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ORIGINAL ARTICLE • SHOULDER - SPORT

Comparative outcomes of combined corticosteroid with low volume compared to high volume of local anesthetic in subacromial injection for impingement syndrome: systematic review and meta-analysis of RCTs

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Abstract Subacromial impingement syndrome (SIS) is one of the most frequent pathologies of the shoulder, which may cause serious restriction of daily activities and lifestyle changes. Corticosteroid injection (CI) into the subacromial space is a palliative treatment option. Currently, there have been no studies that compare between the different volumes of CI injection. We have conducted a systematic review and meta-analysis to answer our specific study questions: Are high volume (< 5 ml) better than low volume (≥ 5 ml) of CI injection with respect to pain reduction? This systematic review was conducted according to the preferred reporting items for systematic reviews and meta-analyses guidelines. Relevant studies were identified from Medline and Scopus from inception to May 11, 2017 that reported American shoulder and elbow surgeons (ASES) function score, pain visual analog score (VAS), and postoperative complications of either group. Fifteen studies were included for the analysis of high volume (more than or equal 5 ml), and 5 studies were included for analysis of low volume (less than 5 ml). Overall, there were 1101 patients (732 in the high-volume group and 369 in the low-volume group). A pooling of mean VAS and ASES function score was ($N = 557$) 2.02 (95% CI 1.52, 2.53), ($N = 190$) 82.59 (95% CI 76.92, 88.27) in high-volume group and ($N = 179$) 2.60 (95% CI 1.94, 3.26), ($N = 95$) 84.65 (95% CI 81.64, 86.82) in low-volume group, respectively. The unstandardized mean difference of ASES and VAS of high volume was − 0.58 (95% confidence interval (CI): − 1.38, 0.22) and − 2.06 (95% CI − 8.35, 4.23) scores lower than low-volume CI in SIS patients, but without statistical significance. A total of 11 studies in the high-volume group and 4 studies in the low-volume group reported adverse effects. The total complication rate per patient was 6.2% (2.3, 10.1%) in the high-volume group and 11.7% (0.3, 12%) in the low-volume group ($p = 0.091$). No significant differences were noted for complications. In subacromial impingement syndrome, the corticosteroid injection had acceptable pain and functional outcomes. Higher volume had a lower ASES, VAS, and risk of having complication when compared to lower volume. However, there are no statistically significant differences between groups. Larger,

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randomized noninferiority or equivalent trial studies are needed to confirm these findings as the current literature is still insufficient.
Level of evidence I.

Keywords Subacromial impingement syndrome · SIS · Corticosteroid injection · Different volume · VAS

Introduction

Shoulder pain is the third most prevalent type of musculoskeletal disorder following spinal and knee pain and has a tremendous psychosocial impact when it progresses to the chronic stage [25]. The cause of shoulder pain can include bursa (bursitis), muscle, tendon (rotator cuff tendinopathy or tears), ligament (instability), and bony structure (glenohumeral, acromioclavicular, and sternoclavicular joints) [4]. Subacromial impingement syndrome (SIS) is one of the most frequent pathologies of the shoulder, which may cause serious restriction of daily activities and lifestyle changes [37]. Subacromial impingement encompasses many commonly used terms including "tendinosis" "rotator cuff fraying," "partial thickness tears," and "tendinitis" [1, 23]. Initial treatment of SIS is conservative, with oral medications, physical therapy, or subacromial injections. In symptomatic tendinosis, a corticosteroid injection into the subacromial space is a palliative treatment option [17]. Many systematic reviews of corticosteroids injections (CI) reported that CI are effective for improvement of pain for SIS [4, 23, 37, 39]. However, the heterogeneity of CI was quite high and the possible cause of the heterogeneity might be the approach of administration CI (landmark-guided (LMG) and US-guided (USG) approach), different doses (low or high), different site (anterior, lateral, and posterior) and different volume (low or high). Not only two different approaches have small and may not represent clinical difference, but also two different doses (20 and 40 mg) have no significant differences between the high- and low-dose CIs reported in current high methodological study (systematic review [29] and RCT [12]). Whereas the results of different sites of CI injection in patients SIS are debated in previous published studies [14, 16, 20, 30, 31], there have been no studies that compare between the different volumes of CI injection. Therefore, we have conducted a systematic review and meta-analysis to answer our specific study questions: (1) Do the different sites of CI injection in patients SIS have different clinical outcomes? (2) Are high volume (< 5 ml) better than low volume (≥ 5 ml) of CI injection with respect to pain reduction?

Materials and methods

Medline and Scopus databases were used for identifying relevant studies published in English since the date of inception to May 11, 2017. The PubMed and Scopus search engines were used to locate studies with the following search terms: impingement syndrome AND intra-articular steroid injection AND clinical study. Search strategies for Medline and Scopus are described in detail in the "Appendix" section. References from the reference lists of included trials were also explored.

Selection of studies

Identified studies were first selected based on titles and abstracts by two independent authors (M.B. and A.A.). Full papers were retrieved if a decision could not be made from the abstracts. Disagreements were resolved by consensus and discussion with a third party (J.K.). Reasons for ineligibility or exclusion of studies were recorded and described.

Inclusion criteria

Randomized controlled trials (RCTs) and comparative studies that compared clinical outcomes between low-volume corticosteroid injection (low-CI) and high-volume corticosteroid injection (high-CI) for treatment SIS were eligible if they met following criteria: Compared at least one of the following outcomes: American Shoulder and Elbow Surgeons (ASES) function score, pain visual analog score (VAS), and postoperative complications; had sufficient data to extract and pool, i.e., the reported mean, standard deviation (SD), the number of subjects according to treatments for continuous outcomes, and the number of patients according to treatment for dichotomous outcomes.

Data extraction

Two reviewers (S.S. and A.A.) independently performed data extraction using standardized data extraction forms. General characteristics of the study (i.e., mean age, gender, body mass index (BMI), mean follow-up time, mean duration of symptom, pain VAS and ASES scores at baseline) were extracted. The number of subjects, means, and SD of continuous outcomes (i.e., pain VAS and ASES scores) between groups were extracted. Cross-tabulated frequencies between treatment and all dichotomous outcomes (complications) were also extracted. Any disagreements were resolved by discussion and consensus with a third party (J.K.).

Risk of bias assessment

Two authors (S.S. and A.A.) independently assessed risk of bias for each study following suggestion in the PRISMA guideline [18]. Six domains were assessed, which included sequence generation, allocation concealment, blinding (participant, personnel, and outcome assessors), incomplete outcome data, selective outcome reporting, and other sources of bias. Disagreements between two authors were resolved by consensus and discussion with a third party (J.K.). Level of agreement for each domain and the overall domains were assessed using the kappa statistics.

Outcomes of interest

The outcomes of interests included ASES, pain VAS and postoperative complications. These outcomes were measured as reported in the original studies, which were VAS pain scale from 0 to 10 cm (lower values of these scores refer to better outcomes), ASES score from 0 to 100 (higher values are equivalent to better outcomes). Postoperative complications (diarrhea, infection, rash, hematoma) were also considered.

Statistical analysis

For continuous outcomes (VAS and ASES), unstandardized mean differences (UMDs) were pooled and calculated using the method as follows [34]:

$$\text{UMD}\ (d_i) = (\bar{x})_{1i} - (\bar{x})_{2i},\ \ \text{var}(d_i) = \frac{\text{sd}_{1i}^2}{n_{1i}} + \frac{\text{sd}_{2i}^2}{n_{2i}},\quad w_i = \frac{1}{\text{var}(d_i)}$$

where w_i is the weighting factor, d_i is the standardized/unstandardized difference of means, D_i is the pooled difference of means, n_{1i} and n_{2i} are the number of subjects in group 1 and 2, n_i is $n_{1i} + n_{2i}$, sd_i is the pooled standard deviation, $\text{var}(d_i)$ is variance of difference, and the subscript i is the study i. Heterogeneity was checked using Q statistic as follows: $Q = \sum_i^k w_i\left(d_i - D\right)^2$, $D = \frac{\sum_{i=1}^k w_i d_i}{\sum_{i=1}^k w_i}$, $w_i = \frac{1}{\text{var}(d_i)}$. The Q statistic follows a Chi-square distribution with $k - 1$ degrees of freedom (df).

For dichotomous outcomes (complications), the prevalence was pooled and calculated using the inverse variance method as follows [34] $(\bar{p}) = \frac{\sum w_i p_i}{\sum w_i}$ where p is the pooled prevalence, p_i is the prevalence of complications of each study, w_i is $1/\text{var}(p_i)$, which is the weight of each study. Heterogeneity of prevalence across studies p was checked as follows: $\sum w_i\left(p_i - (\bar{p})\right)^2$. The Q statistic follows a χ^2 distribution with number of studies $(k) - 1$ degree of freedom (df). The degree of heterogeneity was also quantified using the I^2 statistic [11]. This value can range from 0 to 100%, the closer to 100%, the higher the heterogeneity. If heterogeneity was present, between-studies variation was then estimated as follows: $\tau^2 = \frac{Q-(k-1)}{\sum w_i - \frac{\sum w_1^2}{\sum w_1}}$ if Q k 1 or 0 otherwise. This was used to calculate a weight term that accounted for variations between studies $w_i^* = \frac{1}{\text{var}(p_1)=\tau^2}$, and then, the pooled prevalence was estimated using the random effects model as follows: 95% CI $= (\bar{p})^* \pm \frac{1.96}{\sqrt{\sum w_i^*}}(\bar{p})$.

Meta-regression analysis was then applied to explore causes of heterogeneity [11, 35]. Coverable parameters, i.e., mean age, gender, body mass index (BMI), mean follow-up time, mean duration of symptom, pain VAS, and ASES scores at baseline, were considered in the meta-regression model. Power of the test for meta-regression was also assessed [32]. The unstandardized mean difference (UMD) and odds ratio (OR) were estimated by direct and indirect meta-analyses using a random effects model; otherwise, a fixed effects model was applied. All analyses were performed using STATA version 14.0 [33].

Result

Twenty-one and 340 studies were identified from Medline and Scopus, respectively (Fig. 1); 13 studies were duplicates, leaving 348 studies for review of titles and abstracts. Of these, 20 studies were reviewed and data extracted. Characteristics of the 20 studies [1, 3, 5, 6, 10, 12, 14–16, 21, 22, 24, 26–28, 31, 36, 38, 40] are described in Table 1. Fifteen [3, 5, 6, 10, 12, 14–16, 22, 26–28, 31, 38, 40] of 20 studies were high-CI and 5 studies [1, 21, 24, 36] were low-CI studies that reported postoperative VAS, ASES and postoperative complications. In high-CI, VAS, ASES and complication were reported in 10, 5 and 11 studies, while in low-CI those were reported in 4, 2 and 2 studies, respectively (Fig. 1). Mean age, BMI, and mean follow-up time of participants varied from 39.3 to 65 years, 23.4 to 28.5 kg/m^2, and 4 to 24 months, respectively. Percentages of male patients and dominant side ranged from 22 to 73 and 39 to 69, respectively. Steroid injection agents were triamcinolone acetate (TA), betamethasone, Depo-Medral, and Diprophos in 16, 2, 1, and 1 studies, respectively. Most studies used triamcinolone acetate (TA) and lidocaine for steroid injection and local analgesic agents.

Risk of bias in included studies

Risk of bias is described in Table 2.

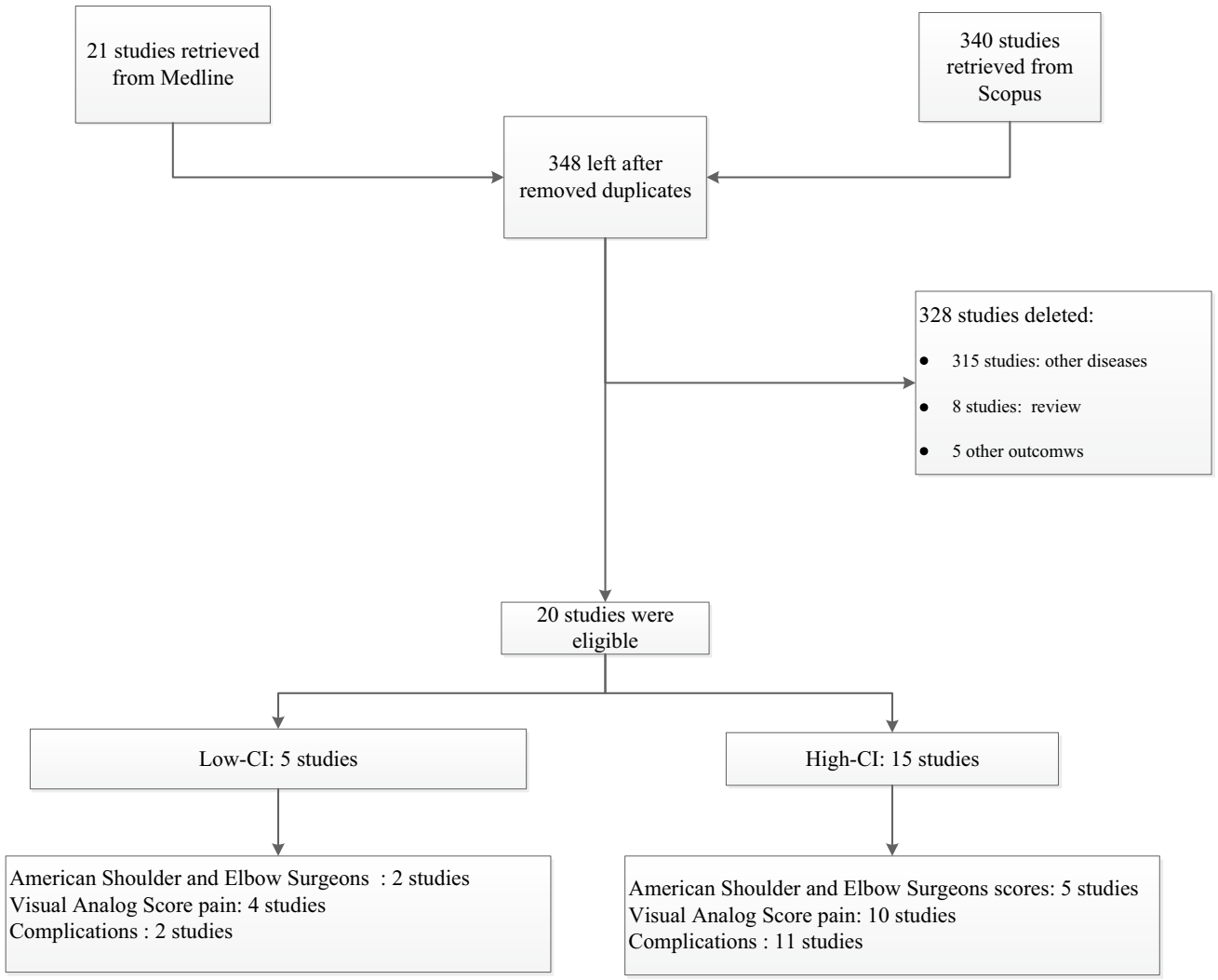

Fig. 1 Flow of study selection

Outcomes

Pooled mean VAS in high-CI and low-CI

Four studies [21, 24, 36] and 11 studies [3, 5, 6, 12, 14, 16, 22, 26, 27, 31, 40] using low-CI and high-CI in SIS were included for pooling of means VAS with 95% confidence intervals (Table 3). In terms of VAS score, with the high-CI group containing 557 patients and low-CI having 179 patients, the pooled mean VAS of high-CI varied highly across studies (I^2 = 93.8) and was 2.02 scores (95% CI 1.52, 2.53) (Table 3). The pooled mean of VAS of 4 low-CI studies varied across studies (I^2 = 97.01) and 2.60 (95% CI 1.94, 3.26). From the result of the indirect meta-analysis, the pooled UMD was − 0.58 (95% CI − 1.38, 0.22), which translates to the mean VAS of high-volume CI being 0.58 scores lower than low-volume CI in SIS but not with a statistically significant difference.

Pooled mean ASES in high-CI and low-CI

Five studies [15, 16, 26, 31, 38] using high-CI and [1, 36] low-CI in SIS were included for pooling of means ASES with 95% confidence intervals (Table 3). For the high-CI group of 190 patients and low-CI group of 95 patients, the pooled mean ASES of high-CI was (I^2 = 87.23) 82.59 (95% CI 76.92, 88.27) and low-CI was (I^2 = 0) 84.65 (95% CI 81.64, 86.82) scores (Table 3). From indirect meta-analysis, the pooled UMD was − 2.06 (95% CI − 8.35, 4.23), translating to the mean ASES of high-CI about 2.06 scores insignificantly lower when compared to low-CI.

Pooled prevalence of adverse effect between high-CI and low-CI

Eleven high-CI studies [3, 6, 10, 12, 15, 26–28, 31, 38, 40] and 2 low-CI studies [21, 36] pooled the prevalence

Table 1 Characteristics of included studies

Author	Years	Type of study	Follow-up (weeks)	Steroid (ml)	Local analgesic agent (ml)	Total volume (ml)	Age (years)	BMI (kg/m^2)	Dominant (right%)	Sex (male%)	Outcomes
High volume (≥ 5 ml)											
Kim DY	2017	I	13	TA 40 mg:1	Lidocaine:4	5	54	23.44	0.5	0.63	VAS and ASES
von WL	2016	I (quasi)	24	40 mg 1 ml	Lidocaine:4	5	54	–	–	0.48	ASES, complications
Carroll MB	2015	I	4	TA 40 mg:2	Lidocaine:4	6	65	–	0.39	0.61	VAS and complications
Rhon DI	2014	I	24	TA 40 mg:2	Marcaine:6	8	41	28.45	0.55	0.35	VAS and complications
Shin SJ	2013	I	16	40 mg 1 ml	Lidocaine:4	5	54.5	–	0.69	0.639	VAS, ASES, complications
Min KS	2013	I	4	TA 40 mg:1	Lidocaine:6	7	39.3	–	0.53	0.21	VAS
Dietrich TJ	2013	I	4	40 mg 1 ml	Lidocaine:4	5	56.2	–	–	0.439	VAS
Zufferey P	2012	I	6	Diprophos:2	Lidocaine:7	9	53.5	–	0.55	0.43	VAS, complications
Penning LIF	2012	I	24	TA 10 mg:2	Lidocaine:8	10	52.5	–	0.58	0.48	VAS, ASES and complication
Dogu B	2012	I	6	Betamethasone:1	Prilocaine:9	10	55.9	–	0.69	0.67	VAS and complications
Hong JY	2011	I	8	TA 40 mg:4	Lidocaine:4	8	49.8	–	0.57	0.53	Complications
Karthikeyan S	2010	I	6	TA 40 mg:1	Lidocaine:5	6	59	–	–	0.45	ASES and complications
Kang MN	2008	I (quasi)	12	Depomedral 80 mg:2	Bupivacaine:5	7	54.7	28.5	–	0.52	VAS
Rutten MJ	2007	I	–	TA 40 mg:1	Prilocaine:4	5	44	–	0.65	0.4	Complications
Hay EM	2003	I	24	TA 40 mg:1	Lidocaine:4	5	57.55	–	–	0.53	Complications
Low volume (< 5 ml)											
Aksakal M	2017	I	4	Betamethasone: 1	–	1	–	–	–	0.31	ASES
Ucuncu F	2009	II	6	TA 40 mg:1	Lidocaine:1	2	53	–	–	0.63	VAS, ASES and complications
Naredo E	2004	I	6	TA 40 mg:1	Lidocaine:1	2	52.4	–	0.52	0.73	VAS
McInerney JJ	2003	I	6	TA 40 mg:1	Bupivacaine:2	3	–	–	–	–	VAS and complications
Petri M	1987	I	12	TA 40 mg:1	Lidocaine:3	4	48	–	–	0.48	VAS

BMI body mass index, *TA* triamcinolone acetate, *VAS* visual analog score, *ASES* American shoulder and elbow function score, *quasi* quasi-randomized controlled trial

Table 2 Risk of bias assessment

Author	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective outcome report	Free of other bias	Description of other bias
Kim DY	Y	Y	N	Y	Y	N	Per-protocol analysis
von WL	N	N	N	Y	Y	N	Per-protocol analysis
Carroll MB	Y	Y	Y	Y	Y	Y	–
Rhon DI	Y	Y	N	Y	Y	Y	–
Shin SJ	Y	Y	N	Y	Y	N	Per-protocol analysis
Min KS	Y	Y	Y	Y	Y	Y	–
Dietrich TJ	N	N	N	N	Y	N	Per-protocol analysis
Zufferey P	U	U	Y	N	Y	N	Per-protocol analysis
Penning LIF	Y	Y	Y	Y	Y	Y	–
Dogu B	U	U	Y	N	Y	N	Per-protocol analysis
Hong JY	Y	Y	Y	N	Y	N	Per-protocol analysis
Karthikeyan S	U	Y	Y	N	Y	N	Per-protocol analysis
Kang MN	U	U	Y	Y	Y	Y	–
Rutten MJ	Y	Y	N	Y	Y	Y	–
Hay EM	U	N	N	N	Y	N	Per-protocol analysis
Aksakal M	Y	Y	Y	N	Y	N	Per-protocol analysis
Ucuncu F	U	N	N	N	Y	N	Per-protocol analysis
Naredo E	Y	U	Y	Y	Y	Y	–
McInerney JJ	Y	Y	Y	Y	Y	Y	–
Petri M	Y	N	Y	Y	Y	Y	–

Table 3 Estimation of the pooled mean of ASES and VAS pain of high-CI and low-CI

Author	Follow-up	Age	Male	*N*	VAS		ASES	
					Mean	SD	Mean	SD
Kim DY	13	54	0.63	46	2.1	0.4	76.75	22.67
von WL	24	54	0.48	25	–	–	87.5	12.3
Carroll MB	4	65	0.61	13	2.29	0.84	–	–
Rhon DI	24	41	0.35	52	2.2	2.2	–	–
Shin SJ	16	54.5	0.639	41	1.4	0.5	87.1	3.2
Min KS	4	39.3	0.21	15	0.9	1.86	–	–
Dietrich TJ	4	56.2	0.439	98	2.55	2.34	–	–
Zufferey P	6	53.5	0.43	65	2.85	0.29	–	–
Penning LIF	24	52.5	0.48	51	0.37	3.71	80.4	16.31
Dogu B	6	55.9	0.67	46	0.5	0.31	–	–
Hong JY	8	49.8	0.53	60	2.6	0.61	–	–
Karthikeyan S	6	59	0.45	27	–	–	73.5	34.2
Kang MN	12	54.7	0.52	60	3.43	2.91	–	–
Rutten MJ	–	44	0.4	20	–	–	–	–
Hay EM	24	57.55	0.53	103	–	–	–	–
Pooled mean high-CI (95% CI)					2.02 (1.52, 2.53)		82.59 (76.92, 88.27)	
Aksakal M	4	–	0.31	35	–	–	85.5	14.1
Ucuncu F	6	53	0.63	60	3.02	0.47	85.6	3.85
Naredo E	6	52.4	0.73	40	2.1	0.51	–	–
McInerney JJ	6	–	–	54	1.38	0.7	–	–
Petri M	12	48	0.48	25	2.04	0.31	–	–
Pooled mean low-CI (95% CI)					2.60 (1.94, 3.26)		84.65 (81,64, 86.82)	
UMD (95% CI) of high-CI versus low-CI					− 0.58 (− 1.38, 0.22)		− 2.06 (− 8.35, 4.23)	

of adverse effect after injection. For the high-CI group of 466 patients and low-CI group of 114 patients, the pooled prevalence of high-CI and low-CI was ($I^2 = 0$ and 53.87) 0.062 (95% CI 0.022, 0.102) and 0.117 (95% CI 0.03, 0.198) (Table 4). From indirect meta-analysis, the difference in the risk of having adverse effect between two groups was 0.57 (95% CI 0.24, 1.36) indicating that the chance of having a diarrhea, infection, rash and hematoma of high-CI group was about 43 percent insignificantly lower than the low-CI group (Table 4).

Sources of heterogeneity and subgroup analysis

Meta-regression was applied for exploring the cause of heterogeneity by fitting a co-variable (i.e., mean age, gender, body mass index (BMI), mean follow-up time, mean duration of symptom, pain VAS, and ASES scores at baseline), and meta-regression was applied to assess this. None of the co-variables could explain the heterogeneity. However, the administering CI might be the source of heterogeneity. Therefore, subgroup analyses were performed as described in Table 5. Four studies had assessed the VAS between landmark-guided (LMG) and ultrasound-guided (USG) CI in SIS. There were 106 and 105 patients in USG and LMG

Table 4 Estimation of the pooled prevalence of postoperative complication of high-CI and low-CI

Author	Follow-up	Age	Male	*N*	Complication	
					Yes	No
Kim DY	13	54	0.63	46	–	–
von WL	24	54	0.48	25	0	25
Carroll MB	4	65	0.61	13	3	0
Rhon DI	24	41	0.35	52	–	–
Shin SJ	16	54.5	0.639	41	10	31
Min KS	4	39.3	0.21	15	1	14
Dietrich TJ	4	56.2	0.439	98	–	–
Zufferey P	6	53.5	0.43	65	0	65
Penning LIF	24	52.5	0.48	51	0	51
Dogu B	6	55.9	0.67	46	0	46
Hong JY	8	49.8	0.53	60	2	58
Karthikeyan S	6	59	0.45	27	0	27
Kang MN	12	54.7	0.52	60	–	–
Rutten MJ	–	44	0.4	20	0	20
Hay EM	24	57.55	0.53	103	0	103
Pooled prevalence high-CI (95% CI) 0.062 (0.022, 0.102)						
Aksakal M	4	–	0.31	35		–
Ucuncu F	6	53	0.63	60	7	53
Naredo E	6	52.4	0.73	40		–
McInerney JJ	6	–	–	54	0	54
Petri M	12	48	0.48	25		
Pooled prevalence low-CI (95% CI) 0.117 (0.03, 0.198)						
RR of high-CI versus low-CI 0.57 (0.24, 1.36)						

Table 5 Mean differences of VAS pain between ultrasound-guided and blinded CI injection in SIS with high-CI and low-CI subgroups

Author	Ultrasound guided			Landmark guided		
	N	Mean	SD	*N*	Mean	SD
Zufferey P	32	3.2	1	33	2.5	1
Dogu B	23	0.57	0.95	23	0.43	1.16
High-CI	UMD (95% CI) − 0.45 (− 0.99, 0.09), $I^2 = 71.6$					
Ucuncu F	30	3.77	1.65	30	2.27	1.94
Naredo E	21	3.49	2.13	20	0.71	0.82
Low-CI	UMD (95% CI) − 2.13 (− 3.38, − 0.87)*, $I^2 = 49.2$					
All volume CI UMD (95% CI) − 1.21 (− 2.18, − 0.24)*, $I^2 = 86.6$						

groups, respectively. The pooled unstandardized mean difference (UMD) of USG had high heterogeneity across studies ($I^2 = 86.6$) with VAS of − 1.21 (95% CI − 2.18, − 0.24) statistically significant lower than LMG. Subgroup analysis performed for high-CI in 2 studies and low-CI in 2 studies showed that the low-CI studies were statistically significantly different between USG and LMG while the high-C studies were insignificantly different between two groups (Table 5, Fig. 2).

Discussion

Until now, there have been no studies in the literature comparing the results of different volumes of CI in SIS. The purpose of this study was to assess whether there is a difference in the pain, function and adverse effect of high-CI versus low-CI in SIS based on the current evidence base. The results indicated that high-CI had no statistically significantly different lower pain and function score when compared to low-CI. The magnitude of these differences was only 0.6 score of VAS and 2.1 score of ASES which were considered not to be a statistically and clinically meaningful difference. Adverse effects include diarrhea, infection, rash, and hematoma; high-CI had lower risk of 42 percent than low-CI in treatment SIS. However, there is no statistically significant difference.

The mean VAS pain, ASES score and prevalence of complications among included studies were heterogeneous, possibly due to methodological and clinical differences. Attempts were made to explore sources of heterogeneity by considering clinical (i.e., mean age, gender, body mass index (BMI), mean follow-up time, mean duration of symptom, pain VAS, and ASES scores at baseline) and methodological variables (i.e., type of studies) in the meta-regression model. None of the co-variables could explain the heterogeneity (the degree of heterogeneity, however, did not decrease after pooling by all subgroups, indicating the presence of other sources of heterogeneity.). However, some important clinical factors that may have had effect include side of injection (anterior, lateral, and posterior) and precision of CI in SIS (USG vs LMG) that are suspected to be the source of heterogeneity of CI in SIS. After subgroup analyses, the results show that there are still no differences in ASES, VAS, and adverse effects between different sides of injection. The difference in precision of injection could be the source of heterogeneity ($I^2 = 86.6$ and 49.2). High-CI with USG or LMG there has no significant difference pain. While low-CI with USG has significant difference pain when compared to low-CI with LMG. Therefore, we recommended using USG

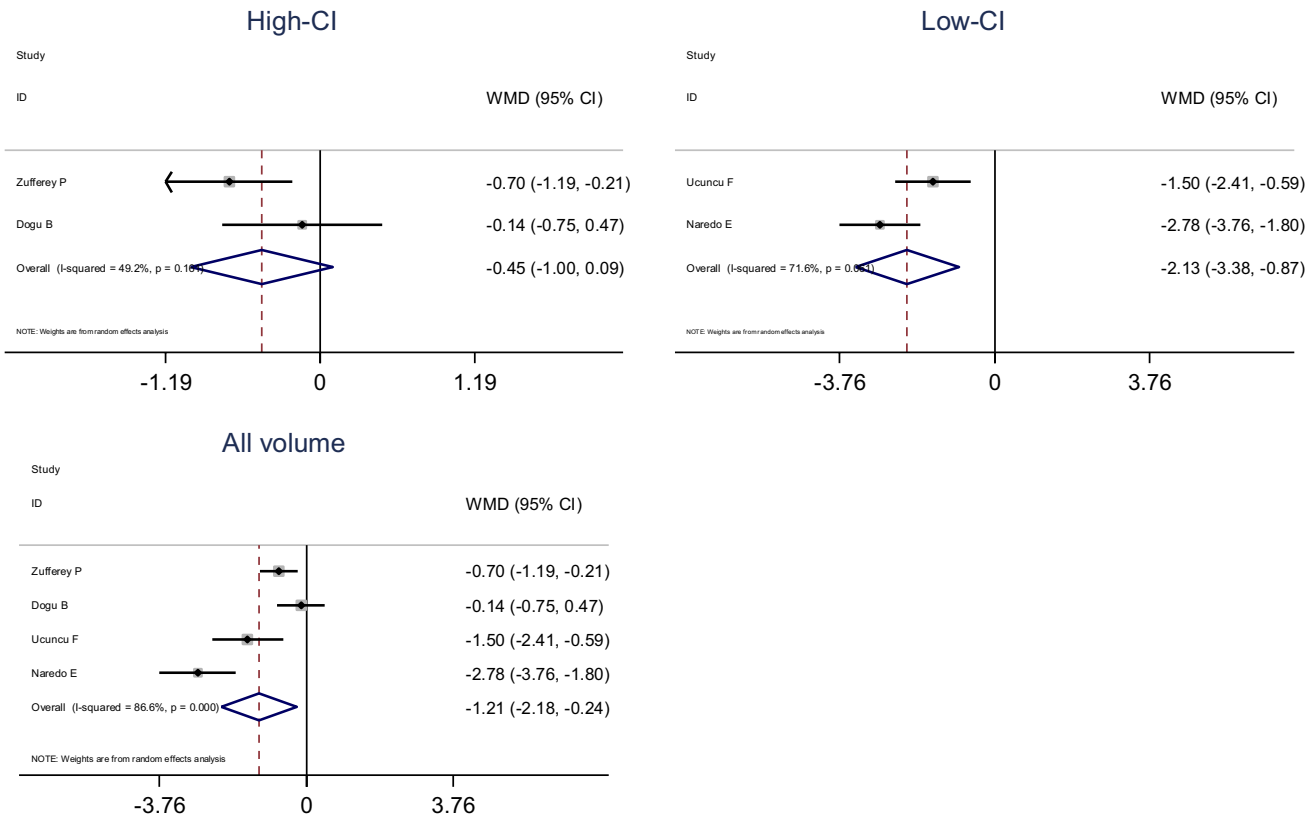

Fig. 2 Subgroup analysis of VAS pain between ultrasound-guided and blinded CI injection in SIS

technique in low-CI to improved outcome of CI injection in SIS while high-CI can use LMG technique.

Corticosteroids, such as triamcinolone, impart both anti-inflammation and direct analgesic effects through reducing proinflammatory mediators and influencing the cells involved in inflammatory responses [2]. The possible mechanisms include anti-inflammatory effects, local hyperemia, reflex muscle spasm relaxation, influence of local tissue metabolism, pain relief, mechanical improvement, and placebo effect [7, 24, 36]. In addition to these effects, corticosteroid injections can cause temporary increases in pain, skin atrophy, depigmentation, and septic arthritis as well as deleterious effects on intra-articular cartilage or tendon degeneration and even tendon ruptures [6, 7, 9, 19, 28]. The onset of action of corticosteroid is 24–48 h, and the duration of action is approximately 2–3 weeks [8]. Local anesthetics, such as lidocaine, act by membrane stabilization with a preferential block to small fibers that carry pain and autonomic impulses. Although the pharmacologic action is dissimilar, both corticosteroid and local anesthetic produce similar effects with regard to pain and subsequent improvement in strength and upper limb function [13]. However, in clinical practice, physicians often use a combination of corticosteroid suspension with local anesthetics during local soft tissue injection. But the optimal dosage, concentration, and volume in the subacromial space remain unclear. This study shows that there is no clinical benefit of high-volume lidocaine combined with corticosteroid injection when compared to low volume.

The strengths of this study were that it included the quality of studies for the meta-analysis was high. Ideal evidence for systematic review is a randomized controlled trial (RCT), which is most commonly used in testing the efficacy of interventions. There is adequate methodology of systematic review in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18] as well as exploration and reduction in the heterogeneity of the studies with subgroup analysis and adequate statistical analysis.

There are some limitations in this study. Firstly, there are no studies that directly compare high- and low-volume CI in SIS and the number of included studies that evaluated volume effect was not enough to detect a statistical difference between groups (type II error). Secondly, heterogeneity remains an important factor to be considered in the conduct and interpretation of meta-analysis and the heterogeneity between the studies were huge. The third limitation is that indirect meta-analysis was used for calculating the mean difference and odd ratio between two groups because all included studies were reports of only one group (low or high volume). The fourth limitation is that there is no another group of intervention that can be used to prove that lidocaine has no effect to treat SIS such as pure corticosteroid injection (CI without analgesic agent). Therefore, this group could not be analyzed because of insufficient data.

In conclusion, subacromial impingement syndrome, the corticosteroid injection had acceptable pain and functional outcomes. Higher volume had a lower ASES, VAS, and risk of having complication when compared to lower volume. However, there are no statistically significant differences between groups. Low-CI should be used with USG technique in treating SIS, while LMG can be used either. Larger, randomized noninferiority or equivalent trial studies are needed to confirm these findings as the current literature is still insufficient.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflicts of interests.

Ethical standards This article does not contain any studies with human participants performed by any of the authors.

Appendix: Search term and search strategy

#1 impingement syndrome.
#2 intra-articular steroid injection.
#3 clinical study.
#4 #1 AND #2 AND #3.

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