# Platelet-Rich Plasma Augmentation in Meniscal Repair Surgery: A Systematic Review of Comparative Studies



Eric D. Haunschild, B.S., Hailey P. Huddleston, B.S., Jorge Chahla, M.D., Ph.D., Ron Gilat, M.D., Brian J. Cole, M.D., M.B.A., and Adam B. Yanke, M.D., Ph.D.

Purpose: To systematically review the literature on meniscal repair surgery and assess functional and radiographic outcomes of platelet-rich plasma (PRP)-augmented repair compared with standard repair techniques. Methods: A systematic review of the literature was completed according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines using the PubMed, MEDLINE, Embase, and Cochrane databases. The inclusion criteria included all human studies testing PRP augmentation of meniscal repair written in the English language. All cadaveric, animal, and basic science studies were excluded from review. The quality of the included publications was assessed prior to data extraction through the Jadad score. Risk of bias was further determined by Methodological Index for Non-randomized Studies (MINORS) and Cochrane risk-of-bias assessments. Heterogeneity in outcomes reported across studies was evaluated using  $I^2$  statistic calculations. **Results:** A total of 5 studies (1 with Level I evidence; 1, Level II; and 3, Level III) met the inclusion criteria for this review, all comparing PRP augmentation of meniscal repair surgery versus meniscal repair with no augmentation. Overall quality and risk of bias in the included studies varied substantially (Jadad score, 1-5; Methodological Index for Non-randomized Studies score, 7-18). Three comparative studies found no significant difference in outcome or failure, whereas the other two showed a significant improvement in PRP-augmented repairs at final follow-up. Two studies assessed healing with postoperative magnetic resonance imaging or second-look arthroscopy, with both showing significantly improved outcomes in the PRP-treated groups (P < .01 and P = .048). PRP preparation techniques and composition differed among all studies and were inconsistently reported. Conclusions: In early and limited investigations, there is insufficient evidence to support PRP augmentation of meniscal repair surgery improving functional and radiographic outcomes and resulting in lower failure rates compared with standard repair techniques. There is considerable heterogeneity in the reporting and preparation of PRP used for augmentation. Level of Evidence: Level III, systematic review of Level I to III studies.

See commentary on page 1775

Meniscal lesions occur frequently in athletes and the general population, with approximately 1 million meniscal surgical procedures in the United States alone each year.<sup>1</sup> The long-term effects of meniscal injury can be severe, often causing functional impairment and an early onset of symptomatic osteoarthritis.<sup>2</sup>

© 2020 by the Arthroscopy Association of North America 0749-8063/191050/\$36.00 https://doi.org/10.1016/j.arthro.2020.01.038 Meniscal injuries are heterogeneous in morphology and etiology, with some tears unable to heal and requiring meniscectomy. In addition, for degenerative tears, recent evidence has shown that surgical intervention may have no effect on long-term outcomes compared with conservative management.<sup>3,4</sup> In select peripheral and well-vascularized lesions traditionally treated by meniscectomy, meniscal repairs have shown significantly improved outcomes and a reduced onset of osteoarthritis at long-term follow-up.<sup>5</sup> Correspondingly, the incidence of meniscal repairs relative to meniscectomy has increased in recent years,<sup>6</sup> with continued efforts focused on optimizing treatment and functional outcomes.

As defined by the American Academy of Orthopaedic Surgeons, "orthobiologics" are naturally occurring substances in the body used to accelerate healing after

From Midwest Orthopedics at Rush University, Chicago, Illinois, U.S.A. The authors report that they have no conflicts of interest in the authorship and publication of this article. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

Received September 3, 2019; accepted January 18, 2020.

Address correspondence to Brian J. Cole, M.D., M.B.A., Midwest Orthopedics at Rush University, 1611 W Harrison St, Chicago, IL, 60612, U.S.A. E-mail: bcole@rushortho.com

injury.<sup>7</sup> One type of orthobiologic, platelet-rich plasma (PRP), has recently emerged as a promising treatment to promote healing in soft-tissue and chondral injury. With its high concentrations of platelets and growth factors, PRP has enhanced the activity and regeneration of meniscal cells using in vitro models.<sup>8,9</sup> However, in the available literature, clinical uses of PRP in meniscal repair have been more variable, with differing indications, PRP preparation techniques, and outcomes.

The aim of this investigation was to systematically review the literature on meniscal repair surgery and assess functional and radiographic outcomes of PRPaugmented repair compared with standard repair techniques. We hypothesized that PRP augmentation would result in improved outcomes and lower failure rates after meniscal repair.

## Methods

#### Search Strategy

This investigation was completed in accordance with the 2009 Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. A systematic review of the use of PRP during surgical repair of meniscal tears was completed with a comprehensive published literature search in the MEDLINE, PubMed, and Embase databases; Cochrane Database of Systematic Reviews; and Cochrane Central Register of Controlled Trials. The references of the investigations found in this search were cross-referenced to identify additional pertinent studies not identified in the original searches. All searches were performed in July 2019. They were performed combining the following keywords: (1) "PRP" or "platelet-rich plasma" or "plasma rich fibrin" or "leukocyte-poor" or "leukocyte-rich"; (2) "meniscus" or "meniscal" or "medial meniscus" or "lateral meniscus" or "meniscal tear"; and (3) "repair" or "surgery" or "augmentation." Systematic review registration was performed in July 2019 using the PROSPERO International Prospective Register of Systematic Reviews (No. 145250).

## **Study Selection and Data Extraction**

This study included all clinical investigations meeting the following inclusion criteria: PRP use during arthroscopic meniscal repair surgery, English language, and human subjects. The exclusion criteria included all animal studies, cadaveric studies, basic science investigations, review articles, expert opinions, investigations not using PRP, studies in which concomitant procedures were performed with meniscal repair, and investigations on other surgical treatments unrelated to meniscal repair. The investigations included in this study were independently reviewed for inclusion and exclusion criteria by 2 graduate student authors (E.D.H., H.P.H.) under the supervision of a practicing

orthopaedic surgeon (A.B.Y.), with discordant findings reviewed by the senior author (A.B.Y.) as needed. Because of the significant heterogeneity in meniscal tear types and PRP preparation techniques, as well as a number of included studies with low levels of evidence, we elected not to proceed with a meta-analysis and instead provide a narrative reporting of functional outcomes and rates of healing in the included studies.

For each included investigation, demographic information including patient cohort size and average age, with age ranges, was recorded if available. Type of meniscal tear, as well as meniscal repair and PRP preparation technique, was also collected if included. Outcome measures used in each investigation were identified and collected, with continuous data recorded including mean value and range as available in the studies. All extracted data were organized in a Microsoft Excel spreadsheet in a table format prior to review.

## Assessment of Study Quality and Risk of Bias

The quality of the included studies was assessed using the Jadad score.<sup>10</sup> The Jadad score is a criterion for the evaluation and appraisal of randomized clinical trials. It is based on a composite score calculated from the 5 following metrics, with 1 point for a yes answer and 0 points for a no answer: (1) Is the study self-described as randomized? (2) Is the randomization method described and appropriate? (3) Is the study double blinded? (4) Is the method for double blinding appropriate? (5) Does the study provide descriptions of dropouts and withdrawals?

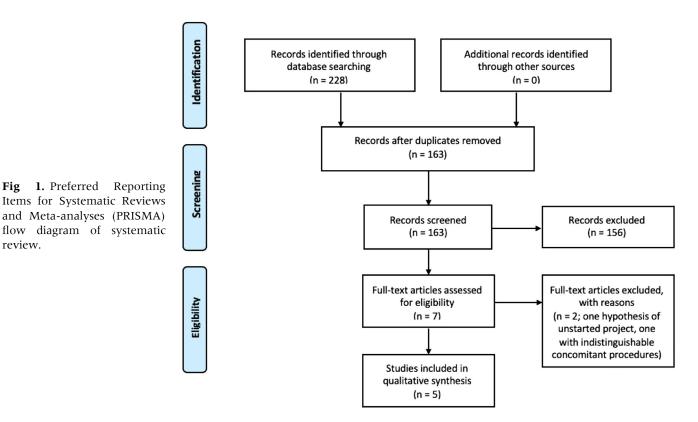
Risk of bias in individual nonrandomized studies was assessed with the Methodological Index for Nonrandomized Studies (MINORS) score. For comparative studies, MINORS assesses 12 items that are scored as 0 if unreported, 1 if reported but inadequate, and 2 if reported and adequate, with an optimum score of 24.<sup>11</sup> Higher scores indicate a lower risk of bias and vice versa. For the included randomized trial, the Cochrane risk-of-bias tool for randomized trials (RoB 2) was used.

All assessments were independently performed by 2 authors (1 graduate student [E.D.H.] and 1 orthopaedic resident [R.G.]), with discordant scores reviewed and resolved by consensus. Inter-rater reliability in assessment scoring was evaluated through calculation of Fleiss  $\kappa$  values.

# Results

# Study Demographic Characteristics and Quality Assessment

The searches performed in this study produced 228 results; when reviewed for duplicates, this number was reduced to 163 distinct publications for screening (Fig 1). After assessment of titles and abstracts for inclusion and exclusion criteria, the full-text articles of 7



investigations were assessed for eligibility. Of these, 1 was excluded because it presented only a hypothesis.<sup>12</sup> Another included a cohort of PRP-augmented meniscal repairs but did not adequately delineate results between cases that received concomitant ACL reconstruction and those that did not.<sup>13</sup> The remaining 5 studies met all criteria and were included in this investigation. Of the 5 included studies, 3 were retrospective studies with Level III evidence,<sup>14-16</sup> 1 was a prospective randomized controlled trial with Level I evidence,<sup>17</sup> and 1 was a nonrandomized prospective trial with Level II evidence.<sup>18</sup>

Study quality assessment in all included studies varied significantly, with Jadad scores ranging from 1 to 5 and MINORS scores ranging from 7 to 18 in nonrandomized studies. The randomized trial by Kaminski et al.<sup>17</sup> was evaluated to have a low risk of bias on Cochrane risk-of-bias assessment. Independent scoring of Jadad scores and Cochrane risk-of-bias assessment between the 2 raters was congruent. For MINORS scoring, inter-rater reliability was acceptable ( $\kappa = 0.687$ ).

All 5 trials included in this study compared outcomes of patients receiving PRP augmentation during meniscal repair but differed in PRP preparation technique and type of meniscal tear treated. The findings regarding functional and radiographic outcomes with PRP augmentation were variable. Details of the 5 included studies are presented in Table 1.

## **Comparative Study Results**

The subjects receiving PRP with meniscal repair in all trials were compared against control groups either receiving a sham saline solution injection or receiving no augmentation at the time of repair (Table 2). Pujol et al.<sup>16</sup> compared standard repair of horizontal tears of the medial or lateral meniscus with repair augmented by PRP. They found modest improvements in outcomes in the PRP cohort, with significant improvements in the Knee Injury and Osteoarthritis Outcome Score (KOOS) pain (P = .046) and sports (P = .03) parameters at a mean of 32.2 months' follow-up. However, the KOOS symptoms, daily activity, and quality-of-life parameters, as well as International Knee Documentation Committee (IKDC) outcomes and postoperative failure rates, were insignificantly different from the control group at final follow-up. Dai et al.<sup>14</sup> retrospectively compared PRP augmentation of discoid meniscal tears, finding no difference in failure rates or Lysholm (P = .306), visual analog scale (P = .321), and Ikeuchi (P = .601) outcome scores at a mean follow-up of 20.6 months. Similarly, an investigation by Griffin et al.<sup>15</sup> of a comparably sized cohort of patients undergoing PRP-augmented repairs of several different types of meniscal tears found no differences in failure rates (P = .89), return to sport or work, and Lysholm (P = .059) and IKDC (P = .55) outcome scores at a mean of 48 months' follow-up.

Two studies prospectively evaluated the effect of PRP augmentation on meniscal repair. In a nonrandomized

# Table 1. Study Characteristics of Included Investigations

			Jadad	MINORS	i -	Follow-up, Mean (Range),		Definition of		Radiographic	Type of Meniscal Tear	Operative Repair
Authors	Study Design (n)	LOE	Score	Score	Age, Mean (Range), yr	mo	Outcomes Measured	Treatment Failure	Findings	Outcomes	Repaired	Technique
Dai et al. <sup>14</sup>	Retrospective cohort (29: 14 in PRP group and 15 in control group)	Ш	1	16	PRP: 32.4 (13-52) Control: 30.3 (14-50)	20.6 (12-27)	VAS score, Lysholm score, Ikeuchi score, treatment failure	Development of joint- line pain and/or locking or swelling development after surgery; symptoms in ipsilateral knee requiring repeated arthroscopy within follow-up period	improvements in	Not assessed	All lateral meniscal tears of discoid menisci: 11 longitudinal, 10 complex, 7 horizontal, and 1 radial	Inside-out technique
Griffin et al. <sup>1</sup>	<sup>5</sup> Retrospective cohort (35: 15 in PRP group and 20 in control group)	ш	1	9	PRP: 26 (19-46) Control: 35 (19-68)	48 (24-72)	IKDC score, Lysholm score, RTW/RTS, treatment failure	Any reoperation on repaired meniscus within follow-up period	<ul> <li>(1) No significant differences in outcomes of Lysholm score, IKDC score, and RTW/RTS between PRP and control groups at final follow-up (2) Insigni- ficant difference in treatment failure rates (27% in PRP group vs 25% in control group)</li> </ul>	Not assessed	Medial and lateral meniscal repairs: 16 longitudinal, 1 complex, 3 horizontal, 9 bucket handle, 4 vertical, and 2 undersurface	Inside-out technique, all-inside technique, outside- in technique, combination of techniques
Pujol et al. <sup>16</sup>	Retrospective cohort (34: 17 in PRP group and 17 in control group)	ш	1	18	PRP: 32.3 Control: 28.3 Overall range: 13- 40	32.2 (24-40)	KOOS, IKDC score, treatment failure	Any reoperation on same knee for meniscectomy or iterative repair of same meniscus within follow-up period	(1) Significant improvements in KOOS parameters for pain and sports in PRP group compared with control group; no difference in KOOS symptoms, daily activities, and quality- of-life parameters or IKDC score(2) No significant difference in treatment failure rates (11.8% in PRP group vs 5.8% in control group)	MRI performed at 1 yr; PRP group had significantly improved radiographic healing (5 of 17 repairs with no hypersignal; control had 0 without hypersignal, P < .01); no correlation between radiographic and functional outcomes in either group	All horizontal tears of medial and lateral meniscus	Open repair, anchoring technique not specified

(continued)

# Table 1. Continued

Authors	Study Design (n)	LOE	Jadad Score	MINORS Score	Age, Mean (Range), yr	Follow-up, Mean (Range), mo	, Outcomes Measured	Definition of Treatment Failure	Findings	Radiographic Outcomes	Type of Meniscal Tear Repaired	Operative Repair Technique
Kaminski et al. <sup>17</sup>	Prospective randomized controlled trial (37: 19 in PRP group and 18 in control group)	I	5	_	PRP: 30 (18-43) Control: 26 (19-44)	54 (45-69)	IKDC score, WOMAC score, VAS score, treatment failure	No visible healing, healing of <50% of tear width, or unstable repair on follow-up MRI or second-look arthroscopy	(1) IKDC score, WOMAC score, and KOOS significantly improved in PRP group compared with control group at 42-mo follow-up; no significant difference in VAS outcome(2) Signi- ficantly lower treatment failure rate in PRP group vs control group (15% vs 53%)	MRI at 18 wk with insignificant differences; however, second- look arthroscopy at same time point with significant improvements in healing in PRP group compared with control group	vertical longitudinal tears in Cooper zone 2	All-inside technique, inside-out technique
Kemmochi et al. <sup>18</sup>	Prospective nonrandomized trial (22: 17 in PRP group and 5 in control group)	П	1	7	PRF: 32.4 ± 16.3 (15- 69) Control: 20.8 ± 8.8 (13-38)	6	Lysholm score, IKDC score	Not provided	No significant differences in IKDC or Lysholm scores at final follow-up	MRI at 6 mo; not objectively quantified, with "a tendency toward healing"	Tears defined by location: 7 in anterior segment, 2 in middle segment, 2 in middle segment, 2 segment, 1 in anterior-posterior segment, 3 in middle-posterior segment, and 3 in anterior-middle- posterior segment	All-inside technique

IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; LOE, level of evidence; MINORS, Methodological Index for Non-randomized Studies; MRI, magnetic resonance imaging; PRF, platelet-rich fibrin; PRP, platelet-rich plasma; RTW/RTS, return to work/return to sport; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Outcome Measurement	Dai et al. <sup>14</sup>	Griffin et al. <sup>15</sup>	Pujol et al. <sup>16</sup> (Average FU, 31.4 mo)	Kaminski et al. <sup>17</sup>	Kemmochi et al. <sup>1</sup>	
IKDC score	(Average FU, 20.6 III0)	(Average FU, 48 1110)	(Average FU, 51.4 III0)	(Average FU, 42 1110)	(Average FU, 6 III	5) 1 , %
PRP treatment	_	$69 \pm 26$	90.7	$97.56 \pm 0.63$	$87.4\pm10.4$	0
Control		$76 \pm 17$	87.9	$97.36 \pm 0.03$ $84.77 \pm 0.92$	$91.5 \pm 1.2$	0
<i>P</i> value		.55	07.7	.001	.13	
Lysholm score		.))		.001	.15	
PRP treatment	$79.8 \pm 9.6$	$66 \pm 31.9$	_	_	$95.8 \pm 7.1$	78
Control	$79.8 \pm 9.0$ $74.6 \pm 11.6$	$89 \pm 9.7$			$97.2 \pm 1.8$	78
<i>P</i> value	.306	.059 .059			97.2 ± 1.8 .69	
Tegner score	.300	.039			.09	
PRP treatment					$5.9 \pm 2.3$	
Control					$7.8 \pm 1.6$	
P value					7.8 ± 1.0 .11	
VAS score					.11	
PRP treatment	$1.2 \pm 1.0$			$0.84 \pm 0.10$		
Control	$1.2 \pm 1.0$ $1.6 \pm 1.1$	—	—	$0.84 \pm 0.10$ $0.89 \pm 0.08$	_	
<i>P</i> value	.321			.15		
Reoperation or	.321			.15		
treatment failure, %						
PRP treatment	7.1	27	5.8	15	_	0
Control	13.3	27	11.8	50		51
P value	.58	.89	11.0	.048		51
WOMAC score	.38	.89	—	.048		_
PRP treatment				$0.95\pm0.13$		
Control				$0.95 \pm 0.13$ $3.95 \pm 0.33$		
<i>P</i> value				.002		
KOOS pain				.002		
PRP treatment	_		93.3	$96.06 \pm 0.23$	_	_
Control			78.4	$92.85 \pm 0.43$		
<i>P</i> value			.046	.035		
KOOS symptoms			.040	.055		
PRP treatment	_		90.9	$96.23 \pm 0.31$	_	_
Control			86.1	$92.33 \pm 0.48$		
P value				.029		
KOOS daily activities				.027		
PRP treatment	_	_	97.2	$98.8 \pm 0.13$	_	_
Control			93.8	$95.14 \pm 0.38$		
<i>P</i> value				.0004		
KOOS sports				.0004		
PRP treatment	_	_	88.8	$89.44 \pm 0.86$	_	_
Control			74.4	$77.65 \pm 1.26$		
<i>P</i> value			.03	.009		
KOOS quality of life			.02	.007		
PRP treatment	_	_	78.3	$80.9 \pm 1.09$	_	_
Control			74.6	$66.18 \pm 1.17$		
<i>P</i> value			/4.0	$.008 \pm 1.17$ .008		
value				.000		

 Table 2. Selection of Surgical Outcomes

NOTE. Data are presented as mean  $\pm$  standard deviation or mean unless otherwise indicated.

FU, postoperative follow-up; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; PRP, platelet-rich plasma; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

trial of short-term outcomes, Kemmochi et al.<sup>18</sup> found that patients receiving PRP and platelet-rich fibrin membrane augmentation showed no significant difference in Lysholm (P = .69) or IKDC (P = .13) outcome scores at 6 months after surgery. Kaminski et al.<sup>17</sup> completed a double-blind, randomized controlled trial of PRP augmentation and tracked long-term outcomes. At 42 months after surgery, patients with PRP augmentation had significantly improved IKDC scores (P = .001), Western Ontario and McMaster Universities

Osteoarthritis Index scores (P = .002), and scores for all 5 KOOS parameter functional outcomes but showed no difference in visual analog scale scores (P = .15) compared with control. In addition, they found significantly lower failure rates (P = .048) in the PRP-treated repair group compared with the control group.

## **PRP** Preparation

Each of the 5 investigations used different preparation techniques and amounts of PRP at the time of surgery,

						Leukocyte Status		
		Post-Preparation	Initial Platelet	Final	Platelet	(Increase Factor	Growth	Final
Authors	Activation	Analysis	Concentration	Platelet Count	Increase Factor	If Provided)	Factors	Volume, mL
Dai et al. <sup>14</sup>	_	Yes	—	—	$ imes 6.4 \pm 1.4$	Leukocyte rich	_	4
						$( imes 6.1 \pm 1.6)$		
Griffin et al. <sup>15</sup>		—	—	—	—	Leukocyte poor	—	—
Pujol et al. <sup>16</sup>		—	—	—	—	Leukocyte rich	—	5
Kaminski	Thrombin	Yes	150-400 ( $\times 1000/\mu L$ )	1,980 (×1,000/ $\mu$ L)	—	Leukocyte rich	Yes	8
et al. <sup>17</sup>								
Kemmochi et al. <sup>18</sup>	_	Yes	_	_	×5.5 (3.4-9.1)	Leukocyte rich	—	2.4

Table 3. Reporting of PRP Preparation Process: Part 1

PRP, platelet-rich plasma.

as shown in Tables 3 and 4. Griffin et al.<sup>15</sup> used a Cascade PRP system (MTF Biologics) to prepare leukocyte-poor platelet-rich fibrin in all patients. Kemmochi et al.<sup>18</sup> prepared leukocyte-rich platelet-rich fibrin for all patients undergoing PRP augmentation. Pujol et al.<sup>16</sup> used the GPS III system (Zimmer Biomet) to produce leukocyte-rich PRP. Finally, Dai et al.<sup>14</sup> and Kaminski et al.<sup>17</sup> prepared leukocyte-rich PRP of differing concentrations for all subjects. Among the investigations that reported data, the amount of PRP used during augmentation ranged from 2.7 to 8 mL.

## Postoperative Arthroscopic and Radiographic Findings

In 2 of the 5 included studies, healing on postoperative imaging or second-look arthroscopy was used as an outcome measure. Pujol et al.<sup>16</sup> investigated magnetic resonance imaging (MRI) 1 year postoperatively, finding that the PRP group had significantly fewer patients with meniscal hypersignaling than the control group (12 of 17-PRP augmented MRI scans vs 17 of 17 control MRI scans, P < .01). However, no correlation was found between radiographic and functional outcomes in either group. In the study of Kaminski et al.,<sup>17</sup> patients received MRI scans 18 weeks after surgery, and no significant difference in their objective findings was observed (P = .54). A subset of patients from either group received second-look arthroscopy prior to final follow-up, with the PRP group showing significantly improved healing rates compared with the control group (P = .003). On cumulative analysis of second-look arthroscopy and MRI

outcomes, a significant improvement in healed or partially healed repair rates was found when receiving PRP augmentation (P = .048). Kemmochi et al.<sup>18</sup> performed MRI in all patients 6 months after surgery but did not provide objective radiographic outcomes, only commenting that some MRI scans showed signs of healing whereas others did not.

# Discussion

The primary finding of this review was that in preliminary investigations, there is insufficient evidence to support a clinical benefit of PRP augmentation of meniscal repair surgery compared with standard repair techniques. Although, in aggregate, the studies included in this investigation show some promising results, they are limited by small cohort sizes and a paucity of high levels of evidence. Further prospective investigations with larger cohorts are essential to better evaluate the role of PRP augmentation in this procedure. This study also found significant heterogeneity and inconsistencies in the reporting and preparation of PRP, showing the need for standardization of PRP reporting and use to allow for reproducibility and higher-quality comparisons in future trials.

The outcomes included in this review varied regarding the efficacy of PRP augmentation. Two studies reported significant improvements in functional outcome as well as decreased failure rates at final follow-up ranging from 32 to 54 months.<sup>16,17</sup> However, the other 3 studies reported no clinical benefit of PRP compared with standard repair.<sup>14,15,18</sup> Reported

**Table 4.** Reporting of PRP Preparation Process: Part 2

	Initial Whole			Spin	n l	Spin 2		
Authors	Blood Volume, mL	Anticoagulant	Processing Machine	Speed	Time, min	Speed	Time, min	
Dai et al. <sup>14</sup>	37	Sodium citrate		2,000 RPM	10	2,000 RPM	10	
Griffin et al. <sup>15</sup>	—	—	Cascade	—	—	—		
Pujol et al. <sup>16</sup>	_	—	GPS III	_	_	_	—	
Kaminski et al. <sup>17</sup>	120	Sodium citrate	_	—	—	—	—	
Kemmochi et al. <sup>18</sup>	—	—	—	1,000g	6	800g	8	

GPS III, Gravitational Platelet Separation System III; PRP, platelet-rich plasma.

radiographic outcomes were similar, with 1 study showing significant evidence of outcome improvement in patients receiving PRP augmentation and another showing no difference on MRI. It should be noted that assessment of meniscal healing after repair by MRI has its limitations, with multiple investigations showing low accuracy in detecting healing compared with secondlook arthroscopy.<sup>19,20</sup> Only Kaminski et al.<sup>17</sup> reported second-look arthroscopy in 14 PRP-treated repairs (77.8% of cohort) and 12 control repairs (63.2% of cohort) at 18 weeks after surgery. In those cases, they found a significantly greater incidence of healing when treated with PRP augmentation, but future studies using second-look arthroscopy as an outcome measurement are needed to confirm these benefits.

Meniscal repairs are being performed more frequently, with recent investigations showing favorable long-term outcomes and a return to baseline activity levels compared with patients undergoing partial meniscectomy.<sup>21,22</sup> However, indications for repair remain limited by the poor vascular supply and healing of the meniscus, resulting in significantly more reoperations after repair than after meniscectomy.<sup>21</sup> Basic science investigations have elucidated the role of growth factors and cytokines, including platelet-derived growth factor, hepatocyte growth factor, epidermal growth factor, insulin-like growth factor 1, and interleukin 1, in promoting DNA synthesis and cell migration across all zones of meniscal tissue.<sup>23</sup> Plateletderived growth factor has been found to be particularly efficacious,<sup>8,24,25</sup> supporting the promise of PRP in augmenting healing and improving surgical outcomes of meniscal repair. Ishida et al.9 proved this efficacy in an in vitro and in vivo animal model, but as our review shows, clinical investigations of PRP use in meniscal repair remain preliminary.

PRP treatment is one of many augmentation techniques proposed in meniscal repair procedures. Several preclinical and Level IV clinical studies have tested autologous fibrin glues and clots,<sup>26-33</sup> which have both shown promise in healing and low failure rates. Others have looked at wrapping meniscal repairs with fascial sheaths and collagen matrices, which have also yielded favorable outcomes in limited Level IV studies.<sup>34-36</sup> In an in vitro study recently published, bone marrow aspirate concentrate was found to promote superior healing compared with PRP in avascular meniscal lesions.<sup>37</sup> There are currently no high-quality studies comparing the effectiveness of these different modalities, and further research is necessary to elucidate the optimal augmentation therapy.

A significant challenge in assessing the effectiveness in PRP is a lack of standardization in PRP dosing and preparation. In this review, different amounts and concentrations of leukocyte-rich PRP, leukocyte-poor PRP, and platelet-rich fibrin were tested, with no 2 studies using the same method. The effect of leukocyte count on tissue healing has been well studied, with leukocyte-rich formulations found to produce greater acute inflammatory responses, suggesting a benefit to leukocyte-poor PRP preparations.<sup>38,39</sup> Because no studies in this review compared leukocyte-rich and leukocyte-poor PRP, no conclusions can be made as to the relative effects, if any, of leukocyte count on meniscal healing or functional outcomes. Moreover, there were no consistent methods of reporting the PRP preparation technique and final PRP composition in any of the studies, limiting the ability to compare outcomes across different trials. Without detailed documentation of the methods used to produce PRP and analysis of PRP composition, it will remain challenging to complete and compare any reproducible, highquality studies on PRP augmentation.

## Limitations

Some limitations and sources of bias were identified in this study. A significant limitation was the heterogeneity of study populations and follow-up time points measured in the included studies, inhibiting the ability to directly compare their results and precluding a metaanalysis of the data extracted. In addition, only 5 studies met the criteria for this investigation, and aside from the study by Kaminski et al.,<sup>17</sup> all included studies were nonrandomized or retrospectively performed. Moreover, several confounders including type of tear, meniscal zone of tear, operative technique, timing of surgery, and type of meniscal tear repaired varied by study, which may partially explain the differences in reported outcomes because some tears are more amenable to operative repair than others. These limitations, in addition to nonstandardized PRP preparation technique, are significant and limit the strength of the findings and the ability to generalize the conclusions obtained from this initial review. Finally, although the investigations included were found through a systematic search, there is the potential that pertinent studies were not included in this review.

## Conclusions

In early and limited investigations, there is insufficient evidence to support PRP augmentation of meniscal repair surgery improving functional and radiographic outcomes and resulting in lower failure rates compared with standard repair techniques. There is considerable heterogeneity in the reporting and preparation of PRP used for augmentation.

## References

- 1. Cook JL. The current status of treatment for large meniscal defects. *Clin Orthop Relat Res* 2005;435:88-95.
- **2.** Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and

meniscus injuries: Osteoarthritis. *Am J Sports Med* 2007;35: 1756-1769.

- **3.** Brignardello-Petersen R, Guyatt GH, Buchbinder R, et al. Knee arthroscopy versus conservative management in patients with degenerative knee disease: A systematic review. *BMJ Open* 2017;7:e016114.
- **4.** van de Graaf VA, Wolterbeek N, Mutsaerts EL, et al. Arthroscopic partial meniscectomy or conservative treatment for nonobstructive meniscal tears: A systematic review and meta-analysis of randomized controlled trials. *Arthroscopy* 2016;32:1855-1865.e4.
- Stein T, Mehling AP, Welsch F, von Eisenhart-Rothe R, Jäger A. Long-term outcome after arthroscopic meniscal repair versus arthroscopic partial meniscectomy for traumatic meniscal tears. *Am J Sports Med* 2010;38:1542-1548.
- **6.** Abrams GD, Frank RM, Gupta AK, Harris JD, McCormick FM, Cole BJ. Trends in meniscus repair and meniscectomy in the United States, 2005-2011. *Am J Sports Med* 2013;41:2333-2339.
- Helping fractures heal (orthobiologics), https://orthoinfo. aaos.org/en/treatment/helping-fractures-heal-orthobio logics/ Published 2010. Accessed December 4, 2019.
- **8.** Bhargava MM, Hidaka C, Hannafin JA, Doty S, Warren RF. Effects of hepatocyte growth factor and platelet-derived growth factor on the repair of meniscal defects in vitro. In *Vitro Cell Dev Biol Anim* 2005;41: 305-310.
- **9.** Ishida K, Kuroda R, Miwa M, et al. The regenerative effects of platelet-rich plasma on meniscal cells in vitro and its in vivo application with biodegradable gelatin hydrogel. *Tissue Eng* 2007;13:1103-1112.
- **10.** Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Control Clin Trials* 1996;17:1-12.
- 11. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): Development and validation of a new instrument. *ANZ J Surg* 2003;73:712-716.
- **12.** Wei LC, Gao SG, Xu M, Jiang W, Tian J, Lei GH. A novel hypothesis: The application of platelet-rich plasma can promote the clinical healing of white-white meniscal tears. *Med Sci Monit* 2012;18:HY47-HY50.
- 13. Everhart JS, Cavendish PA, Eikenberry A, Magnussen RA, Kaeding CC, Flanigan DC. Platelet-rich plasma reduces failure risk for isolated meniscal repairs but provides no benefit for meniscal repairs with anterior cruciate ligament reconstruction. *Am J Sports Med* 2019;47:1789-1796.
- 14. Dai WL, Zhang H, Lin ZM, Shi ZJ, Wang J. Efficacy of platelet-rich plasma in arthroscopic repair for discoid lateral meniscus tears. *BMC Musculoskelet Disord* 2019;20:113.
- **15.** Griffin JW, Hadeed MM, Werner BC, Diduch DR, Carson EW, Miller MD. Platelet-rich plasma in meniscal repair: Does augmentation improve surgical outcomes? *Clin Orthop Relat Res* 2015;473:1665-1672.
- 16. Pujol N, Salle De Chou E, Boisrenoult P, Beaufils P. Platelet-rich plasma for open meniscal repair in young patients: Any benefit? *Knee Surg Sports Traumatol Arthrosc* 2015;23:51-58.
- 17. Kaminski R, Kulinski K, Kozar-Kaminska K, et al. A prospective, randomized, double-blind, parallel-group, placebo-controlled study evaluating meniscal healing,

clinical outcomes, and safety in patients undergoing meniscal repair of unstable, complete vertical meniscal tears (bucket handle) augmented with platelet-rich plasma. *Biomed Res Int* 2018;2018:9315815.

- **18.** Kemmochi M, Sasaki S, Takahashi M, Nishimura T, Aizawa C, Kikuchi J. The use of platelet-rich fibrin with platelet-rich plasma support meniscal repair surgery. *J Orthop* 2018;15:711-720.
- **19.** Miao Y, Yu JK, Ao YF, Zheng ZZ, Gong X, Leung KK. Diagnostic values of 3 methods for evaluating meniscal healing status after meniscal repair: Comparison among second-look arthroscopy, clinical assessment, and magnetic resonance imaging. *Am J Sports Med* 2011;39:735-742.
- **20.** Vives MJ, Homesley D, Ciccotti MG, Schweitzer ME. Evaluation of recurring meniscal tears with gadoliniumenhanced magnetic resonance imaging: A randomized, prospective study. *Am J Sports Med* 2003;31:868-873.
- **21.** Paxton ES, Stock MV, Brophy RH. Meniscal repair versus partial meniscectomy: A systematic review comparing reoperation rates and clinical outcomes. *Arthroscopy* 2011;27:1275-1288.
- **22.** Xu C, Zhao J. A meta-analysis comparing meniscal repair with meniscectomy in the treatment of meniscal tears: The more meniscus, the better outcome? *Knee Surg Sports Traumatol Arthrosc* 2015;23:164-170.
- **23.** Bhargava MM, Attia ET, Murrell GA, Dolan MM, Warren RF, Hannafin JA. The effect of cytokines on the proliferation and migration of bovine meniscal cells. *Am J Sports Med* 1999;27:636-643.
- 24. Buma P, Ramrattan NN, van Tienen TG, Veth RP. Tissue engineering of the meniscus. *Biomaterials* 2004;25: 1523-1532.
- **25.** Lietman SA, Hobbs W, Inoue N, Reddi AH. Effects of selected growth factors on porcine meniscus in chemically defined medium. *Orthopedics* 2003;26:799-803.
- **26.** Biedert RM. Treatment of intrasubstance meniscal lesions: A randomized prospective study of four different methods. *Knee Surg Sports Traumatol Arthrosc* 2000;8:104-108.
- 27. Ishimura M, Ohgushi H, Habata T, Tamai S, Fujisawa Y. Arthroscopic meniscal repair using fibrin glue. Part II: Clinical applications. *Arthroscopy* 1997;13:558-563.
- 28. Ishimura M, Tamai S, Fujisawa Y. Arthroscopic meniscal repair with fibrin glue. *Arthroscopy* 1991;7:177-181.
- 29. Jang SH, Ha JK, Lee DW, Kim JG. Fibrin clot delivery system for meniscal repair. *Knee Surg Relat Res* 2011;23: 180-183.
- **30.** Kamimura T, Kimura M. Repair of horizontal meniscal cleavage tears with exogenous fibrin clots. *Knee Surg Sports Traumatol Arthrosc* 2011;19:1154-1157.
- **31.** Kamimura T, Kimura M. Meniscal repair of degenerative horizontal cleavage tears using fibrin clots: Clinical and arthroscopic outcomes in 10 cases. *Orthop J Sports Med* 2014;2:2325967114555678.
- **32.** Ra HJ, Ha JK, Jang SH, Lee DW, Kim JG. Arthroscopic inside-out repair of complete radial tears of the meniscus with a fibrin clot. *Knee Surg Sports Traumatol Arthrosc* 2013;21:2126-2130.
- **33.** van Trommel MF, Simonian PT, Potter HG, Wickiewicz TL. Arthroscopic meniscal repair with fibrin clot of complete radial tears of the lateral meniscus in the avascular zone. *Arthroscopy* 1998;14:360-365.

- 34. Henning CE, Lynch MA, Yearout KM, Vequist SW, Stallbaumer RJ, Decker KA. Arthroscopic meniscal repair using an exogenous fibrin clot. *Clin Orthop Relat Res* 1990;252:64-72.
- **35.** Henning CE, Yearout KM, Vequist SW, Stallbaumer RJ, Decker KA. Use of the fascia sheath coverage and exogenous fibrin clot in the treatment of complex meniscal tears. *Am J Sports Med* 1991;19:626-631.
- **36.** Piontek T, Ciemniewska-Gorzela K, Naczk J, et al. Complex meniscus tears treated with collagen matrix wrapping and bone marrow blood injection: A 2-year clinical follow-up. *Cartilage* 2016;7:123-139.
- **37.** Koch M, Hammer S, Fuellerer J, et al. Bone marrow aspirate concentrate for the treatment of avascular meniscus tears in a one-step procedure—Evaluation of an in vivo model. *Int J Molec Sci* 2019;20.
- **38.** Braun HJ, Kim HJ, Chu CR, Dragoo JL. The effect of platelet-rich plasma formulations and blood products on human synoviocytes: Implications for intra-articular injury and therapy. *Am J Sports Med* 2014;42:1204-1210.
- **39.** Dragoo JL, Braun HJ, Durham JL, et al. Comparison of the acute inflammatory response of two commercial plateletrich plasma systems in healthy rabbit tendons. *Am J Sports Med* 2012;40:1274-1281.