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Effect of Intraoperative Platelet-Rich Plasma Treatment on Postoperative Donor Site Knee Pain in Patellar Tendon Autograft Anterior Cruciate Ligament Reconstruction

A Double-Blind Randomized Controlled Trial

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Background: Donor site morbidity in the form of anterior knee pain is a frequent complication after bone–patellar tendon–bone (BPTB) autograft anterior cruciate ligament (ACL) reconstruction.

Hypothesis/Purpose: The purpose was to examine the effect of the intraoperative administration of platelet-rich plasma (PRP) on postoperative kneeling pain. It was hypothesized that PRP treatment would reduce knee pain.

Study Design: Randomized controlled trial; Level of evidence, 2.

Methods: Fifty patients (mean ± SD age, 30 ± 12 years) undergoing BPTB ACL autograft reconstruction were randomized to the PRP (n = 27) or sham (n = 23) treatment. In either case, 10 mL of venous blood was drawn before the induction of anesthesia and either discarded (sham) or processed (PRP) for preparation of a PRP gel to be later mixed with donor site bone chips and inserted into the patellar defect. At 12 weeks, 6 months, 1 year, and 2 years after surgery, patients completed International Knee Documentation Committee (IKDC) forms and visual analog scale pain scores for activities of daily living and kneeling. Healing indices at the donor site were assessed by routine noncontrast magnetic resonance imaging (MRI) at 6 months. Mixed-model analysis of variance was used to assess the effect of PRP on patient symptoms and MRI indices of donor site healing, as measured by the width of the donor site defect.

Results: Kneeling pain, pain with activities of daily living, and IKDC scores were not different between treatment groups at any of the time intervals (P = .08-.83). Kneeling pain improved from 12 weeks to 6 months and from 1 to 2 years ($P < .05$). IKDC scores improved substantially from 12 weeks to 6 months ($P < .001$) and continued to improve to 2 years (PRP, 86 ± 19; sham, 89 ± 10). MRI indices of donor site healing were not different between treatment groups (P = .53-.90).

Conclusion: Whether randomized to receive PRP in their patellar defect or not, patients continued to have similar levels of kneeling pain and patellar defect sizes after autograft BPTB ACL reconstruction.

Registration: NCT01765712 (ClinicalTrials.gov identifier).

Keywords: knee; ACL; patella; biologic healing enhancement

Platelet-rich plasma (PRP) has been explored as a way to introduce increased concentrations of growth factors and other bioactive molecules to injury sites in an attempt to optimize the biologic milieu and enhance healing. It has been used extensively in dental and cosmetic surgery for almost 30 years, and its safety and efficacy in these areas are well established.[1,15] The past decade has seen a near exponential rise in the number of studies aimed at determining whether PRP could enhance tissue repair and regeneration in a variety of orthopaedic conditions.[4,35] At the turn of the century, excitement over the use of PRP in orthopaedics was fueled by promising early clinical outcomes in the treatment of various tendinopathies.[12,16,21,30] Today, PRP is just 1 of several types of orthobiologics. Since 2003, studies on the use of orthobiologics for tendon repair have nearly tripled.[13] Despite the emerging popularity and early promise of PRP, there remains a paucity

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of well-designed level 1 studies to support its widespread use.[2,4,22,35]

Autologous bone–patellar tendon–bone (ABPTB) is a popular graft choice in anterior cruciate ligament (ACL) reconstruction because it has excellent bony-healing potential and aperture fixation and comes without the risk of disease transmission that accompanies allograft use. A recent meta-analysis by Xie et al[40] comparing postoperative biomechanics after ABPTB versus 4-strand hamstring tendon autograft for ACL reconstruction found that ACL reconstruction with ABPTB may be more effective at restoring rotational stability to the knee. This in turn allows for a return to higher levels of activity. Not surprising, the authors also found a significantly higher incidence of donor site morbidity in the form of postoperative anterior knee pain and kneeling pain among patients undergoing ABPTB reconstruction. This study serves as an important reminder that despite decades of technological advance in the area of ACL reconstruction, the high incidence of anterior knee pain after ABPTB reconstruction remains a legitimate concern.[6,20]

Outcomes in early animal studies and preliminary clinical results of the use of PRP in ACL reconstruction showed promise in the areas of graft ligamentization, bone tunnel incorporation, and donor site morbidity.[28,29,31,33,34] A recent systematic review of the literature on the use of PRP in ACL reconstruction identified just 15 clinical trials, of which 5 involved the use of bone–patellar tendon–bone (BPTB). Within this group, only 2 used postoperative pain scores as the primary outcome[8,10]; however, there was additional focus on elements of graft healing and incorporation, as seen on magnetic resonance imaging (MRI).[3] Thus, at the outset of our study, we thought that there was a paucity of level 1 clinical studies that carefully and comprehensively investigated what role, if any, PRP in ACL reconstruction with ABPTB may have on the incidence of postoperative donor site morbidity. Given the need for a highly powered study to demonstrate the clinical efficacy of PRP in ACL reconstruction with ABPTB, we designed a prospective randomized double-blinded study to evaluate the specific primary outcome of donor site pain.

The aim of this study is to evaluate the efficacy of intraoperatively applied autologous PRP in reducing postoperative kneeling pain after ACL reconstruction with ABPTB.

METHODS

A single-center prospective randomized double-blinded study enrolled patients undergoing ACL reconstruction with ABPTB graft under the care of 2 sports medicine fellowship–trained surgeons. Before beginning the study, approval was sought and obtained from our institutional review board (Northwell Health; No. 12-160A), and the study was registered at the national registry of clinical trials: clinicaltrials.gov (NCT01765712).

Between 2011 and 2015, patients were recruited for participation in the study. Inclusion criteria included those who were undergoing primary ACL reconstruction without evidence of other ligamentous or chondral injury (determined by preoperative MRI and intraoperative diagnostic arthroscopy) and who were willing to participate in the study, including follow-up at regular intervals and completion of subjective questionnaires. Exclusion criteria included history of ipsilateral anterior knee pain, any previous knee injury, a failed prior ACL reconstruction, diabetes, smoker, workers' compensation, and an Outerbridge classification $\geq$3 based on diagnostic arthroscopy performed at the time of surgery.

Patients were randomized with a computer-generated simple randomization table (Excel 2010; Microsoft Corp) into 1 of 2 treatment arms: ABPTB ACL reconstruction with and without application of PRP.

The patient, surgeon, research personnel, and individuals collecting all objective outcome measures were blinded to the randomization. Randomization and patient assignments were done through sequentially numbered opaque sealed envelopes opened by the circulating nurse in the operating room at the time of surgery. Randomization information was then recorded and placed into a sealed envelope with the patient's randomization ID and deposited into a locked reception box. This box was opened only upon completion of the study.

Surgical Procedures

ACL reconstruction was performed with a transtibial technique. The surgical procedures were performed by 1 of 2 surgeons (S.J.N. or B.B.B.), and diagnostic arthroscopy was performed to verify that the inclusion criteria were met. After diagnostic arthroscopy, the central third of the patellar tendon was harvested with an 11 $\times$ 20–mm patellar bone block and an 11 $\times$ 25–mm tibial bone block. The bony portion of each graft end was debulked and tubularized to fit a 10-mm tunnel. The remaining bone chips were placed into a sterile cup for later use as bone graft within the patellar defect site. Two 7 $\times$ 20–mm titanium cannulated interference screws (Linvatec) were used for fixation. The femoral side was fixed first, and the ACL was next cycled under tension and fixed in near full extension with a posterior drawer based on graft isometry. After

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Figure 1. Magnetic resonance imaging showing a 10.3-mm patellar graft site defect 6 months after surgery.

fixation of the graft, the senior surgeon left the room to remain blinded to the treatment arm. The application of either PRP-soaked or untreated cancellous bone chips to the patellar donor site was performed by a physician assistant. The paratenon was closed over the donor site to seal the contents, and the defect in the patellar tendon was then reapproximated. The wound was closed in standard fashion.

PRP Preparation

The PRP was prepared directly in the operating room during the surgical intervention with a PRP separation kit and centrifuge system (ACP PRP; Arthrex). The blood sample was obtained at the same time that the anesthetist obtained a dedicated intravenous line, thus eliminating any lengthening of the operative time.

Regardless of randomization, 10 mL of venous blood was withdrawn for each patient. The blood of the control group was discarded, being drawn only to blind the physician investigator to treatment arm. For the treatment group, the blood was next mixed with 1 mL of ACD-A (citrate anticoagulant) and centrifuged for 5 minutes at 1500 rpm. The purpose of this step was to separate the blood into red blood cells and a supernatant "buffy coat" layer containing platelets (PRP) at a concentration approximately 2 to 3 times above baseline and with leukocyte depletion. The supernatant PRP layer (approximately 3-5 mL) was aspirated into the inner smaller-diameter syringe of the double-syringe system and set aside until ready for use. Just before the initiation of closing and after fixation of the graft, the PRP was activated by mixing it with 0.25 mL of $CaCl_2$. After activation, the PRP was mixed with the autologous cancellous bone chips and placed into the patellar donor site. For the sham group, the untreated bone chips were placed in the donor site as described for the other group. The physician investigator was not present during the PRP activation with the bone chips to remain blinded to the treatment allocation.

Data Collection

Preoperative data included intake forms (International Knee Documentation Committee [IKDC] and current health assessment), demographics, and a radiographic grading of osteoarthritis with the Kellgren-Lawrence classification scale performed by 1 senior musculoskeletal radiologist (D.A.K.).

Intraoperative data collection included Outerbridge classification of medial, lateral, and patellofemoral compartments, as well as blood loss, time of surgery, tourniquet time, and meniscal injury and its treatment.

Postoperative data collection included subjective and objective outcome measures. Subjective outcomes of donor site morbidity were collected at 12 weeks and 6, 12, and 24 months and included a visual analog scale (VAS) for pain during activities of daily living (ADLs) and kneeling and the IKDC subjective knee evaluation form. A normal IKDC score for 25- to 34-year-olds was reported to be 89 $\pm$ 16 (mean $\pm$ SD). For the purposes of this study, an abnormal IKDC score at final follow-up is defined as <73 (>1 SD below normal).

MRI Analysis

MRI was obtained before patients were cleared to return to full activities. Typically, this would occur between 6 and 9 months after surgery, depending on the patient's target activity level and progress in rehabilitation. With fluid-sensitive axial sequences obtained as part of routine knee MRI sequences, the largest transverse signal defect in normal bone marrow of the patella at the graft site was recorded (Figure 1). The anteroposterior (AP) dimensions of the tendon were also measured at 2 separate levels: the superior tibial cortex and the roof of the intercondylar notch. Since the PRP treatment could have also affected tendon healing, any effect on tendon healing would be expected to be more apparent at the level of the intercondylar notch than at the tibial insertion, given the proximity to the PRP application. All interpretations were performed by 1 senior musculoskeletal radiologist (D.A.K.).

Statistics

The primary outcome measure was kneeling pain. Secondary outcome measures were pain with ADLs, IKDC score, and MRI indices of graft site healing. Power analysis was based on previous studies of postoperative morbidity among patients undergoing ACL reconstruction with ABPTB graft harvest. It was estimated that with 25 patients per group, there would be 80% power to detect a 1.5-point difference in kneeling pain between treatments at $P < .05$, assuming a between-subject standard deviation of 2 for VAS scores. A between-group difference of 1.5 points in VAS scores was deemed to represent a clinically relevant difference.[9,37]

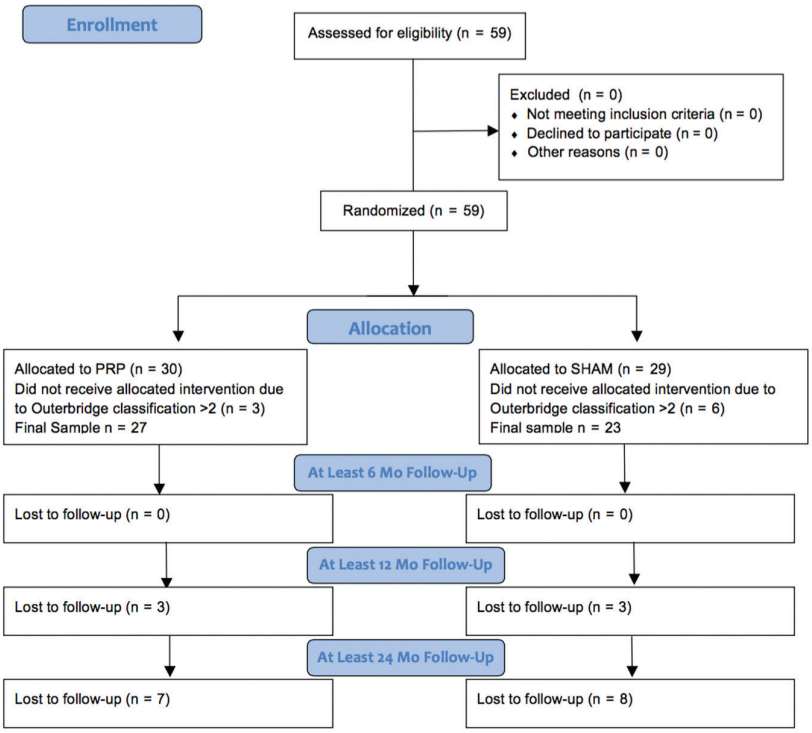

Figure 2. A CONSORT diagram of the study randomization procedure, including enrollment, allocation, follow-up, and analysis. PRP, platelet-rich plasma.

The effect of PRP on outcome measures (VAS and IKDC) was assessed with mixed-model analysis of variance, with treatment as a between-subjects factor and time as a within-subjects factor. Between-group differences at particular time intervals were assessed with the least significant difference method. As different numbers of patients were available at each follow-up interval, data were analyzed separately for periods of 12 weeks to 6 months, 6 months to 1 year, and 1 year to 2 years. This method of analysis maximized the sample size for analysis of changes over time. Independent samples t tests were used to compare MRI indices of graft site healing between treatment groups. Mean ± SD are reported.

RESULTS

Patient Enrollment

Fifty-nine patients undergoing ABPTB ACL reconstruction and eligible to enter the study were randomized to the treatment (PRP, n = 30) or nontreatment (sham, n = 29) arm of the study just before surgery (Figure 2). Subsequently, during surgery, 9 patients with Outerbridge classifications >2 were excluded from the study (3 PRP, 6 sham). Thus, the final sample included 50 patients (age, 30 ± 12 years) undergoing ACL reconstructions with a BPTB autograft (PRP: 10 men, 17 women; sham: 12 men, 11 women). Fifteen patients had concomitant meniscal tears (6 lateral, 7 medial, 2 medial and lateral). All meniscal tears were debrided. Eight patients had chondral lesions (3 medial femoral condyle, 2 lateral femoral condyle, 1 patella, 1 medial femoral condyle and patella, 1 all 3). Based on inclusion criteria, all lesions were <3 on the Outerbridge classification.

All 50 patients were followed at least 6 months postoperatively (Figure 2); 44 patients had at least 1-year follow-up (PRP, n = 24; sham, n = 20); and 35 patients (PRP, n = 20; sham, n = 15) had 2-year follow-up (24.6 ± 0.8 months; range, 24-27 months). There were zero ipsilateral ACL injuries and 2 contralateral ACL injuries during the follow-up period. The only subsequent surgical procedure on the ipsilateral knee was hardware removal 8 months after reconstruction in 1 patient.

Kneeling Pain

Kneeling pain was not different between treatment groups at any of the time intervals (Table 1). Kneeling pain improved from 12 weeks to 6 months ($P < .05$), with no significant change from 6 months to 1 year but further improvement from 1 year to 2 years ($P < .05$). Kneeling pain scores were still significantly greater than zero at 2 years (2.1 ± 2.3).

Pain With ADLs

Pain with ADLs was not different between the PRP and sham groups at any time point (Table 1). At all time points,

TABLE 1
VAS Scores for Pain During Kneeling and ADLs: Effects of PRP vs Sham and Postoperative Changes Over Time[a]

	VAS, Mean ± SD						
	12 wk (n = 50)	6 mo (n = 50)	Change, 12 wk vs 6 mo	1 y (n = 44)	Change, 6 mo vs 1 y	2 y (n = 35)	Change, 1 y vs 2 y
Kneeling							
PRP	5.1 ± 3.9	3.8 ± 3.3	1.3 ± 2.6[b]	3.1 ± 3.0	0.6 ± 2.7	2.4 ± 2.7	1.2 ± 2.3[b]
Sham	6.7 ± 2.1	5.1 ± 2.8	1.9 ± 2.6[b]	4.5 ± 3.0	0.3 ± 3.3	1.9 ± 1.6	2.4 ± 2.8[b]
PRP vs sham, *P* value	.11	.17	.44	.17	.76	.55	.20
ADLs							
PRP	2.3 ± 2.9	1.7 ± 2.2	0.5 ± 1.4	1.2 ± 1.8	0.6 ± 1.0	1.1 ± 2.1	–0.1 ± 1.6
Sham	2.6 ± 2.0	1.9 ± 2.3	0.7 ± 2.1	2.1 ± 2.1	0.2 ± 3.2	0.6 ± 0.7	1.4 ± 2.1[b]
PRP vs sham, *P* value	.83	.55	.82	.18	.18	.44	.15

[a]Data are reported as mean VAS scores ± SD, unless otherwise indicated. ADLs, activities of daily living; PRP, platelet-rich plasma; VAS, visual analog scale.
[b]$P < .05$ for change over time.

kneeling pain scores were significantly greater than those for ADLs ($P < .01$). This highlights that kneeling pain is a significant problem after BPTB autograft ACL reconstruction; pain with ADLs was negligible for most patients by 6 months after surgery (mean, <1.7), while pain with kneeling was a problem (mean, 4.4).

IKDC Outcome Scores

IKDC scores were not different between the PRP and sham groups at any postoperative interval (Table 2). IKDC scores improved substantially from 12 weeks to 6 months ($P < .001$) and continued to improve from 6 months to 1 year in the PRP group and from 1 year to 2 years in the sham group. These improvements were not different between groups. Final IKDC scores indicated good outcomes for both groups (86 ± 19 for PRP, 89 ± 10 for sham). Of the 35 patients with 2-year follow-up, only 3 had abnormal IKDC scores (2 PRP, 1 sham). An additional 9 patients with no 2-year follow-up had follow-up at 1 year. Three of these patients had abnormal IKDC scores (all in sham group). Of the 6 abnormal IKDC scores at 1- to 2-year follow-up, 1 patient had arthrofibrosis with debridement between 1- and 2-year follow-up; 1 had a partial meniscectomy in the study knee between 6 months and 1 year; and 2 patients had removal of hardware. None of the other patients had additional procedures.

MRI Indices of Healing

MRI was performed on 49 of 50 patients at a mean 7.5 ± 2.7 months postoperatively (PRP, 7.5 ± 2.3 mo; sham, 7.5 ± 3.2 mo; $P = .95$). The transverse width of the osseous defect at the largest patellar graft site was not different between groups (PRP, 11.6 ± 2.4 mm; sham, 12.0 ± 3.1 mm; $P = .53$). Similarly, the AP tendon dimensions at the levels of the superior tibial cortex (PRP, 8.9 ± 1.9 mm; sham, 9.1 ± 2.5 mm; $P = .74$) and the roof of the intercondylar notch (PRP, 6.9 ± 1.8 mm; sham, 6.9 ± 2.2 mm; $P = .90$) were not different between treatment groups. Time from surgery to MRI was unrelated to the width of the patellar defect ($r = -0.05$, $P = .74$) and the AP tendon dimension at the level of the roof of the intercondylar notch ($r = 0.21$, $P = .15$). Time from surgery to MRI was related to the AP tendon dimension at the level of the tibial cortex ($r = -0.34$, $P = .019$).

Factors Associated With Kneeling Pain

IKDC scores for patients with at least 1 year of follow-up were strongly correlated with kneeling pain ($r = -0.72$, $P < .001$). MRI indices of graft site healing were unrelated to kneeling pain ($P = .67$-$.37$). Kneeling pain at final follow-up was not different between male and female patients ($P = .86$) and not related to patient age ($P = .77$).

DISCUSSION

Initial excitement over the application of PRP to enhance patellar tendon healing had been sparked by the findings of Lyras et al,[24] who demonstrated increased force to failure, ultimate stress and stiffness, and collagen synthesis in the healing patellar tendons of rabbits that had received PRP versus controls. Additional animal studies provided more encouragement by proving that PRP led to the safe biomechanical enhancement, revascularization, reinnervation, and gene expression in animal models of PRP-augmented ACL reconstruction.[23,25,41,42] Vavken et al[38] published a systematic review of the clinical literature on the use of PRP in human ACL reconstruction with BPTB. The authors concentrated on 8 clinical studies performed between 2005 and 2010 that met their search criteria. All these studies focused primarily on the elements of graft bone healing and ligamentization through postoperative MRI analysis. Two of the 8 studies were performed in the setting of BPTB, and only 1 included allograft BPTB exclusively.[28,31] In that study, differences in VAS pain scores were statistically insignificant between treatment

TABLE 2
IKDC Scores for PRP vs Sham and Postoperative Changes Over Time[a]

	12 wk (n = 50)	6 mo (n = 50)	Change, 12 wk vs 6 mo	1 y (n = 44)	Change, 6 mo vs 1 y	2 y (n = 35)	Change, 1 y vs 2 y
PRP	65 ± 17	75 ± 20	9 ± 12[b]	86 ± 15	11 ± 9[b]	86 ± 19	3 ± 14
Sham	66 ± 13	73 ± 11	8 ± 12[b]	77 ± 15	2 ± 16	89 ± 10	8 ± 13[b]
PRP vs sham: *P* value	.74	.68	.72	.08	.06	.59	.34

[a]Data are reported as mean IKDC scores ± SD, unless otherwise indicated. IKDC, International Knee Documentation Committee; PRP, platelet-rich plasma.
[b]$P < .05$ for change over time.

arms.[28] Despite a hypothesis for the acceleration of graft maturation, the application of PRP in the setting of ACL reconstruction in this systematic review did not show any significant differences in clinical outcomes. The authors cautioned against drawing conclusions, however, since only 2 of the 8 studies could be classified as level 1 and all had follow-up <2 years.[38] Taking into account the basic principles of PRP and extrapolating its positive effects on postoperative pain in other musculoskeletal conditions,[1,19] we believed that it made sense to explore the effect, if any, on postoperative pain in the setting of ACL reconstructive surgery in a level 1 study with longer-term follow-up.

Over the past 5 years, clinical research has appropriately shifted more of its focus toward the clinical outcomes of PRP application in the setting of ACL reconstruction with BPTB autograft, specifically anterior knee pain. In 2012, a prospective randomized controlled nonblinded level 1 study concluded that postoperative pain was significantly reduced after ABPTB ACL reconstruction with PRP augmentation.[8] That study enrolled 40 patients (20 per treatment arm) and examined Victorian Institute of Sport Assessment (VISA) and VAS postoperative pain scores as well as evidence of graft healing on MRI at 12 months. While the VISA scores were significantly higher in the PRP treatment arm, the VAS scores were not significantly different. One reason for this discrepancy may be that the study was underpowered to detect a significant difference in the VAS scoring system. Perhaps another reason why this particular study did not show a significant difference is that a single data point was collected at 12 months, which could have been too late to detect the clinical effect of PRP, as its benefit is most pronounced in the early postoperative time frame. A comparable study later the same year by de Almeida et al[10] examined similar MRI assessments of postoperative tendon healing at 6 months and immediate postoperative pain scores with the VAS. In this study, the authors found that PRP had a significant effect on patellar tendon gap healing on MRI at 6 months, and while it seemed to reduce pain in the immediate postoperative period (first 24 hours), there was no observed effect at 6 months. The significance of this study is that it suggests that there may be some statistically significant improvement in early postoperative pain when PRP is used; however, there were several limitations. The authors randomized just 27 patients, and neither the patient nor the surgeon was blinded to treatment arm. In addition, the use of the VAS pain scale with such a small sample size significantly increases the chance of type I error.

More recently, there have been several well-designed clinical studies prospectively examining the effects of PRP on BPTB autograft ACL reconstruction outcomes. Interestingly, the majority of these studies have focused on parameters of graft healing, including ligamentization and incorporation, and less so on the common postoperative complaint of anterior knee pain. One review separated studies pertaining to the application of PRP as a biologic enhancer during ACL reconstructive surgery into those that analyzed preclinical performance (histological and biomechanical) and those that analyzed clinical performance.[3] In a synopsis of clinical studies, 5 included BPTB graft. Only 4 of those involved the use of autograft, and just 3 focused on BPTB alone. Of those 3 studies, only 2 examined postoperative pain as a secondary measure, and each of those was a small nonblinded randomized trial that was powered to detect a primary outcome measure of tendon healing rather than anterior knee pain with a VAS scoring system.[8,10] We believe that the current study is the first well-designed, appropriately powered randomized controlled trial to critically assess whether PRP plays a role in the postoperative clinical outcome of donor site pain in ACL reconstruction with ABPTB.

Kneeling Pain

The differences in kneeling pain between the PRP and sham treatment at 12 weeks and 6 months postoperatively were not statistically significant. It was estimated a priori that the current sample size would have been sufficient to find a >1.5-point difference statistically significant with 80% power. However, the pain scores showed greater between-subject variability than expected, particularly in the PRP group, where the between-subject SD exceeded 3.0 at 12 weeks and 6 months (a value closer to 2.0 was expected). Given the actual sample sizes at each postoperative time point, there was 80% power to detect a 2.4-point difference in kneeling pain between the PRP and sham treatment groups at 12 weeks and 6 months and a 2.6-point difference at 1 year and 2 years after surgery at $P < .05$. Two years after surgery, kneeling pain was 2.4 ± 2.7 in the PRP group and 1.9 ± 1.6 in the sham group. While there was insufficient power to detect a difference between groups at this time, it is notable that (1) there is

no longer a trend for lower pain values in the PRP group and (2) kneeling pain is still a clinical problem regardless of treatment. Two years after ACL reconstruction, 9 of 20 patients in the PRP group had kneeling pain scores $\geq$3, as opposed to 2 of 15 in the sham group. Thus, regardless of any potential early benefit of PRP, a significant proportion of patients continue to have residual kneeling pain. PRP does not seem to be an effective treatment to address this problem in our study.

The lack of long-term benefit of PRP in reducing kneeling pain is in agreement with similarly designed clinical trials performed over the past decade.[17] This finding is in contradiction to the findings of Cervellin et al,[8] who found significant and sustained improvement in their pain assessment at 12 months with VISA assessment. In that same study, however, the authors failed to find any significant clinical difference in postoperative pain with the more widely accepted VAS pain scoring system. In a similar study, de Almeida et al[10] found a significant reduction in immediate (24-hour) postoperative pain among patients treated with PRP but no difference at 6 months. It is possible that PRP exerts its most profound effects on postoperative healing and pain control in the immediate to short-term postoperative period. Studies measuring outcomes further out from surgery may lose their ability to detect any significant clinical differences, if there is in fact a difference or if the effect of PRP has diminished. The present study demonstrates that PRP does not provide any long-term relief against kneeling pain after patellar tendon autograft ACL reconstruction and that kneeling pain remains a problem for a significant proportion of patients even 2 years after surgery. Of note, the PRP treatment was directed at the patellar defect because in our clinical experience that has been the source of postoperative kneeling pain. If some kneeling pain were due to pain at the tibial tubercle, the PRP treatment could not have been effective, since that site was not treated. This is an inherent limitation of this study.

Previous authors remarked on the limitations of the current evidence for or against the use of PRP based on clinical outcomes. The majority of the published clinical studies were not designed to detect postoperative pain as the primary outcome, nor were their follow-up time points long enough to detect true clinical differences, such as graft failure and incidence of revision. By examining the primary postoperative outcome of donor site morbidity in the form of anterior knee pain in the setting of ACL reconstruction with ABPTB and PRP, the current study uniquely contributes to the current literature. Not only do the results demonstrate no effect of PRP on the clinical outcome measures associated with donor site morbidity, but they also highlight the fact that anterior knee pain after ACL reconstruction with BPTB autograft continues to be a significant clinical problem and that patient expectations should be set accordingly.

Tendon Healing

Similar to Cervellin et al[8] and de Almeida et al,[10] we chose to look at postoperative tendon healing based on gap defect analysis with MRI. Cervellin et al[8] observed 25% better bone healing at the donor sites at 12 months (although this was not significant), and de Almeida et al[10] found significantly greater tendon gap healing at 6 months with PRP. We found no differences between the treatment groups (P = .76) in terms of AP tendon gap and patellar donor site defect gap, bringing into question the effect of PRP on donor site healing.

IKDC Scores

Overall, the outcomes in terms of IKDC scores were good (86 $\pm$ 19 in PRP group, 89 $\pm$ 10 in sham group). It is notable that IKDC scores improved from 6 months to 1 year in the PRP group with no further change from 1 to 2 years, while in the sham group, they did not improve from 6 months to 1 year but did improve from 1 to 2 years. IKDC scores were comparable between groups at 6 months (PRP, 75 $\pm$ 20; sham, 73 $\pm$ 11), suggesting that subsequent differences between groups may have been unrelated to the PRP treatment intervention.

Limitations

One of the more significant limitations in our study is the manner in which our platelet concentrates were prepared and the dilution of bioactive molecules. Owing to the relatively easy manner in which manufacturers can bring their own version of PRP systems to market through the 510(K) pathway—which allows them to bypass the Food and Drug Administration's stricter regulatory pathway—there are now many systems from which to choose, with widespread variation in their PRP formulations.[5,18] As a result, there are many commercially available systems for autologous platelet preparation, and the concentration of growth factors, white blood cells, and other bioactive molecules may be vastly different.[7,32] Unfortunately, this lack of standardization has led to a discrepancy in platelet preparation; therefore, studies citing the generic name PRP can be using largely different formulations, limiting its widespread clinical applicability.[32] Using the Platelet, Activation, White Blood Cell classification system for PRP products,[11] we selected a plasma-based system that uses a double-spin process to produce a leukocyte-depleted final product with inactivated platelet concentrations 2 to 3 times greater than baseline but <750,000 platelets/μL (Arthrex ACP). This enabled us to draw a minimal blood sample while mitigating the potentially deleterious effects of leukocytes and neutrophils at the tendon repair site.[14,26,36] In keeping with what is known about the concentration-dependent effects of growth factors and the diminishing gains beyond PRP concentrations 3 times that of baseline in ligamentous healing, we selected what we thought was the most appropriate system.[25,27] Of note, the PRP system used in this study was shown to be ineffective in improving rotator cuff tendon-bone healing.[39]

Another potential weakness of this study is the manner in which the PRP concentrates were applied. We chose to mix the bone graft with the concentrate just before placing

the solution within the patellar defect site. However, we believe that the systematic manner in which this was done actually reduced internal error and increased the reproducibility of our results. In a study designed to examine similar outcomes, Cervellin et al[8] selected a very different PRP preparation system, without leukocyte depletion but with thrombin added. Application was within the patellar defect; however, it did not include autogenous bone chips. In that study, a significant reduction in postoperative pain was observed; therefore, variance in preparation and application may have contributed to our contrary findings.

Since PRP has demonstrated pain reduction early in the postoperative course, another data point that we could have collected was 24 to 48 hours postoperatively. As evidenced in the previously mentioned studies, it is possible PRP's greatest potency in reducing anterior knee pain may be in the very early postoperative period. Well-designed long-term prospective level 1 clinical trials with larger sample sizes are clearly needed with homogeneous PRP preparations and applications to delineate the best utilization of this particular orthobiologic. Last, based on the relatively small number of participants in this study, there is the potential for type 2 error occurring.

CONCLUSION

The intraoperative administration of PRP in the patellar defect after ACL reconstruction with BPTB autograft has no significant effect on postoperative knee pain when kneeling, postoperative pain with ADLs, IKDC scores, or donor site healing.

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