Effectiveness of platelet-rich plasma in the treatment of anterior cruciate ligament injuries: A Systematic Review and Meta-analysis

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Research Article

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Abstract

Background: Recently, a number of randomized controlled trials (RCTs) have researched the efficacy of anterior cruciate ligament reconstruction (ACLR) combined with platelet-rich plasma (PRP) in the treatment of anterior cruciate ligament (ACL) injuries. Therefore, we updated a systematic review based on these RCTs to evaluate the effects of PRP on knee function and pain with different time.

Methods: We searched in PubMed, Embase, Cochrane, Web of Science(WOS), China National Knowledge Infrastructure(CNKI), and WANFANG DATABASE, for human RCTs comparing the efficacy of intraarticular injection with no injection of PRP. Descriptive summaries and quality assessments were performed for all studies included in this meta-analysis. The outcomes of the study included the International Knee Documentation Committee (IKDC), Visual Analogue Scale (VAS), and Lysholm score.

Results: Finally, we included 6 RCTs studies, involving 315 patients. The control group consisted of blank group or placebo group. Follow-up periods ranged from 3 to 18 months. The results of bias risk assessment showed that all the 6 studies are unclear risk of bias. Compared with the control group, PRP group significantly improved IKDC score at 3, 6 and 12 months after operation (P = 0.00, 0.01, respectively). Lysholm score and VAS score also has significant differences at 3 months after operation (both P = 0.00).

Conclusion: Our study has proved that PRP was more effective in the recovery of knee function and early pain relief after the ACLR than the ACLR alone. Review registration: PROSPERO CRD42021224182. Registered 6 April 2021. Keywords:anterior cruciate ligament injury; anterior cruciate ligament reconstruction; platelet rich plasma; system review; META analysis

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Background

With the development of economy, more and more people do exercise. And anterior cruciate ligament(ACL) injury becomes a common injury in sports. Chen Lianxu et al. conducted an epidemiological analysis of 352 patients with anterior cruciate ligament and found that compared with women, men were more prone to ACL injuries, and most of the injuries in men were caused by sports injuries (such as basketball, football, skiing and badminton) [1]. An Anterior Cruciate Ligament Reconstruction (ACLR) epidemiological survey with 248,234 Italians (adults over 15 years old) in 2001 to 2015 measured by Longo et al. showed that the annual incidence rate of ACL injury ranged from 21.70 to 33.60 per 100,000 population, with a male-to-female ratio of 4.54, and the highest occurrence age ranged from 15 to 39 years. The number of patients undergoing ACLR was predicted to increase by 24.16% in 2016 to 2025, reaching a platform [2]. However some studies have shown that female athletes were more prone to ACL injuries than male athletes [3].

The function of the ACL is to stabilize the knee joint and prevent the tibia from moving forward. The injury of the ACL will cause knee instability, damage to articular cartilage and meniscus, and increase the risk of knee osteoarthritis [1, 4, 5, 6, 7, 8].
The causes of anterior cruciate ligament injury are not only mechanical factors but also anatomical factors. Kızılgöz et al. found that the notch width, notch width index, and medial tibial slope were the most important parameters in risk assessment of ACL injury[9]. There are many factors relating to the occurrence of ACL injury, such as the narrow tibial intercondylar ridge, the larger posterior inclination of the lateral tibial plateau, and the smaller ratio of the width of the tibial intercondylar ridge to the width of the femoral intercondylar concave [10].

The main repair treatment of ACL injury is arthroscopic ACLR, which contains autologous tendon transplantation, allogeneic tendon transplantation and artificial ligament transplantation. The tendons subjects of transplantation compose of hamstring tendon, peroneus longus tendon, semitendinosus and gracilis tendon, and artificial ligaments are mainly LARS ligaments [1, 11, 12, 13, 14, 15].

Platelet rich plasma (PRP) is the platelet concentrate obtained from autologous blood after centrifuging, which contains a large number of growth factors, such as PDGF, TGF-β, IGF-1 etc. [16]. These growth factors can repair and regenerate tissues[17, 18, 19]. PRP can shorten the healing time of acute wounds, relieve trauma pain, and control post-injury infection [20].

PRP was first used in orthopedic surgery, and then continuous research, platelet-rich plasma has also been used in the treatment of orthopedic diseases. For example, it can promote the healing of bone and cartilage and improve the symptoms of knee osteoarthritis [21, 22, 23, 24, 25, 26].

Some randomized controlled trials and meta-analyses suggested that PRP had no promoting effect on graft healing, pain relief and knee function after ACLR [27, 28]. This study was a systematic review and meta-analysis based on the use of ACLR in combination with PRP to observe whether ACLR can relieve pain and improve knee function after ACL injury.

Methods

This systematic review was registered online in PROSPERO (registration number: ) and was performed following the guidelines of the PRISMA statement.

2.1 Inclusion and exclusion criteria

Inclusion criteria: 1 Patients with ACL rupture after diagnosis and need to undergo ACLR (or with meniscus injury); 2 Patients in the intervention group received ACLR combined with PRP, and patients in the control group received ACLR combined with placebo or no treatment; 3 Follow-up time was divided into 3 months, 6 months, 9 months and 12 months; 4 Outcomes should contain one of the International Knee Documentation Committee (IKDC) and the Visual Analogue Scale (VAS), Lysholm score, KT1000/2000 arthrometer, measured value of bone tunnel.

Exclusion criteria: 1 MRI or physical examination suggests collateral ligament injury, muscle injury or combined with fracture; 2 Middle-advanced osteoarthritis (Kellgren-Lawrance grade ≥2), complicated with rheumatoid arthritis, gout, and obvious varus deformity (> 5°); 3 Diabetes mellitus, blood disease, severe
2.2 search strategy

The two researchers separately searched the literature from June 1996 to June 2020 in PubMed, Cochrane, Web of Science, Embase, China National Knowledge Infrastructure (CNKI), and Wanfang DATABASE. The search method in PubMed as follow:((((((((((("Platelet-Rich Plasma"[Mesh]) OR (Plasma, Platelet-Rich[Title/Abstract])) OR (Platelet Rich Plasma[Title/Abstract])) AND ('Anterior Cruciate Ligament'[Mesh]) OR (ACL Injuries[Title/Abstract]) OR (ACL Injury[Title/Abstract]) OR (Injuries, ACL[Title/Abstract]) OR (Injury, ACL[Title/Abstract]) OR (Anterior Cruciate Ligament Injury[Title/Abstract]) OR (Anterior Cruciate Ligament Tear[Title/Abstract]) OR (ACL Tears[Title/Abstract]) OR (ACL Tear[Title/Abstract]) OR (Tear, ACL[Title/Abstract]) OR (Tears, ACL[Title/Abstract]) OR (Anterior Cruciate Ligament Tears[Title/Abstract]). If two researchers find discrepant literature, they will discuss inclusion with a third researcher. We registered on PROSPERO, the number is CRD42021224182.

2.3 Main Outcomes

The primary outcomes were IKDC score, VAS score, Lysholm score, KT1000/2000 arthrometer, and measured value of bone tunnel.

2.4 Data analysis

Data was analyzed by State16.0. Mean difference (MD) was used for continuous variables, and hazard ratio (RR) was used for dichotomous variables as effect analysis statistics. All statistics were rated by 95% Confidence Interval (CI) values. We assumed heterogeneity and used a random-effects model in all pooled analyses. I² was used to test for heterogeneity, and there is no heterogeneity when I² ≤ 50% (otherwise there is heterogeneity). If there is heterogeneity, the source of heterogeneity can be further analyzed by subgroup analysis or sensitivity analysis. If over 10 articles were included, funnel plots were used to assess publication bias. A P value less than 0.05 was considered to be statistically significant.

Results

3.1 Study Characteristics

Finally, a total of 6 RCTs studies were included in our study [29, 30, 31, 32, 33, 34]. The retrieval strategy is shown in Figure 1.

A total of 325 patients received experimental treatment, but 10 patients were lost during the follow-up [30, 33], so 315 patients were included in the final results. There were 157 in the PRP group and 158 in the placebo group. Baseline data of all patients and surgical procedures were shown in Figure 2. In the
included literatures, the results of the control group and the PRP group showed that PRP did not promote graft healing, pain relief and knee function after ACLR [32, 33]. Others literature showed that compared with the control group, the PRP group showed that PRP had a promoting effect on graft healing, pain relief and knee function in the early stage [29, 30, 31, 34]. All studies used IKDC to evaluate knee function. Although all the studies were followed up for at least 3 months, only one study was followed up for only 3 months, the longest was followed up for 18 months, and the rest were followed up for 12 months. Table 1

The procedure and use of PRP are different in different therapeutic conditions. Table 2.

3.2 Risk of Bisa Assessment

We used RoB2 software to accomplish bias analysis, and the results are shown in Figure 2. Blind method was impossible for both researchers and patients owing to surgery, leading to an unclear risk of bias of intervention [29-34]. One study described only the population baseline of the total patients, but did not describe the population baseline of the PRP group and the control group, so its random process bias is unclear risk of bias[32]. Figure 2

3.3 IKDC

At 3 months, IKDC scores were reported in 4 studies, and PRP treatment was statistically significant compared with the control group (MD, 6.68 [95%CI, 3.01 to 10.34] I²=63.75%, P =0.00). At 6 months, three studies showed a statistically significant difference between the PRP group and the control group (MD, 5.47 [95%CI, 3.95 to 6.99] I²=0.00%, P =0.00). At 12 months, four studies also favored the PRP group (MD, 3.75 [95%CI, 0.75 to 6.75] I²=76.81%, P =0.01). The overall response rate in the PRP group was also statistically significant compared with the control group (MD, 5.00 [95%CI, 3.14 to 6.85] I²=74.25%, P =0.00). Figure 3

3.4 Lysholm

At 3 months, Lysholm scores were reported in 3 studies, and PRP treatment was found to be statistically significant compared with the control group (MD, 5.83 [95%CI, 2.36 to 9.31] I²=62.12%, P =0.00). However, in 3 studies at 6 months (MD, 7.01 [95%CI, -0.38 to 14.41] I²=92.75%, P =0.06) and 12 months (MD, 2.60 [95%CI, -3.10 to 8.30] I²=95.28%, P =0.37), the PRP group was not statistically significant compared with the control group. In totally, the PRP group was superior to the control group in terms of overall response rate (MD, 5.47 [95%CI, 3.95 to 6.99] I²=0.00%, P =0.00). Figure 4.

3.5 VAS

VAS scores were reported in two literatures, but their follow-up time was 3, 6, 18 months and 3, 12 months respectively, so we only reported the results of a 3-month meta-analysis of VAS [30, 34]. The final results showed that the PRP group was statistically significant compared with the control group (MD, 5.29 [95%CI, 2.47 to 8.11] I²=95.26%, P =0.00). Figure 5

3.6 Heterogeneity analysis
Heterogeneity of each subgroup was tested by shear and complement method. After the removal of Li[34] and Chen[29] in the IKDC score 3 months after surgery, heterogeneity was reduced (I² ≤ 50%). Heterogeneity of 12 months was caused by Zang[31]. The heterogeneity of Lysholm score 3 months after surgery was also caused by Li[34] and Chen[29]. Heterogeneity at 6 and 12 months after surgery was due to Zang[31]. We analyzed the reasons for the heterogeneity by intensice reading these studies, the results as follows. Patients in Li's study had meniscus injury. Patients in his control group were treated blank, while the others were treated with injections of normal saline. In Li's study, the injection of PRP lasted for the longest time, at 4ml per week for 6 weeks. In Chen's study, PRP was injected only once during surgery. Zang's study also included patients with meniscus injuries, and the number of patients included in his study was larger than the other studies (112 patients).

Discussion

Six articles were included in our study, but only five were used in our meta-analysis. According to the data analysis of the 5 studies at 3, 6 and 12 months, the application of PRP in the reconstruction of the ACL after ACL injury has a significant effect on the recovery of knee function and the relief of early pain.

In the beginning, the expected outcome of two studies all reported the measured value of KT-1000, but one of them did not mention the measured value [31]. We have not been able to contact the author of this study, so only one paper reported the results of KT-1000 at 3 months [33]. We did not conduct a meta-analysis of this outcome.

In a prospective study, Silva et al. divided 40 patients into four groups, all of whom received ACL repair of the hamstring tendon. Patients in the 4 groups were then treated with different PRP treatments: group A without PRP; Group B underwent PRP in the femoral tunnel at the end of operation; Group C: PRP was injected into the femoral tunnel and intraarticular at 2 and 4 weeks postoperatively; Group D: PRP was activated by thrombin in femoral artery. All patients underwent magnetic resonance imaging (MRI) of the knee at 3 months postoperatively to assess signal intensity in the fibrous interzone (FIZ) of the femoral tunnel. Finally, no difference in FIZ signal intensity was found among each group [35]. A RCT by Seijas et al. showed that MRI examination of graft signals in the PRP group and the control group showed higher remodeling at 4 months (P =0.003), 6 months (P =0.0001) and 12 months (P =0.354) than in the control group. However, it was only at 4 and 6 months that the PRP group was statistically significant compared with the control group [36]. Li Yang et al. used rabbit autologous PRP to rebuild the ACL of the grafts and conducted the anti-pull test and dyeing technology. The results showed that after 4-8 weeks, the necrotic tissue was significantly reduced in the PRP group, and a large number of fibroblasts and collagen fibers were grown in regular and orderly arrangement, which was significantly better than that in the control group. The tensile test also showed that the strength of PRP group was significantly stronger than that of the control group [41]. Gao et al. used PRP combined with self-made silk artificial ligament to reconstruct the rabbit ACL and found that the silk ligament was gradually covered with collagen fibers postoperative, and the new blood vessels and new cells gradually grew in. At 16 weeks after surgery, the graft was similar to the normal ACL, and the morphology of new cells was similar to fibroblasts. There were significant
differences in the area of new blood vessels and the number of fibroblasts between PRP group and control group at 4, 8 and 12 weeks postoperatively. There was no statistically significant difference between the two groups 16 weeks after surgery [42].

The Meta-analysis of Lysholm score in our study showed that the PRP group was superior to the control group at 3 months postoperatively, but the overall results showed that the PRP treatment was superior to the control group.

A systematic review of 13 literatures included by Martin et al. showed that only two studies on bone tunnel diameter and grafts on MRI were better in the PRP group than in the control group. Another study showed a statistically significant reduction in postoperative pain levels 12 months after ACLR in the group that received PRP. However, they argue that the current level of evidence does not support the use of PRP to improve graft healing, reduce postoperative pain levels, or improve functional outcomes after ACLR [39]. Figueroa et al.'s systematic review included 11 articles for analysis, of which 3 mentioned the efficacy of PRP for the treatment of ACL injuries. One study showed that after 4-6 weeks, the vascularization of the osteoprotegerin interface was significantly higher in the PRP group than in the control group. One study showed that it took only 48% of the time for PRP group to obtain the same MRI results after ACLR compared with the control group. In one study, CT showed a statistically significant difference in ACL density between the two groups (P<0.01), and ACL density in the PRP group was similar to that in the posterior cruciate ligament [40]. The Meta-analysis of Huang et al. concluded that in Lysholm score, the PRP group was superior to the non-PRP group at 3 and 6 months postoperative, and there was no significant difference between the two groups at 12 months after surgery. In terms of IKDC score, the PRP group was superior to the non-PRP group 3 and 6 months postoperative [38].

As the included literature could only collect VAS scores at 3 months after surgery, it was shown that PRP had a significant effect on pain relief at 3 months after the ACLR. Andre et al.'s meta-analysis showed that PRP significantly alleviated pain effects 6 and 12 months after ACLR surgery, but it had no clinically relevant effect on pain and did not relieve pain effects 24 months after ACLR surgery. It was also shown that PRP did not significantly improve knee function after ACLR [37].

**Limitation**

Six studies were eventually included in our study, but one study was not reported, because the data of KT-1000 at 3 months was reported in this study [33], but there was no matching data for meta-analysis. Although the data of bone tunnel were reported in the included literatures, but different studies used different techniques and locations to measure bone tunnel, so we did not conduct a meta-analysis on this data. Although studies by Mirzatolooeei and Vadala have shown that PRP is not effective in preventing the enlargement of bone tunnels, larger studies with larger sample sizes are needed [33, 43]. Because there was not enough VAS data, we only reported the Meta-analysis data of the VAS at 3 months. It is hoped that these two data results can be completed in the subsequent studies.
In our study, only 325 patients were included in the RCTs, 10 were lost to follow-up, and only 315 patients were finally included in the study. The sample size is too small, and more samples are needed for verification. The RCT experiment we studied did not use blind method in the whole process of the experiment, which resulted in the low quality of the included studies. When we included the studies, we excluded the literatures that reprocessed PRP, such as the trials that used PRP gel, PDGF factor, etc. Because we were not sure whether this procedure would affect the factors in PRP and thus affect the results, it also led to the reduction of the number of included studies.

Meanwhile, the concentration of PRP injected during surgery was not described in detail in the included studies, and animal experiments have shown that different concentrations of PRP have different effects on the bone mineral density at the tendon-bone interface and the expansion of bone tunnel [44]. Therefore, further studies are needed to explore the effect of uniform PRP concentration on ACLR.

None of the included studies indicated the length of the blank period between the time of injury and the time of surgery. Using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database, Agarwalla et al. found that while the overall risk of adverse events after ACL reconstruction remained low, marginal increases in operative time were associated with an increased risk of adverse events. Such as deep vein thrombosis, surgical site infection, sepsis, prolonged stay of hospital, and readmission [52]. Hu et al. believed that autologous ligament transplantation could achieve good results in both early and late ACL reconstruction; However, the knee function and quality of life improved better in early stage patients. Therefore, early autologous ligament grafting is recommended for ACLR. In the knee joint function test after 3 weeks and 3 weeks after surgery, the former group was better than the latter group [53]. Zhang et al. believed that although arthroscopic reconstruction in the early and late stages had the same efficacy in the treatment of ACL injury, the risk of early complications was low, and early surgery was beneficial to the recovery of knee function for patients with meniscus injury [54].

Some of the included studies included patients with combined meniscus injury, but there was no mention of treatment of the injured meniscus in their study[29,34]. Westermann et al. ’s Meta-analysis showed that ACLR combined with total or internal and external meniscus repair had a statistically significant difference in the failure rate of the final ACLR, with the latter having a higher failure rate than the former [55]. Melton et al. believed that ACL injury combined with meniscus tear with ACLR and meniscus repair would have a better effect on knee function recovery than ACLR and meniscus removal [56].

Different grafts also affect the treatment of ACL injuries. Sajovic et al. used hamstring and patellar ligament grafts respectively, and the results showed good subjective effects and objective stability 5 years postoperative. There was no significant difference in the incidence of transplant failure. However, patients receiving patellar ligament grafts have a higher incidence of osteoarthritis 5 years postoperative [45]. Gupta et al. performed arthroscopic reconstruction of ACL using patellar tendon graft and hamstring tendon graft with similar pain scores immediately after surgery [46]. Martin-Alguacil et al. believed that compared with ACLR using hamstring tendon, ACLR using quadriceps tendon transplantation has more advantages [47]. Vilchez-Cavazos et al. found that the clinical effect and postoperative pain of patients with ACL injury treated with autologous quadriceps femoris tendon were similar to those of patients
treated with autologous hamstring tendon [48]. Sajovic et al. found that both semitendinosus tendon and gracilis tendon autograft and autologous patellar tendon autograft had good subjective effects after ACLR. There were no significant differences in graft failure or clinical instability. However, significantly more patients in the semitendinosus and gracilis groups were found to have increased translational volume using the KT-1000 measurement and a higher incidence of knee arthritis 17 years postoperative in the patellar tendon autologous group [49]. Aglietti et al. found no clinical difference between the use of the patellar tendon and the double semitendinosus tendon and gracilis tendon grafts for ACLR [50]. Feller et al. obtained satisfactory functional results for ACLR with two grafts of patellar tendon and hamstring tendon, but knee pain and extension dysfunction increased in the patellar tendon group, knee relaxation increased in the hamstring tendon group, and the femoral tunnel widened radiographic results [51].

**Conclusion**

The use of PRP for ACLR significantly improved IKDC scores at 3, 6 and 12 months postoperatively. Lysholm score and VAS score 3 months after surgery. It is proved that PRP is effective in the recovery of knee function and early pain relief after ACLR.

**Declarations**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

Not applicable.

**CONSENT FOR PUBLICATION**

We all authors decide to publication(supplementary material **File 1**).

**AVAILABILITY OF DATA AND MATERIALS**

Not applicable.

**COMPETING INTERESTS**

The authors declare no competing interests

**FUNDING**

Not applicable.

**AUTHORS’ CONTRIBUTIONS**
XG, WF, ZL, and JZ conceived and designed the experiments. XG, WF, ZL, and ZX searched and screened the studies. XG, WF, and ZL extracted and analyzed the data. XG, WF, ZL, JZ, and CM wrote and revised the manuscript. All authors read and approved the final manuscript.

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Abbreviations

randomized controlled trials: RCTs; anterior cruciate ligament: ACL; platelet-rich plasma: PRP; anterior cruciate ligament reconstruction: ACLR; anterior cruciate ligament reconstruction: ACLR; Visual Analogue Scale: VAS; Mean difference: MD; hazard ratio: RR; Confidence Interval: CI

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Tables

Tables 1 and 2 can be found in the supplementary files section.

Figures
Figure 1
The process of literatures selection.

|                         | Randomization process | Deviations from intended interventions | Missing outcome data | Measurement of the outcome | Selection of the reported | Overall |
|-------------------------|-----------------------|----------------------------------------|----------------------|---------------------------|--------------------------|---------|
| Li Weifeng 2018.06      | +                     | ?                                      | +                    | +                         | +                        | ?       |
| Chen Rongjin 2020.04    | +                     | ?                                      | +                    | +                         | +                        | ?       |
| Ji Qingming 2017.04     | +                     | ?                                      | +                    | +                         | +                        | ?       |
| Zang Yefeng 2019.09     | +                     | ?                                      | +                    | +                         | +                        | ?       |
| F. Mirzatolooei 2013.01 | +                     | ?                                      | +                    | +                         | +                        | ?       |
| M. Komzák 2015          | ?                     | ?                                      | +                    | +                         | +                        | ?       |

Risk of bias summary of all included studies. Methodological quality assessment of each study at 8 domains was illustrated. “+” means low risk of bias, “?” means unclear risk of bias, and “?” means high risk of bias.

Figure 2
Results of bias analysis with RoB2 software.
Figure 3

Forest plots of PRP on IKDC at 3, 6 and 12 months.
### Figure 4

Forest plots of PRP on Lysholm at 3, 6 and 12 months.

| Study or Subgroup | PRP | Control | Mean Diff. with 95% CI | Weight (%) |
|-------------------|-----|---------|-----------------------|------------|
| **Lysholm At 3 months** |     |         |                       |            |
| Li 2018.06        | 21  | 71.33   | 3.18 [ 0.48, 5.88]    | 12.31      |
| Chen 2020.04      | 20  | 65.09   | 7.61 [ 4.59, 10.63]   | 11.98      |
| Ji 2017.04        | 17  | 71.18   | 8.07 [ 1.46, 14.68]   | 7.87       |

Heterogeneity: $\chi^2 = 5.56$, $I^2 = 62.12\%$, $H^2 = 2.64$

Test of $\theta = 0$: $Q(2) = 5.28$, $p = 0.07$

Test of $\theta = 0$: $z = 3.30$, $p = 0.00$

| **Lysholm At 6 months** |     |         |                       |            |
| Li 2018.06            | 21  | 84.66   | 3.46 [ 0.63, 6.29]    | 12.17      |
| Chen 2020.04          | 20  | 68.92   | 3.63 [ -1.83, 9.19]   | 9.01       |
| Zang 2019.09          | 56  | 86.2    | 13.50 [ 10.75, 16.25] | 12.26      |

Heterogeneity: $\chi^2 = 38.88$, $I^2 = 92.75\%$, $H^2 = 13.80$

Test of $\theta = 0$: $Q(2) = 27.60$, $p = 0.00$

Test of $\theta = 0$: $z = 1.86$, $p = 0.06$

| **Lysholm At 12 months** |     |         |                       |            |
| Chen 2020.04           | 20  | 84.23   | 0.51 [ -1.39, 2.41]   | 13.06      |
| Ji 2017.04             | 17  | 83.53   | -1.36 [ -8.16, 5.44]  | 7.68       |
| Zang 2019.09           | 56  | 96.3    | 7.20 [ 6.26, 8.14]    | 13.67      |

Heterogeneity: $\chi^2 = 21.95$, $I^2 = 95.28\%$, $H^2 = 21.20$

Test of $\theta = 0$: $Q(2) = 42.40$, $p = 0.00$

Test of $\theta = 0$: $z = 0.89$, $p = 0.37$

**Overall**

Heterogeneity: $\chi^2 = 14.89$, $I^2 = 90.08\%$, $H^2 = 10.09$

Test of $\theta = 0$: $Q(8) = 80.68$, $p = 0.00$

Test of group differences: $Q_{G}(2) = 1.16$, $p = 0.56$

Test of $\theta = 0$: $z = 3.68$, $p = 0.00$

Random-effects DerSimonian-Laird model
Figure 5

Forest plots of PRP on VAS at 3 months.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- PRISMA2009checklist.doc
- Table1.docx
- Table2.docx