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# Platelet-rich Plasma Does Not Reduce Blood Loss or Pain or Improve Range of Motion After TKA

**Timothy M. DiIorio MD, Justin D. Burkholder BS, Robert P. Good MD, Javad Parvizi MD, Peter F. Sharkey MD**

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**Abstract**

*Background* Numerous reports suggest the application of platelet-rich plasma (PRP) during TKA may decrease postoperative bleeding. Because excessive bleeding can increase postoperative pain and inflammation, use of PRP also reportedly decreases the need for narcotics and increases speed of recovery after TKA. Because previous investigations of PRP and TKA reflect a weak level of medical evidence, we sought to confirm these findings.

*Questions/purposes* We asked whether an intraoperative application of PRP gel to the deep wound reduced postoperative bleeding after TKA.

*Methods* We retrospectively reviewed the charts of all 134 patients who received an intraoperative application of PRP during TKA from November 2009 to April 2010 and all 139 patients undergoing TKA who did not receive PRP between September 2009 to November 2009. Patients' charts were reviewed to identify detailed data, including hemoglobin level, ROM, postoperative narcotic use, and length of hospital stay. Blood loss was determined by the hemoglobin drop on postoperative Day 2.

*Results* The blood loss between study groups was similar (3.6 g/dL [study] versus 3.8 g/dL [controls]). Differences in passive ROM (88° versus 88°), narcotic requirement (27 versus 32 morphine equivalent), and length of stay (2.4 versus 2.6 days) were also similar.

*Conclusion* We found no clinically important differences in patients who received an intraoperative application of PRP compared with patients who did not receive PRP and therefore could not confirm the findings of previous studies.

*Level of Evidence* Level III, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

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Each author certifies that his or her institution approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.
This work was performed at Riddle Memorial Hospital, Media, PA, USA.

T. M. DiIorio
Department of Orthopaedic Research, Rothman Institute at Thomas Jefferson University, Philadelphia, PA, USA

J. D. Burkholder
Drexel University, Philadelphia, PA, USA

R. P. Good
Department of Orthopaedic Surgery, Bryn Mawr Hospital, Bryn Mawr, PA, USA

J. Parvizi, P. F. Sharkey (✉)
Department of Orthopaedic Surgery, Rothman Institute at Thomas Jefferson University, and Thomas Jefferson University Hospital, 925 Chestnut Street, 5th Floor, Philadelphia, PA 19107, USA
e-mail: kerrianne.valichka@rothmaninstitute.com

## Introduction

TKA is often associated with considerable postoperative blood loss [3, 11–13]. Substantial bleeding can lead to hematoma formation, arthrofibrosis [1, 6, 8, 16] and increased allogenic blood transfusions [3, 4, 7], which carry additional health risks and costs [5, 9, 14]. Postoperative bleeding has also been linked to increased inflammation and pain, which is most often treated with

various narcotics, each with substantial side effects, including nausea, vomiting, sedation, and respiratory depression [8].

Numerous strategies have been developed to minimize postoperative blood loss, including minimally invasive surgery, tourniquet use, and appliance of a fibrin gel [7, 11, 15]. Platelet-rich plasma (PRP) is obtained from centrifuged autologous blood drawn pre- or perioperatively. PRP is then combined with thrombin and calcium chloride to form PRP gel. Recent studies have suggested the application of PRP gel to the incision during TKA may substantially decrease postoperative bleeding [7, 8]. However, previous studies are limited by factors such as a small number of subjects, absence of a control group, subjective data reporting, and lack of randomization (Table 1).

We determined if an intraoperative application of PRP after TKA would lead to (1) reduced postoperative bleeding; (2) reduced rate of transfusion; (3) increased postoperative PROM; (4) reduced postoperative analgesic use; (5) decreased length of hospital stay; and (6) decreased rate of subsequent manipulation under anesthesia.

## Patients and Methods

We retrospectively reviewed the charts of all 279 patients who underwent elective TKA (unilateral or bilateral) between September 7, 2009, and April 6, 2010. No unicompartmental knees or revision arthroplasties were included in the study. Beginning November 2009, the standard protocol for TKA was modified to include application of PRP gel to the wound before closure for all patients without contraindications; there were 137 patients so treated. Control subjects were selected from among 139 patients operated on from September 2009 to November 2009. We included all patients with documented administration of intraoperative PRP gel in the study. The protocol was reviewed and approved by the Main Line Hospitals Institutional Review Board, Bryn Mawr, PA.

A power analysis for hemoglobin (Hgb) drop with an alpha value of 0.05 and a beta value of 80% was performed. The difference in means among the groups was set at 0.53 based on Hgb change demonstrated in previous studies. SD was 1.33. The analysis suggested we needed 100 patients in each group in a 1:1 ratio, and accordingly more than 100 patients were considered in both the unilateral control and study groups.

Of the 279 patients, 163 were female and 116 were male. Patients' ages ranged from 43 to 94 years. The control group of 139 patients who did not receive PRP gel was selected to best demographically match the study group based on gender, body mass index, and type of surgery (unilateral, n = 100 or bilateral, n = 39) performed. The 100 patients undergoing unilateral TKA who received PRP were an average of 67.1 years old, whereas the control group was an average of 65.4 years old. The gender of the subjects in the unilateral PRP group was 61% female and 39% male (61 females and 39 males) and in the control group 63% were female and 37% male (63 females and 37 males) (Table 2). The two groups who had unilateral TKA were demographically similar with no differences between them (Table 2). Patients undergoing bilateral TKA who received PRP were an average of 65.0 years old, whereas the control group was an average of 63.5 years old. In the bilateral PRP group, the gender of the subjects was 48% female and 52% male (19 females and 21 males) and in the control group 49% were female and 51% were male (20 females and 19 males) (Table 3).

**Table 1.** Recent publications using platelet-rich plasma

| Authors | Type of study | Number of subjects | Amount of autologous blood | Hemoglobin decrease | Need for transfusion | Length of stay | Pain | ROM |
|---|---|---|---|---|---|---|---|---|
| Gardner et al. [8] | Retrospective | 98 | 450 mL | +* | NA | + | + | + |
| Berghoff et al. [2] | Retrospective | 137 | 55 mL | + | + | + | NS | + |
| Everts et al. [7] | Prospective | 165 | 250 mL | + | + | + | + | NA |
| Horstmann et al. [10] | Randomized, prospective | 40 | 128 mL | NS | NS | NS | + | NS |

*+ = significant ($p < 0.05$); NA = not available; NS = nonsignificant.

**Table 2.** Demographics of unilateral control and study groups

| Demographic | Control group (n = 100) | Study group (n = 100)* | p | 95% Confidence interval |
|---|---|---|---|---|
| Average age (years) | 65.4 (43–94) | 67.1 (46–87) | 0.3007 | −4.76 to 1.48 |
| Male:female | 37:63 | 39:61 | 0.8842 | – |
| Average body mass index (kg/m$^2$) | 31.3 (22–47) | 31.9 (18–49) | 0.4409 | −2.43 to 1.06 |
| Anesthesia spinal:GETA† | 99:1 | 98:2 | 1.0 | – |

* Ranges shown in parentheses; †GETA = general endotracheal anesthesia.

We searched the MEDLINE (PubMed, from 1966) database using the MESH-controlled vocabulary, which includes the Cochrane Controlled Trials Register. The terms "platelet rich plasma," "autologous platelet gel," "arthroplasty," and "replacement" were used. A comprehensive literature review was performed to evaluate blood loss after TKA and to ascertain the current usefulness of PRP gel in achieving postoperative hemostasis.

The surgical technique and choice of implants were similar for study and control subjects. In all cases, the surgical technique included: medial parapatellar approach, extramedullary guides for tibial preparation, intramedullary guides for femoral preparation (intramedullary hole plugged with bone before closure), posterior-stabilized components (one design used), and use of cement to fixate all three components. No drains were used and no patient donated autologous blood.

Sixty milliliters of blood was drawn from each study patient into the 60-mL syringe supplied in the disposable PRP kit (AMS300; Arteriocyte Medical Systems, Cleveland, OH) immediately before the procedure. The syringe was then loaded into the Magellan Autologous Platelet Separator system (AMS100; Arteriocyte Medical Systems). The Magellan system was used to produce a highly concentrated 6-mL aliquot of PRP. PRP was then deposited into the supplied 10-mL syringe and maintained within the sterile environment until injected. The thrombin solution was prepared by adding 1000 units of thrombin (JPI Jones) per each milliliter of 10% CaCl2 solution provided in the disposable PRP kit. After final components were in place and after wound irrigation, the PRP in combination with the activator was uniformly applied to all accessible surfaces of the deep wound. Closure of the wound immediately followed PRP application.

Preoperative and postoperative (Day 2) levels of Hgb were documented, and the difference between the two was noted as the Hgb drop. Units of blood transfused were documented. Passive ROM of the affected knee on the day of discharge was also noted as well as the total number of days each patient remained in the hospital (length of stay [LOS]) and the amount of total postoperative narcotic use per patient. All narcotics were converted into grams of intravenous morphine equivalents for comparison purposes. Demographic data, including body mass index, gender, and race, were recorded.

## Results

The 100 patients undergoing unilateral TKA who received PRP did not have substantially less postoperative blood loss than the 100 patients undergoing unilateral TKA who did not receive PRP as demonstrated by Hgb drop (3.6 mg/dL for control subjects versus 3.8 mg/dL for PRP recipients) and transfusion rate (Table 5).

The intraoperative use of PRP gel had no effect on patients' postoperative passive ROM. Average passive ROM of control subjects at the time of discharge was identical to passive ROM of patients receiving PRP (88°).

PRP application did not alter ($p = 0.23$) the need for narcotic use postoperatively. On average, PRP recipients received 27.4 mg morphine equivalents, whereas patients who did not receive PRP received an average of 31.7 mg.

There was no difference in LOS between study groups. For the control group, the average LOS was 2.6 days. For the study group, the average LOS was 2.4 days (Table 4).

The 40 patients undergoing bilateral TKA who received PRP had similar postoperative blood loss compared with

**Table 3.** Demographics of bilateral control and study groups

| Demographic | Control group (n = 39)* | Study group (n = 40)* | p | 95% Confidence interval |
|---|---|---|---|---|
| Average age (years) | 63.5 (43–82) | 65.0 (47–80) | 0.374 | −5.17 to 1.96 |
| Male:female | 19:20 | 21:19 | 0.912 | – |
| Average body mass index (kg/m$^2$) | 31.7 (19–46) | 31.3 (23–42) | 0.928 | −2.26 to 2.48 |
| Anesthesia spinal:GETA$^\dagger$ | 36:3 | 37:4 | 0.973 | |

* Ranges shown in parentheses; $^\dagger$GETA = general endotracheal anesthesia.

**Table 4.** Postoperative findings in unilateral control and study groups

| Variable | Controls (n = 100) | Study (n = 100) | p | 95% Confidence interval |
|---|---|---|---|---|
| Average hemoglobin drop (mg/dL) | 3.6 | 3.8 | 0.414 | −0.54 to 0.22 |
| Average passive ROM at discharge (degrees) | 88.1 | 87.9 | 0.918 | −4.35 to 4.83 |
| Average postoperative narcotics ($MSO_4$ equivalents) | 31.7 | 27.4 | 0.230 | −2.76 to 11.43 |
| Average length of stay (days) | 2.6 | 2.4 | 0.101 | −0.04 to 0.41 |

the 39 patients undergoing bilateral TKA who did not receive PRP as demonstrated by Hgb drop (5.0 mg/dL for control subjects versus 5.2 mg/dL for PRP recipients) and transfusion rate (Table 5).

In patients receiving bilateral TKA, passive ROM was not affected by application of PRP. Average passive ROM of bilateral TKA control subjects at the time of discharge was 86° compared with 85° for PRP recipients.

For patients undergoing bilateral TKA, PRP application did not result in less consumption of postoperative narcotics among patients undergoing bilateral TKA. On average, PRP recipients received 34 mg morphine equivalents, whereas patients who did not receive PRP received an average of 33 mg.

The average patient's LOS for the bilateral control group was identical to the bilateral study group. For the bilateral TKA control and study groups, the average LOS was 2.6 days (Table 6).

Manipulation under anesthesia was needed tended to be used more frequently ($p = 0.44$) among patients who received PRP. Among the 140 PRP recipients (100 unilateral and 40 bilateral), 10 patients ultimately underwent manipulation under anesthesia after TKA. Among the 139 control subjects who did not receive PRP (100 unilateral and 39 bilateral), six resulted in manipulation under anesthesia after TKA.

## Discussion

Several published studies report benefits of PRP application during TKA. The benefits provided by PRP reportedly include: reduced postoperative blood loss, reduced risk of hematoma, less postoperative pain, faster recovery after TKA, and improved wound healing with less risk of infection. Interpretation of these previous studies is controversial as a result of enrollment of a small number of patients, lack of control groups, and measurements of subjective parameters such as observers' impression of patient quality of wound healing. Because these previous investigations provide a weak level of medical evidence supporting the use of PRP during TKA, we sought to confirm these findings.

Our study has several weaknesses. First, it was retrospective and while we included all patients with complete data, not all patients during the study period had complete data. However, a large number of subjects were evaluated over a short time period measuring objective parameters, including Hgb changes, transfusion rates, narcotic requirements converted to morphine equivalents, ROM measured by blinded observers, and hospital LOS. Furthermore, this study closely demographically matched case and control patients, and no other known variables existed. Surgeon, surgical technique, type of implant, and postoperative regimen were identical for both evaluated groups. Further, we did not have confounding variables such as preoperative autologous blood donation and use of suction drains. Second, we assessed blood loss by drop in Hgb and did so only on one day. It is possible greater blood loss by this measure would have been recorded later, but we assessed all patients in a uniform fashion. Other measures might result in different calculations of blood loss. Third, we did not randomize the groups. However, we attempted to match the groups and distinguished blood loss in those with unilateral TKA and bilateral TKA. Fourth, we evaluated only one PRP product and, therefore, results obtained

**Table 5.** Transfusions

| Numbers of patients with transfusions | Unilateral | | | Bilateral | | |
|---|---|---|---|---|---|---|
| | Controls (n = 100) | Study (n = 100) | p | Controls (n = 39) | Study (n = 40) | p |
| Number of patients who received 1 unit | 2/100 | 6/100 | 0.279 | 5/39 | 3/40 | 0.681 |
| Number of patients who received 2 units | 7/100 | 4/100 | 0.535 | 9/39 | 7/40 | 0.736 |
| Number of patients who received 3 units | 1/100 | 0/100 | 0.316 | 3/39 | 1/40 | 0.590 |
| Number of patients who received 4 units | 1/100 | 0/100 | 0.316 | 1/39 | 2/40 | 0.556 |

**Table 6.** Postoperative findings in bilateral control and study groups

| Variable | Controls (n = 39) | Study (n = 40) | p | Confidence interval (95%) |
|---|---|---|---|---|
| Average hemoglobin drop (mg/dL) | 5.0 | 5.1 | 0.56 | −0.498 to 0.915 |
| Average passive ROM at discharge (degrees) | 85.5 | 85.0 | 0.477 | −2.68 to 5.70 |
| Average postoperative narcotics ($MSO_4$ equivalents) | 32.5 | 34.1 | 0.790 | −9.950 to 13.032 |
| Average length of stay (days) | 2.58 | 2.83 | 0.414 | −0.35 to 0.84 |

may not be applicable for other PRP products. The use of PRP application in orthopaedics is growing rapidly and nearly a dozen manufacturers now produce this produce in the United States. Many variables distinguish these products, including amount of autologous blood collected, platelet concentration, parity of formulation as measured by separation of platelets from white blood cells, and choice of platelet activation.

Activation of platelets on PRP application to an open wound may generate hemostasis and reduce postoperative bleeding. Berghoff et al. reported in a retrospective study that PRP application during TKA improved postoperative hemoglobin values on postoperative Days 1 and 2 but not on Day 3 [2]. Everts et al. prospectively reported improved postoperative hemoglobin values with use of PRP during TKA, but this study had many variables, including use of suction drains in control but not study patients [7]. In another retrospective study, Gardner et al. reported higher postoperative Hgb on postoperative Day 3 for patients receiving PRP application during TKA [8]. However, this study fails to discuss other important variable such as use of suction drains, predonation of autologous blood, and postoperative transfusion requirements for each group studied. In a prospective, randomized but small study of 40 patients, Horstmann et al. found that patients treated with a PRP application during TKA, when compared with untreated patients, had nearly identical postoperative Day 1 Hgb levels and nontreated patients received less blood from reinfusion drains [10]. Nonetheless, they also reported that subjectively, treated patients had fewer and smaller hematomas and these same patients seemed to have better wound healing as determined by an undescribed observer. Results of our study, in part, concur with Horstmann et al., and we found no objective measure of decreased postoperative bleeding for patients treated with PRP during TKA. Although our study did not document hematoma severity, no patient from either limb of the study required surgical evaluation of a hematoma.

It has been proposed that the severity of postoperative bleeding correlates with the amount of pain perceived by the degree of postoperative inflammation. Both Horstmann et al. and Berghoff et al. describe reduced pain in patients treated with PRP application when measured by a visual analog scale. However, Berghoff et al. also measured postoperative narcotic requirements in morphine equivalents for PRP-treated and untreated patients and found no difference for this parameter between groups. In our study, pain perception was not measured using a visual analog scale, but like Berghoff et al., when pain was measured by considering narcotic use, no difference was found between patients treated with PRP and untreated controls.

Reduced pain and inflammation after TKA likely would accelerate speed that ROM is achieved and shorten LOS. Furthermore, when platelets are activated, numerous types of growth factors are released and it has been suggested that this phenomenon could accelerate wound healing after surgery, possibly reducing infection incidence. It has been reported that patients treated with PRP during TKA have small but improved ROM in the early postoperative period.

Other investigations were unable to confirm PRP-induced enhancement of recovery of ROM after TKA. Additionally, several studies demonstrated a shorter hospital LOS when PRP was applied during TKA. Although some have reported subjectively perceived improved healing when PRP is used during TKA, all studies to date have enrolled too few subjects to make definitive statements regarding what effect PRP may have on the incidence of infection after this procedure.

We found application of PRP during TKA did not improve early postoperative ROM. ROM in our study was measured by physical therapists who were unaware that a protocol change instituting use of PRP had occurred. Hospital LOS is an arbitrary measure of recovery speed and likely depends more on factors such as clinical pathways than surgical technique. LOS differences in our study for treated and untreated patients were not clinically important. Finally, we found no reduction in postoperative complications in PRP-treated patients but did not a nonsignificant trend toward treated patients having a greater number of manipulations under anesthesia.

In conclusion, the preponderance of previously existing literature on PRP use during TKA suggested that this product had numerous beneficial effects. However, analysis of this same literature suggests that the conclusions by the authors represent a relatively weak level of scientific evidence. Furthermore, because PRP is obtained by removing substantial blood through an invasive phlebotomy and the cost of this product is substantial, we sought to confirm findings noted in previous literature. Our investigation demonstrated that application of PRP during TKA did not reduce blood loss or postoperative pain, had no effect on transfusion rates, and did not increase improve ROM or decrease LOS. Our findings do not justify the routine use of PRP when performing TKA.

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