Platelet-Rich Plasma Reduces Failure Risk for Isolated Meniscal Repairs but Provides No Benefit for Meniscal Repairs With Anterior Cruciate Ligament Reconstruction

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Background: The effect of platelet-rich plasma (PRP) on the risk of meniscal repair failure is unclear. Current evidence is limited to small studies without comparison between isolated repairs and meniscal repairs with concomitant anterior cruciate ligament (ACL) reconstruction. It is also unclear whether the efficacy of PRP differs between preparation systems in the setting of meniscal repair.

Purpose: (1) To determine whether intraoperative PRP affects the risk of meniscal repair failure. (2) To determine whether the effect of PRP on meniscal failure risk is influenced by ACL reconstruction status or by PRP preparation system.

Study Design: Cohort study; Level of evidence, 3.

Methods: The study entailed 550 patients (mean ± SD age, 28.8 ± 11.2 years) who underwent meniscal repair surgery with PRP (n = 203 total; n = 148 prepared with GPS III system, n = 55 prepared with Angel system) or without PRP (n = 347) and with (n = 399) or without (n = 151) concurrent ACL reconstruction. The patients were assessed for meniscal repair failure within 3 years. The independent effect of PRP on the risk of meniscal repair failure was determined by multivariate Cox proportional hazards modeling with adjustment for age, sex, body mass index, ACL status, tear pattern, tear vascularity, repair technique, side (medial or lateral), and number of sutures or implants used.

Results: Failures within 3 years occurred in 17.0% of patients without PRP and 14.6% of patients with PRP (P = .60) (Angel PRP, 15.9%; GPS III PRP, 14.2%; P = .58). Increased patient age was protective against meniscal failure regardless of ACL or PRP status (per 5-year increase in age: adjusted hazard ratio [aHR], 0.90; 95% CI, 0.81-1.0; P = .047). The effect of PRP on meniscal failure risk was dependent on concomitant ACL injury status. Among isolated meniscal repairs (20.3% failures at 3 years), PRP was independently associated with lower risk of failure (aHR, 0.18; 95% CI, 0.03-0.59; P = .002) with no difference between PRP preparation systems (P = .84). Among meniscal repairs with concomitant ACL reconstruction (14.1% failures at 3 years), PRP was not independently associated with risk of failure (aHR, 1.39; 95% CI, 0.81-2.36; P = .23) with no difference between PRP preparation systems (P = .78).

Conclusion: Both PRP preparations used in the current study had a substantial protective effect in terms of the risk of isolated meniscal repair failure over 3 years. In the setting of concomitant ACL reconstruction, PRP does not reduce the risk of meniscal repair failure.

Keywords: knee ligaments; ACL; knee meniscus; platelet-rich plasma

Intraoperative injections of platelet-rich plasma (PRP) have been used with increased frequency in orthopaedic soft tissue reconstructive procedures. Activation of a high concentration of platelets at the operative site may increase the concentration of growth factors that enhance healing at the site of injury.[34,42] Despite widespread use of PRP, it is unclear which surgical procedures can benefit from intraoperative PRP administration, and the ideal PRP cell concentrations likely vary among surgical procedures. A review by Marx[27] suggested that, in general, a platelet count should be 1 million platelets/μL to achieve a therapeutic effect. However, Anitua et al[2] concluded that any concentration greater than 300,000 platelets/μL is sufficient. Many PRP preparation systems are commercially available, resulting in varying PRP cell concentrations,[10,12,23,33,39] which likely contributes to the uncertainty of the effect of PRP in specific clinical applications.[17]

An intact knee meniscus plays a critical role in preserving normal joint surface contact forces,[7,24,31] and meniscectomy can result in increased joint laxity, decreased shock

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absorption, and the subsequent development of degenerative osteoarthritis.[14,26,40] Therefore, knee meniscal repairs are being performed with increasing frequency,[1] although failure of meniscal repairs is not rare. A systematic review of outcome studies regarding meniscal repair in adults with greater than 5 years of follow-up found a pooled risk of failure of 20% to 24%.[30] Multiple risk factors for meniscal repair failure have been described, including patient age,[22] tobacco use,[5] tear location,[22] and surgeon experience.[22] Some studies suggest that concomitant anterior cruciate ligament (ACL) reconstruction (ACLR) may have a protective effect on meniscal repair failure risk,[11,22] while others have found no association.[30] It has been proposed that the potential beneficial effect of ACLR on meniscal repair healing is due to increased bleeding within the joint[8]; this is also a proposed mechanism for the high rate of healing of small, stable meniscal tears treated nonoperatively at the time of ACLR.[21]

Currently, few published studies are available regarding the effect of PRP on knee meniscal repair outcomes, and all of them are underpowered to assess repair failure as a primary outcome measure.[15,19,20,35] In a small randomized study (n = 19 PRP; n = 18 no PRP), Kaminski et al[19] found higher rates of healing with PRP at 18 weeks as assessed by magnetic resonance imaging (MRI) or second-look arthroscopy ($P = .048$) after repairs of unstable vertical meniscal tears. In a retrospective study conducted in 2015, Griffin et al[15] evaluated 35 patients (n = 15 PRP; n = 20 no PRP) who underwent isolated arthroscopic meniscal repairs, concluding that there was no difference in reoperation rates between the groups at the time of follow-up (mean, 4 years). In a case-control study of isolated horizontal cleavage repairs (n = 17 PRP; n = 17 no PRP), patients who received PRP were more likely to have disappearance of abnormal intrameniscal signal on MRI at 1 year ($P < .01$), but no difference in repair failure (defined by subsequent partial meniscectomy) was found at 2 years.[35]

The primary aim of the current study is to determine whether intraoperative PRP affects the risk of meniscal repair failure. The secondary aim of the study is to determine whether the effect of PRP on meniscal failure risk is influenced by ACLR status or PRP preparation system. We hypothesize that the application of PRP at the time of arthroscopic meniscal repair will lead to a significant reduction in meniscal repair failure risk. We also hypothesize that concomitant ACLR and/or PRP preparation system will not influence the effect of PRP on meniscal repair failure risk.

METHODS

Selection of Patient and Sample Size Estimation

This study was approved by the Biomedical Institutional Review Board of The Ohio State University (2013H0066). We identified all patients at a single institution who underwent primary arthroscopic meniscal repair with or without concomitant ACLR under a single surgeon (D.C.F.) from June 2006 to April 2017. No age or sex criteria were established for study inclusion. Meniscal repairs with concomitant procedures (ACLR or any other procedure) were eligible for inclusion. Meniscal allograft transplants were not considered to be meniscal repairs and were excluded. If a patient underwent subsequent meniscal repair procedures on the contralateral meniscus or contralateral knee (n = 52 patients), only the initial procedure was included. Patients who were incarcerated who underwent meniscal repair were excluded due to the inability to obtain reliable follow-up after completion of rehabilitation (n = 15). After application of these selection criteria, a total of 550 primary meniscal repairs on 550 patients were eligible for inclusion. Of these 550 patients, 399 had concomitant ACLR and 151 were isolated meniscal repairs. Among the 550 eligible patients, 90% (n = 495) had follow-up at 1 year and 83% (n = 458) (no PRP, 85%, n = 294/347; PRP, 81%, 164/203) at 3 years. Follow-up at 4 or more years was less than 80% for the PRP group; the time horizon for the current study was therefore set at 3 years. A 3-year time horizon is adequate to recognize most meniscal repair failures; in a meta-analysis of studies with mean 7.4-year follow-up, 71% of meniscal repair failures occurred within 2 years.[30]

According to an a priori power analysis, the number of patients with 3-year follow-up was adequate to test the primary study hypothesis. A minimum clinically meaningful difference has not been published for risk of meniscal repair failure; in our opinion, a 50% reduction in the risk of meniscal repair failure due to PRP would be substantial enough to justify routine clinical use of PRP. Assuming an estimated 20% risk of meniscal repair failure within 3 years of surgery without PRP use, we determined that the minimum sample size (at 80% power and alpha = .05) needed to detect a 50% reduction in risk of meniscal repair failure due to PRP was n = 266 without PRP and n = 150 with PRP.

Patient Selection for PRP

Use of PRP was based on year of surgery rather than application of specific patient selection criteria. Before 2010,

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PRP was not used by the senior author for meniscal repairs. For meniscal repairs performed from January 2010 to February 2015, the senior author (D.C.F.) used intraoperative PRP that was prepared by the GPS III Platelet Concentration System (Biomet Orthopedics). From March 2015 through April 2017, the author used PRP that was prepared by the Angel Concentrated Platelet Rich Plasma System (Arthrex). The decision to begin to use PRP for meniscal repairs starting in 2010 was based on the belief that PRP may enhance meniscal repair healing. The change in PRP preparation system in 2015 was due to an institutional change in supplier contracts and was not related to perceived clinical performance of either product. Of the patients included in the current study who received PRP (n = 203), 148 received PRP prepared with the GPS III system and 55 received PRP prepared with the Angel system.

Preparation of PRP

In brief, the GPS III system was prepared by first drawing 54 mL of blood from the patient followed by combining the blood with 6 mL of ACD-A (citrate anticoagulant) in a disposable separation tube, which was subsequently centrifuged at 3200 revolutions per minute for 15 minutes. After centrifugation, the platelet-poor plasma was removed from the centrifugate, resulting in 6 to 7 mL of PRP, which was extracted to be injected intraoperatively. For the patients receiving PRP prepared by the Angel system, 60 mL of whole blood was drawn preoperatively and spun down in the Angel centrifuge set at 2% hematocrit. In a comparative study by Degen et al[10] using PRP prepared from whole blood from healthy volunteers, mean ± SD cell counts for the Angel system at 2% hematocrit were 11.0 ± 4.5 k/μL white blood cells (WBCs), 0.2 ± 0.1 M/μL red blood cells (RBCs), 2064 ± 526 k/μL platelets, and 0.6 ± 0.6 k/μL neutrophils; cell counts for the GPS III system were 27.3 ± 7.1 k/μL WBCs, 1.0 ± 0.9 M/μL RBCs, 1343 ± 670 k/μL platelets, and 9.4 ± 7.0 k/μL neutrophils.[10] In their analysis, WBC and neutrophil counts were higher in PRP samples prepared by the GPS III system than the Angel system (P = .017 and P = .007, respectively), and no differences were found in RBC or platelet concentrations.[10] Intraoperatively, the PRP was introduced into the joint with a mixture of 5000 units of thrombin and 5 mL of calcium chloride to activate and clot the platelets. The PRP was administered at the conclusion of the procedure just before closure of the arthroscopic portal sites.

Postoperative Restrictions and Rehabilitation

After meniscal repair, all patients were kept nonweightbearing for 4 weeks with no knee flexion beyond 90° for 8 weeks. No resistive hamstring muscle exercises were used for 8 weeks. In the setting of isolated meniscal repairs, jogging was allowed as early as week 10 and return to sport was allowed as early as week 16. Aside from the initial weightbearing and range of motion restrictions to protect the meniscal repair, patients who underwent meniscal repair and concomitant ACLR were rehabilitated according to the Multicenter Orthopaedic Outcomes Network (MOON) protocol.[41]

Data Collection and Definition of Meniscal Repair Failure

Patient data that were collected included age, sex, height, weight, sport participation, past knee injuries, and surgical procedures. For the purpose of this study, meniscal tears were defined by tear pattern, laterality, vascular zone (vascular, vascular with avascular extension, or avascular), and number of sutures or implants used for repair. Operative time, repair technique, number of sutures or implants used for repair, and concomitant ACLR ligament injury were recorded for the intraoperative data.

For the purpose of this study, meniscal repair failure was defined as subsequent meniscectomy, no evidence of healing on repeat arthroscopy, revision meniscal repair, or subsequent total knee arthroplasty. We do not perform repeat MRI or second-look arthroscopy on asymptomatic patients after meniscal repair; therefore, the current study definition of failure does not include cases of asymptomatic nonhealed repairs. Manipulation under anesthesia and arthroscopic lysis of adhesions, with evidence of healed meniscal repair, were not considered failures, although the occurrence of these procedures was recorded. Meniscal surgery on the contralateral meniscus was not considered a failure.

Statistical Analysis

Statistical analysis was performed by use of a standard software package (JMP 13.0; SAS Institute). Two comparison groups were formed, and descriptive statistics were generated first for the entire sample population and then after stratification by PRP status and PRP preparation system (Table 1). Differences in continuous and categorical variables by PRP status were assessed by 2-tailed Student t test and chi-square test, respectively. A Kaplan-Meier survival plot was created for meniscal repair failure according to ACLR and PRP status, and differences in survival between groups (without adjustment for covariates) were assessed by Wilcoxon rank sum.

Multivariate Cox proportional hazards modeling was used to model the independent association between PRP and risk of meniscal repair failure. Potential covariates in the multivariate analysis included PRP preparation system, patient age, body mass index, meniscal tear pattern, tear vascularity, meniscal repair laterality, repair technique, number of sutures used for meniscal repair, and ACL status. A backward selection method was used with exit criteria of alpha less than .05 and a less than 15% change in estimate of the effect of PRP on failure risk. The change in estimate method has been demonstrated to be a robust method to control for confounding in multivariate analyses.[25,28] To adjust for increased surgeon experience or unaccounted-for changes in practice patterns over time, year of surgery was also assessed as a possible risk factor for meniscal repair failures; this was nonsignificant (P = .26) and was excluded from the final model.

TABLE 1
Descriptive Statistics[a]

	All Patients (N = 550)	No PRP (n = 347)	PRP (n = 203)	*P* Value
Demographics				
Male	348 (63)	219 (63)	129 (64)	.81
Female	202 (37)	128 (37)	74 (36)	
Age, y, mean ± SD	28.8 ± 11.2	28.1 ± 10.5	30.0 ± 12.5	.05
Body mass index, kg/m^2, mean ± SD	27.6 ± 6.0	27.7 ± 6.4	27.4 ± 5.4	.68
Tear pattern				
Vertical	479 (87)	331 (96)	148 (73)	<.001
Radial	38 (7)	7 (2)	31 (15)	
Horizontal	24 (4)	6 (2)	18 (9)	
Root	9 (2)	3 (1)	6 (3)	
Tear vascularity				
Completely vascular	308 (55)	211 (61)	97 (48)	.007
Avascular extension	242 (44)	136 (39)	106 (52)	
ACL status				
Concomitant ACL reconstruction	399 (73)	241 (69)	158 (78)	.02
Repair technique				
All-inside	418 (76)	260 (75)	158 (78)	.05
Inside-out	123 (22)	84 (24)	39 (19)	
Root repair	9 (2)	3 (1)	6 (3)	
Meniscus repaired				
Medial	341 (62)	219 (62)	122 (60)	.63
Lateral	143 (26)	91 (27)	52 (26)	
Both	66 (12)	37 (11)	29 (14)	
Number of sutures or implants, mean ± SD	4.4 ± 3.6	4.6 ± 3.6	4.1 ± 2.9	.18

[a]Values are expressed as n (%), unless otherwise noted. ACL, anterior cruciate ligament; PRP, platelet-rich plasma.

Interaction terms between PRP status and all other covariates were also considered for inclusion; the interaction term between ACLR and PRP status was found to be highly significant, indicating that the effect of PRP on meniscal repair failure risk was dependent on ACLR status. Therefore, the independent risk of meniscal failure due to PRP was determined both for isolated meniscal repairs and for repairs with concomitant ACLR.

RESULTS

Descriptive Statistics

The overall sample population was 63% male, with a mean ± SD age of 28.8 ± 11.2 years and BMI of 27.6 ± 6.0 kg/m^2 (Table 1). Tear pattern differed significantly by PRP status ($P < .001$), with a larger proportion of vertically oriented tears in the non-PRP group (96%) versus the PRP group (73%). Additionally, a larger percentage of tears that received PRP had avascular extension (extension beyond the red zone of the meniscal periphery) (52%) compared with tears that did not receive PRP (39%) ($P = .007$). Concomitant ACLR was more frequent in the PRP group (78%) compared with the non-PRP group (69%) ($P = .02$). There were 21 cases (3.8%) with postoperative stiffness with or without anterior impingement requiring manipulation and arthroscopic debridement with lysis of adhesions: 4.5% (n = 18) with ACLR, 2.0% (n = 3) without ACLR, 4.4% (n = 9) with PRP, and 3.5% (n = 12) without PRP. No significant association was found with use of PRP or difference between PRP systems and rates of arthroscopic lysis of adhesions, including with adjustment for ACLR status ($P > .05$, each comparison).

Meniscal Repair Failures Within 3 Years

Meniscal repair failures over 3 years occurred in 17.0% of repairs without PRP and 14.6% of repairs with PRP ($P = .60$) (Table 2). Failures within 3 years occurred in 20.3% of isolated meniscal repairs and 14.1% of meniscal repairs with concomitant ACLR ($P = .06$). No difference was found in failure risk with versus without use of PRP during year 1 ($P = .86$), year 2 ($P = .52$), or year 3 ($P > .999$) (Table 2). When the risk of failure was compared between repairs with no PRP, PRP prepared by the GPS III system, and PRP prepared by the Angel system, no differences in failure risk were noted over 3 years ($P = .58$) or during year 1 ($P = .75$), year 2 ($P = .21$), or year 3 ($P = .11$) (Table 2).

Independent Risk Factors for Meniscal Repair Failure

In the multivariate analysis, ACLR status and the use of PRP were both independently associated with meniscal repair failure risk (Table 3). Increased age was independently associated with lower risk of failure (adjusted hazard ratio [aHR] per 5-year increase in age, 0.90; 95% CI, 0.81-1.00; $P = .047$), and no other significant independent risk factors were identified. Year of surgery did not influence meniscal repair failure risk ($P = .26$).

TABLE 2
Meniscal Repair Failures Within 3 Years of Surgery[a]

	Year 1	Year 2[b]	Year 3[c]	Total[d]
Comparison of PRP and no PRP				
No PRP (n = 347)	8.0 (25/312)	6.1 (17/280)	3.2 (8/252)	17.0 (50/294)
PRP (n = 203)	7.1 (13/183)	4.2 (7/166)	2.8 (4/145)	14.6 (24/164)
P value	.86	.52	>.999	.60
Comparison of no PRP and the 2 PRP preparation systems				
No PRP (n = 347)	8.0 (25/312)	6.1 (17/280)	3.2 (8/252)	17.0 (50/294)
GPS III PRP (n = 148)	7.5 (10/133)	5.0 (6/120)	1.0 (1/105)	14.2 (17/120)
Angel PRP (n = 55)	6.0 (3/50)	2.2 (1/46)	7.5 (3/40)	15.9 (7/44)
P value	.75	.21	.11	.58

[a]Values given as % (n/N), unless otherwise noted. PRP, platelet-rich plasma.
[b]Excluding failures from year 1 and patients with less than 2 years of follow-up.
[c]Excluding failures from years 1 and 2 and patients with less than 3 years of follow-up.
[d]Excluding patients with less than 3 years of follow-up.

TABLE 3
Adjusted Risk of Meniscal Repair Failure[a]

	Adjusted Hazard Ratio (95% CI)	*P* Value
Sex		
Women	Referent	
Men	0.86 (0.55-1.34)	.50
Age: per 5-year increase	0.90 (0.81-1.00)	.047
Body mass index	1.00 (0.95-1.04)	.87
Tear pattern		
Vertical tear	Referent	
Nonvertical tear	1.76 (0.76-4.75)	.20
Radial tear	Too few observations	
Root tear	Too few observations	
Horizontal cleavage	Too few observations	
Tear vascularity		
Vascular tear	Referent	
Avascular extension	1.07 (0.59-2.01)	.83
ACL injured	0.41 (0.24-0.70)	.001
ACL-PRP interaction[b]	8.62 (2.24-57.1)	.001
Repair technique		
All-inside	Referent	
Inside-out	0.82 (0.27-2.55)	.73
Root repair	Too few observations	
Meniscus repaired		
Medial	Referent	
Lateral	0.97 (0.48-2.01)	.97
Both	0.98 (0.41-2.32)	.97
Number of implants	Per implant: 0.98 (0.91-1.05)	.61
PRP vs no PRP		
No PRP	Referent	
PRP (either brand)	0.16 (0.03-0.54)	.001
GPS III PRP	0.15 (0.02-0.55)	.002
Angel PRP	0.18 (0.03-0.65)	.006
PRP preparation systems		
GPS III PRP	Referent	
Angel PRP	1.19 (0.39-3.01)	.74

[a]ACL status, age, and PRP were included in the final multivariate model. ACL, anterior cruciate ligament; PRP, platelet-rich plasma.
[b]A significant interaction term between PRP and ACL status indicates that the relationship between use of PRP and meniscus repair failure risk is dependent on ACL status, and vice versa.

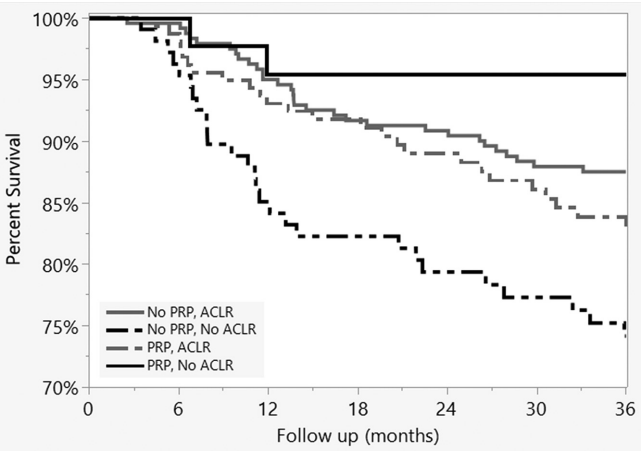

Figure 1. Survival plot by platelet-rich plasma (PRP) and anterior cruciate ligament reconstruction (ACLR) status. Survival rate significantly differed between groups (*P* = .003, Wilcoxon rank sum). Use of PRP resulted in improved survival of isolated meniscal repairs (*P* = .008) but had no effect on survival of meniscal repairs with concomitant ACLR (*P* = .28).

In the multivariate analysis, a highly significant interaction between PRP and ACLR status was identified (*P* = .001 for interaction) (Table 3), indicating that the effect of PRP on meniscal repair failure risk varied based on ACLR status. In a Kaplan-Meier analysis of meniscal repair survival with stratification by PRP and ACLR status, the use of PRP improved survival of isolated meniscal repairs (*P* = .008) but had no effect on survival of meniscal repair with concomitant ACLR (*P* = .28) (Figure 1). In the multivariate Cox proportional hazards analysis, PRP had a strong protective effect on risk of isolated meniscal repairs (aHR, 0.18; 95% CI, 0.03-0.59; *P* = .002) regardless of PRP system (GPS III: aHR, 0.14; 95% CI, 0.01-0.67; *P* = .008) (Angel: aHR, 0.19; 95% CI, 0.01-0.88; *P* = .03) (Table 4). Use of PRP had no effect on risk of meniscal repair failure in the setting of concomitant ACLR (*P* = .23) regardless of PRP system (GPS III, *P* = .29; Angel, *P* = .42) (Table 4).

TABLE 4
Adjusted Risk of Meniscal Repair Failure With Stratification by PRP Formulation and ACL Status[a]

	Both PRP Formulations		GPS III PRP		Angel PRP	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
No PRP, ACL intact	Referent					
PRP, ACL intact	0.18 (0.03-0.59)	.002	0.14 (0.01-0.67)	.008	0.19 (0.01-0.88)	.03
No PRP, ACLR	Referent					
PRP, ACLR	1.39 (0.81-2.36)	.23	1.36 (0.77-2.36)	.29	1.59 (0.47-4.12)	.42
PRP, ACL intact	Referent					
PRP, ACLR	3.54 (1.05-22.0)	.04				
No PRP, ACL intact	Referent					
No PRP, ACLR	0.41 (0.24-0.70)	.001				
	GPS III Versus Angel					
GPS PRP, ACL intact	Referent					
Angel PRP, ACL intact	1.33 (0.05-33.6)	.84				
GPS PRP, ACLR	Referent					
Angel PRP, ACLR	1.17 (0.33-3.12)	.78				

[a]Adjustment performed as needed for risk factors listed in Table 3. ACL, anterior cruciate ligament; ACLR, ACL reconstruction; HR, hazard ratio; PRP, platelet-rich plasma.

No difference was found in the effect of PRP between the GPS III and Angel systems for either isolated meniscal repairs ($P = .84$) or meniscal repairs with concomitant ACLR ($P = .78$) (Table 4). Finally, ACLR reduced meniscal repair failure risk among patients without PRP (aHR, 0.41; 95% CI, 0.24-0.70; $P = .001$) but increased the risk of failure among patients with PRP (aHR, 3.54; 95% CI, 1.05-22.0; $P = .04$).

DISCUSSION

Prior studies of intraoperative PRP for meniscal repairs have been severely underpowered to assess risk of repair failure.[15,19,20,35] The sample size of the current study is adequate to investigate meniscal repair failure risk as a primary outcome measure and demonstrates a strong protective effect of PRP on risk of failure of isolated meniscal repairs over 3 years. Further, both PRP systems used in the current study had similar efficacy in reducing the risk of isolated meniscal repair failure. However, in the setting of meniscal repair with concomitant ACLR, intraoperative PRP was of no benefit. The current study findings may help further define the role of intraoperative PRP in knee meniscal repairs.

The beneficial effect of PRP on meniscal repair failure risk is supported by prior basic science research, as an in vitro and animal study of PRP found the therapy to increase the concentration of various growth factors and upregulate the viability of meniscal cells.[18] However, not all PRP preparations are equivalent, and the cell concentrations produced by different preparation systems vary greatly.[12] This variability is considered a limiting factor in the study and clinical use of PRP.[17] The current study findings may not be applicable to systems with cell concentrations that substantially differ from samples created from the GPS III or Angel (2% hematocrit) systems. Mean platelet counts for samples from both systems were greater than 1000 k/μL in a comparative study by Degen et al,[10] although samples from the GPS III system had higher WBC (27.3 ± 7.1 k/μL) and neutrophil counts (9.4 ± 7.0 k/μL) than samples from the Angel system (WBCs, 11.0 ± 4.5 k/μL; $P = .017$) (neutrophils, 0.6 ± 0.6 k/μL; $P = .007$). Because the PRP preparations made from the GPS III and Angel systems had similar efficacy at reducing the risk of isolated meniscal repair failure, the current study findings suggest that WBC and neutrophil concentrations may be less important than obtaining a high platelet concentration to improve meniscal repair healing potential. Both Marx[27] and Anitua et al[2] suggested that a high platelet concentration, regardless of application, is needed to achieve a therapeutic effect for PRP.

ACL injury and subsequent reconstruction have a complicated effect on the potential for meniscal tear healing and the risk of meniscal repair failure. Bone tunnel bleeding may have an important positive effect on the potential for meniscal tear healing; this was postulated by Lee at al[21] as the reason for a high rate of healing of stable lateral meniscal tears left in situ after ACLR. Other authors have also noted the high healing potential of small tears and particularly lateral tears left untreated at the time of ACLR.[36,43] In animal models, blood clot from ACLR bone tunnels influences graft healing,[44] and Bab and Einhorn[3] reported that multiple growth factors are present within bone marrow–derived clot-including platelet-derived growth factor. Galliera et al[13] demonstrated elevated postoperative levels of vascular endothelial growth factor (VEGF) and VEGF receptor 2 after ACLR compared with arthroscopic partial meniscectomy. In the current study, PRP had no effect on the risk of meniscal repair failure in the setting of ACLR; this suggests that bone tunnel drilling provides sufficient bleeding and introduction of growth factors into the knee joint and that additional

administration of PRP is unnecessary. Further, in patients who did not receive PRP, meniscal repairs with concurrent ACLR had lower failure risk than isolated repairs. Alternatively, concerns have been raised that ACLR does not fully restore rotational stability to the knee and that knee meniscal repairs are at risk for mechanical failure even after ACLR.[37] This has prompted some clinicians to conduct anterolateral ligament reconstruction at the time of ACLR, which has been demonstrated to reduce the risk of posterior medial meniscal repair failure.[37] The current study findings support this concept; among patients who received PRP, meniscal repair failure risk was higher with concurrent ACLR than isolated meniscal repairs, presumably due to residual rotational instability after ACLR.

Our results also indicated that increased patient age was protective against meniscal failure regardless of the ACL or PRP status. These results are consistent with prior reports of lower meniscal repair failure risk among older patients than younger patients.[4,32,38] It is proposed that older age is protective against repair failure because older patients tend to be less active and return to physically demanding activities more slowly than younger patients.[22]

Limitations

This study had several limitations. Rates of asymptomatic nonhealing are likely underappreciated in the current study, as repeat MRI or arthroscopy was not obtained on asymptomatic patients. Some patients were lost to follow-up, which is an inherent source of bias. Due to the use of PRP in later years of the study period, an insufficient percentage of the PRP group had follow-up beyond 3 years to reliably assess risk of failure beyond 3 years in the PRP versus non-PRP groups. Although the majority of failures reported by long-term follow-up studies occur within 2 years,[30] the effect of PRP on risk of late failure of meniscal repairs is unknown. It has been proposed that a PRP clot may dissolve quickly upon exposure to synovial fluid[9,29]; it is possible that techniques to stabilize the clot could enhance intra-articular PRP efficacy, although additional research is needed to determine whether this does in fact improve clinical outcomes. Several differences were noted between PRP and non-PRP groups, including a difference in tear patterns (see Table 1); this is attributable in part to a change in practice patterns by the senior surgeon (D.C.F.) throughout the study period, with an increased tendency in later years of the study to treat nonvertical tear patterns with repair rather than meniscectomy. The multivariate analysis was designed to control for these known imbalances in treatment groups. To account for any changes in practice patterns over time that might have influenced outcomes, year of surgery was assessed as a potential predictor of failure risk and was found to be nonsignificant. Despite these steps to minimize confounding or bias, the potential remains for residual confounding from unknown or unmeasured factors, which is a limitation inherent in all nonrandomized studies. Finally, we followed the manufacturers' recommendations for preparation of PRP throughout the study, and both of the PRP preparations that we used have reported typical values for cell and growth factor concentrations[10]; however, some reports indicate that cell concentrations can vary between samples from the same patient even when PRP is prepared with the same system,[6,16] and these values were not assessed on the PRP samples administered in the current study. It is not known whether individual variations in cell or growth factor concentrations were present among the PRP samples in the current study, and, consequently, the effect of individual variation on meniscal repair failure risk is unknown.

Both PRP preparations used in the current study had a substantial protective effect on the risk of isolated meniscal repair failure over 3 years. In the setting of concomitant ACLR, PRP does not reduce the risk of meniscal repair failure.

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