Original Article

Single-Site Corticosteroid Injection Is as Effective as Multisite Corticosteroid Injection in the Nonsurgical Treatment of Frozen Shoulder: A Systematic Review With Meta-Analysis of Randomized Controlled Trials

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Purpose: To determine whether multisite corticosteroid injection is more effective than a single injection in the nonsurgical treatment of frozen shoulder (FS) via a meta-analysis of randomized controlled trials **Methods:** We identified studies that evaluated the efficacy of multisite corticosteroid injections compared with single-site injection for FS. The Embase, PubMed, and Cochrane Library databases were systematically searched from inception to June 5, 2022. Methodologic quality and risk of bias were assessed using the Modified Coleman Methodology Score and the Cochrane Collaboration risk of bias tool, respectively. Visual analog scale scores, abduction, flexion, internal rotation, external rotation, American Shoulder and Elbow Surgeons Assessment Form scores, Constant−Murley Shoulder scores, and complications were extracted. The meta-analysis was conducted with random effects, and 4 time intervals were analyzed: 3 to 4 weeks, 6 to 8 weeks, 12 to 16 weeks, and 24 to 26 weeks **Results:** The initial search identified 260 studies, and 5 randomized controlled trials that met the inclusion criteria were included. There were no significant differences in visual analog scale scores at 3 to 4 weeks, 6 to 8 weeks, 12 to 16 weeks, or 24 to 26 weeks. There were no significant differences in flexion or external rotation at 3 to 4 weeks, 6 to 8 weeks, 12 to 16 weeks, or 24 to 26 weeks. Multisite injection performed better in terms of abduction (mean difference −15.66 [−30.03, −1.28], $P = .03$) and American Shoulder and Elbow Surgeons Assessment Form score (mean difference −10.13 [−19.54, −0.72] $P = .03$) than single-site injection at 3 to 4 weeks. There were significant differences in internal rotation in favor of the multisite treatment at 3 to 4 weeks, 6 to 8 weeks, 12 to 16 weeks, and 24 to 26 weeks. In addition, there were no significant differences in complications. **Conclusions:** Single-site steroid injection is as effective as multisite corticosteroid injection for the nonoperative treatment of FS. **Level of Evidence:** Level II, meta-analysis of Level I and II studies.

Frozen shoulder (FS), also known as adhesive capsulitis, is a common, self-limiting shoulder disorder, with an incidence rate of 2% to 5% in the general population.[1-3] It has been characterized by the insidious onset of pain coupled with substantial restriction of active and passive movement of the glenohumeral joint.[4,5] As a result, patients often have difficulty performing daily activities and falling asleep at night.[6,7] The current studies attempt to explain the molecular pathways mechanism of shoulder freezing from the perspective of immunobiology, which is still poorly understood.[8,9] The diagnosis of FS is based on recognizing the characteristic features, and radiographs are only valuable for ruling out other pathologies of the shoulder joint.[10,11]

FS comprises 3 overlapping clinical stages: an insidious painful freezing phase (duration 10-36 weeks), a shoulder adhesive phase (duration 4-12 months), and a resolution phase (duration 12-42 months). Most patients experience spontaneously resolution in 2 or 3 years; however, the recovery might be beyond the estimated time frame or incomplete.[10,12,13] In addition, simultaneous bilateral involvement occurs in

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14% of the patients, and 20% of patients develop similar symptoms in the opposite shoulder.[13,14] Therefore, it is necessary to treat patients with FS to improve their quality of life.

A myriad of treatment modalities are available for patients with FS, including oral analgesia, steroid injection, physiotherapy, hydrodistension, acupuncture, manipulation under anesthesia, and arthroscopic or open capsular release.[3] However, there is still uncertainty about the optimal option for patients and treating health care professionals.[3,15] It is worth noting that corticosteroid injections, especially when coupled with physiotherapy exercise, have a better effect than a single treatment and are highly accepted in clinical practice at present.[12,16,17] Numerous previous studies have analyzed the effectiveness of different single injection sites in the shoulder. The effectiveness of multisite corticosteroid injections is unknown.[18,19] The purpose of this study was to determine whether multisite corticosteroid injection is more effective than a single injection in the nonsurgical treatment of FS via a meta-analysis of randomized controlled trials (RCTs). We hypothesized that multisite corticosteroid injection is superior to a single-site injection in pain relief, range of motion (ROM) and function for FS.

Methods

This review of literature adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) statement and checklist.[20]

Search Strategy

Two authors independently searched the Embase, PubMed, and Cochrane Library databases from inception to June 5, 2022, and the reference lists of published systematic reviews for relevant studies. The search specifics were as follows: ''(((((Multisite) OR (sites)) OR (dual-target)) OR (two targets)) AND (((((((((corticosteroid) OR (glucocorticoid)) OR (triamcinolone)) OR (methylprednisolone)) OR (hydrocortisone)) OR (prednisolone)) OR (cortisone)) OR (dexamethasone)) OR (betamethasone))) AND ((((((((((((((((((((((((Bursitides) OR (Bursitis)) OR (Periarthritis)) OR (Frozen Shoulder)) OR (Frozen Shoulders)) OR (Shoulder, Frozen)) OR (Adhesive Capsulitis of the Shoulder)) OR (Shoulder Adhesive Capsulitis)) OR (Adhesive Capsulitides, Shoulder)) OR (Adhesive Capsulitis, Shoulder)) OR (Capsulitides, Shoulder Adhesive)) OR (Capsulitis, Shoulder Adhesive)) OR (Shoulder Adhesive Capsulitides)) OR (Capsulitis)) OR (Capsulitides)) OR (Pes Anserine Bursitis)) OR (Bursitides, Pes Anserine)) OR (Bursitis, Pes Anserine)) OR (Pes Anserine Bursitides)) OR (Adhesive Capsulitis)) OR (Adhesive Capsulitides)) OR (Capsulitides, Adhesive)) OR (Capsulitis, Adhesive)) OR (Stiff Shoulder)).'' No language restrictions or study types were imposed.

Study Selection Process

The same 2 authors independently screened all titles and abstracts for relevance and eligibility. After the screening, chance-adjusted agreement was assessed by kappa value (0-0.20, poor agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, good agreement; and 0.81-1.00, perfect agreement).[21] A third author resolved any disagreements. Studies were reviewed if they met the following PICOS (patients, intervention, comparison, outcome, and study type) criteria:

P: Patients with FS;

I: Multisite corticosteroid injection;

C: Single-site corticosteroid injection;

O: Visual analog scale (VAS) score, ROM, American Shoulder and Elbow Surgeons (ASES) score,[22] or Constant–Murley score[23] (at least 1 outcome); and

S: Level I or II study.

The exclusion criteria were as follows: (1) animal study; (2) cell study; (3) short communication or conference abstracts; and (4) intervention that did not involve steroid injections.

Assessment of Literature and Methodologic Quality

The same 2 authors used the Levels of Evidence for Primary Research Question to assess literature quality[24] and the Modified Coleman Methodology Score (MCMS).[25] The MCMS has a scaled potential score ranging from 0 to 100 to evaluate inclusion criteria, sample size calculation, randomization, follow-up, patient analysis, blinding, similarity in treatment, treatment description, group comparability, outcome assessment, description of rehabilitation protocol, clinical effect measurement, and the number of patients treated.[25] A score of 85 to 100 means excellent, 70 to 84 means good, 55 to 69 means fair, and less than 55 means poor.[25] The kappa score, which evaluates the degree of agreement between authors, was calculated.[21]

Assessment of Risk of Bias

The Cochrane Collaboration risk-of-bias tool was used to evaluate the risk of bias in the included studies; it contains the following domains: bias of random sequence generation (selection bias), bias of allocation concealment (selection bias), bias of blinding participants and personnel (performance bias), bias of blinding outcome assessment (detection bias), bias of missing outcome data (attrition bias), bias of selective reporting (reporting bias), and other bias.[26] The same 2 authors independently assessed the bias of the included RCTs by scoring them as low, unclear, or high risk. Any

discrepancies were resolved by discussion, and the third reviewer made the final decision.

Data-Extraction Process

Two same authors independently collected available data from the included studies. The following essential characteristics were collected: author, year, journal, country, male sex, age, duration of symptoms, follow-up, Level of Evidence, inclusion criteria, injection material, injection content, injection site, ultrasonographic guidance, approach, and physiotherapy program. In addition, VAS pain scores, abduction, flexion, internal rotation, external rotation, ASES Assessment Form scores,[22] Constant–Murley Shoulder scores,[23] and complications were extracted as outcome measurements, and 4 time intervals of these measures were analyzed. We contacted the author to obtain missing data and extracted the mean value using Origin software (Version 2021; OriginLab Corp., Northampton, MA) when data were presented in figures.

Data Synthesis

This meta-analysis was performed with Review Manager, version 5.3 (The Cochrane Collaboration,). Statistical heterogeneity was assessed with I^2 statistics as follows: $0\% < I^2 < 25\%$, unimportant heterogeneity; $25\% < I^2 < 50\%$, moderate heterogeneity; and $I^2 > 50\%$, important heterogeneity. We used a random-effects model for all comparisons because disease phases increase the risk of heterogeneity. The treatment effects of all continuous were measured by mean differences (MDs) with 95% confidence intervals (95% CIs). Dichotomous were measured by risk ratios and 95% CIs. If the comparisons with more than 1 met eligible intervention groups, the control group was divided into more groups with a smaller sample size that allowed all suitable comparisons to be included.[27] If the outcome measures were reported as the mean and 95% CI, standard deviation (SD) values were estimated using "Finding the Standard Deviation using Confidence Intervals" in the Excel version of the RevMan Calculator (Microsoft, Redmond, WA). When the outcome measures were reported in the mean and standard error of the mean, SD values were estimated with the following formula: SD = standard error of the mean × sqrt(n), where sqrt is the square root and n is the number of participants.

In all analyses, a *P* value of .05 was considered statistically significant. Data analyses were performed for the following intervals: (1): 3 to 4 weeks; (2): 6 to 8 weeks; (3): 12 to 16 weeks, and (4): 24 to 26 weeks. When the number of included studies was less than 10, publication bias was not considered.[27] To assess the robustness of the effect sizes, we performed a sensitivity analysis by extracting all high heterogeneity results that synthesized more than 2 studies during 4 time intervals

Results

Identification of Studies

The results of the initial search yielded 260 studies (PubMed = 21, Embase = 126, Cochrane = 113). After the removal of 27 duplicates, 233 studies remained, and 5 were deemed eligible for further screening. Thus, 5 studies were carefully reviewed.[28-32] However, one study[28] was a short communication that did not meet our inclusion criteria, and one additional study[33] was identified from the citation search. Finally, 5 RCTs were included in this review[29-33] (Fig 1). The kappa score was 0.88, indicating perfect agreement.

Basic Characteristics of Included Studies

All of the studies were published in different journals. Of the 5 studies, 2 RCTs[29,30] were from South Korea, and the others were from Norway,[33] India,[31] and Turkey.[32] The minimum follow-up time was 12 weeks.[30] There were three Level I and two Level II studies (Table 1).

All studies included patients with shoulder pain and limited motion. Specifically, one study inclusion criteria were pained with limitation of both active and passive shoulder movements in at least 2 directions (forward flexion <120° or 50% restriction of contralateral external rotation and internal rotation).[29] In addition, patients in two studies were assessed for pain and passive restriction of shoulder motion.[30,33] One study[31] did not report the specific restriction, whereas another study[32] reported that inclusion criteria for patients had lost more than 20% of their shoulder movements in all directions. Cho et al.[30] used 2 different length needles (3 cm and 6 cm) for intra-articular and subacromial injection respectively. One study[31] used a 16-gauge needle, and another study[32] only reported 20-mL needles. Three studies used a 40-mg dose for injection,[29-31] and a 20-mg dose was used in one study.[33] A sham injection was performed in one study.[33] In addition, one RCT used a 40-mg dose for single-site injection and 80 mg for multisite injection.[32] In this study, injection sites include the glenohumeral joint, posteroinferior capsule, subacromial space, posterosuperior capsule, biceps long head, and area around the coracohumeral ligament. Multisite injection was selected for the glenohumeral joint combined with the subacromial space in 2 studies.[29,30] Three injection sites were selected in one RCT,[31] and 4 sites were selected in one study.[32] Ultrasound-assisted injection was reported in 4 studies.[29,30,32,33] Except for 2 studies[30,32,] reporting 2 approaches of multisite injection, all injection approaches were posterior approaches. Three RCTs

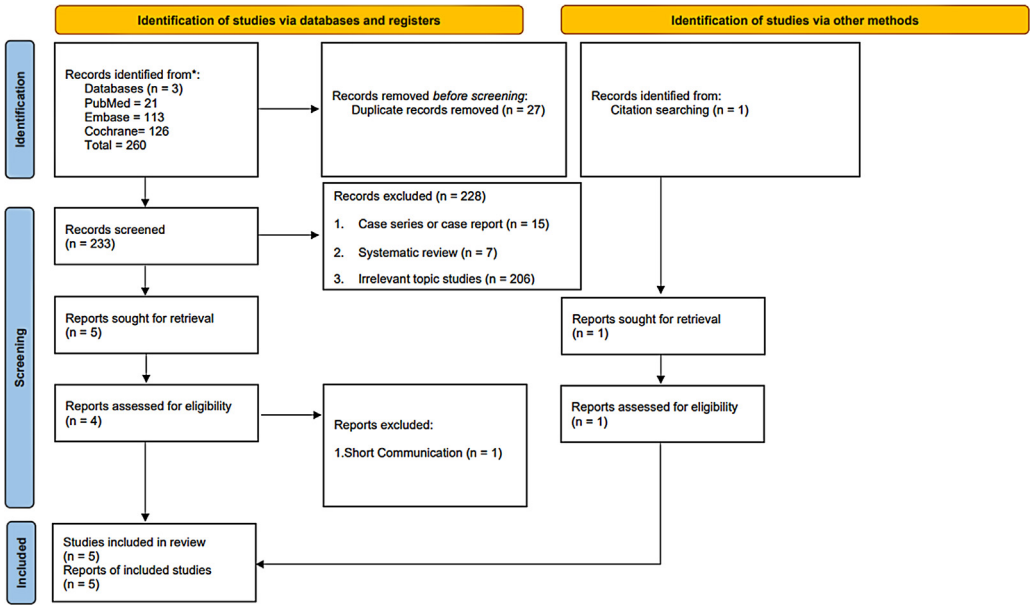

Fig 1. 2020 PRISMA flow chart. The authors followed the 2020 PRISMA guidelines. (PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.)

reported the combination of physical therapy and injections (Table 2).[29,30,32]

Assessment of Literature and Methodologic Quality

According to the MCMS, there were 3 excellent quality studies[29,30,32] and 2 good-quality studies.[31,33] Only one study obtained a score for follow-up, reducing the variability among studies.[32] Two studies[29,33] received fair scores in the description of the surgical procedure, and 2 studies[31,33] did not receive any points for postoperative rehabilitation that may hinder the clinical interpretation of the results. Only 1 study[32] obtained a perfect score in assessing outcomes that enhanced the efficacy of the clinical results. However, the scores of this study[32] were reduced in the description of the subject selection process due to the long assessment period and the small number of patients lost to follow-up (Table 3). There was a very good agreement between authors according to the kappa score (0.88).

Assessment of Risk of Bias

All 5 studies had a low risk of bias in random sequence generation and allocation concealment. One study was a single-blind clinical study, which increased the risk of performance bias.[32] There was no detailed description of the blinding method used in the process in the 3 studies,[29,30,31] and there was an unclear risk of performance bias and detection bias. Pushpasekaran et al.[31] only reported Constant-Murley score, and they did not report total structured values, such as SD or standard error and other outcomes. Thus, this study was rated as having a high risk of attrition bias and reporting bias. Finally, 3 studies did not report the experience of the injectors, indicating that they had unclear risks[29,30,31] (Fig 2).

Visual Analog Scale

Four studies[29,30,32,33] reported VAS scores at 3 to 4 weeks, and one study[29] presented the results in figures (Appendix Table 1, available at www.arthroscopyjournal.org). The results revealed that there were no statistically significant differences in VAS scores (MD 1.19 [−0.05 to 2.43], $P = .06$), and the heterogeneity was high ($I^2 = 90\%$; $P < .00001$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data (Fig 3).

When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 2 studies[30,33] showed no significant differences between multisite group and single-site group for VAS scores (MD 0.77 [−0.46 to 2.01], $P = .22$), and the heterogeneity was 85%. (Appendix Figure 1, available at www.arthroscopyjournal.org)

Three studies[29,30,33] reported VAS scores at 6 to 8 weeks, and one study[29] presented the results in figures. The results revealed that there were no statistically significant differences in VAS scores (MD 0.38 [−0.66 to 1.41], $P = .48$), and the heterogeneity was high ($I^2 = 77\%$; $P = .01$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

Four studies[29,30,32,33] reported VAS scores at 12 to 16 weeks. The results revealed that there were no statistically significant differences in VAS scores (MD 0.54 [−0.10 to 1.17], $P = .10$), and the heterogeneity was

Table 1. Characteristics of the Studies Included in this Systematic Review

Study	Year	Journal	Country	Male	Age	Duration of symptoms	Follow-up	LOE
Shin et al.[29]	2013	*Journal of Shoulder and Elbow Surgery*	South Korea	IA: 16 SA: 14 IA+SA: 14	IA: 55.1 ± 4.6* SA: 53.9 ± 4.16* IA+SA: 56.3 ± 5.86*	IA: 7.4 ± 3.46* mo SA: 7.7 ± 3.36* mo IA+SA: 7.0 ± 2.66* mo	24 wk	II
Prestgaard et al.[33]	2015	*Pain*	Norway	IA: 15 Combined: 15 Sham: 14	IA: 53.2 ± 6.96* Combined: 55 ± 7.26* Sham: 55.4 ± 7.26*	IA: 15.1 ± 4.66* wk Combined: 15.0 ± 5.96* wk Sham: 15.0 ± 5.66* wk	26 wk	I
Cho et al.[30]	2016	*Joint Bone Spine*	South Korea	IA:10 SA: 16 IA+SA: 18	IA: 59.1 ± 7.9[a] SA: 56.0 ± 9.46* IA+SA: 54.8 ± 8.36*	IA: 5.3 ± 3.66* mo SA: 4.6 ± 3.56* mo IA+SA: 5.0 ± 4.56* mo	12 wk	I
Pushpasekaran et al.[31]	2017	*Journal of Orthopaedic Surgery*	India	SS: 12 TS: 17	SS: 56.4 ± 4.326* TS: 56.24±5.42[a]	SS: 15.2 ± 13.746* TS: 14.82 ± 13.656*	24 wk	II
Koraman et al.[32]	2021	*Arthroscopy: The Journal of Arthroscopic and Related Surgery*	Turkey	SI: 9 MI: 13	SI: 54 ± 5.66* MI: 53.7 ± 7.76*	SI: 2.8 ± 1.56* MI: 2.7 ± 1.76*	48 wk	I

IA, intra-articular; LOE, Level of Evidence; MI, multisite injection; SA, subacromial; SD, standard deviation; SI, single injection; SS, single site; TS, three sites.
*Mean ± SD.

high (I^2 = 83%; P < .0001). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data. When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 3 studies[29,30,33] showed no significant differences between multisite group and single-site group for VAS scores (MD 0.20 [−0.08 to 0.48], P = .17), and the heterogeneity was 16%.

Three studies[29,32,33] reported VAS scores at 24 to 26 weeks, and one study[29] presented the results in figures. The results revealed that there were no statistically significant differences in VAS scores (MD 0.50 [−1.26 to 2.27], P = .58), and the heterogeneity was high (I^2 = 87%; P = .006). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

Abduction

Three studies[30,32,33] reported abduction at 3 to 4 weeks (Appendix Table 2, available at www.arthroscopyjournal.org). The results revealed that the multisite group had better abduction than the single-site group (MD −15.66 [−30.03 to −1.28], P = .03), and the heterogeneity was high (I^2 = 83%; P = .0006). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data (Fig 4).

When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 2 studies[30,33] showed no significant differences between multisite group and single-site group for abduction (MD −11.07 [−26.20 to 4.07], P = .15), and the heterogeneity was 80% (Appendix Figure 2, available at www.arthroscopyjournal.org).

Two studies[30,33] reported abduction at 6 to 8 weeks. The results revealed that there were no statistically significant differences in abduction (MD −6.65 [−16.38 to 3.07], P = .18), and the heterogeneity was high (I^2 = 63%; P = .07). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

Three studies[30,32,33] reported abduction at 12 to 16 weeks. The results revealed that there were no statistically significant differences in abduction (MD −13.35 [−28.61 to 1.90], P = .09), and the heterogeneity was high (I^2 = 85%; P = .0001). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data. When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 2 studies[30,33] showed no significant differences between multisite group and single-site group for abduction (MD −5.68 [−12.34 to 0.97], P = .09), and the heterogeneity was 4%.

Two studies[32,33] reported abduction at 24 to 26 weeks. The results revealed that there were no statistically significant differences in abduction (MD −15.11 [−51.44 to 21.23], P = .42), and the heterogeneity was high (I^2 = 91%; P = .0007). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

Flexion

Four studies[29,30,32,33] reported flexion at 3 to 4 weeks, and one study[29] presented the results in figures (Appendix Table 3, available at www.arthroscopyjournal.org). The results revealed that there were no statistically significant differences in flexion (MD −12.21

Table 2. Summary of Injection Administrations

Author	Inclusion Criteria	Injection Material	Injection Content	Corticosteroid Injection Site	US-Guided	Approach	Physiotherapy Program
Shin et al.[29]	Pain with limitation of both active and passive shoulder movement in at least 2 directions (forward flexion <120° or 50% restriction of contralateral external rotation and internal rotation)	NS	IA: 40 mg of triamcinolone (1 mL) with 4 mL of 2% lidocaine.	IA: glenohumeral joint	Yes	Posterior	Yes
			SA: 40 mg of triamcinolone (1 mL) with 4 mL of 2% lidocaine.	SA: Subacromial space			
			IA+SA: 40 mg of triamcinolone (1 mL) with 4 mL of 2% lidocaine equally divided between the 2 sites.	IA+SA: glenohumeral joint combined with subacromial space			
Prestgaard et al.[33]	Pain and stiffness restriction of passive motion 30° in 2 or more planes of movement	NS	IA: 20 mg of triamcinolone hexacetonide (1 mL) with 2.5 mL lidocaine. 3.5 mL lidocaine10 mg/mL into the rotator interval/anterior capsule.	IA: glenohumeral joint	Yes	Posterior	NR
			Combined group: 10 mg of triamcinolone (0.5 mL) + 3 mL lidocaine into the 2 sites.	Combined group: glenohumeral joint + along with the long head of the biceps and into the anterior capsule			
			Sham group: 3.5 mL lidocaine injected into the 2 sites.	Sham group: glenohumeral joint + along with the long head of the biceps and into the anterior capsule			

(continued)

Table 2. Continued

Author	Inclusion Criteria	Injection Material	Injection Content	Corticosteroid Injection Site	US-Guided	Approach	Physiotherapy Program
Cho et al.[30]	Pain with limitation of passive motion of greater than 30° in two or more planes of movement (stage 2 or 3)	IA: a 25-gauge, 6-cm-long needle	IA: 40 mg of triamcinolone acetonide and 4 mL of 1% lidocaine	IA: glenohumeral joint	Yes	IA: Posterior SA: Superior IA+SA: Posterior and Superior	Yes
		SA: a 25-gauge, 3-cm-long needle	SA: 40 mg of triamcinolone acetonide and 4 mL of 1% lidocaine	SA: subacromial space			
		IA+SA: 25-gauge, 3- and 6-cm-long needle	IA+SA: 40 mg of triamcinolone acetonide and 4 mL of 1% lidocaine equally divided between the 2 sites.	IA+SA: glenohumeral joint combined with subacromial space			
Pushpasekaran et al.[31]	Pain and restricted movements	16-gauge needle	SS: 40 mg of methylprednisolone acetate mixed with 2 mL of 2% lignocaine	SS: glenohumeral joint	NS	Posterior	NR
			TS: 40 mg of methylprednisolone acetate mixed with 2 mL of 2% lignocaine and 8 mL of normal saline and instilled at 3 sites	TS: posterior capsule, subacromial and subcoracoid			
Koraman et al.[32]	Pain and a loss of ROM greater than 20% in all directions (stage 2)	20-mL syringes	SI: 40 mg of triamcinolone acetonide (1 mL) and 2 mL of bupivacaine (0.5%)	SI: glenohumeral joint	Yes	SI: Posterior	Yes
			MI*: 80 mg (40 mg/mL) of triamcinolone acetonide (2 mL), 4 mL of bupivacaine (0.5%), and 34 mL of saline solution (total 40 mL).	MI: Glenohumeral joint and posteroinferior capsule (site 1) Subacromial space (site 2) Posterosuperior capsule (site 3) Biceps long head and area around the coracohumeral ligament (site 4)		MI: Posterior (sites 1 and 2) Superomedial (sites 3 and 4)	

DT, dual-target; IA, intra-articular; LOE, Level of Evidence; MI, multisite injection; NS, not shown; ROM, range of motion; SA, subacromial; SI, single injection; SS, single site; ST, standard target; TS, three sites; US-Guided, ultrasonography-guided.

*NOTE: 5 mL into the glenohumeral joint, 5 mL into the posteroinferior capsule, 10 mL into the posterosuperior capsule, and 10 mL into the biceps long head and around the coracohumeral ligament.

Table 3. Modified Coleman Methodology Score (MCMS)

	Assessment	Shin et al.[29]	Prestgaard et al.[33]	Cho et al.[30]	Pushpasekaran et al.[31]	Koraman et al.[32]
Part A	1. Study size	10	10	10	10	10
	2. Mean Follow-up	0	0	0	0	2
	3. Number of different surgical procedures	10	10	10	10	10
	4. Type of study	15	15	15	10	15
	5. Diagnostic certainty	5	5	5	5	5
	6. Description of the surgical procedure given	3	3	5	5	5
	7. Description of postoperative rehabilitation	10	0	10	0	10
Part B	1. Outcome criteria	10	10	10	10	10
	2. Procedure to assess outcomes	8	12	12	9	15
	3. Description of the subject selection process	15	15	15	15	13
	Total score	86	80	92	74	95

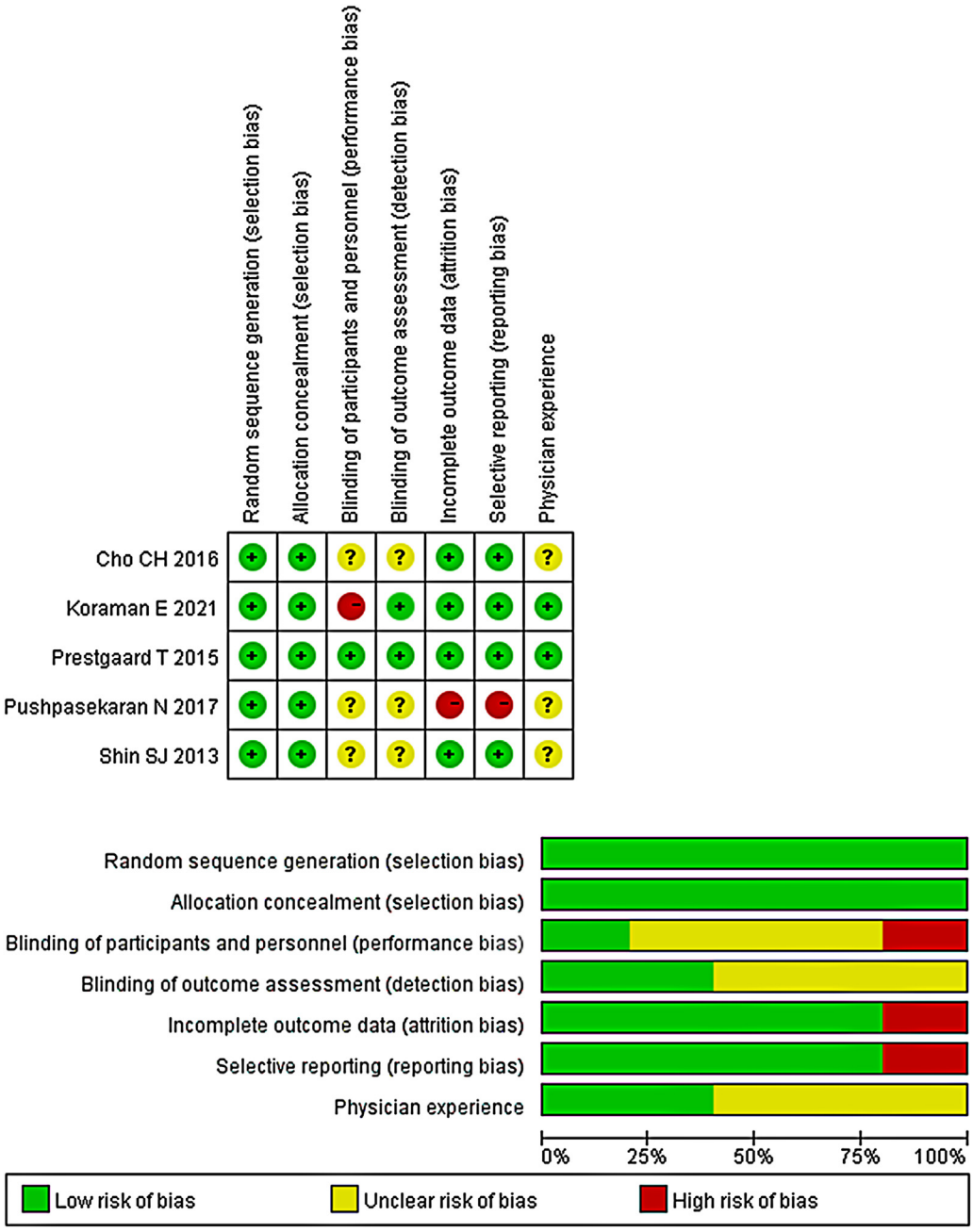

Fig 2. Risk of bias graph and summary.

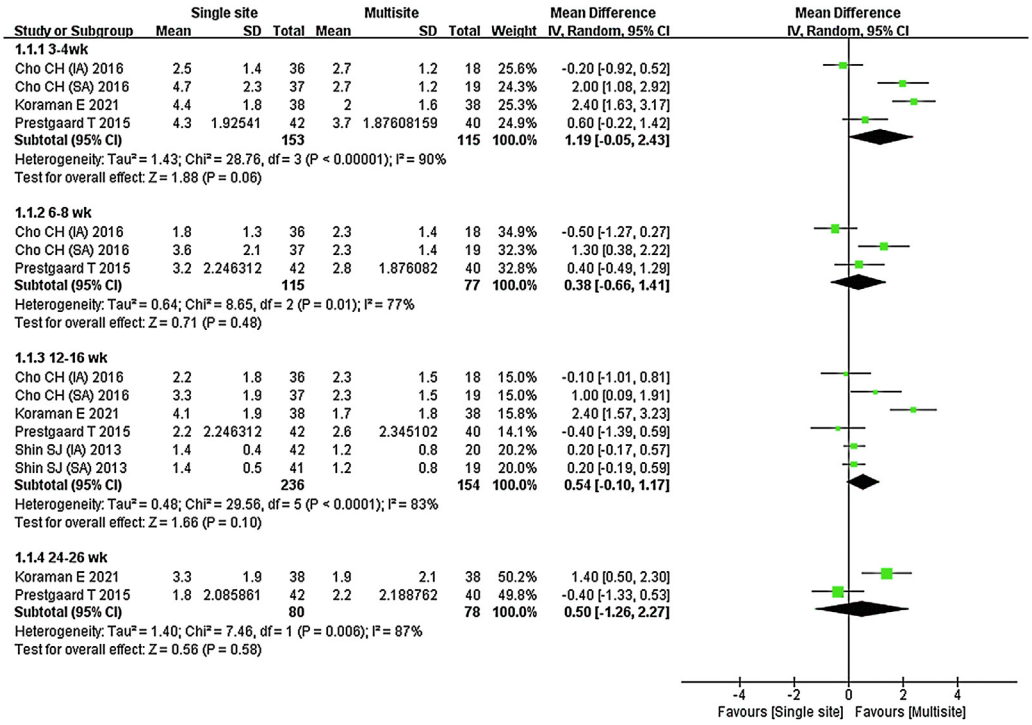

Fig 3. Forest plot showing the results of visual analog scale scores. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)

[−24.49 to 0.08], $P = .05$), and the heterogeneity was high ($I^2 = 85\%$; $P = .0002$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data (Fig 5).

When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 2 studies[30,33] showed no significant differences between multisite group and single-site group for flexion (MD −7.93 [−20.11 to 4.25], $P = .20$), and the heterogeneity

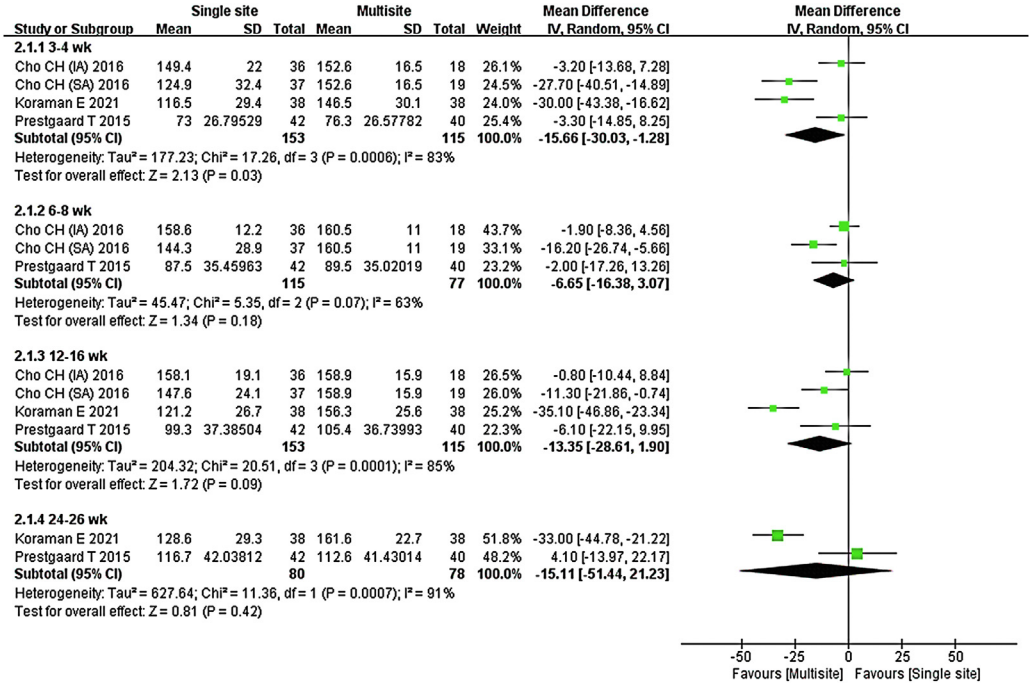

Fig 4. Forest plot showing the results of abduction. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)

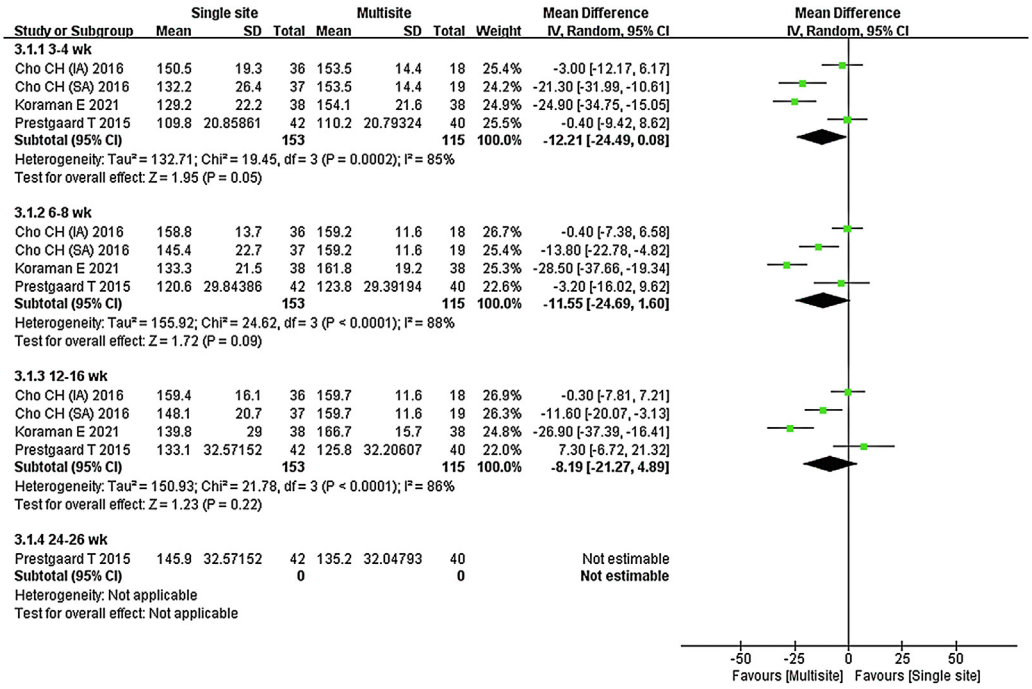

Fig 5. Forest plot showing the results of flexion. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)

was 79% (Appendix Figure 3, available at www.arthroscopyjournal.org).

Four studies[29,30,32,33] reported flexion at 6 to 8 weeks, and one study[29] presented the results in figures. The results revealed that there were no statistically significant differences in flexion (MD −11.55 [−24.69 to 1.60], $P = .09$), and the heterogeneity was high ($I^2 = 88\%$; $P < .0001$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 2 studies[30,33] showed no significant differences between multisite group and single-site group for flexion (MD

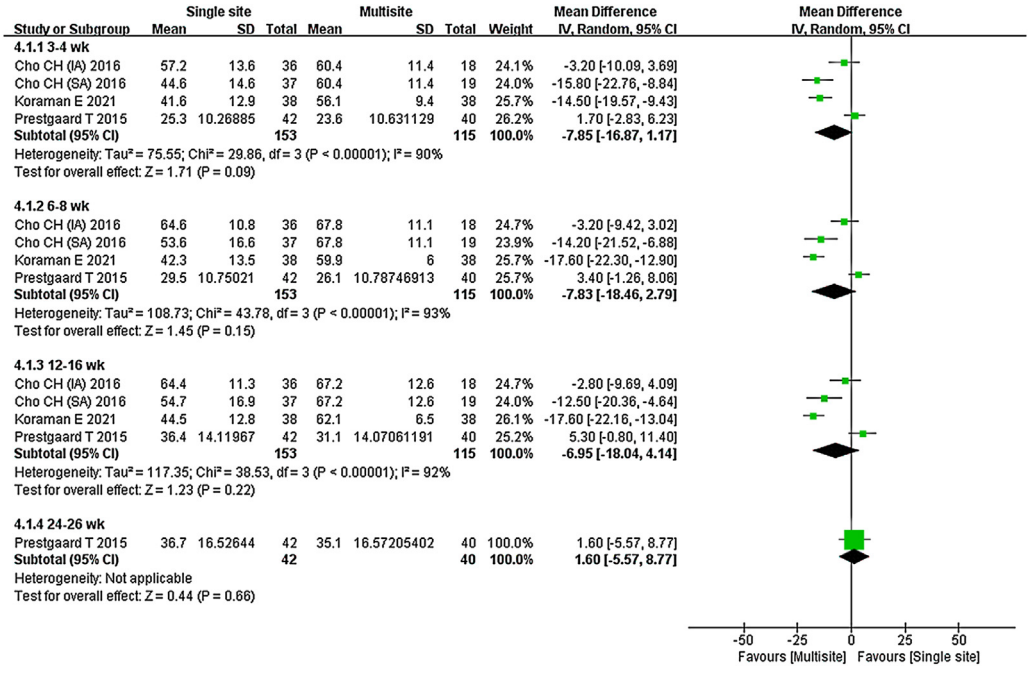

Fig 6. Forest plot showing the results of external rotation. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)

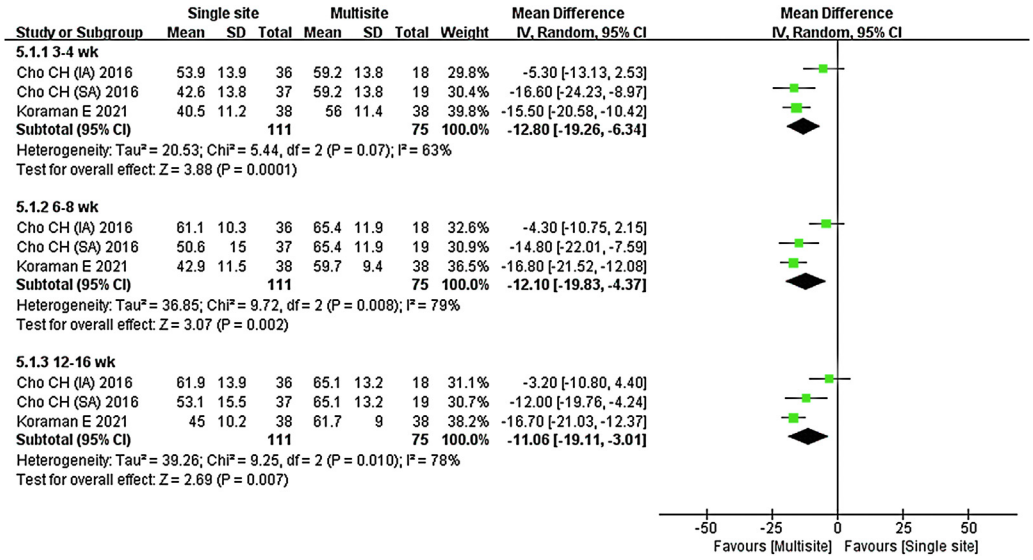

Fig 7. Forest plot showing the results of internal rotation. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)

−5.68 [−14.61 to 3.13], $P = .20$), and the heterogeneity was 63%.

Four studies[29,30,32,33] reported flexion at 12 to 16 weeks, and one study[29] presented the results in figures. The results revealed that there were no statistically significant differences in flexion (MD −8.19 [−21.17 to 4.89], $P = .22$), and the heterogeneity was high ($I^2 = 86\%$; $P < .0001$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 2 studies[30,33] showed no significant differences between multisite group and single-site group for flexion (MD −2.51 [−12.50 to 7.47], $P = .09$), and the heterogeneity was 69%. Two studies[29,33] reported flexion at 24 to 26 weeks, and one study[33] presented the results in figures.

External Rotation

Four studies[29,30,32,33] reported external rotation at 3-4 weeks, and one study[29] presented the results in figures (Appendix Table 4, available at www.arthroscopyjournal.org). The results revealed that there were no statistically significant differences in external rotation (MD −7.85 [−16.87 to 1.17], $P = .09$), and the heterogeneity was high ($I^2 = 90\%$; $P < .00001$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data (Fig 6).

When we excluded the study that caused the greatest heterogeneity due to bias,[33] the pooled analysis of 2 studies[30,32] favor multisite group for external rotation (MD −11.31 [−18.71 to −3.92], $P = .003$), and the heterogeneity was 76% (Appendix Figure 4, available at www.arthroscopyjournal.org).

Four studies[29,30,32,33] reported external rotation at 6-8 weeks, and one study[29] presented the results in figures. The results revealed that there were no statistically significant differences in external rotation (MD −7.83 [−18.46 to 2.79], $P = .15$), and the heterogeneity was high ($I^2 = 93\%$; $P < .00001$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

When we excluded the study that caused the greatest heterogeneity due to bias[33], the pooled analysis of 2 studies[30,32] favor multisite group for external rotation (MD −11.76 [−20.71 to −2.81], $P = .010$), and the heterogeneity was 85%.

Four studies[29,30,32,33] reported external rotation at 12 to 16 weeks, and one study[29] presented the results in figures. The results revealed that there were no statistically significant differences in external rotation (MD −6.95 [−18.04 to 4.14], $P = .22$), and the heterogeneity was high ($I^2 = 92\%$; $P < .00001$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

When we excluded the study that caused the greatest heterogeneity due to bias,[33] the pooled analysis of 2 studies[30,32] favor multisite group for external rotation (MD −11.19 [−20.30 to −2.08], $P = .02$), and the heterogeneity was 84%.

Two studies[29,33] reported external rotation at 24 to 26 weeks, and one study[29] presented the results in figures.

Internal Rotation

Two studies[30,32] reported internal rotation at 3-4 weeks (Appendix Table 5, available at www.arthroscopyjournal.org). The results revealed that there were significant differences in internal rotation in

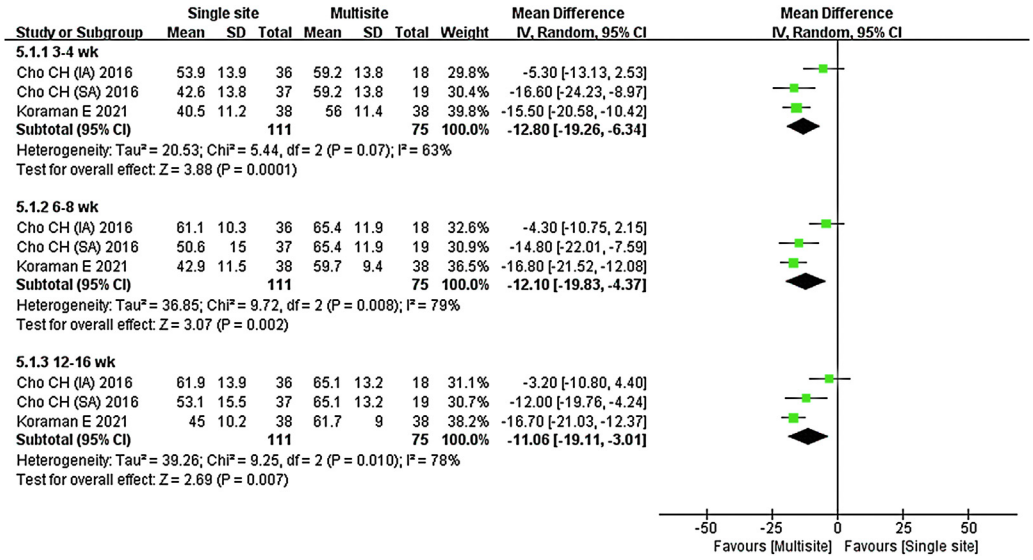

Fig 8. Forest plot showing the results of American Shoulder and Elbow Surgeons Assessment Form scores. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)

favor of the multisite treatment (MD −12.80 [−19.26 to −6.34], $P = .0001$), and the heterogeneity was high ($I^2 = 63\%$; $P = .07$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data (Fig 7).

Two studies[30,32] reported internal rotation at 6 to 8 weeks. The results revealed that there were significant differences in internal rotation in favor of the multisite treatment (MD −12.10 [−19.83 to −4.37], $P = .002$), and the heterogeneity was high ($I^2 = 79\%$; $P = .008$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

Two studies[30,32] reported internal rotation at 12 to 16 weeks. The results revealed that there were significant differences in internal rotation in favor of the multisite treatment (MD −11.06 [−19.11 to −3.01], $P = .007$), and the heterogeneity was high ($I^2 = 78\%$; $P = .010$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

ASES Score

Three studies[29,30,32] reported ASES scores at 3 to 4 weeks (Appendix Table 6, available at www.arthroscopyjournal.org).). The results revealed that there were significant differences in ASES scores in favor of the multisite treatment (MD −10.13 [−19.54, −0.72], $P = .03$), and the heterogeneity was high ($I^2 = 87\%$; $P < .00001$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data (Fig 8).

When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 2 studies[29,30] showed no significant differences between multisite group and single-site group for ASES scores (MD −6.79 [−15.24 to 1.66], $P = .12$), and the heterogeneity was 80% (Appendix Figure 5, available at www.arthroscopyjournal.org).

Three studies[29,30,32] reported ASES scores at 6 to 8 weeks. The results revealed that there were no statistically significant differences in ASES scores (MD −7.46 [−17.45 to 2.53] $P = .14$), and the heterogeneity was high ($I^2 = 88\%$; $P < .00001$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 2 studies[29,30] showed no significant differences between multisite group and single-site group for ASES scores (MD −3.07 [−9.55 to 3.42], $P = .35$), and the heterogeneity was 64%.

Three studies[29,30,32] reported ASES scores at 12 to 16 weeks. The results revealed that there were no statistically significant differences in ASES scores (MD −6.36 [−13.00 to 0.28] $P = .06$), and the heterogeneity was high ($I^2 = 66\%$; $P = .02$). The result suggests that current statistics are underpowered, which makes it hard to draw strong inferences from the available data.

When we excluded the study that caused the greatest heterogeneity due to bias,[32] the pooled analysis of 2 studies[29,30] showed no significant differences between multisite group and single-site group for ASES scores (MD −3.64 [−9.10 to 1.81], $P = .19$), and the

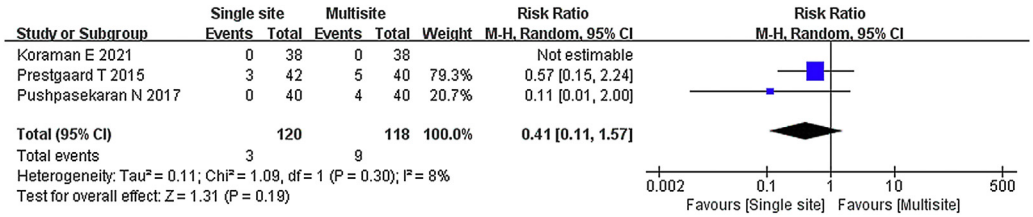

Fig 9. Forest plot showing the results of complications. (CI, confidence interval; MH, Mantel-Haenszel.)

heterogeneity was 32%. One study[29] reported the ASES scores at 24 to 26 weeks.

Complications

Five studies reported complications.[29-33] (Appendix Table 7, available at www.arthroscopyjournal.org) However, 2 studies did not report whether the patients belonged to the multisite injection group or the single site injection group, so the results could not be further analyzed.[29,30] The poor results revealed that there were no statistically significant differences in complication events (risk ratio 0.41 [0.11-1.57]), and the heterogeneity was low ($I^2 = 8\%$; $P = .19$) (Fig 9).

Discussion

Most clinical outcomes assessed in this study (VAS scores, abduction, flexion, external rotation, and ASES scores) showed no significance between multisite group and single-site group with high heterogeneity that make a conclusion from the results unreliable. In most sensitivity analyses, the greatest heterogeneity in Koraman et al.'s study[32] was due to the fact that more than 2 injection sites were used in multisite injection. In addition, the total dose of multipoint injection exceeding the conventional dose also may be the cause of heterogeneity. In the sensitivity analysis of external rotation results, when we excluded Prestgaard et al.'s study[33] which had the greatest heterogeneity, the results tended to be more advantageous for multipoint injection. This may due to the use of lidocaine as a control in the nonsteroid injection area of the joint, which may have somewhat skewed the results. Therefore, it is difficult to draw a clear conclusion. Our hypothesis was not proved according to the results of the current systematic literature and meta-analysis. We only can expect that multisite steroid injection has similarly effective compared with single-site corticosteroid injections for FS.

Identification of the lesion site is essential for treatment. At first, FS was thought to be a glenohumeral joint disorder or associated with subacromial bursa inflammation and thickening.[6] However, a growing body of research suggests that inflammation with vascularity and thickening of the rotator interval, capsule, and glenohumeral ligaments are pathologically pivotal to the driving process.[9,34-36] Therefore, intervention in these structures is vital to alleviate FS.

There are multiple conventional approaches for shoulder injection (the anterior approach, lateral approach, and posterior approach), and practitioners most commonly use the posterior approach.[37-39] Most of the studies we included also adopted this approach, which has the advantage that it is easier to palpate bony surface landmarks, especially for patients with obesity or who are muscular. It is also favorable for simultaneous intra-articular injection and subacromial space injection. In addition, the posterior approach is not affected by osteophytes or a hooked acromion compared to the anterior approach. However, for distant lesions, such as anterior glenohumeral joint lesions and biceps tendon lesions, treatment may be less effective. Therefore, an appropriate approach should be selected according to injection site when using multisite injection. In addition, when the multisite injection is performed using a single approach, the needle passes through the patient's muscle tissue without an anesthetic, which undoubtedly causes fear and pain in the patient and makes the patient's body tense, which may affect the patient and injection at the next point. Multiple approaches to multipoint injection also increase pain in patients initially.

In multisite injection, the choices of injection site and number of injections are not uniform. Only 2 of the 5 studies included selected the glenohumeral joint combined with subacromial space for multipoint injection procedures.[29,30] Prestgaard et al.[33] reported the use of glenohumeral joint and rotator interval as sites for multisite injection. They concluded that there were no significant differences between the groups. However, the remaining 2 studies selected 3 and 4 sites, and they concluded that the differences were significant.[31,32] Therefore, the selection of injection site and number of injections is still worth considering by researchers. If only multiple appropriate sites can be superimposed, ultrasound may be used more frequently to locate these areas accurately.

Another consideration is the dosage of steroids. Increasing the drug dose may be inevitable for multisite injection as the number of injection sites increases. Koraman et al.[32] used 80 mg (40 mg/mL) triamcinolone acetonide for multisite injection. The main side

effects of steroids were transient pain, tendon ruptures, local depigmentation of the skin, disturbance of the menstrual pattern, hot flash-like symptoms, hyperglycemia in diabetes mellitus, nerve damage and infection.[40-43] Therefore, even though the solution is divided into different sites, caution is still needed. However, dividing a drug intended for one injection site equally among multiple injection sites can lead to underdosing and skewing the outcome. The optimal dose is still worth exploring.

Implications for Research

We suggest that future trials investigating the effect of multisite steroid injections on FS use the following parameters:

P: Patients with FS (better to specify the stage of the disease);

I: Multisite steroid injection (20-40 mg dose may be better for one injection site and it is better to have three or more sites for multiple injection);

C: Single steroid injection;

O: VAS, ROM, shoulder function score (such as the ASES score, CMS score, and UCLA score), and adverse events; and

S: Randomized study or other type clinical trial.

In addition, we are still curious about whether similar results could be found for rotator cuff injuries, subacromial impingement syndrome, or other shoulder diseases and whether hyaluronic or platelet-rich plasma injections could be similarly helpful. The most appropriate injection site, the number of injection sites, and the drug dosage also need to be further explored.

Limitations

The primary limitation of this study is that only 5 studies have been conducted on the relevant topic. Although we included the outcomes of each period in the analysis as much as possible, the conclusions were still unstable due to the insufficient number of included studies, Therefore, we cannot determine the optimal dose and injection site. Second, we included the same outcome at 4 time intervals in the data analysis due to the number of included studies. Third, In the process of extracting data, some studies did not report the mean or SD of clinical outcomes, which also limited the analysis data we included. In addition, some literatures did not report specific grouping of patients with postoperative complications, which may lead to biased results. Nevertheless, the duration of each stage of FS was inconsistent among patients, or the onset of each stage overlapped, which may affect the final accuracy of the results. Finally, although most studies used ultrasound injection, there was no literature to report the accuracy of multipoint injection, so we could not compare the accuracy of single and multipoint injection.

Conclusions

Single-site steroid injection is as effective as multisite corticosteroid injection for the nonoperative treatment of FS.

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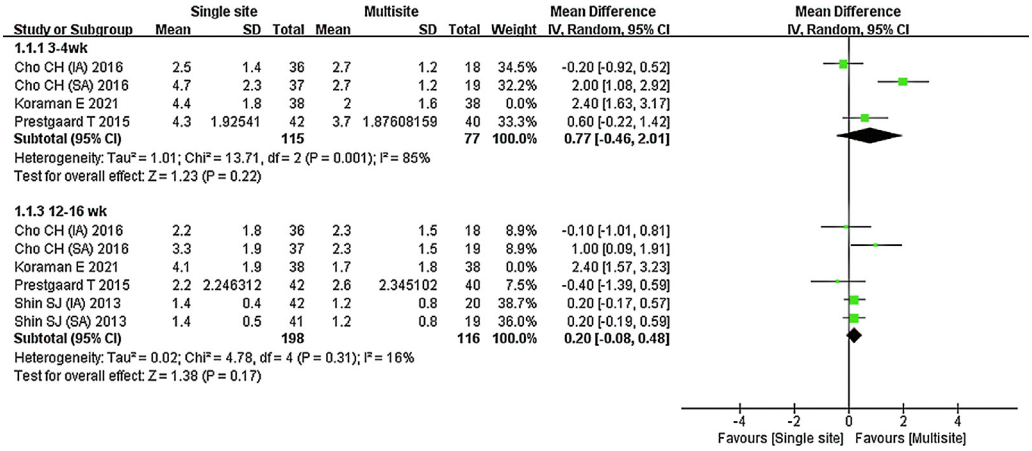
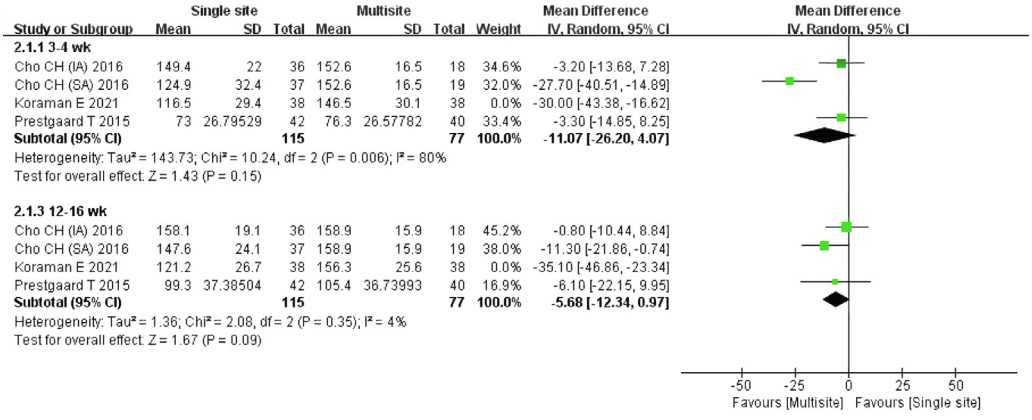
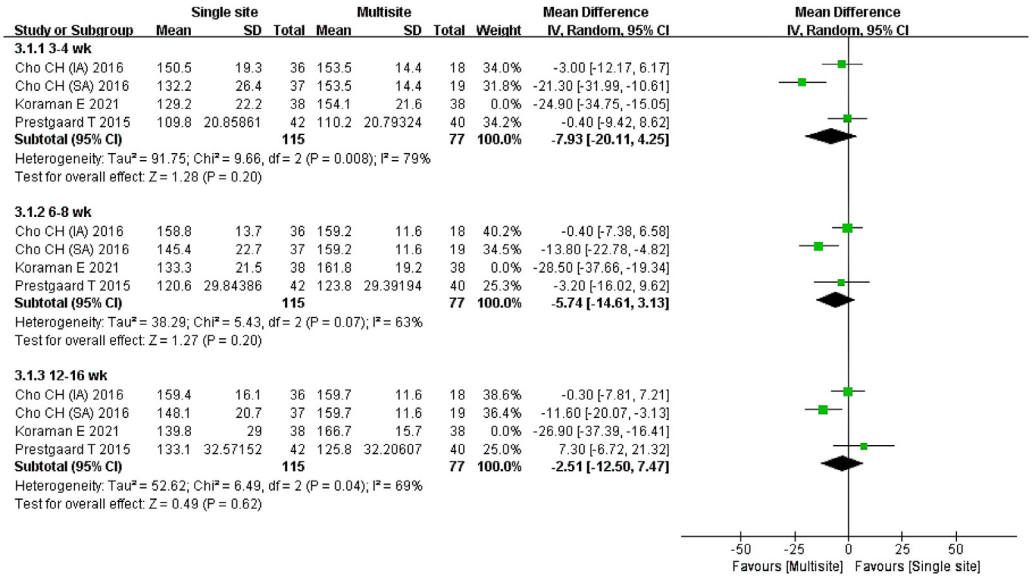


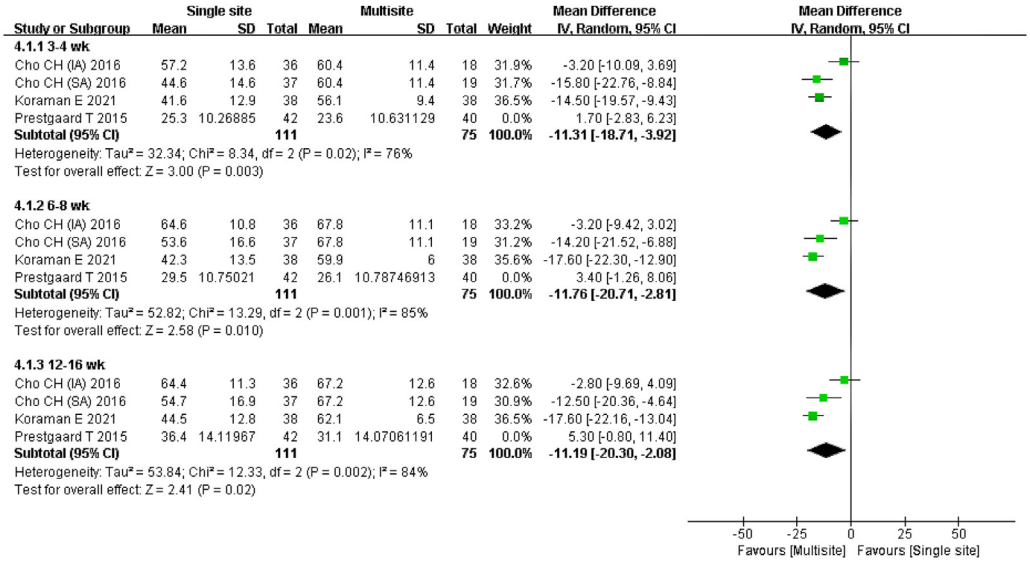
Appendix Fig 1. Forest plot showing of the visual analog scale score after sensitivity analysis. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)



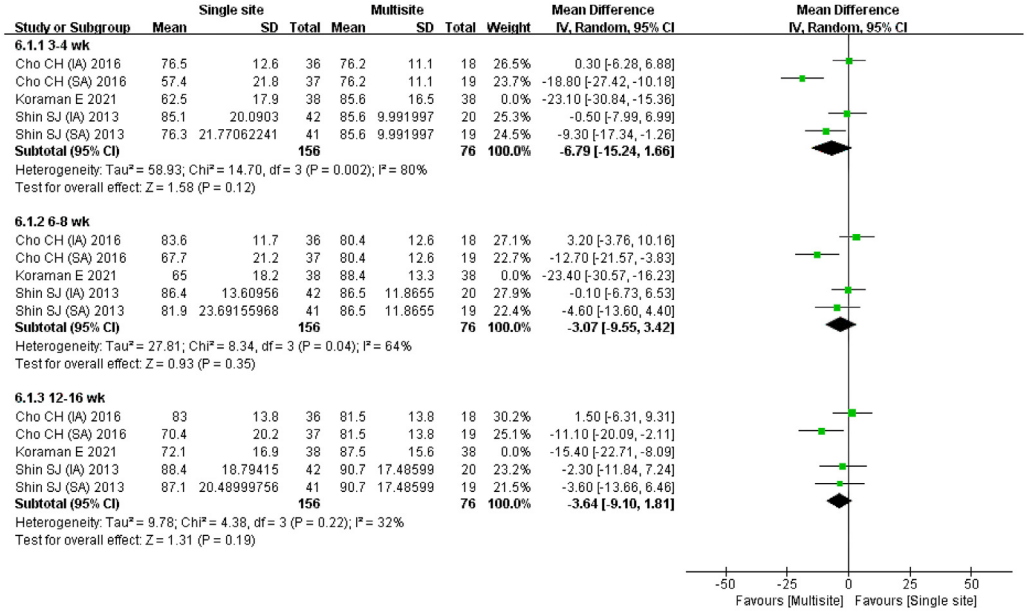
Appendix Fig 2. Forest plot showing of the abduction after sensitivity analysis. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)



Appendix Fig 3. Forest plot showing of the flexion after sensitivity analysis. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)



Appendix Fig 4. Forest plot showing of the external rotation after sensitivity analysis. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)



Appendix Fig 5. Forest plot showing of the American Shoulder and Elbow Surgeons Assessment Form scores after sensitivity analysis. (CI, confidence interval; IV, inverse variance; SD, standard deviation.)

Appendix Table 1. Visual Analog Scale (VAS) Scores, Reported as the Mean Only, Mean With 95% CI, Mean ± SD, or Mean ± SE

	VAS				
Author	Baseline	3-4 wk	6-8 wk	12-16 wk	24-26 wk
Shin et al.[29]	IA: 6.10909*	IA: 1.48021*	IA: 1.49733*	IA: 1.4 ± 0.4‡	IA: 0.96684*
	SA: 7.03316*	SA: 2.53262*	SA: 1.68556*	SA: 1.4 ± 0.5‡	SA: 1.30909*
	IA+SA: 7.15294*	IA+SA: 1.48877*	IA+SA: 1.12941*	IA+SA:1.2 ± 0.8‡	IA+SA: 1.42032*
Prestgaard et al.[33]	IA: 6.1 (5.8-6.4)†	IA: 4.3 (3.7-4.9)†	IA: 3.2 (2.5-3.9)†	IA: 2.2 (1.5-2.9)†	IA: 1.8 (1.2-2.5)†
	Combined group:	Combined group:	Combined group:	Combined group:	Combined group:
	6.4 (6.1-6.7)†	3.7 (3.1-4.3)†	2.8 (2.0-3.5)†	2.6 (1.9-3.3)†	2.2 (1.5-2.8)†
Cho et al.[30]	IA: 7.9 ± 1.5‡	IA: 2.5 ± 1.4‡	IA: 1.8 ± 1.3‡	IA: 2.2 ± 1.8‡	–
	SA: 7.9 ± 1.1‡	SA: 4.7 ± 2.3‡	SA: 3.6 ± 2.1‡	SA: 3.3 ± 1.9‡	
	IA+SA: 8.2 ± 1.6‡	IA+SA: 2.7 ± 1.2‡	IA+SA: 2.3 ± 1.4‡	IA+SA: 2.3 ± 1.5‡	
Koraman et al.[32]	SI: 8.4 ± 1.3‡	SI: 4.4 ± 1.8‡	–	SI: 4.1 ± 1.9‡	SI: 3.3 ± 1.9‡
	MI: 8.7 ± 1.1‡	MI: 2 ± 1.6‡		MI: 1.7 ± 1.8‡	MI: 1.9 ± 2.1‡

CI, confidence interval; IA, intra-articular; MI, multisite injection; SA, subacromial; SD, standard deviation; SI, single injection.
*Mean only (extracted from graphs).
†Mean with 95% CI.
‡Mean ± SD.

Appendix Table 2. Abduction, Reported as the Mean or Mean With 95% CI, Mean ± SD

	Abduction				
Author	Baseline	3-4 wk	6-8 wk	12-16 wk	24-26 wk
Prestgaard et al.[33]	IA: 54.5 (46.7-62.3)*	IA: 73.0 (64.6-81.3)*	IA: 87.5 (76.4-98.5)*	IA: 99.3 (87.7-111.0)*	IA: 116.7 (103.6-129.8)*
	Combined group:	Combined group:	Combined group:	Combined group:	Combined group:
	61.8 (53.6-69.9)*	76.3 (67.8-84.8)*	89.5 (78.3-100.7)*	105.4 (93.6-117.1)*	112.6 (99.3-125.8)*
Cho et al.[30]	IA: 110.0 ± 25.0†	IA: 149.4 ± 22.0†	IA: 158.6 ± 12.2†	IA: 158.1 ± 19.1†	–
	SA: 109.2 ± 29.5†	SA: 124.9 ± 32.4†	SA: 144.3 ± 28.9†	SA: 147.6 ± 24.1†	
	IA+SA: 108.5 ± 24.4†	IA+SA: 152.6 ± 16.5†	IA+SA: 160.5 ± 11.0†	IA+SA: 158.9 ± 15.9†	
Koraman et al.[32]	SI: 73.7 ± 14.4†	SI: 116.5 ± 29.4†	–	SI: 121.2 ± 26.7†	SI: 128.6 ± 29.3†
	MI: 73.2 ± 18.6†	MI: 146.1 ± 30.1†		MI: 156.3 ± 25.6†	MI: 161.6 ± 22.7†

CI, confidence interval; IA, intra-articular; MI, multisite injection; SA, subacromial; SD, standard deviation; SI, single injection.
*Mean with 95% CI.
†Mean ± SD.

Appendix Table 3. Flexion, Reported as the Mean Only, Mean With 95% CI, or Mean ± SD

	Flexion				
Author	Baseline	3-4 wk	6-8 wk	12-16 wk	24-26 wk
Shin et al.[29]	IA: 108.485*	IA: 130.669*	IA: 147.02*	IA: 151.263*	IA: 160.101*
	SA: 106.01*	SA: 131.023*	SA: 143.043*	SA: 144.545*	SA: 156.301*
	IA+SA: 104.154*	IA+SA: 133.586*	IA+SA: 143.838*	IA+SA: 145.96*	IA+SA: 156.212*
Prestgaard et al.[33]	IA: 91.0 (81.1-100.8)†	IA: 109.8 (103.3-116.3)†	IA: 120.6 (111.3-129.9)†	IA: 133.1 (123.0-143.3)†	IA: 145.9 (135.7-156.0)†
	Combined group:	Combined group:	Combined group:	Combined group:	Combined group:
	100.6 (92.3-109.0)†	110.2 (103.6-116.9)†	123.8 (114.4-133.2)†	125.8 (115.5-136.1)†	135.2 (125.0-145.5)†
Cho et al.[30]	IA: 116.9 ± 21.6‡	IA: 150.5 ± 19.3‡	IA: 158.8 ± 13.7‡	IA: 159.4 ± 16.1‡	–
	SA: 112.2 ± 22.1‡	SA: 132.2 ± 26.4‡	SA: 145.4 ± 22.7‡	SA: 148.1 ± 20.7‡	
	IA+SA: 115.7 ± 20.1‡	IA+SA: 153.5 ± 14.4‡	IA+SA: 159.2 ± 11.6‡	IA+SA: 159.7 ± 11.6‡	
Koraman et al.[32]	SI: 88.4 ± 11.7‡	SI: 129.2 ± 22.2‡	SI: 133.3 ± 21.5‡	SI: 139.8 ± 29‡	–
	MI: 80.4 ± 19.8‡	MI: 154.1 ± 21.6‡	MI: 161.8 ± 19.2‡	MI: 166.7 ± 15.7‡	

CI, confidence interval; IA, intra-articular; MI, multisite injection; SA, subacromial; SD, standard deviation; SI, single injection.
*Mean (extracted from graphs).
†Mean with 95% CI.
‡Mean ± SD.

Appendix Table 4. External Rotation, Reported as the Mean Only, Mean With 95% CI, or Mean ± SD

	External rotation				
Author	Baseline	3-4 wk	6-8 wk	12-16 wk	24-26 wk
Shin et al.[29]	IA: 31.0877*	IA: 46.0351*	IA: 57.8246*	IA: 60.2807*	IA: 64.1404*
	SA: 33.9649*	SA: 44.0702*	SA: 53.9649*	SA: 56.0702*	SA: 60.9123*
	IA+SA: 29.7544*	IA+SA: 48.1404*	IA+SA: 60.0702*	IA+SA: 62.0351*	IA+SA: 67.9298*
Prestgaard et al.[33]	IA: 15.8 (12.0-19.7)†	IA: 25.3 (22.1-28.5)†	IA: 29.5 (26.2-32.9)†	IA: 36.4 (32.0-40.8)†	IA: 36.7 (31.5-41.8)†
	Combined group:	Combined group:	Combined group:	Combined group:	Combined group:
	21.9 (18.2-25.6)†	23.6 (20.2-27.0)†	26.1 (22.7-296)†	31.1 (26.6-35.6)†	35.1 (29.8-40.4)†
Cho et al.[30]	IA: 34.4 ± 15.7‡	IA: 57.2 ± 13.6‡	IA: 64.6 ± 10.8‡	IA: 64.4 ± 11.3‡	–
	SA: 32.6 ± 10.2‡	SA: 44.6 ± 14.6‡	SA: 53.6 ± 16.6‡	SA: 54.7 ± 16.9‡	
	IA+SA: 34.8 ± 14.1‡	IA+SA:60.4 ± 11.4‡	IA+SA: 67.8 ± 11.1‡	IA+SA: 67.2 ± 12.6‡	
Koraman et al.[32]	SI :9.7 ± 8.3‡	SI: 41.6 ± 12.9‡	SI: 42.3 ± 13.5‡	SI: 44.5 ± 12.8‡	–
	MI: 10.1 ± 9.7‡	MI: 56.1 ± 9.4‡	MI: 59.9 ± 6‡	MI: 62.1 ± 6.5‡	

CI, confidence interval; IA, intra-articular; MI, multisite injection; SA, subacromial; SD, standard deviation; SI, single injection.
*Mean only (extracted from graphs).
†Mean with 95% CI.
‡Mean ± SD.

Appendix Table 5. Internal Rotation, Reported as the Mean ±SD

	Internal Rotation				
Author	Baseline	3-4 wk	6-8 wk	12-16 wk	24-26 wk
Cho et al.[30]	IA: 30.3 ± 11.3*	IA: 53.9 ± 13.9*	IA: 61.1 ± 10.3*	IA: 61.9 ± 13.9*	–
	SA: 31.7 ± 12.4*	SA: 42.6 ± 13.8*	SA: 50.6 ± 15.0*	SA: 53.1 ± 15.5*	
	IA+SA: 32.4 ± 14.1*	IA+SA: 59.2 ± 13.8*	IA+SA: 65.4 ± 11.9*	IA+SA: 65.1 ± 13.2*	
Koraman et al.[32]	SI: 7.4 ± 7.4*	SI: 40.5 ± 11.2*	SI: 42.9 ± 11.5*	SI: 45 ± 10.2*	–
	MI: 8.4 ± 10.5*	MI: 56 ± 11.4*	MI: 59.7 ± 9.4*	MI: 61.7 ± 9*	

CI, confidence interval; IA, intra-articular; MI, multisite injection; SA, subacromial; SD, standard deviation; SI, single injection.
*Mean ± SD.

Appendix Table 6. ASES Assessment Form Score, Reported as the Mean ± SE or Mean **± SD**

	ASES Assessment Form				
Author	Baseline	3-4 wk	6-8 wk	12-16 wk	24-26 wk
Shin et al.[29]	IA: 42.6 ± 3.1*	IA: 85.1 ± 3.1*	IA: 86.4 ± 2.1*	IA: 88.4 ± 2.9*	IA: 91.1 ± 1.3*
	SA: 38.8 ± 3.6*	SA: 76.3 ± 3.4*	SA: 81.9 ± 3.7*	SA: 87.1 ± 3.2*	SA: 89.4 ± 1.9*
	IA+SA: 39.5 ± 2.6*	IA+SA: 85.6 ± 1.6*	IA+SA: 86.5 ± 1.9*	IA+SA: 90.7 ± 2.8*	IA+SA: 90.7 ± 1.6*
Cho et al.[30]	IA: 31.2 ± 14.6†	IA: 76.5 ± 12.6†	IA: 83.6 ± 11.7†	IA: 83.0 ± 13.8†	–
	SA: 31.2 ± 11.2†	SA: 57.4 ± 21.8†	SA: 67.7 ± 21.2†	SA: 70.4 ± 20.2†	
	IA+SA: 31.3 ± 14.6†	IA+SA: 76.2 ± 11.1†	IA+SA: 80.4 ± 12.6†	IA+SA: 81.5 ± 13.8†	
Koraman et al.[32]	SI: 18.6 ± 10.3†	SI: 62.5 ± 17.9†	SI: 65.0 ± 18.2†	SI: 72.1 ± 16.9†	–
	MI: 18.6 ± 10.3†	MI: 85.6 ± 16.5†	MI: 88.4 ± 13.3†	MI: 87.5 ± 15.6†	

ASES, American Shoulder and Elbow Surgeons; IA, intra-articular; MI, multisite injection; SA, subacromial; SD, standard deviation; SE, standard error; SI, single injection.
*Mean ± SE.
†Mean ± SD.

Appendix Table 7. Complications

Author	Complications
Shin et al.[29]	NC
Prestgaard et al.[33]	IA: 3
	Combined group: 5
Cho et al.[30]	NC
Pushpasekaran et al.[31]	SI: 0
	MI: 4
Koraman et al.[32]	SI: 0
	MI: 0

IA, intra-articular; MI, multisite injection; NC, not clear; SA, subacromial; SI, single injection.