Outcomes After Ultrasound-Guided Platelet-Rich Plasma Injections for Chronic Tendinopathy: A Multicenter, Retrospective Review

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Objective: To determine whether ultrasound-guided platelet-rich plasma (PRP) injections are an effective treatment for chronic tendinopathies.
Design: A retrospective, cross-sectional survey.
Setting: Four academic sports medicine centers from across the United States.
Patients: A total of 180 men and women between the ages of 18 and 75 years who received ultrasound-guided PRP injections for tendinopathy refractory to conventional treatments.
Interventions: Survey on satisfaction and functional outcome.
Main Outcome Measurements: Perceived improvement in symptoms at least 6 months after treatment, perceived change in visual analog scale score, assessment of functional pain, and overall satisfaction.
Results: On average, patients were 48 years old, had symptoms for a median of 18 months before treatment, and answered the survey on average 15 months after treatment. Overall, 82% of patients indicated moderate to complete improvement in symptoms. The most common injection sites were the lateral epicondyle, Achilles, and patellar tendons. Other sites treated included the rotator cuff, hamstring, gluteus medius, and medial epicondyle, among others. Furthermore, 60% of patients received only 1 injection, 30% received 2 injections, and 10% received 3 or more injections. Patients' perceived decrease in visual analog scale score was 75%, from 7.0 ± 1.8 to 1.8 ± 2.0 (−5.2, SD 2.7, 95% confidence interval −5.65 to −4.86, $P < .0001$). In addition, at follow-up, 95% of patients reported having no pain at rest that disrupted their activities of daily living and 68% reported no pain during activities. A total of 85% of patients were satisfied with the procedure.
Conclusions: In this retrospective study, in which we evaluated administration of PRP for chronic tendinopathy, we found that the majority of patients reported a moderate (>50%) improvement in pain symptoms.

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INTRODUCTION

Tendon pain is common in recreational and professional athletes, as well as in sedentary people [1,2]. It occurs in 30%-50% of all sports-related injuries [1]. Tendon injuries are classified as tendinitis during the acute inflammatory process and tendinosis when the healing becomes chronically impaired, evidenced by lack of inflammatory cells in the tissue, abnormal tissue repair, collagen degeneration, neovascularization, and thickening of the tendon [2,3]. The healing response is believed to be different between load-bearing tendons, such as the patellar and Achilles tendons, and non–load-bearing tendons, such as the wrist extensors, which may be related to mechanical stimulation [4,5]. In addition, other extrinsic factors such as overuse of the injured site and poor functional technique also may impair tissue healing, making the treatment of chronic tendon injuries a significant challenge. Clinicians are increasingly using the term *tendinopathy* to refer to tendon disorders without implying a specific pathology and *chronic tendinopathy* for cases that are refractory to conventional treatments.

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Traditionally, physicians have tried using antiinflammatory medications, both oral and injectable, to treat tendinopathies. The rationale for these treatments has been questioned recently. A study on the effect of ibuprofen on rat Achilles tendon cells showed increased activity of the collagen-degrading enzymes, suggesting a detrimental effect on tendon healing [6]. Studies of corticosteroid injections to treat lateral epicondylitis have shown positive short-term results; however, the study authors reported no significant difference in outcomes compared with placebo or physiotherapy and frequent relapses in subjects in the long run [7,8]. Corticosteroid injections also may weaken tendons, leading to rupture, especially in load-bearing tendons [9].

Platelet-rich plasma (PRP) injections have been proposed as a promising alternative for treating tendinopathies. PRP is considered an ideal autologous blood product that promotes the body's own natural healing [10]. It is derived by drawing blood from the patient, which is then centrifuged until the red blood cells and platelets separate, after which the platelet concentrate is extracted from the platelet-rich section of the centrifuged plasma. Platelets are known to contain alpha and dense granules, which release multiple growth factors and cytokines that promote wound healing [11,12]. Authors of in vitro studies have reported an enhancement of the recruitment, proliferation, and differentiation of the cells involved in soft-tissue regeneration [13-15].

PRP injections are widely accepted by patients because the injection is produced from the patient's own blood and the risk of adverse effects is minimal [4]. In addition, in a study on the antibacterial effect of platelet-rich gel in vitro, investigators found that the gel inhibited the growth of *Staphylococcus aureus* and *Escherichia coli* [16]. The risk of acquiring a transmitted blood-borne infection or experiencing an anaphylactic reaction is virtually nonexistent [10]. Finally, PRP has a lower cost and shorter recovery time when compared with surgical management. Surgery has been considered the final option for recalcitrant tendinopathies despite highly variable clinical outcomes [17].

The use of PRP for musculoskeletal injuries has increased significantly during the past few years, given its safety and availability for outpatient preparation and delivery. However, scientific evidence that PRP injections effectively treat chronic tendinopathy is limited; most studies have been case series reports with small sample sizes, and randomized control trials have yielded conflicting results [10,18-25]. Nonetheless, we believe that PRP provides significant improvement in symptoms and ≥50% pain reduction, when measured at ≥6 months after the procedure(s). The objective of this study was to review the outcomes of a large number of patients with various chronic tendinopathies that had been refractory to conventional treatments for longer than 6 months and were treated with ultrasound-guided PRP injections at multiple academic institutions and determine whether PRP is an effective treatment for chronic tendinopathies.

METHODS

This study was conducted at 4 academic institutions across the United States. The protocol was submitted to the Institutional Review Board at each of the institutions that participated. Approval was obtained and the study was completed in accordance with the Institutional Review Board guidelines of each center.

The inclusion criteria were as follows: subjects were men and women between 18 and 75 years of age with a diagnosis of tendinopathy for ≥6 months that had not resolved with conventional treatments, including oral medications, physiotherapeutic modalities, and eccentric exercises (those that involve slow, controlled lengthening of the muscle/tendon unit), among others. For the diagnosis, the patients had to have documented pain upon palpation over the tendon, pain with resisted activation of the tendon, and ultrasound or magnetic resonance imaging findings consistent with tendinopathy. With sonography, the criteria for tendinopathy were as follows: a well-defined hypoechoic area with partial or complete tendon fiber disruption suggestive of a tendon tear, a hyperechoic intratendinous focus with posterior acoustic shadowing suggestive of calcification, or both [26].

The magnetic resonance imaging criteria for tendinopathy were as follows: intratendinous high signal intensity suggestive of a partial tendon tear, absence of a segment of a tendon suggestive of a full tear, or low signal intensity suggestive of intratendinous scarring [27]. The tendinopathy had to be reconfirmed at the time of the procedure with ultrasound evaluation of the tendon after the aforementioned criteria were met. Patients must have received one or more ultrasound-guided PRP injections no less than 6 months before the time of contact for the survey. In addition, the procedure must have followed a defined protocol for preparation and delivery of the PRP that included 2 patient identifiers, aseptic technique, blood draw volume from 20-60 mL depending on the amount of final PRP product needed to inject into a specific tendon, PRP preparation according to manufacturer's recommendations, no activator added, and ultrasound guidance for the injection. Finally, the patients must have completed a rehabilitation program that included eccentric exercises no earlier than 4 weeks after the procedure.

Exclusion criteria included sensory or neurologic complaints affecting the specified region, coagulation disorder, platelet disorder, pregnancy, or a major systemic illness such as diabetes mellitus, rheumatoid arthritis, fibromyalgia, autoimmune disorder, or any other condition that required strict antiplatelet or anticoagulation therapy. Each patient must have had a full work-up on the basis of their history and physical examination to confirm that the exclusion criteria were identified.

All patients who received PRP injection(s) for pain associated to a single tendon according to the aforementioned guidelines during the defined study period and who met the inclusion criteria were identified by the attending physicians, invited to participate in the study, signed the consent and the Health Insurance Portability and Accountability Act forms, and answered the questionnaire. The primary outcome measurement was the perceived improvement in symptoms at least 6 months after the PRP injection(s). This perception was quantified using the following Likert scale: "Not at all," "Slightly," "Moderately," "Mostly," and "Completely." Secondary outcome measurements were the following: perceived change in visual analog scale (VAS) before and after the procedure (from 0 for no pain to 10 for worst pain), functional pain after the procedure using the Nirschl Pain Phase Scale for overuse injuries, and overall satisfaction with the PRP procedure (quantified with the following Likert scale: Completely Dissatisfied, Mostly Dissatisfied, Somewhat Dissatisfied, No Difference, Somewhat Satisfied, Mostly Satisfied, and Completely Satisfied) [28].

The number of PRP injections had to be determined according to specific criteria. If the patient reported (1) 80% global improvement, then no further injection was recommended; (2) <80% global improvement but still improving, no further injection was recommended; and (3) <80% global improvement and plateaued in progress, then an additional injection was recommended.

The primary outcome measurement (improvement in symptoms) was analyzed by calculating a global average for all tendons, average improvement for each of the most commonly treated tendon groups, and average improvement according to the number of injections received. The perceived change in VAS was analyzed using a *t*-test for statistical significance. Averages also were calculated for functional pain after PRP and overall satisfaction with the procedure.

RESULTS

After combining the data from the 4 centers, 180 of the 325 patients (55%) who were contacted answered the survey. The average age was 48 ± 13 years, with a distribution of 100 men and 80 women. The patients' duration of symptoms at the time of the PRP treatment had been a median of 18 months. Thirty-two patients had symptoms for longer than 5 years. Patients answered the survey at 15 ± 6 months from the time they received their last PRP injection. The distribution of the various tendons treated and demographic data are listed in Table 1.

In terms of our primary outcome measurement, 82% of patients recorded a moderate-to-complete resolution of symptoms (≥50% improvement). Furthermore, 70% of patients reported mostly to complete resolution of symptoms (≥75% improvement; Table 2). No significant difference was found between the patients who answered the survey at 1 year or less after the PRP procedure and those who answered more than 1 year after the procedure, refuting the argument that the observed improvements were simply due to spontaneous resolution of symptoms. Specifically, 81% of patients who answered at 1 year or less reported moderate improvement to complete resolution of symptoms (69 patients; mean elapsed time after administration of PRP of 8 months ± 2 months), whereas 82% of patients who answered the survey at more than 1 year after the PRP injection(s) reported the same improvement (111 patients; mean elapsed time after administration of PRP of 19 months ± 5 months).

The 3 most common tendons treated were the insertion of the common extensor tendon at the lateral epicondyle, Achilles, and patellar tendons. Overall, 93% of patients who received an injection at the lateral epicondyle, 100% of patients who received an injection at the Achilles tendon, and 59% of patients who received an injection at the patellar tendon reported moderate to complete resolution of symptoms (≥50% improvement). In addition, more than 80% of patients who received an injection at the rotator cuff, hamstring, gluteus medius, or common flexor tendon at the medial epicondyle reported the same or greater improvement (Table 2).

Regarding the number of PRP injections received by patients, 60% of patients received only 1 injection, 30% received 2 injections, and 10% received 3 or more injections. In terms of the primary outcome, 83% of patients reported moderate-to-complete resolution of symptoms with only 1 injection, 82% reported the same after 2 injections, and 76% reported the same after 3 or more injections.

The perceived change in VAS (Δ) was −5.2 (7.0 ± 1.8 before the PRP treatment and 1.8 ± 2.0 at the time of the survey; Table 1). This perceived change resulted in an average reduction of pain of 75% (−5.2, SD 2.7, 95% confidence interval −5.65 to −4.86, $P < .0001$). No significant difference was found in the estimated change in VAS between the patients who answered the survey at 1 year or less after the PRP procedure ($\Delta = -5.2$) and those who answered more than 1 year after the procedure ($\Delta = -5.3$). Six percent of all the subjects reported a VAS score >5 at final follow-up, including 3 patients who eventually were referred for surgical management.

As for functional pain, 68% of patients reported no pain while performing activities and minimal to no pain before or after activities, 27% reported pain during activities that did not disrupt their activities of daily living or household chores, and only 5% reported having pain at rest that disrupted their daily living. Regarding patient satisfaction, 85% of patients were satisfied with the procedure, 13% were dissatisfied, and 2% were indifferent.

DISCUSSION

This study represents the largest database of patients treated with PRP for tendinopathy that has been published thus far.

Table 1. *Patient demographic information and perceived change in VAS*

Variable	Total	Mean	Median	SD	Range	95% CI	*P* Value
Demographics							
Age, y		48	49	13	19-73		
Gender							
Male	100						
Female	80						
Treatments before PRP, No. patients							
Physical therapy and eccentric exercises	180						
Massage	80						
Corticosteroid injection	74						
Chiropractor	38						
Acupuncture	31						
Nitric oxide patch	5						
Surgery	3						
Prolotherapy	2						
Duration of injury, mo		36	18	44	6-360		
Injury location, No. patients							
Lateral epicondyle	30						
Patella	27						
Achilles	27						
Rotator cuff	21						
Hamstring	17						
Gluteus medius	16						
Medial epicondyle	11						
Plantar fascia	9						
Quadriceps	5						
Hip adductor	4						
Peroneus longus	3						
Tensor fascia lata	3						
Peroneus brevis	2						
Triceps	1						
Biceps	1						
Posterior tibialis	1						
Popliteus	1						
Obturator internus	1						
Elapsed time after PRP, mo		15	14	6	6-29		
Perceived change in VAS		−5.2		2.7		−5.65 to −4.86	<.0001

CI = confidence interval; PRP = platelet-rich plasma; VAS = visual analog scale.

As opposed to the other studies in the literature that have looked only at the response of a specific tendon to PRP, we studied the response of multiple tendons treated throughout the body and determined overall improvement in symptoms. Despite potential differences in etiology, the underlying tissue pathology among these tendinopathies was confirmed to be similar when we used advanced imaging techniques.

Our results show that patients experienced significant improvement in symptoms, evidenced by 82% of patients reporting at least moderate improvement of their symptoms. A similar satisfaction rate also was found, 85% respectively, demonstrating that the improvement in symptoms likely resulted in patient satisfaction. These findings are similar to those of previous smaller studies of PRP. For example, a relatively small cohort study on PRP for chronic elbow tendinopathy reported 81% and 93% improvement in pain at 6 months and 2 years, respectively, and recommended considering PRP before referring patients for surgery [23]. In another study with a larger sample, the authors compared PRP (51 patients) with corticosteroid (49 patients) with a 1-year follow-up and showed a significant difference between PRP and corticosteroid in terms of VAS and Disability of Arm, Shoulder, and Hand (DASH) score [9]. These investigators reported that 49% of patients in the corticosteroid group versus 73% of patients in the PRP group had a successful treatment, defined as >25% improvement in VAS. These outcomes remained positive after 2 years [21].

The 3 most commonly treated tendons in our study correlated with the PRP injection sites that have been investigated the most—that is, the lateral epicondyle, Achilles, and patellar tendons. In our study, 93% of patients with lateral epicondylosis reported at least moderate improvement in symptoms, similar to the findings in the study by Mishra et al [12], and had an 81% decrease in VAS score. In addition, 97% of our patients reported at least a 25% change in VAS score, which is greater than that in previous studies for lateral epicondylosis [10,21]. Several factors could contribute to this difference, such as the platelet concentration, leukocyte

Table 2. *Perceived improvement of symptoms after the platelet-rich plasma procedure*

Subjects' Perceived Improvement of Symptoms After PRP	
Likert Scale	**Subjects (%)**
Not at all	10
Slightly	8
Moderate	12
Mostly	41
Complete	29

Moderate Improvement to Complete Resolution of Symptoms for the Most Commonly Treated Tendons	
Injury Location	**Subjects (%)**
Lateral epicondyle	93
Patella	59
Achilles	100
Rotator cuff	81
Hamstring	82
Gluteus medius	81
Medial epicondyle	82

PRP = platelet-rich plasma.

count in the PRP, and ultrasound guidance for a more specific delivery of PRP.

The Achilles tendon group had the best response, with all patients having at least moderate improvement and 96% of patients reporting mostly to complete improvement. This finding was promising for patients with recalcitrant Achilles tendinopathy because the authors of one systematic review noted that 24%-45.5% of patients with Achilles tendinopathy eventually consider surgery [29]. A case-series report evaluated the effectiveness of PRP for noninsertional Achilles tendinopathy in 14 patients and found significant improvements with American Orthopaedic Foot and Ankle Society (AOFAS) and VAS scores, as well as improved tendon appearance on ultrasound [20].

The additional benefit of PRP for Achilles tendinopathy was not noted in a randomized, double-blind, placebo-controlled trial in which de Vos et al [18] compared patients treated with ultrasound-guided PRP versus saline solution injections. After 24 weeks, both groups showed improvement in the Victorian Institute of Sports Assessment- Achilles (VISA-A) scale; however, no statistically significant difference was found between the 2 groups [18]. de Vos et al examined subjects who reported symptoms for at least 2 months and excluded patients who did not respond to conservative treatment with eccentric exercises before trying PRP, as well as patients with severe symptoms who could not tolerate the eccentric exercises, which led to a sample population of persons with subacute Achilles tendonitis with mild-to-moderate symptoms who had not tried eccentric exercises first. Eccentric exercises have demonstrated favorable outcomes in the treatment of Achilles tendinopathy [30,31]. PRP should be reserved for recalcitrant cases that do not respond to conservative treatments, including eccentric exercises. In addition, the authors provided early eccentric exercises 2 weeks after the injections. It is not yet known whether early eccentric exercises after PRP assist or delay the healing process. Virchenko and Aspenberg [5] reported early tendon repair improvement in a rat's Achilles tendon model after injection of PRP and mechanical stimulation. A controlled, prospective study that compares PRP treatment with eccentric exercises in patients who have failed to respond to eccentric exercises would be beneficial to further understand its effects and its proper application in patients with chronic Achilles tendinopathy.

Of our most commonly treated tendons, patellar tendons had the lowest rate of success. A published study on the prognosis of patellar tendinopathy in male athletes reported that 53% of the patients eventually had to end their sports career, suggesting that patellar tendinopathy may have lower potential for healing [32]. Nonetheless, more than half of our patients in this tendon group reported at least a moderate improvement in symptoms. In addition, 78% of patients reported more than 50% improvement in VAS. When we considered the number of injections given, 89% of these patients received only 1 or 2 injections, whereas the authors of previous studies used 3 PRP treatments for patellar tendinopathy. In one case series report, authors looked at the outcome of 20 athletes after they had received 3 consecutive patellar PRP treatments and reported statistically significant improvement in knee function and quality of life, with 80% of patients eventually returning to their previous sport activity level [22]. In another case-control trial, the same authors compared patients who were treated with 3 PRP injections and physiotherapy with patients who were treated with physiotherapy only. The PRP group showed 39% improvement in sports activity level compared with the control group's 20% improvement [19]. It is possible that providing an additional PRP injection to our patients with patellar tendinopathy may have improved the outcome.

We compared the overall primary outcome measurement based on the number of injections performed and found that more than 80% of patients who received 1 or 2 injections and 76% of those who received 3 injections reported moderate-to-complete resolution of symptoms. This finding suggests that patients who receive one injection and have residual symptoms may benefit from a second or third injection. Some patients did not improve despite receiving 3 injections. Considering this trend, the need for more than 3 injections can be questioned. Other factors may exist that prevent certain patients from responding to PRP treatment, including hormonal and nutritional factors that were not examined in this study and may influence the potential for improvement with PRP treatment. The optimal number of PRP injections requires further investigation.

An average pain reduction of 75% was demonstrated with the VAS, which was greater than our stated goal of 50%. These results differ from those of other published PRP stud-

ies, such as the study by Peerbooms et al, in which they considered >25% reduction in pain as significant and reported that 76% of patients achieved this outcome in this study on lateral epicondyle pain [10]. In our study, 94% of patients, regardless of the tendon, reported ≥25% reduction in VAS. Our greater success could be a result of many factors associated with the preparation and delivery of PRP, including the fact that ultrasound guidance was used to ensure proper placement of the PRP in the tendon. Most of the PRP studies published on tendinopathy did not use ultrasound guidance for the injection [10,19,22,23]. Nevertheless, our study cannot exclude the possibility that other variables could have contributed to the great success, including an average of 15 months follow-up time and not blinding the procedure.

In terms of functional outcome, 68% of patients indicated having no pain during activities and minimal to no pain before or after activities, whereas 27% of patients reported pain during activities and/or at rest. This finding correlates with the VAS at the time of the survey of 1.8 ± 2.0, indicating that at least half of patients had no pain to minimal pain reported.

This study has several limitations that should be considered. First, the response rate in this survey study was 55%. Although this rate is considered good for a survey study of this type, it should be noted that the outcomes might have been worse with a greater percentage of responses. In addition, some patients did not follow up long-term with their physician and thus may have benefited from additional treatments. Also, this study required that a rehabilitation program be completed but did not standardize the specific protocol, and thus confounding variables may exist in the activities that the patients performed after the procedure. We compared a similar treatment across a variety of tendinopathies by defining outcome measurements that would be similar for all tendinopathies; nonetheless, it is difficult to generalize conclusions from mostly subjective outcome measurements. Finally, our study collected retrospective data, which results in recall bias, does not control for confounding factors, and limits the type of questions we can ask. Some of the other PRP studies in the literature reported prospective data, which is certainly more ideal.

This study did not address many of the current controversies pertaining to PRP treatment, including platelet concentration, leukocyte levels, the need for activation before injection, and the number of treatments required; however, the treatment provided represents current clinical practice throughout much of the United States and abroad. The design of this study was to evaluate the perceived improvement in symptoms of a large number of patients treated with PRP for different tendinopathies at 4 separate centers with use of techniques that have been commonly implemented throughout the United States. We acknowledge that additional studies are needed that have more stringent methodology to further evaluate the efficacy of this procedure and hope that these results provide a foundation for these future studies.

CONCLUSION

Patients with painful, chronic recalcitrant tendinopathies have limited options. In this retrospective study of the use of PRP to treat chronic tendinopathy, the majority of patients reported moderate (>50%) improvement in pain symptoms, with almost all tendon groups having similar outcomes. Considering that these patients had pain for an average of 3 years before treatment and a median of 18 months and had undergone traditional treatments that failed for longer than 6 months, the results are encouraging. Also, the similar outcomes seen in patients who answered the survey at 1 year or less after the PRP procedure and in those who answered more than 1 year after the procedure helps refute the possibility that the significant improvement in these patients was related to a spontaneous resolution of the tendinopathy. It appears that PRP has a positive effect in patients with various types of refractory tendinopathy; however, more rigorous studies are needed to confirm these findings.

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