


# Platelet rich plasma versus glucocorticoid for plantar fasciitis

## A protocol for systematic review and meta-analysis of randomized controlled trials

Rongrong Ge, MM, Shuying Chen, MM, Jiawang Jiang, MM, Bangmin Wang, MM, You Zeng, MM, Qianan Cao, MM, Jun Wu, MM\* , Yunfeng Liu, MM

### Abstract

**Background:** Plantar fasciitis (PF) is the most common cause of heel pain in adult. There are a variety of ways to treat PF, but these treatments have varied result in their effectiveness, and exist different degrees of limitations. At present, clinical studies focus on the effect of glucocorticoid (GC) and platelet rich plasma (PRP) in the treatment of PF, but there is a lack of systematic evaluation PRP and GC's clinical effect towards PF. This study aims to evaluate the long-term efficacy of GCs and PRP in the treatment of PF by means of meta-analysis.

**Methods:** The literature of a randomized controlled clinical trial of PRP in the treatment of plantar fasciitis was searched on the Internet. Retrieve 7 databases. EndNote X9 software was used for document management. The Jadad scale was used to score the literature. Risk assessment of the literature was conducted according to Cochrane's systematic evaluation manual 5.0. RevMan5.3 software was used for literature risk bias analysis. Stata12.0 software is used for sensitivity analysis.

**Results:** This study will provide effective evidence-based evidence for the long-term efficacy of PRP and GC in treating PF.

**Conclusion:** A systematic review and meta-analysis were conducted for the comparison of the long-term effect of PRP and GC on plantar fascia in the treatment of PF.

**Abbreviations:** GC = glucocorticoid, PF = plantar fasciitis, PRISMA-P = Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols, PRP = platelet rich plasma, RCT = randomized clinical trial.

**Keywords:** glucocorticoid, meta-analysis, plantar fasciitis, platelet rich plasma, protocol, systematic review

## 1. Introduction

Plantar fasciitis (PF) is a self-limited disease characterized by pain in the medial plantar after getting up or prolonged sitting along with mild plantar flexion and varus in the foot during

walking and localized tenderness in the medial side of calcaneal tuberosity.<sup>[1,2]</sup> PF is the most common cause of chronic heel pain in adults.<sup>[3]</sup> The pathological mechanism of PF is unclear, but it has been widely accepted for medical workers that PF is caused by heavy load or excessive tension results in a slight tear in the fascia. And under continuous micro tears and chronic damage accumulation, the chronic inflammation of the fascia is building up.<sup>[4]</sup> Also, some scholars believe that the emergence of the disease is closely related to obesity, standing up for a long time, incorrect walking posture, unfit shoes, the habit of work and study, and other factors.<sup>[5,6]</sup> According to epidemiological studies, the incidence of PF in the United States is about 10%,<sup>[7]</sup> and it is estimated that PF accounts for 11% to 15% of all foot diseases.<sup>[8]</sup> Besides, studies have found that most PF patients are aged between 25 and 64 years old, with the highest incidence between 45 and 64.<sup>[9]</sup> Moreover, the incidence rate of athletes or regular runners and soldiers is significantly higher than that of the general population, which is about 4% to 22%.<sup>[10]</sup>

At present, the treatment of PF focuses on pain relief, and mainly adopt conservative treatment. Common treatment measures include having a rest, icing plantar locally, using non-steroidal anti-inflammatory drugs, adopting physical therapy, using foot orthoses, injecting corticosteroid, etc.<sup>[1,11]</sup> However, although there are a variety of ways to treat PF, these treatments have varied result in their effectiveness, and exist

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Jiangxi University of Traditional Chinese Medicine, Nanchang, China.

\* Correspondence: Jun Wu, Jiangxi University of Traditional Chinese Medicine, No. 1688 Meiling Avenue, Wanli District, Nanchang City 330004, Jiangxi, China (e-mail: 12188702@qq.com).

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**Table 1**  
**Search strategy used in PubMed database.**

Order	Search items
#1	((Plasma, Platelet-Rich[Title/Abstract]) OR Platelet Rich Plasma[Title/Abstract])
#2	(((((Plantar Fasciitis[Title/Abstract]) OR Policeman's Heel[Title/Abstract]) OR Heel, Policeman's[Title/Abstract]) OR Heels, Policeman's[Title/Abstract]) OR Policeman Heel[Title/Abstract]) OR Policeman's Heels[Title/Abstract]) OR Policemans Heel[Title/Abstract]) OR Heel Spur Syndrome[Title/Abstract]) OR Chronic Plantar Fasciitis[Title/Abstract]) OR Fasciitis, Chronic Plantar[Title/Abstract]) OR Plantar Fasciitis, Chronic[Title/Abstract]) OR Fasciitis, Plantar, Chronic[Title/Abstract])
#3	((((randomized controlled trial[Publication Type]OR randomized[Title/Abstract]OR placebo[Title/Abstract])))
#4	#1 AND #2 AND #3

different degrees of limitations.<sup>[12]</sup> Therefore, it is very important to find effective treatment for PF.

The research shows that PF is a kind of local inflammation triggered by abnormal tension of both abnormalities of foot and fascia plantaris.<sup>[13]</sup> The pathological manifestation turns to be rupture of fascia fiber and local aseptic inflammation. The common treatment in clinical is to inject glucocorticoid (GC) into the specific point on fascia.<sup>[14]</sup> GC does show a distinguished inhibitory effects when it is up to physiological level. But in the late stage of GC treatment, it easily causes rupture of metatarsal fascia and atrophy of plantar fat pad.<sup>[15]</sup> Focus on this question, the clinical discovered platelet rich plasma (PRP) promotes the proliferation of bone marrow mesenchymal stem cell, adipose mesenchymal stem cell, and tendon cell in plantar fascia,<sup>[16]</sup> and accelerates tendon's repair.<sup>[17]</sup> Which can be used in PF's treatment. Whereas, although there have been some randomized controlled trials (RCTs) of PRP and GC in the treatment of PF, there is a lack of systematic evaluation PRP and GC's clinical effect towards PF. To fulfill it, this study was conducted by meta-analysis, to compare the long-term effect between PRP and GC towards PF. Wish to provide evidence for clinical practice.

## 2. Methods

### 2.1. Protocol registration

The protocol study has been registered on the Inplasy website (registration number is INPLASY2021100067: <https://inplasy.com/inplasy-2021-10-0067/>), and the systematic review protocol of us will be performed strictly following the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) for systematic evaluation and meta-analysis.<sup>[18]</sup>

### 2.2. Source of literature and search strategy

CBMdisc, the Wanfang Chinese digital periodical and conference database, China National Knowledge Infrastructure database, the VIP Chinese Science and Technique Journals Database, the Cochrane Library, PubMed, and EMBASE were been searched from their inception to October 10, 2019. And the English terms was: "Plantar Fasciitis, Policeman's Heel, Heel, Policeman's, Heels, Policeman's, Policeman Heel, Policeman's Heels, Policemans Heel, Heel Spur Syndrome, Chronic Plantar Fasciitis, Fasciitis, Chronic Plantar, Plantar Fasciitis, Chronic, Fasciitis, Plantar, Chronic, Plasma, Platelet-Rich, Platelet Rich Plasma". Taking PubMed's search as an example, the literature search strategies are shown in Table 1.

### 2.3. Inclusion criteria

**2.3.1. Types of studies.** This study only considered clinical RCTs of GCs and PRP in the treatment of PF.

**2.3.2. Types of participants.** Diagnosed PF, meeting clinical diagnosis criteria, did not accept GC or PRP treatment recently.

**2.3.3. Types of interventions.** The intervention measures were PRP and GC local injection into metatarsal fascia, PRP and GC were respectively in treatment group and control group.

**2.3.4. Outcome measures.** The primary outcomes were evaluated by Visual Analogue Scale and Ankle Hindfoot Scale.

### 2.4. Exclusion criteria

- (1) Lack of PRP or adopted GC as intervention;
- (2) Adopted different basic therapy;
- (3) Final indicator does not include Visual Analogue Scale or Ankle Hindfoot Scale;
- (4) Repetitive contents;
- (5) Non-clinical RCT; non-human trial;
- (6) Baseline date (age etc) between 2 group shows a statistical difference;
- (7) Being evaluated to low quality research by Jadad scale.

### 2.5. Selection of studies and data extraction

First of all, eliminate repetitive contents been searched, conducted by EndNote X9. Then, exclude contents against standard after reading their title and abstract. Third, exclude contents against standard after reading the whole contents. Fourth, extraction of literature data. These data contain method of research design, interventions, methodology, baseline date (age etc) between 2 group, final indicator, follow-up and missing situation, etc. What have been mentioned above were conducted by 2 independent evaluators, and any differences that were difficult to determine could be solved by the third independent evaluator. The selection process will be shown in Figure 1 with the PRISMA flow diagram.

Next, 2 independent evaluators will extract data from qualified literature according to a pre-designed data extraction table. The extracted content included author's name, year of publication, article title, sample size, gender and age of participants, diagnostic criteria, information about intervention and control groups, intervention measures, follow-up time, outcome indicators, and outcomes. Any disagreement will be resolved through consultation with a third independent evaluator.

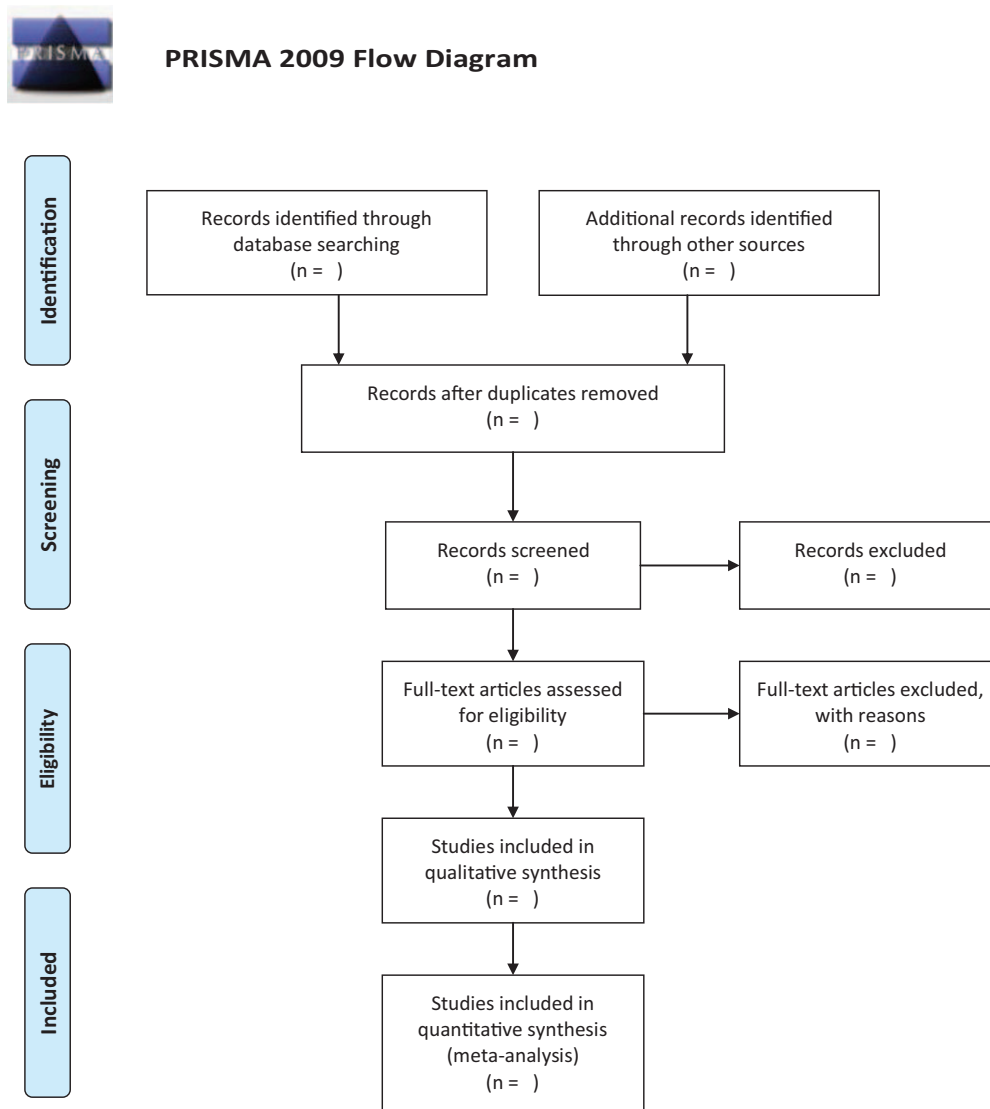


Figure 1. Flow chart of study selection.

### 2.6. Risk of bias assessment

The “risk of bias assessment” tool recommended in Cochrane System Assessment Manual 5.0 was used to evaluate the included clinical randomized controlled studies.<sup>[19]</sup> According to Cochrane Handbook 5.0, ① stochastic method; ② allocation concealment; ③ adopt blinding to volunteers and researchers; ④ adopt blinding to evaluator; ⑤ the completeness of research data; ⑥ selective reporting study outcomes; ⑦ other bias. To decide whether it is low bias risk, bias risk unsure or lack of information. What have been mentioned above were conducted by 2 independent evaluators, and any differences that were difficult to determine could be solved by the third independent evaluator.

### 2.7. Data synthesis and statistical methods

Using Stata12.0 software and RevMan 5.3 software to do statistical treatment, outcome indexes performed in odds ratio. For the dichotomous outcomes, we will use the relative risk to

measure the treatment effect, and for the continuous outcomes, we will use standard mean difference to analyze the effect. Both calculating 95% confidence intervals.

### 2.8. Assessment of heterogeneity

Adopting  $I^2$  test (test level  $\alpha=0.05$ ) to assess statistical heterogeneity of the studies. When  $I^2 < 50\%$ , it indicates that there is a small statistical heterogeneity or no significant statistical heterogeneity between studies, using a fixed effect model; when  $I^2 > 50\%$ , it indicates that the data of studies exist considerable heterogeneity, applying random effects models to do combined analysis. When the heterogeneity is greater, the source of heterogeneity needs to be further analyzed.

### 2.9. Assessment of reporting biases

Galbraith radial plot and Egger test were used to evaluate the potential reporting bias of the inclusion study.

### 2.10. Subgroup analysis and sensitivity analysis

If there is a large heterogeneity between the studies, we will conduct a subgroup analysis to investigate the differences in age and sex, measure of intervention, etc. And we will also use Stata12.0 software for sensitivity analysis to assess the robustness of the study conclusions. If the results showed no qualitative change in the combined effect, the results are stable.

### 2.11. Literature quality evaluation

Using Jaded trial to evaluate clinical RCT's score. The total mark was 5, take scores below (include) 2 as low quality research, scores more than 2 as high quality research. Evaluation standard was: ① randomized blind: The total mark was 2, if there mentioned "randomized blind" and its synonymy gets 1 mark, any specific describe of achieving method about randomized blind add another 1 mark; ② withdraw and loss of follow up: total mark was 1, with explanation about withdraw situation gets 1 mark.

### 2.12. Ethics and dissemination

This study does not collect the personal information of clinical trial participants, so no ethical approval is required. The result of this research will provide reliable evidence-based medical evidence for the long-term efficacy of PRP and GC in treating PF, and the research will be published in peer-reviewed journals.

## 3. Discussion

PF is the most common cause of chronic heel pain in adults, and its pathological manifestations are local aseptic inflammation and fascia rupture. There are many clinical treatment methods, among which GC and PRP are the common treatment methods for PF. However, there is still a lack of systematic evaluation of the clinical efficacy of PRP and GC in the treatment of PF. In this study, a systematic review and meta-analysis were conducted for the comparison of the long-term efficacy of the 2 drugs in the treatment of PF, hoping to provide evidence-based medical evidence for the treatment of PF and guide clinical decision-making.

### Author contributions

**Conceptualization:** Rongrong Ge, Jun Wu.

**Data curation:** Bangmin Wang, Jiawang Jiang, Qianan Cao.

**Formal analysis:** You Zeng, Yunfeng Liu.

**Methodology:** Jiawang Jiang, Bangmin Wang.

**Software:** Rongrong Ge, Qianan Cao.

**Supervision:** Rongrong Ge, Bangmin Wang.

**Writing – original draft:** Rongrong Ge, Bangmin Wang, Shuying Chen, Jiawang Jiang.

**Writing – review & editing:** Rongrong Ge, Shuying Chen, Jiawang Jiang, You Zeng.

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