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# Platelet-rich plasma for the reduction of blood loss after total knee arthroplasty: a clinical trial

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## Abstract

*Purpose* This study aims to clarify the effect of intra-articular platelet-rich plasma (PRP) in total knee arthroplasty (TKA) in preventing postoperative bleeding.

*Methods* There were 315 knees that underwent TKA and were included in this study. The subjects were randomized by paramedical staffs. These were divided into the PRP group who received intra-articular PRP intraoperatively ($n = 109$) and the control group who did not ($n = 206$). We measured postoperative blood loss (drain bag volume), estimated blood loss, and change in hemoglobin (Hb) value at postoperative day 1, 2, 4, and 7. The clinical data were compared between the PRP group and the control group.

*Results* The mean postoperative blood loss of $446.9 \pm 149.7$ mL in the PRP group was significantly less than that in the control group ($550.7 \pm 178.1$ mL, $p < 0.001$). The mean postoperative estimated blood loss of $437.5 \pm 221.3$ mL in the PRP group was significantly less than that in the control group ($552.2 \pm 336.3$ mL, $p < 0.01$). The mean change in Hb value (mg/dL) from baseline was $-1.45$ in the PRP group and $-1.85$ in the control group at postoperative 1 day ($p < 0.05$), $-1.74$ in the PRP group and $-2.11$ in the control group at postoperative day 2 ($p < 0.05$), $-2.30$ in the PRP group and $-2.47$ in the control group at postoperative day 4 ($p < 0.05$), and $-1.98$ in the PRP group and $-2.46$ in the control group at postoperative day 7 ($p < 0.01$).

*Conclusion* In this prospective randomized study, those that received PRP after TKA had significantly less postoperative blood loss and change in Hb level. PRP appears to be effective in reducing postoperative bleeding in TKA.

**Keywords** Blood loss · Osteoarthritis · Platelet-rich plasma · Rheumatoid arthritis · Total knee arthroplasty

## Introduction

Total knee arthroplasty (TKA) is a commonly performed orthopedic procedure for osteoarthritis, rheumatoid arthritis, and osteonecrosis. TKA is an established procedure that can effectively reduce pain and improve function and quality of life. However, some of the complications accompanying TKA are infection, deep vein thrombosis, and bleeding. A perioperative blood loss of 800–1500 mL is associated with a unilateral TKA [1, 2]. Allogeneic red blood cell transfusion is often needed in routine TKA [2–4]; the transfusion rate in TKA was 11 % in a prospective observational study [1]. Allogeneic blood transfusion may lead to increased postoperative bacterial infection rates [5]. Many methods have been reported to reduce bleeding, including autologous re-transfusion drainage, and administration of intra-articular and intravenous tranexamic acid [2, 6].

Platelet-rich plasma (PRP) is plasma with a high concentration of platelets; PRP is extracted by centrifuging whole blood. PRP contains platelet-derived growth factor (PDGF) and transforming growth factor-β (TGF-β), which have been associated with the beneficial wound healing

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cascade [7, 8]. There are many potential clinical applications for PRP; it is used for wound healing in the field of plastic surgery, implant treatment in the field of dentistry, and treatment of lateral elbow tendinosis in orthopedics [9, 10]. Additionally, PRP contains fibrinogen that relates to the coagulation of blood, blood coagulation factor V, adenosine diphosphate (ADP), and thromboxane (TX) $A_2$; it is suggested that these components could potentially reduce bleeding. Some previous studies have reported that the administration of PRP resulted in decreased blood loss, less postoperative pain, and a shorter hospital stay [11–13]. However, other studies support that PRP has not been shown to be effective in TKA [14–16].

The efficacy of PRP for reducing blood loss in TKA is controversial. The purpose of this study is to clarify the effect of PRP in reducing postoperative bleeding after TKA.

## Materials and methods

We investigated the clinical course and background variables of patients with osteoarthritis and rheumatoid arthritis who underwent TKA with or without PRP. This was a randomized, single-blinded, prospective clinical study. The subjects were randomized by paramedical staff, and the surgeon was not blinded to the patients' groups during the TKA procedures. We prospectively enrolled 315 knees that underwent TKA by the same surgeon in our hospital. The exclusion criteria were ankylosed knee and intraoperative lateral patellar release. The patients were divided into the PRP group ($n = 109$) and the control group ($n = 206$). The PRP group and the control group had no significant differences in baseline demographics and characteristics (age, sex, disease, body weight, body mass index, preoperative Hb, preoperative extension angle, preoperative flexion angle, preoperative range of motion, and operation time) (Table 1).

The surgery was done via the medial parapatellar approach using the gap-balancing technique and an intraoperative tourniquet. We opened the tourniquet and used cauterization for a short period intraoperatively. All TKA were done using cemented posterior stabilized implants (Optetrak®; Exactech Inc., Florida, USA). PRP was prepared by adding 5 mL of sodium citrate to 55 mL of blood to make 60 mL in total. This solution was centrifuged at 3500 rpm for 15 min. The PRP that sank to the bottom was then collected. In the PRP group, we closely sutured the joint capsule and then injected PRP into the capsule. Subsequently, 0.5 mL thrombin and 0.5 mL calcium chloride were injected into the capsule (Fig. 1). After the operation, drain clamping was done for 1 h in the PRP group and the control group.

Postoperative blood loss (drain bag volume), estimated blood loss, and change in hemoglobin (Hb) value were measured at postoperative day 1, 2, 4, and 7; range of motion was recorded at postoperative day 7 and 14. The clinical data were compared between the PRP group and the control group. Estimated blood loss was calculated as follows: patient's blood volume $= k1 \times$ height $(m)^3 + k2 \times$ weight (kg) $+ k3$; $k1 = 0.3669$, $k2 = 0.03219$, and $k3 = 0.6041$ for male patients; $k1 = 0.3561$, $k2 = 0.03308$, and $k3 = 0.1833$ for female patients. Estimated blood loss = patient's blood volume $\times$ (preoperative Hct $-$ postoperative Hct) [17]. The postoperative blood loss and estimated blood loss were calculated by paramedical staff.

Univariate analysis was used to compare the PRP group and the control group. The Mann–Whitney $U$ test was used to assess the age, body weight, body mass index, preoperative Hb, preoperative extension angle, preoperative flexion angle, preoperative range of motion, operation time, blood loss, estimated blood loss, and change in Hb. The Fisher exact probability test was used to assess sex and disease. Significance was established at a $p$ value of $<0.05$.

| | PRP group | Control group | $p$ value |
|---|---|---|---|
| Age, years, mean (SD) | 73.0 (7.8) | 73.4 (8.2) | 0.380 |
| Gender, knees; male, female | 17, 92 | 43, 163 | 0.552 |
| Disease, osteoarthritis/rheumatoid arthritis; no (%) | 90/19 | 185/21 | 0.104 |
| Body weight, kg; mean (SD) | 62.0 (11.0) | 61.3 (14.2) | 0.282 |
| Body mass index; mean (SD) | 25.7 (4.1) | 26.0 (5.7) | 0.295 |
| Preoperative hemoglobin, mg/dL; mean (SD) | 11.9 (1.3) | 12.0 (2.3) | 0.884 |
| Preoperative extension angle, degree; mean (SD) | −8.9 (7.9) | −8.3 (7.6) | 0.453 |
| Preoperative flexion angle, degree; mean (SD) | 120.9 (22.9) | 121.1 (21.3) | 0.923 |
| Preoperative range of motion, degree; mean (SD) | 111.9 (26.1) | 112.8 (25.0) | 0.723 |
| Operation time, min; mean (SD) | 77.7 (20.4) | 76.2 (19.9) | 0.792 |

Table 1 Demographic characteristics at baseline in the platelet-rich plasma (PRP) group and the control group
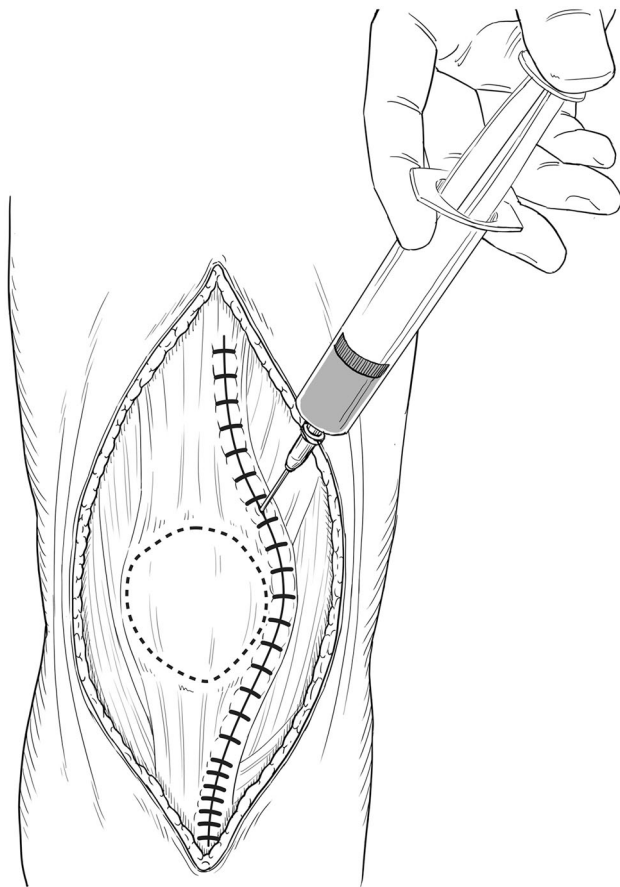
*PRP* platelet-rich plasma

**Fig. 1** Injection of PRP. After finishing the suture of the joint capsule

This study was conducted in compliance with the ethical principles stated in the Declaration of Helsinki and was approved by the ethics committee of Kamagaya General Hospital. All patients provided informed consent.

## Results

The mean postoperative blood loss was $446.9 \pm 149.7$ mL in the PRP group and $550.7 \pm 178.1$ mL in the control group. The mean postoperative blood loss of the PRP group was significantly less than that of the control group ($p < 0.001$, Fig. 2).

The mean postoperative estimated blood loss was $437.5 \pm 221.3$ mL in the PRP group and $552.2 \pm 336.3$ mL in the control group. The mean postoperative blood loss of the PRP group was significantly less than that of the control group ($p < 0.01$, Fig. 3).

The mean change in Hb value from baseline was $-1.45$ mg/dL in the PRP group and $-1.85$ mg/dL in the control group at postoperative day 1 ($p < 0.05$), $-1.74$ mg/dL in the PRP group and $-2.11$ mg/dL in the control group
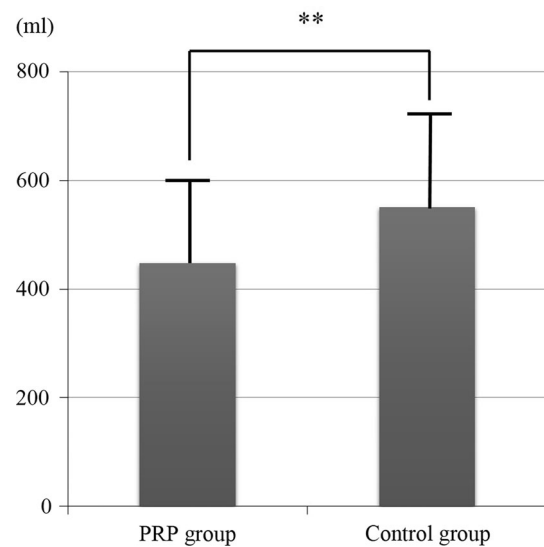


**Fig. 2** Postoperative blood loss volume; comparison of platelet-rich plasma (PRP) group and control group. *PRP* platelet-rich plasma; ***$p < 0.01$
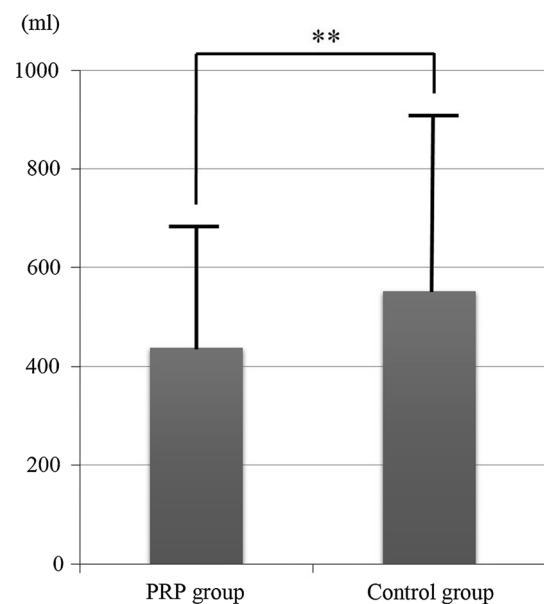


**Fig. 3** Postoperative estimated blood loss volume; comparison of PRP group and control group. *PRP* platelet-rich plasma; ***$p < 0.01$

at postoperative day 2 ($p < 0.05$), $-2.30$ mg/dL in the PRP group and $-2.47$ mg/dL in the control group at postoperative day 4 ($p < 0.05$), and $-1.98$ mg/dL in the PRP group and $-2.46$ mg/dL in the control group at postoperative day 7 ($p < 0.01$, Fig. 4).

The mean range of motion was $106.1° \pm 13.3°$ in the PRP group and $108.2° \pm 15.7°$ in the control group at postoperative day 7 ($p > 0.05$), and $118.5° \pm 10.8°$ in the PRP group and $120.1° \pm 10.7°$ in the control group at postoperative day 14 ($p > 0.05$).
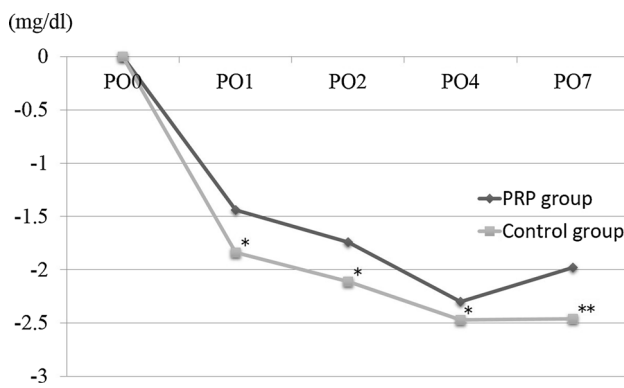
(mg/dl)



Fig. 4 Change in hemoglobin value from baseline; comparison of PRP group and control group. *PRP* platelet-rich plasma, *PO* postoperative day; *$p < 0.05$, **$p < 0.01$

## Discussion

Platelets play an important role in wound healing and hemostasis. Treatment with PRP delivers high concentrations of platelets and growth factors (which play a critical role in wound healing) directly to the wound site, which initiates and enhances wound healing [18, 19]. Further, when there is tissue damage with bleeding, von Willebrand factor (vWF) combines with the collagen in the tissue under vascular endothelial cells and megakaryocytes [20]. Glycoprotein (GP)Ia/IX compound in platelet membrane glycoprotein combines with and attaches to vWF and is then activated by the presence of Ca ions, ADP, and $TXA_2$; ADP and $TXA_2$ are contained in the granules that are released by activated platelets. ADP further activates platelets, while $TXA_2$ promotes hemostasis by causing platelet aggregation and vasoconstriction [21, 22]. Further activated platelets produce GPIIb/IIIa complex and combine with fibrinogen; platelets then condensate with one another to form a blood clot and cause primary hemostasis. Secondary hemostasis occurs when fibrin covers the primary blood clot. This secondary hemostasis, or coagulating system, plays a critical role in efficient blood clotting by phospholipid in platelets. PRP is created by centrifuging autologous blood and contains factor V, ADP and $TXA_2$. Clinically, PRP is 4–7 times more effective than standard platelets [23] and is considered to be effective in reducing postoperative bleeding.

PRP usage in TKA has been previously reported. Everts et al. [11] reported that perioperative application of PRP and fibrin sealant may reduce the incidence of allogeneic blood transfusions. They reported that the PRP and fibrin sealant group ($n = 85$) maintained significantly higher Hb levels than the control group ($n = 80$) (11.3 vs. 8.9 g/dL; $p < 0.001$) at postoperative day 1 and had a significantly lower incidence of allogeneic transfusion (0.17 vs. 0.52 units; $p < 0.001$) [11]. Gardner et al. [12] also reported that

the group using PRP ($n = 61$) had a significantly smaller change in Hb from baseline (−2.68 vs. −3.16 g/dL; $p < 0.05$) at postoperative day 3, and decreased pain and reduced hospitalization period compared with the control group ($n = 37$). Meanwhile, Peerbooms et al. [14] reported that 3 months after surgery, the Hb in the PRP group ($n = 52$) was not different to baseline (−1.58 vs. −1.75 mmol/L; $p > 0.05$). Horstmann et al. [15] reported that there was no difference in the mean Hb and flexion angle of the PRP group ($n = 20$) at postoperative day 1 compared with the control group ($n = 20$).

In our study, the use of PRP significantly reduced postoperative bleeding and significantly suppressed the decrease in Hb at postoperative day 1, 2, 4, and 7. PRP was therefore effective in reducing postoperative bleeding after TKA. This result may have been due to the 1-h drain clamping time after the operation and the larger sample size used in our study. We consider that in the previous studies on PRP in TKA, the PRP may have overflown out from the joint, and therefore the effect of PRP was not manifested; hence, in our study we clamped the drain for 1 h to ensure that the PRP remained in the intra-articular compartment of the knee. The PRP is active by adding thrombin and calcium. The potential beneficial efficacy including reduction of blood loss associated with PRP use may have been due to the growth factors, cytokines, and fibrin products present in the PRP. Moreover, in addition to the growth factors in PRP, $TXA_2$, thrombin and ADP release from platelets. PRP provide a concentrated and directed supply of the growth factor that stimulates the maturation of mesenchymal cells [24]. Collagen aggregation involved in platelet aggregation induced by ADP [25]. These agents lead to earlier hemostasis by enhancing the activity of platelets and forming a platelet plug.

The effect of PRP is a function of many variables, including the platelet concentration and the procedures implemented after injection of PRP. The concentration rate of PRP is increased 3.6 times by single-spinning [26], and 7.9 times by double-spinning [27]. Single centrifugation is simple, but the concentration of the resultant PRP may be low. This study used PRP prepared by single-spinning, so the results using PRP prepared by double-spinning may have been different. However, the role of PRP may not be concentration-dependent, as a previous study reported that the effect of PRP in vitro for neurotrophic function and migration of Schwann cells was not concentration-dependent [28].

PRP is considered to be effective in reducing postoperative bleeding. In the future, it is necessary to determine more effective methods of PRP usage for reducing postoperative blood loss by investigating optimal spin time, concentration rate, volume, and drain clamping time.

## Conclusion

The results of this prospective study suggest that PRP was effective in reducing postoperative bleeding after TKA. Future studies are needed to compare the effectiveness of PRP, tranexamic acid, and autologous transfusion in reducing postoperative bleeding. Moreover, we need to investigate more effective methods of PRP preparation and usage.

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