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REVIEW ARTICLE (META-ANALYSIS)

Rotator Interval vs Posterior Approach Ultrasound-guided Corticosteroid Injections in Primary Frozen Shoulder: A Meta-analysis of Randomized Controlled Trials

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Abstract

Objective: To compare the efficacy of rotator interval (RI) vs posterior approach (PA) ultrasound (US) guided corticosteroid injections into the glenohumeral (GH) joint in primary frozen shoulder (PFS).

Data Sources: A systematic literature search for all relevant studies on Medline, Scopus, Embase, Web of Science, and Cochrane Central, up to January 2023 was conducted.

Study Selection: Randomized controlled trials that directly compared the US-guided corticosteroid injection into the RI and GH joint using PA in patients clinically and radiographically diagnosed with PFS.

Data Extraction: The primary outcome was pain, and the secondary outcomes were function, and range of motion (ROM). Two authors independently assessed the risk of bias using the Cochrane risk-of-bias tool version 2. A random-effects model and generic inverse variance method were performed. Effect sizes were estimated using mean difference (MD) and standardized mean difference (SMD).

Data Synthesis: A total of 5 clinical trials involving 323 subjects were included for the meta-analysis. US-guided corticosteroid injections into the RI revealed significant pain relief (MD 1.33 [95% confidence interval (CI) 0.20 to 2.46]; *P*=.02) and significant functional improvement (SMD 1.31 [95% CI 0.11 to 2.51]; *P*=.03) compared with the PA after 12 weeks.

Conclusion: The results suggest the injection of corticosteroid into RI space is more effective than PA after 12 weeks in improving both pain and functional scores in patients with PFS.

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Ethical approval: This study was previously reviewed and approved by the University's Ethics and Research Committees, making sure it adheres to the Helsinki declaration, and national and international standards of research. The ID number is RVS23-001.

Registration: The study was also registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42022378516.

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Introduction

Primary frozen shoulder (PFS) or adhesive capsulitis is an inflammatory condition of uncertain etiology characterized by a gradual and painful restriction of movement in the glenohumeral (GH) joint.[1-3] It is estimated to affect around 5% of the population and commonly occurs in middle-aged women.[4-7] Non-surgical interventions are the gold-standard treatment option.[8-10] Studies have shown that a single corticosteroid injection produces more favorable short-term outcomes than other conservative approaches.[3,10-13] The mechanical effect of hydrodilatation as well as the reduction of synovitis by the steroid improves pain levels and overall joint function.[3,14]

Accurate injections are crucial to ensure the therapeutic effectiveness. Radiologic guidance is recommended to archive precision and avoid anatomic variations.[15-18] Ultrasound (US) guided corticosteroid injections in the rotator interval (RI), subacromial (SA) space, and GH using a posterior approach (PA) have been widely described.[19-23] However, debate continues regarding which is the most effective.[20] Chen et al performed a meta-analysis of randomized controlled trials (RCTs) comparing intra-articular (IA) and subacromial corticosteroid injections. They found that IA injections were more effective for pain relief, but no significant differences were observed in functional outcomes.[19] Therefore, further comparison and analysis are required.[24]

The RI and coracohumeral ligament involvement in the pathogenesis of the PFS suggests that an intervention directly into the RI may lead to superior clinical results than injections in other sites.[25-29] Trials have compared the RI corticosteroid injection with other articular spaces. However, findings have been inconsistent across the studies.[14,25,26,30,31] These discrepancies suggest that further research about the benefits of RI injection is needed. This systematic review aimed to compare the efficacy of RI vs PA for US-guided corticosteroid injections into the GH joint in patients with PFS.

Materials and methods

The systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist[32] and the guidelines from the Cochrane Handbook for Systematic Reviews of Interventions.[33] The study was reviewed and approved by the university's research and ethics committees (RVS23-001) and by the International Prospective Register of Systematic Reviews (PROSPERO, ID number CRD42022378516).

List of abbreviations:

CI	**confidence interval**
GH	**glenohumeral**
IA	**intra-articular**
MD	**mean difference**
RCT	**randomized controlled trial**
RI	**rotator interval**
ROM	**range of motion**
SMD	**standard mean difference**
SPADI	**shoulder pain and disability index questionnaire**
SSV	**subjective shoulder value**
PA	**posterior approach**
PFS	**primary frozen shoulder**
US	**ultrasound**
VAS	**visual analog scale**

Search strategy

The search strategy was designed by an expert reference librarian using a combination of keywords and MeSH terms based on the population, intervention, comparison, and study design of interest. The principal terms such as "frozen shoulder, "adhesive capsulitis", "ultrasound-guided injection", "intraarticular corticosteroid injection", and "randomized controlled trial" were searched with maximum sensitivity. The search was conducted in multiple electronic databases (MEDLINE, Scopus, Web of Science, EMBASE, and Cochrane Central). The studies were searched from inception to January 2023 (see supplemental table S1).

Eligibility criteria

Studies were screened for inclusion according to the following criteria: RCTs that directly compared the US-guided corticosteroid injection into the RI vs the PA in patients clinically and radiographically diagnosed with PFS. Pain relief (primary outcome), function, and range of motion (ROM) improvement (secondary outcomes) assessed by validated questionnaires or scales (ie, visual analog scale [VAS], Constant score, the subjective shoulder value [SSV], The shoulder pain and disability index questionnaire (SPADI) and goniometer). A minimum of 1 outcome was considered enough for a study to be included. Studies that did not report the demographic characteristics of the sample, undefined sample sources, non-full-text reports, or duplicates were excluded. No studies were excluded based on the risk of bias assessment.

Study selection process

Two reviewers independently screened the titles, abstracts, and full-text of manuscripts for eligibility using a 2-step approach. The reviewers screened only the titles and abstracts of the studies (Step 1). Studies considered by at least 1 reviewer were contemplated for full-text screening. A full-text screening (step 2) was managed to decide the inclusion of studies. Identical inclusion criteria were used for both screening phases. Disagreements were debated and communally resolved by the authors. In case of further disagreements, a third author made the final decision. The chance-adjusted inter-rater agreement was estimated at the calibration and conduction of each phase using the Kappa statistic.[34] Distiller Systematic Review Software (DistillerSR, Evidence Partners, Ottawa, Canada) was used for the data management during the selection process.

Data collection process

Data regarding study characteristics, quality of evidence, and outcomes were extracted independently and in duplicate by 2 reviewers using a standardized data extraction format. Eligible studies were reviewed, and the following data were extracted: first author name; publication year; follow-up; number of participants in the intervention groups; age and sex of the study participants; corticosteroid injection space; description of the intervention; injected volume; type and dose of corticosteroid used; additional activities (physical therapy, home exercise program); and pain, functional scores, and ROMs at baseline and follow-up. Studies

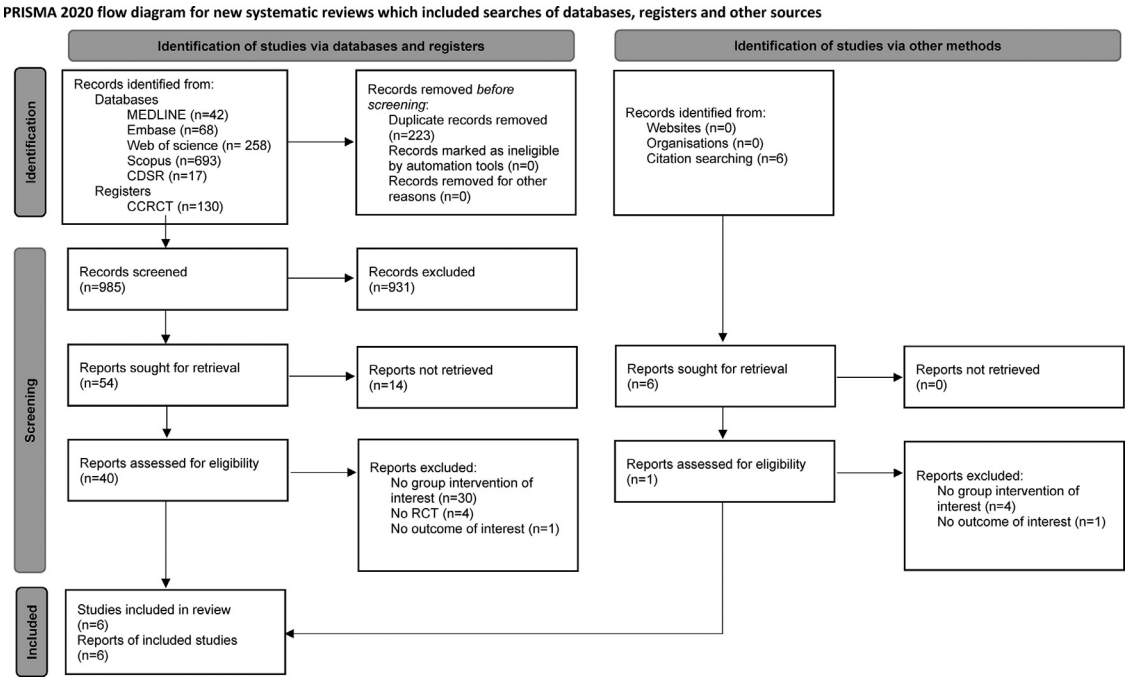

Fig 1 Flow chart of study selection.

were analyzed qualitatively if the intervention could not be possible to pool. Conflicts at this phase were resolved by consensus or arbitration by a third, experienced, reviewer.

Quality assessment of included studies

A systematic assessment of bias in the included studies was performed using the Cochrane Risk of Bias Tool version 2 (RoB 2.0). Two reviewers working independently and in duplicate assessed the methodological quality of each study. The tool covers 5 domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in the measurement of the outcome, and bias in the selection of the reported result.[35] There are 5 possible answers for each domain (yes, probably yes, no, probably not, and no information), and according to the answers, the tool catalogs the risk of bias as low, some concerns, or high.

Statistical analysis

To evaluate the effectiveness of the interventions for each study, a summary of the intervention effect was estimated by mean difference (MD) and standardized mean difference (SMD) with 95% confidence interval (CI). The MD was estimated for pain (VAS), abduction, flexion, and external rotation (goniometry). Because of the different metrics and methods used to evaluate functionality scores (SPADI, SSV, and Constant scores) and internal rotation, SMD was used for effect size estimation. SMD values of 0.2−0.5 were considered small, values of 0.5-0.8 were appraised as medium, and values >0.8 were considered large.[36] The Der Simonian-Laird random-effect model and the generic inverse variance method were used. For MD calculation, net changes in measurements were calculated as follows: measure at the follow-up minus measure at baseline. When only the standard error of the mean (SEM) was reported, the SD was estimated using the following formula: SD = SEM × sqrt (n), where n is the number of subjects. We performed recalculations for the study conducted by Elnady et al.[30] The SD of the mean difference was calculated using the following formula: SD = square root [(SDpre-treatment) 2 + (SDpost-treatment)2 − (2R × SDpre- treatment × SDpost- treatment)], assuming a correlation coefficient (R) of 0.5. These calculations served as fundamental components within the RevMan program, enabling a quantitative comparison of interventions and the generation of forest plots. The heterogeneity of the studies was examined by applying Cochrane's Q statistic test, and a P value <.05 was considered statistically significant. The I^2 was also calculated to evaluate the percentage of variability in the effect estimate that is due to heterogeneity rather than chance, in which >50% suggests substantial heterogeneity. Lastly, we performed a sensitivity analysis to evaluate the influence of individual studies on the overall effect size using the leave-one-out method (ie, removing 1 study each time and repeating the analysis). We did not perform a test for publication bias because such an evaluation is typically performed only when at least 10 studies are included in the meta-analysis. The results are presented in 3 periods of follow-up (3-4, 6-8, and 12 weeks). All statistical analyses were conducted using RevMan (version 5.4; The Cochrane Collaboration, 2020) and the meta package in R (version 3.4.3; R Project for Statistical Computing).

Certainty of evidence

We evaluated the certainty of evidence using the GRADE for complex interventions. Certainty of evidence from non-randomized trials starts at low and can be rated down for methodological limitations, imprecision, indirectness, inconsistency, or publication bias.

Results

The search strategy identified 991 publications. A total of 931 studies did not meet the inclusion criteria and were excluded. Subsequently, 14 reports were not retrieved. Forty full-text articles

were reviewed for eligibility, and 35 were excluded for the following reasons: 30 studies did not include the intervention group of interest, 4 studies were not RCT, and 1 study did not evaluate the outcomes of interest. In addition, 1 study was identified through a citation-searching method. From the 6 RCTs selected in the systematic review, a total of 5 were included for meta-analysis (fig 1). The study conducted by Prestgaard et al[31] was not included in the quantitative analysis because of the differing arm interventions used. Their investigation compared corticoid injections in PFS contrasting IA with a combined approach of IA and RI approaches. The chance-adjusted inter-rater agreement using the Kappa statistic resulted in 0.84 and 0.96 for the 2 selection phases, respectively.

Patient demographics

Data suitable for analysis were reviewed and analyzed from 323 subjects (162 in the RI arm and 161 in the PA arm). The range of publication dates of the studies was from 2015[31] to 2023.[37] The geographic region where the studies were conducted was heterogeneous: 2 studies from China,[26,37] 1 from Egypt,[30] Norway,[31] Taiwan,[14] and South Korea[25] each. All subjects enrolled in the studies included had a confirmed diagnosis of PFS. The duration disease ranged from 8 weeks[30] to 10 months.[31] Three studies did not specify the disease stage of the patients included,[30,31,37] 2 studies included patients in the freezing stage,[25,26] and 1 analyzed a sample through different stages.[14] The final follow-up of patients in each study ranged from 3 months[14,25,26,30,37] to 6 months.[31] The samples included are mainly women between 40 and 50 years old. Detailed information of study characteristics and patients is depicted in table 1, and the intervention characteristics are described in table 2. The approaches were neither planned to be personalized nor modified during the study. The allocation and data collection were blinded across the studies. The results across follow-up and level of evidence are summarized in table 3.

Pain relief

A meta-analysis was performed using 5 studies[14,25,26,30,37] that reported a pain scale (VAS) (fig 2). Statistical differences were found between RI and PA steroid injection for pain relief after 3-4 weeks (n=3, MD 1.44 [95% CI 0.37 to 2.5]; P=.008; I^2=89%), 6-8 weeks (n=4, MD 1.36 [95% CI 0.38 to 2.33]; P=.006; I^2=89%), and 12 weeks (n=5, MD 1.33 [95% CI 0.20 to 2.46]; P=.02; I^2=94%), favoring the RI over the PA. This effect size was robust in the sensitivity analysis (supplemental table S2).

Function improvement

Five studies reported a functional scale, using the SSV,[25] SPADI,[14,30] and Constant[26,37] tools, allowing for a meta-analysis to be performed (fig 3). No statistical differences were found between RI and PA steroid injection for function after 3-4 weeks (n=3, SMD 1.32 [95% CI -0.19 to 2.83]; P=.09; I^2=95%), and 6-8 weeks (n=4, SMD 0.74 [95% CI -0.19 to 1.68]; P=.12; I^2=92%). However, a statistically significant result was obtained after 12 weeks (n=5, SMD 1.31 [95% CI 0.11 to 2.51]; P=.03; I^2=96%), favoring the RI over the PA. It is considered as large effect. The sensitivity analysis shows that the effect size was not robust (supplemental table S2).

Table 1 Demographics of studies included

Author Year Country	Intervention Arms	Follow-up	n	Women	Age	Stage Disease	Disease Duration Weeks	Baseline					
								Pain Score	Function Score	Abduction °	Flexion °	Internal Rotation °	External Rotation °
Prestgaard, 2015	IA	6	42	27 (64%)	53.2±6.9	NR	15.1±4.6	6.1 (5.8-6.4)†	68.9 (63.7-74.1)†	54.5 (46.7-62.3)†	91.0 (81.1-100.8)†	NR	15.8 (12-19.7)†
Norway[31]	PA + RI		40	25 (63%)	55±7.2		15±5.9	6.4 (6.1-6.7)†	67.1 (62.3-71.9)†	61.8 (53.6-69.9)†	100.6 (92.3-109)†	NR	21.9 (18.2-25.6)†
Sun, 2017	RI	3	33	16 (59.2%)	52.6±4.4	Freezing	14.4 ± 4.3	7.6±0.4	20.9±4.4‡	76.4±9.7	87.1±9.8	17.6±0.5	0.6±5
China[26]	PA		30	14 (58.3%)	55.1±3.4		15.2 ± 5	7.6±0.4	21.3±4.3‡	73.1±8.6	88.5±11.4	17.6±0.5	−1.1±6.5
Elnady, 2020	RI	3	30	22 (73.3%)	45.4±4.9	NR	9.1±2.9*	7.2±9.7	90.3±15.1	108.8±22.6	99±19.1	26.5±9	37.3±10.4
Egypt[30]	PA		30	21 (70%)	47.6±3.5		8.3±2.6*	7.2±9.6	89±15.8	110.1±21.8	99.3±19.2	28.6±9.5	40.6±9.8
Wang, 2021	RI	3	32	20 (62.50%)	52.40±6.37	Different stages	NR	5.9±2.2	47.6±14.9	91.7±22.8	131.1±19.2	23.1±28.3	19.5±28.3
Taiwan[14]	PA		32	19 (59.37%)	53.96±7.02			5.1±2.1	49.5±22	89.4±21.4	127.1±17.4	28.1±30	18.2±25.7
Cho, 2022	RI	3	43	18 (41.8%)	54.14±8.87	Freezing	9.3±14.7	6.9±2.5	39.6±21.3	100.3±26.5	119.1±23.8	17.7±2	41.4±18.9
South Korea[25]	PA		45	25 (55.5%)	55.44±9.93		10±11.2	6.4±2.2	41±16.7	98.6±26.7	112.9±24.4	18.1±2.2	39.1±20.5
Deng, 2023	RI	3	30	23 (76.67%)	54.5±5.7	NR	4.4±1.3*	7.23±1.28	41.6±11‡	78.1±16.3	90.1±20.7	22.1±11.9	23.0±9.6
China[37]	PA		30	20 (66.67%)	55.3±3.9		4.3±1.5*	7.10±1.30	42.6±11.9‡	80.1±19.2	88.3±23.6	24.7±12.4	24.3±10

NOTE. Quantitative values are expressed as mean ± standard deviation, and qualitative variables as number (Percentage) unless otherwise indicated.
Abbreviations: °, degrees of movement; NR, no reported.
* Disease duration expressed in months.
† Data expressed as mean and 95% confidence interval.
‡ Constant score.

Table 2 Intervention characteristics

Author	Provider	Steroid	Complement	Support Activities	RI Procedure	PA Procedure
Prestegaard, 2015, Norway[31]	Physicians	IA: 1 mL triamcinolone hexacetonide 20 mg/mL RI + PA: 0.5 mL triamcinolone into RI and IA.	IA group: 2.5 mL lidocaine into IA, and 3.5 mL lidocaine 10 mg/mL into RI Combined:3 mL lidocaine into RI and 3 mL lidocaine into IA	No home exercises were given.	The participants lying in a supine position. The injections were aimed along the long head of the biceps and into the anterior capsule.	Participants lying on their side. The injection was from the posterior portal and guided into the joint.
Sun, 2017 China[26]	Physician	1 mL of 40 mg/mL triamcinolone	2 mL 2% lidocaine	Daily shoulder exercises	In a seated position, the needle was introduced with an angle of 30˚ to the skin into RI.	The injection was from the posterior portal and guided into the joint.
Elnady, 2020 Egypt[30]	Radiologist	1 mL methyl-prednisolone acetate (40 mg)	1 mL of 2% lidocaine and 15 mL saline	Guided stretching and strengthening exercise program	In a supine or semi-supine, the shoulder is slightly extended. A needle is introduced into the RI using an oblique path between the coracohumeral ligament above and biceps tendon.	In semi-prone position, the injection needle is introduced at the skin surface in an oblique lateral to medial direction into GH joint.
Wang, 2021, Taiwan[14]	Physiatrist	4 mL of 40 mg (10 mg/mL) triamcinolone acetonide.	4 mL of 2% lidocaine hydrochloride and 12 mL of normal saline	Exercise program including Codman's exercises, and wall climbing.	The probe was placed lateral to the coracoid process on the deltopectoral groove. After sterile preparation, a needle was inserted from the lateral side of the probe.	The probe was placed parallel to the lateral end of the scapular spine. A needle was inserted using the in-plane approach between the humeral head and the bony glenoid fossa.
Cho, 2022 South Korea[25]	Shoulder-intervention specialist	1 mL of 40 mg triamcinolone acetonide	3 mL of 1% lidocaine, 3 mL of water-soluble unionized contrast, and 3 mL of normal saline.	Home-based exercise	The patient in supine position with external rotation and abduction of the arm. The needle was introduced between the long bicep's tendon and the subscapularis tendon.	In semi lateral decubitus position on the unaffected side with 45˚ anterior tilting of the affected side. The needle was advanced laterally to medially reached the GH joint space.
Deng, 2023, China[37]	Trained joint surgeon	1 mL of 40 mg triamcinolone acetonide	4 mL of 1% lidocaine	Self-exercise program	The elbow joint was placed in the flexion position. The needle was inserted between the coracoid process and the anterolateral angle of the acromion	The soft point inferior and medial to the posterolateral angle of the acromion. The needle was inserted toward the coracoid process.

Abbreviations: ˚, grades; %, percentage.

Table 3 Results of pooled outcomes

	Effect Size		Heterogeneity		
	MD (95% CI)	*P* Value	I^2, %	*P* Value	Level of Evidence
3-4 weeks					
Pain relief	1.44 (0.37, 2.5)	.008	89%	<.001	Low
Function*	1.32 (-0.19, 2.93)	.09	95%	<.001	
Passive abduction	2.38 (-2.03, 6.8)	.29	0%	.83	
Passive flexion	3.5 (-9.04, 16.04)	.58	87%	<.001	
Passive external rotation	6.94 (3.39, 10.49)	<.001	25%	.26	
Passive internal rotation*	0.26 (-0.14, 0.66)	.2	49%	.14	
6-8 weeks					
Pain relief	1.36 (0.38, 2.33)	.006	89%	<.001	Low
Function*	0.74 (-0.19, 1.68)	.12	92%	<.001	
Passive abduction	3.4 (-0.81, 7.61)	.11	0%	.85	
Passive flexion	1.71 (-4.6, 8.01)	.6	55%	.08	
Passive external rotation	6.12 (3.32, 8.92)	<.001	0%	.46	
Passive internal rotation*	0.32 (0.08, 0.57)	.009	0%	.92	
12 weeks					
Pain relief	1.33 (0.2, 2.46)	.02	94%	<.001	Moderate
Function*	1.31 (0.11, 2.51)	.03	96%	<.001	
Passive abduction	7.04 (3.83, 10.26)	<.0001	0%	.76	
Passive flexion	6.31 (0.46, 12.16)	.03	74%	.006	
Passive external rotation	9.89 (2.2, 17.59)	.01	89%	<.001	
Passive internal rotation*	0.99 (0.13, 1.85)	.02	92%	<.001	

NOTE. Values are expressed as mean difference (95% CI) unless otherwise indicated.
* Effect size expressed as standard mean difference (95% CI).

Range of motion

Five studies[14,25,26,30,37] reported in grades measured through a goniometer for abduction, flexion, internal rotation, and external rotation improvement, enabling the performing of a meta-analysis for each movement (supplemental figs S1-S4, respectively). Sensitivity analysis effect sizes were also calculated (supplemental table S2).

Abduction improvement

No statistical differences were found between RI and PA steroid injection after 3-4 weeks (n=3, MD 2.38 [95% CI -2.03 to 6.8]; *P*=.29; I^2=0%), and 6-8 weeks (n=4, MD 3.4 [95% CI -0.81 to 7.61]; *P*=.11; I^2=0%). Nevertheless, a statistically significant result was obtained after 12 weeks (n=5, MD 7.04 [95% CI 3.83 to 10.26]; *P*≤.001; I^2=0%), favoring the RI over the PA. The effect size demonstrated robustness in the sensitivity analysis.

Flexion improvement

No statistical differences were found between RI and PA steroid injection after 3-4 weeks (n=3, MD 3.5 [95% CI -9.04 to 16.04]; *P*=.58; I^2=87%), and 12 weeks (n=5, MD 1.71 [95% CI -4.6 to 8.01]; *P*=.6; I^2=55%). However, a statistically significant result was identified after 6-8 weeks (n=4, MD 6.31 [95% CI 0.46 to 12.16]; *P*=.03; I^2=72%), favoring the RI over the PA. This effect size was not robust in the sensitivity analysis.

Internal rotation improvement

No statistical differences were found between RI and PA steroid injection for flexion after 3-4 weeks (n=3, SMD 0.26 [95% CI -0.14 to 0.66]; *P*=.20; I^2=49%). Nonetheless, a statistical significance was found after 6-8 weeks (n=4, SMD 0.32 [95% CI 0.08 to 0.57]; *P*=.02; I^2=92%), and 12 weeks (n=5, SMD 0.35 [95% CI 0.03 to 0.66]; *P*=.009; I^2=0%), favoring the RI over the PA. However, both SMD are considered as small effect. Sensitivity analysis indicates robustness in the effect size.

External rotation improvement

Statistical differences were found between RI and PA steroid injection for flexion after 3-4 weeks (n=3, MD 6.94 [95% CI 3.39 to 10.49]; *P*≤.001; I^2=25%), 6-8 weeks (n=4, MD 9.89 [95% CI 2.2 to 17.59]; *P*=.01; I^2=89%), and 12 weeks (n=5, MD 6.12 [95% CI 3.32 to 8.92]; *P*≤.001; I^2=0%), favoring the RI over the PA. This effect size was not robust in the sensitivity analysis.

Adverse effects

Overall, the procedure was well tolerated by the patients in both approaches, with no significant adverse events reported. Temporary facial flushing, attributed to needle syncope, was observed in both interventions.[26,30] Additionally, some patients experienced shoulder discomfort or pain during the initial days after the intra-articular injection; however, these symptoms resolved spontaneously.[14,25,26,30,37]

Risk of bias

For the randomization process domain, the 5 studies were classified as low risk of bias. One study[26] was classified as high risk of bias in the domain related to deviations from intended interventions and missing outcome data, the rest of the studies had a low risk of bias. All the studies had a low risk of bias regarding the measurement of the outcome domains. Four studies[14,25,26,37] had some concerns for the selection of the reported results, the rest of the studies had a low risk of bias. Finally, the overall risk of bias

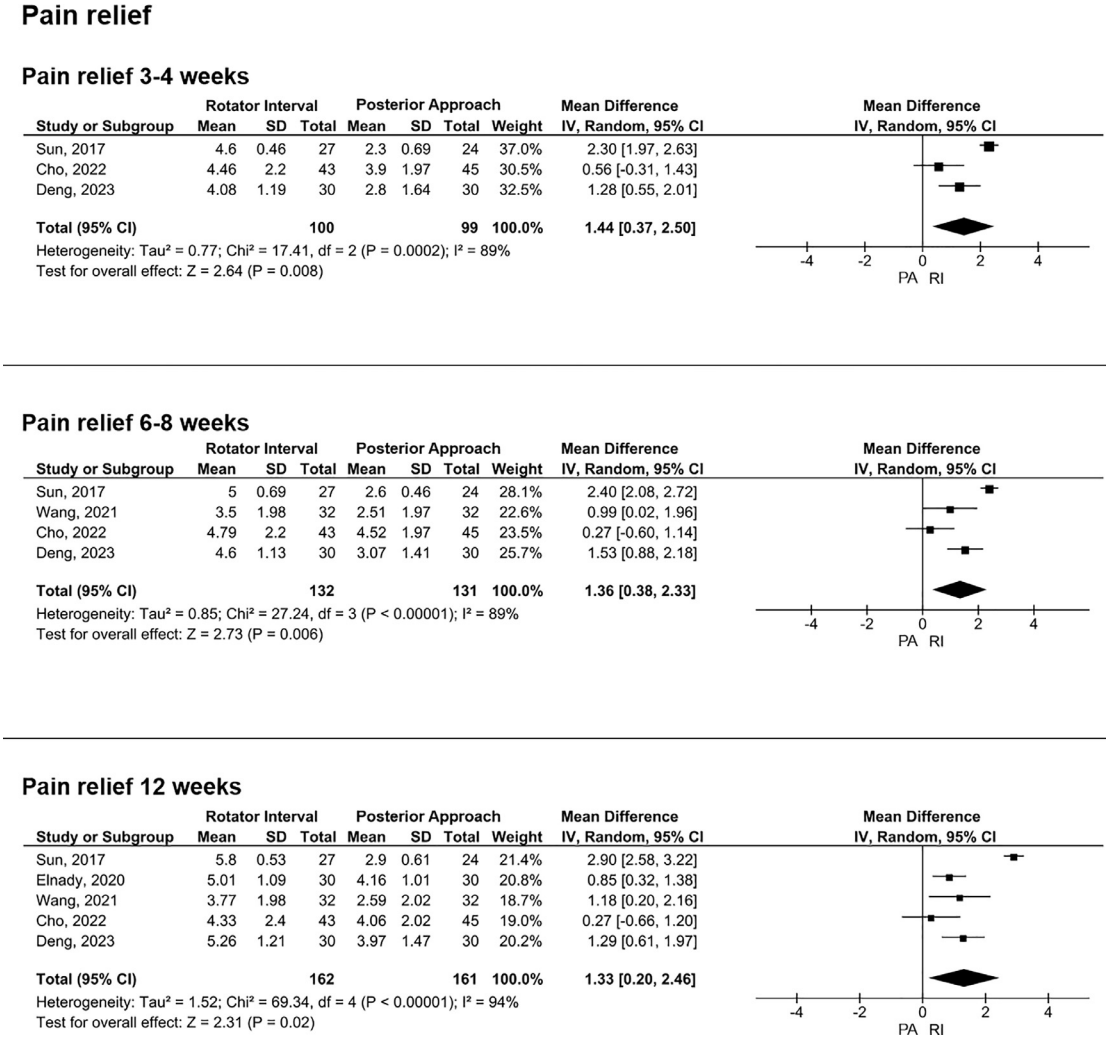

Fig 2 Forest plot displaying the effect size (MD) and 95% CI for pain relief.

was graded with some concerns in 4 studies,[14,25,30,37] low in 1 study,[26] and high in another[31] (supplemental fig S5).

Discussion

The findings of the present meta-analysis suggest that a single US-guided corticosteroid injection led to significant improvements in pain relief, function, and ROMs for at least 12 weeks, as indicated by previous systematic reviews.[19-22,38] The clinical efficacy between RI and PA intra-articular US-guided corticosteroid injection was compared through RCTs. Statistically significant differences for pain relief across all the follow-up periods, and only after 12 weeks post-intervention for function in favor of the RI approach. Regarding ROMs improvement, there were statistically significant differences in abduction, internal rotation, and external rotation at 12 weeks post-injection with the RI approach. However, these differences could be clinically narrow. The sensitivity analysis performed for pain relief and internal rotation improvement displayed no significant influence by individual studies on the overall effect size. In contrast, the function and external rotation improvement revealed a modification in the summary effect.

The RI is a triangular space located in the anterior superior region of the GH joint. It is limited by the subscapularis and supraspinatus tendons, and encompasses the long head of the bicep's tendon, the coracohumeral, and the superior glenohumeral ligaments.[29,39] Although the RI is not the unique area affected by PFS, it has an acknowledged role in its pathogenesis. Imaging and histologic findings show a significantly thickened, increased expression of inflammatory cytokines, and fibrosis in this region.[27,40-42]

Previous RCTs have determined the efficacy of US-guided RI injection.[25,31,37,43,44] The injection via RI increases the local corticosteroid concentration at the anterior joint capsule, and the coracohumeral ligament.[43] The intervention through the rotator cuff interval offers notable advantages over PA such as a better evaluation of the rotator cuff, facility in the procedure, and the infiltration into the subacromial bursa structure if this structure is also affected.[14] Nevertheless, there remain unclear factors that require consideration to understand the heterogeneous results such as disease duration, exercise program implemented, doses, and volume of the interventions.

The features of the participants regarding disease duration differ across the studies. It has been discussed that the intervention is more useful during the early period.[22,25,38,45] The PFS is a self-limiting condition lasting up to 3 years. Normally, 3 representative pathologic phases are described: the freezing phase, the adhesive phase, and the resolution phase.[46] The first phase lasts 10-36

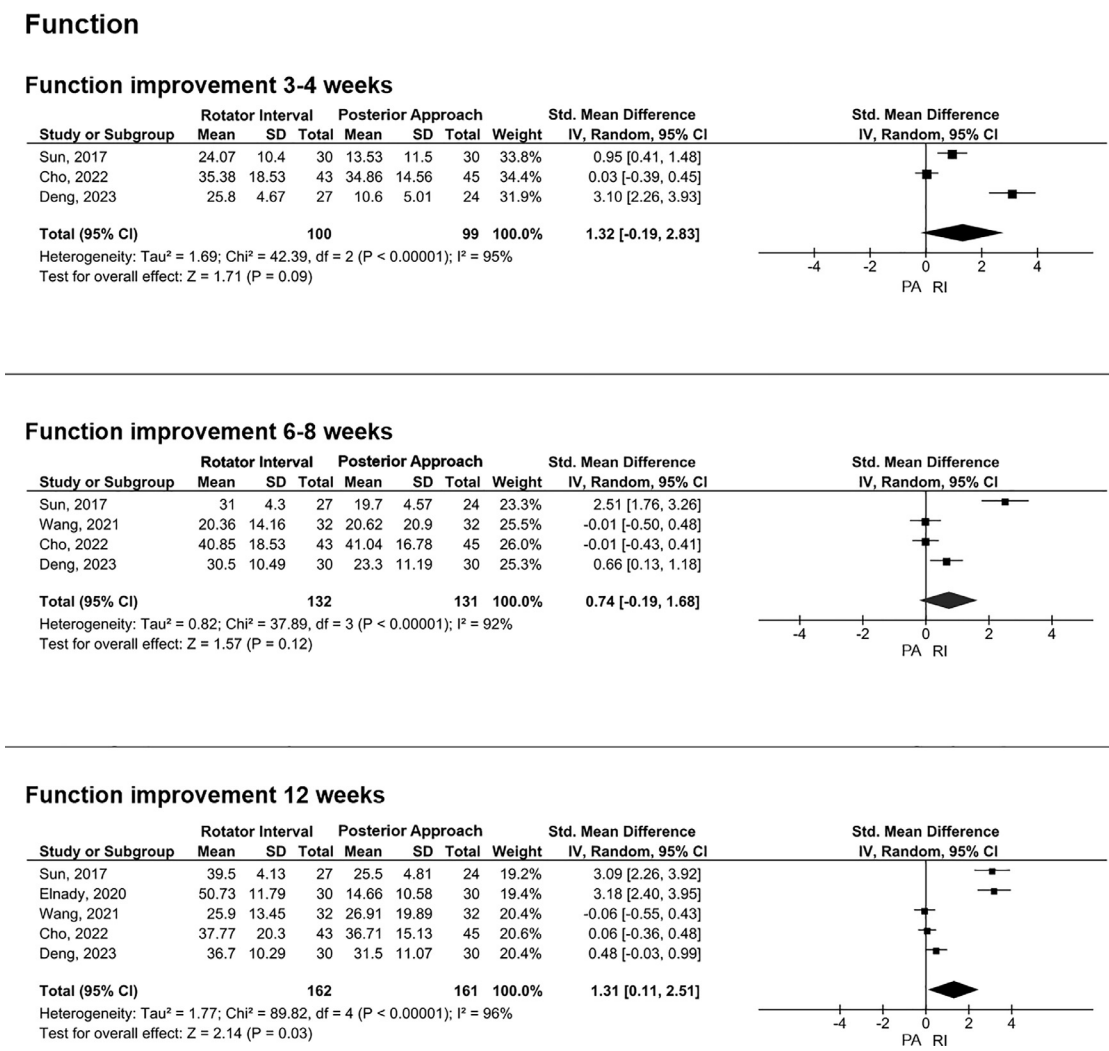

Fig 3 Forest plot displaying the effect size (MD) and 95% CI for function improvement.

weeks, in which the pain and stiffness of the shoulder are predominant. The adhesive phase occurs at 4-12 months where the pain gradually subsides, but the stiffness remains. Lastly, the resolution phase takes between 12 and 42 months, with spontaneous improvement in the range of movement.[3,27,46] Only 2 studies included in the review had patients in the freezing stage,[25,26] while the other ones included participants in various stages or did not specify. However, overlapping of the distinct stages is possible because of the progression of the disease and inaccurate duration report.[24,26]

Because of the natural history of PFS, improvement over time is expected. In addition, long-term studies have shown that 40% of patients have persistent mild pain and shoulder motion limitation and 11% of patients have permanent disability of the shoulder joint.[13] Nevertheless, the trials focus on short follow-ups (3 months) rather than longer. Only 1 study follow-up covered up to 6 months.[31] The no specification of disease phase and the wide range of disease duration reported could explain some of the heterogeneous results between studies due to the expected improvement due to the natural history of the PFS. Some authors could include patients with longer disease duration than other authors.

Injections across the studies share common errors in their implementation that could possibly affect the outcomes. US-guided might not fully prevent steroid leakage.[15,16] Inaccurate administration may reduce the effectiveness of the intervention.[47] Furthermore, it could originate several side effects. Only 1 study assessed the accuracy of steroid administration through axillary fluoroscopic images. The accuracy of injection was 76.7% and 93.3% in the RI and PA groups, respectively.[25] These data suggest some imprecision despite the image guidance.

A triamcinolone dosage of 40 mg has been proven to be effective.[48,49] Four studies administered this dose of triamcinolone[14,25,26,37] and 1 study used 40 mg of prednisolone.[30] The drug combination used across the studies were similar, but the volume content was different. The ideal volume for hydro-dilatation remains uncertain.[24,50] Volumes of 10 mL,[25] 17 mL,[30] and 20 mL[14] have been described, which may produce an additional therapeutic effect distention of the capsule caused by the hydrostatic pressure.[51,52]. However, volumes of injected solution exceeding 18 mL may lead to the rupture of the joint capsule, leading to various adverse effects such as leakage of corticosteroids into the surrounding soft tissues.[24]

Complementary interventions implemented across studies were heterogenous and not included in the analysis. Although all studies employed an exercise regimen after the intervention, these lacked standardization of frequency, intensity, duration, supervision,

compliance assessment, and type of movements. The effectiveness of exercise therapy has been analyzed previously for pain relief, disability, and ROM.[53] Both home-based exercise programs and supervised exercise have demonstrated effectiveness.[10,53-56] A systematic review concluded that steroid injection combined with physical therapy provided more benefits during the freezing phase, whereas joint manipulation provided more benefits in the adhesive phase.[22]

Study limitations

The current study has several limitations. The inclusion of a limited number of studies poses a significant weakness in our research, limiting the generalizability of the results. The omission of searching for gray literature may have resulted in the exclusion of relevant information. The analysis focused solely on short-term outcomes, thereby overlooking potential long-term effects. Moreover, individual studies do not account for error measurement of the outcomes due to the absence of a reliability analysis (Cronbach alpha); this is important because of the reproducibility of the measurements. Additionally, because of the study's context, the administering physician was not blinded. Furthermore, owing to the limited number of incorporated studies, a quantitative assessment of moderators to explain the heterogeneity within the outcomes was not performed. The possible factors for this could be the eligibility criteria used among the studies, exercise practice, disease duration, and intervention protocol. Although the studies implemented an exercise protocol after the corticosteroid injection, the lack of standardization in the procedure poses a limitation. Lastly, the studies did not report restrictions on medication consumption post-intervention, which could have influenced both clinical outcomes and the effects of corticosteroids. These limitations should be considered when interpreting the results.

Future studies should evaluate the effect of corticosteroid injection by incorporating assessment methods such as imaging techniques to appraise the accuracy of the procedure. Longer follow-up periods and PFS recurrence would provide valuable insights. Subsequent research could explore the treatment effectiveness of combined injection approaches, taking into consideration the diverse involvement of various spaces in PFS. The standardization of the exercise program must be specified in future studies.

Conclusion

Both RI and PA groups demonstrated substantial pain relief and enhancement in functionality, and ROMs at 12 weeks post-injection. The data suggest a single US-guided corticosteroid injection into the RI significantly improves pain and function over the PA after 12 weeks. Although there were significant differences in abduction, internal, and external improvement between approaches, these differences could be clinically narrow. Subsequent studies should focus on a longer follow-up and register the recurrence of the PFS.

Keywords

Adhesive capsulitis; Corticosteroid injection; Frozen shoulder; Intra-articular; Meta-analysis; Randomized controlled trial; Rehabilitation; Rotator interval; Ultrasound

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References

1. Zuckerman JD, Rokito A. Frozen shoulder: a consensus definition. J Shoulder Elbow Surg 2011;20:322–5.
2. Cho CH, Song KS, Kim BS, Kim DH, Lho YM. Biological aspect of pathophysiology for frozen shoulder. Biomed Res Int 2018;2018:7274517.
3. Pandey V, Madi S. Clinical guidelines in the management of frozen shoulder: an update!. Indian J Orthop 2021;55:299–309.
4. Van der Windt D, Koes BW, De Jong BA, Bouter LM. Shoulder disorders in general practice: incidence, patient characteristics, and management. Ann Rheum Dis 1995;54:959–64.
5. Hand C, Clipsham K, Rees JL, Carr AJ. Long-term outcome of frozen shoulder. J Shoulder Elbow Surg 2008;17:231–6.
6. White D, Choi H, Peloquin C, Zhu Y, Zhang Y. Secular trend of adhesive capsulitis. Arthritis Care Res (Hoboken) 2011;63:1571–5.
7. Zreik NH, Malik RA, Charalambous CP. Adhesive capsulitis of the shoulder and diabetes: a meta-analysis of prevalence. Muscles Ligaments Tendons J 2016;6:26–34.
8. Arslan S, Celiker R. Comparison of the efficacy of local corticosteroid injection and physical therapy for the treatment of adhesive capsulitis. Rheumatol Int 2001;21:20–3.
9. Neviaser AS, Hannafin JA. Adhesive capsulitis: a review of current treatment. Am J Sports Med 2010;38:2346–56.
10. Challoumas D, Biddle M, McLean M, Millar NL. Comparison of treatments for frozen shoulder: a systematic review and meta-analysis. JAMA Netw Open 2020;3:e2029581.
11. Jacobs LG, Smith MG, Khan SA, Smith K, Joshi M. Manipulation or intra-articular steroids in the management of adhesive capsulitis of the shoulder? A prospective randomized trial. J Shoulder Elbow Surg 2009;18:348–53.
12. Lorbach O, Anagnostakos K, Scherf C, Seil R, Kohn D, Pape D. Nonoperative management of adhesive capsulitis of the shoulder: oral cortisone application versus intra-articular cortisone injections. J Shoulder Elbow Surg 2010;19:172–9.
13. Shin SJ, Lee SY. Efficacies of corticosteroid injection at different sites of the shoulder for the treatment of adhesive capsulitis. J Shoulder Elbow Surg 2013;22:521–7.
14. Wang JC, Tsai PY, Hsu PC, et al. Ultrasound-guided hydrodilatation with triamcinolone acetonide for adhesive capsulitis: a randomized controlled trial comparing the posterior glenohumeral recess and the rotator cuff interval spproaches. Front Pharmacol 2021;12:686139.
15. Aly AR, Rajasekaran S, Ashworth N. Ultrasound-guided shoulder girdle injections are more accurate and more effective than landmark-guided injections: a systematic review and meta-analysis. Br J Sports Med 2015;49:1042–9.
16. Wu T, Song HX, Dong Y, Li JH. Ultrasound-guided versus blind subacromial-subdeltoid bursa injection in adults with shoulder pain: a systematic review and meta-analysis. Semin Arthritis Rheum 2015;45:374–8.
17. Alfaro-Gomez U, Fuentes-Ramirez LD, Chavez-Blanco KI, et al. Anatomical variations of the acromial and coracoid process: clinical relevance. Surg Radiol Anat 2020;42:877–85.
18. Tapia-Nañez M, Quiroga-Garza A, Guerrero-Mendivil FD, et al. A review of the importance of research in Anatomy, an evidence-based science. Eur J Anat 2022;26:477–86.

19. Chen R, Jiang C, Huang G. Comparison of intra-articular and subacromial corticosteroid injection in frozen shoulder: a meta-analysis of randomized controlled trials. Int J Surg 2019;68:92–103.
20. Sun Y, Zhang P, Liu S, et al. Intra-articular steroid injection for frozen shoulder: a systematic review and meta-analysis of randomized controlled trials with trial sequential analysis. Am J Sports Med 2017;45:2171–9.
21. Yoon JP, Chung SW, Kim JE, et al. Intra-articular injection, subacromial injection, and hydrodilatation for primary frozen shoulder: a randomized clinical trial. J Shoulder Elbow Surg 2016;25:376–83.
22. Zhang J, Zhong S, Tan T, et al. Comparative efficacy and patient-specific moderating factors of nonsurgical treatment strategies for frozen shoulder: an updated systematic review and network meta-analysis. Am J Sports Med 2021;49:1669–79.
23. Henkus HE, Cobben LP, Coerkamp EG, Nelissen RG, van Arkel ER. The accuracy of subacromial injections: a prospective randomized magnetic resonance imaging study. Arthroscopy 2006;22:277–82.
24. Cho JH. Updates on the treatment of adhesive capsulitis with hydraulic distension. Yeungnam Univ J Med 2021;38:19–26.
25. Cho C-H, Kim DH, Kim D-H, et al. Comparative efficacy of rotator interval versus posterior capsule approach intraarticular corticosteroid injections for primary frozen shoulder: a single-blind, randomized trial. Pain Physician 2022;25:313–21.
26. Sun Y, Liu S, Chen S, Chen J. The effect of corticosteroid injection into rotator interval for early frozen shoulder: a randomized controlled trial. Am J Sports Med 2018;46:663–70.
27. Tamai K, Akutsu M, Yano Y. Primary frozen shoulder: brief review of pathology and imaging abnormalities. J Orthop Sci 2014;19:1–5.
28. Ozaki J, Nakagawa Y, Sakurai G, Tamai S. Recalcitrant chronic adhesive capsulitis of the shoulder. Role of contracture of the coracohumeral ligament and rotator interval in pathogenesis and treatment. J Bone Joint Surg Am 1989;71:1511–5.
29. Neer CS, Satterlee CC, Dalsey RM, Flatow EL. The anatomy and potential effects of contracture of the coracohumeral ligament. Clin Orthop Relat Res 1992;280:182–5.
30. Elnady B, Rageh EM, Hussein MS, et al. In shoulder adhesive capsulitis, ultrasound-guided anterior hydrodilatation in rotator interval is more effective than posterior approach: a randomized controlled study. Clin Rheumatol 2020;39:3805–14.
31. Prestgaard T, Wormgoor MEA, Haugen S, Harstad H, Mowinckel P, Brox JI. Ultrasound-guided intra-articular and rotator interval corticosteroid injections in adhesive capsulitis of the shoulder: a double-blind, sham-controlled randomized study. Pain 2015;156:1683–91.
32. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev 2021;10:89.
33. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, Welch VA. Cochrane Handbook for Systematic Reviews of Interventions. Chichester, UK: John Wiley & Sons; 2019.
34. Sim J, Wright CC. The kappa statistic in reliability studies: use, interpretation, and sample size requirements. Phys Ther 2005;85:257–68.
35. Sterne JA, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019: 366.
36. Faraone SV. Interpreting estimates of treatment effects: implications for managed care. P T 2008;33:700–11.
37. Deng Z, Li Z, Li X, et al. Comparison of outcomes of two different corticosteroid injection approaches for primary frozen shoulder: a randomized controlled study. J Rehabil Med 2023;55:jrm00361.
38. Lee DH, Yoon SH, Lee MY, Kwack KS, Rah UW. Capsule-preserving hydrodilatation with corticosteroid versus corticosteroid injection alone in refractory adhesive capsulitis of shoulder: a randomized controlled trial. Arch Phys Med Rehabil 2017;98:815–21.
39. Jost B, Koch PP, Gerber C. Anatomy and functional aspects of the rotator interval. J Shoulder Elb Surg 2000;9:336–41.
40. Bunker T, Anthony P. The pathology of frozen shoulder. A Dupuytren-like disease. J Bone Joint Surg Br Vol 1995;77:677–83.
41. Bunker T, Reilly J, Baird K, Hamblen D. Expression of growth factors, cytokines and matrix metalloproteinases in frozen shoulder. J Bone Joint Surg Br Vol 2000;82:768–73.
42. Wu CH, Chen WS, Wang TG. Elasticity of the coracohumeral ligament in patients with adhesive capsulitis of the shoulder. Radiology 2016;278:458–64.
43. Juel NG, Oland G, Kvalheim S, Love T, Ekeberg OM. Adhesive capsulitis: one sonographic-guided injection of 20 mg triamcinolon into the rotator interval. Rheumatol Int 2013;33:1547–53.
44. Yoong P, Duffy S, McKean D, Hujairi NP, Mansour R, Teh JL. Targeted ultrasound-guided hydrodilatation via the rotator interval for adhesive capsulitis. Skeletal Radiol 2015;44:703–8.
45. Cho C-H, Bae K-C, Kim D-H. Treatment strategy for frozen shoulder. Clin Orthop Surg 2019;11:249–57.
46. Dias R, Cutts S, Massoud S. Frozen shoulder. BMJ 2005;331:1453–6.
47. Eustace J, Brophy D, Gibney R, Bresnihan B, FitzGerald O. Comparison of the accuracy of steroid placement with clinical outcome in patients with shoulder symptoms. Ann Rheum Dis 1997;56:59–63.
48. de Jong BA, Dahmen R, Hogeweg JA, Marti RK. Intra-articular triamcinolone acetonide injection in patients with capsulitis of the shoulder: a comparative study of two dose regimens. Clin Rehabil 1998;12:211–5.
49. Yoon SH, Lee HY, Lee HJ, Kwack KS. Optimal dose of intra-articular corticosteroids for adhesive capsulitis: a randomized, triple-blind, placebo-controlled trial. Am J Sports Med 2013;41:1133–9.
50. Cho CH, Kim du H, Bae KC, Lee D, Kim K. Proper site of corticosteroid injection for the treatment of idiopathic frozen shoulder: results from a randomized trial. Joint Bone Spine 2016;83:324–9.
51. Koh ES, Chung SG, Kim TU, Kim HC. Changes in biomechanical properties of glenohumeral joint capsules with adhesive capsulitis by repeated capsule-preserving hydraulic distensions with saline solution and corticosteroid. PM R 2012;4:976–84.
52. Buchbinder R, Green S, Youd JM, Johnston RV, Cumpston M. Arthrographic distension for adhesive capsulitis (frozen shoulder). Cochrane Database Syst Rev 2008:Cd007005.
53. Mertens MG, Meert L, Struyf F, Schwank A, Meeus M. Exercise therapy is effective for improvement in range of motion, function, and pain in patients with frozen shoulder: a systematic review and meta-analysis. Arch Phys Med Rehabil 2022;103:998–1012.e14.
54. Kelley MJ, Shaffer MA, Kuhn JE, et al. Shoulder pain and mobility deficits: adhesive capsulitis. J Orthop Sports Phys Ther 2013;43:A1–31.
55. Jain TK, Sharma NK. The effectiveness of physiotherapeutic interventions in treatment of frozen shoulder/adhesive capsulitis: a systematic review. J Back Musculoskelet Rehabil 2014;27:247–73.
56. Nakandala P, Nanayakkara I, Wadugodapitiya S, Gawarammana I. The efficacy of physiotherapy interventions in the treatment of adhesive capsulitis: a systematic review. J Back Musculoskelet Rehabil 2021;34:195–205.