REVIEW

Platelet-rich plasma versus corticosteroid injections in the management of patients with rotator cuff disease: A systematic review and meta-analysis

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Abstract

Platelet-rich plasma (PRP) is an alternative to corticosteroid (CS) injections in managing rotator cuff disease. This meta-analysis investigated differences between PRP and CS for function and pain scores in significance and minimal clinical important difference (MCID). A literature search of Ovid Cochrane Library, Medline, Embase, Epub, and Scopus was conducted from inception to October 28, 2021. Eligible studies reported patients older than 18 years with a diagnosis of rotator cuff disease. This review was registered in PROSPERO (ID: CRD42021278740). Twelve studies met eligibility criteria ($n = 639$) of patients receiving either PRP or CS. At short-term follow-up, a difference favored CS compared to PRP in baseline change for disability of arm, shoulder, and hand (DASH) score (MD = −5.08, 95% CI: −8.00, −2.15; $p = 0.0007$; $I^2 = 0\%$) and simple shoulder test (SST) (MD = 1.25, 95% CI: 0.33, 2.18; $p = 0.008$; $I^2 = 0\%$). At intermediate follow-up, a difference favored PRP to CS baseline change of the DASH score (MD = 3.41, 95% CI: 0.67, 6.15; $p = 0.01$; $I^2 = 0\%$). At medium-term, a difference favored PRP to CS baseline change of the American Shoulder and Elbow Surgeons Shoulder (ASES) score (MD = −4.42, 95% CI: −8.16, −0.67; $p = 0.02$; $I^2 = 0\%$). Both treatments achieved individual MCID for each score. Despite favoring CS at short-term follow-up and PRP at intermediate- and medium-term follow-up, functional and pain scores did not demonstrate any clinical difference between the two treatment modalities in management of rotator cuff disease at all follow-up periods.

KEYWORDS

corticosteroid, injection, meta-analysis, platelet-rich, rotator cuff

1 | INTRODUCTION

Rotator cuff disease (RCD) is one of the most common shoulder pathologies in the general population, with prevalence of over 60% for those over 80.[1] RCD is an umbrella term that includes numerous pathologies namely partial or full thickness tears, cuff tear arthropathy, tendinopathy, subacromial impingement syndrome, and subacromial bursitis.[2] While the more obvious outcome of RCD is shoulder pain, it can also lead to a significant decrease in the ability to perform daily activities. Conservative management is considered the gold standard[3] and consists of activity modification, oral medication, physical therapy, and subacromial injections of corticosteroids (CS).[4,5] However, CS provides little benefit beyond symptomatic relief which may not last and may even lead to permanent damage to tendon ultrastructure.[6] As a consequence, alternative treatment methods are being considered.[7] One of these is platelet-rich plasma (PRP). PRP injections promote the release of growth factors such as transforming growth factor beta (TGF-β) and vascular endothelial growth factor (VEGF)[8] and it is thought that PRP injections accelerate the process of healing via increasing fibroblast migration and proliferation and tissue vascularization.[9] PRP injections are considered to be more expensive than corticosteroid injections as a single PRP has a mean cost of $707USD.[10] Scarpone et al.[11] noted significant improvement in pain, function, and MRI outcomes following PRP injections for participants with refractory rotator cuff tears, which are unresponsive to standard care including rest, physical therapy, analgesia, CS injections, and surgery. Because of its direct contribution to wound healing, in addition to its role in pain relief, the use of PRP injections in clinical practice has been gaining traction. The relative efficacy of CS injections compared to PRP is currently under debate.

A recent systematic review comparing CS with PRP injections noted no significant difference in the efficacy of these two techniques in the medium to long term with regard to pain relief, functional recovery, and range of motion.[7] In the short-term, two studies favored CS in improving functional outcomes, while pain relief scores favored PRP injections[12]; but the remainder showed no significant difference between the two treatment modalities.

In addition, what has not been discussed is the actual clinical effect of the intervention on the patient. Ultimately the question is— does the treatment reach the threshold for the minimal clinically important differences (MCID)?

To the best of our knowledge, no meta-analysis has analyzed the functional scores with respect to this threshold. The aim of this study is to compare the efficacy of CS and PRP in the treatment of RCD based on functional scores and pain scores to determine if either reach the MCID threshold of patient benefit which will help determine whether there is a clinical difference.

2 | METHODS

2.1 | Data sources and search strategies

A comprehensive search of numerous databases from inception to October 28, 2021 was conducted in compliance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.[13] The databases included Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, Ovid Embase, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus. The search strategy was designed and conducted by an experienced librarian with input from the study's principal investigator. Controlled vocabulary supplemented with keywords was used to search for studies describing corticosteroid versus PRP injection for the treatment of rotator cuff diseases, which include conditions such as rotator cuff tendinopathy, partial- and full-thickness tear, subacromial impingement syndrome, subacromial bursitis, and cuff tear arthropathy. The actual strategy listing all search terms used and how they are combined is available in Supporting Information: Item 1. This review was registered in PROSPERO (ID: CRD42021278740).

2.2 | Eligibility criteria and quality assessment

Eligible studies were randomized control and clinical trials that met all the following inclusion criteria: (1) adults above 18 years old who underwent either a PRP or CS injection for the treatment of rotator cuff disease, (2) patients were either diagnosed with imaging or clinical evaluation, (3) rotator cuff disease includes partial tendon tear, full-thickness tear, rotator cuff tendinosis (tendinopathy), subacromial pain syndrome and rotator cuff impingement. Case reports, case series, conference abstracts and/or abstracts, and articles that were not reported in English were excluded from the study. The quality of each study was independently evaluated by two authors (Maamoun Adra and Nour El Ghazal) using the Newcastle-Ottawa Scale.[14] Results of the quality assessment of all included studies are shown in Supporting Information: Table S1.

2.3 | Statistical analysis

The pooled estimate of mean difference was analyzed using an inverse-variance-weighted average of the individual studies.[15] A direct comparison between the two groups was conducted by assessing studies that reported outcomes of both treatments (two-arm analysis). The data were analyzed using intention-to-treat analysis. When change in standard deviation could not be obtained, it was imputed by performing correlation analysis using standard deviation of baseline and final value. If the correlation coefficient was less than 0.5, the final value of standard deviation was incorporated in our analysis.[15] The heterogeneity of effect size estimates across

the studies was quantified using the Q statistic and I^2 ($p < 0.05$ was considered significant). A value of I^2 of 0%–25% indicates insignificant statistical heterogeneity, 26%–50% low heterogeneity, 51%–100% high heterogeneity.[16] The Random-effects model was used when the value of I^2 was >50% and the fixed-effects model was used for $I^2 < 50\%$. Data analysis was performed usingRevMan software version 5.4 (Review Manager [RevMan] [Computer program]. The Cochrane Collaboration, 2020).

2.4 | Data extraction and MCID interpretation

2.4.1 | Functional scores

The functional scores were assessed using the constant-Murley score (CMS), the American Shoulder and Elbow Surgeons Shoulder Score (ASES), University of California at Los Angeles Shoulder Score (UCLA), disability of the arm, shoulder, and hand (DASH) score and simple shoulder test (SST). Each score was analyzed as a change from baseline at short-term (3–6 weeks), intermediate-term (8–12 weeks), and medium-term (more than 12 weeks) follow-up. The range of reported MCID for rotator cuff tears assessment are 8–10 for CMS,[17] 9–26.9 for ASES,[17] 3.0 for UCLA,[18] 8.1–13.0 for DASH,[17] and 2 for SST.[17] The specific characteristics of MCID, which includes the condition and treatment for which it was determined, can be found in detail in Table 1.

2.4.2 | Pain

The perception of pain was evaluated with visual analog scale (VAS) questionnaire score, and it was analyzed as a change from baseline at short-term (3–6 weeks), intermediate-term (8–12 weeks), and medium-term (more than 12 weeks) follow-up. MCID for rotator cuff tears assessment is reported as 1.4 cm for VAS score.[19]

3 | RESULTS

3.1 | Study selection and characteristics

The initial search yielded 648 potentially relevant articles from which 12 unique studies, involving 321 patients in the CS group and 318 patients in the PRP group, met the eligibility criteria. The PRISMA flow chart (Figure 1) illustrates the details of the study selection process. Furthermore, the baseline characteristics of each included study are comprehensively described in Table 2.

3.2 | Risk of bias

Results of the quality assessment of all included studies are shown in Supporting Information: Table 1. All the studies were judged to be of good quality. The patients appeared to represent the whole experience of the investigator, and the exposure and outcome were adequately ascertained, and the lengths of follow-up were adequate to manifest a change in the clinical outcomes.

The results with respect to the research questions are summarized in Table 3.

3.3 | VAS score

Pain was self-reported by patients using VAS score in a number of papers (Figure 2). The baseline VAS scores along with their change from base-line can be found in Table 4. At short- and intermediate-term follow-up, the change from baseline was comparable between the CS and PRP groups and no difference was observed (short-term: MD = −0.30, 95% CI: −1.40, 0.08; $p = 0.59$; $I^2 = 89\%$[12,26,28,34,32]) (Intermediate-term: MD = 0.28, 95% CI: −0.71, 1.28; $p = 0.58$; $I^2 = 84\%$[26–28,31,32]). At medium-term follow-up, no difference in the change of VAS score from base-line was observed between the PRP and CS groups (MD = 0.39, 95% CI: −1.84, 2.62; $p = 0.73$; $I^2 = 97\%$[12,28,34,32]).

Both the CS and PRP cohorts reached MCID separately. Therefore, no clinical difference was observed between the two treatments.

3.4 | Functional scores

All baseline values of the functional scores along with their subsequent changes at follow-up for the CS and PRP groups are summarized in Table 4. Furthermore, the mean differences (MD) between the two treatments for each outcome is summarized in Table 5.

3.4.1 | ASES score

ASES score was reported in five studies[28,33,32] (Figure 3). At the short-term follow-up, no difference in the change of ASES from base-line was observed between the two groups (MD = 6.10, 95% CI: −3.66, 15.85; $p = 0.22$; $I^2 = 87\%$). Similarly, at the intermediate-term point, no difference in the change from base-line was observed between the two groups (MD = −7.52, 95% CI: −19.88, 4.83; $p = 0.23$; $I^2 = 92\%$). At the medium-term follow-up, there is a difference between the CS and PRP group such that in the latter group, there was a greater change from baseline compared to the former group with a difference of 18.15 and 10.80, respectively (MD = −4.42, 95% CI: −8.16, −0.67; $p = 0.02$; $I^2 = 0\%$).

Both CS and PRP cohorts reached MCID separately. Therefore, there exists no clinical difference between the two treatment modalities.

3.4.2 | CMS score

CMS score was reported in five studies[12,25,28,33,35] (Figure 4). At the short-term follow-up, no difference in the change from base-line was observed between the two groups (MD = 3.18, 95% CI: −5.78, 12.14; $p = 0.49$; $I^2 = 91\%$). Similarly, at the intermediate

TABLE 1 Characteristics of MCID for pain and functional scores

Score	MCID	Study	Condition(s)	Treatment
VAS	1.4	Tashjian et al.[19]	Rotator cuff tendonitis, rotator cuff tear (partial- or full-thickness)	Nonoperative treatment (various combinations of rest, ice, activity modifications, physical therapy, anti-inflammatory pain medications, and subacromial corticosteroid injection)
CMS	8–10	Kukkonen et al.[20]	Partial- or full-thickness rotator cuff tears	Arthroscopic rotator cuff surgery
		Torrens et al.[21]	Massive irreparable rotator cuff tears	Reverse shoulder arthroplasty
ASES	9–26.9	Gagnier et al.[22]	Full-thickness rotator cuff tears	Surgically and nonsurgically
		Tashjian et al.[19]	Tendinitis, partial- or full-thickness rotator cuff tear	Nonsurgical (various combination of rest, ice, activity modifications, physical therapy, anti-inflammatory pain medications, and subacromial corticosteroid injection)
		Werner et al.[23]	Glenohumeral arthritis, rotator cuff tear arthropathy	Total or reverse shoulder arthroplasty
UCLA	3	Xu et al.[18]	Partial- or full-thickness supraspinatus tear	Arthroscopic rotator cuff repair with subacromial decompression surgery
SST	2	Tashjian et al.[19]	Tendinitis, partial- or full-thickness rotator cuff tear	Nonsurgical (various combination of rest, ice, activity modifications, physical therapy, anti-inflammatory pain medications, and subacromial corticosteroid injection)
DASH	8.1–13	Van de Water et al.[24]	Proximal humeral fractures	Rehabilitation

Abbreviations: ASES, American Shoulder and Elbow Surgeons Shoulder Score; CMS, constant-murley score; DASH, disabilities of the arm, shoulder, and hand; MCID, minimally clinically important difference; SST, simple shoulder test; UCLA, University of California at Los Angeles Shoulder Score; VAS, visual analog scale.
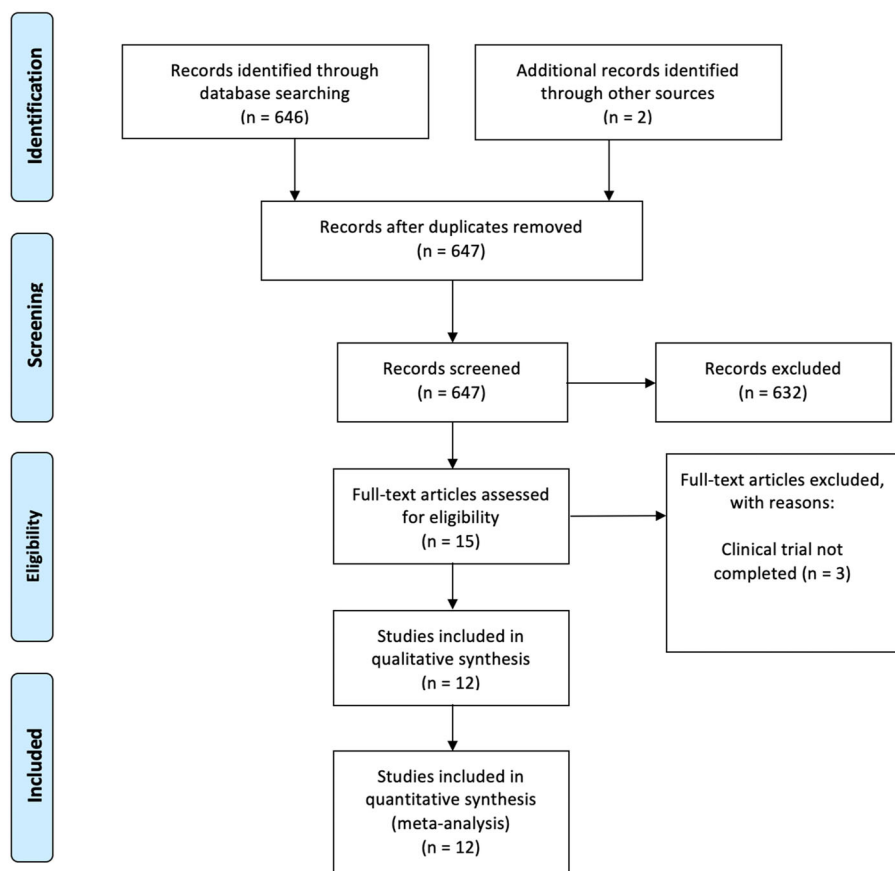

FIGURE 1 Preferred reporting items for systematic reviews and meta-analyses flow diagram

TABLE 2 Baseline characteristics of included studies

Study	Country	Sample size (n)			Males: Females (n)	Mean age ± SD (years)		Indications	Side affected		Duration of symptoms ± SD (months)		Follow-up (weeks)	Outcome assessment method/score
		Total	CS	PRP		CS	PRP		Right	Left	CS	PRP		
Barreto et al.[25]	Brazil	51	25	26	18:33	53 ± 11	53.2 ± 9.4	Rotator cuff impingement syndrome	23	16	NR	NR	Baseline, 4, 12, 24 weeks	CMS DASH UCLA
Dadgostar et al.[26]	Iran	58	28	30	11:47	53.6 ± 7.24	57.33 ± 9.8	Rotator cuff tendinopathy	NR	NR	NR	NR	Baseline, 1, 4, 12 weeks	VAS WORC DASH Supraspinatus thickness ROM Flexion Extension Abduction Adduction External rotation Internal rotation
Ibrahim et al.[27]	Egypt	30	15	15	13:17	41.5 ± 12.5	46.8 ± 10.6	Rotator cuff tendinopathy	23	7	1	2	Baseline, 8 weeks	VAS SDQ Clinical rotator cuff tests US findings ROM Flexion Extension Abduction External rotation Internal rotation
Jo et al.[28]	Korea	60	30	30	20:40	52.5 ± 11.2	55.3 ± 10.3	Rotator cuff disease	NR	NR	13.1 ± 15.6	11.6 ± 11.4	Baseline, 1, 4, 12, 24 weeks	VAS (mean, rest, night, activity, worst) CMS ASES DASHSSTUCLA RC strength ROM Flexion Extension Abduction External rotation Internal rotation
Kwong et al.[29]	Canada	99	52	47	35:64	49.08 ± 9.54	49.94 ± 9.7	Partial thickness rotator cuff tears or tendinopathy	NR	NR	297.84 ± 318.24	404.28 ± 925.32	Baseline, 6, 12, 48 weeks	VAS ASES WORC
Pasin et al.[30]	Turkey	60	30	30	NR	47.73 ± 9.55	49.4 ± 9.1	Subacromial impingement syndrome	NR	NR	0.92 ± 1.12	0.77 ± 0.66	Baseline, 3, 8 weeks	VAS (rest and activity) DASH UCLA

(Continues)

TABLE 2 (Continued)

Study	Country	Sample size (n)			Males: Females (n)	Mean age ± SD (years)		Indications	Side affected		Duration of symptoms ± SD (months)		Follow-up (weeks)	Outcome assessment method/score
		Total	CS	PRP		CS	PRP		Right	Left	CS	PRP		
														SDQ SF-36
Sabaah and Nassif [31]	Egypt	40	20	20	12:28	41.85 ± 10.21	41.85 ± 10.21	Rotator cuff tendinopathy	24	16	NR	NR	Baseline, 12 weeks	VAS WORC
Sari and Eroglu [32]	Turkey	60	30	30	43:77*	NR	NR	Rotator cuff lesions	88	32	4.87 ± 1.76	NR	Baseline, 3, 12, 24 weeks	VAS ASES WORC
Say et al. [12]	Turkey	60	30	30	22:38	50.2 ± 2.7	49.2 ± 7	Subacromial impingement syndrome	35	25	NR	NR	Baseline, 6, 24 weeks	CMS VAS Radiographic outcomes ROM Flexion Abduction External rotation Internal rotation
Shams et al. [33]	Egypt	40	20	20	21:19	50 ± 10	52 ± 12	Symptomatic partial rotator cuff tear	23	17	NR	NR	Baseline, 6, 12, 24 weeks	CMS VAS ASES SST Radiographic outcomes (Pre-op + 6 months post-op) MRI grades
Thepsoparn et al. [34]	Thailand	31	16	15	6:25	62.4 ± 10.5	51.3 ± 10.3	Partial supraspinatus tears	NR	NR	13.5 ± 12.5	8.3 ± 11.6	Baseline, 4, 24 weeks	VAS OSS ROM
von Wehren et al. [35]	Switzerland	50	25	25	26:24	55 ± 10	53 ± 14	Partial rotator cuff tears	30	20	NR	NR	Baseline, 6, 12, 24 weeks	CMS VAS ASES SST

Abbreviations: ASES, American Shoulder and Elbow Surgeons Shoulder Score; CMS, constant-murley score; CS, corticosteroid; DASH, disabilities of the arm, shoulder, and hand; n, number of patients; NR, not reported; OSS, Oxford shoulder score; PRP, platelet rich plasma; ROM, range of motion; SD, standard deviation; SDQ, shoulder disability questionnaire; SF-36, short form 36; SST, simple shoulder test; UCLA, University of California at Los Angeles Shoulder Score; VAS, visual analog scale; WORC, Western Ontario rotator cuff index.

TABLE 3 Summary of the findings

Test		3–6 weeks		8–12 weeks		>12 weeks	
		PRP	CS	PRP	CS	PRP	CS
VAS	Reaches MCID	Yes	Yes	Yes	Yes	Yes	Yes
	Significant difference	No		No		No	
CMS	Reaches MCID	Yes	Yes	Yes	Yes	Yes	Yes
	Significant difference	No		No		No	
ASES	Reaches MCID	Yes	Yes	Yes	Yes	Yes	Yes
	Significant difference	No		No		Yes (PRP > CS)	
DASH	Reaches MCID	Yes	Yes	Yes	Yes	Yes	Yes
	Significant difference	Yes (CS > PRP)		Yes (PRP > CS)		No	
SST	Reaches MCID	No	Yes	Yes	Yes	Yes	yes
	Significant difference	Yes (CS > PRP)		No		No	
UCLA	Reaches MCID	Yes	Yes	Yes	Yes	Yes	Yes
	Significant difference	No		No		No	

Abbreviations: ASES, American Shoulder and Elbow Surgeons Shoulder Score; CMS, constant-murley score; CS, corticosteroid; DASH, disabilities of the arm, shoulder, and hand; MCID, minimally clinically important difference; PRP, platelet rich plasma; SST, simple shoulder test; UCLA, University of California at Los Angeles Shoulder Score; VAS, visual analog scale.
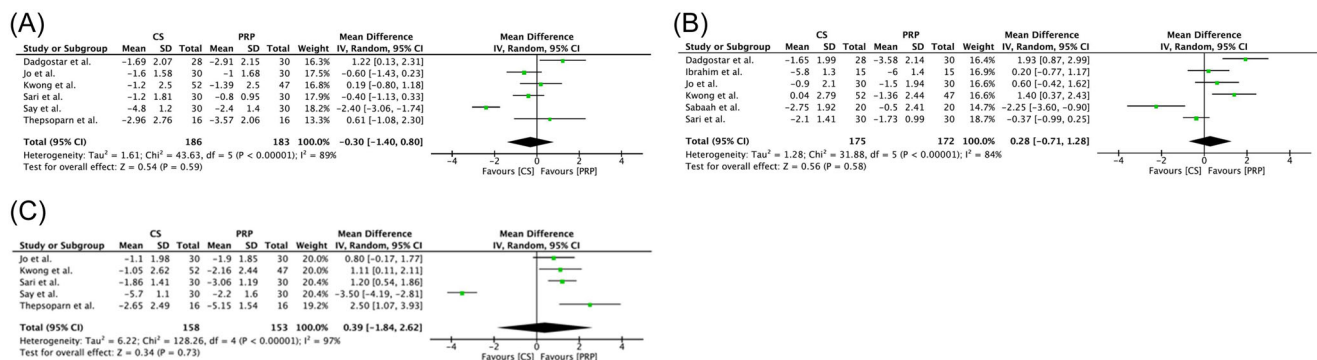

FIGURE 2 Pooled estimate of visual analog scale (VAS) score for corticosteroids versus platelet-rich plasma group at (A) short-term (3–6 weeks), (B) intermediate-term (8–12 weeks), (C) medium-term (>12 weeks). VAS is a negative outcome.

point, no difference in the change from base-line was observed between the treatments (MD = −7.73, 95% CI: −18.68, 3.23; $p = 0.17$; $I^2 = 87\%$.[25,28,33,35] The two groups were comparable at the medium-term point (MD = −2.65, 95% CI: −11.70, 6.40; $p = 0.57$; $I^2 = 91\%$[12,25,28,33,35]).

Both CS and PRP cohorts reached MCID separately. Therefore, there exists no clinical difference between the two treatments.

3.4.3 | DASH score

DASH score was reported in four studies[25,26,28,30] (Figure 5). At the short-term follow-up, there exists a difference between the

two cohorts such that the change from baseline was higher in the CS group in comparison to the PRP group with a mean change of −16.71 and −10.92, respectively (MD = −5.08, 95% CI: −8.00, −2.15; $p = 0.0007$; $I^2 = 0\%$[25,26,28,30]). At the intermediate-term follow-up, there exists a difference with a greater change in the PRP group in comparison to the CS group with a mean DASH score of −25.56 and −24.31, respectively (MD = 3.41, 95% CI: 0.67, 6.15; $p = 0.01$; $I^2 = 0\%$[25,26,28,30]). During medium-term follow-up, the mean change from baseline was comparable between the two groups with no difference (MD = 0.95, 95% CI: −4.88, 6.79; $p = 0.75$; $I^2 = 80\%$[28,28]).

Both CS and PRP cohorts reached MCID separately. Therefore, there exists no clinical difference between the two treatment modalities.

TABLE 4 Baseline and follow-up outcomes

Outcome	Baseline Mean ± SD (N) CS	Baseline PRP	3–6 weeks Mean ± SD (N) CS	3–6 weeks PRP	p-Value	8–12 weeks Mean ± SD (N) CS	8–12 weeks PRP	p-Value	>12 weeks Mean ± SD (N) CS	>12 weeks PRP	p-Value
Shoulder scores											
ASES	55.28 ± 15.75 (5)	53.83 ± 14.02 (5)	17.31 ± 16.49 (5)	11.65 ± 17.83 (5)	0.22	10.80 ± 20.02 (5)	18.15 ± 20.04 (5)	0.23	16.45 ± 20.14 (5)	22.09 ± 19.80 (5)	0.02
VAS	5.53 ± 2.43 (8)	5.94 ± 2.13 (8)	−2.39 ± 2.41 (6)	−1.83 ± 2.12 (6)	0.59	−1.58 ± 2.71 (6)	−2.14 ± 2.54 (6)	0.58	−2.26 ± 2.72 (5)	−2.61 ± 2.16 (5)	0.73
CMS	57.51 ± 19.03 (5)	56.19 ± 17.35 (5)	12.15 ± 11.81 (5)	8.39 ± 13.63 (5)	0.49	9.125 ± 16.80 (4)	15.80 ± 15.81 (4)	0.17	14.68 ± 14.99 (5)	16.48 ± 13.54 (5)	0.57
UCLA	17.51 ± 5.69 (3)	15.95 ± 4.67 (3)	11.01 ± 7.99 (3)	10.40 ± 7.60 (3)	0.52	12.76 ± 10.04 (3)	14.78 ± 9.49 (3)	0.25	8.77 ± 9.59 (2)	9.96 ± 14.35 (2)	0.32
DASH	52.23 ± 23.65 (4)	52.94 ± 22.76 (4)	−16.71 ± 16.70 (4)	−10.92 ± 15.19 (4)	0.0007	−24.31 ± −24.71 (4)	−25.56 ± 24.43 (4)	0.01	−18.64 ± 22.62 (2)	−20.99 ± 19.24 (2)	0.75
SST	6.31 ± 2.53 (3)	6.85 ± 2.41 (3)	2.66 ± 3.16 (3)	1.34 ± 2.71 (3)	0.008*	2.13 ± 3.06 (3)	2.55 ± 2.83 (3)	0.37	2.61 ± 3.25 (3)	3.19 ± 2.71 (3)	0.26

Note: *Indicates statistical significance.

Abbreviations: ASES, American Shoulder and Elbow Surgeons Shoulder Score; CMS, constant-Murley score; CS, corticosteroid; DASH, disabilities of the arm, shoulder, and hand; N, number of studies included; PRP, platelet-rich plasma; SD, standard deviation; SST, simple shoulder test; UCLA, University of California at Los Angeles Shoulder Score; VAS, visual analog scale.

3.4.4 | UCLA score

UCLA score was reported in three studies[25,28,30] (Figure 6). The change from baseline was comparable between the CS and PRP groups at short- and medium-term follow-up (Short-term: MD = 0.47, 95% CI: −0.94, 1.88; $p = 0.52$; $I^2 = 0\%$[25,28,30]) (medium-term: MD = −1.27, 95% CI: −3.75, 1.21; $p = 0.32$; $I^2 = 0\%$[25,28]). Similarly, in the intermediate-term, no difference in the change from base-line was observed amongst the two treatment groups (MD = −2.31, 95% CI: −6.27, 1.66; $p = 0.25$; $I^2 = 76\%$[25,28,30]).

Both CS and PRP cohorts reached MCID separately. Therefore, there exists no clinical difference between the two treatments.

3.4.5 | SST score

SST score was reported in three studies[28,33,35] (Figure 7). At the short-term follow-up, there exists a difference between the two cohorts such that the change from baseline was higher in the CS group in comparison to the PRP group with a mean change of 2.66 and 1.34, respectively (MD = 1.25, 95% CI: 0.33, 2.18; $p = 0.008$; $I^2 = 0\%$). Conversely, at intermediate- and medium-term, the change from baseline was comparable between the PRP and CS groups with no difference (intermediate-term: MD = −0.63, 95% CI: −1.99, 0.73; $p = 0.08$; $I^2 = 61\%$) (medium-term: MD = −0.48, 95% CI: −1.31, 0.35; $p = 0.26$; $I^2 = 0\%$).

Both CS and PRP cohorts reached MCID separately, except during the short-term where PRP had a change of 1.34. Therefore, there exists no clinical difference between the two treatment modalities.

4 | DISCUSSION

The primary aim of this review was to investigate the functional outcomes (UCLA, SST, DASH, ASES, and CMS) and perception of pain (VAS) among patients injected with PRP compared to those injected with CS for managing rotator cuff disease with the critical questions being

(1) Did either treatment reach the MCID threshold for patient benefit?
(2) Was there a significant clinical difference between the treatment modalities?

This meta-analysis demonstrated that:

(1) Both treatment methods separately reached MCID at nearly all time points (apart from PRP failing to reach MCID in the short-term in the SST outcome).
(2) Despite there being a statistically significant difference in the short-term in favor of CS injection and a statistically significant difference in favor of PRP injection in the intermediate and

TABLE 5 Mean difference of functional and pain scores between corticosteroid and platelet-rich plasma treatment

Outcome	3–6 weeks (MD)	3–6 weeks (p-Value)	8–12 weeks (MD)	8–12 weeks (p-Value)	>12 weeks (MD)	>12 weeks (p-Value)
Shoulder scores						
VAS	−0.30 (Favouring CS)	0.59	0.28 (Favouring PRP)	0.58	0.39 (Favouring PRP)	0.73
CMS	3.18 (Favouring CS)	0.49	−7.73 (Favouring PRP)	0.17	−2.65 (Favouring PRP)	0.57
ASES	6.10 (Favouring CS)	0.22	−7.52 (Favouring PRP)	0.23	−4.42 (Favouring PRP)	0.02*
DASH	−5.08 (Favouring CS)	0.0007*	3.41 (Favouring PRP)	0.01*	0.95 (Favouring PRP)	0.75
SST	1.25 (Favouring CS)	0.008*	−0.63 (Favouring PRP)	0.37	−0.48 (Favouring PRP)	0.26
UCLA	0.47 (Favouring CS)	0.52	−2.31 (Favouring PRP)	0.25	−1.27 (Favouring PRP)	0.32

Note: *Indicates statistical significance.

Abbreviations: ASES, American Shoulder and Elbow Surgeons Shoulder Score; CMS, constant-Murley score; CS, corticosteroid; DASH, disabilities of the arm, shoulder, and hand; N, number of studies included; PRP, platelet rich plasma; SD, standard deviation; SST, simple shoulder test; UCLA, University of California at Los Angeles Shoulder Score; VAS, visual analog scale.
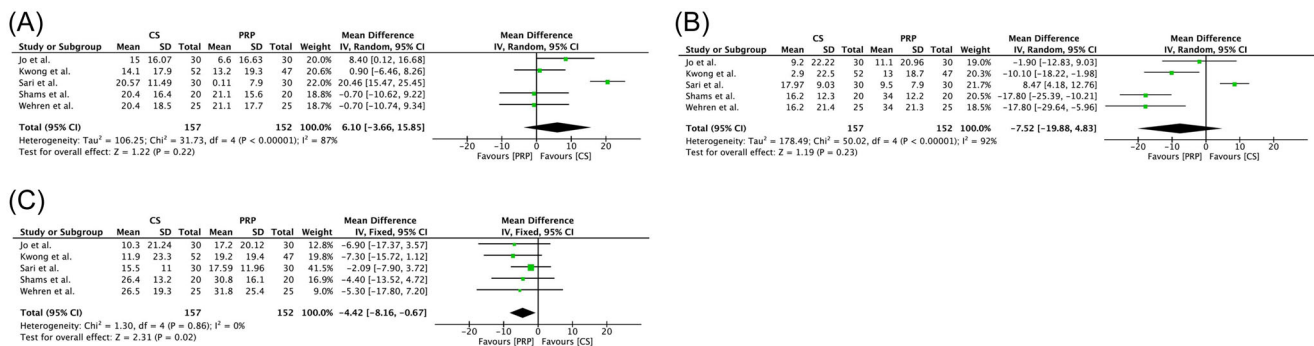
FIGURE 3 Pooled estimate of American shoulder and elbow surgeons shoulder (ASES) score for corticosteroids versus platelet-rich plasma group at (A), short-term (3–6 weeks), (B) intermediate-term (8–12 weeks), (C) medium-term (>12 weeks)
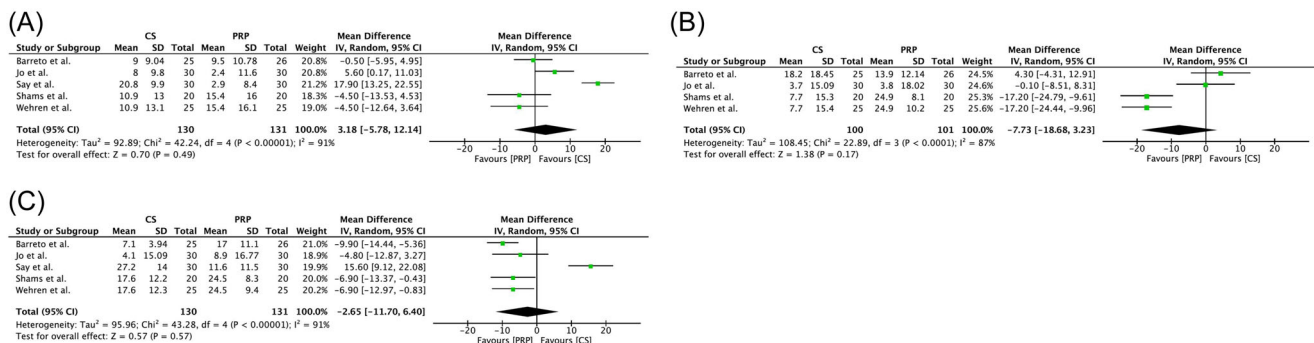
FIGURE 4 Pooled estimate of constant-murley score (CMS) for corticosteroids versus platelet-rich plasma group at (A), short-term (3–6 weeks), (B) intermediate-term (8–12 weeks), (C), medium-term (>12 weeks)

medium term, there is no clinical difference between them since both reached MCID. Thus, neither can be considered clinically superior.

There is consensus that CS suppress acute inflammation by inhibiting protein synthesis of pro-inflammatory products.[36,37] CS injection as a source of symptomatic relief and transient functional improvement is commonly used among many different conditions including rotator cuff lesions.[38] According to the American Academy of Orthopedic Surgeons (AAOS), a single CS injection with a local anesthetic provides short-term pain relief as well as improved shoulder joint function.[39] A systematic review[40] reported that CS injections for the management of shoulder impingement yielded less pain at 6 weeks follow-up but not at
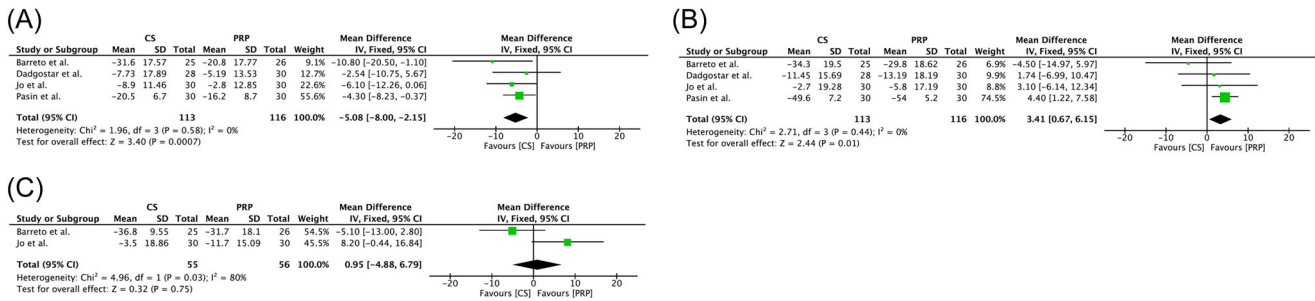
(A)
(B)
(C)

FIGURE 5 Pooled estimate of disabilities of the arm, shoulder, and hand (DASH) score for corticosteroids versus platelet-rich plasma group at (A) short-term (3–6 weeks), (B) intermediate-term (8–12 weeks), (C), medium-term (>12 weeks). DASH is a negative outcome.
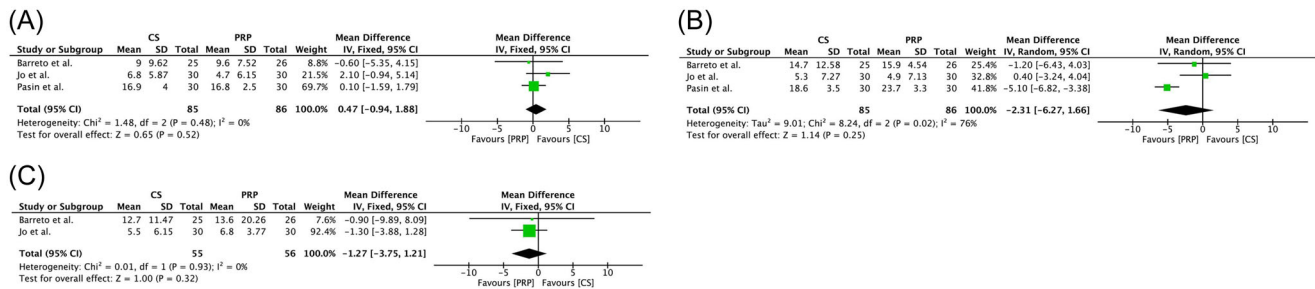
(A)
(B)
(C)

FIGURE 6 Pooled estimate of University of California at Los Angeles Shoulder (UCLA) score for corticosteroids versus platelet-rich plasma group at (A), short-term (3–6 weeks), (B), intermediate-term (8–12 weeks), (C), medium-term (>12 weeks)
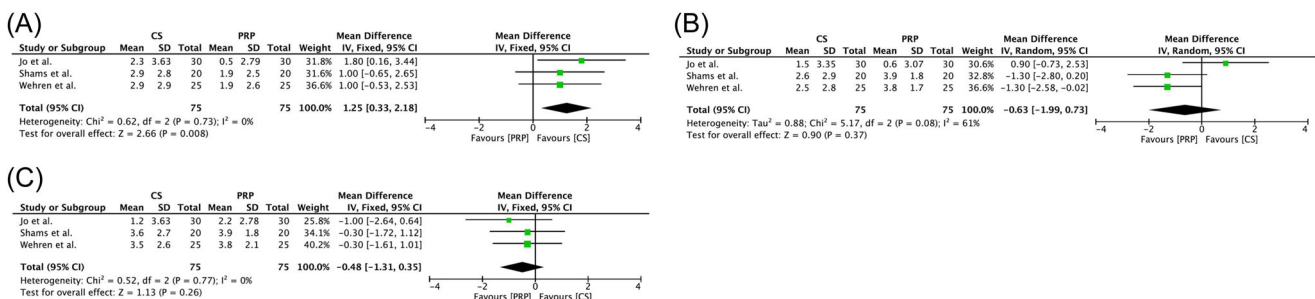
(A)
(B)
(C)

FIGURE 7 Pooled estimate of simple shoulder test (SST) score for corticosteroids versus platelet-rich plasma group at (A), short-term (3–6 weeks). (B), intermediate-term (8–12 weeks), (C), medium-term (>12 weeks)

longer follow-up times such as 3 and 6 months. An RCT[41] found that at 1-month postinjection of CS, lower VAS pain score, improved functional score (ASES), and higher ROM were observed in comparison to the control group, which received a normal saline injection.

A previous meta-analysis[7] demonstrated that CS yielded short-term pain relief as well as better functionality in comparison to PRP, which is in line with our findings, but the results were only reported as being statistically significant.

However, several recent RCTs comparing CS and PRP injections for the treatment of rotator cuff diseases showed controversial results.[25,30] Our findings suggest statistically but not clinically

significant difference in the short term in favor for CS injections possibly allowing better functionality and pain relief in the short-term in the management of patients with rotator cuff disease. Similarly, a review done by Abate et al.[42] has found that CS injection for the treatment of shoulder pain, mainly due to rotator cuff tendinopathy, provided short-term pain relief and functional improvement. However, no long-term benefit was reported by the studies, but no harm was observed either. CS administration generally can cause local skin manifestations such as rash or hypopigmentation which are considered to be minor adverse effects.[43] There exist reviews that mention serious side effects upon local CS injection such as subcutaneous tendon ruptures[42,44] However, such an event is mainly

TABLE 6 Treatment characteristics across the studies

Studies	Type of PRP	# of injections	US-guided	Location of injection	Preparation
Barreto et al.[25]	Autologous	NS	No	Posterior subacromial space	Double centrifugation and manual platelet separation with micropipettes, including the buffy coat. Then transferred to test tube for concentration.
Dadgostar et al.[26]	NS	2	Yes	Intraarticular joint at the tendon	Prepared and processed in ROOYA GEN (Arya Mabna Tashkhis Co., Tehran, Iran)
Ibrahim et al.[27]	Autologous	1	Yes	Lateral subacromial	Double centrifugation protocol. The remaining PRP and platelet plug were reconstituted using gentle manual agitation resulting in 2 ml of PRP ready for injection, thrombin was added to activate PRP in ratio 10:1, it was directly mixed before injection.
Jo et al.[28]	Allogenic pure	1	Yes	Subacromial space	Allogeneic PRPs were obtained with use of an automated plateletpheresis system with a leukoreduction set (COBE Spectra LRS Turbo; Caridian BCT) from healthy donors without rotator cuff disease (n = 3). After activation with calcium gluconate, PRPs were mixed and frozen until use
Kwong et al.[29]	Leukocyte-poor	1	Yes	Affected tendon + subacromial space	A leukocyte-poor preparation was used from a pre-packaged kit (RegenLab, Lausanne, Switzerland). The samples were centrifuged at 1500 g for 5 min to yield approximately 5.5 ml of 80% platelets at 1.6 concentration
Pasin et al.[30]	Autologous	1	NS	Subacromial space	Neotec Biotechnology PRP kit (Neotec Biotechnology Ltd., Istanbul, Turkey) and Elektromag device model 415 P (Elektro-Mag AS) were used. Double centrifugation was done.
Sabaah and Nassif. (2020)	Autologous	2 (2 weeks apart)	Yes	Subacromial subdeltoid bursa	Double centrifugation protocol. The remaining PRP and platelet plug resulted in 5 ml PRP with a concentration of 6.7 times of whole blood ready for use.
Sari and Eroglu. (2020)	Autologous	1	Yes	Lateral subacromial	PRP was prepared using the literature-based double spin method. Before injection, the PRP was activated by adding 1 ml 10% calcium chloride
Say et al.[12]	Autologous	1	NS	Posterolateral below the dorsal acromial edge	The PRP was prepared manually using single spin rotation. The 2.5 ml PRP was activated by 5.5% calcium chloride.
Shams et al.[33]	NS	1	NS	Posterolateral	Patients received PRP injection using MyCells Autologous Platelet Preparation System (ProTech). A single-spin was done.
Thepsoparn et al.[34]	Leukocyte-poor	1	Yes	Posterolateral at tendon site	PRP was prepared using the ACP Double Syringe System (Arthrex).
von Wehren et al.[30]	Autologous	3 (within a 7-day interval)	NS	Lateral subacromial space	Ten milliliters of autologous blood was taken from the antecubital vein with the outer syringe, placed into the Arthrex Centrifuge (Rotofix) and centrifuged for 5 min at 1500 rpm.

Abbreviations: NS, not specified; PRP, platelet-rich plasma.

attributed to multiple injections with poor technique, mostly not US-guided.[45]

PRP is an emerging alternative treatment for many different conditions. During the inflammatory stage of the tendon healing process, platelets will migrate toward the injured area and release growth factors such as transforming growth factor β (TGFβ), platelet-derived growth factor (PDGF), and insulin growth factor (IGF). This collectively promotes acute inflammation.[46] In addition to the anti-inflammatory properties mediated by hepatocyte growth factor (HGF)[47] the regenerative capacity of PRP is facilitated by growth factors, such as PDGF, known to enhance cell migration, tenocyte proliferation, differentiation, and extracellular matrix (ECM) synthesis.[48] PRP also accelerates the healing process via its contribution to the differentiation and proliferation of tendon stem cells into tenocytes, thus maintaining tendon homeostasis, in addition to producing tendon healing-related glycoproteins and proteoglycans involved in matrix assembly and collagen adhesion.[49] Since the effects of PRP have been mainly studied in in-vivo animal studies and in vitro studies,[49] the clinical significance of the tendon healing and tissue regeneration capacity of PRP in humans is still yet to be explored. In our study, PRP suggests that the overall improvement in functional and pain scores seen in this meta-analysis are mainly due to the symptom-modifying effects of PRP which are likely to be associated with the anti-inflammatory component rather than the tissue regeneration component.

A number of recent reviews have suggested that PRP therapy yields a more favorable functional outcome as well as reduced pain in the long-term compared to CS treatment; for a variety of conditions including lateral epicondylitis,[50,51] knee osteoarthritis,[52] lumbar spondylosis and sacroiliac arthropathy.[53] In addition, a randomized control trial[54] reported that there seems to be clinically important improvements disability (>15-point DASH change) at long-term follow-up for treating degenerative tendinopathies.

4.1 | Limitations

This meta-analysis contains several limitations.

A confounding factor in the interpretation of the literature is the method of PRP preparation. It has been demonstrated that an apheresis and buffy coat-derived preparation achieved a higher platelet concentration owing to a possible extra centrifugation step, which in turn allows for higher growth factor levels, as opposed to a tube method preparation, which, on the other hand, showed the highest level of white blood cell contamination.[55] A handful of these studies utilized a similar protocol which involved a double centrifugation that gives rise to PRP derived from the upper plasma layer and the buffy coat (buffy-coat derived).[25,30,31] However,[12] prepared PRP manually using a single spin rotation.

In addition, the baseline characteristics of the participants were different in terms of lifestyle, occupation, weight, and

severity of the rotator cuff disease. The treatment protocols were different not only with respect to the injection itself but also the posttreatment regime. Given that physiotherapy has a strong influence on the recovery from rotator cuff disorders there may be significant effects. Moreover, the final standard deviation (SD) was used for the meta-analysis instead of the change in SD in some studies due to the lack of individual patient data. The authors of the included studies were contacted three times with no response. There is also inconsistency in follow-up period between the studies. With regard to MCID, the values used for the pain and function scores were determined based on treatments involving surgical and nonsurgical regimens for which PRP were not routinely included. This limitation encourages future studies to include PRP injections as a treatment to determine MCID in rotator cuff disease.

As discussed, different platelets preparations may have had variability, but there was also variability in the steroid preparations. Different doses were administered over one or several injections at different sites, the composition of the injections slightly varied and some of them were guided by imaging (ultrasound or MRI) while others were not. Table 6 summarizes the similarities and differences in the treatment protocols across all included studies. Despite the above limitations, this meta-analysis supports no clinical difference between PRP and CS. Future research should address these limitations while continuing to evaluate the efficacy of PRP in the treatment of rotator cuff disease in comparison to CS.

5 | CONCLUSION

Both CS and PRP injections separately reach MCID proving to be clinically beneficial for patients. Therefore, no clinical difference could be concluded. Furthermore, both treatments achieve some statistical differences in various functional scores such that the CS group seems to be in favor of better functionality in the short-term while the PRP group appears to yield better functionality in the intermediate and medium term. In future, studies with prolonged follow-up periods, larger sample sizes, a homogenous treatment protocol, and MCID evaluating rotator cuff disease are required to further assess the clinical difference of CS versus PRP injection in the management of rotator cuff disease.

AUTHOR CONTRIBUTIONS
Maamoun Adra, Nour El Ghazal, Christian A. Than, and Duncan Tennent conceived and designed the study, reviewed the literature,

collected, analyzed, and interpreted the data, and drafted the manuscript. Maamoun Adra, Nour El Ghazal, Hayato Nakanishi, Christian A. Than, Duncan Tennent conceived and designed the study, and critically revised the manuscript. Maamoun Adra, Nour El Ghazal, Hayato Nakanishi, Karen Smayra, Sam S. Hong, Shahid Miangul, Reem H. Matar, Christian A. Than, Duncan Tennent reviewed the literature, collected, analyzed, and interpreted the data, and drafted the manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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