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Effectiveness of Ultrasound-Guided Versus Anatomic Landmark–Guided Corticosteroid Injection on Pain, Physical Function, and Safety in Patients With Subacromial Impingement Syndrome

A Systematic Review and Meta-analysis

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Objective: The aim of the study was to compare the efficacy and safety of ultrasound-guided versus anatomic landmark–guided corticosteroid injection for the treatment of subacromial impingement syndrome.

Design: PubMed, Embase, Web of Science, Cochrane Central Register of Controlled Trials, Scopus, ClinicalTrials.gov, CBM, CNKI, and Wanfang databases were searched from inception to August 15, 2021, for randomized controlled trials comparing ultrasound-guided versus anatomic landmark–guided injections of corticosteroids for the treatment of subacromial impingement syndrome.

Results: Twelve randomized controlled trials with 891 patients were included in this study; 454 patients received ultrasound-guided injections and 437 received anatomic landmark–guided injections. Pooled results showed that ultrasound-guided injection was more beneficial for pain relief (10 trials; mean difference = −0.58; 95% confidence interval = −1.05 to −0.10; $P = 0.017$) and functional improvement (11 trials; standard mean difference = −0.84; 95% confidence interval = −1.41 to −0.27; $P = 0.004$). There was no significant difference in shoulder range of motion. In the subgroup analysis, there was a significant difference in pain relief and functional improvement at 6–8 wks and with methylprednisolone.

Conclusions: Ultrasound-guided injection of corticosteroids is potentially superior to anatomic landmark–guided injection in improving the clinical symptoms of subacromial impingement syndrome; however, these findings should be interpreted with some caution as the quality of evidence was rated as moderate to very low.

Key Words: Subacromial Impingement Syndrome, Adrenal Cortex Hormones, Ultrasonography, Injections, Meta-analysis

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What Is Known

- Previous systematic reviews yielded contradictory results regarding the efficacy and safety of ultrasound-guided (USG) versus anatomic landmark–guided (ALG) corticosteroid injections for the treatment of subacromial impingement syndrome (SIS).

What Is New

- This meta-analysis included the largest sample size of participants to date and compared the most comprehensive set of outcome measures stratified by age, follow-up duration, and type of corticosteroid. We found that the USG injection offers significantly better clinical improvement than ALG corticosteroid injection for the treatment of SIS, with acceptable safety.

BACKGROUND

Subacromial impingement syndrome (SIS) is a of common cause of shoulder pain[1,2] and accounts for 44%–65% of all shoulder complaints[3] in people older than 40 yrs.[4] The pathophysiological mechanism of SIS is the mechanical impingement of the rotator cuff tendons as they pass through the subacromial space, which leads to a condition of inflammation and irritation.[5,6] Shoulder pain occurs when patients elevate their arms at or above the shoulder level,[7] is usually confined to the anterolateral shoulder, and radiates to the medial and lateral sides of the humerus.[8] Physical function and quality of life can be severely affected by shoulder pain.[9]

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The primary aims of SIS treatment are to resolve the mechanical dysfunction and relieve pain.[10] Corticosteroid injection into the subacromial space has been recommended as a standard treatment approach in the management of SIS.[11] Traditionally, corticosteroid injections are administered under the guidance of anatomical landmarks.[12] Henkus et al.[13] reported that 30%–80% of shoulder girdle injections reaching the subacromial capsule were regarded as blind injections. Injections performed by image guidance (fluoroscopy or ultrasonography) have been shown to improve the accuracy of shoulder girdle injections.[14] With recent advances in ultrasound imaging, ultrasound-guided (USG) injections have gained popularity and have been demonstrated to have improved efficacy in the treatment of SIS.[14]

However, despite improvements in the accuracy of injection placement by USG, the current evidence on the effect of USG versus ALG corticosteroid injections for the management of SIS is conflicting. Several studies[15,16] indicated that USG injections for SIS resulted in significant improvements in pain relief and physical function compared with ALG injections, whereas others[17,18] reported no positive results. The results from previous systematic reviews were contradictory and previous studies were limited by small sample sizes, ambiguous definitions of SIS, and increased costs were raised to justify the advantages of using USG injections for SIS.[19–23] Therefore, to address these concerns, a systematic review and meta-analysis were performed to summarize and update the current evidence on the efficacy and safety of applying USG versus ALG corticosteroid injection in the management of SIS.

METHODS

This systematic review and meta-analysis were conducted in accordance with the recommendations of the Cochrane Collaboration[24] and reported based on the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines (see Supplementary Material Appendix A, Supplemental Digital Content 1, http://links.lww.com/PHM/B452).[25] The protocol of this study is available in PROSPERO (CRD42020162682).

Search Strategy

The following electronic databases were searched from inception to August 15, 2021; using search terms shoulder impingement syndrome/impingement and corticosteroid injection: PubMed, Embase, Web of Science, the Cochrane Central Register of Controlled Trials, Scopus, ClinicalTrials.gov, CBM, CNKI, and Wanfang databases. Detailed electronic search strategies are provided in the Supplementary Material Appendix B (Supplemental Digital Content 2, http://links.lww.com/PHM/B453). Open Grey (http://www.opengrey.eu/) was searched for the gray literature research. The reference lists of the included reviews and trials were also screened to identify potentially related studies.

Inclusion and Exclusion Criteria

Types of Studies

All randomized controlled trials comparing the efficacy of USG versus ALG corticosteroid injection in treating SIS were eligible for inclusion. Studies without full text or case reports were excluded. The language of the included randomized controlled trials was limited to English and Chinese.

Types of Participants

Adults participants (older than 18 yrs) with (1) a history of shoulder pain that worsened because of overhead activities and lying on the affected shoulder; (2) painful restriction of active flexion and/or abduction of the shoulder, or limitations in internal and external rotation; and (3) a positive Neer test, Hawkins test, Jobes test, painful arch, or external rotation resistance test[1] were included. Causes of shoulder pain other than SIS were excluded.

Types of Interventions

The intervention was a USG corticosteroid injection, and the comparator was an ALG corticosteroid injection. The doses and types of corticosteroids used were not limited. There was no restriction on the injection approach: anterior, lateral, and posterior approaches.

Types of Outcome Measures

The primary outcome was pain and secondary outcomes were function/disability, range-of-motion (ROM) assessment, and adverse events. The outcomes were prioritized as suggested by Steuri et al.[26] and pain or functional outcomes were assessed by using different scales (Supplementary Material Appendix C, Supplemental Digital Content 3, http://links.lww.com/PHM/B454).

Study Selection

A three-stage screening methodology was used to select relevant randomized controlled trials for this review. First, all titles were screened by one reviewer (XYD) for eligibility, and irrelevant articles were excluded accordingly. Second, two reviewers (SYZ and DSL) independently reviewed the titles and abstracts of each study. Third, two independent reviewers (DSL and XYD) accessed the full text to assess against the eligibility criteria for each potentially eligible study. Disagreements were resolved through discussion with a third party (SYZ).

Data Collection

Two reviewers (XYD and SYZ) independently extracted the data from studies with a standardized spreadsheet, including data on lead author, year of publication, country, sample size, participants (sex and age), interventions, approach, follow-up period, and outcomes. Two reviewers cross-checked the extracted data. For missing data, we emailed the corresponding author or estimated the mean, SD, confidence interval (CI), or *P* values.[24] All discrepancies were arbitrated by another author (YL).

Quality Assessment

We used the Cochrane Collaboration's 2.0 tool (RoB 2)[27] to appraise the risk of bias for eligible studies in the following domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported results, and overall bias. The risk of bias in each domain was judged as "low," "some

concerns," or "high." The Grades of Recommendation Assessment, Development, and Evaluation (GRADE) tool[28] was used to describe the overall quality of the body of evidence. It contains the following domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The certainty of evidence was classified into four categories: high, moderate, low, or very low for each outcome. Two reviewers independently assessed the risk of bias for each study (XZ and DSL), and a third author (YLT) reviewed the final results and resolved any disagreements.

Statistical Analysis

All statistical analyses were performed using Revman (version 5.4) and STATA 15.0 software. Pooled effect assessments were analyzed by comparing changes between baseline and posttreatment outcomes: $\text{outcome}_{\text{posttreatment}}$ and $\text{outcome}_{\text{baseline}}$. The changes in pain scores, function scores, and ROM were expressed as mean differences (MDs) with 95% CIs. If the evaluation scales differed for the same outcome, the standard MD (SMD) was calculated. To summarize the safety outcome (number of adverse events), the risk ratios with 95% CIs were used. We used the I^2 value to detect the heterogeneity of the pooled results, as follows: $I^2 > 50\%$ was defined as significant heterogeneity; $I^2 < 50\%$ was defined as no significant heterogeneity. A fixed-effects model was used to combine studies with $I^2 < 50\%$. Otherwise, random-effects models were used. Subgroup analysis was conducted to detect the effectiveness relative to different age (≥50 and <50 yrs old), follow-up durations (1–2, 4, 6–8, and 12 wks), and different types of corticosteroids (betamethasone, dexamethasone, methylprednisolone). To evaluate the quality and consistency of pooled results, a sensitivity analysis was performed by excluding studies one by one to determine whether the changes had a significant impact on the treatment effect. Publication bias was estimated using a funnel plot if the comparisons included at least 10 trials.[29] Begg test,[30] and Egger test,[31] and trim and fill analyses were used for further quantitative analysis of publication bias. All tests were two-tailed, and statistical significance was set at $P < 0.05$.

RESULTS

Study Characteristics

A total of 298 studies were obtained. Of these, 296 studies were identified using the original databases, and two additional studies were identified from published systematic reviews.[19,20] After deleting the duplicate articles and reviewing the titles and abstracts, 47 studies were selected. Among these, 12 studies that met the inclusion criteria for full-text screening were obtained for the data extraction and analysis (Fig. 1). A total of 891 participants (USG group, $n = 454$; ALG group, $n = 437$) were enrolled. The sample size of individual studies ranged from 14 to 128 participants per group with a mean age between 28.13 and 57.7 yrs. The average disease duration ranged from 1 to 26 mos. The follow-up duration of the included trials ranged from 1 to 12 wks. The injection approach varied across the studies. The characteristics of the included studies are listed in Table 1.

Pain data were obtained from 10 studies[15–18,33–36,38,39] with the use of Visual Analog Scale (VAS) and Numerical Rating Scale, and only one study[34] reported the type of pain (active and passive). Functional and disability outcomes were assessed in 11 trials[15–18,33–39] using different tools (shoulder pain and disability index, modified Constant-Murley score, Oxford shoulder score, shoulder disability questionnaire, physician global assessment, American shoulder, and elbow surgeons score). Four studies[15–17,32] reported ROM assessment. Adverse events were reported in six studies.[17,18,34,35,37,38]

Quality Assessment

Of the 12 included studies, one was rated as having a "low risk of bias" in all domains, and the other studies were classified as having an "unclear risk of bias" for at least one aspect or a "high risk of bias" for at least two aspects. The results of the risk of bias are presented in the Supplementary Material Appendix D (Supplemental Digital Content 4, http://links.lww.com/PHM/B455). According to the GRADE system, the quality of the evidence of the included studies was very low, low, or moderate. For pain, the certainty of the evidence was moderate. The evidence was downgraded because of the risk of bias. For function, the certainty of the evidence was very low. The evidence was downgraded because of the risk of bias, inconsistency, and imprecision. For shoulder ROM, the certainty of the evidence was low or very low. The evidence was downgraded because of the risk of bias, inconsistency, and imprecision. The GRADE results are presented in Table 2.

Effect of Intervention: Pain Relief

Ten trials[15–18,33–36,38,39] (795 participants) were included in the analysis. Moderate certainty evidence showed that the USG injection had a small but significant effect on the reduction of pain (10 trials; MD = −0.58; 95% CI = −1.05 to −0.10; $P = 0.017$) with statistically significant heterogeneity ($I^2 = 76.7\%$, $P = 0.000$; Fig. 2). In the subgroup analysis, follow-up duration of 6–8 wks (8 trials; MD = −0.72; 95% CI = −1.19 to −0.25; $P = 0.002$) and use of methylprednisolone (8 trials; MD = −0.79; 95% CI = −1.28 to −0.29; $P = 0.002$) and betamethasone (1 trial; MD = −0.94; 95% CI = −1.58 to −0.30; $P = 0.004$) showed evidence of a significant difference in pain relief (Table 3). Age and other subgroup factors had no effect on pain relief. No significant changes in heterogeneity or overall effects were observed in the sensitivity analysis (Supplementary Material Appendix E, Supplemental Digital Content 5, http://links.lww.com/PHM/B456).

Effect of Intervention: Function Improvement

Eleven trials[15–18,33–39] (851 participants) were included in the analysis. Very low certainty evidence showed that USG injection had a small but significant effect on the improvement of function (11 trials; SMD = −0.84; 95% CI = −1.41 to −0.27; $P = 0.004$) with statistically significant heterogeneity ($I^2 = 92.8\%$, $P = 0.000$; Fig. 3). In the subgroup analysis, follow-up duration of 6–8 wks (8 trials; SMD = −0.78; 95% CI = −1.36 to −0.21; $P = 0.008$) and use of methylprednisolone (8 trials; SMD = −0.77; 95% CI = −1.36 to −0.18; $P = 0.01$) showed evidence of a significant difference in functional improvement (Table 3). Age and other subgroup factors had no

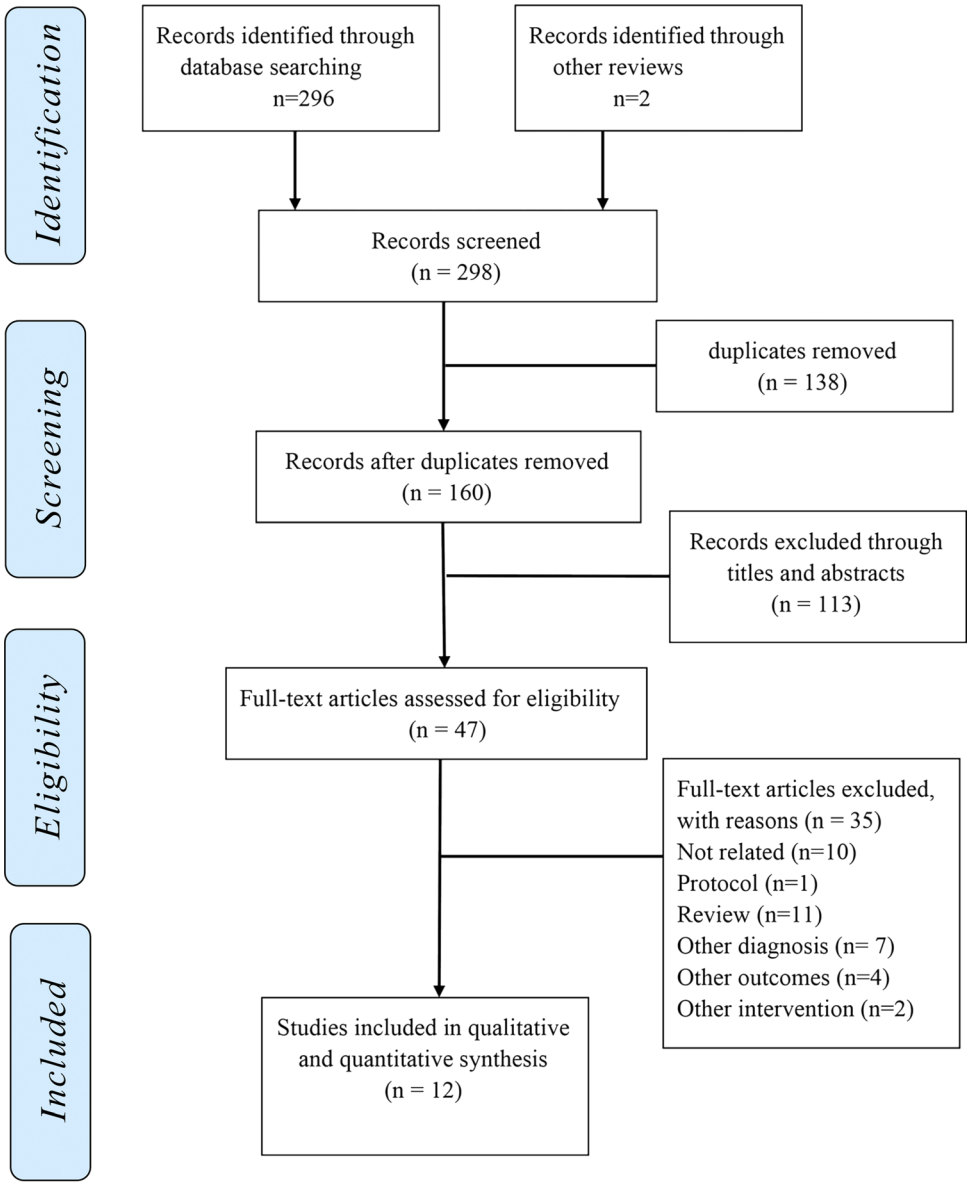

FIGURE 1. Study flow diagram.

effect on functional improvement. The meta-analysis results for function were robust in sensitivity analysis (Supplementary Material Appendix E, Supplemental Digital Content 5, http://links.lww.com/PHM/B456).

Effect of Intervention: ROM

Four trials[15–17,32] (204 participants) were included in the analysis. Very low to low certainty evidence showed that USG injection had no significant effect on the improvement of shoulder ROM (Fig. 4). In the subgroup analysis, follow-up duration of 6 wks (1 trial; MD = 6.50; 95% CI = 4.50 to 8.50; $P < 0.00001$) and use of betamethasone (1 trial; MD = 41.54; 95% CI = 30.95 to 52.13; $P < 0.00001$) showed evidence of a significant difference in shoulder abduction ROM. Age 50 yrs or greater (2 trials; MD = 4.51; 95% CI = 3.29 to 5.74; $P < 0.0001$) and follow-up duration of 6 wks (1 trial; MD = 4.50; 95% CI = 3.27 to 5.37; $P < 0.0001$) showed evidence of a significant difference in shoulder flexion ROM (Table 4). Other subgroup factors had no effect on shoulder ROM. The results showed no major change in the overall findings in the sensitivity analysis, which suggested the stability of the results (Supplementary Material Appendix E, Supplemental Digital Content 5, http://links.lww.com/PHM/B456).

Safety Outcome

Six studies reported adverse events. Two studies[35,38] reported that shoulder pain occurred in a small number of cases. In one study,[38] a serious adverse event was observed in a participant who was hospitalized for pyelonephritis. Four studies reported that no adverse events were observed.[17,18,34,37]

Publication Bias

For pain, the funnel plot was symmetry and Begg test ($z = 1.07$, $P = 0.283$) and Egger ($t = -0.49$, $P = 0.637$) tests

TABLE 1. Characteristics of included studies

Author (Year), Country	No. Patients	Women, *n*/%	Mean Age (SD)/Media (Min–Max)	Type of Intervention and Dose	Approach	Duration, mo/wk	Follow-up	Outcomes Measure
Chen[32] (2006), Taiwan	20	26/33	53 (30–66)	USG: 1 ml of betamethasone and 1 ml of 1% lidocaine	Lateral	>1 mo	1 wk	Abduction ROM (not specified active or passive)
	20			ALG: 1 ml of betamethasone and 1 ml of 1% lidocaine	Lateral			
Panditaratne[33] (2010), United Kingdom	41	36/62	54 (25–80)	USG: 80 mg of Depo-Medrol and 3–10 ml of bupivacaine or lidocaine	NR	NR	6 wks	Pain (not specified active or rest) The Oxford shoulder score
	17			ALG: 80 mg of Depo-Medrol and 3–10 ml of bupivacaine or lidocaine	Lateral			
Dogu[34] (2012), Turkey	23	15/65.2	55.17 (9.24)	USG: 1 ml of 5 mg/ml of betamethasone dipropionate and 9 ml of 10 mg/ml prilocaine hydrochloride	Lateral	7.43 (5.37) mos	6 wks	VAS (rest, activity and sleep) the constant ROM score Constant general pain Constant activities of daily living score SDQ
	23	16/69.6	56.74 (8.02)	ALG: 1 ml of 5 mg/ml betamethasone dipropionate and 9 ml of 10 mg/ml prilocaine hydrochloride	Posterior	9.74 (7.67) mos		
Hsieh[16] (2013), Taiwan	48	27/56	57.59 (10.30)	USG: 0.5 ml (5 $mg{\cdot}ml^{-1}$) of dexamethasone and 3 ml (10 $mg{\cdot}ml^{-1}$) of lidocaine hydrochloride	Lateral	6.28 (3.59) mos	Immediately 1 wk 4 wks	VAS (not specified active or rest) SPADI SDQ SF-36
	48	29/60	55.87 (11.42)	ALG: 0.5 ml (5 $mg{\cdot}ml^{-1}$) of dexamethasone and 3 ml (10 $mg{\cdot}ml^{-1}$) of lidocaine hydrochloride	Lateral	7.14 (4.72) mos		ROM of flexion, abduction, external rotation, internal rotation (active and passive)
Saeed[35] (2014), Ireland	59	79/65	57.7	USG: 40 mg of methylprednisolone acetate with 4 ml of lidocaine hydrochloride	NR	19.64 (1.84) wks	6 wks 12 wks	VAS (not specified active or rest) SFTs PGA
	66			ALG: 40 mg of methylprednisolone acetate with 4 ml of lidocaine hydrochloride	Lateral	20.02 (1.52) wks		
Haghighat[15] (2015), Iran	20	12/60	50.45 (6.78)	USG: 40 mg of methylprednisolone with 1 ml of lidocaine 2%	Lateral	1.8 (0.54) mos	6 wks	VAS (not specified active or rest) SPADI
	20	13/65	52.3 (7.48)	ALG: 40 mg of methylprednisolone with 1 ml of lidocaine 2%	Posterior	1.87 (0.48) mos		ROM of flexion, abduction, external rotation, internal rotation (not specified if active or passive)

(Continued on next page)

TABLE 1. *(Continued)*

Author (Year), Country	No. Patients	Women, *n*/%	Mean Age (SD)/Media (Min–Max)	Type of Intervention and Dose	Approach	Duration, mo/wk	Follow-up	Outcomes Measure
Cole[36] (2016), Australia	28	14/ (50)	46 (19–68)	USG: 1 ml of 40 mg/ml methylprednisolone acetate and 5 ml of 1% lidocaine hydrochloride	Lateral	26 (1–108) mos	6 wks	VAS (active) ASES
	28	18/ (64)	42 (23–62)	ALG: 1 ml of 40 mg/ml methylprednisolone acetate and 5 ml of 1% lidocaine hydrochloride	Posterior	16 (2–108) mos		
Bhayana[18] (2018), India	30	17/56.6	44.53 (9.2)	USG: 2 ml of 40 mg/ml methylprednisolone acetate suspension mixed and 2 ml of 1% lignocaine	Anterior	2 mos	Day 5 3 wks 6 wks 12 wks	VAS (not specified active or rest) Constant score
	30	10/33.3	42.03 (9.9)	ALG: 2 ml of 40 mg/ml methylprednisolone acetate suspension mixed and 2 ml of 1% lignocaine	Lateral			
Cao[37] (2018), China	28	7/25	50.2 (3.6)	USG: 1 ml of betamethasone and 1 ml of 2% lidocaine	Lateral	18 (4) mos	4 wks	CMS ADL
	28	9/25	47.6 (2.6)	ALG: 1 ml of betamethasone and 1 ml of 2% lidocaine	Lateral	16 (5) mos		ROM
Akbari[17] (2020), Turkey	14	8/57.1	39.5 (20–64)	USG: methylprednisolone acetate 40 mg in 1 ml and procaine 2% 4 ml	Anterior	>3 mos	4 wks	VAS (not specified active or rest) Flexion, abduction ROM (active) DASH
	14	9/64.3	42.5 (20–64)	ALG: methylprednisolone acetate 40 mg in 1 ml and procaine 2% 4 ml	Posterior			CMS
Roddy[38] (2021), United Kingdom	128	63/51	53.8 (10.2)	USG: methylprednisolone 40 mg and 1 ml of 1% lidocaine	Anterior	Time varied	6 wks 6 mos	NRS SPADI
	128	67/128	53.8 (10.2)	ALG: methylprednisolone 40 mg and 1 ml of 1% lidocaine	Lateral		12 mos	Patient's Self-reported Global Impression of Change Short-Form 12
Azadvari[39] (2021), Iran	15	10/66.7	33.80 (9.34)	USG: 1 ml of Depo-Medrol along with 2 ml of lidocaine	Lateral	23.46 (14.78) mos	2 wks 2 mos	CONSTANT score VAS
	15	12/80	28.13 (11.02)	ALG: 1 ml of Depo-Medrol along with 2 ml of lidocaine	Lateral	22.53 (14.87) mos		BREF-QOL questionnaire

ADL, activities of daily living; ASES, American Shoulder and Elbow Surgeons score; BREQ, Brief quality of life; CMS, modified Constant-Murley Score; DASH, Disabilities of the Arm, Shoulder, and Hand questionnaire; NR, not reported; NRS, Numerical Rating Scale; PGA, Physician Global Assessment; QOL, quality of life; SDQ, Shoulder Disability Questionnaire; SF-36, 36-item Short-Form Health Survey; SFTs, shoulder function tests; SPADI, Shoulder Pain and Disability Index.

TABLE 2. Results of the GRADE

Outcomes	Certainty Assessment							No. Patients		Effect	
	No. Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	USG Injection	ALG Injection	Absolute (95% CI)	Certainty
Pain	10	Randomized trials	Serious[a]	Not serious	Not serious	Not serious	None	406	389	MD = 0.58 lower (1.05 lower to 0.1 lower)	⊕⊕⊕○ Moderate
Function	11	Randomized trials	Serious[a]	Serious[b]	Not serious	Serious[c]	Publication bias strongly suspected[d]	434	417	SMD = 0.82 SD lower (1.38 lower to 0.26 lower)	⊕○○○ Very low
Abduction of ROM	4	Randomized trials	Serious[a]	Serious[b]	Not serious	Not serious	None	102	102	MD = 9.28 higher (12.13 lower to 30.7 higher)	⊕⊕○○ Low
Flexion of ROM	3	Randomized trials	Serious[a]	Serious[b]	Not serious	Serious[e]	None	82	82	MD = 1.53 lower (15.54 lower to 12.47 higher)	⊕○○○ Very low
External rotation of ROM	2	Randomized trials	Serious[f]	Not serious	Not serious	Serious[g]	None	68	68	MD = 0.28 lower (1.38 lower to 0.38 higher)	⊕⊕○○ Low
Internal rotation of ROM	2	Randomized trials	Serious[f]	Not serious	Not serious	Serious[g]	None	68	68	0.77 lower (1.72 lower to 0.18 higher)	⊕⊕○○ Low

[a] Two trials did not describe the randomization process; in one trial, patients and the physician administering the injections were not blinded.
[b] I^2 value of the combined results was high heterogeneity.
[c] Potential imprecision due to different scales was combined for analysis for functional performance.
[d] There was a suspicion of publishing bias.
[e] Potential imprecision due to availability of three trials of 164 participants.
[f] Patients and the physician administering the injections were not blinded.
[g] Potential imprecision due to availability of two trials of 136 participants.

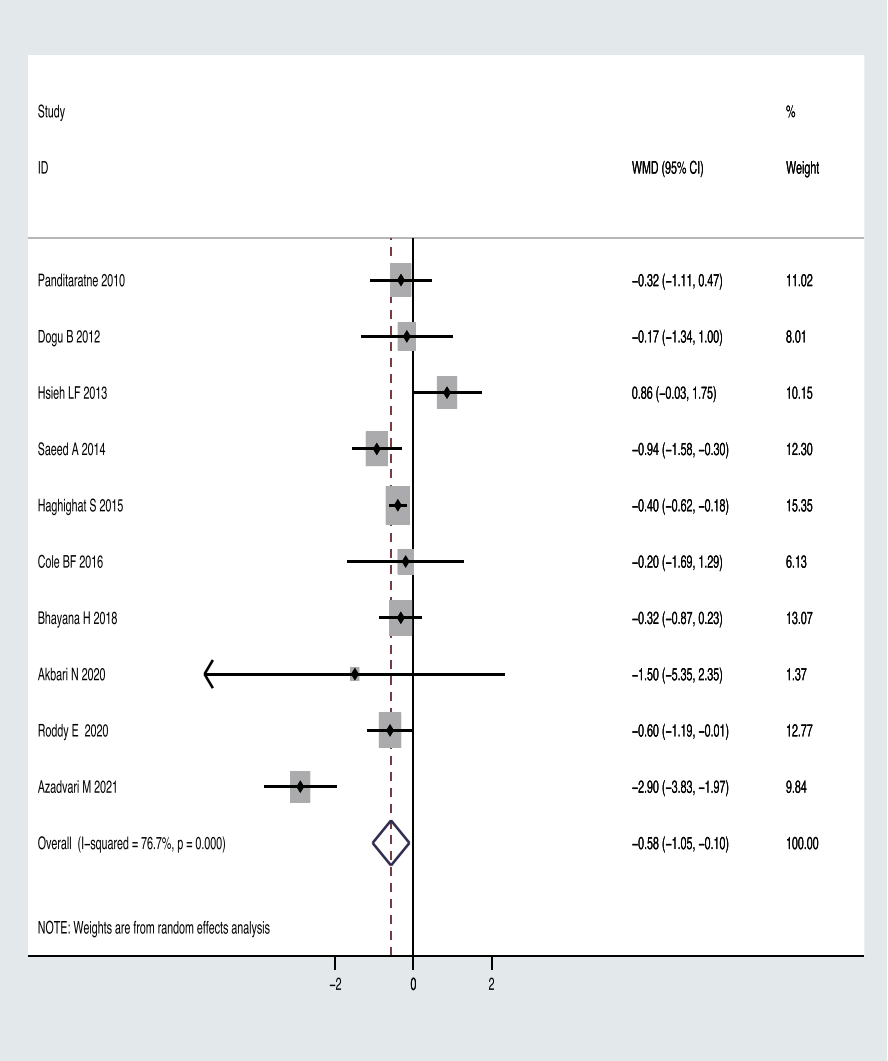

FIGURE 2. Forest plot for effects of USG versus ALG injection on pain.

did not detect publication bias. For function, the funnel plot showed a mild asymmetry and Begg (z = 2.02, P = 0.043), Egger (t = −2.98, P = 0.024) tests indicated publication bias. Trim and filled analyses did not change, which showed that the results were stable. For ROM, the Begg and Egger tests showed no publication bias. The results are presented in

TABLE 3. Subgroup analyses of USG versus ALG injection of corticosteroid for pain and function

	Pain			Function		
Subgroup	**Articles**	**Effect Size (95% CI)**	***P***	**Articles**	**Effect Size (95% CI)**	***P***
Age, yr						
<50	4	−1.20 (−2.84 to 0.44)	0.15	4	−0.076 (−1.95 to 0.43)	0.21
>50	6	−0.35 (−0.73 to 0.03)	0.07	6	−0.46 (−1.05 to 0.13)	0.13
Flow-ups						
1–2 wks	2	−1.51 (−5.22 to 2.21)	0.43	2	−1.35 (−4.72 to 2.01)	0.43
4 wks	2	0.46 (−1.29 to 2.20)	0.61	3	−0.85 (−2.81 to 1.11)	0.39
6–8 wks	8	−0.72 (−1.19 to −0.25)	0.002	8	−0.78 (−1.36 to −0.21)	0.008
12 wks	2	−0.53 (−1.25 to 0.20)	0.15	2	−0.23 (−0.66 to 0.21)	0.31
Drugs						
Dexamethasone	1	0.86 (−0.03 to 1.75)	0.06	1	0.49 (0.08 to 0.90)	0.02
Betamethasone	1	−0.94 (−1.58 to −0.30)	0.004	2	−1.61 (−4.07 to 0.84)	0.2
Methylprednisolone	8	−0.79 (−1.28 to −0.29)	0.002	8	−0.77 (−1.36 to −0.18)	0.01

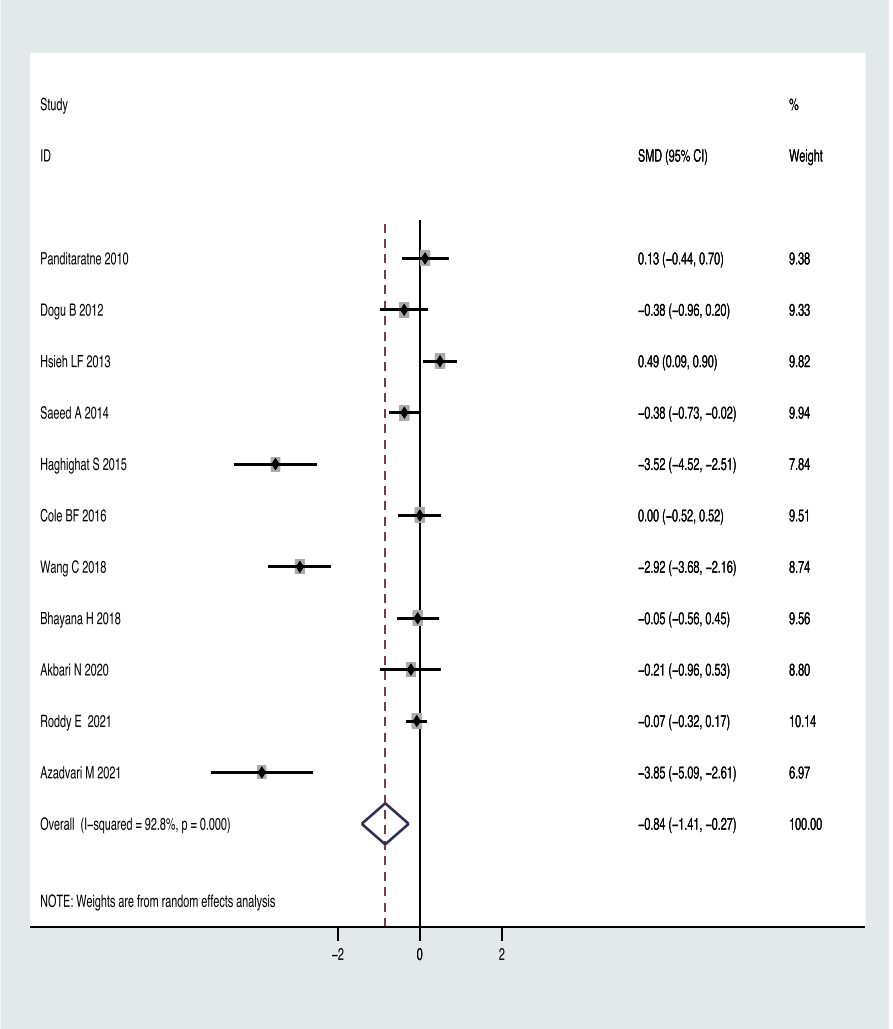

FIGURE 3. Forest plot for effects of USG versus ALG injection on function.

Supplementary Material Appendices F1–F4 (Supplemental Digital Content 6, http://links.lww.com/PHM/B457).

DISCUSSION

This systematic review and meta-analysis of 12 studies involving 891 participants (USG group: 454 participants; ALG group: 437 participants) suggested that USG corticosteroid injection for management of SIS resulted in more effective pain relief and functional improvement than ALG injections; however, there was no significant difference in shoulder ROM. In the subgroup analysis, follow-up of 6–8 wks and use of methylprednisolone showed evidence of a significant difference in pain relief and functional improvement.

Our findings are in consistent with those of several previously published systematic reviews.[20,40,41] Several mechanisms have been suggested to explain the significantly greater improvement in pain reduction and functional gain in the USG group. The main mechanism is the greater accuracy of USG versus ALG for all shoulder girdle joints, which led to improved efficacy in outcome measures of pain and function.[41] Another important factor resulting in the improvement to consider is the increased patient comfort and less needle manipulation with USG injections, although it was not assessed across all studies.[20] Ultrasound-guided injections also provide real-time monitoring during needle placement without any risk of radiation exposure. Furthermore, a short-term retention of the therapeutic efficacy may exist as reported by the findings in our subgroup analysis, and another systematic review measured the changes between 6-wk follow-up and baseline VAS and shoulder function scores.[40] However, several factors should be considered when interpreting these positive findings such as the varied quality of included studies, inclusion of specific populations with small sample sizes, substantial heterogeneity across studies, and small clinical effect. The reasons for these weaknesses could be attributed to different periods of follow-up, heterogeneous pathologies of painful shoulder, inadequate patient blinding potentially causing bias, and placebo effect.[14] In our study, although there was an evidence of substantial heterogeneity among the included trials, our sensitivity analysis detected no changes in the levels of heterogeneity and effect, and the results of publication bias confirmed the robustness.

In contrast, a recent Cochrane review and another systematic review did not detect improved efficacy or advantages of USG corticosteroid injection for the management of SIS.[19,23]

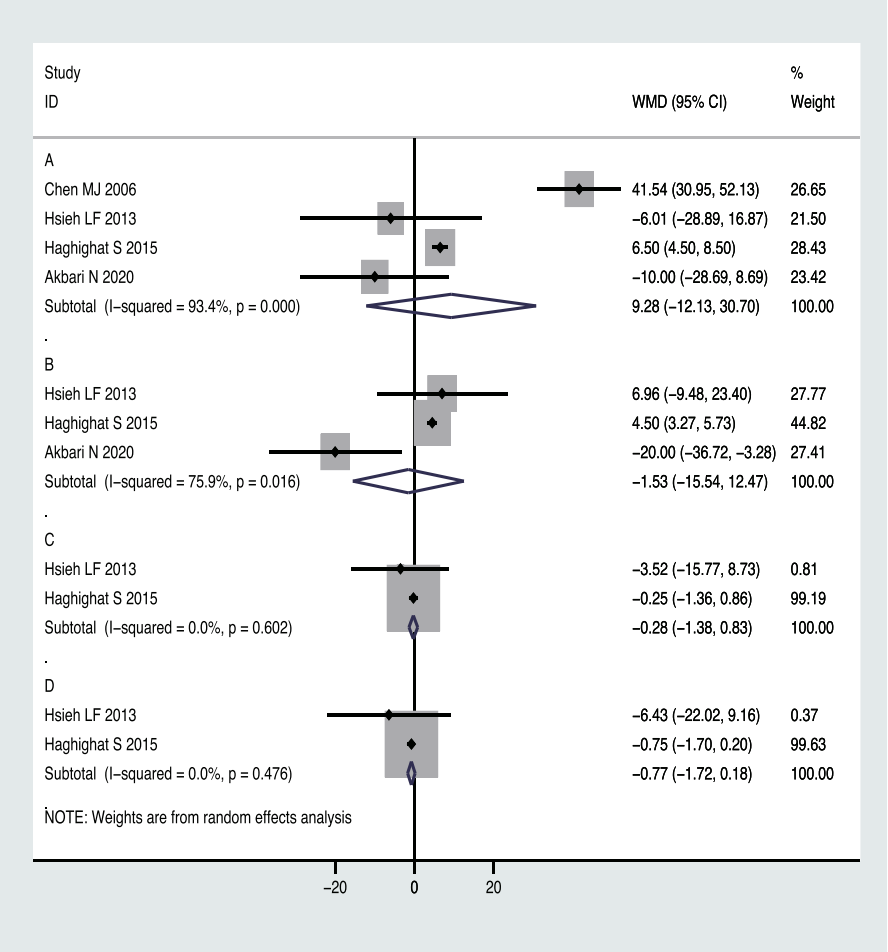

FIGURE 4. Forest plot for effects of USG versus ALG injection on ROM. A, Shoulder abduction ROM. B, Shoulder flexion ROM. C, Shoulder external rotation ROM. D, Shoulder internal rotation ROM.

Bloom et al.[19] included patients with various pathologies for shoulder pain (one of which was SIS), whereas Ayekoloye et al.[23] included patients with SIS under the injection of the subacromial bursa only. However, these previous systematic reviews,[19,23] which obtained negative results, included only 4–5 studies involved 234–290 patients with different causes of shoulder pain, whereas our study included 12 trials involving 891 participants with SIS. In addition, participants included in previous studies were in the chronic stage of SIS, which is less responsive to corticosteroid injections reported,[42] and these patients received additional treatments with the corticosteroid injection, which may have influenced the outcome measures.[43] Other notable limitations of the abovementioned Cochrane review include the use of the final pain and functional outcome MD between groups instead of the mean change difference and the fact that negative conclusion in terms of pain, function, shoulder range of motion, or safety was made mainly based on a single study.[44]

Strengths and Limitations

This review has several strengths. To our knowledge, this study had the largest sample size of participants (891 participants in 12 trials) with SIS and evaluated the treatment efficacy of USG versus ALG injections. Our study used the most comprehensive set of outcome measures including pain, function, ROM, and safety, which were stratified by age, follow-up duration, and the type of corticosteroid. These results will guide clinicians in making a decision regarding the use of USG injections for the management of SIS or similar musculoskeletal disorders. Furthermore, to optimize data gathering and to ensure that no study was missed in compliance with the study protocol, we sought the help of a librarian familiar with the development of searches and the mechanism of living systematic reviews. Finally, this study strictly adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses checklist and was carefully performed according to guidelines to ensure the robustness of the findings.

Nevertheless, this review also has several limitations. First, the level of evidence assessed by the GRADE criteria ranged from moderate to very low, which suggests that the quality of studies included needs to be further improved by including studies with a larger sample size and well-designed methodology to eliminate any potential risk of bias. Moreover, there were remarkable variations in the measures of pain and functional outcomes used between studies; therefore, we used SMD for all functional measures in the analysis. Pain measures across studies were converted to a 10-point scale, where some

TABLE 4. Subgroup analyses of USG versus ALG injection of corticosteroid for ROM

	ROM of Abduction			ROM of Flexion		
Subgroup	**Studies**	**Effect Size (95% CI)**	***P***	**Studies**	**Effect Size (95% CI)**	***P***
Age, yr						
<50	1	−10.00 (−28.69 to 8.69)	0.29	1	−20.00 (−36.72 to −3.28)	0.02
≥50	3	15.03 (−11.46 to 41.52)	0.27	2	4.51 (3.29 to 5.74)	<0.0001
Flow-ups						
1 wk	2	21.59 (−19.99 to 63.17)	0.31	1	10.23 (−5.78 to 26.23)	0.21
4 wks	2	−8.40 (−22.88 to 6.08)	0.26	2	−6.21 (−33.08 to 20.66)	0.65
6 wks	1	6.50 (4.50 to 8.50)	<0.00001	1	4.50 (3.27 to 5.73)	<0.0001
Type of corticosteroid						
Dexamethasone	1	−6.01 (−28.89 to 16.87)	0.61	1	6.96 (−9.48 to 23.40)	0.41
Betamethasone	1	41.54 (30.95 to 52.13)	<0.00001			
Methylprednisolone	2	0.97 (−14.29 to 16.24)	0.90	2	−6.27 (−30.11 to 17.56)	0.61
	ROM of External Rotation			**ROM of Internal Rotation**		
Subgroup	**Studies**	**Effect Size (95% CI)**	***P***	**Studies**	**Effect Size (95% CI)**	***P***
Age, yr						
<50	0			0		
≥50	2	−0.28 (−1.38 to 0.83)	0.62	2	−0.77 (−1.72 to 0.18)	0.11
Flow-ups						
1 wk	1	−2.80 (−12.01 to 6.41)	0.55	1	−8.24 (−22.98 to 6.51)	0.27
4 wks	1	−3.52 (−15.77 to 8.73)	0.57	1	−6.43 (−22.02 to 9.16)	0.42
6 wks	1	−0.25 (−1.36 to 0.86)	0.66	1	−0.75 (−1.70 to 0.20)	0.12
Type of corticosteroid						
Dexamethasone	1	−3.52 (−15.77 to 8.73)	0.56	1	−6.43 (−22.02 to 9.16)	0.81
Betamethasone						
Methylprednisolone	1	−0.25 (−1.36 to 0.86)	0.44	1	−0.75 (−1.70 to 0.20)	0.12

unspecified pain outcomes were added. Finally, SIS definitions in the included studies varied because of a lack of well-defined diagnostic criteria for SIS,[45] and the systematic search was limited to the English and Chinese languages, which may have resulted in some relevant trials being missed.

Implications

Ultrasound-guided injections are associated with several advantages including the lack of radiation exposure; therefore, this technique has gained widespread use in recent years, replacing the conventional ALG injection, also known as "blind" approach.[46] In our study, few cases of adverse events were reported in the safety analysis, although only six studies reported this outcome. Therefore, based on our findings, we recommend USG corticosteroid injection as an efficient and safe intervention for patients with SIS, particularly when a physician or therapist is not well trained and proficient in using ALG injection, both of which can achieve similar accuracy and efficacy when administered by an experienced provider.[41] Although some researchers have expressed concerns regarding the lack of efficacy of USG injections to justify their higher cost, a cost-effectiveness analysis has not been performed in current evidence to address these concerns.[41] Until this analysis is conducted, the decision regarding the use of USG versus ALG injections should be primarily informed by evidence from currently available efficacy analysis.

CONCLUSIONS

The meta-analysis in this study provides moderate to very low evidence that USG corticosteroid injection for the management of SIS results in significant pain relief and improvement in physical function of the shoulder as compared with ALG injection. Short-term retention between 6 and 8 wks after injection and the type of corticosteroid used potentially affect the treatment efficacy of USG as reported in this study. Adverse events were relatively low in both groups, which justifies the safety and efficacy of USG injection in treating SIS. Future research should optimize the study design (taking factors not limited to a clear definition of SIS), perform a cost-effective analysis, include longer follow-up periods and larger sample size, and perform an intention-to-treat analysis to generate high certainty evidence.

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