoulder stiffness and pain after repair surgery for rotator cuff injuries[23, 24]. It was found that compared with hyaluronic acid, fibroblast proliferation was lower and the rate of healing failure was higher when the corticosteroids were injected at the surgical site in the studies in animal repair models of rotator cuff injury[25, 26]. In addition, human tissue cytology studies have shown that corticosteroid treatment is associated with higher cell apoptosis at the surgical site[27]. Although some basic studies have shown that corticosteroids may have a negative effect on postoperative tissue healing, some clinical studies have shown that early intraarticular injection of corticosteroids after arthroscopic rotator cuff repair does not increase the tear rate[21, 28]. Our research demonstrated that there was no significant difference in tear rate, constant score, ASES score and UCLA score. However, corticosteroids injection within 1 month after arthroscopic shoulder surgery will significantly increase the early infection rate.

The results of this meta-analysis showed that the corticosteroids injection group had no significant difference in tear rate compared with the control group, which is inconsistent with the research of BAVEREL[21]. We consider that different characteristics of the included patients may be one of the potential reasons. only severely injured patients with rotator cuff full-thickness tearing were included in BAVEREL's research[21]. In this study, patients with partial or full-thickness rotator cuff tears and a mixture of the two were included. The differences of the study subjects may lead to inconsistent conclusions. Secondly, betamethasone is the intervention of the former study, while triamcinolone acetonide is the main intervention of this study. To some extent, the difference of corticosteroid types will affect the conclusion.

In this research, 2 included articles mentioned that no postoperative adverse reactions were found after corticosteroids administration. The most likely reason was that the sample size was relatively small. KEW [19]compared the incidence of infection of 3946 patients undergoing shoulder arthroscopy operation between two groups. Finally, they found that the infection rate of patients who received corticosteroid injection within 1 month after operation was significantly higher, but there was no significant change in the infection rate of patients who received corticosteroid injection within 2–4 months after operation and this result is in line with previous studies[29, 30]. Postoperative infections are caused when pathogens enter the body during surgery or corticosteroid injection. The first month after the operation is considered as the inflammatory response period. Due to the immunosuppressive effect of corticosteroid, the ability of bacteria resistance declines causing infection.

Previous studies have reported that long-term use of corticosteroid will increase the incidence of complications within 30 days after arthroscopic shoulder surgery[29–31]. MARTIN [31]reported the incidence of corticosteroid relevant complications such as reoperation (0.31%), superficial infection of the surgical site (0.16%), deep infection (0.01%), deep vein thrombosis or thrombophlebitis (0.09%), peripheral nerve injury (0.01%), pulmonary embolism (0.06%) in a study involving 9410 patients. HEYER [29] found that in addition to the long-term use of corticosteroid, patients older than 65 years old, male patients, ASA rating greater than level 2, history of chronic obstructive pulmonary disease, hypertension and operation time more than 90 minutes were all related to the increased incidence of adverse reactions.

The shortcomings of the research: First, only one of the included literatures is an RCT, which may be one of the sources of heterogeneity. Second, all the literatures are short-term observation studies with a follow-up time of no more than 3 years. This conclusion should not be applied to long-term observation results.

Conclusion

The use of corticosteroids after shoulder arthroscopy will not increase the rate of postoperative tears, but the injection of corticosteroid within 1 month will increase the postoperative infection rate.

Abbreviations

RCT
Randomized controlled trial; RCS:retrospective controlled trial; OR:Odds Ratio; WMD:Weighted Mean Difference; CI:Confidence interval; SD:Standard Deviation. UCLA:ASES:rating scale of the American shoulder and elbow surgeons; UCLA:the university of California at Los Angeles shoulder rating; NOS:Newcastle-Ottawa Scale; ROBINS-I:Risk Bias in Non-randomized intervention studies.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

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Authors' contributions

Wen-chen Lu conceived of the design of the study. Ting-jiang Wang performed and collected the data and contributed to the design of the study. Zhi-hong Tang prepared and revised the manuscript. All authors read and approved the final content of the manuscript.

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References

1. Memon M, Kay J, Ginsberg L, de Sa D, Simunovic N, Samuelsson K, Athwal GS, Ayeni OR. Arthroscopic Management of Septic Arthritis of the Native Shoulder: A Systematic Review, Arthroscopy: the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association, 34 (2018) 625–646.e621.
2. Darrieutort-Laffite C, Blanchard F, Le Goff B. Calcific tendonitis of the rotator cuff: From formation to resorption. Joint bone spine. 2018;85:687–92.
3. Kanbe K. Clinical outcome of arthroscopic capsular release for frozen shoulder: essential technical points in 255 patients. J Orthop Surg Res. 2018;13:56.
4. Flemming DJ, Gustas-French CN. Rapidly Progressive Osteoarthritis: a Review of the Clinical and Radiologic Presentation. Curr Rheumatol Rep. 2017;19:42.
5. Saltzman BM, Leroux T, Cole BJ. Management and Surgical Options for Articular Defects in the Shoulder, Clinics in sports medicine, 36 (2017) 549–572.
6. Ho AG, Gowda AL, Wiater JM. Evaluation and treatment of failed shoulder instability procedures. J Orthop Traumatol. 2016;17:187–97.
7. Xu Y, Wu K, Ma Q, Zhang L, Zhang Y, Xu W, Guo JJ. Comparison of clinical and patient-reported outcomes of three procedures for recurrent anterior shoulder instability: arthroscopic Bankart repair, capsular shift, and open Latarjet. J Orthop Surg Res. 2019;14:326.
8. Jain NB, Higgins LD, Losina E, Collins J, Blazar PE, Katz JN. Epidemiology of musculoskeletal upper extremity ambulatory surgery in the United States. BMC Musculoskelet Disord. 2014;15:4.
9. Ruiz-Suarez M, Barber FA. Postoperative pain control after shoulder arthroscopy. Orthopedics. 2008;31:1130.
10. Conn RA, Cofield RH, Byer DE, Linstromberg JW. Interscalene block anesthesia for shoulder surgery, Clinical orthopaedics and related research, (1987) 94–98.
11. Gialanella B, Prometti P. Effects of corticosteroids injection in rotator cuff tears, Pain medicine (Malden, Mass.), 12 (2011) 1559–1565.
12. Donohue NK, Prisco AR, Grindel SI. Pre-operative corticosteroid injections improve functional outcomes in patients undergoing arthroscopic repair of high-grade partial-thickness rotator cuff tears, Muscles, ligaments and tendons journal, 7 (2017) 34–39.

13. Omar M, Haas P, Ettinger M, Krettek C, Petri M, Simultaneous Bilateral Quadriceps Tendon Rupture following Long-Term Low-Dose Nasal Corticosteroid Application, Case reports in orthopedics, 2013 (2013) 657845.
14. Hiemstra LA, Macdonald PB, Froese W. Subacromial infection following corticosteroid injection. Journal of shoulder elbow surgery. 2003;12:91–3.
15. Forsythe B, Agarwalla A, Puzzitiello RN, Sumner S, Romeo AA, Mascarenhas R. The Timing of Injections Prior to Arthroscopic Rotator Cuff Repair Impacts the Risk of Surgical Site Infection, The Journal of bone and joint surgery. American volume. 2019;101:682–7.
16. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6:e1000097.
17. Lee W, Kim SJ, Choi CH, Choi YR, Chun YM. Intra-articular injection of steroids in the early postoperative period does not have an adverse effect on the clinical outcomes and the re-tear rate after arthroscopic rotator cuff repair, Knee surgery, sports traumatology, arthroscopy: official journal of the ESSKA, 27 (2019) 3912–3919.
18. Kim YS, Jin HK, Lee HJ, Cho HL, Lee WS, Jang HJ. Is It Safe to Inject Corticosteroids Into the Glenohumeral Joint After Arthroscopic Rotator Cuff Repair? Am J Sports Med. 2019;47:1694–700.
19. Kew ME, Cancienne JM, Christensen JE, Werner BC. The Timing of Corticosteroid Injections After Arthroscopic Shoulder Procedures Affects Postoperative Infection Risk, The American journal of sports medicine, 47 (2019) 915–921.
20. Kim IB, Jung DW. An Intra-articular Steroid Injection at 6 Weeks Postoperatively for Shoulder Stiffness After Arthroscopic Rotator Cuff Repair Does Not Affect Repair Integrity, The American journal of sports medicine, 46 (2018) 2192–2202.
21. Baverel L, Boutsiadis A, Reynolds RJ, Saffarini M, Barthélémy R, Barth J. Do corticosteroid injections compromise rotator cuff tendon healing after arthroscopic repair? JSES open access. 2018;2:54–9.
22. Shin SJ, Do NH, Lee J, Ko YW. Efficacy of a Subacromial Corticosteroid Injection for Persistent Pain After Arthroscopic Rotator Cuff Repair. Am J Sports Med. 2016;44:2231–6.
23. Itoi E, Arce G, Bain GI, Diercks RL, Guttmann D, Imhoff AB, Mazzocca AD, Sugaya H, Yoo YS. Shoulder Stiffness: Current Concepts and Concerns. Arthroscopy: the journal of arthroscopic related surgery : official publication of the Arthroscopy Association of North America the International Arthroscopy Association. 2016;32:1402–14.
24. Favejee MM, Huisstede BM, Koes BW. Frozen shoulder: the effectiveness of conservative and surgical interventions–systematic review. Br J Sports Med. 2011;45:49–56.
25. Nakamura H, Gotoh M, Kanazawa T, Ohta K, Nakamura K, Honda H, Ohzono H, Shimokobe H, Mitsui Y, Shirachi I, Okawa T, Higuchi F, Shirahama M, Shiba N, Matsueda S. Effects of corticosteroids and hyaluronic acid on torn rotator cuff tendons in vitro and in rats. Journal of orthopaedic research: official publication of the Orthopaedic Research Society. 2015;33:1523–30.
26. Muto T, Kokubu T, Mifune Y, Inui A, Harada Y, Yoshifumi F, Takase R, Kuroda M, Kurosaka. Temporary inductions of matrix metalloprotease-3 (MMP-3) expression and cell apoptosis are associated with tendon degeneration or rupture after corticosteroid injection. Journal of orthopaedic research: official publication of the Orthopaedic Research Society. 2014;32:1297–304.
27. Ramírez JP, Bonati-Richardson F, García MP, Hidalgo C, Stoore C, Liendo R, Soza F, Landerer E, Paredes R. Intra-articular treatment with corticosteroids increases apoptosis in human rotator cuff tears. Connect Tissue Res. 2019;60:283–90.
28. Bonnevialle N, Bayle X, Faruch M, Wargny M, Gomez-Brouchet A, Mansat P. Does microvascularization of the footprint play a role in rotator cuff healing of the shoulder? Journal of shoulder elbow surgery. 2015;24:1257–62.
29. Heyer JH, Kuang X, Amdur RL, Pandarinath R. Identifiable risk factors for thirty-day complications following arthroscopic rotator cuff repair. The Physician sportsmedicine. 2018;46:56–60.
30. Hill JR, McKnight B, Pannell WC, Heckmann N, Sivasundaram L, Mostofi A, Omid R, Rick GF, Hatch, 3. Risk Factors for 30-Day Readmission Following Shoulder Arthroscopy. Arthroscopy: the journal of arthroscopic related surgery : official publication of the Arthroscopy Association of North America the International Arthroscopy Association. 2017;33:55–61. rd, .
31. Martin CT, Gao Y, Pugely AJ, Wolf BR. 30-day morbidity and mortality after elective shoulder arthroscopy: a review of 9410 cases. Journal of shoulder elbow surgery. 2013;22:1667–75.e1661.

Tables

Table 1 The basic characteristics of included studies.

Author	Year	Country	Study design	Intervention	Study Group		Gender		Age		Fo up
					Corticosteroid	Control	Corticosteroid (M/F)	Control (M/F)	Corticosteroid	Control	
Lee	2019	Korea	RCS	Triamcinolone	56	262	24/32	106/156	69.7±7.3	61.3±7.8	24 month
Shin	2016	Korea	RCS	Triamcinolone	72	386	38/34	203/183	57.3±8.6	57.3±8.5	28.9± month
Baverel	2017	France	RCS	Betamethasone	31	35	21/10	21/14	52.7±8.0	52.3±13.0	3.3±1 years 3.3±0 years
Kim	2019	Korea	RCT	Triamcinolone	40	40	12/23	21/19	59.8±8.4	60.4±8.6	23.1± month 27.0± month
Kim	2018	Korea	RCS	Triamcinolone	39	135	21/18	63/72	62.7±6.6	60.4±8.6	≥24 month
Kew	2019	USA	RCS	NA	3946	2640	1694/2252	1150/1490	NA	NA	≤3 month

Tear rate Postoperative infection Constant score ASES score UCLA score

#Corticosteroidgroup

*Controlgroup

Table 2 BiasassessmentbyTools ofRisk Bias In Non-randomized intervention studies (ROBINS-I)

Author	Year	Risk of bias assessment	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
Lee	2019	Moderate	Moderate	Low	Low	Low	Moderate	Moderate	Moderate
Shin	2016	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate
Baverel	2017	Serious	Serious	Moderate	Moderate	Low	Moderate	Moderate	Serious
Kim	2018	Moderate	Serious	Moderate	Moderate	Moderate	Moderate	Moderate	Serious
Kew	2019	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate

Table 3 The qualityassessmentfortheoutcomes

The Comparison for safety and effectiveness of intra-articular corticosteroid injection following arthroscopic shoulder surgery						
Patient or population: patients with relevantshoulderdisease **Settings:**safety and effectiveness of intra-articular corticosteroid injection **Intervention:corticosteroid injection**						
Outcomes	**Illustrative comparative risks* (95% CI)** Assumed risk **Control**	Corresponding risk **New Comparison**	**Relative effect (95% CI)**	**No of Participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
Tear rate	**Study population**		**OR 0.71** (0.45 to 1.13)	1000 (5 studies)	⊕⊕⊖⊖ **low**	
	166 per 1000	**123 per 1000** (82 to 183)				
	Moderate					
	143 per 1000	**106 per 1000** (70 to 159)				
Constant score	Themeanconstantscorein the intervention groups was **0.99 lower** (12.44 lower to 10.46 higher)			524 (2 studies)	⊕⊕⊖⊖ **low**	
ASES score	ThemeanASES scorein the intervention groups was **0.12 lower** (1.8 lower to 1.56 higher)			776 (2 studies)	⊕⊕⊖⊖ **low**	
UCLA score	ThemeanUCLA scorein the intervention groups was **1.46 lower** (3.22 lower to 0.3 higher)			492 (2 studies)	⊕⊕⊖⊖ **low**	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Figures

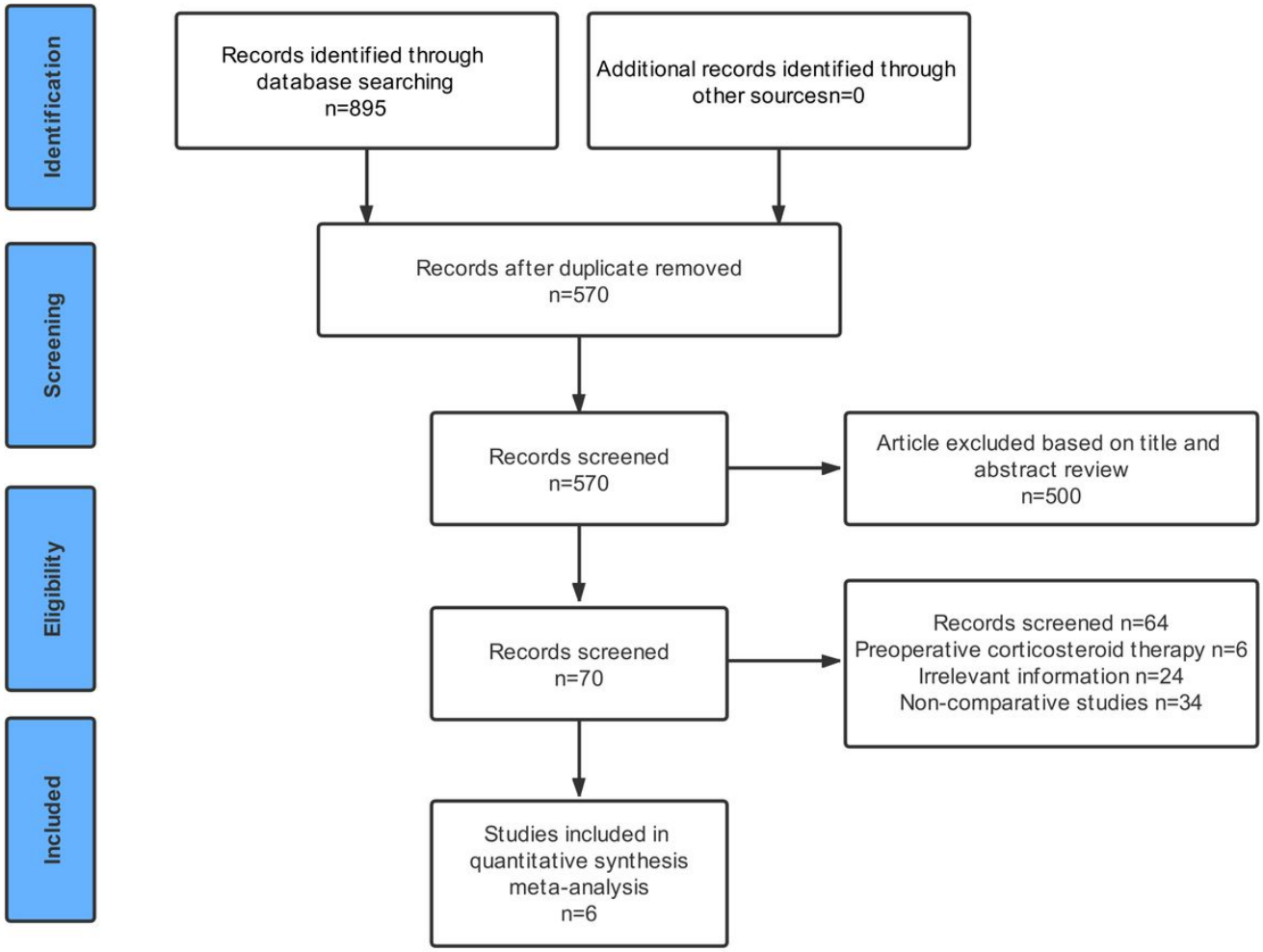

Figure 1

Flowchart of the study selection process

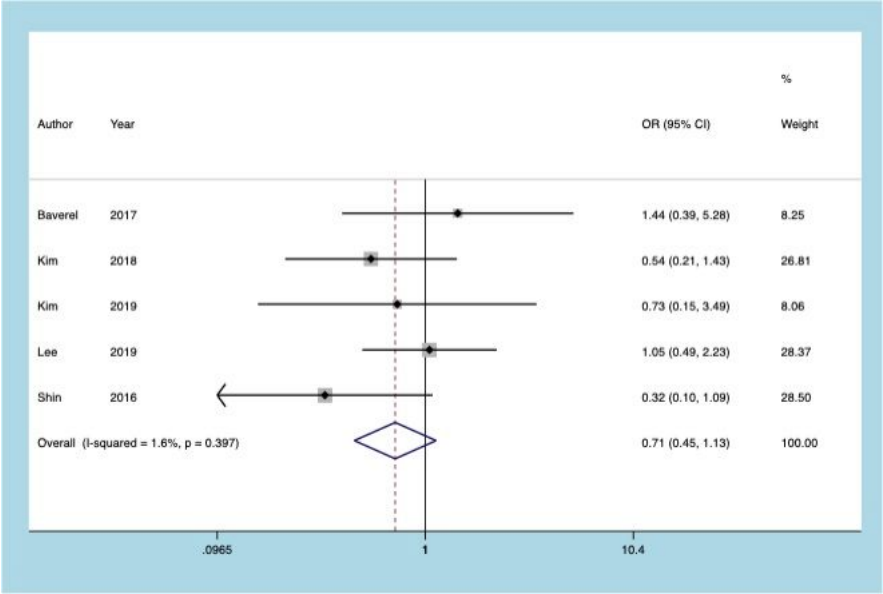

Figure 2

Forest plot diagram showing thetear rate

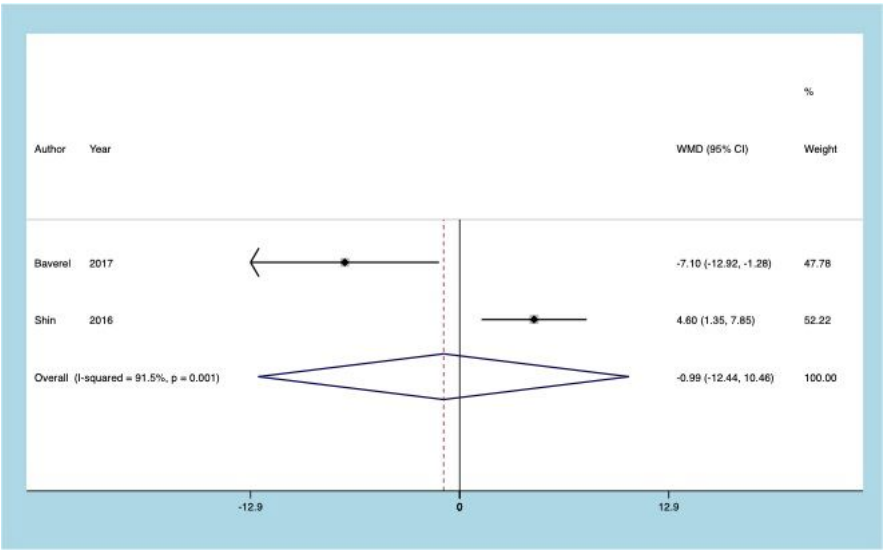

Figure 3

Forest plot diagram showing the constantscore

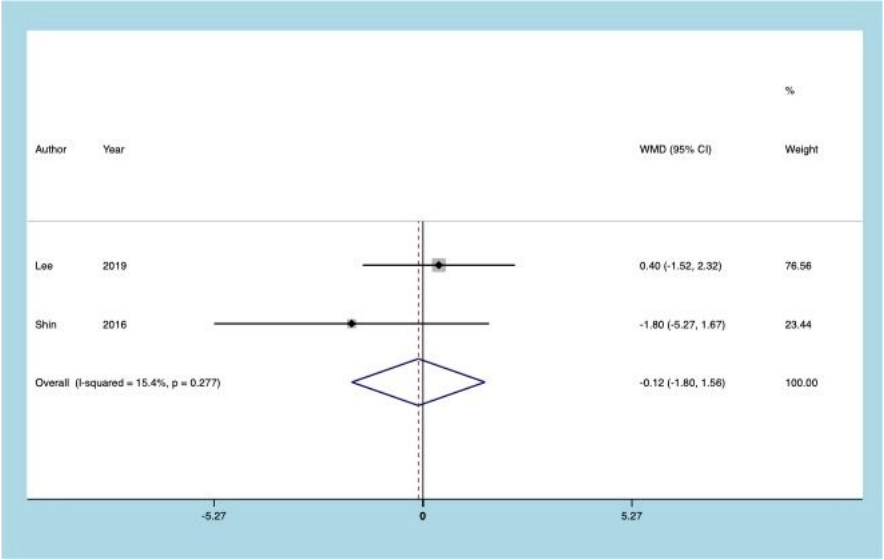

Figure 4

Forest plot diagram showing the ASES score

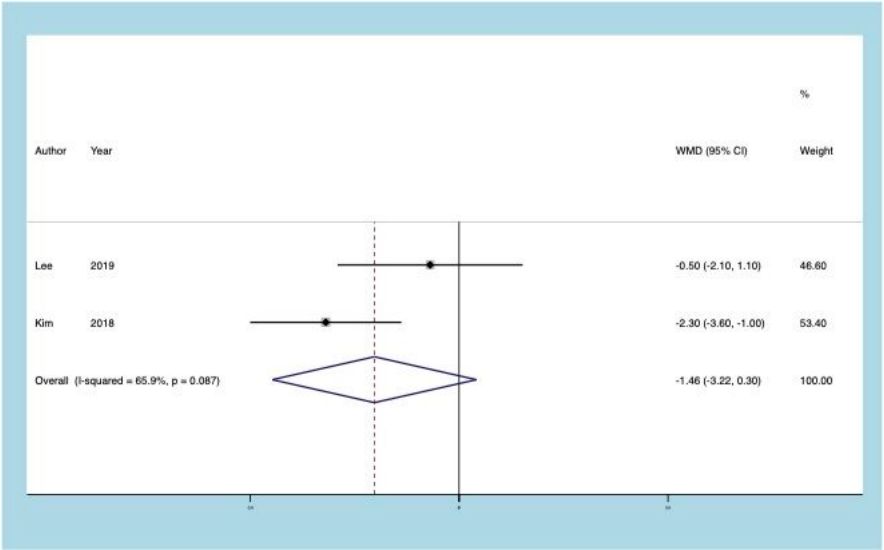

Figure 5

Forest plot diagram showing the UCLA score

Supplementary Files

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