

Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy

A Double-Blind, Randomized Controlled Trial

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Background: Previous studies have shown improvement in patellar tendinopathy symptoms after platelet-rich plasma (PRP) injections, but no randomized controlled trial has compared PRP with dry needling (DN) for this condition.

Purpose: To compare clinical outcomes in patellar tendinopathy after a single ultrasound-guided, leukocyte-rich PRP injection versus DN.

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

Methods: A total of 23 patients with patellar tendinopathy on examination and MRI who had failed nonoperative treatment were enrolled and randomized to receive ultrasound-guided DN alone (DN group; $n = 13$) or with injection of leukocyte-rich PRP (PRP group; $n = 10$), along with standardized eccentric exercises. Patients and the physician providing follow-up care were blinded. Participants completed patient-reported outcome surveys before and at 3, 6, 9, 12, and ≥ 26 weeks after treatment during follow-up visits. The primary outcome measure was the Victorian Institute of Sports Assessment (VISA) score for patellar tendinopathy at 12 weeks, and secondary measures included the visual analog scale (VAS) for pain, Tegner activity scale, Lysholm knee scale, and Short Form (SF-12) questionnaire at 12 and ≥ 26 weeks. Results were analyzed using 2-tailed paired and unpaired t tests. Patients who were dissatisfied at 12 weeks were allowed to cross over into a separate unblinded arm.

Results: At 12 weeks after treatment, VISA scores improved by a mean \pm standard deviation of 5.2 ± 12.5 points ($P = .20$) in the DN group ($n = 12$) and by 25.4 ± 23.2 points ($P = .01$) in the PRP group ($n = 9$); at ≥ 26 weeks, the scores improved by 33.2 ± 14.0 points ($P = .001$) in the DN group ($n = 9$) and by 28.9 ± 25.2 points ($P = .01$) in the PRP group ($n = 7$). The PRP group had improved significantly more than the DN group at 12 weeks ($P = .02$), but the difference between groups was not significant at ≥ 26 weeks ($P = .66$). Lysholm scores were not significantly different between groups at 12 weeks ($P = .81$), but the DN group had improved significantly more than the PRP group at ≥ 26 weeks ($P = .006$). At 12 weeks, 3 patients in the DN group failed treatment and subsequently crossed over into the PRP group. These patients were excluded from the primary ≥ 26 -week analysis. There were no treatment failures in the PRP group. No adverse events were reported. Recruitment was stopped because interim analysis demonstrated statistically significant and clinically important results.

Conclusion: A therapeutic regimen of standardized eccentric exercise and ultrasound-guided leukocyte-rich PRP injection with DN accelerates the recovery from patellar tendinopathy relative to exercise and ultrasound-guided DN alone, but the apparent benefit of PRP dissipates over time.

Keywords: tendinopathy; tendon injuries; patellar tendon; platelet-rich plasma; symptoms; randomized controlled trial

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Patellar tendinopathy (PT) is a degenerative disease of the patellar tendon resulting in anterior knee pain associated with focal and palpable tenderness at the inferior pole of the patella.^{3,43} Typical findings on magnetic resonance imaging (MRI) include smaller tendon cross-sectional area⁸ and abnormalities of the posterior border of the patellar tendon and infrapatellar fat pad.⁴⁴ Patellar tendinopathy is often caused by overuse in activities that require jumping, running, or rapid changes in direction^{14,28} and has a reported prevalence ranging from 14% to 32% and 45% in basketball and volleyball athletes, respectively.²⁸ The condition appears to be more common

in males; an increased prevalence of PT in males versus females has been reported in recreational athletes,⁴⁷ adolescent athletes,⁶ and elite athletes.⁴⁰

Eccentric exercise has been a critical component of the standard treatment for chronic PT. One clinical study comparing eccentric to concentric exercises in PT found a statistically significant improvement in visual analog scores (VAS) and Victorian Institute of Sports Assessment (VISA) scores within the eccentric group but no improvement within the concentric group.²³ However, a systematic review of clinical trials studying eccentric exercises in PT found no significant improvement in return to activity, concluding that there is limited evidence to support eccentric exercise in PT treatment regimens.⁴⁶ Eccentric exercises remain a component of most treatment programs, but many patients fail to improve and need additional treatment.

Beyond eccentric exercise, there is currently no consensus on the optimal treatment method.^{1,33,34} Since most tendinopathies have minimal or no inflammation, ibuprofen and other nonsteroidal anti-inflammatory drugs are generally not helpful.³⁴ Similarly, although glucocorticoids may be effective in the treatment of acute tendon inflammation, they inhibit collagen production and may contribute to poor long-term outcomes in PT.²⁷

Newer therapies have focused on intratendinous injection of substances believed to inhibit neovascularization (sclerotherapy), stimulate tendon repair (prolotherapy and platelet-rich plasma [PRP]), or improve pain through other pathways (acupuncture, shock wave therapy). Previous randomized controlled trials and prospective cohort studies have investigated the use of aprotinin,³² corticosteroids,^{17,27} and sclerosing^{19,20} injections on PT. However, there is little evidence to support the efficacy of prolotherapy, sclerotherapy, matrix metalloproteinase inhibitors, acupuncture, or shock wave therapy in the treatment of PT.^{39,41} One prospective study of ultrasound-guided dry needling (DN) with autologous blood injection found a significant improvement in VISA score and return to sport,²² suggesting that DN with autologous injections could be a promising therapy.

Platelet-rich plasma is an autologous blood fraction rich in platelets and their associated growth factors that is injected at the site of muscle or tendon injury as an adjuvant to the natural healing process. The logic behind PRP is that platelets are the first to arrive at the site of tissue injury and thus have the potential to release growth factors that play a critical role in mediating healing.⁹ While PRP has been used and studied since the 1970s, there has been a recent spike in interest in using PRP for sports-related injuries,¹⁶ and PRP is now commonly used throughout the world.^{2,30}

The goal of this investigation is to compare a regimen of eccentric exercises combined with either ultrasound-guided leukocyte-rich PRP injection (including dry needling) or ultrasound-guided dry needling alone in the treatment of PT that has failed to respond to at least 6 weeks of physical therapy.

METHODS

The study has been designed and reported in accordance with the CONSORT and CONSORT PRO Extension

guidelines for reporting patient-reported outcomes in randomized trials (Figure 1).^{5,21,36}

Trial Design

After institutional review board approval was obtained and the trial was registered with clinicaltrials.gov (NCT01406821), 30 consecutive patients from our sports medicine clinic were assessed for eligibility and 23 were subsequently enrolled in the study from October 2009 to June 2012. No changes to the trial design were made after the first patient was enrolled.

Participants

The diagnosis of PT was made by clinical examination performed by an attending orthopaedic surgeon and was confirmed by MRI read by an attending musculoskeletal radiologist. Inclusion criteria were age ≥ 18 years, diagnosis of PT, and persistence of symptoms after 6 weeks (12 sessions) of physical therapy with eccentric exercise. Exclusion criteria were previous injection or surgery in the affected knee and inability to complete patient-reported outcome surveys. Clinical examination features indicative of PT included tenderness to palpation at the inferior pole of the patella with the knee fully extended and the quadriceps relaxed. The MRI features consistent with PT included enhanced signal intensity in the proximal patellar tendon, increased tendon size in the antero-posterior direction, and poor definition of the posterior tendon border.

Randomization and Blinding

The random allocation sequence was generated by a medical assistant based on coin toss, a form of simple (unrestricted) randomization.³⁷ The coin was tossed 30 times, assigning tails to DN ($n = 17$) and heads to PRP ($n = 13$). To conceal treatment allocations, treatment group assignments were placed in opaque envelopes that were numbered sequentially and remained sealed until the day of treatment. After opening the next sealed envelope in the sequence, the medical assistant communicated the treatment allocation directly to the radiologist and nursing staff responsible for performing the ultrasound-guided injection.

Both the treating orthopaedic surgeon and the patient remained blinded with respect to treatment group at least until the ≥ 26 -week outcomes had been reported, except for those patients who defined their treatment as a failure at 12 weeks after injection. The radiologist and assistants who performed the ultrasound-guided treatment were not blinded, but they were not involved in reporting any patient outcomes. To maintain patient blinding, patients were blindfolded throughout the DN or PRP procedure. Care was also taken to remove language from billing and other written communications that could potentially unblind the patient.

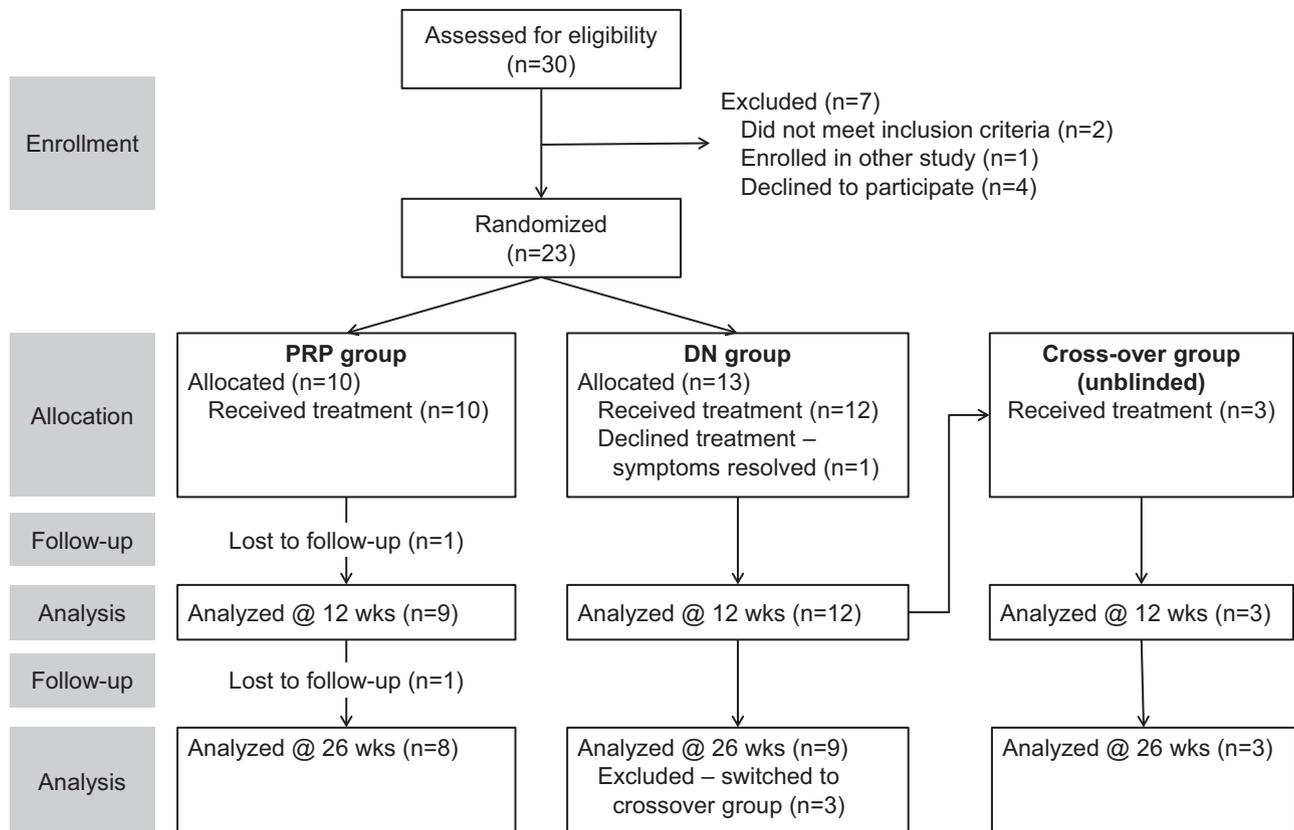


Figure 1. CONSORT flowchart. DN, dry needling; PRP, platelet-rich plasma.

Patients in a treatment group who completed the 12-week questionnaires and were dissatisfied with their progress were then allowed to receive the other treatment and were followed for at least 14 more weeks, for a total of ≥ 26 weeks. Patients who were satisfied with treatment at 12 weeks remained blinded and were followed for a minimum of 26 weeks (6 months). All patients were instructed to avoid nonsteroidal anti-inflammatory drugs for 4 weeks before and after treatment.

Ultrasound-Guided Dry Needling and PRP

Patients received either a single DN or PRP procedure, according to their assigned treatment group. A registered nurse obtained 55 mL of peripheral blood by venipuncture for all patients regardless of treatment group. For patients in the PRP group, blood was then processed with a GPS III (Biomet Inc, Warsaw, Indiana, USA) PRP kit according to manufacturer instructions. For patients in the DN group, the 55 mL of blood was discarded. For all patients, a board-certified radiologist localized the area of tendinopathy by ultrasound and patient feedback and then injected 3 mL of 0.25% bupivacaine with 1:100,000 epinephrine subcutaneously using sterile technique. Care was taken not to anesthetize the tendon or tendon sheath. All patients were then blindfolded, and the radiologist penetrated the area of tendinopathy 10 times. In the PRP

group, approximately 6 mL of leukocyte-rich PRP was injected into the patellar tendon during the DN procedure. The blindfold was then removed and patients were instructed to resume weightbearing as tolerated.

Eccentric Exercises

All patients were instructed to follow a standardized 5-phase program of eccentric exercises, which was provided directly to their physical therapists. Each patient was assessed to determine the appropriate starting phase based on his or her current abilities. Treatment plans focused on eccentric strengthening and on improving flexibility, cardiovascular fitness, balance, core strength, and sport-specific skills. Patients attended physical therapy twice per week and were instructed to perform standardized additional exercises at home throughout the study period. Physical therapists reported patients' overall progress directly to the principal investigator.

Outcomes

Participants were asked to complete written questionnaires at baseline and at 5 additional follow-up appointments: 3, 6, 9, and 12 weeks and ≥ 6 months. The primary patient-reported outcome was the VISA score at

TABLE 1
Description of the Patient Groups Analyzed at 12 Weeks^a

	DN (n = 12)	PRP (n = 9)	Mean (All Patients)	P Value
Age, y	40 ± 14	28 ± 8	35 ± 13	.04
% male	100	89	95	.24
Height, in.	69 ± 5	70 ± 4	69 ± 4	.46
Weight, lb	171 ± 18	185 ± 37	177 ± 28	.26
Baseline scores				
VISA	47.4 ± 18.0	41.0 ± 14.3	43.7 ± 15.6	.39
Tegner	4.0 ± 2.1	3.7 ± 2.5	3.9 ± 2.2	.75
Lysholm	48.5 ± 16.5	58.3 ± 14.5	53.6 ± 16.0	.17
VAS	3 ± 2.3	4.1 ± 1.5	3.5 ± 2.0	.22
SF-12	50 ± 7.5	49.2 ± 3.7	49.6 ± 5.8	.75

^aValues are reported as mean ± standard deviation unless otherwise indicated. Statistically significant differences between groups are in boldface ($P < .05$, independent samples t tests). DN, dry needling group; PRP, dry needling + platelet-rich plasma group; SF-12, Short Form-12; VAS, visual analog scale; VISA, Victorian Institute of Sports Assessment.

12 weeks, because the VISA is a validated questionnaire that can be used to quantitatively assess severity of symptoms specifically in patients with PT.⁴² Secondary patient-reported outcomes were Tegner activity scale (Tegner),³⁸ Lysholm knee scoring scale (Lysholm),²⁹ visual analog scale for pain (VAS),¹¹ and Short Form-12 (SF-12) measure of health-related quality of life⁴⁵ at 3, 6, 9, and 12 weeks and at 6 months.

Sample Size

An a priori power analysis was conducted to estimate the minimum sample size needed to achieve 80% power ($1 - \beta$) at the .05 significance level (α) for the primary outcome measure, VISA score at 12 weeks. Variables used in the power calculation were taken from the literature including an assumed effect size of 13¹⁸ and standard deviation (SD) of 8.⁴² This analysis suggested that a minimum of 6 patients per group would suffice. To allow room for potential loss to follow-up and to ensure a robust data set, we created 30 sealed envelopes, as indicated above.

Statistical Analysis

All 12-week data were analyzed using the “intention-to-treat” principle. Statistical analysis on all patient-reported outcome measures was conducted using paired 2-tailed t tests to compare 12-week and baseline scores. Independent samples 2-tailed t tests were used to compare the mean change at 12 weeks between the DN and PRP groups. The 26-week data were analyzed using a “per protocol” approach, which included only data from patients who had maintained their original group assignments and remained blinded for at least 26 weeks; individuals who crossed over at 12 weeks were excluded from this analysis. A secondary intention-to-treat analysis was also conducted as recommended by the CONSORT guidelines to maintain randomization and minimize the introduction of systematic bias from crossover, adherence, and loss to follow-up.³² In this secondary intention-to-treat analysis,

patients were analyzed according to their original group assignments; the 3 patients who voluntarily crossed over from the DN group to the PRP group at 12 weeks were analyzed according to their original group assignment. Results for all analyses were considered significant at $P < .05$. The proportion of treatment failures at 12 weeks was compared by use of a chi-square test.

Interim Analyses and Stopping Guidelines

Interim analyses were conducted annually, with the intent of stopping recruitment early if 12-week analyses revealed a statistically significant difference in VISA score improvement between the DN and PRP groups. No additional participants were recruited after this criterion was met in the 2-year interim analysis. All currently enrolled participants were still followed as outlined above.

RESULTS

A total of 23 patients were enrolled and randomized into the DN (n = 13) and PRP (n = 10) groups. By 12 weeks, 12 DN and 9 PRP patients had completed treatment and all follow-up surveys and were included in the primary analysis; their characteristics are summarized in Table 1. Patient sex, height, weight, and baseline VISA score were all similar between groups, indicating successful randomization. However, the mean age (\pm SD) was higher in the DN group (40 ± 14 years) than in the PRP group (28 ± 8 years) ($P = .04$).

The primary statistical analysis at ≥ 26 weeks was performed per protocol, which excluded data from the 3 patients who crossed over from the DN to the PRP groups after “failing treatment” at 12 weeks. The statistical analyses at ≥ 26 weeks were also repeated using intention-to-treat principles. In this secondary analysis, the 3 DN patients who eventually received PRP as part of the crossover group were still analyzed as part of the original DN group. The results from the intention-to-treat and per

TABLE 2
Scores for the Dry Needling (DN) and Platelet-Rich Plasma (PRP) Groups^a

	Baseline		12 Weeks		26 Weeks	
	DN	PRP	DN	PRP	DN	PRP
VISA	47.4 ± 18.0 (37.2-57.6)	41.0 ± 14.3 (31.7-50.3)	52 ± 20.3 (40.0-64.0)	66.4 ± 20.2 (53.2-79.7)	83.9 ± 9.0 (78.0-89.8)	67.8 ± 21.9 (53.4-82.1)
Tegner	4.0 ± 2.1 (2.8-5.2)	3.7 ± 2.5 (2.0-5.3)	4.0 ± 1.6 (3.0-4.9)	4.9 ± 2 (3.6-6.2)	6.4 ± 1.4 (5.5-7.4)	5.8 ± 2.4 (4.1-7.4)
Lysholm	48.5 ± 16.5 (39.2-57.8)	58.3 ± 14.5 (48.9-67.8)	74.8 ± 19.4 (63.3-86.3)	82.1 ± 22.1 (67.7-96.5)	91.8 ± 13.4 (83.0-100.5)	76.3 ± 20.7 (60.8-91.7)
VAS	3.0 ± 2.3 (1.7-4.3)	4.1 ± 1.5 (3.2-5.1)	2.3 ± 1.6 (1.4-3.2)	1.7 ± 1.7 (0.5-2.8)	0.3 ± 0.5 (0.0-0.7)	1.7 ± 1.5 (0.6-2.8)
SF-12	50.0 ± 7.5 (45.8-54.3)	49.2 ± 3.7 (46.7-51.6)	50.0 ± 8.5 (44.9-55.0)	50.7 ± 2.7 (48.9-52.5)	50.6 ± 5.0 (47.4-53.8)	49.0 ± 4.2 (45.8-52.1)

^aValues are reported as mean ± standard deviation (95% confidence interval). SF-12, Short Form-12; VAS, visual analog scale; VISA, Victorian Institute of Sports Assessment.

TABLE 3
Net Change in Scores From Baseline to 12 and ≥26 Weeks^a

MCID ^b	Change From Baseline at 12 Weeks						Change From Baseline at ≥26 Weeks					
	DN		PRP		DN vs PRP	DN		PRP		DN vs PRP		
	Δ	P	Δ	P	P	Δ	P	Δ	P	P		
VISA	13	5.2 ± 12.5 (-2.2 to 12.6)	.20	25.4 ± 23.2 (10.3 to 40.6)	.01	.02	33.2 ± 14.0 (24.1 to 42.4)	.0001	28.9 ± 25.2 (11.4 to 46.3)	.01	.66	
Tegner	1	0.0 ± 1.4 (-0.9 to 0.8)	.92	1.2 ± 3.5 (-1.0 to 3.5)	.32	.28	2.0 ± 1.5 (1.0 to 3.0)	.004	2.5 ± 3.5 (0.0 to 5.0)	.09	.70	
Lysholm	10	26.5 ± 22.7 (13.2 to 39.9)	.003	23.8 ± 27.0 (6.2 to 41.4)	.03	.81	45.4 ± 18.8 (33.1 to 57.8)	.0001	14.7 ± 19.1 (0.6 to 28.8)	.09	.006	
VAS	2	-0.9 ± 2.2 (-2.2 to 0.4)	.20	-2.4 ± 2.1 (-3.8 to -1.1)	.008	.13	-2.5 ± 2.7 (-4.2 to -0.8)	.02	-2.6 ± 1.7 (-3.7 to -1.4)	.003	.96	
SF-12	6.8	-0.4 ± 6.0 (-4.0 to 3.1)	.82	1.5 ± 3.0 (-0.4 to 3.5)	.16	.39	1.9 ± 4.4 (-1.0 to 4.8)	.24	-0.6 ± 4.8 (-4.1 to 2.9)	.75	.30	

^aValues are reported as mean change (Δ) ± standard deviation (95% confidence interval). Statistically significant differences are in bold-face. The ≥26-week statistical analyses were performed “per protocol,” which excluded data from the 3 patients who crossed over from the dry needling (DN) to the platelet-rich plasma (PRP) group. MCID, minimum clinically important difference; SF-12, Short Form-12; VAS, visual analog scale; VISA, Victorian Institute of Sports Assessment.

^bBased on published MCIDs for VISA,¹⁸ Tegner,⁴ Lysholm,⁴ VAS,^{11,24} and SF-12.³⁵

protocol analyses were nearly identical, with no differences in statistical significance. The proportion of treatment failures at 12 weeks did not significantly differ between groups ($P = .103$).

Mean VISA, Tegner, Lysholm, VAS, and SF-12 scores at baseline, 12 weeks, and ≥26 weeks are summarized for the DN and PRP groups in Table 2, and the trajectories are shown in Figure 2. The change from baseline at 12 and ≥26 weeks is reported for all outcome measures in Table 3.

Patellar Tendinopathy Symptoms (VISA)

The DN group improved only modestly by 5.2 ± 12.5 points at 12 weeks ($P = .20$) but achieved a net improvement of

33.2 ± 14.0 points ($P = .001$) by ≥26 weeks. The VISA scores improved significantly within the PRP group at 12 weeks by a mean ± SD of 25.4 ± 23.2 points ($P = .01$) and at ≥26 weeks by a total of 28.9 ± 25.2 points ($P = .01$). The PRP group had improved significantly more than the DN group at 12 weeks ($P = .02$), but the difference between groups was not significant at ≥26 weeks ($P = .66$). All statistically significant changes in VISA scores were also clinically important based on the published minimum clinically important difference (MCID) of 13 points.¹⁸

Activity (Tegner)

Mean Tegner scores for the DN group were unchanged at 12 weeks but improved by 2.0 ± 1.5 points at ≥26 weeks

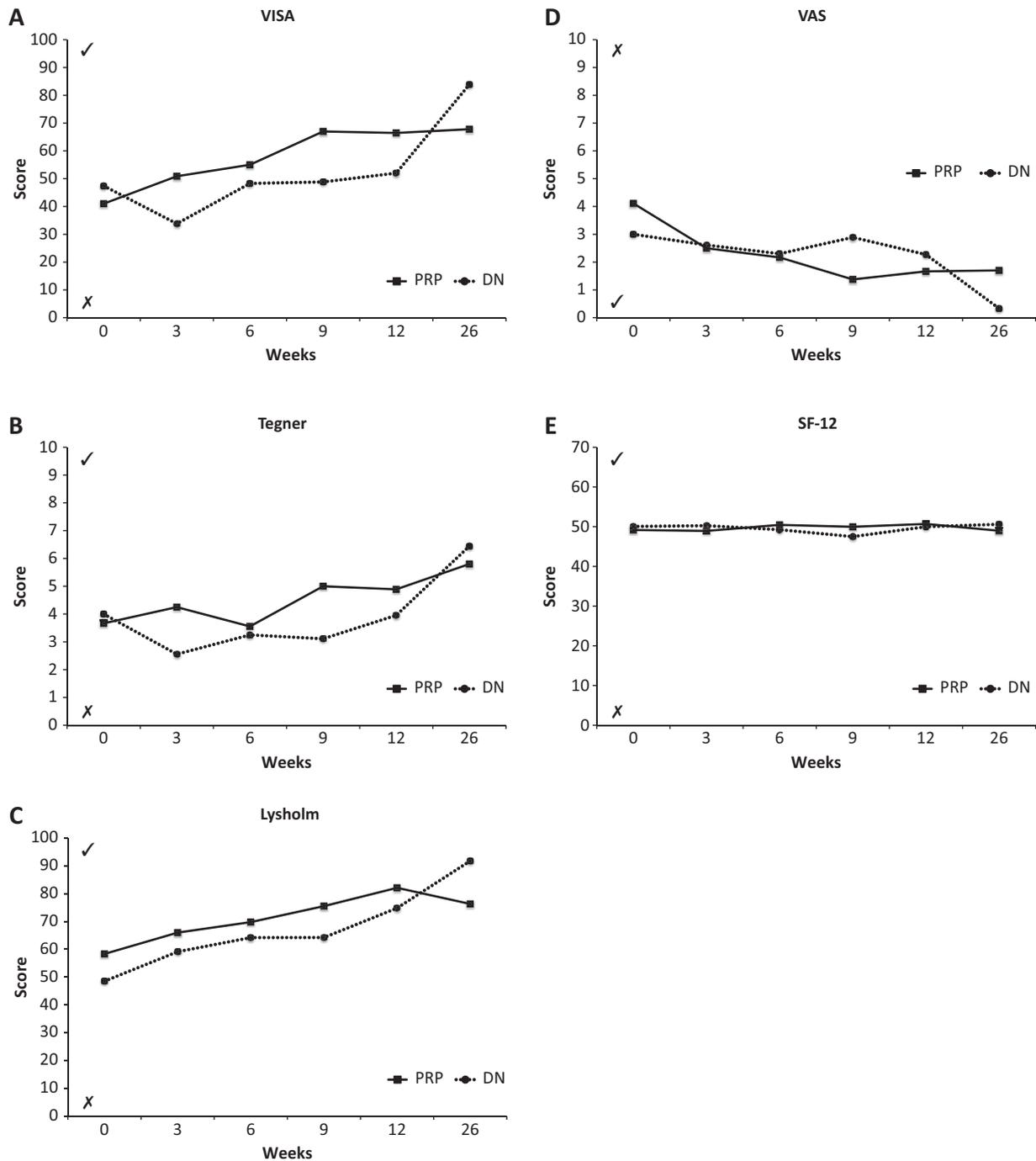


Figure 2. Patient-reported outcomes for patients in the randomized and blinded dry needling (DN) and platelet-rich plasma (PRP) groups at 3, 6, 9, 12, and ≥ 26 weeks after a single treatment. A check mark indicates the best possible score and an X indicates the worst possible score for each outcome measure. Data reported here include only patients who remained blinded throughout the full 26 weeks; patients who voluntarily switched to the crossover cohort after 12 weeks are excluded.

relative to baseline ($P = .004$). Within the PRP group, Tegner scores improved by 1.2 ± 3.5 points ($P = .32$) at 12 weeks and by 2.5 ± 3.5 points ($P = .09$) at ≥ 26 weeks, neither of which was significant. There were no significant

differences between the DN and PRP groups at 12 ($P = .28$) or ≥ 26 weeks (0.70). Both groups showed clinically meaningful improvement by ≥ 26 weeks based on the published MCID of 1 point.⁴

Function and Stability (Lysholm)

The DN group showed statistically significant improvements of 26.5 ± 22.7 points ($P = .003$) at 12 weeks and 45.4 ± 18.8 points ($P = .0001$) at ≥ 26 weeks, both of which met criteria for clinical importance based on the MCID of 10.⁴ Although the PRP group initially improved by 23.8 ± 27.0 points ($P = .03$) at 12 weeks, much of this progress was lost by ≥ 26 weeks, at which time the PRP group showed a net improvement of only 14.7 ± 19.1 points ($P = .09$). There was no significant difference between the DN and PRP groups at 12 weeks ($P = .81$), but the DN group had improved significantly more than the PRP group at ≥ 26 weeks ($P = .006$).

Pain (VAS)

Within the DN group, VAS pain score decreased by 0.9 ± 2.2 points ($P = .20$) at 12 weeks and by a net 2.5 ± 2.7 points ($P = .02$) by ≥ 26 weeks. The PRP group decreased significantly by 2.4 ± 2.1 points at 12 weeks ($P = .008$) and by 2.6 ± 1.7 points ($P = .003$) at ≥ 26 weeks. There was no significant difference between the DN and PRP groups at either 12 ($P = .13$) or ≥ 26 weeks ($P = .96$). All statistically significant results also met the 2-point threshold for clinical importance.^{11,24}

Health-Related Quality of Life (SF-12)

Neither the DN nor PRP groups showed any statistically significant or clinically important changes at any time point, based on the published MCID of 6.8 points.³⁵

DISCUSSION

The results of this double-blind, randomized controlled trial indicate that a therapeutic regimen of standardized eccentric exercise and ultrasound-guided leukocyte-rich PRP injection (including dry needling) accelerates the recovery from patellar tendinopathy relative to exercise and ultrasound-guided dry needling alone, but the apparent benefit of PRP dissipates over time.

The PRP group demonstrated statistically significant and clinically important improvements in symptoms (VISA), pain (VAS), and function and stability (Lysholm) at 12 weeks. The DN group also showed statistically significant and clinically important improvements on the Lysholm knee questionnaire. Statistical comparison between the two groups at 12 weeks showed that the PRP group had improved significantly more than the DN group based on the VISA score of patellar tendinopathy symptoms. However, by ≥ 26 weeks these benefits of PRP had dissipated. At ≥ 26 weeks, the DN group had made clinically and statistically significant improvements on VISA, Tegner, Lysholm, and VAS scores, whereas the PRP group achieved statistically significant gains only on the VISA and VAS scores. Notably, the improvements in VISA, Tegner, VAS, and SF-12 scores were not

significantly different between the DN and PRP groups at ≥ 26 weeks, and in fact the DN group had improved significantly more than the PRP group on the Lysholm score.

Since the VISA score was designed to assess symptoms among patients diagnosed with patellar tendinopathy in particular, VISA score is especially relevant to our patient population and was our primary outcome measure. On the basis of this metric, we conclude that PRP appears to accelerate recovery from patellar tendinopathy relative to dry needling but does not affect the patient's ultimate outcome at a minimum of 6 months. However, patients may in fact place equal or even more emphasis on pain (VAS), function and stability (Lysholm), and activity levels (Tegner), since these scores more directly reflect the extent to which patients' daily lives are affected by PT. When discussing treatment options with patients, practitioners may take into account the specific goals of the patient, such as reduction in pain and return to sport.

Our results are generally consistent with other reports supporting the efficacy of PRP in the treatment of chronic patellar tendinopathy. A prospective cohort study of 47 knees showed a significant 34-point mean improvement in VISA score and a reduction in overall tendon thickness and interstitial tears by ultrasound at 6 to 22 months after 2 separate ultrasound-guided autologous blood injections combined with dry needling²²; this is similar to the 30-point improvement reported in our study at ≥ 26 weeks. The improvement in VAS pain score and Tegner activity scale observed in our PRP group is also reflected in reports by Kon et al²⁶ and Filardo et al.¹⁵ Finally, in a randomized controlled trial comparing PRP to extracorporeal shock wave therapy in patellar tendinopathy, Vetrano et al⁴¹ found no significant difference between the two groups at 2 months, but the PRP group scored significantly better on VISA and VAS at 6 and 12 months. We have built on these studies by demonstrating that the positive effect of PRP compared with alternative treatments such as dry needling is greatest in the first few weeks and months after PRP. This benefit was attenuated by 26 weeks, at which time dry needling led to equivalent improvement in patellar tendinopathy symptoms.

Our findings raise an important question: Why does PRP appear more effective than DN initially, but no different over longer follow-up? For example, the PRP group initially improved significantly on the Lysholm score for function and stability at 12 weeks, but this gain was lost by 26 weeks. In fact, the DN group improved significantly more than the PRP group at ≥ 26 weeks by this measure. Similarly, the VISA score of patellar tendinopathy symptoms had improved significantly more within the PRP group than within the DN group, but by ≥ 26 weeks there was no longer a statistically significant difference between groups. In contrast to our results, the study by Vetrano et al⁴¹ demonstrated an increasing effect of PRP with time. One possible explanation for this discrepancy is that the effect of a single PRP injection may wear off over time. Other protocols, including the Vetrano study, have included 2 or more PRP injections,^{15,22,26,41} whereas ours involved only a single PRP injection or dry needling treatment.

A second possibility is that our results were biased toward the null hypothesis (that PRP and DN are no different) at the final time point because of changes in the patient groups at ≥ 26 weeks. One patient in the PRP group was included in the 12-week data but unfortunately was lost to follow-up at ≥ 26 weeks. It is possible that this patient failed to follow up because his symptoms had improved, causing the 26-week PRP group scores to appear lower than they would have been if this patient had been included. In addition, since all 3 excluded patients were in the DN (control) group and had poor outcomes, this approach may make the DN group appear to be improving more than it actually is. Therefore, this method is statistically sound because we would expect it to bias our results toward the null hypothesis (no difference between PRP and DN treatments). We also conducted a second intention-to-treat analysis that maintained those 3 patients in their original DN group, and the results from this analysis were nearly identical to those of the per protocol analysis.

It is also possible that the high leukocyte content of the PRP used in our study¹² triggered a particularly robust inflammatory response in the initial weeks after treatment, accelerating the recovery of the PRP group relative to the DN group in the first 12 weeks after treatment. Over time the benefit of this early inflammatory response may be attenuated, as both DN and PRP treatments appear to be effective over 26 weeks. This is supported by histologic studies in animals. Dragoo et al¹² demonstrated a large acute inflammatory response with increased cellularity and vascularity in rabbit tendons 5 days after treatment with leukocyte-rich relative to leukocyte-poor PRP, whole blood, and saline. However, the overall cellularity in the other treatment groups improved over time and was the same in all groups by 14 days. One surprising finding in our study was that PRP patients did not report increased pain relative to DN patients in the initial weeks after treatment, despite our hypothesis that PRP induces a larger inflammatory response.

A limitation of our study is that we did not document anatomic tendon changes by ultrasound or MRI after treatment. However, multiple prospective studies have shown that patellar tendon sonographic hypochoic areas can resolve, remain unchanged, or expand in athletes without predicting symptoms of patellar tendinopathy and therefore should not dictate treatment decisions.^{7,25} Additionally, the younger age of the PRP group could potentially bias our results. PRP generated from younger patients tends to contain higher concentrations of growth factors, which could lead younger patients to benefit from PRP more than their older peers.¹³ Similarly, aging tendon fibroblasts may be less responsive to PRP or other treatment modalities. However, whereas previous studies have shown that Tegner activity level is inversely correlated with age, the Tegner scores were not different between our DN and PRP groups (Table 1), despite the age difference. Therefore, we do not think that the age difference between groups in our study had a meaningful influence on patients' clinical outcomes. Furthermore, we

used a simple randomization technique to allocate patients to treatment groups, which has been noted to offer the best possible unpredictability and bias prevention.³⁷ The disparity in our group sizes is also to be expected with this randomization technique.

It is possible that the volume of the PRP injection plays a role in its biological effects. This volume, regardless of the injected contents, may improve tendinopathies via mechanical disruption of neoneurovascularization. For example, Crisp et al¹⁰ found that 22- to 50-mL combination injections of bupivacaine, hydrocortisone, and normal saline generated significant improvements in VAS and VISA scores among patellar tendinopathy patients. Dragoo et al¹² recently demonstrated that the cellular response in healthy rabbit tendons to PRP, saline, and whole blood injections was equivalent, suggesting that volume may be at least as important as contents. In contrast to PRP injection, dry needling does not introduce additional volume into the tendon but rather is intended to stimulate a healing response within the tendon by initiating bleeding. Additional studies could compare the effect of PRP injection versus equivalent volume saline injection to better understand the importance of injection composition and injection volume. Longer follow-up of the same cohorts described in this study may also elucidate the long-term trajectory for patellar tendinopathy patients treated with PRP versus dry needling. Finally, a larger multicenter trial comparing PRP, dry needling, corticosteroid injections, and possibly other treatment options may offer even greater statistical power.

REFERENCES

1. Andres BM, Murrell GA. Treatment of tendinopathy: what works, what does not, and what is on the horizon. *Clin Orthop Relat Res*. 2008;466(7):1539-1554.
2. Anitua E, Sanchez M, Nurden AT, et al. Autologous fibrin matrices: a potential source of biological mediators that modulate tendon cell activities. *J Biomed Mat Res A*. 2006;77(2):285-293.
3. Blazina ME, Kerlan RK, Jobe FW, Carter VS, Carlson GJ. Jumper's knee. *Orthop Clin North Am*. 1973;4(3):665-678.
4. Briggs KK, Lysholm J, Tegner Y, Rodkey WG, Kocher MS, Steadman JR. The reliability, validity, and responsiveness of the Lysholm score and Tegner activity scale for anterior cruciate ligament injuries of the knee: 25 years later. *Am J Sports Med*. 2009;37(5):890-897.
5. Calvert M, Blazeby J, Altman DG, Revicki DA, Moher D, Brundage MD. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO extension. *JAMA*. 2013;309(8):814-822.
6. Cook JL, Khan KM, Kiss ZS, Griffiths L. Patellar tendinopathy in junior basketball players: a controlled clinical and ultrasonographic study of 268 patellar tendons in players aged 14-18 years. *Scand J Med Sci Sports*. 2000;10(4):216-220.
7. Cook JL, Khan KM, Kiss ZS, Purdam CR, Griffiths L. Prospective imaging study of asymptomatic patellar tendinopathy in elite junior basketball players. *J Ultrasound Med*. 2000;19(7):473-479.
8. Coupe C, Kongsgaard M, Aagaard P, et al. Differences in tendon properties in elite badminton players with or without patellar tendinopathy. *Scand J Med Sci Sports*. 2013;23(2):e89-95.
9. Creaney L, Hamilton B. Growth factor delivery methods in the management of sports injuries: the state of play. *Br J Sports Med*. 2008;42(5):314-320.

10. Crisp T, Khan F, Padhiar N, et al. High volume ultrasound guided injections at the interface between the patellar tendon and Hoffa's body are effective in chronic patellar tendinopathy: a pilot study. *Disabil Rehabil.* 2008;30(20-22):1625-1634.
11. Crossley KM, Bennell KL, Cowan SM, Green S. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil.* 2004;85(5):815-822.
12. Dragoo JL, Braun HJ, Durham JL, et al. Comparison of the acute inflammatory response of two commercial platelet-rich plasma systems in healthy rabbit tendons. *Am J Sports Med.* 2012;40(6):1274-1281.
13. Dragoo JL, Korotkova T, Wasterlain AS, Pouliot MA, Kim HJ, Golish SR. Age-related changes of chondrogenic growth factors in platelet-rich plasma. *Oper Tech Orthop.* 2012;22(2):49-55.
14. Ferretti A. Epidemiology of jumper's knee. *Sports Med.* 1986;3(4):289-295.
15. Filardo G, Kon E, Della Villa S, Vincentelli F, Fornasari PM, Marcacci M. Use of platelet-rich plasma for the treatment of refractory jumper's knee. *Int Orthop.* 2010;34(6):909-915.
16. Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: from basic science to clinical applications. *Am J Sports Med.* 2009;37(11):2259-2272.
17. Fredberg U, Bolvig L, Pfeiffer-Jensen M, Clemmensen D, Jakobsen BW, Stengaard-Pedersen K. Ultrasonography as a tool for diagnosis, guidance of local steroid injection and, together with pressure algometry, monitoring of the treatment of athletes with chronic jumper's knee and Achilles tendinitis: a randomized, double-blind, placebo-controlled study. *Scand J Rheumatol.* 2004;33(2):94-101.
18. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Responsiveness of the VISA-P scale for patellar tendinopathy in athletes [published online September 25, 2012]. *Br J Sports Med.* doi:bjsports-2012-091163.
19. Hoksrud A, Ohberg L, Alfredson H, Bahr R. Ultrasound-guided sclerosis of neovessels in painful chronic patellar tendinopathy: a randomized controlled trial. *Am J Sports Med.* 2006;34(11):1738-1746.
20. Hoksrud A, Torgalsen T, Harstad H, et al. Ultrasound-guided sclerosis of neovessels in patellar tendinopathy: a prospective study of 101 patients. *Am J Sports Med.* 2012;40(3):542-547.
21. Hopewell S, Clarke M, Moher D, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet.* 2008;371(9609):281-283.
22. James SL, Ali K, Pocock C, et al. Ultrasound guided dry needling and autologous blood injection for patellar tendinosis. *Br J Sports Med.* 2007;41(8):518-521; discussion 522.
23. Jonsson P, Alfredson H. Superior results with eccentric compared to concentric quadriceps training in patients with jumper's knee: a prospective randomised study. *Br J Sports Med.* 2005;39(11):847-850.
24. Kelly AM. The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. *Emerg Med J.* 2001;18(3):205-207.
25. Khan KM, Cook JL, Kiss ZS, et al. Patellar tendon ultrasonography and jumper's knee in female basketball players: a longitudinal study. *Clin J Sport Med.* 1997;7(3):199-206.
26. Kon E, Filardo G, Delcogliano M, et al. Platelet-rich plasma: new clinical application: a pilot study for treatment of jumper's knee. *Injury.* 2009;40(6):598-603.
27. Kongsgaard M, Kovanen V, Aagaard P, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. *Scand J Med Sci Sports.* 2009;19(6):790-802.
28. Lian OB, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports: a cross-sectional study. *Am J Sports Med.* 2005;33(4):561-567.
29. Lysholm J, Gillquist J. Evaluation of knee ligament surgery results with special emphasis on use of a scoring scale. *Am J Sports Med.* 1982;10(3):150-154.
30. Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *Am J Sports Med.* 2006;34(11):1774-1778.
31. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ.* 2010;340:c869.
32. Orchard J, Massey A, Brown R, Cardon-Dunbar A, Hofmann J. Successful management of tendinopathy with injections of the MMP-inhibitor aprotinin. *Clin Orthop Relat Res.* 2008;466(7):1625-1632.
33. Peers KH, Lysens RJ. Patellar tendinopathy in athletes: current diagnostic and therapeutic recommendations. *Sports Med.* 2005;35(1):71-87.
34. Rees JD, Wilson AM, Wolman RL. Current concepts in the management of tendon disorders. *Rheumatology.* 2006;45(5):508-521.
35. Schmitt JS, Di Fabio RP. Reliable change and minimum important difference (MID) proportions facilitated group responsiveness comparisons using individual threshold criteria. *J Clin Epidemiol.* 2004;57(10):1008-1018.
36. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ.* 2010;340:c332.
37. Schulz KF, Grimes DA. Generation of allocation sequences in randomised trials: chance, not choice. *Lancet.* 2002;359(9305):515-519.
38. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res.* 1985;198:43-49.
39. van Ark M, Zwerver J, van den Akker-Scheek I. Injection treatments for patellar tendinopathy. *Br J Sports Med.* 45(13):1068-1076.
40. van der Worp H, Zwerver J, Kuijjer PP, Frings-Dresen MH, van den Akker-Scheek I. The impact of physically demanding work of basketball and volleyball players on the risk for patellar tendinopathy and on work limitations. *J Back Musculoskelet Rehabil.* 2011;24(1):49-55.
41. Vetrano M, Castorina A, Vulpiani MC, Baldini R, Pavan A, Ferretti A. Platelet-rich plasma versus focused shock waves in the treatment of jumper's knee in athletes. *Am J Sports Med.* 2013;41(4):795-803.
42. Visentini PJ, Khan KM, Cook JL, Kiss ZS, Harcourt PR, Wark JD. The VISA score: an index of severity of symptoms in patients with jumper's knee (patellar tendinosis). Victorian Institute of Sport Tendon Study Group. *J Sci Med Sport.* 1998;1(1):22-28.
43. Warden SJ, Brukner P. Patellar tendinopathy. *Clin Sports Med.* 2003;22(4):743-759.
44. Warden SJ, Kiss ZS, Malara FA, Ooi AB, Cook JL, Crossley KM. Comparative accuracy of magnetic resonance imaging and ultrasonography in confirming clinically diagnosed patellar tendinopathy. *Am J Sports Med.* 2007;35(3):427-436.
45. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care.* 1996;34(3):220-233.
46. Woodley BL, Newsham-West RJ, Baxter GD. Chronic tendinopathy: effectiveness of eccentric exercise. *Br J Sports Med.* 2007;41(4):188-198; discussion 199.
47. Zwerver J, Bredeweg SW, van den Akker-Scheek I. Prevalence of jumper's knee among nonelite athletes from different sports: a cross-sectional survey. *Am J Sports Med.* 39(9):1984-1988.