

## EFFICIENCY OF APPLYING PLATELET- RICH PLASMA (PRP) IN THE REGENERATION OF TENDINOPATHY: A SYSTEMATIC REVIEW STUDY

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**Abstract:** **Introduction:** The tendon is a fundamental tissue for providing lever movements in the joints, absorbing impacts and stabilizing the joint and, due to its high demands, it becomes susceptible to overuse injuries, called tendinopathies. In this context, it is necessary to understand the efficiency of interventions aimed at regenerating this tissue, such as the infiltration of platelet-rich plasma. **Objective:** The present study aimed to systematically review the literature in order to elucidate the methods of preparing platelet-rich plasma and their effectiveness in the regeneration of tendinopathies. **Methodology:** To carry out this study, a systematic review of the literature was carried out, using as a basis the Preferred Reporting Items for Systematic review and Meta-Analysis, and adopting the following descriptors from the Medical Subject Headings, in English: platelet-rich plasma (plasma rich in platelets), physiotherapy, tendinopathy and tendon injury, in the Pubmed electronic database. **Results:** In this study, 4 articles were selected, 3 of which showed significant efficacy in improving function and pain in the injured limb after the application of PRP (GAUTAM, et al, 2015; CAI, et al, 2019; KAMBLE, et al, 2022), however, the study by Keene et al, (2019), did not detect a significant improvement with the use of PRP in relation to placebo, considering that the application of PRP in this study was guided only by the doctor's palpation. **Discussion:** In the studies by Gautam et Al, (2015), Cai et Al, (2019) and Kamble et Al, (2022) US-guided application was used, demonstrating more positive results compared to the study by Keene et Al, (2019), which used the application guided by the doctor's palpation. Regarding the preparation method, the double centrifugation demonstrated in the studies by Cai et Al, (2019) and Kamble et Al, (2022), was also associated with greater benefits compared to a single centrifugation in the study by

Keene et Al, (2019). **Conclusion:** Most studies have demonstrated the effectiveness of using PRP in the regeneration of tendinopathies. The preparation method involving double centrifugation and US-guided application presents more positive results compared to the preparation technique involving only one centrifugation and application guided by the doctor's palpation. More studies are needed to verify the possible role of temperature in the preparation, PRP activation and duration of injury.

**Keywords:** Regeneration, physiotherapy, platelet-rich plasma, infiltration, tendinopathies.

## INTRODUCTION

Tendinopathies are injuries to tendon tissue due to excessive use, they are a part of the daily lives of healthcare professionals today due to their high incidence. According to Andarawis-Puri, Flatow and Soslowsky (2015), tendinopathies affect more than 30% of musculoskeletal injuries in people who seek care, and Aicale, Tarantino and Maffulli (2018), state that football athletes suffer, on average, 2 injuries per season (300-day period). As a result, treatments for this type of injury are being further studied in an attempt to improve the effectiveness of remodeling and speed up this process, which can take years to complete tissue remodeling. (LEONG, et al. 2020)

The tendon tissue is resistant and elastic, with the function of fixing the muscles in the entheses (site of osteotendinous insertion), absorbing impacts, stabilizing the joint to which it is inserted and transmitting the contraction forces of the muscle to the bone. Therefore, the movements performed require alignment, biomechanics, strength and resistance from the tendon, muscle and bone to avoid injuries, in addition to requiring sliding and stability of the tendon so that lever actions can occur appropriately, avoiding tendinopathies. On the other hand, the tissue can suffer other

extrinsic and intrinsic influences that can influence the tissue, such as the low level of local vascularization, genetic factors, speed of the immune response, variation in sexual hormones (testosterone and estradiol), rest time after activity physical, training volume, among other factors. With this, you can enjoy directing the possible responses that the body can give, causing progress in the healing process and remodeling of the affected tissue. (BENJAMIN and RALPHS, 1997. CLEGG et. Al, 2007. ABATE, et. Al, 2009. DYMENT, et. Al, 2013. ANDARAWIS-PURI et. Al, 2015. DERRICKSON and TORTORA, 2017)

One of the studies that brought the possibility of speeding up this process is the infiltration of platelet-rich plasma (PRP) in the tendon injury, consisting of increasing tissue growth factors, improving the quantity of local immune system cells with the aim of favoring the healing process and tissue remodeling, reducing treatment time and pain, using autologous material to avoid possible known rejections, with few contraindications for treatment. However, despite this material being studied for more than 60 years, there is no consensus on its preparation, with more than 40 types of techniques for application, with results varying from beneficial to non-significant, with a lack of standardization of a model that has more effectiveness, with the need for a systematic investigation and review to carry out a comparative analysis of existing preparations. (EVERTS, et. Al, 2020. LEONG, et. Al, 2020. NARAYANASWAMY, et. Al, 2023).

## GOAL

The present study aimed to systematically review the literature in order to elucidate the methods of preparing platelet-rich plasma and their effectiveness in the regeneration of tendinopathies.

## METHODOLOGY

To carry out this study, a systematic review of the literature was carried out, a method that consisted of a broad search for articles, with the aim of finding relevant articles on the subject that were filtered by inclusion and exclusion criteria, with the aim of comparing the results regarding to the application of platelet-rich plasma for tendon healing and its effectiveness, using as a basis the items described in Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA 2020) (ANNEX A) to establish points to be followed. (DONATO, 2019)

To select scientific articles, the following Medical Subject Headings (MeSH - MEDLINE) descriptors in English were used: platelet-rich plasma, physiotherapy, tendinopathy and tendon injury. tendon), in the electronic database Pubmed. The terms were combined in 3 ways: [platelet-rich plasma + physiotherapy], [platelet-rich plasma + tendinopathy] and [platelet-rich plasma + tendon injury], using the “AND” operator to combine the descriptors. A search was carried out in the selected database, considering the period from 2013 to 2023.

The inclusion criteria adopted for the study selection process were: 1) original articles; 2) studies showing the method for preparing platelet-rich plasma (PRP); 3) studies that analyze the effectiveness of PRP in tendon repair; 4) studies that presented a summary; 5) articles published in the last 10 years; 6) studies without techniques combined with PRP, except physical exercise and ice; 7) studies with double or triple-blind methodology and 8) studies that had their text available free of charge.

## DISCUSSION

In this study, it was possible to analyze data from four experimental studies, which demonstrated the effectiveness of PRP in tendon recovery, clarifying the preparation method used. Of these, three studies demonstrated significant patient improvement in pain and function (GAUTAM, et al, 2015; CAI, et al, 2019; KAMBLE, et al, 2022), however, the study by Keene et. Al, (2019) demonstrated no significant changes in patients receiving PRP compared to placebo. However, the PRP preparation method used by Keene et. Al, (2019) was different compared to other studies.

Keene et. Al, (2019) used patients in the acute stage of the injury, in an average period of 5.3 days after partial rupture of the Achilles tendon, from these, 50 ml of blood were collected to produce 8ml of plasma rich in platelets and leukocytes (PRPL). The separation of this material was performed by the machine (MAG 200 MAGELLAN Autologous Platelet Separator, Arteriocyte Medical Systems, MA, 2015) for 10 min, in just one centrifugation at a speed of 4000 rpm. Of the 8 ml of PRPL produced, 4 ml were injected into the patient at the injured site detected by the doctor's palpation, and the other 4 ml were separated to analyze the quality of the material. The studies by Cai et. Al, (2019); Kamble et. Al, (2022); and Gautam et. Al, (2015) used a different form of preparation, and also applied it to the exact location of the lesion using an ultrasound (US) guided technique, demonstrating effective results.

In the study by Kamble et. Al, (2022), chronic patients were used, with pain at the site of the injury for a minimum period of three months, with the aim of comparing the effectiveness of PRP and CS in the recovery of lateral elbow tendinopathies, as well as the study of Gautam et. Al, (2015). Both presented results of long-term analgesia,

tissue recovery and improved function of the affected limb after PRP application. However, there were considerable differences between the methods used for such studies, Kamble et. Al, (2022) applied two centrifuges to 30 mL of venous blood, the first lasting 15 minutes at 1800 rpm (revolutions per minute), and the second lasting 10 minutes and 3500 rpm, obtaining the final result of 3 ml of PRP that were injected into the injury site under US guidance.

Gautam et. Al, (2015), performed only one centrifugation on 20 ml of venous blood, which lasted 15 minutes at 1500 rpm, producing 2 ml of PRP that was also injected at the site of the injury, with the aid of US.

The study by Cai et. Al, (2019), used double centrifugation at 4°C, both lasting 10 minutes, the first at a speed of 1500 rpm, and the second at a speed of 2500 rpm, resulting in a final product of 5 to 6 mL of PRP with low amounts of leukocytes. Whereas 4 mL were activated and injected into the injury site in each patient. 4 injections were performed, once a week, for 4 weeks, with the aid of US during application, showing that PRP has high long-term effectiveness, but if used in conjunction with SH it provides better short and long-term results, in compared to the isolated form of PRP. Contrasting the study by Keene et. Al, (2019), in which only one application of PRP was performed without activation, the preparation method with just one centrifugation and application guided by the doctor's palpation, presenting a non-significant result of the effectiveness of the treatment compared to placebo.

When comparing the results obtained in the aforementioned studies, it is possible to observe that the preparation technique involving two centrifuges, with speeds varying between 1500 and 3500 rpm, with a prevailing time of 15 minutes and US-guided application tends to produce more positive results

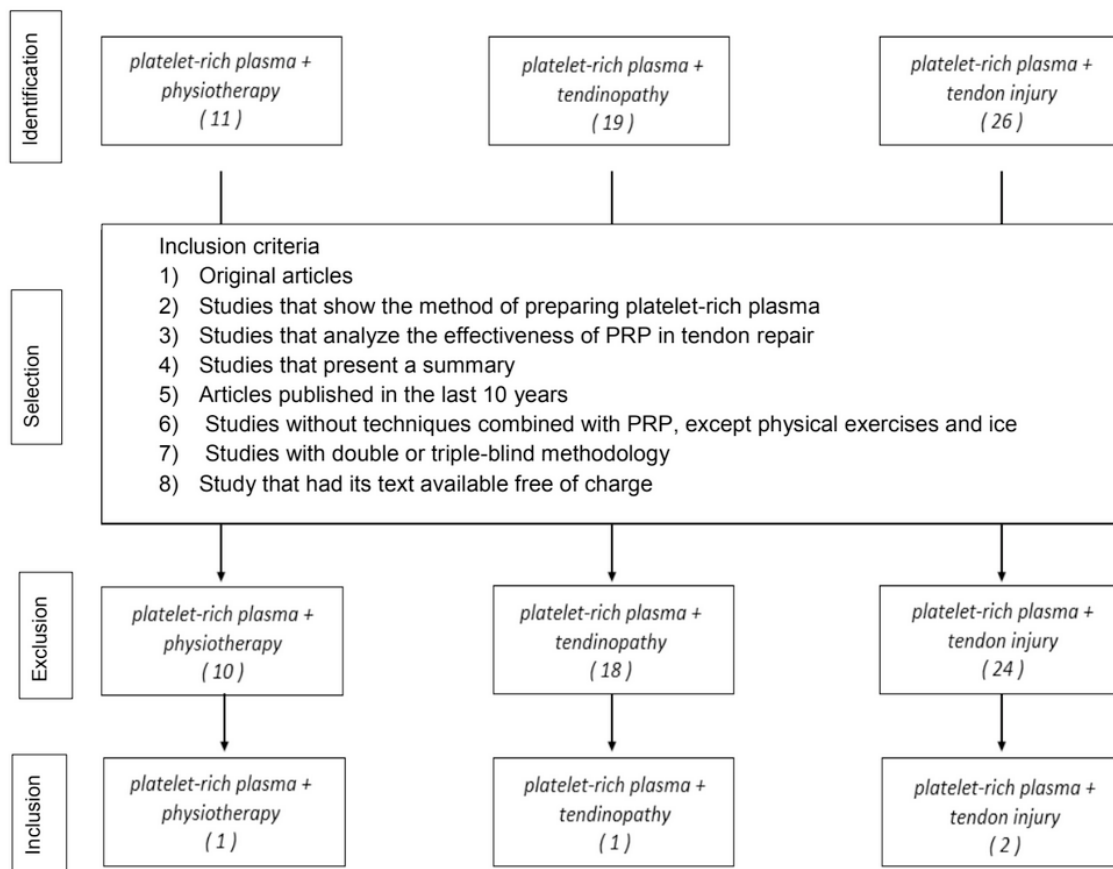


Figure 1.

Authors	Newspaper	Sample	Age (years)	Type of study
KAMBLE, Prashant, et al. (2022)	<i>Is Ultrasound (US)-Guided Platelet-Rich Plasma Injection More Efficacious as a Treatment Modality for Lateral Elbow Tendinopathy Than US-Guided Steroid Injection? A Prospective Triple-Blinded Study with Midterm Follow-up</i>	64 non-athletes	20 to 65 years	triple-blind randomized clinical trial
KEENE, David J. et al. (2019)	<i>Platelet rich plasma injection for acute Achilles tendon rupture: PATH-2 randomised, placebo controlled, superiority trial</i>	230 adults	18 years or over	double-blind randomized clinical trial
CAI, YU et al. (2019)	<i>Sodium Hyaluronate and Platelet-Rich Plasma for Partial-Thickness Rotator Cuff Tears</i>	184 patients	18 to 55 years	prospective, randomized, controlled and double-blind study.
GAUTAM, V. K. et al. (2015)	<i>Platelet-rich plasma versus corticosteroid injection for recalcitrant lateral epicondylitis: clinical and ultrasonographic evaluation.</i>	30 patients	18 to 60 years	double-blind randomized clinical trial

Table 1. Articles included in the study.



## RESULTS

Author	Subjects	Groups	Evaluations	Result
KAMBLE, Prashant, et al. (2022)	64 non-athlete patients 29M 35F	PRP injection: 32 patients Corticosteroid injection (CS): 32 patients	visual analog scale (VAS) Arm-Hand-Shoulder Disability Scores (DASH) Patient Rated Tennis Elbow Assessment (PRTEE) scores hand grip strength period of 2 weeks, 1 month, 3 months, 6 months, 1 year and 2 years	2 weeks: ↑CS 1 month: ↑CS 3 months: ↑PRP 6 months: ↑PRP 1 year: ↑PRP 2 years: ↑PRP
KEENE, David J. et al. (2019)	230 patients 57 F 173 M	PRP injection: 114 patients dry needle: 116 patients	symmetry index function Quality of life VAS achieving goals Follow-up: 4, 7, 13, 24 weeks	↑PRP in all weeks of follow-up, however to a lesser extent compared to placebo
CAI, YU et al. (2019)	200 patients	PRP injection: 50 patients sodium hyaluronate (SH) injection: 50 patients SH+PRP injection: 50 patients Normal saline (NS) injection: 50 patients	follow-up: 1, 3, 6 and 12 months VAS Constant score secondary outcome measures were American Shoulder and Elbow Surgeons (ASES)	up to 3 months: ↑SH than PRP and NS after 3 months: ↑PRP that NA and SH ↑SH+PRP that all applications throughout the monitoring
GAUTAM, V. K. et al. (2015)	30 patients	PRP: 15 patients CS: 15 patients	VAS DASH Oxford Elbow Score modified Mayo score hand grip strength Follow-up: 3 and 6 months	↑PRP: healing ↑CS: relief up to 3 months CS demonstrated reduced tendon thickness and increased cortical erosion

Table 2. Results of articles included in the study

↑: the person showed greater effectiveness

M: male

F: female

compared to preparation technique involving only one centrifugation, with a speed of 4000 rpm and a time period of 10 minutes, with application guided by palpation.

## CONCLUSION

Most studies have demonstrated the effectiveness of using PRP in the recovery from tendinopathies, however, they present considerable differences regarding preparation methods. Through this review, it was possible to observe that the preparation technique involving two centrifuges, with speeds varying between 1500 and 3500 rpm, with a prevailing time of 10 minutes and US-

guided application tends to produce more positive results compared to the preparation technique involving only one centrifuge, with a speed of 4000 rpm and a period of time of 10 minutes, with application guided by palpation.

However, more studies are needed in order to elucidate the influence of other variables, such as: temperature at which centrifugation occurred, as only the study by Cai et. Al, (2019) treated this data; the activation of PRP, evidenced only in studies by Cai et. Al, (2019) and de Keene et. Al, (2019); and the duration of the injury that the patient had, demonstrated only in the studies by Keene et. Al, (2019) and Kamble et. Al, (2022).

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## **ANEXO A:**

Guia prático *Preferred Reporting Items for Systematic review and Meta-Analysis* (PRISMA): [www.prisma-statement.org](http://www.prisma-statement.org)