Systematic Review and Meta-Analysis

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The effect of platelet-rich plasma on reducing blood loss after total knee arthroplasty

A systematic review and meta-analysis

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Abstract

Background: Efficacy and safety of platelet-rich plasma (PRP) compared with control for preventing postoperative bleeding after total knee arthroplasty (TKA) is controversial. We performed a meta-analysis of randomized controlled trials (RCTs) to determine whether PRP might reduce blood loss and improve function following TKA.

Methods: PubMed, Medline, Embase, Web of Science, and the Cochrane Library were searched to identify RCTs comparing PRP with control for patients undergoing unilateral TKA. The mean difference (MD) of total blood loss, hemoglobin (Hb) level, Hb drop, drain volume, range of motion (ROM), Western Ontario and McMaster Osteoarthritis Index (WOMAC) scores, length of hospital stay (LOS), and odds ratios of transfusion rate and postoperative complications in the PRP and control groups were pooled throughout the study. Relevant data were meta-analyzed using RevMan v5.3.

Results: Six RCTs involving 529 patients were included (208 PRP vs. 321 controls). The application of PRP in TKA had a significantly less calculated total blood loss (MD = −98.11; 95% confidence interval [CI]: −153.63 to −42.59, $P = .0005$) and lower Hb drop (MD = −0.34; 95% CI: −0.59 to −0.09, $P = .008$) than the control in the early postoperative period while decreasing the LOS (MD = −2.12; 95% CI: −3.47 to −0.76, $P = .002$). No significant differences were seen in drain volume, Hb level, transfusion rate, ROM, WOMAC scores, and complications between the 2 groups ($P > .05$).

Conclusions: Our meta-analysis suggests that PRP appears to be effective in reducing postoperative blood loss and lowering Hb drop without increasing the risks of postoperative complications after TKA. However, owing to the variation of included studies, no firm conclusions can be drawn.

Abbreviations: CI = confidence interval, Development and Evaluation, DVT = deep vein thrombosis, GRADE = Grading of Recommendations Assessment, Development, and Evaluation, Hb = hemoglobin, LOS = length of hospital stay, MD = mean difference, PE = pulmonary embolism, POD = postoperative day, PRP = platelet-rich plasma, RCTs = randomized controlled trials, ROM = range of motion, TKA = total knee arthroplasty, VTE = venous thrombus embolism, WOMAC = Western Ontario and McMaster Osteoarthritis Index.

Keywords: blood loss, meta-analysis, platelet-rich plasma, randomized controlled trial, systematic review, total knee arthroplasty, transfusion

1. Introduction

Total knee arthroplasty (TKA) is a very successful surgical procedure used to treat end-stage knee osteoarthritis so that pain can be relieved and joint function restored. However, TKA can be associated with several complications including blood loss, pain, infection, wound complications, stiffness and deep vein thrombosis in the perioperative period.[1] Besides, any surgery transiently induces the fibrinolytic action, which is aggravated by the use of pneumatic tourniquet in TKA.[2] So, the resulting hyperfibrinolysis may further contribute to higher blood loss following TKA. Thus, many patients have lower postoperative Hb that usually results in allogeneic blood transfusion. However, blood transfusion can lead to serious complications and increased costs.[3,4] Therefore, more effective and safer measures for reducing bleeding and blood-transfusion requirements during and after TKA are needed. Various blood-preservation protocols, such as the application of PRP, tranexamic acid, and fibrin sealant, have been used to prevent blood loss and decrease the requirements of blood transfusion.[5–9] And there are numerous studies indicating the advantages of TXA and FS on reducing the blood loss after TKA,[8,10] so our meta-analysis mainly concentrates on the effect of PRP.

PRP is plasma with a higher concentration of platelets than that found in blood.[11] PRP releases much more growth factors,

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JM and JS are joint first authors.

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thromboxane A2, thrombin, adenosine diphosphate, and several growth factors including platelet-derived growth factor and transforming growth factor-b, which attract more platelets to the wound site. A platelet plug is formed by these huge amounts of platelets, which enhance the inflammatory cascade and lead to hemostasis.[5,11–14] In 2000, for the first time, one study showed that autologous platelet gel played an important role in preventing postoperative blood loss when it was administrated during the postoperative period following implantation of prostheses.[15] After that, multiple studies have reported that the application of PRP during TKA could lead to decreased blood loss, less postoperative pain, and a shorter hospital stay. However, different conclusions have been reached by some scholars who have not found significant differences in preventing blood loss when applying PRP for TKA patients. Kuang et al's[16] meta-analysis indicates that autologous platelet gel (APG) has no effectiveness on blood loss, functional recovery, postoperative narcotics, and length of hospital stay; however, APG can reduce pain after TKA. Li et al[17] did not study the effect of PRP on reducing blood loss after TKA, indicating the conclusion on increasing the ROM after TKA in short term and long term. There is controversy over whether PRP leads to a safer and effective hemostatic effect after TKA. We conducted a meta-analysis of RCTs to ascertain whether PRP is superior to control in reducing postoperative blood loss for TKA patients.

2. Materials and methods

Ethical approval for this study was unnecessary because it was a review of existing literature and did not involve any handling of individual patient data.

2.1. Search strategy

This meta-analysis was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis[10] reporting guidelines for the meta-analysis of intervention trials. PubMed, Medline, Embase, Web of Science, and the Cochrane Library were searched up to September 2016 for RCTs comparing PRP with control for reducing blood loss in patients undergoing primary unilateral TKA. The search terms were as follows: "platelet rich plasma" OR "PRP" OR "autologous platelet concentrate" OR "platelet gel" AND "knee arthroplasty" OR "knee replacement". No restrictions were imposed on language and publication status. The title and abstract of studies identified in the search were reviewed to exclude clearly irrelevant studies. Reference lists of all eligible studies and relevant reviews were searched manually for additional trials.

2.2. Inclusion criteria and study selection

We identified RCTs comparing PRP with control in patients undergoing primary unilateral TKA. The primary outcomes included total blood loss, Hb level, Hb drop, drain volume, and transfusion rate. Secondary outcomes included ROM, WOMAC scores, LOS, and postoperative complications (including wound healing disturbances/superficial infection). Articles that reported at least 1 outcome were included and those without the outcome measures of interest were excluded. Quasi-RCT or non-RCT, observational studies, letters, comments, editorials, and practice guidelines were excluded.

2.3. Data extraction and quality assessment

Two authors (JM and JS) independently reviewed all titles and abstracts of studies identified by searches according to the eligibility criteria described above. Full texts of articles that met the inclusion criteria were reviewed thoroughly. Disagreements were resolved by discussion to reach consensus. Data on patient characteristics (age, sex, and other baseline characteristics), intervention, and outcomes were extracted in duplicate by the 2 authors using a standardized form. Data in other forms (ie, median, interquartile range, and mean ± 95% confidence interval [CI]) were converted to mean ± SD according to the Cochrane Handbook.[18] If data were not reported numerically, we extracted them by manual measurements from published figures.

Two authors (JM and JS) independently assessed the risk of bias of the included studies, based on the following items: random sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias.[18] Disagreement was resolved by the third author. The quality of evidence of outcomes was judged according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) [19] criteria. The 2 authors independently evaluated 5 factors (risk of bias, inconsistency, indirectness, imprecision, and publication bias) that may downgrade the quality level of evidence. The recommendation level of evidence was classified into 4 categories: high, moderate, low, or very low.[19] High-quality: further research is very unlikely to change our confidence in the estimate of effect; moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low quality: we are very uncertain about the estimate.

2.4. Statistical analysis

All calculations were made using RevMan 5.3 software. Mean difference (MD) with a 95% CI was calculated for continuous data. Odds ratio (OR) or risk difference (RD) with 95% CI was calculated for dichotomous data. Heterogeneity among studies was estimated using the I^2 statistic; substantial heterogeneity was represented by $I^2 > 50\%$. A fixed-effects model was used if the heterogeneity test did not reveal significance ($I^2 < 50\%$; $P > .1$). Otherwise, we adopted the random-effects model. $P < .05$ was considered significant. Sensitivity analysis was performed to explore the impact of an individual study by deleting one study each time.

3. Results

3.1. Search results

The initial search yielded 102 citations, of which 91 were excluded owing to duplication. After screening the titles and abstracts and reading full text, 5 studies were excluded based on inclusion criteria. Finally, 6 studies[5,14,20–23] involving 529 patients were eligible for data extraction and meta-analysis (Fig. 1). Of these 529 patients, 208 patients belonged to the PRP group and 321 to the control group.

Table 1 summarizes the characteristics of the 6 included RCTs, which were published between 2009 and 2016. Sample size of the studies was 21 to 315 patients. All of the trials involved primary unilateral TKA, and all patients were diagnosed with knee

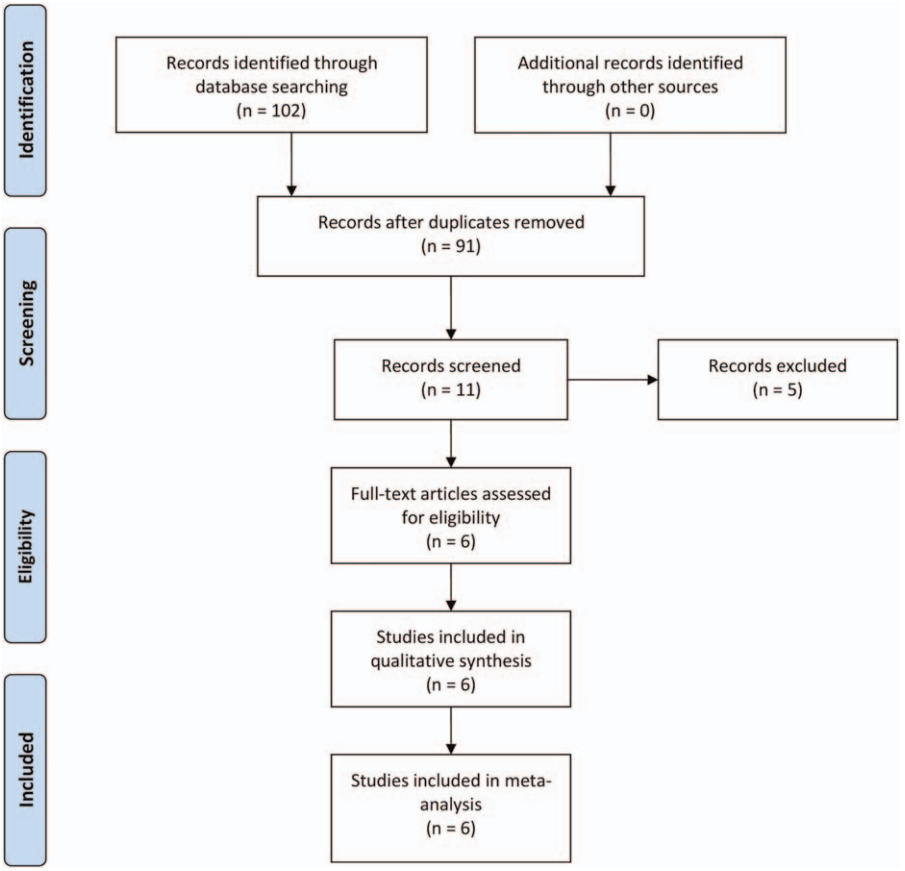

Figure 1. Flow chart of the literature search.

osteoarthritis except one study,[22] which included the patients with rheumatoid arthritis. All of the included studies were compared with blank control. Baseline characteristics between the two groups in each study were well matched. Two trials[5,23] used spinal anesthesia, one trial[5] involved combined sciatic nerve and femoral nerve block, and the remaining trials did not mention the type of anesthesia used. A pneumatic tourniquet was applied in all the included studies except one study,[21] which did not report the use of a tourniquet. Two studies[14,22] reported use of a drain during TKA, and no postoperative drains were applied in the other 4 studies. Two studies[5,21] described an indication for transfusion associated with a fall in hemoglobin level or hematocrit and clinical symptoms. Variation in the amount of PRP used was noted. Thromboembolic complications such as deep vein thrombosis, pulmonary embolism, and venous thrombus embolism were reported in all studies except 1 study.[22] Outcome of units transfused was reported in 1 study,[5] which was not analyzed owing to insufficient data.

3.2. Study quality and GRADE of evidence

Risk of bias in the included studies and GRADE of evidence are shown in Fig. 2 and Table 2, respectively. Among the included studies, 2 included studies[21,23] were randomized by randomization table or computer-generated numbers, and the remaining studies did not report the method of random sequence generation. All studies reported allocation concealment using sealed envelope except 2 studies[22,23]. We used the GRADE criteria to measure the strength of recommendations. The evidence quality for each outcome was mostly moderate.

4. Results of the meta-analysis

4.1. Calculated total blood loss

Data from 2 studies[22,23] involving 355 patients were available to examine the calculated total blood loss assessed by the Gross formula. The formula was proven to be an accurate method.[24] The application of PRP in TKA had a significantly less calculated total blood loss than the control (MD = −98.11; 95% CI: −153.63 to −42.59, $P = .0005$) (Fig. 3, Table 2). There was no significant heterogeneity between studies ($I^2 = 29\%$, $P = .24$).

4.2. Drainage volume

Two studies[14,22] involving 355 patients reported the drainage volume after TKA. There was no significant difference in the drainage volume between the 2 groups (MD = − 38.73, 95% CI: −185.97 to 108.51, $P = .61$) with considerable heterogeneity ($I^2 = 83\%$, $P = .02$) (Fig. 4, Table 2).

4.3. Hemoglobin level

Two studies[14,21] involving 80 patients reported the Hb level on the first postoperative day (POD). Meta-analysis revealed no significant difference in hemoglobin levels between the 2 groups (MD = –0.18; 95% CI, –0.79 to –0.43, $P = .01$) on the POD 1.

Table 1

Characteristics of the included studies.

Study (year)	No. PRP/ control	Male patients (PRP/control)	Mean age (PRP/control)	Anesthesia	PRP preparation	Intervention	Follow-up	DVT prophylaxis	Outcomes
Aggarwal et al (2014)[5]	7/14	NR	56.43±7.59/ 53.79±9.755	Regional spinal/ epidural	50 mL of the patient's blood, centrifuged for 15 min at 1500 rpm on a table-top centrifuge, extracted, passed through a leucocyte filter	8 mL of PRP and calcium chloride were injected into the posterior recess, gutters and capsule in a ratio of 4:1. The remaining platelet gel was infiltrated into the repaired extensor mechanism and prepatellar fat.	6 mo	Aspirin 150 mg one day before surgery and 150 mg daily through the 10th postoperative day	b, f, g, h
Mochizuki et al (2016)[22]	109/206	17/43	73.0±7.8/73.4 ±8.2	NR	60 mL of the solution containing 5-mL sodium citrate and 55-mL patient's blood was centrifuged at 3500 rpm for 15 min	PRP was injected into the capsule after suturing the joint capsule. Subsequently, 0.5-ml thrombin and 0.5-ml calcium chloride were injected into the capsule.	2 wk	NR	a, c, d, f
Guerreiro et al (2015)[21]	20/20	6/8	66.4/71.6	NR	20 mL of the patient's blood, centrifuged for 10 minutes at 1200 rpm at room temperature, and then the plasma was decanted into a 10-ml sterile tube, centrifuged again in the same machine at the same speed for 5 min	PRP was applied to the entire exposed portion of the knee joint.	2 mo	A dose of 40 mg of enoxaparin subcutaneously, 24–48 h after the surgery, and 10 mg of rivaroxaban daily, for a further 10 days at home	b, e, f, g, i
Morishita et al (2014)[23]	20/20	2/0	72±4.1/74.7± 5.7	Spinal anesthesia	60 mL container containing 3-mL citrate and 57-mL patient's blood was centrifuged at 3500 rpm for 15 min to separate PRP-containing buffy coat layers.	Platelet gel was sprayed (5 mL of PRP, combined with the 5 mL of 5000 U of thrombin in 2% calcium chloride solution) to all accessible surfaces of the deep wound.	4 wk	10,000 IU of heparin sodium intravenously in addition to mechanical prophylaxis with an intermittent pneumatic compression device until postoperative day 1	a, c, e, f, i
Peerbooms et al (2009)[20]	32/41	6/8	76±4.1/78± 5.2	NR	60-mL container containing 7-mL citrate phosphate dextrose and 53 ml whole blood was centrifuged at 3200 rpm for 15 min to separate 6 ml of PRP.	The subcutaneous tissues of the patients were sprayed with the PPP fraction (approximately 10 mL) after closure of the joint capsule.	3 mo	0.3 mL LMWH subcutaneously daily before the operation, and then the oral anticoagulants (acenocoumarol) were used up to 12 weeks postoperatively.	c, f, g, i
Horstmann et al (2011)[14]	20/20	14/13	67/66	Combined sciatic nerve and femoral nerve block	Two 60-mL containers were filled with 54 mL of fresh whole blood and 6-mL citrate, centrifuged at 3200 rpm for 12 min	After implantation of the knee prosthesis, 11 mL of platelet gel was sprayed into the medial and lateral recessus, onto exposed cut bone surfaces, and into the fossa suprapatellaris. Consecutively, 11 mL of activated platelet-poor plasma was sprayed onto the capsule after closure of it, and onto the subcutis before closure of the wound.	5 days	0.3 mL nadroparin subcutaneously before the operation, which continued daily until 6 weeks postoperatively.	b, c, d, e, h, i

a = calculated total blood loss, b = hemoglobin level, c = hemoglobin drop, d = drain volume, DVT = deep vein thrombosis, e = transfusion rate, f = range of motion, g = WOMAC scores, h = length of hospital stay, i = postoperative complications, LMWH = low molecular weight heparin, NR = not report, PRP = platelet-rich plasma, rpm = revolutions per minute.

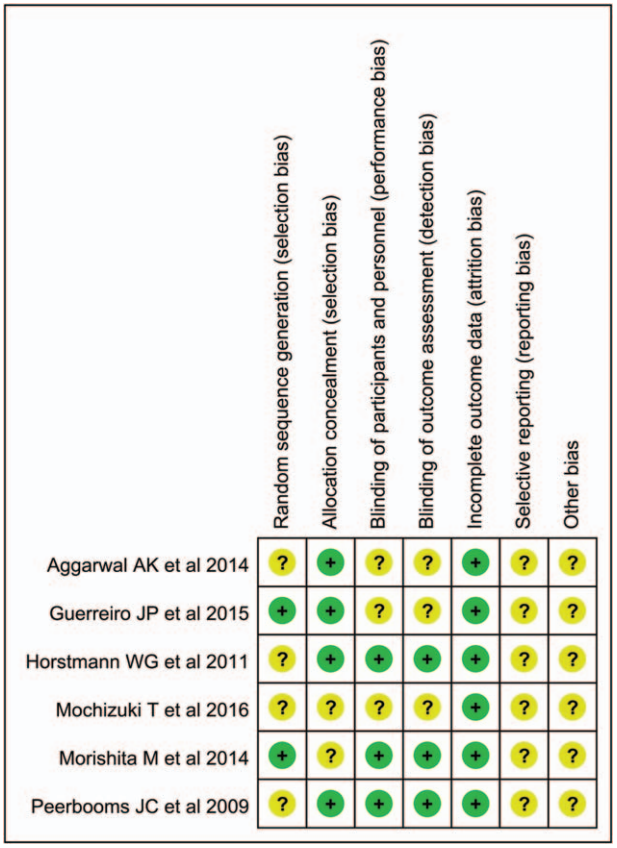

Figure 2. Risk of bias assessment of the included studies.

There was no significant heterogeneity between studies ($I^2=0\%$, $P=.46$) (Fig. 5, Table 2).

4.4. Hemoglobin drop

Two studies[20,22] involving 388 patients reported the Hb drop on POD 1. The PRP group had a significantly lower Hb drop (MD = –0.34; 95% CI: –0.59 to –0.09, $P=.008$) on POD 1 after TKA. There was no significant heterogeneity between studies ($I^2=0\%$, $P=.47$) (Fig. 6, Table 2).

4.5. Transfusion rate

Three studies[14,21,23] involving 120 patients were used to carry out a meta-analysis on the requirements of blood transfusion. Meta-analysis revealed no significant difference in transfusion rate between the 2 groups (RD = 0.00; 95% CI: −0.06 to 0.06; $P=1.00$). There was no significant heterogeneity between studies ($I^2=0\%$, $P=1.00$) (Fig. 7, Table 2).

4.6. Range of motion

Five studies[5,14,20–22] with 489 patients reported range of motion (ROM) postoperatively at POD 2, POD 5, POD 7, POD 2W, and POD 6W. Meta-analysis revealed no significant difference in ROM between the PRP and control groups postoperatively at POD 2 (MD POD 2 = 0.80, 95% CI: −2.87 to 4.46, $P=.67$], POD 5 (MD POD 5 = 2.93, 95% CI: −0.60 to 6.46, $P=.10$), POD 7 (MD POD 7 = −1.64, 95% CI: −4.54 to 1.27, $P=.27$), POD 2W (MD POD 2W = −0.88, 95% CI: −3.70 to 1.94, $P=.54$), and 6W (MD POD 6W = 3.93, 95% CI: −5.17 to 13.02, $P=.40$) (Fig. 8, Table 2).

4.7. WOMAC score

Two studies[5,20] with 94 patients reported WOMAC score postoperatively at POD 6W and POD 3M. There were no significant differences in WOMAC score between the 2 groups postoperatively at POD 6W (MD POD 6W = −2.78, 95% CI: −10.03 to 4.46, $P=.45$) and POD 3 M (MD POD 3M = −1.09, 95% CI: −8.72 to 6.54, $P=.78$) (Fig. 9, Table 2).

4.8. Length of hospital stay

Data were available from 2 studies[5,14] involving 61 patients. The PRP group decreased the LOS than the control group (MD = −2.12; 95% CI: −3.47 to −0.76, $P=.002$) with moderate heterogeneity ($I^2=58\%$, $P=.13$) (Fig. 10, Table 2).

Table 2

The GRADE evidence quality for each outcome.

Outcomes	No. of included studies	No. of patients		MD or OR (95% CI)	Heterogeneity	Quality of evidence (GRADE)
		PRP	Control			
Calculated total blood loss, mL	2	129	226	−98.11 (−153.63, −42.59)	$I^2=29\%$, $P=.24$	Moderate
Drainage volume, mL	2	129	226	−38.73 (−185.97, 108.51)	$I^2=83\%$, $P=.02$	Low
Hemoglobin level, g/dL	2	40	40	−0.18 (−0.79, −0.43)	$I^2=0\%$, $P=.46$	Moderate
Hemoglobin drop, g/dL	2	141	247	−0.34 (−0.59, −0.09)	$I^2=0\%$, $P=.47$	Moderate
Transfusion rate	3	60	60	−0.00 (−0.06, 0.06)	$I^2=0\%$, $P=1.00$	Moderate
Range of motion at POD 2	2	52	61	0.80 (−2.87, 4.46)	$I^2=0\%$, $P=.48$	Low
Range of motion at POD 5	2	27	34	2.93 (−0.60, 6.46)	$I^2=0\%$, $P=.78$	High
Range of motion at POD 7	2	129	226	−1.64 (−4.54, 1.27)	$I^2=0\%$, $P=.56$	Moderate
Range of motion at POD 2W	2	141	247	−0.88 (−3.70, 1.94)	$I^2=15\%$, $P=.28$	High
Range of motion at POD 6W	2	39	55	−3.93 (−5.17, 13.02)	$I^2=88\%$, $P=.004$	Low
WOMAC score at POD 6W	2	39	55	−2.78 (−10.03, 4.46)	$I^2=67\%$, $P=.08$	Moderate
WOMAC score at POD 3M	2	39	55	−1.09 (−8.72, 6.54)	$I^2=71\%$, $P=.06$	Moderate
Length of hospital stay	2	27	34	−2.12 (−3.47, −0.76)	$I^2=58\%$, $P=.13$	Low
Postoperative complications	4	92	101	0.43 (0.17, 1.10)	$I^2=5\%$, $P=.37$	High

CI = confidence interval, MD = mean difference, OR = odds ratio, POD = postoperative day, PRP = platelet-rich plasma, WOMAC = Western Ontario and McMaster Osteoarthritis Index, GRADE = Grading of Recommendations Assessment, Development, and Evaluation.

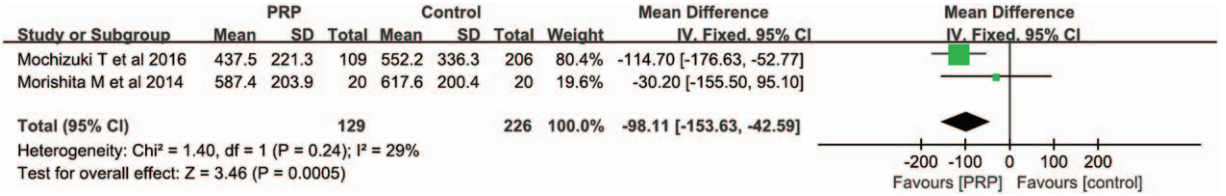

Figure 3. Forest plot analyses of calculated total blood loss in total knee arthroplasty.

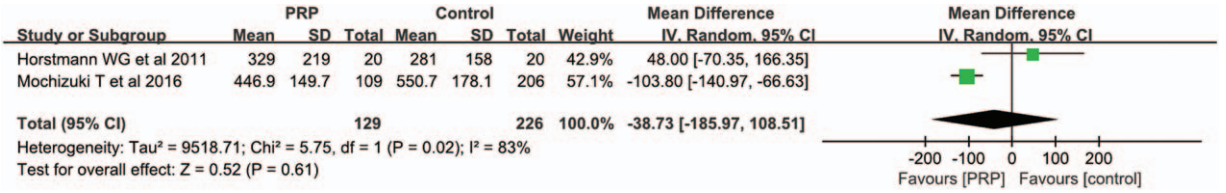

Figure 4. Forest plot analyses of drain volume in total knee arthroplasty.

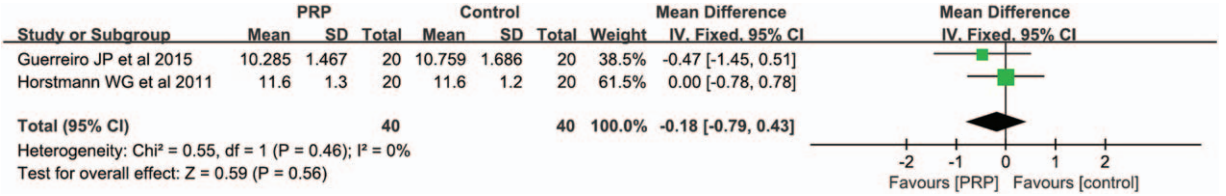

Figure 5. Forest plot analyses of hemoglobin level in total knee arthroplasty.

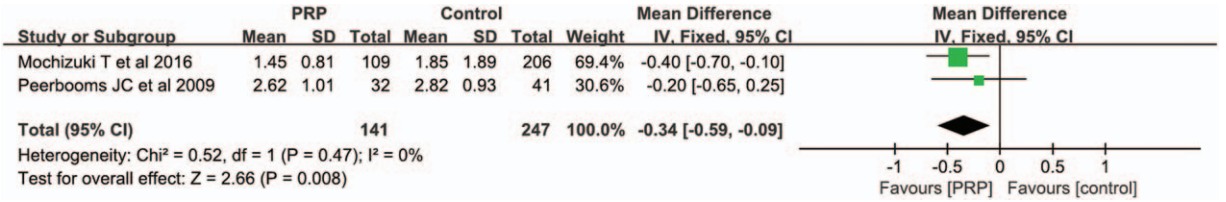

Figure 6. Forest plot analyses of hemoglobin drop in total knee arthroplasty.

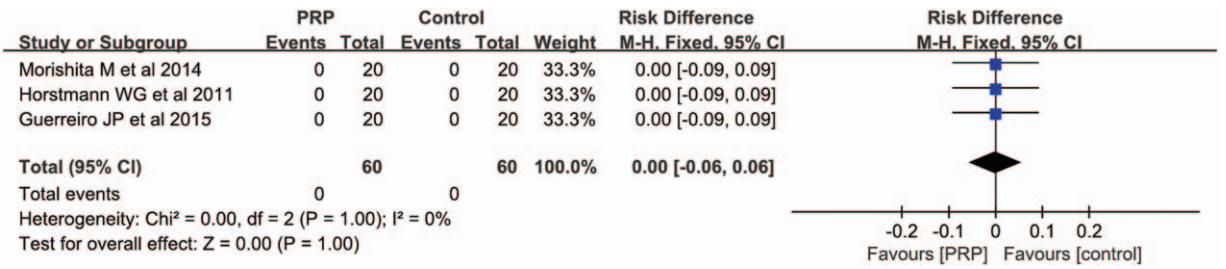

Figure 7. Forest plot analyses of blood transfusion rate in total knee arthroplasty.

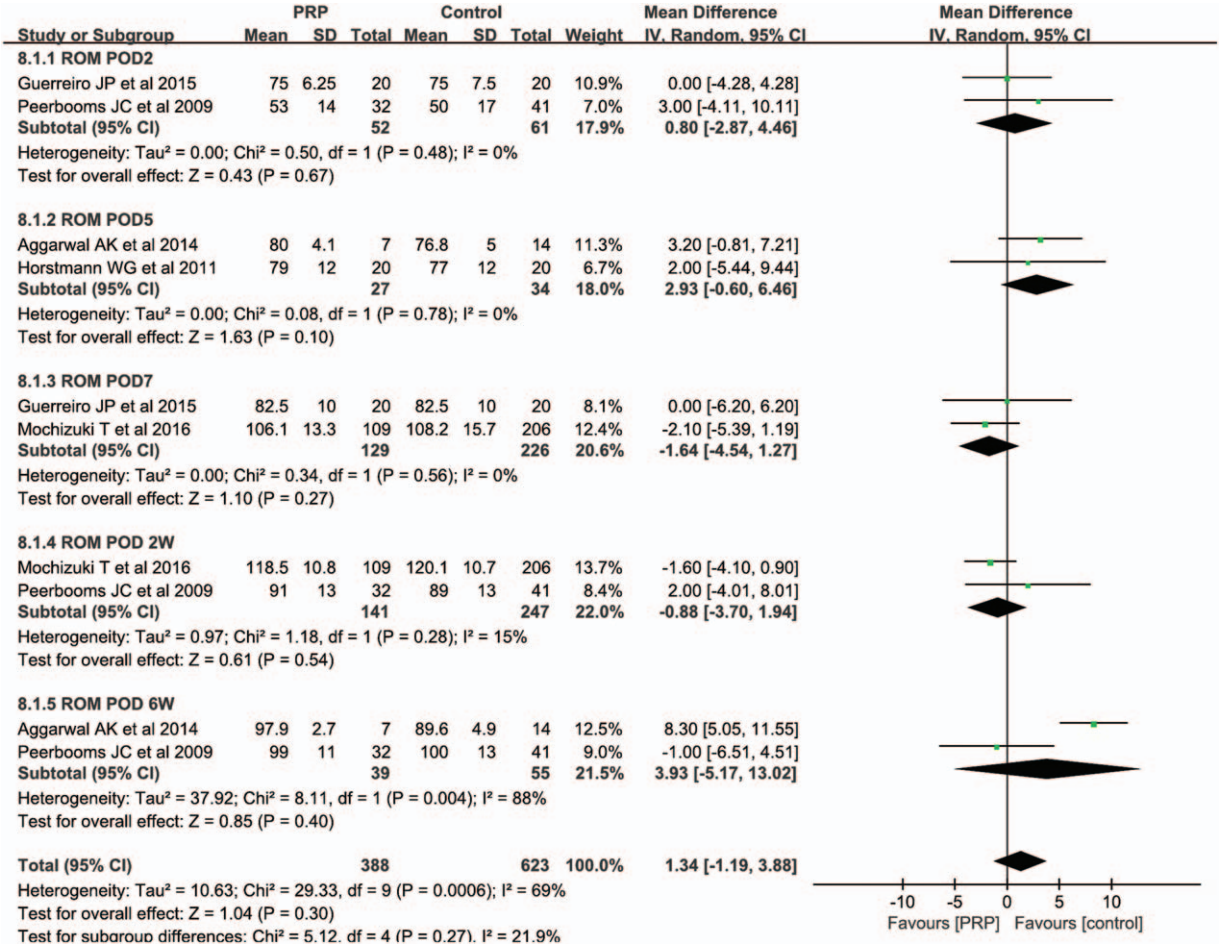

Figure 8. Forest plot analyses of range of motion in total knee arthroplasty.

4.9. Postoperative complications

Four studies[14,20,21,23] described complications such as wound healing disturbances, superficial infection, and hematoma. There was no significant difference observed in terms of any postoperative complications between the 2 groups (OR = 0.43; 95% CI: 0.17–1.10; $P = .08$). There was no evidence of heterogeneity between trials ($I^2 = 5\%$, $P = .37$) (Fig. 11, Table 2).

4.10. Sensitivity analysis

Sensitivity analysis was performed to investigate the influence of a single study on the overall outcome estimate by omitting one study in each turn. Postoperative complications in the PRP group were significantly different from that in the control group when omitting anyone of the studies except Guerreiro et al.[21] The results of sensitivity analysis of other outcomes were not

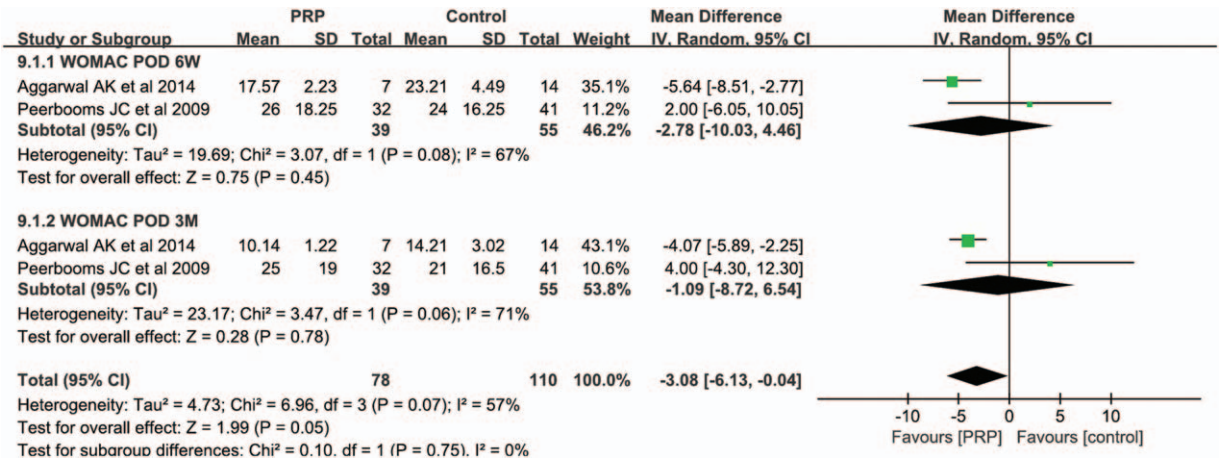

Figure 9. Forest plot analyses of WOMAC score in total knee arthroplasty.

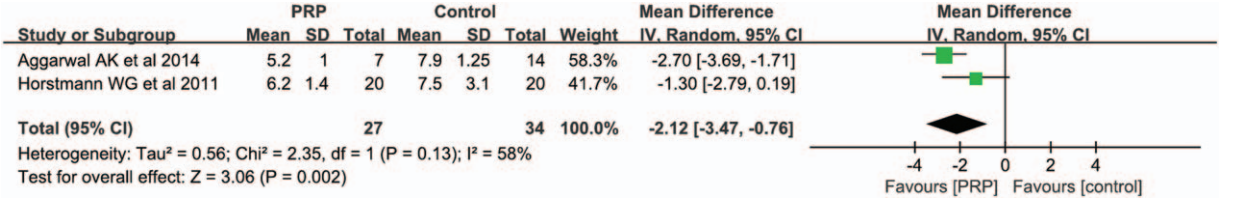

Figure 10. Forest plot analyses of length of stay in total knee arthroplasty.

materially differentiated compared with those of the original analysis.

5. Discussion

To our knowledge, this is the first meta-analysis of RCTs comparing the efficacy and safety of PRP with control for reduction of blood loss after TKA. We found that the application of PRP for patients undergoing TKA reduced more calculated total blood loss and lowered Hb drop compared with control in the early postoperative period; however, there were no significant differences in the drain volume, Hb level, transfusion rate, ROM, and WOMAC scores between the 2 groups. Furthermore, the administration of PRP did not increase the risk of postoperative complications.

PRP applied during TKA has been shown to be effective and safe in reducing blood loss and lowering Hb drop. Mochizuki et al[22] concluded that the administration of PRP significantly reduced postoperative blood loss and calculated total blood loss and significantly maintained lower decrease in Hb in patients undergoing TKA compared with the control group. Aggarwal et al[5] also revealed that a less decrease in Hb was found in the patients of APG group compared with the control group. Similar outcomes were found by 2 pieces of retrospective studies written by Gardner et al[13] and Berghoff et al,[12] which were not included in our meta-analysis. However, Morishita et al[23] did not find a significance in blood loss. Peerbooms et al[20] and Horstmann et al[14] revealed no statistically significant difference in lowering Hb drop. In our meta-analysis, we found blood loss and Hb drop on POD 1 after TKA in the PRP group to be significantly lower than those in the control group.

Postoperative bleeding may cause formation of hematomas and seromas resulting in pain, restricting the ROM, prolonging length of hospital stays.[25] Therefore, Minimizing the blood loss may avoid these condition, and we compared these indicators to assess the blood loss indirectly. Our meta-analysis revealed the PRP group may decrease length of hospital stay in patients undergoing a TKA compared with the control group. Aggarwal et al[5] found that the length of hospital stay in the APG group was 4 to 8 (mean 5.2) days compared with the control group with 6 to 11 (mean 7.9) days. Horstmann et al[14] found that the total length of hospital stay was 6.2 (1.4) days in the platelet gel group against 7.5 (3.1) days in the control group with 1.3 days shorter in the experimental group. These results are similar to the previous researches performed by Everts et al[25] and Gardner et al.[13] The shorter length of hospital stay could also save the hospitalization costs.

However, statistically significant differences were not found in drainage volume, Hb level, transfusion rate, ROM, WOMAC score, and complications between the 2 groups. Among the included studies, different kinds of drainage and different methods to calculate drainage volume were used, which may be the reason why PRP did not significantly reduce drainage volume compared with the control group. In addition, requirements of blood transfusion were associated with the hemoglobin level. Horstmann et al[14] and Guerreiro et al[21] revealed that there was no significant difference in postoperative hemoglobin level, so was transfusion rate, the possible reason of which may be the small number of patients. Even though Aggarwal et al[5] indicated clearly that APG group had increased ROM on POD5, at 6 weeks, and 12 weeks and lower WOMAC scores at 6 and 3 months, respectively than the control group, our meta-analysis did not found that the WOMAC score and ROM in the PRP group significantly differed from that in the control group.

We found that administration of PRP for patients undergoing TKA did not increase the occurrence of complications compared with the control group and then may shorten the period of hospitalization. Moreover, PRP with high concentrations of immune cell could act as antibacterial agents, inhibiting inflammatory response.[26]

Most of the observed heterogeneity appeared to be attributed to clinical practice or methodology of the trial. The use of drainage and the way each experiment applied PRP may resulted in the high risk of the inaccurate outcomes but subgroup analyses

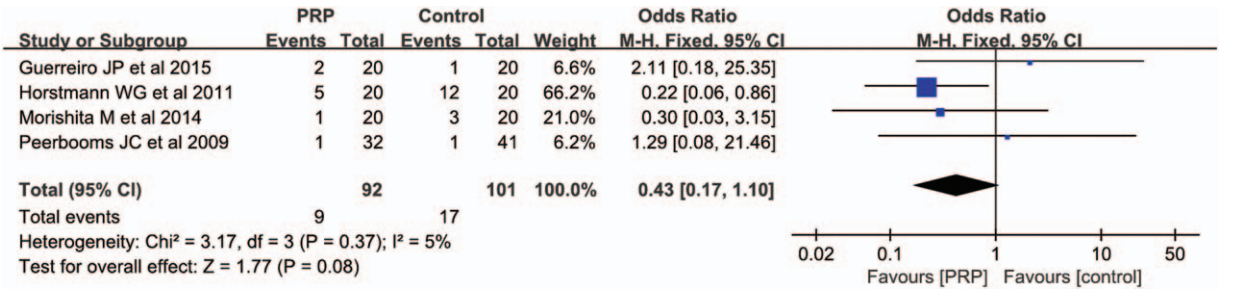

Figure 11. Forest plot analyses of complications in total knee arthroplasty.

based on the number of participants were not carried out owing to the insufficient data required for further confirmation.

There are 4 main limitations in our meta-analysis. First, we included only studies written in English, so some relevant studies in other languages may have been missed. Second, only 6 reports were included, and the sample size of each study was small, which limited the statistical power of our meta-analysis. Third, the variation of the doses of PRP among the studies might also be a problem. Finally, outcomes of hidden blood loss, cost, and postoperative swelling were not analyzed owing to insufficient data. Hence, further research into the comparative efficacy and complications between the application of PRP and control for blood preservation during TKA is required.

6. Conclusion

The application of PRP has significant effect in reducing postoperative blood loss and lowering Hb drop without increasing the risk of postoperative complications compared with the control for blood management in patients undergoing TKA. No significant differences were seen in the drain volume, Hb level, transfusion rate, ROM, and WOMAC scores between the 2 groups. However, owing to the limitations in the included studies, more large-sample and high-quality clinical trials and systemic reviews are needed in the future to demonstrate the efficacy and safety of PRP applied in TKA.

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References

[1] Cheung A, Goh SK, Tang A, et al. Complications of total knee arthroplasty. Curr Orthop 2008;22:274–83.
[2] Maniar RN, Kumar G, Singhi T, et al. Most effective regimen of tranexamic acid in knee arthroplasty: a prospective randomized controlled study in 240 patients. Clin Orthop Relat Res 2012; 470:2605–12.
[3] Klein HG. Allogeneic transfusion risks in the surgical patient. Am J Surg 1995;170:21S–6S.
[4] Varney SJ, Guest JF. The annual cost of blood transfusions in the UK. Transfus Med 2003;13:205–18.
[5] Aggarwal AK, Shashikanth VS, Marwaha N. Platelet-rich plasma prevents blood loss and pain and enhances early functional outcome after total knee arthroplasty: a prospective randomised controlled study. Int Orthop 2014;38:387–95.
[6] Tenholder M, Cushner FD. Intraoperative blood management in joint replacement surgery. Orthopedics 2004;27:s663.
[7] Lemaire R. Strategies for blood management in orthopaedic and trauma surgery. J Bone Joint Surg Br 2008;90:1128–36.
[8] Molloy DO1, Archbold HA, Ogonda L, et al. Comparison of topical fibrin spray and tranexamic acid on blood loss after total knee replacement: a prospective, randomised controlled trial. J Bone Joint Surg Br 2007;89:306–9.
[9] Benoni G1, Fredin H. Fibrinolytic inhibition with tranexamic acid reduces blood loss and blood transfusion after knee arthroplasty: a prospective, randomised, doubleblind study of 86 patients. J Bone Joint Surg Br 1996;78:434–40.
[10] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;10:1006.
[11] Mehta S, Watson JT. Platelet rich concentrate: basic science and current clinical applications. J Orthop Trauma 2008;22:432–8.
[12] Berghoff WJ, Pietrzak WS, Rhodes RD. Platelet-rich plasma application during closure following total knee arthroplasty. Orthopedics 2006;29: 590–8.
[13] Gardner MJ, Demetrakopoulos D, Klepchick PR, et al. The efficacy of autologous platelet gel in pain control and blood loss in total knee arthroplasty. An analysis of the haemoglobin, narcotic requirement and range of motion. Int Orthop 2007;31:309–13.
[14] Horstmann WG, Slappendel R, van Hellemondt GG, et al. Autologous platelet gel in total knee arthroplasty: a prospective randomized study. Knee Surg Sports Traumatol Arthrosc 2011;19:115–21.
[15] Gardner MJ, Demetrakopoulos D, Klepchick PR, et al. The efficacy of autologous platelet gel in total knee arthroplasty: an analysis of range of motion, hemoglobin, and narcotic requirements. Int Orthop 2007;31:309–13.
[16] Kuang MJ, Han C, Ma JX, et al. The efficacy of intraoperative autologous platelet gel in total knee arthroplasty: A meta-analysis. Int J Surg 2016;36:56–65.
[17] Li FX, Li Y, Qiao CW, et al. Topical use of platelet-rich plasma can improve the clinical outcomes after total knee arthroplasty: A systematic review and meta-analysis of 1316 patients. Int J Surg 2016;38:109–16.
[18] Higgins JPT, Green S. Cochrane handbook for systematic reviews of 389 interventions version 5.1.0 [updated March 2011]. The Cochrane collaboration; 390 2011. Available at: http://www.cochrane-handbook.org. Accessed March 20, 2011.
[19] Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. BMJ 2004;328:1490.
[20] Peerbooms JC, de Wolf GS, Colaris JW, et al. No positive effect of autologous platelet gel after total knee arthroplasty. Acta Orthop 2009;80:557–62.
[21] Guerreiro JP, Danieli MV, Queiroz AO, et al. Platelet-rich plasma (PRP) applied during total knee arthroplasty. Rev Bras Ortop 2015;50: 186–94.
[22] Mochizuki T, Yano K, Ikari K, et al. Platelet-rich plasma for the reduction of blood loss after total knee arthroplasty: a clinical trial. Eur J Orthop Surg Traumatol 2016;26:901–5.
[23] Morishita M, Ishida K, Matsumoto T, et al. Tsumura N Intraoperative platelet-rich plasma does not improve outcomes of total knee arthroplasty. J Arthroplasty 2014;29:2337–41.
[24] Gross JB. Estimating allowable blood loss: corrected for dilution. Anesthesiology 1983;58:277–80.
[25] Everts PA, Devilee RJ, Brown Mahoney C, et al. Platelet gel and fibrin sealant reduce allogeneic blood transfusions in total knee arthroplasty. Acta Anaesthesiol Scand 2006;50:593–9.
[26] Bielecki TM, Gazdzik TS, Arendt J, et al. Antibacterial effect of autologous platelet gel enriched with growth factors and other active substances: an in vitro study. J Bone Joint Surg Br 2007;89:417–20.