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Platelet Rich Plasma Use in Allograft ACL Reconstructions: Two-Year Clinical Results of a MOON Cohort Study

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Introduction

The anterior cruciate ligament (ACL) is commonly injured and frequently reconstructed. Modern intra-articular reconstructive techniques produce clinically stable ligament reconstruction in the majority of cases; however, graft tears after reconstruction continue to be a problem. The use of allograft tissue in ACL reconstruction have been associated with increased graft failure rates.¹ Animal studies have demonstrated slower incorporation of allograft tissue² and demonstrated decreased failure loads for allografts up to one year following reconstruction.³

Platelet rich plasma (PRP) is a preparation of autologous platelets and plasma that are concentrated to a level greater than their naturally occurring levels in blood.⁴ PRP is typically prepared by centrifuging anti-coagulated autologous blood. When platelets are activated, they release numerous growth factors that have been shown to enhance tissue healing. These factors include platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-Beta), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and insulin-like growth factor 1 (IGF-1). These preparations have been shown in cell cultures to enhance fibrocyte growth and collagen production.⁵⁻⁷ Animal studies have demonstrated positive effects of PRP on collagen healing.⁸⁻¹² An MRI study of ACL grafts treated with PRP showed a shorter time to the development of a homogenous signal within the graft.¹³ Intra-operative PRP application has been shown to decreased post-operative pain and improved short-term clinical results in a variety of orthopaedic procedures.¹⁴⁻¹⁷

The purpose of this study was to evaluate the effect of intra-operative PRP application on the outcome of allograft ACL reconstruction surgery. We hypothesized that intra-operative application of PRP to the ACL allograft results in 1) Decreased effusions at 10 days and 8 weeks post-operative, 2) Decreased re-operations rates in the first two years following reconstruction, and 3) Improved patient-reported outcomes (KOOS and IKDC scores) at two years post-operative.

Methods

Patients

The study was approved by the IRB at our institution. The senior author began augmenting all allograft ACL reconstructions with PRP in 2007. Prior to this time, allograft ACL reconstructions were performed without PRP augmentation. Between January 1, 2007, and August 31, 2009, 50 patients underwent allograft ACL reconstruction augmented with PRP. These patients form the study group.

A control group of 50 patients matched by age, gender, and whether revision or primary ACL reconstruction was performed was selected from the senior author's ACL reconstruction database. These patients underwent allograft ACL reconstructions between January 1, 2003, and December 31, 2006, without PRP augmentation. No information regarding outcomes was available at the time the controls were selected to avoid selection bias. No other changes were made to the senior author's ACL reconstruction technique between January 1, 2003, and August 31, 2009. Allograft tissue was obtained from a variety of sources during this time period including the Musculoskeletal Transplant Foundation (Edison, NJ) and Community Tissue Services (Dayton, OH).

Surgical Technique and Rehabilitation

The surgical technique was identical for the two surgical groups. A single surgeon performed all of the procedures and each patient underwent identical postoperative protocols. The allografts (all tibialis tendons) were fixed in the femoral tunnel with an absorbable cross pin and in the tibial tunnel with an absorbable interference screw. In the PRP group following fixation of the graft, the knee was drained of arthroscopic irrigation solution and the intra-articular portion of the graft was coated with PRP prepared by following the manufacturer instructions (GPS II Platelet Concentrate Separation Kit, Biomet, Inc., Warsaw, IN, USA). The application of the PRP was done in the knee as the final step prior to wound closure.

A standard accelerated rehabilitation protocol focusing on early knee range of motion and restoration of quadriceps function was utilized. Weight-bearing as tolerated was allowed immediately and crutches were weaned as gait improved. No post-operative bracing was used.

Follow-up

A chart review was performed for each subject. Data extracted from clinic visits at 10 ± 4 days and 8 ± 4 weeks post-operative included the presence and size of any effusion. Effusions were characterized as none, trace, 1+, 2+, or 3+. Any subsequent surgical procedures, including revision ACL reconstruction, were recorded.

As part of an ongoing prospective cohort study, a subset of the patients were contacted at two years post-operative and asked to complete a questionnaire. Data from this questionnaire allowed calculation of the Knee Injury and Osteoarthritis Outcome Score

(KOOS),¹⁸ Marx activity score,¹⁹ and International Knee Documentation Committee (IKDC) score²⁰ for each patient.

Statistical Analysis

Stata 10.1 (College Station, TX, USA) was used for all data analysis. Continuous variables were compared between the two groups using paired t-tests. Categorical variables were compared using Fisher's exact test. A power analysis indicated a sample size of 29 patients in each group was sufficient to detect a clinically significant difference in the KOOS quality of life subscale (10 points) and IKDC score (11.5 points) with 80% power at an alpha of 0.05.

Results

The 50 patients treated with PRP and 50 matched controls did not differ significantly pre-operatively in terms of sex, age, or mechanism of injury (Table 1). Thirty-five patients in each group underwent primary ACL reconstruction, while fifteen underwent revision ACL reconstruction. The 29 pairs of patients (58%) with pre-operative patient-reported outcome scores (KOOS scores, IKDC score, and Marx activity score) exhibited no differences between the two groups (Table 1).

The same twenty-nine matched pairs (58%) of patients completed the questionnaire two years following ACL reconstruction. Overall, significant improvements in all patient-reported outcome scores were noted; although Marx activity scores were significantly lower post-operatively compared to pre-injury levels (Figure 1). No significant differences in post-operative KOOS subscales, IKDC score, Marx activity score, or number of additional operative procedures were noted between the PRP and control groups (Table 2).

The presence of and size of any effusion was documented in all fifty pairs of patients at 10 ± 4 days after surgery and in 45 pairs of patients at 8 ± 4 weeks after surgery. The two groups differed at 10 ± 4 days ($p = 0.014$) but no difference was noted at 8 ± 4 weeks ($p = 0.31$) (Figure 2). There were no major complications (such as pulmonary embolism) in either group.

Discussion

The most significant finding of this study is that the application of PRP to tibialis allografts during ACL reconstruction does not significantly improve patient-reported outcomes or activity level at two years post-operative. We noted no increase in complications with PRP application, suggesting that this application of PRP is safe. We did note decreased effusions in the early (10 ± 4 days) post-operative period, but this advantage was noted to disappear by 8 ± 4 weeks post-operative. The difference between the two groups appeared to be primarily driven by a smaller number of patients with trace effusions and a larger number of patients with no effusion in the PRP group. The clinical significance of such a difference in unknown.

We are aware of no other studies in the literature assessing the effect of intra-operative PRP on patient-reported outcomes following ACL reconstruction, but our results are consistent with the findings of Nin et al, who demonstrated no differences in pain, overall IKDC score, or knee stability as assessed with KT-1000 measurements two years following ACL reconstruction with patellar tendon allograft.²¹ In an imaging study, Silva et al noted no difference in MRI signal 3 months post-operatively with PRP augmentation of autologous hamstring ACL reconstruction.²²

In contrast, Ventura et al noted difference in MRI signal density in ACL grafts augmented with growth factors intra-operatively 6 months following hamstring autograft reconstruction compared with a control.²³ These results suggested more rapid incorporation in this group. Vogrin et al recently reported a positive effect of PRP application to ACL hamstring autografts on anterior laxity measures at three and six months following reconstruction.²⁴

This study has several limitations. Primarily, two-year patient reported outcomes data were not collected in all patients. Sufficient patients were present for adequate power, but selection bias is possible based on subject loss. In addition, this study did not evaluate the biologic healing enhancement effect of the PRP application but focused on the clinical outcome. If PRP had a positive influence on the biologic incorporation of the allograft, it was not reflected in patient-reported outcome data. Further, the data in this study are based entirely on ACL reconstruction with tibialis allograft. While there is no evidence that other grafts would behave differently with PRP augmentation, one must consider this limitation when applying our results to patients treated with other types of allografts. Finally, the reliance on chart review to retrospectively collect effusion data is not ideal because these data were not collected by a blinded observer solely focused on assessing effusions. They were collected during the course of normal clinical care, which may contribute to some bias.

Though the study was not randomized, the use of a single surgeon using allograft from the same source with a standardized surgical technique and post-operative protocol reduces confounders as a source of bias. The control group was effectively matched for age, gender, and primary versus revision surgery.

Conclusions

The study demonstrated that although PRP application in tibialis allograft ACL reconstructions appeared safe, no differences in patient-reported outcomes or number of additional surgeries at two years were noted.

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Figure 1.

Improvements in International Knee Documentation Committee (IKDC) and Knee Injury Outcome and Osteoarthritis Score (KOOS) subscales (Symptoms, Pain, Activities of Daily Living, Sport/Recreation Function, and Knee Related Quality of Life) following ACL reconstruction.

Figure 2.

The incidence of effusions 10 ± 4 days and 8 ± 4 weeks following ACL reconstruction in the platelet-rich plasma (PRP) and control groups. Significant differences between the two groups are noted at 10 ± 4 days ($p = 0.014$) but no difference was noted at 8 ± 4 weeks ($p = 0.31$).

Table 1
Pre-operative Comparison of the PRP and Control Groups

	PRP group (n = 50)	Control group (n = 50)	Significance
Sex	28 male 22 female	28 male 22 female	p = 1.0
Age at surgery (years)	35.1 ± 11.5	35.3 ± 11.5	p = 0.93
Mechanism of Injury			p = 0.14
<i>Non-contact</i>	16 (32%)	22 (44%)	
<i>Contact</i>	10 (20%)	14 (28%)	
<i>No specific injury reported</i>	24 (48%)	14 (28%)	
KOOS Subscales*			
Symptoms	63.7 ± 16.5	60.0 ± 21.2	p = 0.47
Pain	72.4 ± 14.5	68.1 ± 21.1	p = 0.40
Activities of Daily Living	82.6 ± 12.9	77.1 ± 21.6	p = 0.27
Sport/Recreation Function	46.8 ± 30.7	45.3 ± 25.3	p = 0.74
Knee-Related Quality of Life	37.7 ± 19.7	35.1 ± 17.7	p = 0.53
IKDC Score*	50.2 ± 13.3	44.9 ± 17.2	p = 0.21
Marx Activity Score*	9.5 ± 6.1	9.2 ± 6.1	p = 0.83

KOOS = Knee Injury and Osteoarthritis Outcome Score

IKDC = International Knee Documentation Committee

* Pre-operative KOOS, IKDC, and Marx scores are only available in 29 pairs of patients

Table 2
Patient-reported Outcomes at Two Years Post-operative

	PRP group (n = 29)	Control group (n = 29)	Significance
KOOS Subscales			
<i>Symptoms</i>	79.2 ± 11.9	70.8 ± 23.8	p = 0.10
<i>Pain</i>	82.7 ± 15.1	80.2 ± 26.3	p = 0.55
<i>Activities of Daily Living</i>	88.1 ± 14.6	86.3 ± 23.4	p = 0.63
<i>Sport/Recreation Function</i>	70.9 ± 21.5	64.3 ± 32.1	p = 0.31
<i>Knee-Related Quality of Life</i>	58.4 ± 21.8	56.7 ± 30.0	p = 0.79
IKDC Score	70.7 ± 13.3	68.8 ± 17.2	p = 0.72
Marx Activity Score	3.9 ± 4.2	5.7 ± 4.7	p = 0.10
Additional surgery on the index knee	6 (21%)	7 (24%)	p = 1.0
<i>Revision ACL reconstruction</i>	1 (3.4%)	0 (0%)	p = 1.0

KOOS = Knee Injury and Osteoarthritis Outcome Score

IKDC = International Knee Documentation Committee