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Steroid Injection Versus Physiotherapy for Patients With Adhesive Capsulitis of the Shoulder

A PRISMA Systematic Review and Meta-Analysis of Randomized Controlled Trials

Yaying Sun, MB, Shuai Lu, MB, Peng Zhang, MD, Zhaohui Wang, and Jiwu Chen, MD

Abstract: To compare the effect of steroid injection and physiotherapy for patients with adhesive capsulitis of the shoulder (ACS).

An electronic search was performed on Pubmed, Embase, and Cochrane library, and reference lists were also reviewed for randomized controlled trials (RCTs) comparing steroid injection and physiotherapy for patients with ACS. The quality of included studies were assessed using PEDro scale. Standardized mean differences (SMDs) and 95% confidence interval (CI) were used for comparisons. The primary outcome was functional improvement.

Nine RCTs including 453 patients were identified. From 6–7 weeks to 24–26 weeks postintervention, no superiority was noted in favor of either steroid injection or physiotherapy for functional improvement (SMD 0.28; 95% CI –0.01–0.58; $P=0.06$) or pain relief (SMD –0.10; 95% CI –0.70–0.50; $P=0.75$). Steroid injection provided more improvement in passive external rotation at 24 to 26 weeks (3 studies, SMD 0.42; 95% CI 0.11–0.72; $P=0.007$) but not at 6 to 7 weeks (4 studies, SMD 0.63; 95% CI 0.36–0.89; $P=0.32$) or 12 to 16 weeks (3 studies, SMD –0.07; 95% CI –0.79–0.65; $P=0.85$). Steroid injection was as safe as physiotherapy for patients with ACS (risk ratio 0.94; 95% CI 0.67–1.31).

Both steroid injection and physiotherapy are equally effective for patients with ACS. One steroid injection might be the 1st choice for ACS. Results should be interpreted with caution due to the heterogeneity among the studies.

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From the Department of Sports Medicine, Huashan Hospital, Fudan University, Shanghai (YS, PZ, JC); and Department of Cardiology, Union Hospital, Huazhong University of Science and Technology, Wuhan, People's Republic of China (SL, ZW).

Correspondence: Jiwu Chen, Department of Sports Medicine, Huashan Hospital, Fudan University, 12# Middle Wulumuqi Road, Shanghai 200040, People's Republic of China (e-mail: jeevechen@gmail.com).

Zhaohui Wang, Department of Cardiology, Union Hospital, Huazhong University of Science and Technology, Wuhan 430000, People's Republic of China (e-mail: wuxiaohongtian@163.com).

YS and SL contributed equally to this work.

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Abbreviations: ACS = adhesive capsulitis of the shoulder, CI = confidence interval, NSAID = nonsteroidal antiinflammatory drug, RCT = randomized controlled trial.

INTRODUCTION

Adhesive capsulitis of the shoulder (ACS), entitled in 1945 by Neviaser,¹ is a common shoulder complaint affecting 2% to 5% of the population.² The condition leads to a progressive loss of glenohumeral movements, especially external rotation, and shoulder pain.^{3,4} It is believed that inflammation happened in rotator interval, results in painful motion and subsequent fibrosis, and stiffness that limits movements.^{5–7}

Based on the current pathological findings, many treatment strategies are introduced into practice, aiming at antiinflammation and antiadhesion. The most commonly used treatments are steroid injection and physiotherapy.^{8,9} Steroid injection has strong antiinflammation effect and has long been used for ACS, but invasion to the body and complications such as pain, vasovagal reaction, and serum glucose level changes may prevent patients from accepting this method.^{10,11} Compared with steroid injection, physiotherapy, with no or minimal invasion to the body, may be more applicable for patients with ACS though the non-invasive character might limit the antiinflammation effect. Components of physiotherapies are various, including active glenohumeral motion, shockwave, ice and hot pack, ultrasound, and proprioceptive neuromuscular facilitation.^{12–15}

A previous systematic review compared the effect of physiotherapy with isolated steroid injection and found that steroid injection improved significantly more degree of shoulder function than physiotherapy from 6–7 to 24–26 weeks postintervention.² Since new randomized controlled trials (RCTs) comparing steroid injection with physiotherapy for ACS were identified,^{16,17} we undertook a systematic review and meta-analysis of RCTs to reevaluate the effect of 2 interventions for this condition.

MATERIALS AND METHODS

This systematic review was written in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist.¹⁸ Review Manager, Version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration; Copenhagen, Denmark) was used for comparisons. Ethical approval was not necessary according to local legislation because of the type of study (meta-analysis).¹⁹

Search Strategy

Searching strategy was formulated based on former meta-analyses. The last search was performed independently by the

1st 2 authors in December, 2015 on Pubmed, Embase, and Cochrane library. Detailed searching key words for Pubmed is in Appendix 1, <http://links.lww.com/MD/A964>. Reference lists of previous reviews with regard to physiotherapy in ACS were also reviewed.

Inclusion Criteria

The following inclusion criteria were applied:

- (i) population: adult with either primary or secondary ACS;
- (ii) intervention: steroid injection;
- (iii) comparison: physiotherapy. Physiotherapy was defined as non-injectable conservative treatments, including but not limited to electrotherapy, shockwave, and acupuncture;
- (iv) outcome measures: primary outcome was functional improvement, i.e., Shoulder Pain and Disability Index, or The American Shoulder and Elbow Surgeons score, while secondary outcomes were pain relief, passive external rotation, and adverse effect; and
- (v) study design: RCT in English. Comparisons were performed at 3 follow-up time points, 6 to 7, 12 to 16, and 24 to 26 weeks.

Study Selection

Titles and abstracts were screened independently by the first 2 authors. Full text was retrieved when a judgment could not be made. Inconsistencies were resolved by discussion and consensus.

Data Collection and Management

A piloted data-extraction sheet, which covered the following items: first author and year, number of patients (steroid injection group/physiotherapy group), intervention protocol (steroid injection group and physiotherapy group), cointervention, and summary of findings were used. The first 2 authors independently extracted information from included RCTs. Disagreement would be resolved by discussion and consensus.

Data Analysis

A random-effects model was used regardless of heterogeneity because patient information, intervention details, and other confounding factors were inconsistent among studies. Heterogeneity was assessed by I^2 statistic, which describes the percentage of total variation across studies due to heterogeneity rather than chance. An I^2 statistic $>50\%$ would be regarded as significant heterogeneity.²⁰ Standardized mean difference (SMD) and 95% confidence intervals (CIs) were used to compare continuous variable, and risk ratio and 95% CI were used to compare dichotomous variable. The difference on scales pre- and posttreatment was input for comparisons with the purpose of investigating the difference in the degree of improvement between 2 modalities. For cases in which the standard deviation was known for baseline and endpoint instead of change, a correlation of 0.5 was used to estimate the dispersion.²¹ Publication bias was not detected because the number of studies included was less than 10.²² Whenever heterogeneity was significant, we looked for the origin of heterogeneity. One study would be omitted in each turn to figure out the origin of heterogeneity. A P value <0.05 was regarded as statistically significant.

Assessments of Quality of Evidence

Eligible articles were assessed for methodological quality using the PEDro scale.²³ This scale, which is based on both Jadad and Verhagen scales, is designed specifically for studies focusing on physiotherapy.²⁴ This scale has already been proved to be moderately-to-highly reliable.²⁵ Besides, the quality of evidence was evaluated by the Grading of Recommendations Assessment, Development, and Evaluation approach.²⁶ Four levels of evidence, that is, high quality, moderate quality, low quality, and very low quality, were entitled to the pooled results according to risk of bias, publication bias, inconsistency, indirectness, and imprecision.^{27–31}

RESULTS

A total of 691 titles were obtained from electronic databases after removing duplicates. One additional article was identified from previous reviews.¹⁴ After reading titles and abstracts, 521 were excluded and 18 were left for further screening. Six were abstracts with no full text available.^{32–37} Three were not written in English.^{38–40} Finally, all 9 RCTs with full text were eligible and included.^{14,16,36,41–46} Two were included in qualitative synthesis,^{14,47} and the left 7 in quantitative synthesis, as shown in the flow diagram.

Study Characteristics

Basic information of included studies were listed in Table 1. A total of 453 patients were included, of whom 227 received steroid injection, while 226 received physiotherapy. Patients in 1 study received steroid injection for 3 times weekly.⁴⁷ In another study, patients received no more than 3 injections at weekly interval.¹⁵ Patients in the rest 7 studies received only 1 steroid injection.

Risk of Bias

Given the nature of interventions, all patients and clinicians were not blindly to treatments. Four studies did not mention the method of concealment.^{14,44,47,48} Two studies, in which the data at follow-up was not suitable for meta-analysis, did not compare the baseline data between 2 intervention groups.^{14,47} Intention-to-treat method was employed in only 2 studies.^{15,49} The included studies satisfied 3 to 8 criteria of 10 items in the checklist (Table 2).

QUANTITATIVE SYNTHESIS

Primary Outcome

Compared with patients who received steroid injection, physiotherapy provided equally functional improvement at 6 to 7 weeks (4 studies, SMD 0.32; 95% CI -0.32 – 0.96 ; $P=0.32$) with significant heterogeneity ($I^2=82\%$, $P=0.0009$), 12 to 16 weeks (4 studies, SMD 0.11; 95% CI -0.28 – 0.49 ; $P=0.60$) with marginal heterogeneity without significance ($I^2=50\%$, $P=0.11$), and 24 to 26 weeks (3 studies, SMD 0.28; 95% CI -0.01 – 0.58 ; $P=0.06$) without heterogeneity ($I^2=0\%$, $P=0.72$) (Figure 1). Subsequently, we performed sensitivity analysis to detect the origin of heterogeneity ($I^2=82\%$) at 6 to 7 weeks. The study conducted by Maryam et al⁴³ showed results that were completely out of range of the others and probably contributed to the heterogeneity. After excluding this study, the pooled result was in favor of steroid injection (SMD 0.66; 95% CI 0.30–1.01) with no significant heterogeneity ($I^2=28\%$, $P=0.25$).

TABLE 1. Basic Characteristics of Included Studies

Study	Number of Patients Included		Intervention Protocol	Physiotherapy	Cointerventions	Outcome Measures	Summary of Findings
	(Steroid/Physiotherapy)	Steroid Injection					
Maryam 2012	27/31	Triamcinolone acetamide 60 mg and 3 cc lidocaine in shoulder joint + triamcinolone acetamide 20 mg and 1.5 cc lidocaine in subacromial bursa. Injection technique: palpation guidance.	Transcutaneous electrical nerve stimulation, active range of motion exercises, and ice application in 10 sessions.	Shoulder exercise program and acetaminophen	SPADI; Active ROM (Hand behind back); Passive ROM (flexion, abduction, and external rotation); At 6 and 24 weeks after interventions.	Steroid injection was effective for patients with adhesive capsulitis while physiotherapy was of limited effect.	
Calis 2006	26/22	Intraarticular injection of 40 mg triamcinolone acetamide. Injection technique: palpation guidance.	Hot pack for 20 minutes, ultrasonic therapy at 1.5 W/cm ² for 5 minutes, transcutaneous electrical nerve stimulation for 20 minutes, and stretching exercises. Daily for 10 days	Stretching and Codman exercises and paracetamol drug	Constant score; Pain VAS; Passive ROM (external rotation and abduction); at 15 days and 3 months after interventions.	Both interventions were effective for adhesive capsulitis. Physiotherapy was more beneficial than steroid injection.	
Ryans 2005	19/20	Triamcinolone 20 mg (1 mL) and normal saline 2 mL equally injected into intraarticular and subacromial space. Injection technique: palpation guidance.	Proprioceptive neuromuscular facilitation, Maitland mobilizations, and interferential modality, and active exercise therapy, 8 sessions for 4 weeks.	Home exercise program and paracetamol tablets	SDQ (shoulder disability questionnaire); Pain VAS; Passive external rotation; at 6 and 16 weeks after interventions.	Steroid injection was effective in improving disability, and physiotherapy was effective in improving ROM in external rotation 6 weeks after treatment.	
Carette 2003	23/26	Intraarticular injection of 40 mg triamcinolone hexacetamide. Injection technique: fluoroscopic guidance.	Transcutaneous electrical nerve stimulation, ultrasound, mobilization, active and auto-assisted range of motion exercises, isometric strengthening exercises, and ice application.	Ten-minute exercise program at home twice daily for 3 months + acetaminophen tablets	SPADI; SF-36 (The Short Form); Active ROM (hand behind back); Passive ROM (flexion, abduction, and external rotation); at 6 weeks, 3, 6 and 12 months after interventions.	A single intraarticular steroid injection was effective in improving shoulder pain and disability in patients with adhesive capsulitis. Physiotherapy was of limited efficacy.	
Arslan 2001	10/10	Intraarticular injection of 40 mg methylprednisolone acetate and 1 mL 2% lidocaine. Injection technique: palpation guidance.	Hot pack for 20 minutes, ultrasonic therapy at 3.5 W/cm ² for 5 minutes, passive glenohumeral stretching exercise, Codman exercise, and wall climbing + acemetazine 120 mg/day.	Home exercise	Pain VAS; Active and passive ROM (flexion, abduction, internal rotation, and external rotation); at 2 and 12 weeks after interventions.	Intraarticular injection was equally effective for patients with adhesive capsulitis compared with physiotherapy.	

Number of Patients Included Intervention Protocol

Study	(Steroid/ Physiotherapy)	Steroid Injection	Physiotherapy	Cointerventions	Outcome Measures	Summary of Findings
Van der Windt 1998	49/54	Intraarticular injections of 40 mg triamcinolone acetamide no more than 3 times during the 6 weeks. Injection technique: not mentioned.	Twelve sessions of 30 minutes physiotherapy including passive joint mobilization and exercise treatment. Ice, hot packs, or electrotherapy during the 6 weeks.	Analgesic drug	Pain during day and night; Improvement in rating of shoulder disability; at 3, 7, 13, 26, and 52 weeks after interventions. ROM (external rotation and abduction); at 3, 7, and 26 weeks after interventions.	Steroid injections were superior to physiotherapy for this condition and provided significantly faster pain relief and more symptom remission.
Dacre 1989	22/20	Triamcinolone 20 mg and 1 mL 2% lignocaine into shoulder joint. Injection technique: not mentioned.	Mobilization for 4–6 weeks	No	Pain VAS (day, night, and during active and passive movement); Passive ROM (abduction, external rotation, and hand behind back); at 6 and 26 weeks after interventions.	Steroid injection was as effective as physiotherapy for adhesive capsulitis for 26 weeks.
Bulgen 1984	11/11 + 12	Methyl-prednisolone acetate 20 mg and 2% lignocaine 0.5 mL into subacromial bursa and similar amount into shoulder joint 1 time/week for 3 weeks. Injection technique: not mentioned.	Eleven received Maitland mobilization and 12 received icepacks and proprioceptive neuromuscular facilitation. Three times/week for 6 weeks.	Pendular exercise 2–3 minutes/hour. Diazepam 5 mg and nonsalicylate analgesics at night.	Component analysis: C = (0.536 × total flexion) + (0.201 × glenohumeral flexion) + (0.263 × glenohumeral abduction) + (0.079 × external rotation) + (0.369 × total rotation) – 137.7; At 1, 2, 3, 4, 5, and 6 weeks, and 1, 2, 3, 4, 5, and 6 months after interventions.	Compared with physiotherapy, steroid injection benefited pain and range of motion in early stages of condition but did not have long-term advantage.
Lee 1973	(20 + 20)/20	Twenty received intraarticular injection of 25 mg hydrocortisone acetate; 20 received injection of 25 mg hydrocortisone acetate into the synovial sheath of biceps tendon. Injection technique: not mentioned.	Infrared irradiation for 6 weeks	Exercise program + analgesics	Active abduction, lateral rotation, and medial rotation. Passive abduction.	All 3 groups showed improvement with no significant difference between them.

TABLE 2. Quality Assessment of Included Studies Using the Physiotherapy Evidence Database Scale

	Random Allocation	Concealed Allocation	Baseline Comparability	Blind Subject	Blind Clinician	Blind Assessor	Adequate Follow-Up	Intention-to-Treat Method	Between-Group Analysis	Point Estimates and Variability	Total Score
Maryam 2012	1	1	1	0	0	1	1	0	1	1	7
Calis 2006	1	1	1	0	0	1	1	0	1	1	7
Ryans 2005	1	1	1	0	0	1	1	0	1	1	7
Carette 2003	1	1	1	0	0	1	1	1	1	1	8
Arsilan 2001	1	0	1	0	0	0	1	0	1	1	5
Van der Windt 1998	1	1	1	0	0	1	1	1	1	1	8
Dacre 1989	1	0	1	0	0	1	1	0	1	1	6
Bulgen 1984	1	0	0	0	0	0	1	0	0	0	3
Lee 1973	1	0	0	0	0	0	1	0	0	0	3

Secondary Outcomes

Compared with patients who received steroid injection, patients who received physiotherapy gained significantly less passive external rotation at 24 to 26 weeks (3 studies, SMD 0.42; 95% CI 0.11–0.72; $P=0.007$) with no heterogeneity ($I^2=0%$, $P=0.92$) but not at 6 to 7 weeks (4 studies, SMD 0.63; 95% CI 0.36–0.89; $P=0.32$) with significant heterogeneity ($I^2=82%$, $P=0.0009$) or 12 to 16 weeks (3 studies, SMD -0.07 ; 95% CI -0.79 – 0.65 ; $P=0.85$) with significant heterogeneity ($I^2=75%$, $P=0.02$) (Figure 2).

Compared with steroid injection, physiotherapy had equally effect in pain relief at 6 to 7 weeks (5 studies, SMD 0.32; 95% CI -0.10 – 0.75 ; $P=0.14$) with significant heterogeneity ($I^2=66%$, $P=0.02$), 12 to 16 weeks (4 studies, SMD 0.13; 95% CI -0.28 – 0.53 ; $P=0.54$) with no significant heterogeneity ($I^2=44%$, $P=0.15$), and 24 to 26 weeks (4 studies, SMD -0.10 ; 95% CI -0.70 – 0.50 ; $P=0.75$) with significant heterogeneity ($I^2=76%$, $P=0.006$) (Figure 3).

Only 1 study reported complications.¹⁵ Thirty out of 57 patients in steroid injection group and 32 out of 57 patients in physiotherapy group reported adverse events, mainly pain after treatment ($P>0.05$), indicating similar safety of both interventions for this condition.

Grade of Evidence

For the pooled results, Grading of Recommendations Assessment, Development, and Evaluation Working Group grades of evidence were low for functional improvement, improvement in passive external rotation, and pain relief at 6 to 7 weeks, moderate for functional improvement and pain relief, low for improvement in passive external rotation at 12 to 16 weeks, and moderate for functional improvement and improvement in passive external rotation, low for pain relief at 24 to 26 weeks.

Qualitative Synthesis

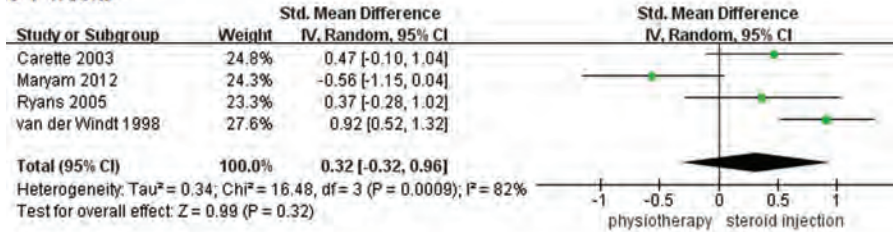
Bulgen et al⁴⁷ used a component analysis to evaluate the degree of improvement of patients in both steroid injection and physiotherapy group. They found that patients who received 3 steroid injections had faster improvement in the first 6 weeks ($P=0.02$). At 6 months after the 1st injection, both steroid injection and physiotherapy group had similar functional improvement.⁴⁷ Contrary to these findings, Lee et al¹⁴ found that both interventions were equally effective for ACS for 6 weeks.

DISCUSSION

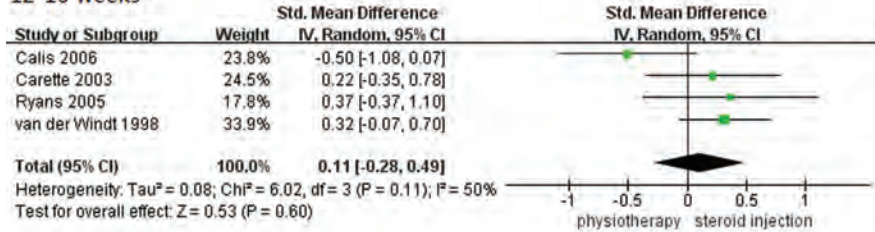
This is a further systematic review and meta-analysis of 9 RCTs to evaluate the efficacy and safety of steroid injection compared with physiotherapy for patients with ACS. The present results showed that both interventions had similar effect in improving glenohumeral function, increasing passive external rotation, and decreasing pain for ACS. Steroid injection was as safe as physiotherapy.

A previous meta-analysis on the same topic found that, though both interventions were effective for ACS compared with placebo, isolated steroid injection was superior to physiotherapy in improving shoulder function from 6 to 7 weeks to 26 weeks postintervention, recovering passive external rotation at 26 weeks but not at 6 to 7 or 12 to 16 weeks, and was as effective as physiotherapy in pain relief at 6 to 7 weeks and last to 26 weeks.² However, no primary or secondary outcomes were

6-7 weeks



12-16 weeks



24-26 weeks

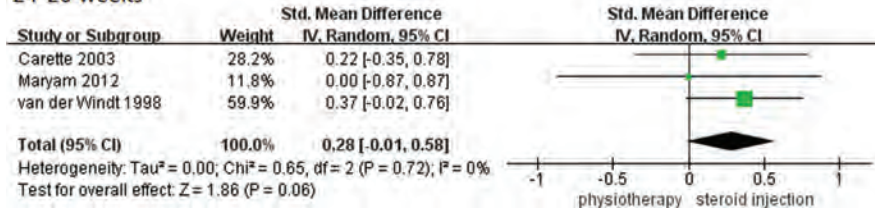
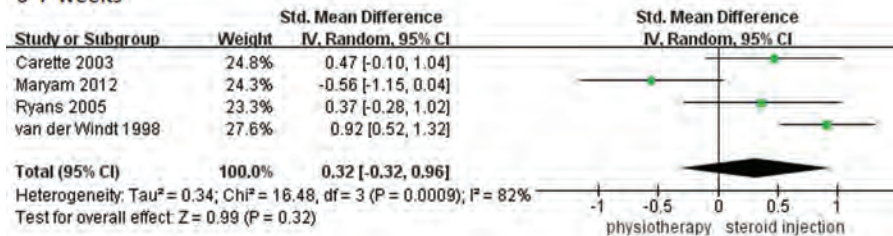
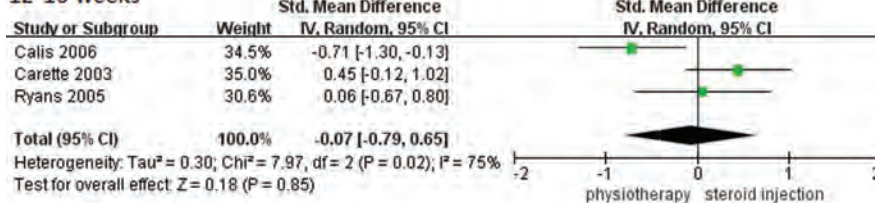


FIGURE 1. Functional improvement.

6-7 weeks



12-16 weeks



24-26 weeks

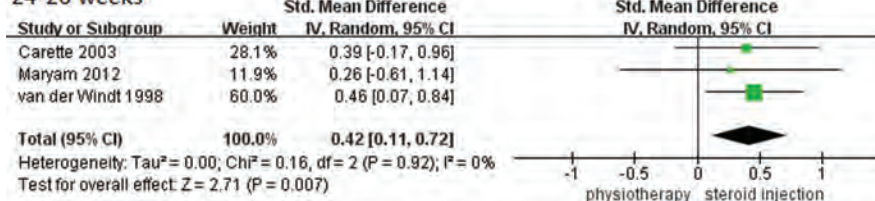


FIGURE 2. Improvement in passive external rotation.

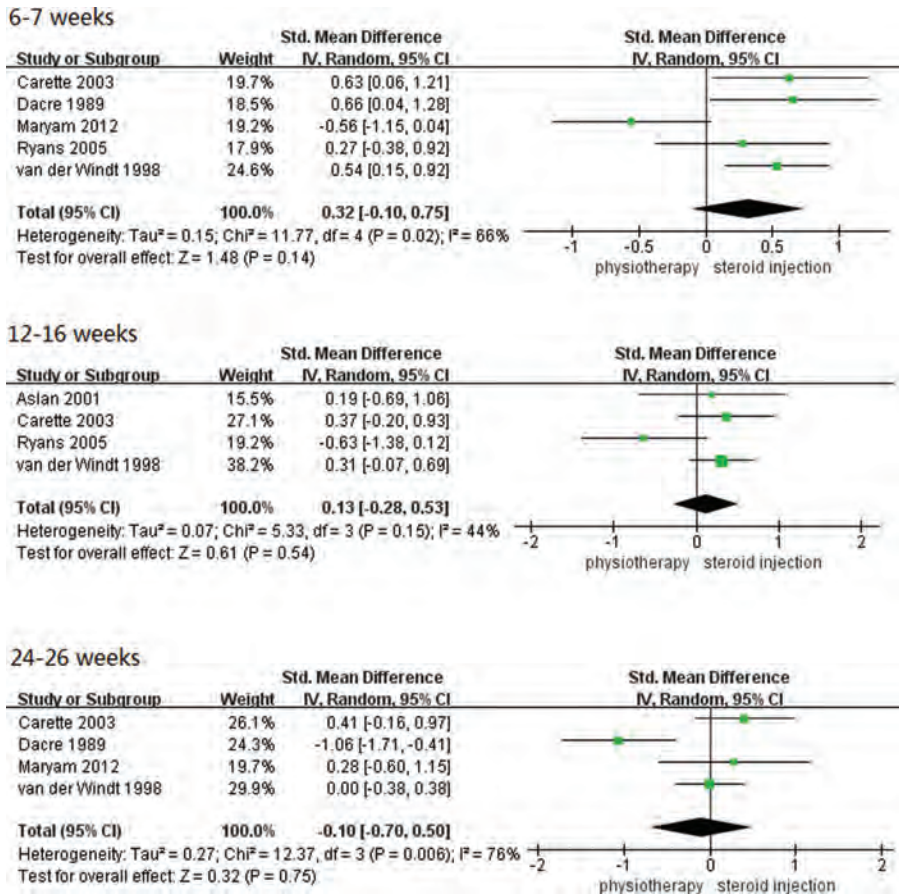


FIGURE 3. Pain relief.

entitled to either index. As ACS was a condition of functional defect caused by shoulder pain and range of motion limitation, we chose improvement in shoulder function as primary outcome, and improvement in passive external rotation, and pain relief as secondary outcomes. Besides, we also studied the difference of adverse effect of 2 interventions, in an attempt to figure out the safety of steroid injection and physiotherapy.

Contrary to the results of the former meta-analysis, after pooling all available studies into comparison, we found that both interventions had similar effect in improving shoulder disability at 6 to 7 weeks and last to 24 to 26 weeks post-intervention. Significant heterogeneity was observed in the comparison at 6 to 7 weeks and the origin of heterogeneity was caused by the study conducted by Maryam et al.⁴³ In this study, 45 out of 58 patients included had diabetic mellitus, while only 4 out of 197 patients included the other 3 studies in this comparison had diabetic mellitus.^{15,49,50} As ACS can be more serious and refractory when concomitant with diabetic mellitus, and was often more resistant to conventional treatment,⁵¹⁻⁵³ it might be this difference in population accounting for the heterogeneity. Besides, the number of patients recruited in this study did not reach the prespecified sample size, which could also exert an influence on outcomes, though might not be remarkable. These results of primary outcome provided significance for patients who had contradictions for steroid injection, such as diabetic mellitus. Since steroid injection could influence the level of blood sugar, current evidence suggested that physiotherapy could be an alternative.

Contradictory results were obtained regarding the improvement in passive external rotation. Although both interventions had equally effect at 6 to 7 and 12 to 16 weeks, patients who received steroid injection had significantly more improvement in passive external rotation at 24 to 26 weeks. It should be noted that heterogeneity was significant at this time point, hence downgrading the level of evidence to low, which indicated that the current estimate of effect was not robust and was probably changed by future trials. Of the 3 included RCTs, Calis et al¹⁶ arranged physiotherapy of 10 consecutive days for patients with ACS, while other 2 studies had a frequency of no more than 3 times per week.^{49,50} This disconformity might explain the reason why the result of Calis et al was beyond the range of other 2 studies, which might indicate that physiotherapy of consecutive days could have different treatment effect compared with physiotherapy with several sessions per week for several weeks.

In line with the former findings, we also found that both interventions provided similar pain relief for patients with ACS. However, components of physiotherapy did not contain modalities for continuous pain relief. The current result was possible caused by the use of nonsteroidal antiinflammatory drugs (NSAIDs) as cointervention or for physiotherapy group, since it has been proven that NSAIDs could provide similar effect to steroid injection for ACS in pain relief.⁵⁴ The dose of NSAIDs was not clearly stated in the included RCTs, which could contribute to the significant heterogeneity in the result at 6 to 7 weeks.

Compared with the pooled results which showed equally effect between 2 interventions for functional improvement, and the result of Lee et al, Bulgen et al⁴⁷ found that steroid injection provided significantly more functional improvement at 6 weeks and was similar at 26 weeks, compared with physiotherapy. The contradictory findings might be in relation to the frequency of steroid injection. Patients in the study conducted by Bulgen et al⁴⁷ received 3 injections at weekly interval, while only a single injection was performed in the study of Lee et al¹⁴ and all studies pooled for the comparison of functional improvement at 6 to 7 weeks.^{15,17,49,50} The inconsistency indicated that more injections was probably related to faster functional improvement compared with physiotherapy.

This systematic review provides a distinct evidence that, steroid injection might be the first choice for ACS, as 1 injection was equal to sessions of physiotherapy from 6–7 to 24–26 weeks postintervention, according to the pooled results. However, caution must be taken when interpreting outcomes. According to the pathological progress, this condition can be divided into the following three stages, freezing stage with increasing pain, frozen stage with decreasing pain, and thawing stage.⁵⁵ In the current analysis, patients with different stages of condition were included for comparison, undermining the strength of outcomes. Limited information about steroid injection technique precluded us from making subgroup analysis. Besides, a cost-effective analysis was not launched due to lack of details in articles. Compared with a single steroid injection in most studies, physiotherapy consisted of several sessions with different modalities, adding financial burden to patients and decreasing compliance. Third, components of physiotherapy were various, and detailed prescription of NSAIDs were not detailed among studies. It is the variety that precludes us from performing subgroup analysis to refine results. Finally, some data input for calculation was an estimate one, and detailed exercise programs were not always reported, which might have exert an impact on the pooled outcomes.

In summary, both steroid injection and physiotherapy are equally effective for patients with ACS. One steroid injection might be the 1st choice for ACS. Results should be interpreted with caution due to the heterogeneity among the studies.

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