



# Platelet-rich plasma injections for chronic plantar fasciopathy: a systematic review

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## Abstract

**Introduction:** There is an increasing interest in platelet-rich plasma (PRP) injection as a treatment for chronic plantar fasciopathy (PF). We wished to evaluate the evidence for the use of PRP in PF/fasciitis.

**Sources of data:** We performed a systematic review on the effects of PRP in PF. In June 2014, we searched Medline, Cochrane, CINAHL and Embase databases using various combinations of the commercial names of each PRP preparation and 'plantar' (with its associated terms). We only included prospectively designed studies in humans.

**Areas of agreement:** Eight articles met the inclusion criteria, three of them were randomized. All studies yielded a significantly greater improvement in symptoms between baseline and last follow-up assessment. None of the papers recorded major complications.

**Areas of controversy:** Only three randomized studies were identified; none of them had a true controlled group treated with placebo and one of the three studies had a very short (6 week) follow-up. A non-randomized study evaluating PRP versus corticosteroids (CCS) injections, and a randomized controlled trial comparing PRP and dextrose prolotherapy reported no statistical significant differences at 6 months. Most studies did not have a control group and imaging evaluation.

**Growing points and areas for research:** Evidence for the use of PRP in PF shows promising results, and this therapy appears safe. However, the

number of studies available is limited and randomized placebo-controlled studies are required. Characterizing the details of the intervention and standardizing the outcome scores would help to better document the responses and optimize the treatment.

**Key words:** PRP, platelet-rich plasma, plantar fasciopathy, fasciitis, systematic review

## Introduction

Plantar fasciopathy (PF) is a frequent disorder involving the plantar fascia: it has a bimodal distribution and occurs in both athletes and sedentary subjects.

Usually syndromes that involve manifestation of the typical heel pain are called plantar fasciitis, but that term is not correct, because no histological evidence of inflammation is present in this condition; the terms 'fasciosis' or 'fasciopathy' are most appropriate terms to define heel pain associated with degeneration of the plantar fascia and atrophy of the abductor digiti minimi muscle.<sup>1,2</sup>

Even though the exact aetiology is unknown, collagen degeneration at the origin of the plantar fascia, caused by repetitive microtears, appears to be the basis of the pain.<sup>3</sup>

To our knowledge, all authors have agreed that, in the first phases of the condition, the management should be non-operative. Several treatment options have been described with variable results, including rest, weight loss, deep massage, heel cups, night splint, anti-inflammatory drugs and stretching exercises.<sup>4-7</sup>

However, ~10% of patients do not respond to conservative therapies, necessitating further aggressive procedures such as injection therapy, extracorporeal shock wave therapy and, in some cases, surgical release of the plantar fascia.<sup>4-6,8</sup>

CCS injections can be effective in improving symptoms, but are associated with various complications such as rupture of the plantar fascia, calcaneal osteomyelitis and fat pad atrophy.<sup>9,10</sup>

Platelet-rich plasma (PRP) is an autologous blood product in which the platelets have been concentrated. Several preclinical studies have shown PRP to be beneficial to tendon healing, possibly because of

its anti-inflammatory property and the ability of the platelets to release several growth factors upon activation.<sup>11</sup>

There is an increasing interest in PRP injections as a treatment for chronic PF, and recently several papers on this topic have been published.<sup>12-19</sup>

This review aims to provide a complete evaluation of all studies concerning PRP injection therapy for PF as well as a detailed assessment of the methodological quality of these studies.

## Methods

This systematic review was performed following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.<sup>20,21</sup>

## Literature search

A comprehensive, systematic literature search was performed in June 2014. The databases of MEDLINE (PubMed), EMBASE, CINAHL (Cumulative Index to Nursing and Allied Health Literature) and the Cochrane library were searched without time limits. The following key words were used in different combinations: 'plantar fasciitis', 'plantar fasciosis', 'plantar fasciopathy', 'heel pain', 'platelet rich plasma', 'platelet transfusion', 'prp' or 'injection'. We limited the search to articles in English, and only human studies were included. All titles and abstracts were assessed by two researchers (E.F. and M.P.), and all relevant articles were obtained. All bibliographies were also hand searched to identify further relevant literature.

All relevant articles were read independently in full text by two researchers to assess whether they met the inclusion criteria. If there was a difference in

opinion on their suitability, a consensus was reached by consulting a third senior reviewer.

### Study selection

All participants in the trials had to have a clinical diagnosis of PF/fasciitis.

Studies were included if their design could be classified into one of the three categories: randomized controlled trial, prospective comparative study and prospective cohort study. We imposed no exclusion relying on publication year. Articles were included if reporting clinical outcomes of at least a group of patients undergoing PRP injection, and the intervention had to be well described.

### Data extraction

Two researchers independently recorded the study design, population, intervention, outcome measure and outcome using standardized data extraction forms. To assess the efficacy of the interventions, mean values of the continuous outcomes were extracted from the published articles.

### Quality assessment

The Coleman methodology score (CMS), a 10-items validated system,<sup>22</sup> was used to evaluate each paper. Two different authors (R.P. and M.P.) assessed the methodological quality of each study, first separately, and then discussing to reach an agreement when a difference >2 points was found. An investigation scoring 100 would represent the ideal design of a study, without bias or influence of casual factors.

## Results

### Literature search

Of the 164 articles initially identified by the search, 8<sup>2,13,14,16–19,23</sup> met the inclusion criteria (Fig. 1).

### Study design, level of evidence

All studies included were prospective;<sup>2,13,14,16–19,23</sup> of these, three<sup>14,17,23</sup> were level I controlled randomized trials.

### Subjects' selection and inclusion criteria

Selection criteria of patients were reported with fairly detailed descriptions in all the papers.

In all studies, patients needed to have a diagnosis of PF to be enrolled in the trials and receive injection therapies. Martinelli *et al.*<sup>18</sup> and Kim and Lee<sup>17</sup> required, in addition to the clinical diagnosis, a radiographic evidence of calcaneal spur and a plantar fascia thickness  $\geq 4$  mm at ultrasound, respectively. In all studies, a failure of other previous conservative treatments was mandatory to be included in the trials (Table 1 for full details).

### Participants

Based on the available data, the 8 papers selected evaluate a total of 256 participants (264 plantar fascias treated), of whom 180 underwent PRP injections (188 plantar fascia). Ninety-three patients were male and 163 were female, with a ratio male/female of 0.63. The mean age of the patients involved in all the studies was 45.43 years (Table 1).

### Interventions

Each study used a different device to prepare PRP. Two studies were used a double centrifugation instead of a single cycle. The PRP volume injected ranged from 2.5<sup>16</sup> to 5 ml.<sup>18,19</sup> Four out of eight studies<sup>13,17,19,23</sup> reported the final concentration of platelets; it ranged from at least 2x<sup>19</sup> (double of standard concentration) to 8x.<sup>23</sup> Anticoagulation methods were used in all but two trials,<sup>13,16</sup> while buffering was provided in two studies,<sup>13,16</sup> and only Aksahin *et al.*<sup>2</sup> used an activator as calcium. The details in PRP preparation are shown in Table 2.

All but two studies treated patients with only one injection of PRP. Kim and Lee<sup>17</sup> used two injections, with a 2-week interval, while Martinelli *et al.*<sup>18</sup> injected each foot three times.

All studies advised a rest period ranging from 2 days to 4 weeks; five studies<sup>2,14,16,19</sup> provided also a post-procedure rehabilitation programme, often involving stretching exercises. (Table 2)

The duration of the follow-up ranged from 6 weeks<sup>23</sup> to 24 months.<sup>14</sup>

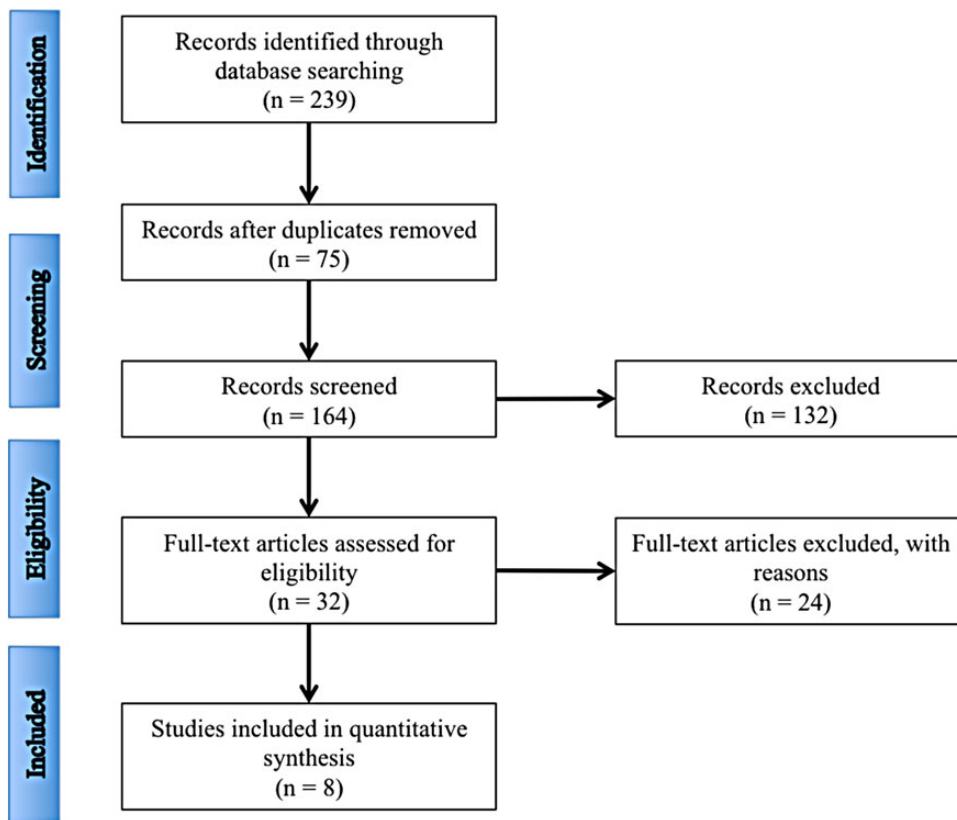


Fig. 1 PRISMA 2009 flow diagram

## Outcome measures

Different scores were used to evaluate the outcomes (Figs. 2 and Table 3). The most frequently used test was the VAS (Visual analogue scale) score. Roles and Maudsley scores were recorded in three of eight studies. The AOFAS (American Orthopaedic Foot and Ankle Society) score were used in two studies. Plantar fascia bands thickness was evaluated by ultrasound in one article.

## Outcomes data

### Effectiveness of PRP

Ragab and Othman<sup>19</sup> in 2012 evaluated 25 participants treated with a single injection of PRP. At 12 months post-intervention, the average VAS pain decreased from 9.1 to 2.1. The patient's questionnaire showed no limitation of activity for 15 patients (60%), minimal limitation for 8 of them (32%), and

moderate limitation for 2 (8%), with 22 of 25 patients completely satisfied of the therapy (88% of success rate). Ultrasonography thickness measurements of the plantar fascia revealed improvements for both medial and central bands.

In a prospective uncontrolled study, Martinelli *et al.*<sup>18</sup> obtained, after 12 months, a marked improvement in terms of VAS after the treatment with PRP, namely from  $7.1 \pm 1.1$  to  $1.9 \pm 1.5$ . Eleven of 14 patients were classified excellent or good based on the Roles and Maudsley score.

Kumar *et al.*<sup>16</sup> evaluated, through VAS, AOFAS and Roles and Maudsley scores, 44 patients (50 heels) prospectively enrolled. At all follow-up appointments planned (3rd and 6th month), a statistically significant improvement was recorded in all scores.

The most recent trial to date to assess the efficacy and safety of PRP<sup>13</sup> showed a statistically significant improvement in terms of FAAM score (Foot and

**Table 1** Demographic data of the studies

Author	Year	Type of study	Indication	PRP group	Control group	M/F (n)	Mean age (years)	Follow-up
Wilson <i>et al.</i> <sup>13</sup>	2014	Prospective case series	Symptoms of PF for a minimum of 3 months, unresponsive to other conservative treatments for at least 3 months. Diagnosis confirmed by imaging	22 (24 plantar fascia)	No	9/13	44	32 weeks
Monto <i>et al.</i> <sup>14</sup>	2014	Randomized controlled single-blinded study	Symptoms of PF for a minimum of 4 months, unresponsive to other conservative treatments	20	20 CCS (40 mg DepoMedrol)	PRP group: 8/12 CCS group: 9/11	PRP group: 51 CCS group: 59	24 months
Kumar <i>et al.</i> <sup>16</sup>	2013	Prospective cohort study	Symptoms of PF for a minimum of 12 months, unresponsive to other conservative treatments	44 (50 plantar fascia)	No	15/29	51	6 months
Kim <i>et al.</i> <sup>17</sup>	2013	Randomized controlled single-blinded study	Symptoms of PF for a minimum of 6 months, unresponsive to other conservative treatments. PF thickness $\geq 4$ mm at US	10 (9 at final follow-up)	11 DP	PRP group: 4/6 DP group: 7/4	PRP group: 36.2 DP group: 37.8	6 months
Martinelli <i>et al.</i> <sup>18</sup>	2013	Prospective cohort study	Symptoms of PF for a minimum of 6 months, unresponsive to other conservative treatments for at least 3 months. Radiographic evidence of calcaneal spur	14	No	5/9	42.9	12 months
Ragab and Othman <sup>19</sup>	2012	Prospective cohort study	Chronic PF unresponsive to other conservative treatments for at least 6 months.	25	No	11/14	44	10.3 months (mean)
Aksahin <i>et al.</i> <sup>2</sup>	2012	Non-randomized controlled single-blinded study	PF unresponsive to other conservative treatments for at least 3 months.	30	30 CCS (40 mg methylprednisolone)	PRP group: 12/18 CCS group: 13/17	PRP group: 46.36 CCS group: 45.67	6 months
Omar <i>et al.</i> <sup>23</sup>	2011	Randomized controlled single-blinded study	Patients with diagnosis of PF and inferior heel pain and tenderness	15	15 CCS	PRP group: 0/15 CCS group: 0/15	PRP group: 42.5 CCS group: 44.5	6 weeks

CCS, corticosteroid; DP, dextrose prolotherapy; PF, plantar fasciopathy/fasciitis; n.r., not reported.

**Table 2** PRP procedure descriptions

References	PRP centrifugation	PRP concentration	PRP volume (ml)	Volume of blood drawn (ml)	N of injections	Activation	Anticoagulant	Buffering	Post-procedure rehabilitation
Wilson <i>et al.</i> <sup>13</sup>	Magellan Arterioocyte Platelet Concentrator System centrifuge (Arterioocyte Medical Systems, Inc, Cleveland, OH)	7x	3	45	1	No	Citrate dextrose solution	Sodium bicarbonate 0.05 ml/ml PRP	Physical therapy regimen as tolerated within 2 weeks of the procedure. Supervising not mandatory
Monto <i>et al.</i> <sup>14</sup>	Accelerate Sport Platelet Concentration System (Exactech, Inc., Gainesville, FL), soft spin centrifugation at 2400 rpm for 12 min	n.r.	3	27	1	No	3 ml citrate dextrose-A solution (ACDA)	No	Daily home eccentric exercise (Swedish heel drop programme) and calf/arch stretching
Kumar <i>et al.</i> <sup>16</sup>	GPSIII system (Biomet Biologics, Warsaw, IN), 15 min centrifugation at 3200 revolutions per minute	n.r.	2.5–3.5	27	1	No	3 ml sodium citrate	8.4% sodium bicarbonate	Eccentric stretching programme and cushioned insoles
Kim <i>et al.</i> <sup>17</sup>	Huons HC-1000 System (Huons Co. Ltd., Sungnam, South Korea), centrifugation at 3200 g for 3 min	7.6x	n.r.	20	2 (2 weeks apart)	No	Sodium citrate 22 mg, citric acid 7.3 mg, glucose monohydrate 24.5 mg	No	n.r.
Martinelli <i>et al.</i> 2013 <sup>18</sup>	Arthrex ACP Double Syringe System (Arthrex, Naples, FL), centrifugation for 5 min at 1500 rpm	n.r.	5	10	3	No	2 ml citrate dextrose solution	No	n.r.

Ragab and Othman <sup>19</sup>	Centrifugation for ~15 min (3000 rounds per minute) using desk top centrifuge	6-8x	5	50	1	No	5 ml sodium citrate	No	Supervised stretching exercises for 2 weeks and strengthening exercises for additional 2 weeks
Aksahin <i>et al.</i> <sup>2</sup>	Double centrifugation technique, first 1800 rpm for 15 min, second time 3500 rpm for 10 min	n.r.	3	25	1	Calcium	n.r.	No	Standardized stretching programme for Achilles tendon and PF
Omar <i>et al.</i> <sup>23</sup>	Two-step centrifugation, 15 min at 320 g (soft spin) then at 2000g for 15 min (hard spine)	at least 2x	n.r.	150	1	No	63 ml citrate phosphate dextrose (CPD)	No	n.r.

Ankle Ability Measure), Foot-SANE (Foot-Single Assessment Numeric Evaluation), SF-12v2 (Short Form 12 item Health Survey version 2) after 32 weeks for 22 patients undergoing a single PRP injection.

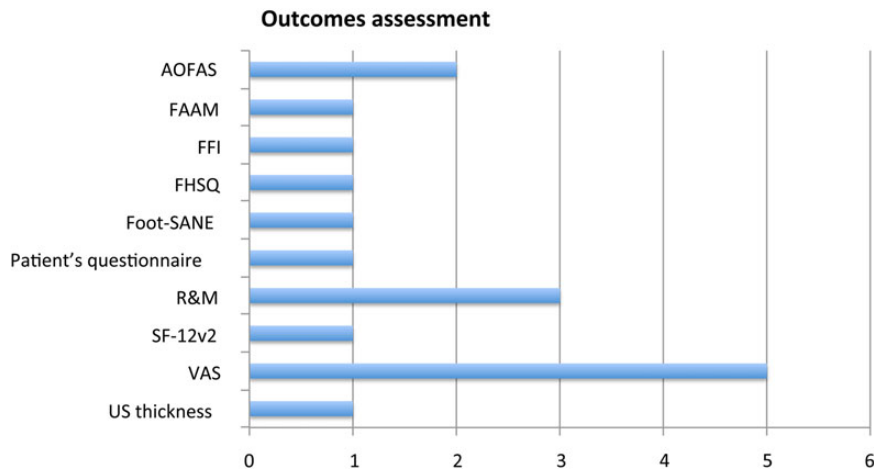
#### PRP vs. dextrose prolotherapy (DP)

Kim and Lee<sup>17</sup> in a 2013 prospective randomized single-blinded study compared 10 patients undergoing two PRP injections with 11 patients treated with 2 injections of dextrose/lidocaine solution (DP). They lost one patient from the PRP group. At the 2- and 6-month follow-up appointments, they evaluated pain, disability and activity limitation of the 20 remaining patients, using the Foot Functional Index (FFI). The mean final FFI total score was improved for both the PRP group and the DP group, from  $151.5 \pm 37.9$  at the baseline to  $81.6 \pm 55.3$  for the PRP group and from  $132.5 \pm 31.1$  to  $97.7 \pm 52.5$  for the DP group. The improvement was greater for the PRP group (30.4 vs. 15.1%), but there was no statistically significant difference between the two groups at any follow-up (see Table 3 for FFI subscales details).

#### PRP vs. CCS therapy

In 2011 an Egyptian study<sup>23</sup> compared steroid injection ( $n = 15$ ) (control group) with PRP injection ( $n = 15$ ) (PRP group). After a follow-up of 6 weeks, a statistically significant difference was recorded for VAS and FHSQ (Foot Health Status Questionnaire) scores between the PRP and control groups ( $2.6 \pm 2$  vs.  $6.5 \pm 2.6$ ,  $P = 0.001$  and  $25.1 \pm 12.4$  vs.  $49.0 \pm 19.1$   $P = 0.001$ ), where at baseline VAS and FHSQ values showed no significant differences (8.2 vs. 8.8 and 58.5 vs. 57.5).

Aksahin *et al.*<sup>2</sup> prospectively studied results in terms of VAS and Roles and Maudsley of 60 patients assigned non-randomly to PRP or CCS injection therapies. VAS improved both from baseline to 3 months and from 3 to 6 months of follow-up ( $P = 0.001$ ) reaching  $3.93 \pm 2.02$  in the PRP group and 3.4 in the CCS group. The Roles and Maudsley score also significantly improved from 3 to 6 months post-injection. Comparing the two groups, however, the authors found no statistical difference for both VAS and Roles and Maudsley ( $P > 0.05$ ).



**Fig. 2** Outcome measures, frequency of use. AOFAS, American Orthopaedic Foot and Ankle Society score; FAAM, foot and ankle ability measure; FFI, foot functional index; FHSQ, Foot Health Status Questionnaire; Foot-SANE, Foot-Single Assessment Numeric Evaluation; R&M, Roles and Maudsley score; SF-12v2, Short Form 12 item Health Survey version 2; VAS, visual analogue scale; US, ultrasound

In 2014, Monto *et al.*<sup>14</sup> compared PRP and DepoMedrol injection therapy by means of AOFAS score. Their results showed a clinically significant difference in favour of PRP ( $P = 0.001$ , 95% confidence interval) at 3-, 6-, 12- and 24-month follow-up evaluations. Patients treated with cortisone significantly improved at 3 months, but subsequently worsened up to values similar to baseline.

#### Success of PRP therapy

Four on eight articles<sup>2,16,18,19</sup> provided a further outcome measure in terms of success rate of the therapy. Only two studies<sup>2,18</sup> used the same method to define a successful result, namely the amount of patients with good or excellent score at Roles and Maudsley assessment. They obtained divergent results with 33.3 and 78.6%, respectively. Another study<sup>19</sup> investigated patients' satisfaction through a questionnaire, reaching 88% of success. Kumar *et al.*<sup>16</sup> asked patients to evaluate the therapy, recorded 64% of positive responses and 68% of AOFAS scores  $\geq 80$  (Table 4).

#### Safety of PRP therapy

None of the articles analysed in this systematic review recorded any complication or adverse effect related to PRP administration.

#### Methodological quality

The modified CMS ranged from 61 to 81,<sup>17</sup> with a mean value of 74.23 and a standard deviation of 6.27 (Table 5).

The Spearman correlation coefficient showed no significant correlation between Coleman data and the year of publication ( $P = -0.27$ ).

#### Discussion

This systematic review evaluated the current evidence for application of PRP in PF, focusing on the effectiveness and safety of this therapeutic modality.

Plantar fasciopathy is the most common cause of heel pain, accounting for >1 million medical consultations per year only in the USA, with an incidence rate of ~10%.<sup>24</sup>

A careful medical evaluation of clinical symptoms usually allows diagnosing the condition.

PF occurs especially in athletes and is supposed to be caused by continuous excessive overload.<sup>25</sup> Similarly to other overuse injuries, PF is often self-resolving.

However, the continuous microtrauma caused by overuse initially results in microtears of the tissue substance, but then, if the noxious insult continues, it produces a macro injury, and the condition becomes chronic.<sup>25,26</sup>



**Table 3** Outcomes of the studies

References	Score	Baseline score outcomes	Last follow-up score outcomes	Complications
Wilson <i>et al.</i> <sup>13</sup>	FAAM-ADL	58.00 ± 14.48	76.78 ± 18.48	No
	FAAM-Sports	31.33 ± 18.73	57.31 ± 30.66	
	Foot-SANE	43.30 ± 19.38	67.66 ± 25.18	
	SF-12v2	37.40 ± 10.40	SF-12v2: 47.92 ± 12.87	
Monto <i>et al.</i> <sup>14</sup>	AOFAS	PRP group: 37 (range 30–56), CCS group: 52 (range 24–60)	PRP group: 92 (range 77–100), CCS group: 56 (range 30–75) <sup>#</sup>	No
Kumar <i>et al.</i> <sup>16</sup>	AOFAS	60.6 ± 13.1	81.9 ± 16.6	No
	R&M	7.7 ± 1.4	4.2 ± 3.2	
	VAS	4 (inter-quartile 0.0)	2 (inter-quartile 1.0) <sup>†</sup>	
Kim <i>et al.</i> 2013 <sup>17</sup>	Total FFI	PRP group 151.5 ± 37.9; DP group 132.5 ± 31.1*	PRP group 81.6 ± 55.3; DP group 97.7 ± 52.5*	No
	Pain FFI	PRP group 60.4 ± 14.7; DP group 56.5 ± 14.0*	PRP group 33.7 ± 23.4; DP group 41.1 ± 21.4*	
	Disability FFI	PRP group 55.8 ± 19.5; DP group 53.4 ± 15.7*	PRP group 31.9 ± 23.4; DP group 40.3 ± 21.8*	
	Activity limitation FFI	PRP group 31.3 ± 10.2; DP group 22.6 ± 9.8*	PRP group 17.3 ± 11.6; DP group 16.4 ± 12.9*	
	VAS	7.1 ± 1.1	1.9 ± 1.5	
Martinelli <i>et al.</i> <sup>18</sup>	R&M	n.r.	9(64.3%) excellent, 2 (14.3%) good, 2(14.3%) acceptable, 1(7.1%) poor	No
	VAS	VAS: 9.1	VAS: 2.1	No
Ragab and Othman <sup>19</sup>	Patient's questionnaire	Moderate limitation of activity 7 (28%), Severe limitation of activity (72%)	No limitation of activity 15(60%), Minimal limitation of activity 8(32%) Moderate limitation of activity 2(8%)	No
	US thickness	Medial band: 7.1 mm	Medial band: 4.8 mm	
		Central band: 6.6 mm Lateral band: 4.6 mm	Central band: 5.4 mm Lateral band: 4.6 mm	
Aksahin <i>et al.</i> <sup>2</sup>	VAS	PRP group 7.33 ± 0.62, CCS group 6.2 ± 1.61*	PRP group 3.93 ± 2.02, CCS group 3.4 ± 2.32*	No
	R&M	PRP group: 1(3.3%) excellent, 10(33.3%) good, 13 (43.3%) acceptable, 6(20%) poor, CCS group 2(6.7%) excellent, 8(26.7%) good, 14(46.7%) acceptable, 6(20%) poor*	PRP group: 6(20%) excellent, 4(13.3%) good, 16(53.3%) acceptable, 4(13.3%) poor, CCS group 8(26.7%) excellent, 6(20%) good, 12(40%) acceptable, 4(13.3%) poor*	
Omar <i>et al.</i> <sup>23</sup>	VAS	PRP group 8.2 ± 1.3, CCS group 8.8 ± 0.9*	PRP group 2.6 ± 2.1, CCS group 6.5 ± 2.6 <sup>#</sup>	No
	FHSQ	PRP group 58.5 ± 9.6, CCS group 57.5 ± 9.4*	PRP group 25.1 ± 12.4, CCS group 49.0 ± 19.1 <sup>#</sup>	

All scores statistically significant improved from baseline to last follow-up evaluation except CCS group in Monto *et al.* n.r., not reported. See text for full wording of the scores.

\*No statistically significant difference between the two groups compared.

<sup>#</sup>Statistically significant difference between the two groups compared.

**Table 4** Success rates of PRP injection therapy

References	Success definition	Success rate (%)
Kumar <i>et al.</i> 2013 <sup>16</sup>	Patients satisfaction at the question 'would have the procedure again'	64
Martinelli <i>et al.</i> 2013 <sup>18</sup>	R&M excellent and good	78.6
Ragab and Othman 2012 <sup>19</sup>	Satisfaction at patient's questionnaire	88
Aksahin <i>et al.</i> 2012 <sup>2</sup>	R&M excellent and good	33.3

A combination of intensive use (so-called repetitive microtrauma) and anomalous microvascular response results in reduced blood flow; reduced vascularization provides less oxygen and nutrients, slowing the healing processes and encouraging degenerative ones. Histological studies confirm this hypothesis, showing no acute inflammation, but rather a failure of the healing process associated with angiofibroblastic degeneration, collagen necrosis, chondroid metaplasia and matrix calcification.<sup>27–29</sup>

In conclusion, in plantar fasciopathy, similarly to other tendinopathies, a failed healing response of the tendon occurs.<sup>30</sup>

The rationale of the use of PRP is based on the growth factors stored in the alpha granules of platelets. Those factors, such as TGF- $\beta$  (transforming growth factor beta), VEGF (vascular endothelial growth factor) and PDGF (platelet-derived growth factor), stimulate tissue regeneration from mesenchymal cells, acting on both cell replication and differentiation. The tissue microenvironment determines phenotypic differentiation. Furthermore, platelets activated by thrombin release additional cytokines able to promote tendon cell proliferation.<sup>11</sup>

In this systematic review, we analysed all prospectively designed studies focusing on PRP injection therapy for the treatment of PF. We included eight publications,<sup>2,13,14,16–19,23</sup> of which three studies<sup>14,17,23</sup> were randomized controlled clinical trials.

We analysed the methodological quality of the papers included using the CMS,<sup>22</sup> an evaluation score first developed to assess the methodological

quality for studies investigating surgical management of patellar tendinopathy, and successively used for published studies about other conditions and procedures such as surgery for Achilles tendinopathy,<sup>22</sup> knee arthroplasty,<sup>31</sup> treatment for combined knee ligaments injury,<sup>32</sup> augmentation techniques for rotator cuff repair,<sup>33</sup> etc. The average CMS was 74.23, which indicates a moderate overall quality of the eight studies reviewed.

Most the studies analysed<sup>13,16,18,19</sup> reported a significantly greater improvement in symptoms between baseline and last follow-up assessment to testify the effectiveness of PRP in treating plantar fasciopathy.

Also, retrospective studies not included in the present review reported good results after PRP injections. In 2004, Barrett and Erredge<sup>34</sup> first assessed the effectiveness of this therapy achieving complete resolution of PF symptoms in seven of nine patients; O'Malley and Vosseller<sup>15</sup> reviewed a series of 24 patients reporting success in 66.6% of patients after 6 months.

However, the randomized controlled trial by Kim and Lee<sup>17</sup> did not find any significant difference comparing PRP and dextrose prolotherapy at 6 months.

The controlled study by Aksahin *et al.*<sup>2</sup> also failed to note the difference between PRP and CCS therapy in terms of FFI scores.

Conversely, in other two randomized studies,<sup>14,23</sup> PRP had a significantly greater efficacy than CCS, both after a short-term follow-up of 6 weeks and after a longer period (24 months).

Also in the retrospective cohort study by Shetty *et al.*,<sup>12</sup> at 3 months PRP was superior in all the evaluated scores compared with CCS injection.

Although other studies have shown that injection of CCS are effective in treating the PF,<sup>35–37</sup> the effect seems to be limited and short lived; furthermore, the use of CCSs is not a pathology-based therapy and has been associated with the risks of fat pad atrophy and rupture of the plantar fascia.<sup>6–8</sup>

Surgery remains the last treatment option when all previous therapy fail, but carries the risk of nerve injury, infection, plantar fascia rupture and does not always ensure a symptoms improvement.<sup>38</sup>

Although the current evidence suggests that PRP may be of benefit as an injection therapy to treat

Table 5 Modified CMS

References	Study size	Mean duration of follow-up	Number of surgical procedures	Type of study	Diagnostic certainty	Description of surgical procedure	Description of post-Op rehabilitation	Outcome measurements	Outcome assessment	Selection process	Total score
Wilson <i>et al.</i> <sup>13</sup>	4	0	10	0	5	5	5	10	8	14	61
Monto <i>et al.</i> <sup>14</sup>	4	2	10	15	5	5	5	8	10	12	76
Kumar <i>et al.</i> <sup>16</sup>	7	0	10	10	5	5	5	10	11	13	76
Kim <i>et al.</i> <sup>17</sup>	7	0	10	15	5	5	5	8	11	15	81
Martinelli <i>et al.</i> <sup>18</sup>	4	2	10	10	5	5	5	8	11	15	75
Ragab and Othman <sup>19</sup>	7	0	10	10	5	5	5	7	10	14	73
Aksahin <i>et al.</i> <sup>2</sup>	7	0	10	10	5	5	5	9	11	13	75
Omar <i>et al.</i> <sup>2,3</sup>	7	0	10	15	5	5	5	7	11	12	77

plantar fasciopathy, a greater number of studies are needed to draw better conclusions on the use of PRP in PF.

To date, indeed, the total amount of patients treated with this therapy is still too limited to properly assess both effectiveness and safety.

Most of the articles included in this review were published in the last 2 years, showing the growing interest on the topic. Some level I studies are currently under way, such as the multicentre, randomized controlled study by Peerbooms *et al.*<sup>39</sup>

Future studies should characterize the details of the intervention and standardize the outcome scores to help to find the best procedure and optimize treatment.

Furthermore, only one of the studies in our review reported an imaging evaluation of the plantar fascia: this is not enough to provide useful information; future studies should include an ultrasound evaluation before and after injection, given the role that this technique can play in assessing healing.<sup>40,41</sup>

This systematic review has some limitations. First, only articles published in English were included.

Moreover, no other kind of autologous blood injection, other than PRP, was considered. Our aim was to focus only on PRP products in which platelet concentrations were increased compared with standard autologous blood.

Most of the studies analysed do not have control groups and provide only results of patients undergoing PRP injection. Moreover, not even one of the controlled studies has a real placebo control group: randomized clinical trials comparing PRP with placebo are necessary, given the nature of PF, which is often self-limiting.

## Conclusion

PRP injection therapy may be of benefit over purely conservative treatment and other injection therapy modalities to treat plantar fasciopathy. The current evidence is promising but limited, and therefore further high-quality research must be undertaken to both compare PRP versus placebo and better characterize the optimal preparation of PRP, the appropriate recipient, and the timing of the intervention to maximize any benefit it may have. To complement

the clinical parameters that may be used to designate successful treatment, addressing the current lack of imaging documentation of the response to PRP therapy is also recommended.

## Conflict of interest

The authors report no conflict of interest.

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