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Am J Sports Med 2013 41: 795 originally published online February 13, 2013
DOI: 10.1177/0363546513475345

Platelet-Rich Plasma Versus Focused Shock Waves in the Treatment of Jumper's Knee in Athletes

Mario Vetrano,*† MD, Anna Castorina,† MD, Maria Chiara Vulpiani,† MD, Rossella Baldini,‡ PhD, Antonio Pavan,§ MD, and Andrea Ferretti,‖ MD
Investigation performed at the Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy

Background: Tendinopathies represent a serious challenge for orthopaedic surgeons involved in treatment of athletes.

Purpose: To compare the effectiveness and safety of platelet-rich plasma (PRP) injections and focused extracorporeal shock wave therapy (ESWT) in athletes with jumper's knee.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: Forty-six consecutive athletes with jumper's knee were selected for this study and randomized into 2 treatment groups: 2 autologous PRP injections over 2 weeks under ultrasound guidance (PRP group; n = 23), and 3 sessions of focused extracorporeal shock wave therapy (2.400 impulses at 0.17-0.25 mJ/mm^2 per session) (ESWT group; n = 23). The outcome measures were Victorian Institute of Sports Assessment–Patella (VISA-P) questionnaire, pain visual analog scale (VAS), and modified Blazina scale. A reviewer who was blinded as to the group allocation of participants performed outcome assessments before treatment and at 2, 6, and 12 months after treatment. Nonparametric tests were used for within-group (Friedman/Wilcoxon test) and between-group (Kruskal-Wallis/Fisher test) testing, and the significance level was set at .05.

Results: The 2 groups were homogeneous in terms of age, sex, level of sports participation, and pretreatment clinical status. Patients in both groups showed statistically significant improvement of symptoms at all follow-up assessments. The VISA-P, VAS, and modified Blazina scale scores showed no significant differences between groups at 2-month follow-up (P = .635, .360, and .339, respectively). The PRP group showed significantly better improvement than the ESWT group in VISA-P, VAS scores at 6- and 12-month follow-up, and modified Blazina scale score at 12-month follow-up ($P < .05$ for all).

Conclusion: Therapeutic injections of PRP lead to better midterm clinical results compared with focused ESWT in the treatment of jumper's knee in athletes.

Keywords: jumper's knee; platelet-rich plasma; extracorporeal shock wave therapy; tendinopathy/therapy

Jumper's knee is an insertional tendinopathy of the extensor apparatus of the knee that may affect athletes practicing several sports at every level of participation but is found mainly in elite athletes involved in jumping activities. This syndrome is characterized by pain at the insertion either of the quadriceps tendon at the upper pole of the patella (20%) or of the patellar tendon at the lower pole of the patella (70%) or at the tibial tuberosity (10%).[12]

The characteristic complaint is an anterior knee pain with insidious onset, localized in the involved area, which is unleashed during or immediately after repetitive running or jumping activity. The pain usually disappears after a short period of rest but comes back after resumption of physical activity.

Diagnosis is clinical and is typically based on medical history and clinical findings. Imaging techniques such as color-Doppler sonography and magnetic resonance imaging are valuable tools to confirm the diagnosis and provide guidance for treatment.

Lian et al[26] reported an overall prevalence of jumper's knee of 14% in athletes practicing different sports activities, with a 45% recurrence in volleyball players and 32% in basketball players, confirming the data reported by Ferretti et al[11] in 1984 in their study on volleyball players. No cases were reported in cycling and orienteering. Hence,

*Address correspondence to Mario Vetrano, MD, Physical Medicine and Rehabilitation Unit, Sant'Andrea Hospital, Via di Grottarossa 1035-1039, Rome, Italy 00189 (email: mariovetrano@gmail.com).
†Physical Medicine and Rehabilitation Unit, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy.
‡Department of Statistical Sciences, Sapienza University of Rome, Rome, Italy.
§Department of Immunohematology and Transfusion, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy.
‖Orthopaedic Unit and Kirk Kilgour Sports Injury Centre, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy.
The authors declared that they have no conflicts of interest in the authorship and publication of this contribution.

The American Journal of Sports Medicine, Vol. 41, No. 4
DOI: 10.1177/0363546513475345

jumper's knee shows a high prevalence in sports characterized by high-impact ballistic loading of the knee extensors and low prevalence in sports with low loads, suggesting a link between the prevalence of jumper's knee and total tendon load. Epidemiological data support the pathogenetic hypothesis of disease overload, sustained by histological data. Ferretti et al[10] examined 18 fragments of the patellar tendon obtained during surgery and found histological abnormalities localized at the bone-tendon junction, whereas the patellar tendon itself, far from the osteotendinous junction, appeared normal. Similar alterations have been described previously in other insertional tendinopathies. As with other tendinopathies, all authors have agreed that in the first phases of this disease, the therapy should be nonoperative, including relative rest, cryotherapy, stretching, and physical therapy focusing on hamstrings flexibility and strengthening of quadriceps. The effectiveness of extracorporeal shock wave therapy (ESWT) and platelet-rich plasma (PRP) injection in the treatment of jumper's knee was reported in previous studies.[12,15,42,44,45]

With the assumption that tendinopathy is a failed healing response of the tendon,[28] the rationale for the use of PRP is promotion of tendon healing through high content of growth factors and cells in hyperphysiologic doses, which should enhance tissue repair mechanisms. Numerous studies have examined the effects of PRP in vitro and in vivo, demonstrating benefits that include improved cellular remodeling and decreased healing time.[1,13,15,21,39]

Extracorporeal shock wave therapy works through similar mechanisms in addressing the failed healing response of a tendon. Studies have indicated that mechanical loading increases the expression of several growth factors and cytokines, such as insulin-like growth factor 1 (IGF-1), transforming growth factor (TGF)–β1, and interleukin 6.[14] Most recent studies have demonstrated that shock wave treatment can increase the number of neovessels at the normal bone-tendon junction[46] and promote cell growth and collagen synthesis[25,43] through the release of growth factors and other active substances.

To our knowledge, no prospective randomized controlled trials have been performed to assess the effectiveness of ESWT compared with PRP injections in patients with insertional tendinopathies such as jumper's knee, Achilles tendinopathy, and plantar fasciopathy. The purpose of this randomized controlled clinical study was to compare the effectiveness and safety of ESWT and PRP injections in athletes with jumper's knee.

MATERIALS AND METHODS

Patient Recruitment

We recruited 46 patients who had consulted one of the participating physicians for jumper's knee during the period from January 2009 to May 2011. At the time of the enrollment, the diagnosis of jumper's knee for all patients was confirmed clinically by the same clinician, and all the patients underwent an ultrasound (US) examination performed by a clinician with 10 years of experience in musculoskeletal US. Both clinicians were not aware of the study details. For the purpose of this study, we included only patients with chronic unilateral tendinopathy at the insertion of the patellar tendon at the lower pole of the patella and identified at the US examination as proximal tendon anterior-posterior thickening with focal area of hypoechoic change and fibril discontinuity, evident in both the longitudinal and the transverse scans. The patients were informed in detail by an oral presentation of the scope and procedures of the study. They were then asked to take part in a clinical trial, in which they were randomly allocated to PRP injection group or ESWT group according to a computer-generated randomization list.

The criteria used for inclusion in the study were an established diagnosis of chronic jumper's knee at the insertion of the patellar tendon at the lower pole of the patella for at least 6 months before treatment and failure of nonoperative management. A washout period of 12 weeks was required between any nonoperative therapy and inclusion in the study. Patients were to be in the age range from 18 to 50 years and capable of completing questionnaires and of giving informed consent. All patients were to be athletic participants, involved in various sports activities as elite and nonelite athletes. Exclusion criteria were bilateral complaints; signs or symptoms of other, coexisting knee lesions; knee surgery or injection therapy with corticosteroids in the past 3 months; systemic disorders such as diabetes, rheumatoid arthritis, coagulopathies, cardiovascular diseases, infections, immunodepression, or neoplastic diseases; therapy with anticoagulants-antiaggregants; platelet values of fewer than 150,000/mm^3; or pregnancy.

The study protocol was approved by the Ethics and Experimental Research Committee of the Sant'Andrea Hospital, Sapienza University of Rome (RS:95/2012), and a randomized placebo-controlled study was not permitted. All patients gave written, informed consent to participate in this randomized controlled clinical study.

Fourteen of the 60 patients who underwent the first evaluation did not satisfy the inclusion criteria: 3 patients with bilateral complaint, 4 patients with pain for fewer than 3 months, 4 patients undergoing corticosteroids injections, and 3 patients undergoing knee surgery in the 3 months before recruitment. Therefore, in the end, a total of 46 participants were randomized to either PRP injection group or ESWT group.

Methods of Treatment

PRP Preparation. A PRP gel was supplied by the Immunohaematology and Transfusion Unit (SIMT) of the hospital. The PRP was obtained by a single centrifugation of whole blood to isolate platelets using MyCells Autologous Platelet Preparation System (Kaylight Ltd, Ramat-Hasharon, Israel).

The Recover platelet separation kit (Kaylight Ltd) was used to prepare PRP, in accordance with the system's instructions. Ten milliliters of venous blood was collected from the cubital vein. The whole blood was mixed in

a disposable sterile tube with acid-citrate-dextrose to prevent early clotting. After blood collection and 10 minutes of centrifugation at 1500*g*, PRP was obtained. One milliliter of this PRP was sent to the laboratory for analysis of platelet concentration, whereas the remaining 3 to 5 mL was used for patient injection without activation.

PRP Injection Group. All 23 patients in this group received 2 autologous PRP injections over 2 weeks (1 injection per week for 2 weeks) under ultrasound guidance. All treatments were performed by the same trained author (M.V.), who was not involved in assessing the patients before or after the treatment. The special MyCells tube containing separation gel and anticoagulant was used to collect 10 mL of blood from the patient. The tube was then centrifuged for 10 minutes at 1300 to 1500 rpm. Centrifugation resulted in 6 to 7 mL of plasma with a mean platelet concentration of 0.89 to 1.1 $\times$ 10^9 mL that was 3 to 5 times baseline concentration (which resulted from the above-mentioned analysis of platelet concentration). The designated injection location was recorded before the injection (hypoechogenicity of the tendon). The injection technique involved a single skin portal using a 22-g needle and then multiple small aliquots into the tendinous lesion, with color Doppler guidance. Approximately 2 mL of PRP was injected, and no local anesthesia was applied. After the injections, the patient rested in a supine position without moving the leg for 15 minutes, and a moderate compression bandage was applied with indication to remove it at the end of the day. Patients were allowed full loading of the limb immediately and could perform normal activities of daily living. If necessary, patients were allowed to use acetaminophen, but the use of nonsteroidal anti-inflammatory medication was prohibited.

ESWT Group. All 23 patients in this group received treatment from the same experienced author, who was not involved in assessing the patients before or after the treatment. A focused electromagnetic shock wave device (Modulith SLK, STORZ Medical, Switzerland) was used. Each participant received 3 sessions at 48- to 72-hour intervals. In each session, 2.400 impulses were administered with an energy flux density of 0.17 to 0.25 mJ/mm^2, depending on patient's pain tolerance. The treatment area was prepared with a coupling ultrasound gel to minimize the loss of shock wave energy at the interface between applicator tip and skin. Inline ultrasonic guidance was used to focus the shock waves on the injury area in the patellar tendon. No local anesthesia was applied.

Posttreatment Protocol

One week after the last treatment session, patients of both PRP injection group and ESWT group were given a standardized stretching and muscle strengthening protocol to be followed for 2 weeks, and subsequently they were allowed to begin water activities if these activities could be performed with only mild discomfort or pain.

The conventional stretching program included hip flexors, quadriceps, hamstrings, and heel cord before and after activity (30 s $\times$ 3-4 times). The proximal hip and thigh strengthening program included isometric and isotonic exercises to be performed daily. Isometric exercises included quad sets, flattening the knee against the floor with straight leg (10 s $\times$ 10 repetitions), and knees bent at 90° with the back against a wall (60 s $\times$ 6 repetitions). Isotonic exercises included straight leg raise (10 sets $\times$ 25 repetitions, 25 s rest between series), hip abduction side leg raise (4 sets $\times$ 25 repetitions, 25 s rest between series), hip adduction inside leg raise (4 sets $\times$ 25 repetitions, 25 s rest between series), and hip extension prone leg raise (4 sets $\times$ 25 repetitions, 25 s rest between series).

After 4 weeks patients were allowed to gradually return to previous training activity if there was minimal or no pain. Complete return to sports activities took place in accordance with the patient's pain tolerance and absence of clinical signs.

TABLE 1
Classification of Jumper's Knee According to Symptoms (Modified Blazina Scale)

Classification	Symptoms
Stage 0	No pain
Stage 1	Pain only after intense sports activity; no undue functional impairment
Stage 2	Pain at the beginning and after sports activity; still able to perform at a satisfactory level
Stage 3	Pain during sports activity; increasing difficulty in performing at a satisfactory level
Stage 4	Pain during sports activity; unable to participate in sport at a satisfactory level
Stage 5	Pain during daily activity; unable to participate in sport at any level

Outcome Assessments

Patients were assessed before treatment and 2, 6, and 12 months after the end of treatment. One clinical investigator, who was blinded with regard to treatment group allocation, performed all assessments.

VISA-P Score. At each visit, patients were requested to complete the Italian version of the Victorian Institute of Sports Assessment–Patella (VISA-P) questionnaire,[31] which was designed specifically for patients suffering from patellar tendinopathy to assess severity of symptoms, function, and ability to participate in sport. VISA-P is the only published clinical scale validated for patellar tendinopathy. The questionnaire contains 8 questions that cover the 3 domains of pain (questions 1-3), function (questions 4-6), and sport activity (questions 7 and 8). Questions 1 through 7 are scored out of 10, while question 8 carries a maximum of 30. Scores are summed to give a total out of 100. For question 8, participants must answer only part A, B, or C. The maximum score possible, which corresponds to an asymptomatic athlete, is 100 points. The theoretical minimum is 0 points.

Visual Analog Scale. Patients recorded the severity of their knee pain during the execution of 5 single-legged squats on a 10-cm continuous line marked "no pain" on one end and "worst pain I have ever had" on the other. The 10-cm visual analog scale (VAS) has been shown to

TABLE 2
Baseline Characteristics of Patients[a]

Characteristic	PRP Injection Group (n = 23)	ESWT Group (n = 23)	*P* Value
Age, mean (SD), y	26.9 (9.1)	26.8 (8.5)	.947
Sex, n (%)			.270
Men	20 (86.9)	17 (73.9)	
Women	3 (13.1)	6 (26.1)	
Duration of symptoms, mean (SD), mo	18.9 (19.1)	17.6 (20.2)	.935
Affected knee, n (%)			1.000
Left	12 (52.1)	12 (52.1)	
Right	11 (47.9)	11 (47.9)	
Previous treatments, n (%)			.832
CO_2 laser therapy	8 (34.8)	5 (21.7)	
Tecar therapy	19 (82.6)	16 (69.6)	
Therapeutic ultrasound	3 (13.0)	5 (21.7)	
Therapeutic exercises	21 (91.3)	22 (95.7)	
NSAIDs	9 (39.1)	12 (52.2)	
Sport activity, n (%)			1.000
Elite athletes	18 (78.3)	18 (78.3)	
Nonelite athletes	5 (21.7)	5 (21.7)	
Sport involved, n (%)			.902
Basketball	11 (47.8)	12 (52.2)	
Volleyball	11 (47.8)	9 (39.1)	
Soccer	1 (4.4)	2 (8.7)	

[a]ESWT, extracorporeal shock wave therapy; NSAIDs, nonsteroidal anti-inflammatory drugs; PRP, platelet-rich plasma.

be a reliable and sensitive scale for pain and has been used extensively in orthopaedic investigations.[24]

General Assessment and Response to Treatment. General assessment was scored by the patients with the use of a slightly modified version of the classification described by the Blazina scale, currently used in clinical settings to grade clinical status and monitor response to treatment, as reported by some authors in previously published studies.[9,45] Patients were requested to estimate their subjective symptoms and the current status of their treated patellar tendon using this classification scale, graded from 0 to 5 (Table 1). This scale is currently used. The result was considered excellent when it was stage 0 at the time of follow-up, good when it was stage 1 with a posttreatment improvement of at least 2 stages, fair when there had been improvement but the final result was stage 2 or higher, and poor when there had been no improvement. Excellent+good indicated satisfactory results, whereas fair+poor indicated unsatisfactory results.

Statistical Analysis

The aim of this study was to compare the clinical outcome after PRP injections or after focused ESWT. The efficacy end points were prospectively defined as improvement of the VISA-P score, reduction of the VAS from baseline to 2-, 6-, and 12-month follow-up, and a percentage of satisfactory results at 2-, 6-, and 12-month follow-up. Descriptive statistics were reported. The VISA-P and VAS data were summarized using mean and standard deviation. Modified Blazina scale scores and satisfactory/unsatisfactory results were summarized using a frequency distribution with percentages.

Since analysis of all parameters showed a nonnormal distribution, Kruskal-Wallis test was used to compare VISA-P and VAS, and Fisher exact test was used to compare satisfactory/unsatisfactory percentages between the treatment groups. Friedman and Wilcoxon tests were used for within-group analyses. All data analysis was performed using SPSS for Windows (version 13.0; SPSS Inc, Chicago, Illinois). *P* values less than .05 were considered statistically significant.

RESULTS

The 2 groups were homogeneous in terms of age, sex, level of sports participation, and pretreatment clinical status (Table 2). No patients were lost to follow-up or had undergone a surgical intervention during the follow-up period (Figure 1).

VISA-P Score

Both treatments were effective in improving the baseline VISA-P score values at 2-, 6-, and 12-month follow-up ($P < .005$ for all).

The VISA-P score showed no significant difference before treatments (PRP injection group, 55.3 ± 14.3; ESWT group, 56.1 ± 19.9; $P = .817$) and at the 2-month follow-up in the groups (PRP injection group, 76.2 ± 16.5; ESWT group, 71.3 ± 19.1; $P = .635$). The PRP injection group showed significantly better improvement than the ESWT group at 6-month (86.7 ± 14.2 vs 73.7 ± 19.9; $P = .014$) and 12-month (91.3 ± 9.9 vs 77.6 ± 19.9; $P = .026$) follow-up (Table 3).

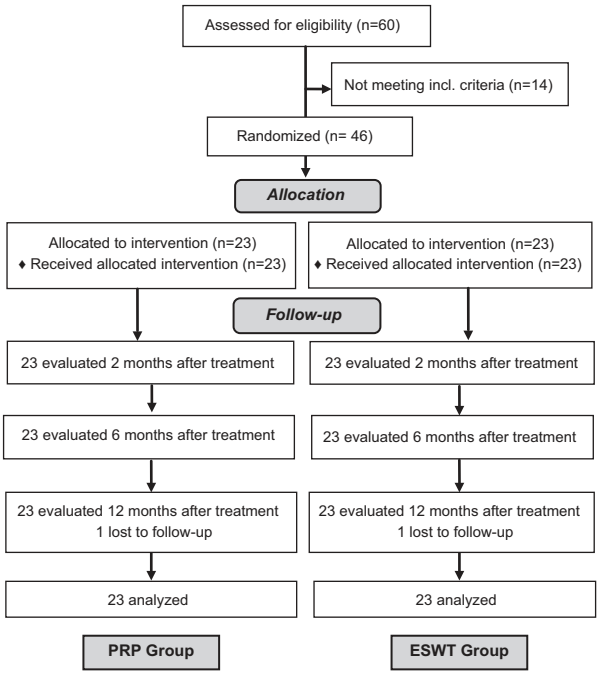

Figure 1. CONSORT flow diagram. ESWT, extracorporeal shock wave therapy; PRP, platelet-rich plasma.

Visual Analog Scale

Both treatments were effective in reducing the baseline VAS values at 2-, 6-, and 12-month follow-up (all P values $<.005$).

Assessment of load-induced pain on the VAS showed no significant difference between the groups before interventions (PRP injection group, 6.6 ± 1.8; ESWT group 6.3 ± 2.0; $P = .358$) and at the 2-month follow-up (PRP injection group, 3.2 ± 1.8; ESWT group, 3.9 ± 1.9; $P = .360$). The PRP injection group showed significantly better results than did the ESWT group at 6-month (2.4 ± 1.9 vs 3.9 ± 2.3; $P = .028$) and 12-month follow-up (1.5 ± 1.7 vs 3.2 ± 2.4; $P = .009$) (Table 3).

General Assessment

Significant improvement of baseline modified Blazina scale scores was shown in both treatment groups at all follow-up time points ($P < .005$ for all).

Assessment of classification of jumper's knee according to symptoms (modified Blazina scale) showed no significant difference before treatments in the groups ($P = .545$) at the 2-month follow-up ($P = .339$) and at the 6-month follow-up ($P = .130$). The PRP injection group showed significantly better results than did the ESWT group at 12-month follow-up ($P = .015$) (Table 3).

Response to Treatment

At the 2- and 6-month follow-ups, no statistically significant differences were reported between groups, with satisfactory results, respectively, in 47.8% and 82.6% of PRP injection group patients and in 43.4% and 65.2% of ESWT group patients ($P = .767$ and .314, respectively). The PRP injection group showed higher success rates (91.3% of satisfactory results) than the ESWT group (60.8%) at 12-month follow-up ($P = .035$) (Table 3).

Side Effects

No clinically relevant side effects were seen in either group. Three patients in the PRP injection group reported local pain and discomfort that started from the day of injection and gradually subsided. In the ESWT group, transient reddening of the skin occurred after treatment, but no bruising was seen. No device-related complications occurred.

DISCUSSION

Jumper's knee is a relatively frequent disorder that most commonly occurs in athletes participating in jumping activities; it is due to overuse of the knee extensor mechanism.

Volleyball, basketball, and soccer players, as well as dancers are at particular risk for the development of patellar tendinopathy because rapid acceleration, deceleration, jumping, and landing concentrate a tremendous stress on the extensor mechanism. As with other overuse injuries, jumper's knee is a self-resolving disease: Patellar tendinosis heals when the extensor mechanism stops being overloaded. To our knowledge, all authors have agreed that in the first phases of this disease, the therapy should be nonoperative. Several treatment options have been described in the literature, such as rest, anti-inflammatory drugs, eccentric exercises, injections, and surgical treatments.[29,30]

Extracorporeal shock wave therapy and PRP injections seem to be a safe and promising part of the rehabilitation program for jumper's knee, although, given current knowledge, it is impossible to recommend a specific treatment protocol. Both treatments share the same disputes: lack of hard evidence through randomized clinical and no standardized treatment protocols.

In 2009, van Leeuwen et al[42] published a review about ESWT for treating patellar tendinopathy. Only 7 studies were included in the review, and all of them concluded that ESWT seems to be an effective treatment for patellar tendinopathy with an estimate of approximately 74.7% of patients resulting in improvement of pain and knee function. But the findings should be interpreted with caution since only 2 of 7 studies boasted a high methodological quality.

In a randomized clinical trial in 2011 by Zwerver et al,[47] the effectiveness of ESWT on patellar tendinopathy was evaluated in 62 actively competing jumping athletes during the competitive season, and the investigators reported no benefit over placebo treatment over the 22-week study period. An explanation for the absence of a beneficial ESWT effect might be that athletes continued

TABLE 3
Outcome Assessment Before Treatment and at 2-, 6-, and 12-Month Follow-up[a]

Characteristic	PRP Injection Group (n = 23)	ESWT Group (n = 23)	*P* Value[b]
VISA-P score [0-100], mean (SD)			
Baseline	55.3 (14.3)	56.1 (19.9)	.817
2-month follow-up	76.2 (16.5)	71.3 (19.1)	.635
6-month follow-up	86.7 (14.2)	73.7 (19.9)	**.014**
12-month follow-up	91.3 (9.9)	77.6 (19.9)	**.026**
VAS [0-10], mean (SD)			
Baseline	6.6 (1.8)	6.3 (2.0)	.358
2-month follow-up	3.2 (1.8)	3.9 (1.9)	.360
6-month follow-up	2.4 (1.9)	3.9 (2.3)	**.028**
12-month follow-up	1.5 (1.7)	3.2 (2.4)	**.009**
Modified Blazina scale [0-5], n (%)			
Baseline			.545
Stage 0	—	—	
Stage 1	2 (8.7)	2 (8.7)	
Stage 2	8 (34.8)	12 (52.2)	
Stage 3	9 (39,2)	4 (17,4)	
Stage 4	3 (13.0)	3 (13.0)	
Stage 5	1 (4,3)	2 (8.7)	
2-month follow-up			.339
Stage 0	3 (13.0)	—	
Stage 1	9 (39.2)	12 (52.2)	
Stage 2	11 (47.8)	7 (30.4)	
Stage 3	—	4 (17.4)	
Stage 4	—	—	
Stage 5	—	—	
6-month follow-up			.130
Stage 0	6 (26.0)	5 (21.7)	
Stage 1	13 (56.6)	8 (34.8)	
Stage 2	4 (17.4)	8 (34.8)	
Stage 3	—	2 (8.7)	
Stage 4	—	—	
Stage 5	—	—	
12-month follow-up			**.015**
Stage 0	13 (22.3)	6 (20)	
Stage 1	8 (22.3)	9 (20)	
Stage 2	2 (22.3)	8 (20)	
Stage 3	—	—	
Stage 4	—	—	
Stage 5	—	—	
Results, n (%)			
2-month follow-up			.767
Satisfactory	11 (47.8)	10 (43.4)	
Unsatisfactory	12 (52.2)	13 (56.6)	
6-month follow-up			.314
Satisfactory	19 (82.6)	15 (65.2)	
Unsatisfactory	4 (17.4)	8 (34.8)	
12-month follow-up			**.035**
Satisfactory	21 (91.3)	14 (60.8)	
Unsatisfactory	2 (8.7)	9 (39.2)	

[a]ESWT, extracorporeal shock wave therapy; PRP, platelet-rich plasma; VAS, visual analog scale; VISA-P, Victorian Institute of Sports Assessment–Patella. Statistically significant data are in boldface.
[b]Kruskal-Wallis test.

participating in their usual training and matches during the treatment and follow-up period and received no restrictions with regard to sports participation during the season, so that the total load on the tendon was too high and there was insufficient time for recovery.

There are no randomized controlled trials about PRP application in patellar tendinopathy. To date, 2 studies are available in the literature. One was a prospective comparative study[13] that evaluated the effects of PRP injections and physiotherapy on 15 patients who had failed

previous nonsurgical or surgical treatments, compared with 16 patients primarily treated exclusively with the physiotherapy approach. The results documented no statistically significant differences in pain level or in time to recover and patient satisfaction, whereas there was a statistically significant improvement in EQ-VAS and Tegner score at the end of the therapy and at 6-month follow-up in either group; therefore, patients who had previously failed nonsurgical or even surgical treatments were able, through the combination of multiple PRP injections and physiotherapy, to achieve the same results obtainable in less severe cases.

The second prospective cohort study[15] evaluated the outcome of 36 patients with patellar tendinopathy treated with PRP injections, examining the differences between a group of patients receiving previous treatment that failed (injection of steroids, injection of polidocanol, and/or surgical treatment) and another group that received no prior therapy. The PRP treatment resulted in statistically significant improvement mainly in the group of patients who were not treated before, showing largest healing potential.

There is a lack of standardized treatment protocols for both therapies examined in our study. The literature describes various protocols for ESWT that have been used, as well as a number of sessions ranging from 1 to 5, number of impulses from 1000 to 2500, and energy levels usually titrated according to individual pain tolerance up to a possible maximum ranging from 0.44 to 0.58 mJ/mm^2.[42,47] As described in the study by Vulpiani et al,[45] we applied shock waves according to the guidelines of the Italian Society of Shock Wave Therapy, and the variability of energy flux density for patellar tendinopathy (0.17-0.25 mJ/mm^2) can be referred to some individual parameters of the single patient that we must take into consideration: degree of tendinopathy, presence of calcifications, and tolerance to pain.

The same variability is found in PRP treatment protocols. Extending research on PRP treatment of other tendinopathies, we deduce that authors use different treatment methods and PRP preparation techniques. Number of injections ranges from 1 to 3[6,36,41] performed every 2 weeks[13] or every 4 weeks.[5] There are differences in the dose of injected PRP, with a minimum of 2 mL and a maximum of 5 mL. In a 2011 review, Taylor et al[40] reported that all the selected studies used nonhomogeneous methods for PRP preparation (different volume blood drawn, different platelet separation system, different activating agent) and application (injection, PRP gel, PRP scaffold, PRP fibrin membrane). Also, studies used various activating agents, including autologous thrombin, calcium chloride, both, and none at all. In our study we have chosen to perform 2 weekly PRP injections because after the initial burst of PRP-related growth factors, the platelets synthesize and secrete additional growth factors for the remaining 7 days of their life span.[32]

Controversy also exists regarding the concomitant use of local anesthesia for the application of PRP and ESWT. In 2005, a comparative study[38] evaluated the effects of ESWT performed with or without anesthesia on plantar fasciitis. At 3 months, patients in the group without local anesthesia achieved significantly more reduction of pain compared with the group treated with local anesthesia. A more recent study[22] on healthy participants provided evidence that ESWT dose dependently activates and sensitizes primary afferent nociceptive C-fibers and that both activation and sensitization were prevented if local anesthesia was applied. Activation of C-fibers in humans is accompanied by the release of neuropeptides (CGRP and substance P), which not only act on microcirculation but also stimulate fibroblasts and osteoclastic/osteoblastic cells. Hence, application of local anesthesia significantly alters the biological effects of ESWT and should be avoided. A recent study[2] evaluated the effects of mixing anesthetics or corticosteroids with PRP on human tenocytes in vitro. The addition of either anesthetics or corticosteroids to PRP resulted in statistically significant decreases in tenocyte proliferation and cell viability; hence, anesthetics or corticosteroids, either alone or in combination, should be used carefully to preserve the proposed positive effects of PRP in the treatment of tendon injury. Given these findings, in our study all injections and all ESWT applications were performed without anesthetics.

The results of the current study show that PRP injections yielded better medium-term results than ESWT in the management of athletes with jumper's knee. The VISA-P and VAS scores showed no significant differences between groups at 2-month follow-up ($P = .635$ and .360, respectively). The PRP group showed significantly better improvement than the ESWT group in both scores at 6- and 12-month follow-up ($P < .05$ for all). The analysis showed comparable results in both treatment groups at short term, with an even higher satisfaction level in the PRP group at 6 and 12 months of follow-up. Eight weeks after the procedure, the PRP group reported satisfactory results in 47.8% of cases (11/23 tendons), similar to the ESWT group, which reported satisfactory results in 43.4% of cases (10/23 tendons). Subsequently, the PRP group satisfactory results increased to 82.6% at 6-month follow-up (19/23 tendons), reaching 91.3% at 12-month follow-up (21/23 tendons), whereas in the ESWT group satisfactory results increased to 65.2% at 6-month follow-up (15/23 tendons) but decreased to 60.8% at 12-month follow-up (14/23 tendons). In the last evaluation, results showed a high level of satisfaction in the PRP group, with 91.3% of patients (21/23 patients) able to pursue sports at their preinjury level, compared with 60.8% of satisfied patients (14/23 patients) in the ESWT group. We reported 82.6% satisfied patients at 6-month follow-up, and this result is in line with 6-month data reported by Filardo et al,[13] who reported a satisfaction level of 86.7% in PRP group.

Two hypotheses could explain the better results of PRP over ESWT. The PRP injections may have a multifaceted mechanism of action involving platelet action as well as injection-related effects. Several studies have shown that needling of tendinopathic tissue has a positive effect itself on tendon healing.[4,18] Injection-produced needle trauma causes local bleeding, and some studies suggested that autologous blood injection might be associated with improved symptoms of lateral epicondylitis and Achilles tendinopathy.[8,20,35] Injections change the pressure-

volume relationship in a given anatomic space, and these local mechanical effects are hypothesized to destroy pathological vascular and neural growth. All these factors inherent in the route of administration of PRP may enhance the biological mechanisms and increase the tendon's healing response.

The pathway of chronic tendinopathies is very complex and involves, in addition to growth factors, many other pathogenetic factors that operate at different stages of the disease. Furthermore, the exact action mechanisms of ESWT and PRP are not yet fully understood. Many laboratory studies that have investigated the molecular mechanisms of PRP and ESWT have demonstrated that both may enhance tendon healing by increasing the number of tenocytes and production of collagen, which, including collagen types I and III, is a major component of the tendon. Different mechanisms have been described in explaining ESWT effects, including release of growth factors (TGF-β1, IGF-1), which occurs through mechanical stimulation of the treated site and stimulation of tenocyte proliferation, and collagen synthesis.[14,25,28,33,34,43]

The molecular effects of PRP are dose-dependent.[19] The number of platelets needed to obtain the optimal effect in bone regeneration has been shown to be between 503,000 and 1,729,000 platelets/μL of PRP. Concentrations below 3.8×10^5 platelets/μL have a suboptimal effect, and concentrations above 1.8×10^6 platelets/μL paradoxically may have an inhibitory effect.[27] Commonly used PRP manufacturing methods concentrate the platelets within this range, optimizing the therapeutic effect. Probably PRP injection provides the optimal amount of growth factors, thus stimulating more effectively the mechanisms of tissue repair compared with the action of ESWT.

Further explanation for better results in the PRP group may be related to high expectations of patients about this new technology, which has had a great influence especially in sports medicine. All these reasons, as well as the relatively low age and the high motivation of the patients in our study, could justify the surprisingly high VISA-P mean scores reached at 6- and 12-month follow-up in the PRP injection group (86.7 and 91.3, respectively). However, these VISA-P values are not unreasonable, since the maximum score possible is 100 points, and several authors[3,7,16,17,23,37] have reported a VISA-P mean score above 85 in asymptomatic athletes with diagnosed jumper's knee.

This study has the following principal limitations: (1) small number of patients enrolled, (2) lack of a placebo control group, and (3) follow-up assessment through qualitative outcome measures (VISA-P, VAS, modified Blazina score) in the absence of clinical and instrumental quantitative assessments (color ultrasonography, magnetic resonance imaging). In addition, although the assessment was blinded, there was no way to blind the patients to the treatment. Therefore, it is possible that their awareness of the treatment modality may have had some effect on their perception of their response to the treatment. Finally, the results may be specific to the specific formulation of PRP and the specific ESWT protocol used in the study.

In conclusion, this report describes the first comparison of PRP injection with ESWT as a treatment for jumper's knee. Both PRP injections and ESWT are safe and effective in the treatment of athletes with jumper's knee. The analysis showed comparable results in both treatment groups at short term, with better results in the PRP group at 6 and 12 months of follow-up.

ACKNOWLEDGMENT

The authors thank Mauro Masci for his help in the preparation of the PRP and his contributions to this research.

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