

Platelet-Rich Plasma Augmentation of Arthroscopic Rotator Cuff Repair Lowers Retear Rates and Improves Short-Term Postoperative Functional Outcome Scores: A Systematic Review of Meta-Analyses



Zafar Ahmad, M.D., Swee Ang, M.D., Neil Rushton, M.D., Adrian Harvey, M.D., Kash Akhtar, Sebastian Dawson-Bowling, M.D., and Ali Noorani, M.D.

Purpose: The purpose of this study is to conduct a systematic review of meta-analyses of rotator cuff repair using platelet-rich plasma (PRP) to identify whether PRP improves clinical function and rate of tendon retears. We will (1) conduct a systematic review of the current meta-analyses of rotator cuff repair using platelet-rich plasma available in the literature, (2) evaluate the quality of these meta-analyses using the Preferred Reporting Items for Systematic Review (PRISMA) methodology, (3) identify whether PRP improves clinical function and rate of tendon retears, and develop guidance to improve future studies in this area.

Methods: We carried out a systematic review of previous meta-analyses published on the clinical outcomes of PRP used in the treatment of rotator cuff tears. We performed a comprehensive search of PubMed, Medline, Cochrane, CINAHL (Cumulative Index to Nursing and Allied Health Literature), and Embase databases, using various combinations of the commercial names of each PRP preparation and “rotator cuff” (with its associated terms), looking specifically at human meta-analysis studies involving the repair of the rotator cuff tendon surgically in the English language. Data validity was assessed and collected on clinical outcomes. Following this, a meta-analysis was undertaken. **Results:** Thirteen meta-analyses met the inclusion and exclusion criteria. All were considered of similar quality with Oxman-Guyatt index of 9 and PRISMA score of more than 24. A total of 1,800 patients with an average follow up of 12 to 36 months. The use of PRP for arthroscopic rotator cuff tear, when compared with controls, leads to a lower number of retears, improved short-term postoperative scores, and functional outcome. The following postoperative scores were reported: Constant: 12, Simple Shoulder Test: 10, ASES (American Shoulder and Elbow Surgeons): 9, UCLA (University of California, Los Angeles) 11, SANE (Single Assessment Numeric Evaluation) 1, VAS (visual analog scale): 6, and Retears: 13. Subgroup analysis showed that leukocyte content and gel application make no difference in the effectiveness of PRP. VAS score subgroup analysis showed short-term pain relief. **Conclusions:** Our study shows that PRP is effective in reducing retears after rotator cuff repair and improving functional outcome scores and reducing short-term pain. **Level of Evidence:** Level III, systematic review of Level I-III studies.

Introduction

The number of rotator cuff repairs continues to increase with overall satisfactory results, but the

number of reported retears is still significant.¹ Factors that may affect outcomes include those related to the surgeon, the surgery, and the patient. Surgeon factors include the amount of experience a surgeon has, which shows a correlation with lower re-tear rates.² Surgical factors include the nature of the tear and the method of repair. Patient factors include the age, comorbidities, and quality of the remnant tissue.¹ The tissue is often of poor quality in larger chronic tears, and when repaired, the remnant tissue heals with scar tissue, forming a weaker biomechanical structure.² The normal healing of tendon heals with scar tissue, which is an inferior construct compared with normal tissue.³ Biological augmentation using methods such as platelet-rich plasma (PRP) has the potential to enhance tissue healing for tendon repairs. It can either lead to

From the Barts Health NHS Trust, London, United Kingdom.

The authors report the following potential conflicts of interest or sources of funding: Supported by charitable grants of Charnlee Latta trust and the Winston Churchill Memorial Trust. Full ICMJE author disclosure forms are available for this article online, as [supplementary material](#).

Received April 4, 2020; accepted December 12, 2021.

Address correspondence to Zafar Ahmad, M.D., Barts Health NHS Trust, Royal London, Whitechapel Road, E1 1BB, London, United Kingdom. E-mail: ziazj@hotmail.com

© 2022 THE AUTHORS. Published by Elsevier Inc. on behalf of the Arthroscopy Association of North America. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). 2666-061X/20406

<https://doi.org/10.1016/j.asmr.2021.12.012>

enhanced tissue repair, improving the scar tissue strength, or ultimately, it could lead to tissue regeneration that has the potential to heal tears with high-quality tendon tissue.^{4,5}

Platelet-rich plasma is an autologous blood-derived concentrate of plasma, which has a high amount of growth factors. The initial research showed little promise; however, a number of later studies, including meta-analyses, have shown a reduction of retear rates in rotator cuff repair.⁴ This suggests with adequate power an effect can be detected. It stands to reason that an analysis of all the current potential meta-analyses may reveal trends not identified in individual studies.

The purpose of this study is to conduct a systematic review of meta-analyses of rotator cuff repair using PRP to identify whether PRP improves clinical function and rate of tendon retears. These include (1) to conduct a systematic review of the current meta-analyses of rotator cuff repair using platelet-rich plasma available in the literature, (2) to evaluate the quality of these meta-analyses using the Preferred Reporting Items for Systematic Review (PRISMA) methodology, (3) to identify whether PRP improves clinical function and rate of tendon retears, (4) and to develop guidance to improve future studies in this area. We hypothesize that PRP does improve clinical outcomes and reduces retears for rotator cuff repair.

Methods

This study is a level III systematic review of previous meta-analyses. This systematic review was performed in line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.

Search Strategy

We performed a comprehensive search of PubMed, Medline, Cochrane, CINAHL (Cumulative Index to Nursing and Allied Health Literature), and Embase databases for the years 1966 to Jan 1, 2020. To minimize the number of articles that may be missed, we used various combinations of the commercial names (Smartprep, Cascade, Harvest, GPS, etc.) of each PRP preparation and the following key words: tendon, rotator cuff, supraspinatus, infraspinatus, platelet, platelet-rich plasma, PRP, "shoulder", "subscapularis", "external rotators", "systematic review", "meta-analysis", and platelet concentrate (see [Appendix 1](#)). All articles relevant to the subject were retrieved, and their bibliographies were searched for further references in the context of the use of orthobiologics in the treatment of rotator cuff tears. We identified 180 citations from the initial electronic searches looking at published meta-analyses. These were then streamlined to only include surgical repair of rotator cuff tendons augmented with PRP.

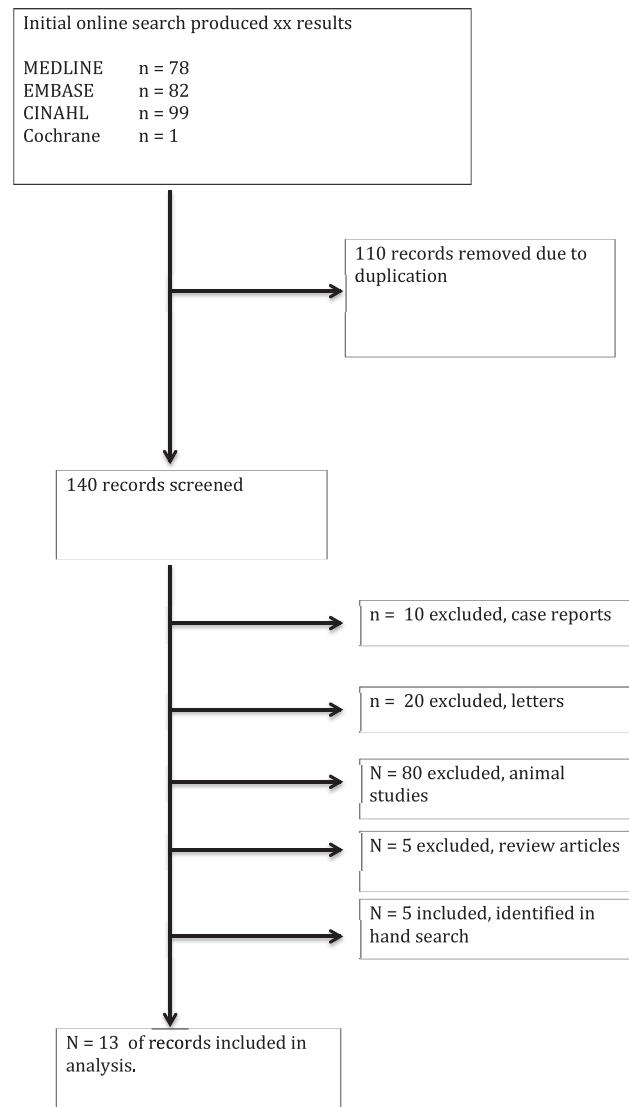


Fig 1. Search strategy.

Eligibility Criteria

The search was limited to meta-analysis articles published in peer-reviewed journals and the English language without date restrictions up to Jan 1, 2020 ([Fig 1](#)). Case reports, literature reviews, abstract-only publications, and letters to the editors were all excluded. Animal studies were not included. Studies were included if they reported on clinical outcomes of PRP augmentation in patients with surgical repair of rotator cuff tears and were meta-analyses or systematic reviews. All types of tears were included. All types of PRP preparations and applications were included. No limit was set for minimum follow-up duration.

Extraction of Data

Data were extracted from all eligible articles restricted to meta-analyses. Each study was reviewed for the quality of its methodology, and differences were

Table 1A. List of Meta-Analysis: Summary of Articles with Number of Articles Analyzed and the Article Citation

First Author	Journal	Date of Publication	Date of Last Literature Search	Level of Evidence	No. of articles reviewed	No of systematic reviews/ Meta-analysis to cite	No of systematic reviews/ Meta-analysis cited
Chahal	<i>Arthroscopy</i>	Nov 2012	December 2011	3	5	0	0
Zhang	<i>PLoS One</i>	July 2013	April 2013	2	7	1	1
Moraes	<i>Cochrane</i>	April 2014	March 2013	2	3	1	1
Li	<i>Arthroscopy</i>	November 2014	May 2013	2	7	1	1
Zhao	<i>Arthroscopy</i>	January 2015	September 2013	2	8	2	2
Warth	<i>Arthroscopy</i>	February 2015	September 2013	2	11	2	0
Vavken	<i>AJSM</i>	March 2015	August 2014	2	13	3	1
Cai	<i>JSES</i>	December 2015	January 2015	1	8	4	0
Yang	<i>Journal of Sports Medicine and Physical Fitness</i>	November 2016	Not stated	1	8	5	1
Fu	<i>Clinical Rehabilitation</i>	February 2017	December 2015	1	11	6	4
Han	<i>Journal of Orthopaedic Surgery and Research</i>	June 2019	September 2016	1	13	7	6
Hurley	<i>AJSM</i>	March 2019	March 2017	1	18	8	7
Chen	<i>AJSM</i>	November 2019	December 2017	1	18	9	7

resolved by discussion among the authors. A descriptive summary of the results is presented. A total of 13 articles met the inclusion criteria (Table 1). If data were missing, the authors of the articles were contacted to determine whether those potential data were available.

The characteristics of the meta-analyses are demonstrated in Tables 1-6. The data points evaluating effect size and mean differences between these points were extracted. The number of retears, patient function, and pain score were analyzed and compared. Methodologies of each study were compared.

The QUOROM (Quality Of Reporting Of Meta-analysis) used previously by Saltzman et al.⁶ has been superseded by PRISMA.⁷ The PRISMA (Preferred Reporting Items for Systematic reviews and Meta-analyses) is a 27-item checklist that is used to evaluate the quality of reporting. New items included are an evaluation of objective, presence of protocol, a full description of electronic search, outcome level of assessment, risk of bias, limitations, and sources of

funding. The meta-analysis was further assessed by the Oxman-Guyatt⁸ score as a quality appraisal tool. This is a 10-point questionnaire looking at the search method, criteria of included studies, the bias in selection, the validity of the studies, and whether the results supported the conclusion the authors had undertaken. The Oxman-Guyatt score provides an opportunity for subjective feedback, which the PRISMA method is lacking. The Jadad decision algorithm⁹ was used to evaluate discordant reviews. Two authors independently applied the search method and the evaluation of the scoring system to analyze these studies.

Results

Thirteen studies met the criteria (Table 1). The range of date of publications was from November 2012 to November 2019. Publications were published in a number of journals, including *Arthroscopy*, *American Journal of Sports Medicine*, *Journal of Shoulder and Elbow Surgeons*, and *PLoS One*. The earliest study was

Table 1B. Summary of Conclusion of Meta-Analysis and Risk of Bias

Study Name	Retear	Pain	Function	Risk of Bias	Subgroup Analysis
Chahal	N	N	N	Low to medium	X
Zhang	N	N	N	X	Tear Size
Moraes	N	N	N	Low to medium	X
Li	N	N	N	Low to medium	X
Zhao	N	N	N	Low to medium	X
Warth	Small-moderate tears	N	N	5 out of 11	Tear size, Surgical fixation; PRP: preparation/application/consistency
Vavken	Small-moderate tears	N	N	X	Tear size
Cai	Small-moderate tears	N	N	low x	Tear size
Yang	Small-moderate tears	Y	N	low x	Tear size
Fu	N	Y	Y	low	X
Han	Y	N	Y	X	X
Hurley	Y	Y	Y	Low	Tear size; VAS
Chen	Y	Y	Y	X	Leukocyte content and Gel Application \

N, not effective; Y, effective.

Table 2. Scores Used in Meta-Analysis

	Chahal	Zhang	Moraes	Li	Zhao	Warth	Vavken	Cai	Yang	Fu	Han	Hurley	Chen
Clinical Indices													
Constant score	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
SST score	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	N	Y
ASES score	Y	Y	N	Y	N	Y	N	Y	Y	N	Y	Y	Y
UCLA Shoulder score	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y
SANE score	Y	N	N	N	N	N	N	N	N	N	N	N	N
Overall Function	N	N	Y	N	N	N	N	N	N	Y	N	N	N
Subjective measures													
Patient VAS for pain	N	N	N	Y	N	Y	N	N	Y	Y	Y	Y	Y
Constant Pain Score	N	N	N	N	N	N	N	N	N	Y	N	N	N
Complications													
Retear rate (MRI)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Revision surgery	N	N	N	N	Y	N	Y	N	N	N	N	N	N
Overall complications	N	N	N	N	N	N	Y	N	N	N	N	N	N

published by Chahal et al.¹⁰ in *Arthroscopy* that reviewed 5 studies; however, it did not include only randomized controlled trials. This is in contrast to Chen et al.,¹¹ who published in November 2019 and reviewed 18 studies, which were all level I randomized controlled trials. The majority of articles cited previous meta-analyses.

The mean age of the patients in the studies ranged from 58 to 62, with a range reported from 28 to 79. Initial studies suggested that PRP did not affect the clinical and radiological outcomes.^{10,12,13,14,15} Radiological outcomes were all measured using MRI on all follow-up patients as standard procedure. However, later studies used a subgroup analysis and noted a reduced retear rate in the repair of small and medium tears with PRP. Warth et al.¹³ noted that injecting PRP between the tendon-bone interface improved outcomes.¹⁶ With the increasing amount of patient data, later meta-analyses were able to detect reduced retear, improved pain, and functional outcome in all types of tears. This suggests that the earlier studies were inadequately powered to note this difference.

Data Collection

All of the meta-analyses collected retear rates (see Table 2). Only the Vavken et al.¹⁶ looked at complications of surgery. Both Vavken et al.¹⁶ and Zhao et al.¹⁷ looked at the topic of revision surgery. Only 7 studies looked at the VAS pain score. The timing of these scores was vastly different from some studies looking at 1-month postoperation and others looking further ahead at 6 months or more. The clinical indices analyzed were different. The majority of articles looked at the Constant score. However, early articles, like Chahal et al. in 2012,¹⁰ looked at 5 different scores, whereas Zhao et al.¹⁷ in 2015 only looked at the Constant score. Vavken et al. in 2014¹⁶ looked at no clinical indices. Fortunately, the later articles, including Han et al.,¹⁸ Hurley et al.,¹⁹ and Chen et al.¹¹ analyzed the majority of clinical scoring.

Quality of Search

The majority of articles searched were found in PUBMED, EMBASE, and the Cochrane library (Table 3). Only Vavken et al.¹⁶ was quoted as using

Table 3. Database Analyzed

Article	PubMed	EMBASE	Cochrane Library of					Ovid	No of primary studies	Primary Studies Included
			Databases	CINAHL	LILACS	BIOSIS	Only RCTS or Quasi-RCTS			
Chahal	Y	Y	Y	N	N	N	N	5	N	
Zhang	Y	Y	Y	N	N	N	N	7	N	
Moraes	Y	Y	Y	N	Y	N	N	7	Y	
Li	Y	Y	Y	N	N	Y	Y	7	Y	
Zhao	Y	Y	Y	N	N	N	N	8	Y	
Warth	Y	Y	N	N	N	N	N	11	N	
Vavken	Y	Y	Y	Y	N	N	N	13	N	
Cai	Y	Y	N	N	N	N	N	8	Y	
Yang	Y	Y	Y	N	N	N	N	8	Y	
Fu	Y	Y	Y	N	N	N	Y	11	Y	
Han	Y	Y	Y	N	N	N	N	13	Y	
Hurley	Y	Y	Y	N	N	N	N	18	Y	
Chen	Y	N	Y	N	N	N	Y	18	Y	

Table 4. Studies Included

Primary Study	Chahal 2012	Zhang 2013	Moraes 2014	Li 2014	Zhao 2015	Warth 2015	Vavken 2015	Cai 2015	Yang 2016	Fu 2017	Han 2019	Hurley 2019	Chen 2019
Castricini 2010	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
Randelli 2011	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
Barber 2011	Y	N	N	N	N	N	Y	N	N	N	N	N	N
Buford 2011	N	N	N	N	N	N	Y	N	N	N	N	N	N
Longo 2011	N	N	N	N	N	N	Y	N	N	N	N	N	N
Bergeson 2012	Y	N	N	N	N	N	Y	N	N	N	N	N	N
Jo 2011	Y	Y	N	N	N	Y	Y	Y	N	N	N	N	N
Gumina 2012	N	Y	Y	Y	Y	Y	N/A	N	Y	Y	N	Y	Y
Weber 2013	N	Y	N	Y	Y	Y	Y	Y	Y	N	N	Y	Y
Antuna 2013	N	Y	Y	Y	N	Y	N/A	N	Y	N	N	N	N
Jo 2013	N	N	N	N	Y	Y	N/A	N	N	N	N	Y	Y
Ruiz-Moneo 2013	N	N	N	Y	Y	Y	N/A	N	Y	Y	N	Y	Y
Malavolta 2014	N	N	Y	N	N	Y	N/A	Y	Y	Y	N	Y	Y
Sanchez 2011	N	N	N	N	Y	Y	N/A	N	N	N	N	Y	N
Rodeo 2012	N	Y	Y	Y	Y	Y	N/A	N	Y	Y	N	Y	N
Rha 2013	N/A	N	N	N	N	N	N	N	N	N	N	N	Y
Antuna 2013	N/A	N	N	N	N	N	N	N	N	N	N	N	N
Kesikburun 2013	N/A	N	N	N	N	N	N	N	N	Y	N	N	Y
Zumstein 2014	N/A	N/A	N	N	N	N	N	N	N	N	N	Y	Y
Hak 2014	N/A	N/A	N	N	N	N	N	N	N	Y	N	Y	N
Jo 2015	N/A	N/A	N/A	N/A	N	N	N	N	N	Y	Y	Y	Y
Pandey 2016	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N	N	Y	Y	Y
D'Ambrosi 2016	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N	N	N	Y	Y
Holtby 2016	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N	N	Y	Y	N
Ebert 2017	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N	N	N	Y
Flury 2017	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N	N	Y	Y
Malavolta 2018	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N	N	N
Walsh 2018	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N	N	N

N, no; N/A, not applicable; Y, yes.

Table 6B. Clinical Outcomes

UCLA	Total No. of Studies	No. of Studies Used for Analysis	Only RCT	Overall				
				Z	P Value	Range	I (%)	Cross Line of No Effect
Chahal 2012	5		N					
Zhang 2013	5	3	N	1.09	.28	-2.2-.63	0	Y
Li 2014	6	2	Y	.42	.67	-1.55-1	90	Y
Zhao 2015	8	4	N	1	.32	-2- -.65	0	Y
Warth 2015	11	6	N		.48	-1.03-1.63	0	Y
Vavken 2015	7		N					
Cai 2015	5	4	N	.38	.7	-1.48-2.19	60	Y
Yang 2016	8	4	Y	.25	.8	-1.64-2.13	0	Y
Fu 2017	11	-	Y					
Han 2019	13	7	Y	2.69	.007	.27-1.69	47	N
Hurley 2019	18	6	Y		<.05	.55-2.05	0	N
Chen 2019	18		Y					

SST	Total no. of studies	No. of studies used for analysis	Only RCT	Overall				
				Z	P Value	Range	I (%)	Cross Line of No Effect
Chahal 2012	5		N					
Zhang 2013	5	3	N	1.73	.08	.48-1.05	24	Y
Li 2014	6	2	Y	1.93	.05	-.01-.69	47	Y
Zhao 2015	8		N					
Warth 2015	11	4	N		.85	-.37-.71	0	Y
Vavken 2015	7		N					
Cai 2015	5	2	N	1.6	.11	-.11-1.09	0	Y
Yang 2016	8	3	Y	1.93	.15	-.01-.69	47	Y
Fu 2017	11		Y					
Han 2019	13		Y	2.65	.008	.1-.75	0	N
Hurley 2019	18		Y					
Chen 2019	18		Y					

noting 5 out of 11 studies had a high risk of selection bias. They also noted that 6 out of 11 studies had a performance bias. Cai et al.,²¹ Yang et al.,²² and Fu et al.²³ found a low risk of bias. Hurley et al.¹⁹ undertook a Jaddad score⁹ of $3.8 \pm .7$, suggesting an overall high quality of study but noted that 3 out of the 18 studies had a high risk of bias.

Heterogeneity and Subgroup Analyses

The majority of the meta-analysis undertook *I* squared tests for clinical and radiological outcomes. The issue with heterogeneity is that the outcomes were recorded with a variety of scoring methods and that these were not universally employed. Seven studies undertook *I* squared tests for retears. Earlier studies, including Li et al.¹² and Warth et al.¹³ both found moderate heterogeneity. Zhang et al.²⁴ decided to undertake a subgroup analysis by tear size, and as a result, were the first to find PRP effective for small and medium tears with low heterogeneity. Articles by Vavken et al.¹⁶ and Cai et al.²¹ echoed this. Recent studies included Hurley et al.¹⁹ and Chen et al.¹¹ found PRP effective for reducing retears in all types of tears.

Only Chen et al.¹¹ and Hurley et al.¹⁹ looked at leukocyte concentration in PRP. Chen et al.¹¹ undertook a subgroup analysis for leukocyte content and gel application (thickened with coagulants), showing low

heterogeneity for both, and these were not factors in determining the effectiveness of PRP to reduce retear rates. Leukocyte content and commercial brand was not shown to make any impact on outcome.¹⁹

The VAS pain analysis showed a low heterogeneity; again, only the later studies would show PRP of benefit over the control. Hurley et al.¹⁹ undertook a subgroup analysis analyzing VAS score at different time periods, showing both had low heterogeneity and that PRP was effective in reducing pain scores. Chen et al.¹¹ showed PRP was effective for the short term, but not in the long term. Subgroup analysis with low heterogeneity at leukocyte content and gel application led to no difference in the results.

The Constant score had low heterogeneity in the majority of studies. This is not surprising, as these are the most common scores employed in clinical studies. Warth et al.¹³ undertook a subgroup analysis of Constant scores. They undertook subgroup analysis of levels of evidence; tear size, fixation method, PRP preparation PRP application, and PRP consistency. Despite this, they found a difference between the treatment groups. They employed a Leave-One-Out analysis for ASES (American Shoulder and Elbow Surgeons), UCLA (University of California, Los Angeles), Constant, Simple Shoulder Test (SST), VAS (visual analog scale) pain scores, again concluding no difference. A recent paper by Hurley

Table 6C. Overall Recommendation for PRP

Studies	Retears	Clinical	Comment
Chahal 2012	N	N	Small study size. Only 5 studies reviewed of which only 2 randomized. Study is too small for quantitative synthesis undertaken.
Zhang 2013	N	N	7 studies reviewed of which 3 were randomized controlled trial. Insufficient numbers appropriate for meta-analysis.
Li 2014	N	N	7 studies reviewed of which only 4 were randomized trials. Insufficient evidence to make a conclusion
Zhao 2015	N	N	8 studies reviewed, all randomized controlled trials. Patient number was low (under 500 patients).
Warth 2015	N	N	11 studies reviewed of which 8 were randomized. They did note improvement of Constant scores and retear rates of PRP, but that was statistically significant at this point.
Vavken 2015	N	N	13 studies. Effective for small and medium tears.
Cai 2015	Y	N	5 studies were reviewed, which showed a reduce retear rate in small- to moderate-sized tears
Yang 2016	N	Y	8 studies reviewed. Noted improvement in postoperative pain but not in retear rate.
Fu 2017	N/A	N	11 studies reviewed. Did not look at retears. No clinical improvements noted.
Han 2019	Y	Y	13 studies showed improvement in pain, function, and retear rates.
Hurley 2019	Y	Y	18 studies showed improvement in pain, function, and retear rates.
Chen 2019	Y	Y	18 studies showed improvement in retear rate and functional outcomes.

et al.¹⁹ and Chen et al.¹¹ showed that PRP was effective in improving Constant scores. Chen et al.¹¹ showed in subgroup analysis with low heterogeneity that despite the leukocyte content and gel application method, PRP improved Constant scores over control.

Eight studies looked at the UCLA scores. Li et al.¹² noted high heterogeneity for the UCLA scores, where the majority noted low to moderate. The issue with the UCLA score is that few of the randomized controlled trials utilized it. The SST score was noted as low-to-moderate heterogeneity. The ASES and the SST score, though used less frequently, also noted low-to-moderate heterogeneity.

Overall, the data are suggestive of low-to-moderate heterogeneity, which suggests that the data are comparable. This strengthens the conclusions of these articles, though it should be noted that this changed with time,

Overall Recommendations

Early studies did not recommend PRP for clinical or radiological benefit (See Table 6B and 6C). Warth et al.¹³ first noted in 2015 of possible reduced retear and Constant score, but it was not statistically significant. Following this Vavken et al.¹⁶ and Cai et al.²¹ noted a statistically significant improvement of retear rate in small and medium retears. The four meta-analyses that were recently published all now show a clinical and radiological benefit of PRP over control. The reasons are potential improvement in technology of PRP production, application (improved retear rates with bone-tendon implementation), and larger number of patients that results in adequate power that allows the detection of effect of PRP. Also, the previous meta-analyses had small numbers and fewer randomized controlled trials, and they used nonrandomized controlled trials. Strict meta-analysis rules do not advise or allow it.

Jaddad Decision Algorithm

Four of the authors applied the Jaddad methodology⁹ to identify which of the studies provided the strongest evidence. After analysis, it was determined 11 out of 13 studies delivered high-quality evidence, including Jaddad scores,⁹ Detsky scores,²⁵ and appropriate subgroup analysis. The current evidence suggests that PRP reduces the rate of retear, can reduce short-term pain, and provides better functional outcomes as compared to control. This is despite the tear size or the leukocyte content. It has been found that the application of PRP at the tendon-bone interface provides the most benefit, whether a gel is employed or not.

Discussion

In our study, PRP augmentation for arthroscopic rotator cuff tear led to lower retear rates and improved short-term postoperative functional outcome scores

We critically analyzed 13 studies, of which 6 were level I, 6 were level II and 1 was level III. These studies were deemed of high quality after analysis with PRISMA and Oxman-Guyatt scores, lending credence to their findings. There is a conflict of conclusions between early and later studies, the effectiveness of PRP only being shown in later articles. The resolution of this conflict is apparent from our study, with a subgroup analysis of later meta-analyses showing that with appropriate numbers, PRP is effective in improving functional outcome, as well as the rate-of retear. Certain factors such as gel application and high numbers of leukocytes have shown no difference to the effectiveness of PRP, but the application at the tendon-bone interface was superior to the application over the repair site.

According to our findings, platelet-rich plasma is recommended for augmenting rotator cuff repair. PRP

preparation, application, and consistency do not seem to affect outcomes. This finding is in contrast to Saltzman et al.,⁶ who also conducted a systematic review of meta-analyses in May 2016. The effect of PRP application timing (before and after repair) could not be commented on, as the large majority did the application after repair, as the PRP could affect the surgical visualization.

Saltzman et al.⁶ only included 7 meta-analyses, of which six were level of evidence II and one was level of evidence I. Out of the 7 studies, only one by Li et al.¹² looked exclusively at randomized controlled trials, the others included cohort studies, lowering the quality of data produced. The most recent meta-analysis reviewed by Saltzman et al.⁶ was Vavken et al.¹⁶ from 2015, which looked only at 11 studies, of which only 8 were randomized.

They undertook an analysis of these 7 studies and scored them according to Oxman-Guyatt and QUORUM. They found that looking at re-tear rates, Constant, UCLA, ASES, and SST there was no difference between PRP-treated groups and controls. However, they did note the trend in their subgroup analysis findings, suggesting small-to-moderate tears, and using PRP in the tendon-bone interface had improved outcomes.

In contrast, our study looked at 13 meta-analyses, the latest being published in 2019. These studies included 6 level I, 6 level II, and 1 level III. The last meta-analysis of our study looked at 18 randomized controlled trials.

Our study differs from Saltzman et al.⁶ due to the fact we had a number of higher-quality studies available to us. We also had a larger number of patients. This suggests that with an adequately powered data, the clinical and radiological benefit can be seen in the use of PRP.

The meta-analyses presented have limitations. Aside from the six level I studies, we included one level II and six level III studies. As a result, there may be bias, including selection and publication bias. These studies included low-to-moderate heterogeneity. The other issue is that the preparation and application are so variable that it can be difficult to compare. Subgroup analysis did not show any differences; however, these subgroup analyses had a limited number of studies. The employment of scoring systems still varies between studies, so a limited comparison could be made. Also, there is no standardization of surgical technique, including the use of acromioplasty, the method of repair, and the postoperative physiotherapy.

Even if PRP does have some positive effect, the issue of how substantial and whether this is cost-effective needs to be seen. Vavken et al.,¹⁶ who undertook a meta-analysis in March 2015 of 13 studies, of which only 7 were randomized controlled trials, suggested that PRP is not cost-effective. Making a cost-effectiveness statement of PRP at this early stage is

presumptuous. Early adopters of new treatments will always be expensive in the short term. However, as the treatment evolves and the use becomes more widespread through an economy of scales, the treatment will be substantially less costly. With a better technique in hand, PRP has the potential to be cost-effective and prevent the need for further surgery. This reduction in morbidity may also lead to more economic benefits for society as a whole.

Limitations

The majority of the meta-analyses unfortunately included low-level evidence. If we did not include them, we would be essentially missing half of published meta-analyses in the literature. Also, a large proportion of current thinking of PRP was based on these early reviews. Including these studies to address their weaknesses is important to help clinicians understand why prevalent thinking is incorrect and how more powerful recent studies of higher-quality data has led to a different understanding. However, as a result, this creates limitation in our analysis.

Another limitation is that we are reviewing meta-analyses, not individual randomized controlled trials. We are depending on the findings of the group who wrote the article. The information extracted from the article could be incorrect due to method or human error. By analyzing the conclusions of other groups, we create another level of error, based on the distance from the actual evidence. We do our best to minimize this by undertaking stringent criteria to evaluate each article.

Conclusion

Our study shows that PRP is effective in reducing retears after rotator cuff repair and improving functional outcome scores and reducing short-term pain.

References

1. Wani Z, Abdullah M, Habeebullah A, et al. Rotator cuff tears: Review of epidemiology, clinical assessment and operative treatment. *Trauma* 2016;18:190-204.
2. Ahmad Z, Parkar A, Shepherd J. Revolving doors of tendinopathy: definition, pathogenesis and treatment. *Postgrad Med J* 2020;96:94-101.
3. Ahmad Z, Al-Wattar Z, Rushton N, et al. Holding on by a thread: the continuing story of rotator cuff tears. *Br J Hosp Med (Lond)* 2021;82:1-10.
4. Ahmad Z, Howard D, Brookset RA, et al. The role of platelet rich plasma in musculoskeletal science. *JRSM Short Rep* 2012;3:40.
5. Ahmad Z, Brooks R, Kang S-N, et al. The effect of platelet-rich plasma on clinical outcomes in lateral epicondylitis. *Arthroscopy* 2013;29:1851-1862.
6. Saltzman BM, Jain A, Campbellet KA, et al. Does the use of platelet-rich plasma at the time of surgery improve clinical outcomes in arthroscopic rotator cuff repair when

- compared with control cohorts? A systematic review of meta-analyses. *Arthroscopy* 2016;32:906-918.
7. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;339:b2700.
 8. Oxman AD, Guyatt GH. Validation of an index of the quality of review articles. *J Clin Epidemiol* 1991;44:1271-1278.
 9. Jadad AR, Haynes RB, Hunt D, Browman GP, et al. The Internet and evidence-based decision-making: a needed synergy for efficient knowledge management in health care. *CMAJ* 2000;162:362-365.
 10. Chahal J, Van Thiel GS, Mall N, et al. The role of platelet-rich plasma in arthroscopic rotator cuff repair: A systematic review with quantitative synthesis. *Arthroscopy* 2012;28:1718-1727.
 11. Chen X, Jones IA, Togashi R, Park C, Vangsness CT Jr, et al. Use of platelet-rich plasma for the improvement of pain and function in rotator cuff tears: A systematic review and meta-analysis with bias assessment. *Am J Sports Med* 2019;48:2028-2041.
 12. Li X, Xu C-P, Hou Y-L, Song J-Q, Cui Z, Yu B, et al. Are platelet concentrates an ideal biomaterial for arthroscopic rotator cuff repair? A meta-analysis of randomized controlled trials. *Arthroscopy* 2014;30:1483-1490.
 13. Warth RJ, Dornan GJ, James EW, Horan MP, Millett PJ. Clinical and structural outcomes after arthroscopic repair of full-thickness rotator cuff tears with and without platelet-rich product supplementation: A meta-analysis and meta-regression. *Arthroscopy* 2015;31:306-320.
 14. Zhao JG, Wang ZL, Zhao L. Platelet-rich plasma in arthroscopic rotator cuff repair. *Arthroscopy* 2015;31:9-10.
 15. Zhang Q, Ge H, Zhou J, Cheng B, et al. Are platelet-rich products necessary during the arthroscopic repair of full-thickness rotator cuff tears: A meta-analysis. *PLoS One* 2013;8:e69731.
 16. Vavken P, Sadoghi P, Palmer M, et al. Platelet-rich plasma reduces retear rates after arthroscopic repair of small- and medium-sized rotator cuff tears but is not cost-effective. *Am J Sports Med* 2015;43:3071-3076.
 17. Zhao JG, Zhao L, Jiang Y-X, Wang Z-L, Wang J, Zhang P, et al. Platelet-rich plasma in arthroscopic rotator cuff repair: A meta-analysis of randomized controlled trials. *Arthroscopy* 2015;31:125-135.
 18. Han C, Na Y, Zhu Y, et al. Is platelet-rich plasma an ideal biomaterial for arthroscopic rotator cuff repair? A systematic review and meta-analysis of randomized controlled trials. *J Orthopaed Surg Res* 2019;14:183.
 19. Hurley ET, Lim Fat D, Moran CH, Mullett H. The efficacy of platelet-rich plasma and platelet-rich fibrin in arthroscopic rotator cuff repair: A meta-analysis of randomized controlled trials. *Am J Sports Med* 2019;47:753-761.
 20. Moraes VY, Lenza M, Tamaoki MJ, Faloppa F, Belloti JC, et al. Platelet-rich therapies for musculoskeletal soft tissue injuries. *Cochrane Database Syst Rev* 2013;12:Cd010071.
 21. Cai YZ, Zhang C, Lin XJ. Efficacy of platelet-rich plasma in arthroscopic repair of full-thickness rotator cuff tears: A meta-analysis. *J Shoulder Elbow Surg* 2015;24:1852-1859.
 22. Yang J, Sun Y, Xu P, Cheng B. Can patients get better clinical outcomes by using PRP in rotator cuff repair: A meta-analysis of randomized controlled trials. *J Sports Med Phys Fitness* 2016;56:1359-1367.
 23. Fu CJ, Sun J-B, Bi Z-G, Wang X-M, Yang C-Y. Evaluation of platelet-rich plasma and fibrin matrix to assist in healing and repair of rotator cuff injuries: A systematic review and meta-analysis. *Clin Rehabil* 2017;31:158-172.
 24. Zhang Z, Wang Y, Sun J. The effect of platelet-rich plasma on arthroscopic double-row rotator cuff repair: A clinical study with 12-month follow-up. *Acta Orthop Traumatol Turc* 2016;50:191-197.
 25. Detsky AS, Naylor CD, O'Rourke K, McGeer AJ, L'Abbé KA. Incorporating variations in the quality of individual randomized trials into meta-analysis. *J Clin Epidemiol* 1992;45:255-265.

Appendix 1

Terminology used for search:

Tendon, rotator cuff, supraspinatus, infraspinatus, platelet, platelet-rich plasma, PRP, shoulder, subscapularis, external rotators, and platelet concentrate.

Commercial names searched:

GPS II (Biomet Biologics, Warsaw, IN)
Cascade (MTF, Edison, NJ)
Regenkit; Regen Lab, Switzerland
Haemonetics MC+ (Haemonetics Corp.)
GPS III Platelet concentration system (Biomet Biologics, Warsaw, IN)
PRGF System 1, (BTI Biotechnology, Spain)
PRF Process, Nice, France
Cobe spectra LRS Turbo, Caridian BCT, Lakewood, CO
Vivostat PRF, Alleroed, Denmark
ACP Arthrex (USA)
Harvest Smartprep (Harvest, Plymouth, MA)
Terumo Penpol (Terumo, Japan)
ACP Arthrex (USA)