

## Review

# Comparison of intra-articular and subacromial corticosteroid injection in frozen shoulder: A meta-analysis of randomized controlled trials

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## ARTICLE INFO

## Keywords:

Frozen shoulder  
Intra-articular  
Subacromial  
Pain  
Meta-analysis

## ABSTRACT

**Objective:** To compare the efficacy and safety of intra-articular injection and subacromial injection in the treatment of primary frozen shoulder (FS).

**Methods:** We conducted a systematic literature search for all relevant studies on Medline, Embase, Web of Science and Cochrane Central, up to April 2019 with no restrictions to language of publication. The primary outcome was visual analog scale (VAS) score, range of motion (ROM), and Constant shoulder score. The secondary outcome was injection-related adverse effects. Two authors independently assessed the risk of bias using the Cochrane risk-of-bias tool. Data were conducted using STATA version 12.0 (STATA corp., College Station, TX).

**Results:** Seven randomized controlled trials (RCTs) involving 421 participants were finally included in the present meta-analysis. Our study indicated that intra-articular injection was associated with a statistically significant reduction in the outcome of pain score compared with the subacromial injection. No significant differences were identified between two groups regarding the ROM or post-injection adverse events.

**Conclusion:** Intra-articular injection of corticosteroid was associated with an improved outcomes for pain relief compared to subacromial injection. There was no significant difference regarding the shoulder function or adverse effects.

## 1. Introduction

Frozen shoulder (FS), also known as “adhesive capsulitis” is a common shoulder disorder, which has a distinct pattern of symptoms resulting in severe shoulder pain, loss of shoulder function and eventually stiffness [1,2]. It was reported that approximately 2.4 of 1000 general population suffered from FS, especially occurred in patients aging 50 years old [3]. The pathogenesis of FS remains controversial. It is believed that FS is the concept of a musculotendinous or tenosynovitis-induced inflammation giving rise to the formation of adhesions and capsular thickening [4,5]. Recent studies indicated that 40% of patients have persistent mild pain and functional disorder and that 11% of patients have permanent functional disability of the shoulder joint [6]. The ultimate goal of treatment is to relieve pain and improve joint function.

Several methods have been used for treating FS, including physical exercises, medicine treatment, suprascapular nerve block, and arthroscopic release [7–9]. Local steroid injection is considered gold standard in primary FS, which enables the early acceleration of functional

recovery and reduces pain by inhibiting synovial inflammation [10,11]. Intra-articular injection is popular, which can be performed without the guidance of ultrasound. However, it has reported the accuracy of blind intra-articular injection reached only about 10–42% [12]. Besides, an inappropriate injection into the soft tissue may be associated with severe complications and nullify the therapeutic effects of the corticosteroid. Subacromial injection is also an alternative approach to treat rotator cuff disorders and is considered to be relatively straightforward with a higher injection accuracy rate.

However, no reliable evidence regarding the optimal approach of corticosteroid injection has been proposed. Therefore, we perform the meta-analysis from randomized controlled trials (RCTs) to compare the efficacy and safety of two injection methods: intra-articular injection and subacromial injection in the treatment of primary FS. The hypothesis of the study was that both two methods has the comparable therapeutic effect and achieves the similar joint function.

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<https://doi.org/10.1016/j.ijisu.2019.06.008>

Received 7 April 2019; Received in revised form 10 June 2019; Accepted 12 June 2019

Available online 27 June 2019

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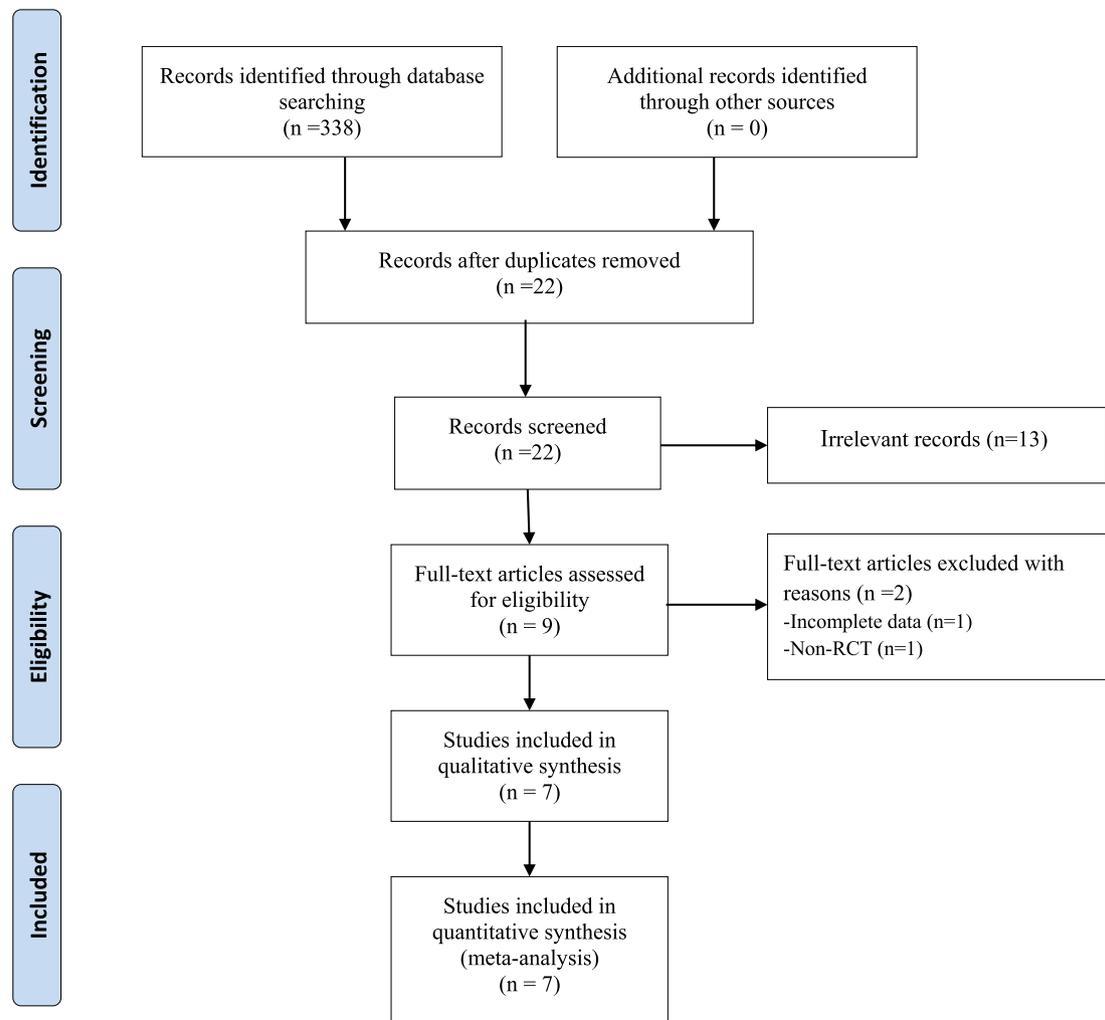


Fig. 1. Flow diagram for study selection.

## 2. Materials and methods

The work has been reported in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines.

### 2.1. Search strategy

We conducted a systematic literature search on Medline, Embase, Web of Science and Cochrane Central, up to April 2019 with no restrictions to language of publication. A retrieval strategy was defined such that the terms “frozen shoulder or adhesive capsulitis”, “intra-articular” and “subacromial” were searched with maximum sensitivity. Furthermore, the reference lists from published original articles and relevant reviews were also assessed to identify more relevant studies.

### 2.2. Inclusion and exclusion criteria

Included studies were considered eligible if they met the following population, intervention, comparison, outcome and study design (PICOS) criteria: Population: Patients (older than 18 years) with FS; Intervention: intra-articular injection of corticosteroid; Comparator: subacromial injection of corticosteroid; Outcomes: The primary outcome was visual analog scale (VAS) score, range of motion (ROM) and Constant shoulder score. The secondary outcome was injection-related

adverse effects; Study design: RCTs. Studies were excluded if any of the following existed: non-RCTs, undefined sample and control sources, nontherapeutic clinical studies, nonoriginal studies, non-full-text reports, and undefined grouping.

### 2.3. Data extraction

Standard data extraction was performed to collect the following data from included trials: author's name, publication year, study design, sample size, intervention, control group, outcomes, and follow-up. Relevant data were extracted independently by two authors after all eligible studies were identified. In studies in which data were incomplete or unclear, attempts were made to contact investigators for clarification. All data were extracted; any discrepancy was cross-checked and resolved by a third author to reach a final consensus.

### 2.4. Risk of bias assessment and evidence level

Two authors independently assessed the risk of bias using the Cochrane risk-of-bias tool. The risk of bias in RCTs was assessed across the following seven domains: (1) random-sequence generation (selection bias); (2) allocation concealment (selection bias); (3) blinding of participants and personnel (performance bias); (4) blinding of outcome assessment (detection bias); (5) incomplete outcome data (attrition bias); (6) selective reporting (reporting bias); (7) other bias. Disagreements between two researchers were resolved by discussion.

**Table 1**  
Study characteristics and patient demographic details.

Study	Year	Study type	Sample size		Age	Gender (Female)	Intervention of IA		Intervention of SA	Follow up
			IA	SA						
Oh et al.	2011	RCT	37	34	55.7	58.3	20	19	IA: 1 mL triamcinolone (40 mg), 4 mL of 2% lidocaine, and 4 mL of normal saline SA: 1 mL triamcinolone (40 mg), 4 mL of 2% lidocaine, and 4 mL of normal saline	3 months
Shin et al.	2013	RCT	42	41	55.1	53.9	26	27	IA: 4 mL of 2% lidocaine and 40 mg of triamcinolone (1 mL) SA: 4 mL of 2% lidocaine and 40 mg of triamcinolone (1 mL)	1.5 months
Kim et al.	2015	RCT	23	23	58.8	52.1	11	11	IA: 1 mL of 40 mg triamcinolone acetamide mixed with 4 mL of 1% lidocaine SA: 1 mL of 40 mg triamcinolone acetamide mixed with 4 mL of 1% lidocaine	3 months
Cho et al.	2016	RCT	36	37	59.1	56.0	26	21	IA: 1 mL of 40 mg/mL triamcinolone and 2 mL 2% lidocaine SA: 1 mL of 40 mg/mL triamcinolone and 2 mL 2% lidocaine	3 months
Yoon et al.	2016	RCT	29	29	53	57	18	23	IA: 1 mL of 40 mg/mL triamcinolone (40 mg), 4 mL of 2% lidocaine, and 5 mL of normal saline SA: 1 mL of 40 mg/mL triamcinolone (40 mg), 4 mL of 2% lidocaine, and 5 mL of normal saline	1.5 months
Khallaf et al.	2018	RCT	20	20	49.6	45.1	12	12	IA: methylprednisolone acetate (40 mg) and 1 mL 2% lidocaine SA: methylprednisolone acetate (40 mg) and 1 mL 2% lidocaine	3 weeks
Sun et al.	2018	RCT	24	26	55.1	54.2	14	16	IA: 1 mL of 40 mg/mL triamcinolone and 2 mL 2% lidocaine SA: 1 mL of 40 mg/mL triamcinolone and 2 mL 2% lidocaine	3 months

RCT: randomized controlled trial, IA: intra-articular, SA: sub-acromial.

**Table 2**  
Risk of bias summary.

	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
Cho, 2016	+	-	?	+	+	+	+
Khallaf, 2018	+	-	?	+	?	?	?
Kim, 2015	+	+	+	?	+	+	+
Oh, 2011	+	+	+	?	+	+	+
Shin, 2013	+	?	+	?	+	+	+
sun, 2018	+	+	?	?	+	+	+
Yoon, 2016	+	?	-	?	+	+	+

Recommendations Assessment, Development and Evaluation (GRADE) system was used to grading the evidence level.

2.5. Statistical analysis

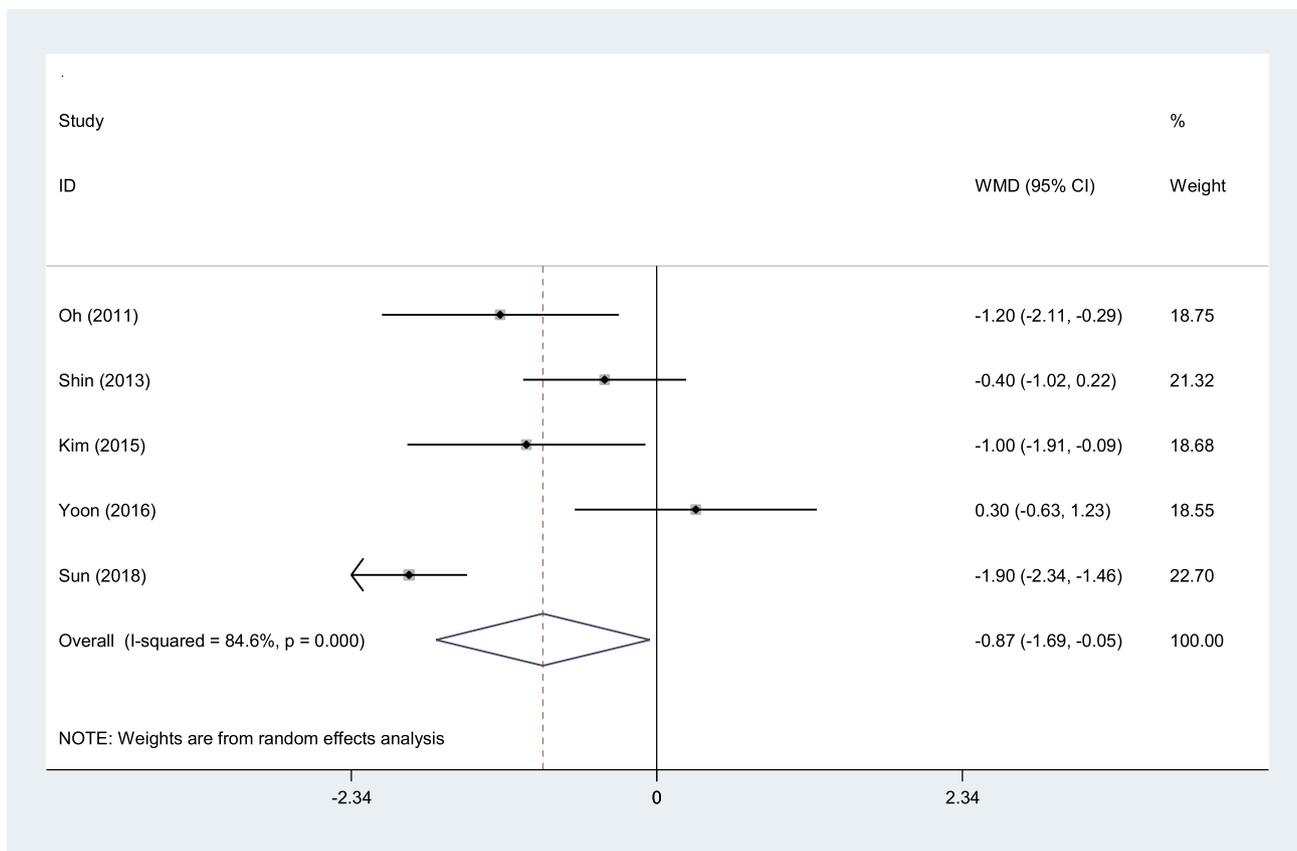
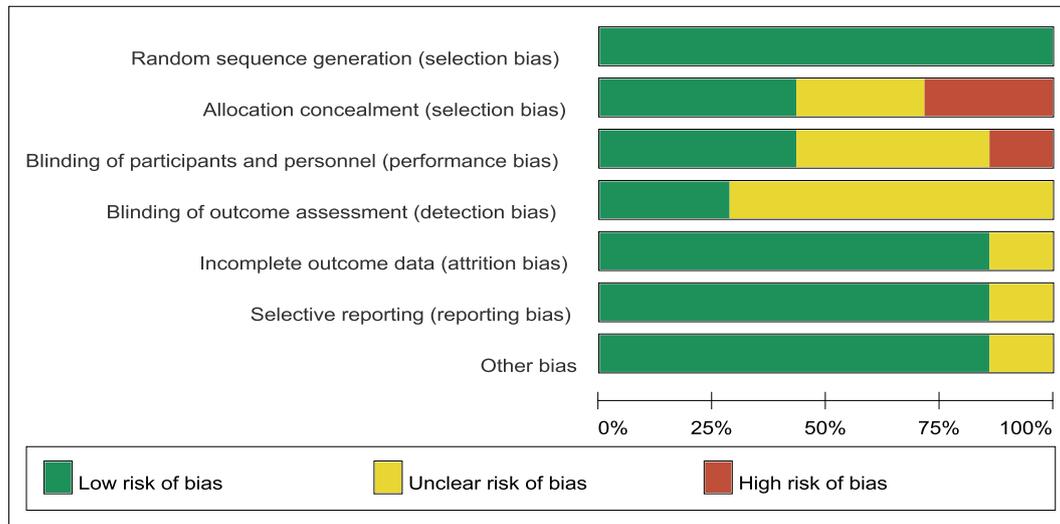
For continuous outcome data, weighted mean difference (WMD) was calculated. For dichotomous outcomes, risk difference (RD) and confidence intervals (CIs) was calculated to estimate the difference between groups.  $I^2$  was used to assess the heterogeneity among trials. For both continuous and dichotomous outcomes, a random-effects model was used when heterogeneity was high ( $I^2 > 50\%$ ) and a fixed effects model when heterogeneity was low ( $I^2 < 50\%$ ). Most of the statistical analyses were conducted using STATA version 12.0 (STATA corp., College Station, TX). Publication bias were conducted using Review Manager 5.3 (The Cochrane Collaboration, Oxford, UK).

3. Results

3.1. Study selection

Our search of the database using keywords yielded 338 studies; 316 studies were removed because of duplication. After careful review of 22

**Table 3**  
Risk of bias graph.



**Fig. 2.** Forest plot diagram of pain score at 1 month.

papers, 15 of them were excluded for a variety of reasons, including irrelevant content, incomplete data and non-RCT. Finally, 7 studies [13–19] were included for analysis. Manual search of relevant reference did not identify any additional studies. A flow diagram depicting the selection process of eligible studies was shown in Fig. 1.

### 3.2. Study characteristics

The characteristics of all the included studies were presented in Table 1. All included studies were single-centered RCTs, which were published between 2011 and 2018. In total, 421 patients with FS for

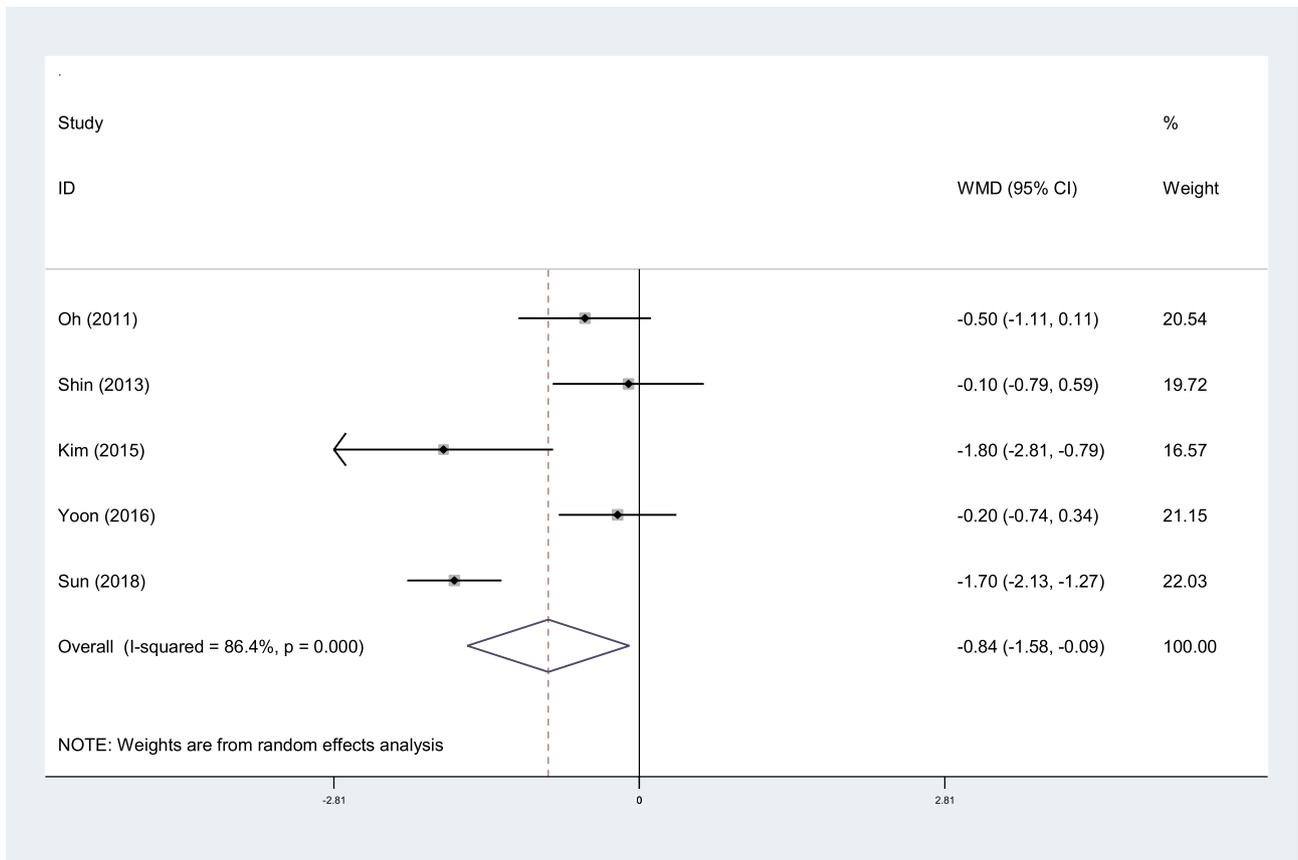


Fig. 3. Forest plot diagram of pain score at 2 month.

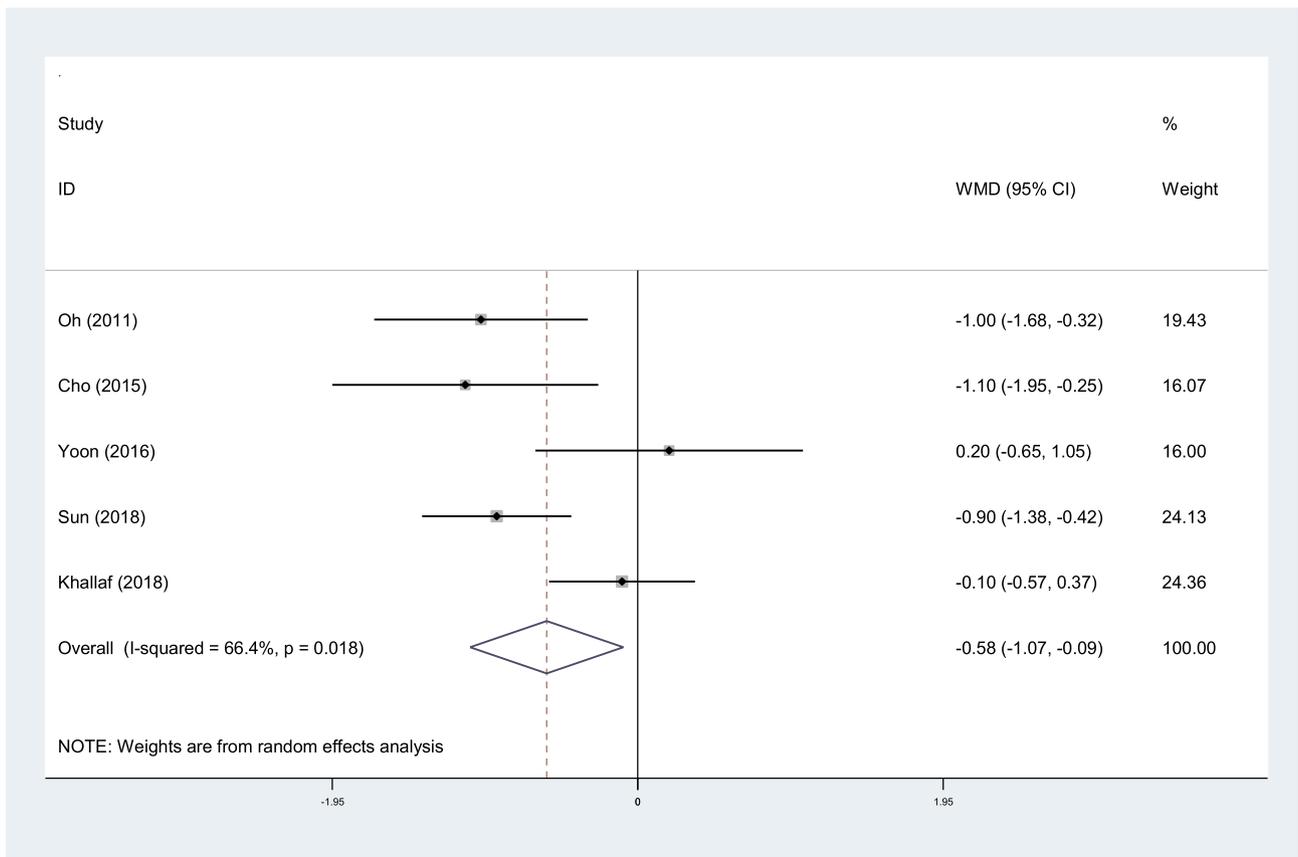


Fig. 4. Forest plot diagram of pain score at 3 month.

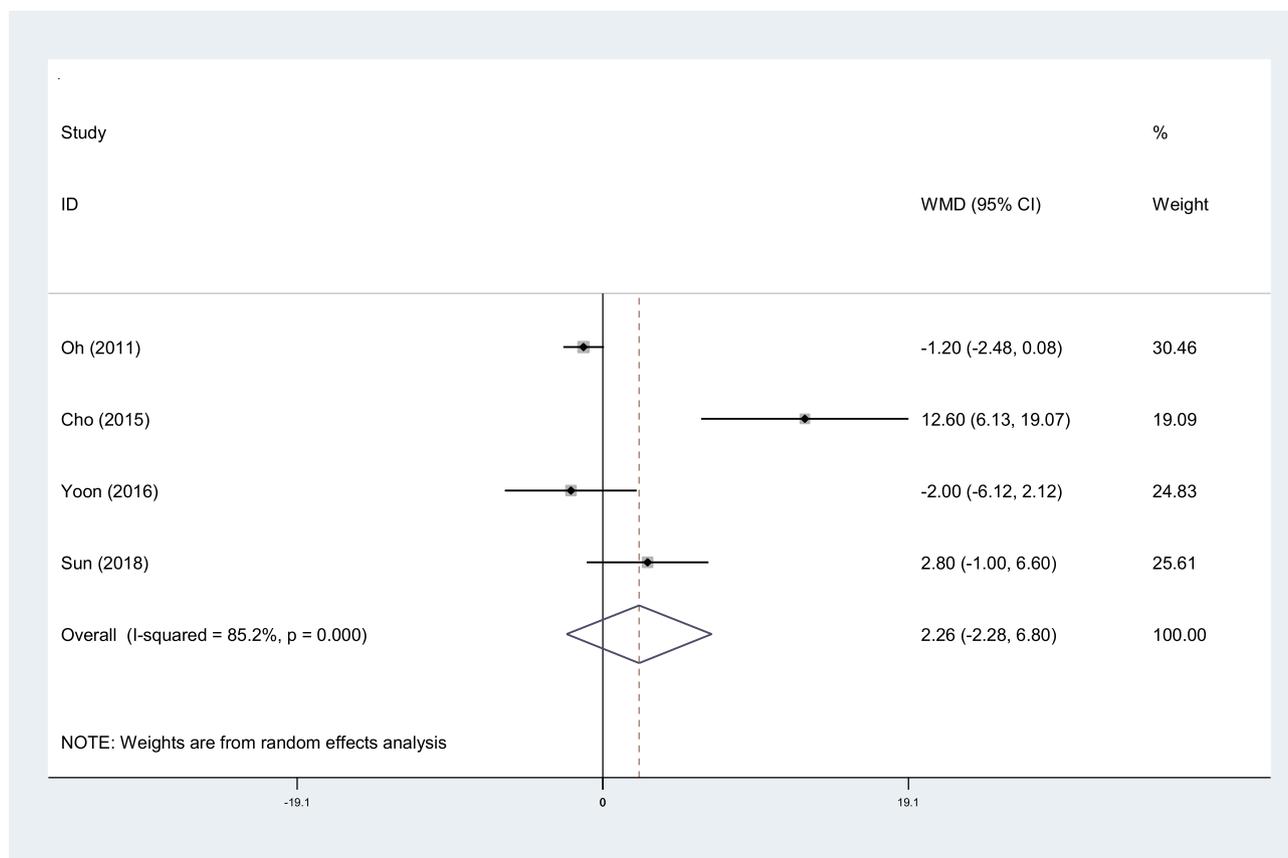


Fig. 5. Forest plot diagram of ROM at 1 month.

corticosteroid injection were included in the meta-analysis. The sample sizes ranged from 40 to 83. The duration of follow up ranged from 1.5 to 3 months.

### 3.3. Risk of bias

A summary of quality assessment was provided in Table 2. Methodological quality of 7 RCTs were evaluated with the Cochrane Handbook for Systematic Reviews of Interventions. The randomization was achieved by a random number table in 3 RCTs, centralized randomization system in 4 RCTs. Only 3 RCTs described the concealment of allocation. Only 3 RCTs performed the double-blind. All RCTs mentioned the information about withdrawal and dropout. Each risk of the bias item was expressed in terms of the percentage across all the included studies, which indicated the proportion of risk levels for each item bias (Table 3).

### 3.4. Meta-analysis results

#### 3.4.1. Pain score at 1 month

5 articles showed the outcome of VAS at 1 month after treatment. There was significant heterogeneity among studies ( $I^2 = 84.6%$ ,  $p < 0.001$ ) and a random effect model was used. The pooled data showed that intra-articular injection demonstrated significantly lower pain score compared with the subacromial injection at 1 month (WMD: -0.873; 95% CI: -1.693 to -0.052;  $p = 0.037$ , Fig. 2).

#### 3.4.2. Pain score at 2 month

A total of 5 RCTs reported the outcome of VAS at 2 month after treatment. A random effect model was used ( $I^2 = 86.4%$ ,  $p < 0.001$ ). Our study indicated that intra-articular injection demonstrated significantly lower pain score compared with the subacromial injection at

2 month (WMD: -0.837; 95% CI: -1.582 to -0.092;  $p = 0.028$ , Fig. 3).

#### 3.4.3. Pain score at 3 month

VAS at 3 month was reported in 5 RCTs. There was significant heterogeneity ( $I^2 = 66.4%$ ,  $p = 0.018$ ) and a random effect model was used. Meta-analysis revealed a benefit of intra-articular injection compared to subacromial injection in pain relief at 3 month (WMD: -0.581; 95% CI: -1.069 to -0.093;  $p = 0.020$ , Fig. 4).

### 3.5. Range of motion (ROM) at 1 month

4 studies provided the outcome of ROM at 1 month after local injection. There was significant heterogeneity among studies ( $I^2 = 85.2%$ ,  $p < 0.001$ ) and a random effect model was used. The present meta-analysis showed that there was no significant difference between two groups regarding the ROM at 1 month (WMD: 2.261; 95% CI: -2.276 to 6.798;  $p = 0.329$ , Fig. 5).

### 3.6. ROM at 2 month

A total of 6 studies reported ROM at 2 month after treatment. A random effect model was used ( $I^2 = 83.4%$ ,  $p < 0.001$ ). No significant difference in terms of ROM at 2 month was identified (WMD: -0.680; 95% CI: -4.984 to 3.624;  $p = 0.757$ , Fig. 6).

### 3.7. Constant shoulder score

Three RCTs reported Constant shoulder score. A random effect model was used ( $I^2 = 97.5%$ ,  $p < 0.001$ ). The present meta-analysis indicated there was no significant difference in terms of Constant shoulder score at 1 month (WMD: 3.952; 95% CI: -1.071 to 8.974;  $p = 0.123$ , Fig. 7) or 2 month (WMD: 10.159; 95% CI: -3.717 to 24.035;

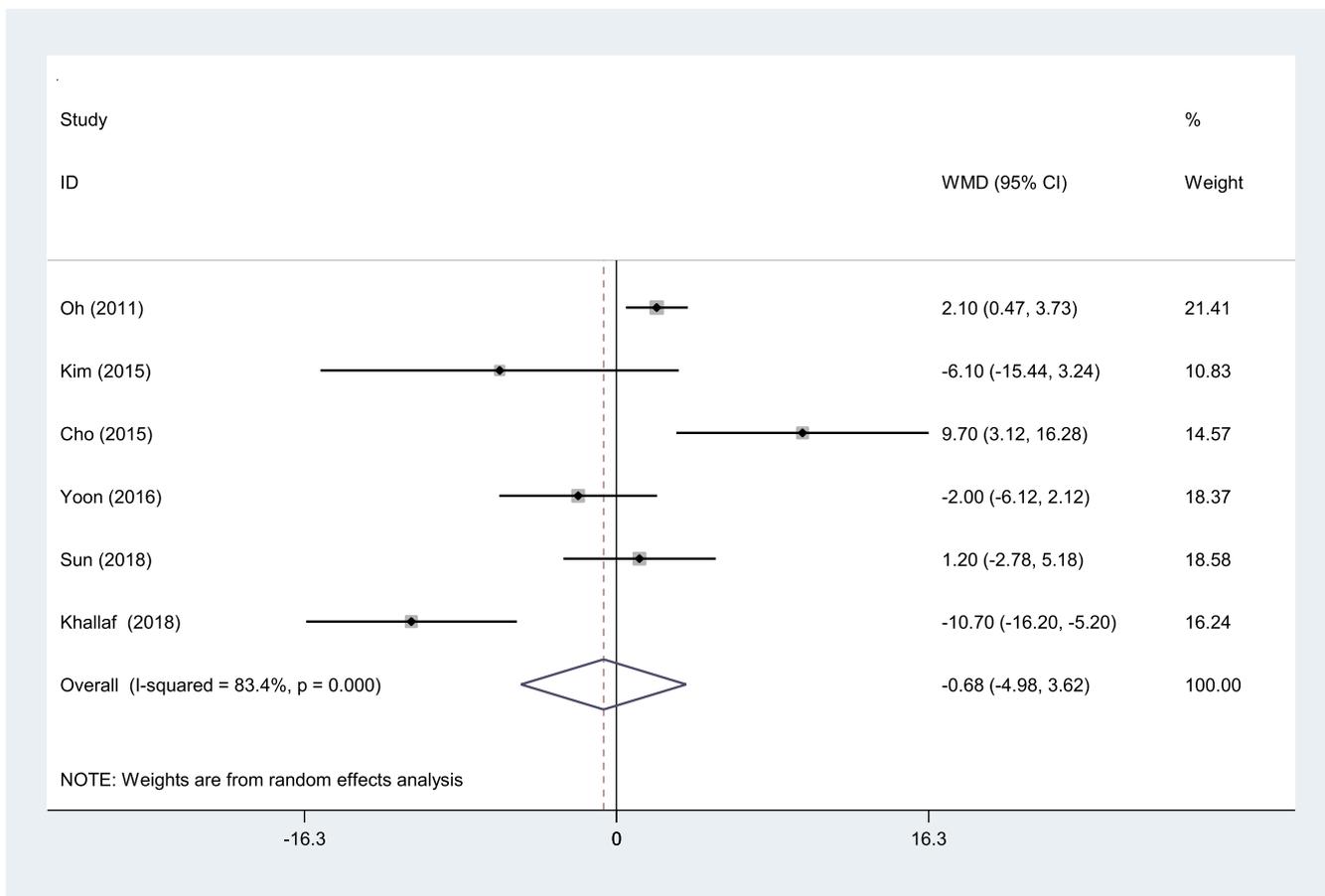


Fig. 6. Forest plot diagram of ROM at 2 month.

$p = 0.151$ , Fig. 7).

### 3.8. Adverse effects

Four RCTs showed the adverse effects, such as dizziness and infection after local corticosteroid injection. The present meta-analysis indicated that there was no significant difference regarding the risk of adverse effects (WMD: 0.009; 95% CI: -0.023 to 0.041;  $p = 0.585$ , Fig. 8).

### 3.9. Publication bias and subgroup analysis

A low risk of publication bias was identified for the ROM at 2 month (Table 4).

Subgroup analysis was performed based on the type of corticosteroid. Only Khallaf et al. used methylprednisolone, after exclusion, there was still huge heterogeneity among studies (Table 5).

### 3.10. Quality of the evidence and recommendation strengths

The evidence quality for each outcome was high to moderate. Therefore, we agreed that the overall evidence quality was moderate, which indicated that further research was likely to significantly alter confidence in the effect estimate and may change the estimate (Table 6).

## 4. Discussion

To the best of our knowledge, this is the first meta-analysis from recent published RCTs to compare the efficacy and safety of intra-articular injection and subacromial injection for patients with FS. The most important finding of the present meta-analysis was that intra-articular injection was associated with a significant reduction in VAS score, with a benefit lasting for at least 3 month. There was no significant difference between groups regarding the risk of adverse effects.

FS is a condition in which the shoulder is painful and loses motion because of inflammation. FS syndrome affects females slightly more than males [20]. Patients typically develop FS syndrome in the fifth and sixth decades of life. 12% of the patients develop the bilaterally FS. Previous studies reported that 40% of patients have persistent mild pain and limitation of activity and that 11% of them have permanent functional disability of the shoulder joint [21,22]. Arthroscopy biopsy material demonstrated that the chronic inflammation and proliferative fibrosis, as well as the presence of high vascularity results in the painful shoulder [23]. The essential goal for treatment was to relieve pain and improve shoulder joint function.

Many strategies have been used to reduce pain and to enable an early return to daily activities. Local inflammation plays an essential role for the pathogenesis of FS. Immune mechanisms may be also associated with the pathogenesis of FS syndrome. Local injection of steroid was first introduced since the 1950s and it has been viewed as a

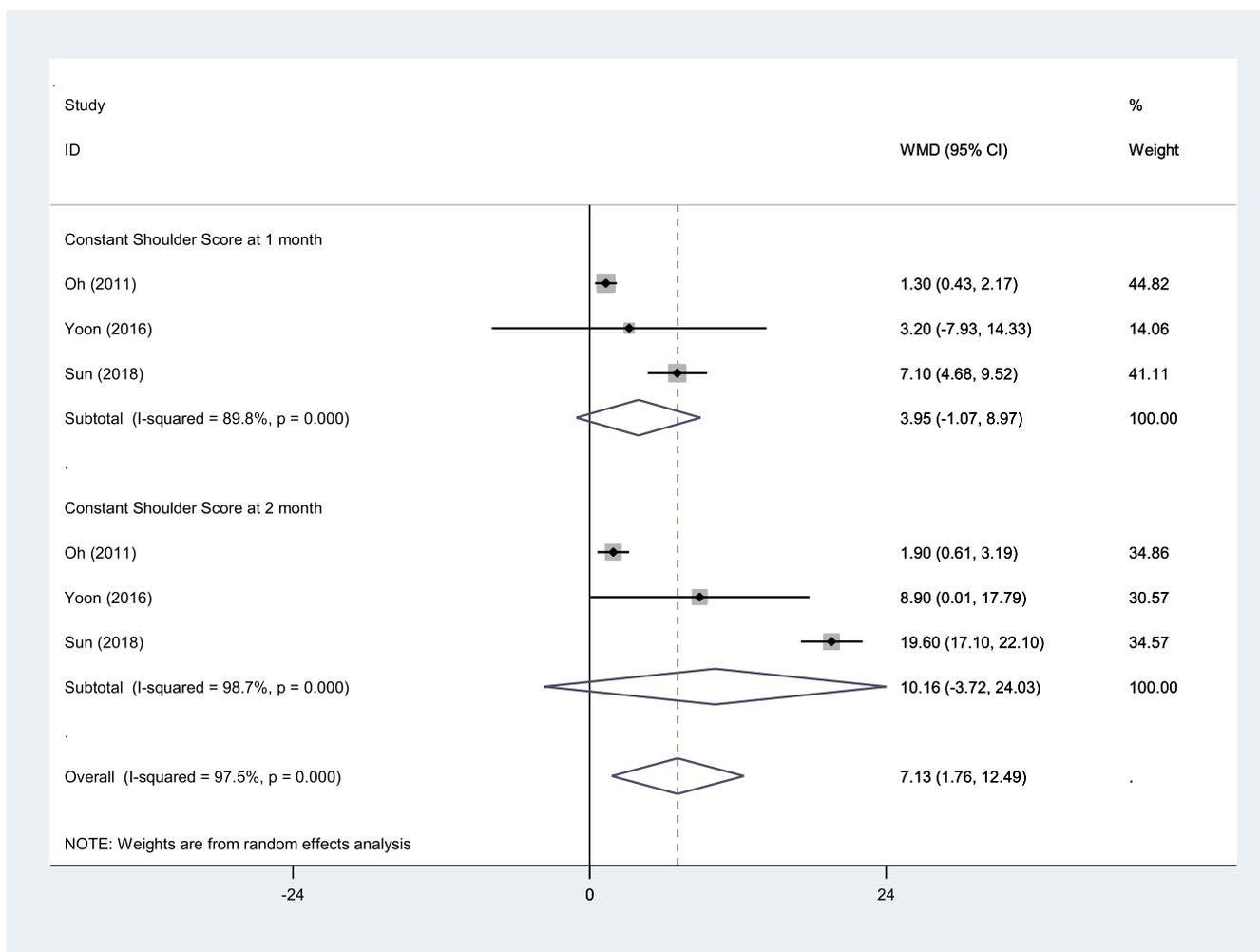


Fig. 7. Forest plot diagram of Constant shoulder score.

conservative treatment modality that achieves good clinical outcomes. Among various treatment approach, subacromial injection and intra-articular injection were commonly used, however, the intra-articular injection was technically more demanding without radiologic guidance compared to subacromial injection which was more easily to accomplish. It was considered to be relatively safe and cost-effective with a rapid and satisfactory outcome. The optimal approach of corticosteroid injection remained controversial. It was well known that intra-articular corticosteroid was associated with short term effect on pain relief in FS. Previous articles have shown that subacromial injection was as effective as intra-articular injection in reducing pain [24]. Rizk et al. [25] reported that intra-articular and subacromial injections achieved similar pain scores at 4 weeks, 12 weeks, and 24 weeks. However, Kim et al. [15] indicated that the efficacy of corticosteroid injection into the subacromial space in FS was inferior to intra-articular injection up to 12 weeks. In our study, 5 RCTs with 307 patients showed the outcome of VAS (0–10 cm) from different follow up period. The present meta-analysis indicated that intra-articular injection showed superior outcome for reducing pain in FS at 1 month, 2 month and 3 month.

Functional outcome is an important parameter to assess the efficacy of local corticosteroid injection for FS. The chronic inflammation

process may influence the shoulder joint function. It was well recognized that corticosteroid had the properties of anti-inflammation. Therefore, the use of corticosteroid was associated with the improved outcome of joint function. The Constant Score was first published in 1987 [26] and it has become the most commonly used outcome measure for assessing the treatment of shoulder disorders. It combines a subjective assessment of the patient's perception of pain and function along with an objective measurement of range of motion and strength, which was recommended by the European Society of Shoulder & Elbow Surgery. Intra-articular injection could maintain a high concentration of corticosteroid which may achieve a better functional outcome. Sun et al. [10] reported an improvements of Constant score in intra-articular group compared to subacromial group. In our study, a total of 3 RCTs were analyzed for the Constant score. The aggregated results of these studies suggest that Constant scores were similar for both groups and continuously improved throughout the follow-up period. There was no significant difference between the two groups. Khallaf et al. [18] used methylprednisolone for local injection, while others used triamcinolone. We performed a subgroup analysis for the ROM at 2 month. After exclusion, there was still huge heterogeneity. More RCTs were required for further analyzing.

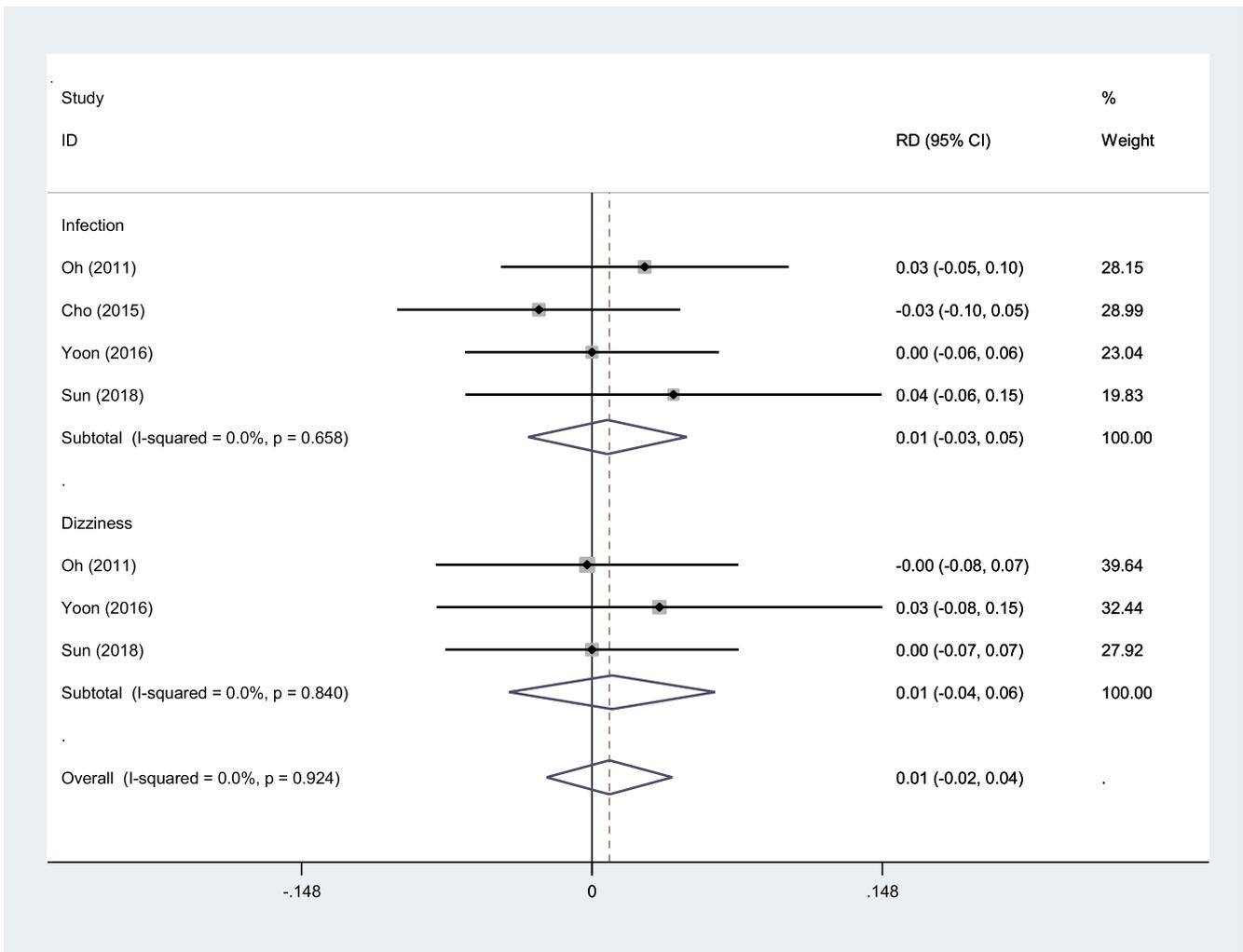
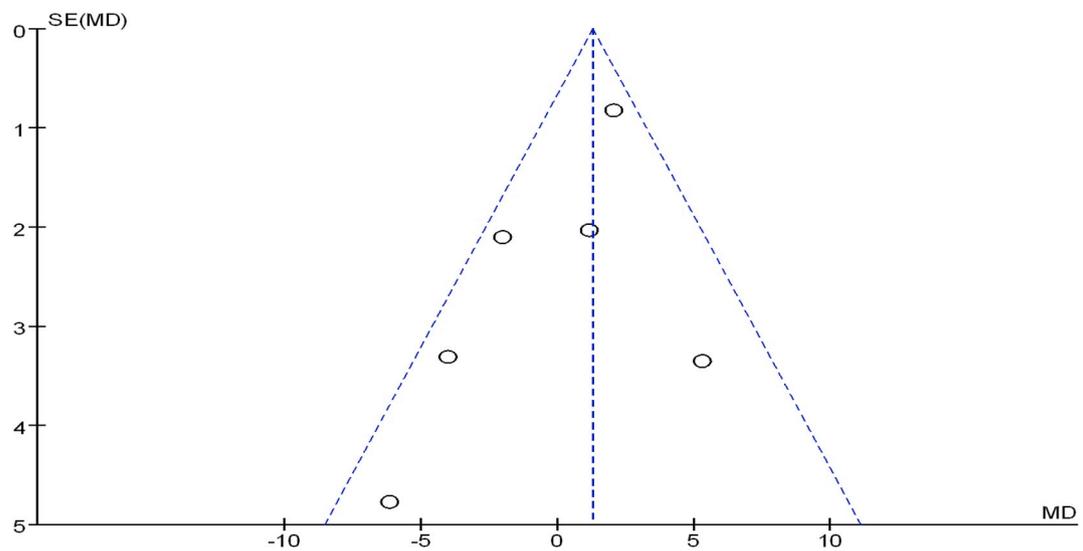
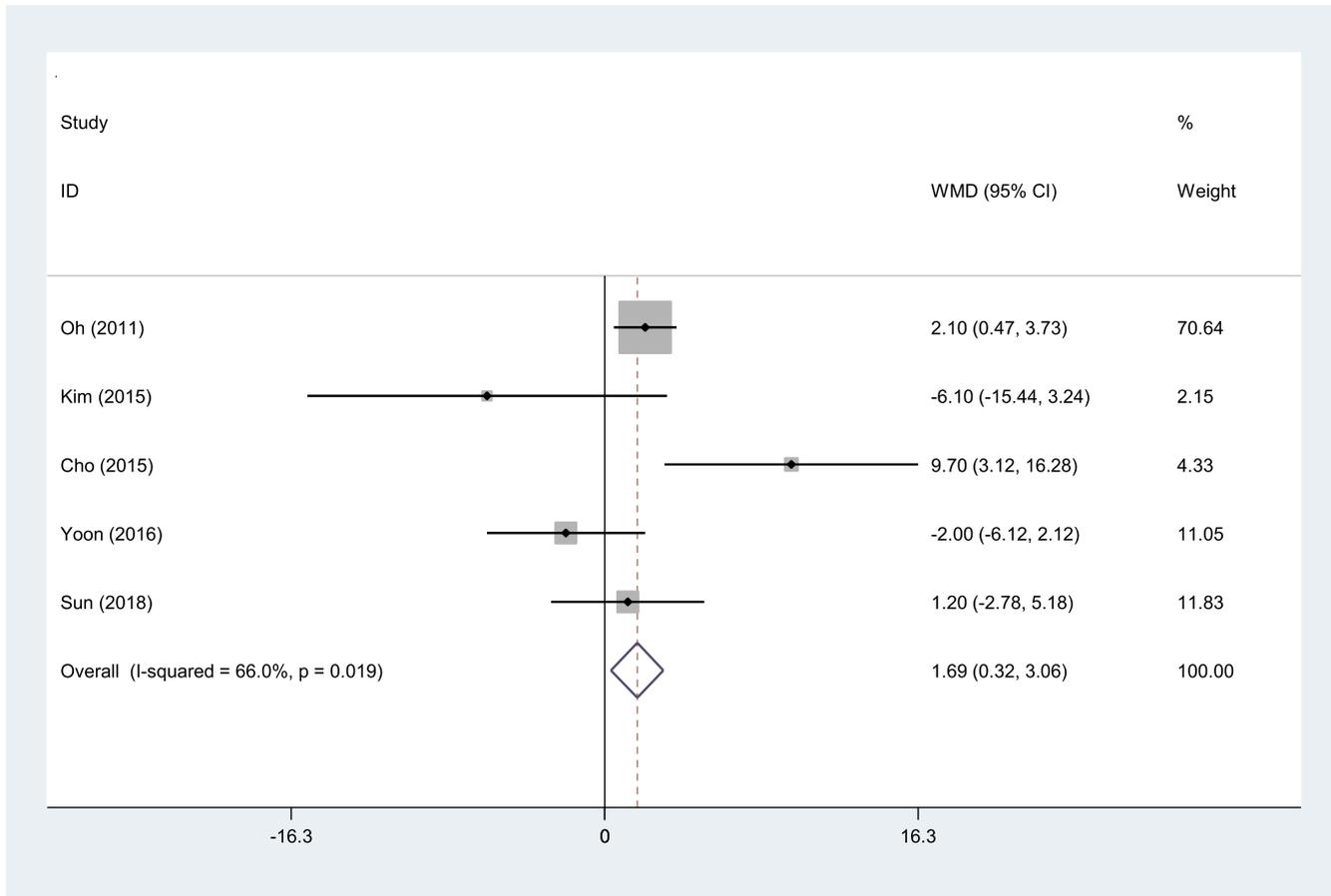


Fig. 8. Forest plot diagram of adverse effects.

Table 4  
Publication bias.



**Table 5**  
The outcome of subgroup analysis for ROM at 2 month.



Adverse effects were also an important parameter to compare the efficacy and safety between intra-articular and subacromial injection. Local injection will have less clinical value if there was a relatively high incidence of adverse effects. Local infection is common and may cause the degeneration of articular cartilage. In our study, four studies reported the adverse effects after local injection. All of them were mild and no treatment were required. There was no significant difference between groups in terms of adverse effects between two kinds of injection. Large sample size of RCTs were still needed for further research.

Several limitations in present meta-analysis were as followed: (1) only seven RCTs with 421 patients were included, so the conclusion should be treated cautiously; (2) heterogeneity among the included RCTs could potentially have increased bias. Due to the small number of the studies, we did not conduct a subgroup analysis for all outcomes, therefore, source of heterogeneity was unclear; (3) short term follow up may cause underestimation of adverse effects; (4) only English studies were included, publication bias is unavoidable.

**5. Conclusion**

Intra-articular injection of corticosteroid was associated with an improved outcomes for pain relief compared to subacromial injection.

There was no significant difference regarding the shoulder function or adverse effects.

**Provenance and peer review**

Not commissioned, externally peer-reviewed.

**Ethical approval**

Ethical approval was not application.

**Sources of funding**

We did not receive funding.

**Author contribution**

Rui Chen: writing.  
Cuihua Jiang: data analysis.  
Guiming Huang: study design and data collections.

**Table 6**  
Quality of the evidence and recommendation strengths.

Quality assessment	Effects				Quality	Importance	
	Limitations	Inconsistency	Indirectness	Imprecision			
Number of studies							
Pain score at 1 month							
5	no serious limitations	serious inconsistency	no serious indirectness	no serious imprecision	WMD: -0.873; 95% CI: -1.693 to -0.052	moderate	CRITICAL
Pain score at 2 month							
5	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	WMD: -0.837; 95% CI: -1.582 to -0.092	high	CRITICAL
Pain score at 3 month							
5	no serious limitations	serious inconsistency	no serious indirectness	no serious imprecision	WMD: -0.581; 95% CI: -1.069 to -0.093	moderate	CRITICAL
Range of motion at 1 month							
4	no serious limitations	serious inconsistency	no serious indirectness	no serious imprecision	WMD: 2.261; 95% CI: -2.276 to 6.798	moderate	CRITICAL
Range of motion at 2 month							
6	no serious limitations	serious inconsistency	no serious indirectness	no serious imprecision	WMD: -0.680; 95% CI: -4.984 to 3.624	moderate	CRITICAL
Constant shoulder score at 1 month							
3	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	WMD: 3.952; 95% CI: -1.071 to 8.974;	high	CRITICAL
Constant shoulder score at 2 month							
3	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	WMD: 10.159; 95% CI: -3.717 to 24.035	high	CRITICAL
Adverse effects							
3	no serious limitations	serious inconsistency	no serious indirectness	no serious imprecision	WMD: 0.009; 95% CI: -0.023 to 0.041	moderate	IMPORTANT

**Conflicts of interest**

We declared that there is no conflicts of interest.

**Research registry number**

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<https://www.researchregistry.com/browse-the-registry#registryofsystematicreviewsmeta-analyses/registryofsystematicreviewsmeta-analysesdetails/5ca8b9f7906687361e0b7ecf/>

**Guarantor**

Guiming Huang.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijssu.2019.06.008>.

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