Are Multiple Platelet-Rich Plasma Injections Useful for Treatment of Chronic Patellar Tendinopathy in Athletes?: A Prospective Study

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Are Multiple Platelet-Rich Plasma Injections Useful for Treatment of Chronic Patellar Tendinopathy in Athletes?

A Prospective Study

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Background: Chronic patellar tendinopathy (PT) is one of the most common overuse knee disorders. Platelet-rich plasma (PRP) appears to be a reliable nonoperative therapy for chronic PT.

Purpose: To evaluate clinical and radiological outcomes of 3 consecutive ultrasound (US)–guided PRP injections for the treatment of chronic PT in athletes.

Study Design: Case series; Level of evidence, 4.

Methods: A total of 28 athletes (17 professional, 11 semiprofessional) with chronic PT refractory to nonoperative management were prospectively included for US-guided pure PRP injections into the site of the tendinopathy. The same treating physician at a single institution performed 3 consecutive injections 1 week apart, with the same PRP preparation used. All patients underwent clinical evaluation, including the Victorian Institute of Sport Assessment–Patella (VISA-P) score, visual analog scales (VAS) for pain, and Lysholm knee scale before surgery and after return to practice sports. Tendon healing was assessed with MRI at 1 and 3 months after the procedure.

Results: The VISA-P, VAS, and Lysholm scores all significantly improved at the 2-year follow-up. The average preprocedure VISA-P, VAS, and Lysholm scores improved from 39 to 94 ($P < .001$), 7 to 0.8 ($P < .0001$), and 60 to 96 ($P < .001$), respectively, at the 2-year follow-up. Twenty-one of the 28 athletes returned to their presymptom sporting level at 3 months (range, 2-6 months) after the procedure. Follow-up MRI assessment showed improved structural integrity of the tendon at 3 months after the procedure and complete return to normal structural integrity of the tendon in 16 patients (57%). Seven patients did not recover their presymptom sporting level (among them, 6 were considered treatment failures): 3 patients returned to sport at a lesser level, 1 patient changed his sport activity (for other reasons), and 3 needed surgical intervention.

Conclusion: In this study, application of 3 consecutive US-guided PRP injections significantly improved symptoms and function in athletes with chronic PT and allowed fast recovery to their presymptom sporting level. The PRP treatment permitted a return to a normal architecture of the tendon as assessed by MRI.

Keywords: patellar tendinopathy; jumper's knee; platelet-rich plasma; treatment

Chronic patellar tendinopathy, also called jumper's knee, is a common disease characterized by pain, swelling, and reduced load-bearing capacity.[27] It occurs mostly in athletes but can also occur in sedentary people.[27] Jumper's knee is the most common injury in sports, characterized by high demand on the knee extensors for speed and power.[25] Forty percent of professional players have experienced symptoms of this condition during their career.[10] This tendinopathy affects athletes in many sports: volleyball (40%), basketball (35%), soccer, jumping, and sprinting.[2,24] In a prospective 15-year follow-up study, Kettunen et al[18] found that chronic patellar tendinopathy commonly leads to athletes abandoning their careers and causes mild but long-lasting symptoms after their careers.

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Although the precise mechanism of this tendinopathy remains unclear, several histopathological observations concluded that tendinosis was associated with microruptures of the patellar tendon, incomplete healing, and extensive neovascularity[13] that may lead to a chronic degenerative process.[7,11,26]

One biological therapeutic approach is the use of autologous growth factors, which stimulate tendon healing through collagen regeneration and a well-ordered angiogenesis.[29,36,44] The degranulation of the alpha granules in the platelets releases many different growth factors in high quantities.[5] Autologous growth factors are delivered locally in the form of platelet-rich plasma (PRP) by injection to the tendon repair site, and PRP has gained popularity as a potentially useful regenerative therapy to address many musculoskeletal injuries.[5] However, most growth factors are short-lived, and thus repeated administration is needed.[15,31]

Repeated injection of PRP is a promising procedure for jumper's knee and has already shown pain relief and improved tendon healing.[12,14,22] The aim of our study was to evaluate clinical and radiological outcomes after 3 consecutive ultrasound (US)–guided PRP injections for athlete's chronic patellar tendinopathy in a single-institution, continuous, prospective series.

MATERIALS AND METHODS

Patient Selection

The study protocol was given local ethical committee approval. Inclusion of study patients was between February and November 2010. All patients had failed previous nonoperative treatment for at least 4 months (mean, 18 months; range, 4-60 months). Such treatment included relative rest; nonsteroidal anti-inflammatory drugs (NSAIDs); formal eccentric exercises on a flat board (despite pain during exercise), as described by Stanish et al[39]; peritendon corticosteroid injections (previously performed by their own personal physician); laser therapy; and extracorporeal shockwave therapy (ESWT).

Patients were included if they had the following clinical symptoms: anterior chronic knee pain, tenderness at the inferior pole of the patella, or pain during provocative tests of the knee extensors and morphological signs of chronic patellar tendinopathy. All patients underwent previous recent ultrasonography and magnetic resonance imaging (MRI) (median, 19 days; range, 9-49 days). Hypoechoic regions with the loss of the normal fibrillar architecture on US[19,32] as well as hypersignal in T2-weighted MRI (microrupture) near the lower pole of the patella[17,20] were used to confirm the diagnosis before the inclusion (Figure 1). Exclusion criteria were systemic disorders, diabetes, rheumatoid arthritis, infections, coagulopathies, immunodepression, hemoglobin values of <11 g/dL, platelet values of <150,000/mm^3, and therapy with antiaggregants, anticoagulants, and NSAIDs in the 10 days before the procedure.

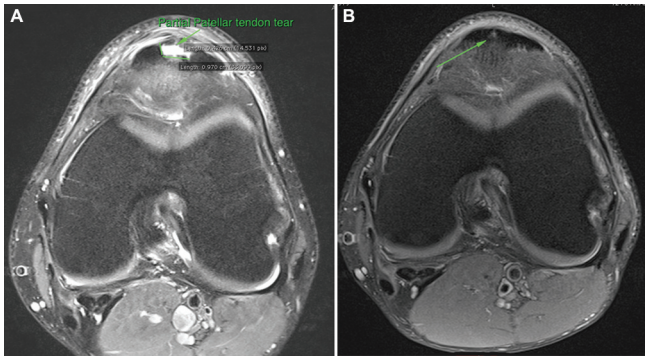

Figure 1. T2-weighted axial magnetic resonance imaging showing partial (A) patellar tendon tear before treatment and (B) patellar tendon healing 3 months after 3 ultrasound-guided injections of pure platelet-rich plasma.

Platelet-Rich Plasma Preparation

We prepared the PRP using the Arthrex ACP system (Arthrex Inc, Naples, Florida, USA), which gives pure PRP,[8,9] without leukocytes.[8,40] The density of platelets is more than twice as high in the ACP versus whole blood. The concentration levels of growth factors are significantly higher in the ACP compared with whole blood, with an increase in concentration by a factor of 25 for platelet-derived growth factor–AB; by a factor of 5 to 11 for epidermal growth factor, vascular epidermal growth factor, and platelet-derived growth factor–BB; and up to a factor of 5 for insulin-like growth factor–1 and transforming growth factor–β.[4,46]

In total, 15 mL of venous blood was drawn into the Arthrex Double Syringe System (Arthrex Inc) and then centrifuged at 1700 rpm for 5 minutes. A final volume of 6 mL of pure PRP was obtained (Figure 2). No activating agent was used. The PRP was extemporaneously prepared and immediately delivered.

Ultrasound-Guided Autologous PRP Injection Procedure

The investigator injected 6 mL of PRP with a 22-gauge needle under sterile conditions (Figure 2). With use of a single skin portal, injections were guided under ultrasonography (Viamo Toshiba, Tokyo, Japan) using a 16-MHz linear probe to better identify the tendinous lesion and to distribute the PRP within and around the hypoechoic area (Figure 2). The PRP injections were tolerated without the need for any sedation or local injected anesthesia. The procedure was repeated weekly for a total number of 3 injections. Supplementary injections (1-2) were scheduled when needed based on the clinical outcome and the return to the normal fibrillar pattern of the tendon.

After the initial injection, the patient was sent home with instructions to limit the use of the treated leg for 24 hours. The use of ice and nonsteroidal drugs was prohibited.

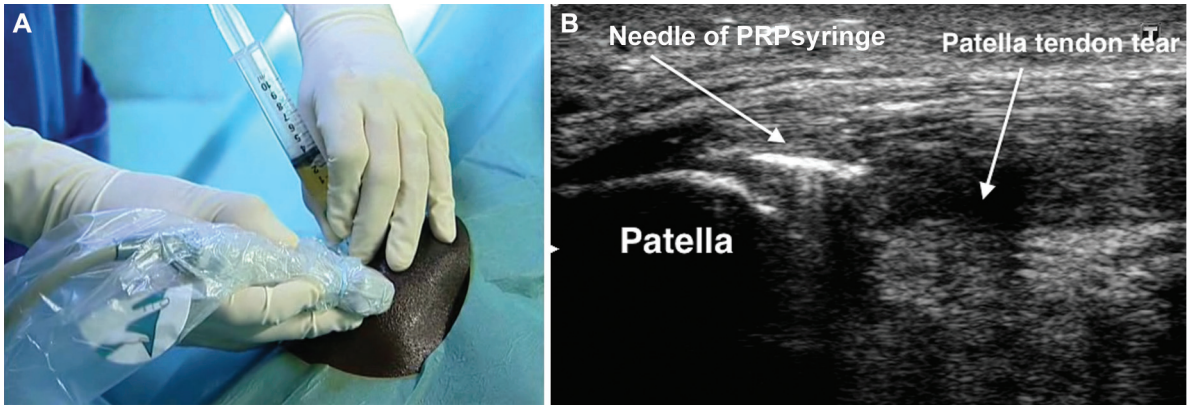

Figure 2. (A) Pure platelet-rich plasma (PRP) injection under ultrasound guidance. (B) The ultrasound image shows the needle within the pathologic area of the tendon.

Postprocedure Protocol

At the end of the injection protocol, all patients were enrolled in the same rehabilitation program, starting with warm-up exercises, stretching, and formal eccentric exercises on a flat board, as described by Stanish et al,[39] followed by progressive training such as cycling and mild exercises in the pool with a pool buoy. Running was authorized from postoperative week 6. Patients were allowed to resume their sport as tolerated 8 weeks after the last injection.

Outcome Measures

The postprocedure follow-up was begun after the last injection at 4 weeks, 3 months, and every 6 months with a 2-year minimum follow-up. The Victorian Institute of Sport Assessment–Patella (VISA-P) score, visual analog scale (VAS) for pain, and Lysholm knee scale were used for clinical evaluation after return to practice sports.

To evaluate tendon healing, MRI was performed at 1 and 3 months after the procedure using a 1.5-T magnet (1.5-T MRI system; Siemens Avanto, Munich, Germany) and an extremity-array coil. The MRI protocol consisted of the following pulse sequences: coronal and axial T2 fat-saturated WI and T1 SPAIR WI after gadolinium injection (Dotarem; Guerbert Healthcare, Villepinte, France). All MRI scans were evaluated by a single independent musculoskeletal radiologist who was blinded to the patient's treatment and was not involved in the clinical evaluation. The images were used for structural and qualitative assessment. The MRI criteria for healing were the absence of the hypersignal on T2-weighted images.

Clinical recurrences of symptoms with radiological findings of tendon healing at any time were considered treatment failures.

Statistical Analysis

Descriptive statistics were used to present data at baseline. Comparison was made between the pre- and postprocedure for all clinical and radiological outcomes with the Fisher exact test for categorical variables and the Mann-Whitney *U* test for continuous variables. Logistic regression models were used to explore risk factors of treatment failure; level of statistical significance was set at $P < .05$. All statistical analysis was carried out with STATA 12 (Stata Corp, College Station, Texas, USA).

RESULTS

Twenty-eight patients were included in this study. The mean age of the patients was 27 years (range, 16-37 years). All were athletes (17 professionals and 11 semiprofessionals). Patients were graded according to the classification of Blazina et al[3] and modified by Roels et al[35]; 5 patients were graded as 3A (permanent pain during sports activity resulting in a reduction in training time) and 23 patients were graded 3B (unable to participate in sports at the same level as before the onset of symptoms). The average number of PRP injections needed was 3 (1 supplementary injection was needed for 3 patients and 2 supplementary injections for 1 patient). Table 1 shows the baseline characteristics of the entire population of patients treated with pure PRP.

Clinical Outcomes After PRP Injections

All patients were satisfied with this procedure. No complications were observed during the treatment or 2-year follow-up period. None of the patients were lost to follow-up. At the 2-year follow-up, the entire group significantly improved after the procedure. The mean VISA-P score improved from 39 to 94 ($P < .001$), mean VAS decreased from 7 to 0.8 ($P < .0001$), and mean Lysholm knee rose from 60 to 96 ($P < .001$) (Table 2). At the 2-year follow-up, 21 of the 28 athletes (75%) were able to return to their presymptom sporting level (same number of hours per week) after a mean period of 3 months (range, 2-6 months) following the end of the PRP injections procedure (high jump, n = 5; basketball, n = 4; soccer, n = 3; gymnastics, n = 2; volleyball, n = 2; badminton, n = 2; judo, n = 1; tennis, n = 1; artistic dancing, n = 1).

TABLE 1
Baseline Characteristics of the Enrolled Patients (N = 28)[a]

Characteristic	Value
Age, y, mean (range)	27.3 (16.3-36.8)
Height, cm, mean (range)	184 (160-218)
Weight, kg, mean (range)	72 (50-120)
BMI, kg/m^2, mean (range)	21.6 (18.9-33.2)
Duration of symptoms, mo, mean (range)	18 (4-60)
Type of sport	
Jumpers	19
Other	9
Hours of training per week, mean (range)	18 (8-24)
Level of sport	
Professional	17
Semiprofessional	11
Patellar tendinopathy grade[b]	
3A	5
3B	23
Previous treatments	
Rest (at least 2 months)	28
Eccentric exercises	28
ESWT	24
Laser therapy	6
Peritendon corticosteroid injections	8

[a]BMI, body mass index; ESWT, extracorporeal shockwave therapy.
[b]According to Blazina et al.[3]

Seven patients did not recover their presymptom sporting level (among them, 6 were considered treatment failures): 3 patients returned to sport at a lesser level, 1 patient changed his sport activity (for other reasons), and 3 needed surgical interventions.

Effect of PRP Injections on the Tendon Structure

The MRI control of patellar tendon integrity showed complete return to normal structural integrity in 16 tendons (57%) (Figure 1) at 3 months and partial healing in 12 tendons (43%). The 6 patients considered to have treatment failure showed partial healing as assessed on MRI.

Prognosis Predictive Factors

For all items analyzed, the number of injections was the only significant risk factor, with a threshold superior to 3 injections ($P < .02$). Among the 4 patients treated with >3 injections, 3 were considered treatment failures. We found no correlation between previous treatments and actual failures ($P = .14$ for peritendon corticosteroid injections, $P = .6$ for laser therapy, and $P = .19$ for ESWT) or with pretreatment clinical or radiological findings.

DISCUSSION

Chronic patellar tendinopathy or jumper's knee is one of the most common overuse knee disorders. It affects athletes in many sports and at all levels of participation.

TABLE 2
Comparison of Clinical Outcomes Before the Procedure and at the 2-Year Follow-up[a]

Outcome Measure	Preprocedure	2-Year Follow-up	*P* Value
Lysholm score	60 (40-70)	96 (70-100)	<.001
VISA-P score	39 (28-60)	94 (60-100)	<.001
VAS	7 (4-8)	0.8 (0-3)	<.0001

[a]Values are expressed as mean (range).

The nonoperative treatment of patellar tendinopathy recorded in the literature may not be effective in all cases despite several months of treatment.[1,23,43] In our study, we found that 3 US-guided injections of PRP significantly improved function. In fact, all athletes had failed previous nonoperative treatment for at least 4 months (mean, 18 months); 75% were able to return to their presymptom sporting level after a mean period of 3 months, and this sporting level was maintained until the 2-year follow-up. A complete repair of the tendon was confirmed by the 3-month MRI in 57% of patients. This conservative procedure is an alternative treatment to surgery, which has allowed only 50% to 70% of the treated patients (either arthroscopic or open surgery) to return to a presymptom sporting level.[6,33]

Coleman et al[6] compared open (29 tendons) versus arthroscopic (25 tendons) patellar tenotomy with a 4-year follow-up. They found sporting success in 54% of open and 46% of arthroscopic tenotomy patients, with a median time to return to a preinjury level of activity of 10 months and 6 months, respectively. Pascarella et al,[33] who studied clinical outcomes after arthroscopic management of patellar tendinopathy with a 10-year follow-up, found a return to presymptom levels in 19 of 27 (70%) professional athletes at 3 months after the procedure.

The biological study of tendon healing revealed that growth factors are one of the most important molecular families for tissue healing.[41] The rationale of using PRP for tendon disorders is that alpha granules in the platelets release many different growth factors, which stimulate tendon healing through collagen regeneration and a well-ordered angiogenesis. Thus, the use of PRP in the treatment of tendon lesions over several years has led to a significant improvement in healing.[16,30,34,37,38]

Commercial preparations of PRP vary in their ability to concentrate platelets and leukocytes. McCarrel and Fortier[28] demonstrated that leukocyte concentration is positively correlated with catabolic gene expression in tendons and ligaments, which suggested that delivery of concentrated leukocytes to a site of injury might not provide a favorable environment for tissue healing. In our study, we used the Arthrex ACP Double Syringe System, which is a pure PRP that concentrates platelets and minimizes leukocytes.[8,40]

Filardo et al[12] treated 15 patients with multiple PRP injections and observed a statistically significant improvement in Tegner and pain scores evaluated at the end of the therapy and at a 6-month follow-up. Knee function and

quality of life markedly improved, and most patients had a good recovery and returned to their previous sporting activity level. In a prospective cohort study that measured pain and sporting ability in patients with chronic patellar tendinopathy, Gosens et al[14] showed a statistically significant improvement in the PRP-treated group.

Vetrano et al,[42] in a randomized controlled trial, found that PRP injections led to better clinical results compared with focused ESWT in the treatment of jumper's knee in athletes.

The major limitation of our study is the absence of a control group. To our knowledge, no published studies have evaluated 3 consecutive US-guided PRP injections for the treatment of patellar chronic tendinopathy in athletes at a 2-year follow-up. We believe that ultrasonography is helpful for PRP injections. In fact, sonography permits precise localization of the pathologic area of the tendon, precise control of the area to be treated, and a tendon healing follow-up.[21,45]

Another limitation is that available preparations of PRP vary in terms of growth factors, platelet concentration, and platelet activation, and we did not independently measure the cellular content of our PRP; the ideal preparation has yet to be determined. Besides, the ideal protocol of PRP application (eg, the volume, number of injections, and timing of injections) remains imprecise. We found that 3 consecutive US-guided injections of pure PRP is a reliable nonoperative therapy for the treatment of refractory jumper's knee. Most growth factors contained in platelets are short-lived, and thus repeated administration is needed. Several clinical studies[12,14] suggested that weekly repeated injection of PRP permitted better clinical outcomes. Furthermore, our findings support PRP use in sport medicine patients who need a return to their preinjury level.

In July 2011, the World Anti-Doping Agency deemed all musculoskeletal PRP injections legal with no notification required. Clinical studies are needed to investigate if PRP therapy would permit faster recovery in professional athletes.

The clinical and radiological evaluation of our study showed improved results in athletes with chronic patellar tendinopathy at a minimum 2-year follow-up. Ultrasound-guided PRP injection in the pathologic area of the tendon could be considered a potential regenerative treatment for jumper's knee. Long-term randomized controlled trials are needed to corroborate our findings.

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