Clinical Sports Medicine Update

Nonsurgical Treatments of Patellar Tendinopathy: Multiple Injections of Platelet-Rich Plasma Are a Suitable Option

A Systematic Review and Meta-analysis

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Background: Patellar tendinopathy is a condition characterized by anterior knee activity–related pain. It has a high incidence among athletes engaged in jumping sports and may become a chronic condition. Nonoperative management is the first choice in these patients, and several nonsurgical treatment options have been proposed. Nonetheless, clear indications on the most effective approach to address patellar tendinopathy are still lacking.

Purpose: To analyze the evidence on nonoperative options to treat chronic patellar tendinopathy through a systematic review of the literature and to perform a meta-analysis to identify the most effective nonsurgical option.

Study Design: Systematic review and meta-analysis.

Methods: The search was conducted with the PubMed and Cochrane databases on January 4, 2017. All clinical English-language reports of any level of evidence on nonsurgical treatment of patellar tendinopathy were included. The quality of each article was assessed by use of the Coleman score. A meta-analysis was performed on all articles reporting the Victorian Institute of Sport Assessment scale for patellar tendinopathy to evaluate the results of the most described treatments.

Results: A total of 70 studies involving 2530 patients were included in the qualitative data synthesis. The Coleman score showed an overall poor study quality. The most described treatment groups that could be included in the meta-analysis were reported in 22 studies on eccentric exercise, extracorporeal shockwave therapy (ESWT), and platelet-rich plasma (PRP). Single and multiple PRP injections were evaluated separately. Eccentric exercise therapies obtained the best results ($P < .05$) at short-term (<6 months, mean 2.7 ± 0.7 months). However, multiple injections of PRP obtained the best results ($P < .05$), followed by ESWT and eccentric exercise, at long-term follow-up (≥6 months, mean 15.1 ± 11.3 months).

Conclusion: The literature documents several nonsurgical approaches for the treatment of chronic patellar tendinopathy with important limitations in terms of study quality. The available evidence showed an overall positive outcome, but some differences have been highlighted. Eccentric exercises may seem the strategy of choice in the short-term, but multiple PRP injections may offer more satisfactory results at long-term follow-up and can be therefore considered a suitable option for the treatment of patellar tendinopathy.

Keywords: patellar tendinopathy; jumper's knee; nonoperative treatment; eccentric exercise; ESWT; PRP

Patellar tendinopathy is a condition characterized by anterior knee activity–related pain and tenderness at the inferior pole of the patella.[19] This condition has a high incidence among athletes engaged in jumping sports, with 32% of basketball players and 44% of volleyball players affected, leading to the term *jumper's knee*.[9,56] Patellar tendinopathy is also common in the sedentary population and as a work-related condition,[86,98] with an incidence of 17% reported in the general population.[4] Acute cases mostly heal spontaneously, but in up to 20% of cases this condition becomes recalcitrant or recurs after resolution.[28,37]

Many theories have been proposed on the pathogenesis of patellar tendinopathy, including vascular, mechanical, impingement-related, and nervous system causes.[5,45,58,59,78,80] Prominent features include histopathological changes such as disorganization of collagen fibers, an increase in the number of vessels and sensory nerves, an increase of hydrated components of the extracellular matrix, and, in the end, an overall

The American Journal of Sports Medicine
1–18
DOI: 10.1177/0363546518759674

breakdown of tissue organization, leading to the apoptotic death of tenocytes.[55] These changes are considered to result from several intrinsic and extrinsic factors, where repetitive tendon overload plays a key role in the onset of microscopic cell and matrix failures that lead to the weakening of the mechanical properties of the tendon and, finally, to chronic tendinopathy.[15]

The healing response is impeded by recurring microtrauma with a failed or slow healing response to overuse injury, which results in a degeneration of tissue with compromised functional properties and disabling symptoms.[31,73,75] The onset is typically insidious, and the prognosis for a patient with chronic symptoms is either resolution at a frustratingly slow pace or failure to resolve and inability to return to full activity.[79] The mean duration of symptoms is more than 2 years, but knee symptoms can persist for more than 15 years and can be devastating for an athletic career; more than 50% of athletes with patellar tendinopathy have had to stop sports participation because of knee pain.[76] The most refractory cases may even require operative treatments (ie, open or arthroscopic debridement of the proximal patellar tendon and the inferior patellar pole region, resection of part of the distal pole of the patella, removal of hypertrophic synovium and fat pad), which may provide good results with a 90% success rate; however, no indication about different procedures has been established, and the invasive approach is affected by longer recovery time and concerns related to surgery.[12] Thus, nonoperative management is still the first choice, and several nonsurgical treatment options have been proposed, ranging from specific exercise protocols and physical therapies to the more ambitious novel regenerative injective treatments.[29] Nonetheless, despite the increasing number of treatments and of articles analyzing their results, clear indications on the most effective approach to address patellar tendinopathy are still lacking, and clinicians thus lack support in making treatment decisions.

The aim of this study was to analyze the evidence on nonoperative treatments for chronic patellar tendinopathy through a systematic review of the literature and to perform a meta-analysis to compare the different strategies and identify the most effective nonsurgical option to treat patellar tendinopathy.

METHODS

The search was conducted on the PubMed and Cochrane databases on January 4, 2017, by use of the following parameters: ((patellar) AND ((tendinopathy) OR (tendinitis) OR (tendon pathology))) AND (treatment). The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines were used.[61] A flowchart of the study selection for qualitative and quantitative data synthesis is reported in Figure 1.

Screening and analysis were conducted separately by 2 independent observers (D.R. and S.A.A.). In the first step, the articles were screened by title and abstract. The following inclusion criteria for relevant articles were used during the initial screening of titles and abstracts: clinical reports of any level of evidence, written in the English language, on nonsurgical treatment of patellar tendinopathy. Exclusion criteria were articles written in other languages, preclinical studies, studies reporting surgical treatment of patellar tendinopathy, and reviews. In the second step, the full texts of the selected articles were retrieved and screened, with further exclusions according to the previously described criteria. Moreover, the articles not reporting clinical results were excluded. Reference lists from the selected papers and from the systematic reviews found with the first and second screening were also screened, and all selected studies were included in the qualitative data synthesis. Relevant data (year of publication, type of study, number of patients, sex, age, follow-up time, results, and scores reported) were then extracted and collected in a database with consensus of the 2 observers, to be analyzed for the purposes of the present study. The quality of each article was assessed independently by 2 authors (D.R. and S.A.A.) with disagreements resolved by consensus with a third author (L.A.), using the Coleman Methodology Score (CMS).[18] This score uses 10 criteria to assess each study's method, and the 10 criteria are analyzed to give a total CMS between 0 and 100, where a score of 100 represents a study design that largely avoids the influence of chance, different biases, and confounding factors.

Finally, a meta-analysis on the clinical results of the most documented nonoperative treatments was performed. In particular, all articles reporting the Victorian Institute of Sport Assessment scale for patellar tendinopathy (VISA-P)[92] were selected. The VISA-P score was developed in 1998[92] and is specifically designed for patellar tendinopathy. It demonstrated an excellent interobserver (0.95) and intraobserver (0.99) reliability,[92] with a minimal clinically important difference (MCID) of 13 points.[38] To analyze the real benefit of the treatments, the VISA-P improvement had to be calculated, and thus studies not reporting both pretreatment and posttreatment VISA-P scores were excluded.

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One or more of the authors has declared the following potential conflict of interest or source of funding: G.F. is a consultant for and receives institutional support from Finceramica Faenza SpA (Italy), Fidia Farmaceutici SpA (Italy), and CartHeal (2009) Ltd (Israel); is a consultant for EON Medica SRL (Italy); and receives institutional support from IGEA Clinical Biophysics (Italy), BIOMET (USA), and Kensey Nash (USA). S.Z. has received financial support from I+ srl, Italy; has royalties from Springer (Germany); and receives institutional support from Fidia Farmaceutici SpA (Italy), CartHeal (2009) Ltd (Israel), IGEA Clinical Biophysics (Italy), BIOMET (USA), and Kensey Nash (USA).

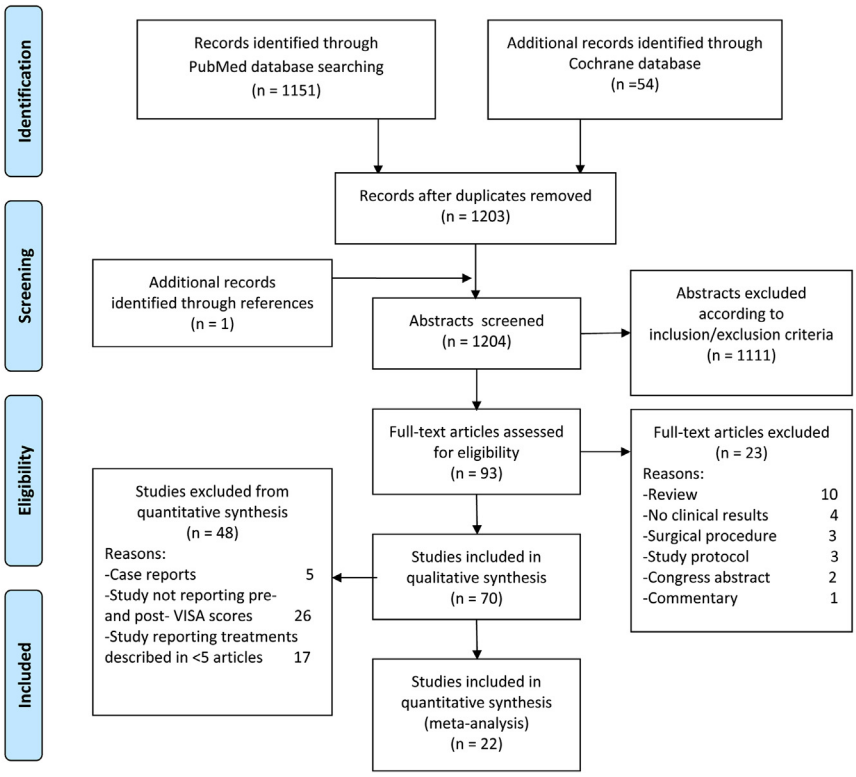

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) flowchart of the systematic literature review.

Moreover, only treatments assessed in at least 5 studies were included in the meta-analysis, to obtain homogeneous and statistically meaningful results.

Articles were divided by treatment. In case of comparative studies with more treatment groups in which patients underwent different nonoperative procedures, each treatment group was analyzed independently according to the treatment applied. Articles not reporting pre- and posttreatment VISA-P, treatments described in fewer than 5 studies, and case reports were excluded from the meta-analysis. For the treatment groups included in the analysis, the VISA-P score was analyzed separately at short-term follow-up (<6 months) and at long-term follow-up (≥6 months). In particular, the improvement provided by each treatment was analyzed, both at short- and long-term follow-up, and collected data were compared by statistical analysis to evaluate the most effective treatment.

Statistical Analysis

Statistical analysis and Forest plotting were carried out according to Neyeloff et al[65] using Microsoft Excel. The comparison among the groups was based on analysis of variance (ANOVA)[10]: 1-way repeated-measures ANOVA with random effect adjustment for heterogeneity when I^2 was greater than 50% was used for the estimation of the pretreatment and posttreatment scores; 1-way ANOVA with Sidak correction for multiple comparisons was used for testing the effects of the 4 treatment groups considering the difference between pretreatment and posttreatment scores (mean difference). With no heterogeneity, the estimation of the mean difference and its 95% confidence interval was based on fixed-effect analysis of variance; the random effects model was preferred otherwise. P less than .05 was used as the level of statistical significance. Statistical heterogeneity among the 4 included groups was evaluated by the I^2 test.

RESULTS

The PubMed and Cochrane search after removal of duplicates identified 1203 records. Abstracts were screened and selected according to the inclusion-exclusion criteria (Figure 1): 1111 abstracts were excluded, and 1 article was identified through the reference lists, which gave a total of 93 full-text articles assessed for eligibility. Twenty-three full-text articles were further excluded for the following reasons: 10 articles were reviews, 3 were study protocol descriptions, 3 reported outcomes of surgical procedures, 4 did not report clinical results, 2 were congress abstracts, and 1 article was a commentary of another article included in this review. Thus, 70 studies were included in the qualitative data synthesis (see the Appendix, available in the online version of this article), and 22 studies were included in the quantitative data synthesis (Table 1 and the Appendix).

TABLE 1
Detailed Description of the 22 Studies Included in the Quantitative Data Synthesis[a]

Article, Type of Study	Treatment Groups	Treatment Details	No. of Patients (Dropouts)	Age Sex BMI	Minimum Follow-up	Pathological Condition (Symptom Duration) Previous Treatment	Results	CMS
Eccentric Exercise								
Bahr[8] (2006), RCT	Eccentric training (vs surgical treatment—not reported)	Eccentric training program on a 25° decline board twice daily, with 3 sets of 15 repetitions at each session. Downward (eccentric) component performed with the affected leg, upward (concentric) component performed with the asymptomatic leg.	20 (0)	31 18 M, 2 W 25.0	12 mo	Chronic (>3 mo) (33 mo) —	5 patients had no improvement and underwent surgery. Of the remaining 15 knees, 7 had no symptoms and 8 had improvement but were still symptomatic. Improvement of VISA.	69
Frohm[33] (2007), RCT	Eccentric overload training group	The Browsman eccentric overload training device consists of a barbell. The patients resisted the movement of the barbell using both legs during 4 sets × 4 repetitions. During the ascending phase, the patients followed the barbell without resisting the movement.	11 (0)	26 9 M, 2 W 24.5	3 mo	Chronic (continuous >3 mo or recurrent >6 mo) (—) —	Significant improvement of VISA-P in both groups of athletes. No significant differences between the groups in terms of pain and function. After a 3-mo rehabilitation period, most patients could be regarded as improved enough to be able to return to training and sports.	57
	Single-leg eccentric training group	Single-leg eccentric training according to Curwin was carried out on a 25° decline board, with 3 sets × 15 repetitions of unilateral squats on the injured leg, holding an extra weight in front of the chest.	9 (0)	28 7 M, 2 W 24.1				
Jonsson[46] (2005), RCT	Eccentric quadriceps training on a decline board	3 sets of 15 repetitions each, performed twice a day, 7 d/wk, for 12 wk. The starting position was standing on the 25° decline board. From that position the knee was slowly flexed 70°.	8 (0)	24.1 7 M, 1 W 24.0	12 wk	Chronic (>8 mo) (33 mo) —	Athletes in the eccentric training group were more satisfied with the treatment than those in the concentric group and had returned to their preinjury sporting activity at 12 wk follow-up.	48
	Concentric quadriceps training on a decline board	3 sets of 15 repetitions each, performed twice a day, 7 d/wk, for 12 wk. The starting position was standing on the 25° decline board with the knee in 70° flexion. From that position, the knee was slowly straightened to full extension.	7 (3)	25.7 6 M, 1 W 24.4		Chronic (>8 mo) (33 mo) —		
Kongsgaard[51] (2009), RCT	Peritendinous corticosteroid injections	US-guided injections of 1 mL of 40 mg/mL methylprednisolone in 0.5 mL lidocaine. A second injection was administered 4 wk later according to normal clinical practice.	12 (1)	34.3 12 M 24.8	6 mo	Chronic (>3 mo) (18 mo) —	Significant improvement of VISA-P and VAS in all groups of recreational athletes at 12-wk follow-up. Worsening of VISA and VAS after 12 wk in the corticosteroid group. Corticosteroid had good short-term but poor long-term clinical effects. HSR and eccentric training had good short- and long-term clinical effects with increased collagen turnover. Patients in the HSR group were more satisfied.	89
	Eccentric decline squat training	3 sets of 15 slow repetitions of eccentric unilateral squats on a 25° decline board twice daily for 12 consecutive wk.	12 (3)	31.3 12 M 24.4		Chronic (>3 mo) (19 mo) —		
	Heavy slow resistance training	3 weekly sessions of 3 bilateral exercises: squat, leg press and hack squat. All exercises were performed from complete extension to 90° of knee flexion and back again.	13 (2)	31.7 13 M 24.8		Chronic (>3 mo) (19 mo) —		

(continued)

TABLE 1
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Article, Type of Study	Treatment Groups	Treatment Details	No. of Patients (Dropouts)	Age Sex BMI	Minimum Follow-up	Pathological Condition (Symptom Duration) Previous Treatment	Results	CMS
Stasinopoulos[82] (2012), RCT	Eccentric training of patellar tendon + static stretching exercises of quadriceps-hamstrings	For eccentric exercises, participants carried out 3 sets of 15 repetitions of unilateral squat on a 25° decline board. Static stretching exercises were performed before and after the eccentric training. Each stretch lasted 30 s and there was a 1-min rest between each stretch.	22 (0)	26.4 16 M, 6 W —	6 mo	Chronic (>3 mo) (6 mo) Drugs (n = 14), rehabilitation (n = 3), injections (n = 5)	Eccentric training and static stretching exercises are superior to eccentric training alone to reduce pain and improve function in patients at follow-up.	60
	Eccentric training of patellar tendon	For eccentric exercises, participants carried out 3 sets of 15 repetitions of unilateral squat on a 25° decline board.	21 (0)	27.0 15 M, 6 W —		Chronic (>3 mo) (6 mo) Drugs (n = 14), rehabilitation (n = 1), injections (n = 6)		
Young[101] (2005), RCT	Eccentric training on a decline board	Single-leg squats on a 25° decline board. 3 sets of 15 repetitions twice a day for 12 wk.	9 (—)	27.3 13 M, 4 W 26.0	12 mo	Chronic (—) —	Both groups of elite volleyball players had improved significantly from baseline in both outcome measures at 12 wk and 12 mo, but there was no difference between groups for either outcome measure at any time.	71
	Step eccentric protocol	Single-leg squats on a 10-cm step, exercising without tendon pain. Three sets of 15 repetitions twice a day for 12 wk.	8 (—)	27.3 13 M, 4 W 22.5				
Eccentric Exercise vs ESWT								
Thijs[85] (2017), RCT	ESWT + eccentric training	3 sessions at 1-wk intervals of ESWT. All participant performed eccentric exercises (3 sets of 15 repetitions twice a day) for 3 mo on a decline board.	22 (7)	30.5 14 M, 8 W 23.9	24 wk	Chronic (>8 wk) (65 wk) —	Both groups significantly improved in VISA and Likert score. No significant differences were found between groups.	73
	Sham shockwave therapy (placebo) + eccentric training	3 sets of 15 repetitions twice a day for 3 mo of eccentric training. 3 sessions at 1-wk intervals of ESWT. Transmission gel was not applied between the applicator and the focusing pad, so shockwaves were hardly conducted.	30 (4)	27.3 24 M, 6 W 23.4		Chronic (>8 wk) (99 wk) —		
ESWT								
Furia[34] (2013), retrospective comparative study	Single application of ESWT	Each patient received a single, low-energy administration: 2000 shocks at a session of 4.0 bars; 10 shocks/s; procedure performed with patient seated with knee at 90°.	33 (0)	Not specified	12 mo	Chronic (—) NSAIDs, hamstring stretching, physical therapy, ice, iontophoresis	ESWT was safe and effective up to 12 mo from the last application and provided significantly better results than current conservative cases.	60
	Other forms of nonoperative therapy		33 (0)					
van der Worp[89] (2014), RCT	Focused ESWT therapy + eccentric training	3 focused ESWT sessions with a 1-wk interval + eccentric training were carried out.	21 (1)	28.8 16 M, 5 W 24.2	14 wk	Chronic (>3 mo) (33 mo) —	Significant improvement of VISA-P in both groups. No difference between treatment groups in improvement on the VISA-P questionnaire after 14 wk or any other follow-up time point.	82
	Radial ESWT therapy + eccentric training	3 radial ESWT sessions with a 1-wk interval + eccentric training were carried out.	22 (0)	23.4 16 M, 6 W 23.9	14 wk	Chronic (>3 mo) (39 mo) —		

(continued)

TABLE 1
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Article, Type of Study	Treatment Groups	Treatment Details	No. of Patients (Dropouts)	Age Sex BMI	Minimum Follow-up	Pathological Condition (Symptom Duration) Previous Treatment	Results	CMS
Wang[95] (2007), RCT	ESWT	Treatment began with slow frequency at 1 impulse of shock/s and gradually increased to 2 shocks/s as the patient could tolerate the procedure.	27 (2)	29.4 14 M, 13 W —	36 mo	Chronic (>6 mo) (16 mo) —	At 2- to 3-year follow-up, overall results for the study group were 43% excellent, 47% good, 10% fair, and 0% poor. For the control group, results were 0% excellent, 50% good, 25% fair, and 25% poor. Satisfactory results were observed in 90% of the study group vs 50% of the control group.	74
	Nonoperative treatment	Patients in the control group were treated with nonoperative treatments including NSAIDs, physical therapy, an exercise program, the use of a knee strap, and modification of activity levels.	23 (1)	30.2 13 M, 10 W —		Chronic (>3 mo) (11 mo) —		
Zwerver[103] (2010), prospective case series	ESWT	Each patient received 2000 impulses at each visit, and the shockwave treatment was repeated each week for 3 wk.	19 (0)	37 19 M —	3 mo	Chronic (<3 mo) (28 mo) 16 patients received nonspecified previous treatment	Patients were recreational athletes and tolerated the treatment well with no serious complications. Mean VISA-P score improved, VAS decreased.	48
Zwerver[104] (2011), RCT	ESWT	ESWT was administered in 3 sessions at 1-wk intervals using a piezoelectric ESWT device.	31 (1)	24.2 20 M, 11 W —	6 mo	Chronic (>3 mo) (7 mo) —	One week after final treatment, significantly more athletes in the ESWT group reported subjective improvement. This was the only difference noted between the 2 groups.	68
	Placebo		31 (4)	25.7 21 M, 10 W —		Chronic (>3 mo) (8 mo) —		
ESWT vs PRP								
Vetrano[90] (2013), RCT	Multiple (2) PRP injections	All 23 patients in this group received 2 autologous PRP injections over 2 wk.	23 (1)	26.9 20 M, 3 W —	12 mo	Chronic (>6 mo) (19 mo) Laser (n = 8), TECAR (n = 19), US (n = 3), exercises (n = 21), NSAIDs (n = 9)	Both treatments were effective in improving baseline VISA-P, VAS, and Blazina scale values in athletes. The PRP group showed significantly better improvement than the ESWT group in VISA-P, VAS scores at 6- and 12-mo follow-up, and modified Blazina scale score at 12-mo follow-up.	84
	ESWT	A focused electromagnetic shockwave device (Modulith SLK; STORZ Medical) was used.	23 (1)	26.8 17 M, 6 W —	12 mo	Chronic (>6 mo) (18 mo) Laser (n = 5), TECAR (n = 16), US (n = 5), exercises (n = 22), NSAIDs (n = 12)		
PRP								
Charousset[16] (2014), prospective case series	Multiple PRP injections	US-guidance injection of 6 mL of PRP with a 22-gauge needle. The procedure was repeated weekly for a total number of 3 injections.	28 (0)	27 — 21.6	24 mo	Chronic (>4 mo) (18 mo) Rest (n = 28), eccentric exercises (n = 28), ESWT (n = 24), laser (n = 6), steroid injections (n = 8)	Improvement of VISA and Lysholm knee score. Significant reduction of pain. All patients were satisfied. Most of the athletes were able to return to their presymptom sporting level.	74

(continued)

TABLE 1
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Article, Type of Study	Treatment Groups	Treatment Details	No. of Patients (Dropouts)	Age Sex BMI	Minimum Follow-up	Pathological Condition (Symptom Duration) Previous Treatment	Results	CMS
Dragoo[25] (2014), RCT	US-guided DN alone	US-guidance injection of 3 mL of 0.25% bupivacaine with 1:100,000 epinephrine subcutaneously. All patients were then blindfolded, and the radiologist penetrated the area of tendinopathy 10 times.	12 (0)	40 12 M —	26 wk	Chronic (persistence of symptoms after 6 wk of therapy with eccentric exercise) (—)	The PRP group showed a significant improvement compared with the DN group at 12 wk, but the difference between groups was not significant at 26 wk.	84
	US-guided injection of leukocyte-rich PRP	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.	9 (1)	28 8 M, 1 W —		Eccentric exercises	Lysholm scores were not significantly different between groups at 12 wk, but the DN group had improved significantly more than the PRP group at 26 wk.	
Ferrero[27] (2012), prospective case series	Multiple (2) US-guided PRP injections	6 mL of autologous PRP prepared from a previously collected sample was injected into the degenerated region of the tendon under US guidance.	24 (6)	37.4 14 M, 10 W —	6 mo	Chronic (>6 mo) (—) —	Improvement of clinical symptoms and recovery of the tendon matrix potentially helping to prevent degenerative lesions. Mean VISA improved.	67
Filardo[31] (2013), prospective case series	Multiple PRP injections	3 intratendinous injections of 5 mL PRP, 2 wk apart from each other. US controlled injection of PRP directly into the lesion site with multiple penetrations of the tendon.	43 (—)	30.6 42 M, 1 W 24.7	49 mo (mean)	Chronic (>3 mo) (—) —	Good overall results (improvement of VISA, EQ-VAS, and Tegner); clinical improvement was stable. Patients with bilateral involvement and a long history of pain and limited function obtained significantly poorer results.	73
Gosens[36] (2012), prospective comparative study	Single PRP injection with no previous treatment	Injection of 3 mL of PRP. 1 mL of PRP + bupivacaine HCL 0.5% + epinephrine was injected directly into the area of maximum tenderness. Then the remaining PRP + bupivacaine HCL 0.5% + epinephrine was injected into the patellar tendon origin on the patella.	22 (—)	32.2 14 M, 8 W —	18 mo	Chronic (41 mo) No previous treatments	Significant improvement of VISA-P and VAS in both groups. No significant difference between the 2 groups.	67
	Single PRP injection with previous treatment (steroid, ethoxysclerol, and/or surgical treatment)	Injection of 3 mL of PRP. 1 mL of PRP + bupivacaine HCL 0.5% + epinephrine was injected directly into the area of maximum tenderness. Then the remaining PRP + bupivacaine HCL 0.5% + epinephrine was injected into the patellar tendon origin on the patella. Previous treatments included cortisone, ethoxysclerol, and/or surgery.	14 (—)	28.7 16 M, 6W —		Chronic (39 mo) Steroid injections (n = 13), ethoxysclerol (n = 6), surgical treatment (n = 5)		
Kaux[48] (2016), RCT	Single PRP injection	6 mL of PRP injected into the patellar tendon after disinfection and US tracking.	10 (0)	31.1 10 M —	12 mo	Chronic (>3 mo and resistance to nonoperative treatment) (17 mo) Painkillers, NSAIDs, eccentric exercises, shockwaves	Infiltration of PRP associated with a submaximal eccentric protocol improves symptoms in recreational athletes. However, the application of 1 or 2 infiltrations of PRP did not reveal any difference.	69
	Multiple (2) PRP injection	After 1 wk of rehabilitation, a second infiltration of 6 mL of PRP was administered.	10 (0)	29.5 10 M —				

(continued)

TABLE 1
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Article, Type of Study	Treatment Groups	Treatment Details	No. of Patients (Dropouts)	Age Sex BMI	Minimum Follow-up	Pathological Condition (Symptom Duration) Previous Treatment	Results	CMS
Kaux[47] (2015), prospective case series	Single PRP injection + eccentric rehabilitation	6 mL of PRP infiltration. 1 wk of rest was followed by a progressive submaximal eccentric program, 3 times/wk, 5 sessions of 15 repetitions, for 6 wk.	20 (0)	28.8 17 M, 3 W —	12 mo	Chronic (>3 mo and no satisfactory improvement after 3 mo of nonoperative management) (18 mo) Nonoperative treatment	Good results at 3 mo in recreational patients with a good evolution at 12 mo. Improvement of VISA-P, VAS, and IKDC.	62
Van Ark[88] (2013), prospective case series	Single PRP injection + exercise-based physical therapy program	Single US-guided PRP injection + exercise-based physical therapy program consisting of exercise for muscle strength, endurance, power, and retraining sport-specific function and eccentric exercise.	5 (0)	27 2 M, 3 W 25.7	6 mo	Chronic (symptoms >12 mo, current symptoms >3 mo) (38 mo) —	5 of the 6 tendons showed an improvement of at least 30 points on the VISA-P after 26 wk.	66
Zayni[102] (2015), prospective comparative study	Single PRP injection	Injections performed under US control within and around the hypoechogenic tendon area.	16 (4)	24.6 14 M, 2 W —	34 mo (mean)	Chronic (>3 mo, resistance to nonoperative treatment) (—) Rest, NSAIDs, eccentric exercises, shockwaves	Patients who received 2 PRP injections had significantly better clinical scores than those who received a single PRP injection.	69
	Multiple (2) PRP injections 2 wk apart	Injections performed under US control within and around the hypoechogenic tendon area.	14 (1)	24.1 12 M, 2 W —				

[a]Dashes indicate data not available. BMI, body mass index; CMS, Coleman Methodology Score; DN, dry needling; EQ-VAS, EuroQol visual analog scale; ESWT, extracorporeal shockwave therapy; HSR, heavy slow resistance training; IKDC, International Knee Documentation Committee; M, men; NSAID, nonsteroidal anti-inflammatory drug; PRP, platelet-rich plasma; RCT, randomized controlled trial; TECAR, Transfer Electrical Capacitive and Resistive; US, ultrasound; VAS, visual analog scale; VISA, Victorian Institute of Sport Assessment; VISA-P, Victorian Institute of Sport Assessment for Patellar Tendon; W, women.

Systematic Review

Among the 70 articles included in the qualitative data synthesis, the evaluation of the study type showed 29 randomized controlled trials (RCTs), 5 prospective comparative studies, 1 retrospective comparative study, 25 prospective case series, 4 retrospective case series, 1 combined retrospective and prospective case series, and 5 case reports (Table 1 and the Appendix, available online).

The evaluation with the CMS showed an overall poor quality of the included studies. In fact, only 9 studies obtained a score higher than 80 and 8 studies had a score higher than 70, whereas 20 studies reached a score between 60 and 69, 18 studies were between 50 and 59, and 15 studies obtained a score lower than 50.

A total of 2530 patients affected by patellar tendinopathy were managed with nonsurgical treatments (a detailed description of the analyzed data, with the number of patients and the specific data reported, is provided in Table 1 and the Appendix, available online). The studies described and analyzed the outcome of different types of nonsurgical treatments, which are summarized in the following paragraphs: rehabilitative treatments, including eccentric exercises (15 studies) and other rehabilitative protocols (11 studies); physical instrumental therapies, such as extracorporeal shockwave therapy (ESWT) (9 studies), intratissue percutaneous electrolysis (EPI) (3 studies), and other physical therapies (10 studies); oral therapies (1 study); injective therapies, including injection of platelet-rich plasma (PRP) (15 studies), other biological agents (5 studies), hyaluronic acid (2 studies), corticosteroids (2 studies), sclerosing polidocanol injection (5 studies), and other substances (7 studies).

Rehabilitative Treatment

Eccentric Exercise. Fifteen articles reported the outcome of eccentric protocols, documenting improvement of clinical scores for these protocols, but with more controversial results in comparative studies. In particular, analyzing the benefit of eccentric versus concentric exercises, an RCT showed superior results in 15 active patients for eccentric exercise[46] while another RCT[14] showed no differences in an athletic population, with both trainings providing a high rate of return to sport at 12-week follow-up. Moreover, 1 RCT demonstrated no difference with surgical treatment at 12-months follow-up,[8] and 2 RCTs[44,93] failed to find superiority versus other rehabilitative treatments: 1 RCT reported an overall lack of improvement with eccentric exercises versus usual training at 6 months' follow-up in volleyball players during the competitive season,[93] and the other RCT reported no benefits of adding eccentric exercise to a home stretching

program of quadriceps and hamstrings.[44] Two other RCTs suggested a superiority of eccentric exercises compared with other treatments such as pulsed ultrasound,[83] transverse friction,[83] and ultrasound-guided injections of methylprednisolone.[51]

Other articles investigated eccentric training with treatment combinations. One RCT[85] showed good results for eccentric exercise and demonstrated that the association with ESWT provided no additional benefits. Another RCT[24] investigated the efficacy of eccentric training associated with static stretching exercise of quadriceps and hamstrings in athletic patients, showing better results than eccentric exercises alone at 6 months' follow-up. Two studies by the same author investigated heavy slow resistance training (which combines eccentric and concentric training): One of these was a prospective comparative study[52] and showed better improvement in clinical scores and pain during activity at 12 weeks' follow-up versus no intervention; the other was an RCT[51] and showed good improvement and no differences in pain and clinical scores for heavy slow resistance training and eccentric exercises at 6 months' follow-up but better results in term of satisfaction of the patients for heavy slow resistance training.

Finally, other authors investigated different eccentric training procedures: 1 prospective study[70] and 1 RCT[96] demonstrated the superiority of eccentric training on a decline board, compared with eccentric training in standard position, and 1 RCT[33] showed no differences between single- and double-leg eccentric training. Moreover, these studies suggested that a minimum of 20 training sessions appears to be necessary to ensure that the treatment is effective, with series typically performed at a 15-repetition maximum.[33,101] The program of submaximal eccentric contractions needs to be prolonged from 6 weeks to 1 year, depending on the severity of the condition, to significantly reduce symptoms of tendinopathy.[49,78,101]

Other Rehabilitative Treatments. Several studies applied different rehabilitative protocols, including concentric exercise,[14,46] heavy slow resistance training,[51,52] stretching exercises,[24,76] isometric and isotonic exercises,[87] fascial manipulation,[68] use of orthoses,[23] and use of augmented soft tissue mobilization (ASTM) advantEDGE[100] (or Astym treatment; Performance Dynamics, Inc), thus making a group of very heterogeneous studies.

One prospective case series[68] showed good improvement in pain and clinical scores for fascial manipulation at 1-month follow-up. One RCT[87] demonstrated how isometric and isotonic exercises are effective options in improving pain and clinical scores at 1-month follow-up with no significant differences between the 2 techniques. A case report[76] showed a complete resolution of symptoms with a program of hip extensor strengthening and landing-strategy modification at 6 months' follow-up. Another RCT[23] showed no additional relief in pain with the use of a patellar strap or sport tape and no effect of these orthoses on jumping height or distance. Finally, an RCT[100] investigated the use of ASTM advantEDGE, showing a resolution in 100% of the patients using this product, while in the traditional rehabilitation group the resolution rate was 60%.

Physical Instrumental Therapies

ESWT. An ESWT treatment consists of the application of shockwaves, which are sonic pulses generating high-stress forces in the tissue, with beneficial effects attributed to an analgesic process, the mechanical disintegration of calcium deposits (if present), and a tissue regeneration stimulating process.[105] Nine studies were found describing the outcome of ESWT for patellar tendinopathy, reporting an overall improvement in pain and clinical outcome.

Three prospective case series showed good results for ESWT: 1 case series[69] reported a reduction of pain and an improvement in clinical score at 24-month follow-up; another case series[94] showed overall good results in pain and clinical improvement at 24-month follow-up, with better results in performing athletes than in patients practicing sport only occasionally; finally, the most recent study[103] investigated the outcome at 3 months showing an improvement in pain and clinical scores.

Three comparative studies[34,95,104] evaluated ESWT compared with other nonoperative treatments or placebo. A retrospective comparative study[34] reported better results in ESWT at 12-month follow-up, compared with other, not better specified, nonoperative treatments. One RCT[95] demonstrated a better rate of satisfaction in ESWT (90% good and excellent results in ESWT vs 50% in the control group of heterogeneous nonoperative treatments), and another RCT[104] reported no differences in pain and clinical scores between ESWT and placebo in athletes at 5 months' follow-up but better subjective improvement in ESWT 1 week after the final treatment compared with the placebo group. One RCT compared ESWT with a minimally invasive treatment, multiple injections of PRP[90] (2 injections over 2 weeks), reporting good improvement of VISA-P, visual analog scale, and Blazina scale in both groups at 2, 6, and 12 months' follow-up but significantly better results in the PRP group.

Another RCT investigated a treatment combination, the effectiveness of adding ESWT to an eccentric training protocol[85]; or results showed no differences in pain and VISA-P improvement at 24-week follow-up between patients treated with eccentric training plus ESWT and patients treated with eccentric training plus sham shockwave therapy (placebo).

Finally, an RCT compared radial and focused ESWT when used in an eccentric training protocol. These types of ESWT differ in terms of the wave generation mechanism and the type of wave produced. It was found that radial shockwaves had a more superficial effect, reaching maximal energy at the skin, whereas focused shockwaves reached maximal energy deeper in the body tissues. This RCT demonstrated good results in both groups and no differences between radial and focused ESWT.

Intratissue Percutaneous Electrolysis. Intratissue percutaneous electrolysis (EPI) treatment leads to a nonthermal electrochemical ablation and causes an organic reaction leading to highly localized inflammation, exclusively in the region of treatment, which should lead to a rapid regeneration of the injured tendon.[2]

Three studies by the same author group[1-3] reported good results of EPI in terms of clinical improvement. A prospective case series[1] showed a significant improvement of VISA, and all patients returned to their preinjury level of physical activity at 2-year follow-up. Another prospective case series[2] reported a significant improvement of clinical scores and a satisfaction rate of 97.5% at 120 months' of follow-up. The most recent study[3] was an RCT comparing EPI with a treatment protocol that consisted of pulsed ultrasound, laser CO_2, and interferential currents; the authors reported better results in the EPI group in terms of clinical improvement and success probability (72.4% vs 36.1%) at 2 months' follow-up.

Other Physical Instrumental Therapies. Several other physical instrumental therapies have been investigated: laser therapy CO_2, cryo-ultrasound therapy, transfer electrical capacitive and resistive (TECAR) therapy, pulsed ultrasound, low-intensity pulsed ultrasound (LIPUS), wired iontophoresis, wireless iontophoresis patch, heated lidocaine-tetracaine patch, and topical glyceryl trinitrate. A prospective case series[35] showed good results in terms of clinical improvement and reduction of pain using a heated lidocaine-tetracaine patch. One prospective comparative study[20] showed better improvement of pain for cryo-ultrasound than laser CO_2 and no differences with TECAR therapy at 8 months' follow-up. One RCT[72] investigated the efficacy of wired and wireless iontophoresis with dexamethasone sodium phosphate placed in the drug reservoir, showing better results for both treatments than placebo but no differences between the 2 treatments at 2 weeks' follow-up. The use of LIPUS was investigated in an RCT,[96] showing a significant improvement in pain and clinical scores but no differences with the control group. Finally, another RCT[84] reported no differences between treatment with topical glyceryl trinitrate patch and placebo at 24 weeks' follow-up.

Oral Therapies

One prospective case series[7] investigated an oral treatment with a daily dose of 435 mg of mucopolysaccharides, 75 mg of type I collagen, and 60 mg of vitamin C for 90 consecutive days, showing a significant reduction in pain and improvement of clinical scores.

Injective Therapies

Platelet-Rich Plasma. Fifteen articles described the use of PRP, reporting overall good results in terms of clinical improvement, return to sport, and pain at short-term and long-term follow-up.

Two prospective case series[27,50] showed significant improvements in pain and clinical scores at short-term follow-up with multiple injections of PRP. In 1 study,[27] the authors used a protocol of 2 PRP injections of 6 mL over a mean of 3 weeks; in the other study,[50] the authors used a protocol of 3 PRP injections of 5 mL, 1 injection every 15 days. Moreover, a case report[13] and a prospective comparative study[36] demonstrated, respectively, good results in pain and clinical scores with a single injection of 3 mL of PRP and no difference at 6-month follow-up between patients who had undergone previous treatment (13 steroid injection, 6 Ethoxysclerol [Chemische Fabrik Kreussler & Co GmbH] injection, 5 surgical treatment) before the injection of PRP and patients who did not. Two prospective case series showed good results for multiple injections of PRP at long-term follow-up: 1 of these series[16] showed a significant improvement in clinical scores at 24 months' follow-up, with most of the athletes returning to their presymptom sport level; the other series[31] showed a significant clinical improvement after 6 months, with scores remaining stable at a longer mean follow-up of 48.6 months. Moreover, both studies demonstrated poorer results at both short-term and long-term follow-up for patients with bilateral involvement and a long history of pain. Finally, a retrospective study[22] showed a significant clinical improvement with an 88.8% patient satisfaction rate for a single injection of PRP in a large series of 393 patients at a mean follow-up of 20.2 months.

Among comparative studies, 1 prospective study compared multiple PRP injections together with physical therapy for recalcitrant tendinopathy versus physical therapy for less complex cases,[30] showing a clinical score improvement in both groups and higher improvement in sports activity level with multiple injections of PRP at 6 months' follow-up. One RCT[90] compared multiple PRP injections versus ESWT, demonstrating better improvement in pain and clinical scores in the PRP group at 6 months' and 12 months' follow-up. Another RCT[25] compared a single injection of leukocyte-rich PRP versus dry needling, showing better results in clinical scores for the PRP group at 26 weeks' follow-up.

With respect to treatment combinations, 1 prospective case series[47] investigated the association of a single injection of PRP and eccentric exercises, showing a significant improvement of clinical scores at a 12-month follow-up. Another study[88] showed good results in clinical improvement at a mean follow-up of 38.4 months with a single injection of PRP and an exercise-based physical therapy program. Moreover, 1 case report[74] described an athlete who returned to preinjury level of competition 6 months after a single injection of 2 mL of PRP with buffy coat and 3 mL of fat cells. Conversely, another case report study on 3 patients[11] described some potentially adverse clinical and radiological findings after treatment with PRP, including patellar tendon thickening, worsening pain, discontinuation of athletic participation in all 3 patients, and osteolysis of the distal pole of the patella in 1 patient.

Finally, an RCT and a prospective comparative study compared single versus multiple injections of PRP. The prospective comparative study[102] demonstrated better improvement in clinical scores for multiple injections at a follow-up of 34 months. The RCT[48] showed good results and no significant differences at 12-month follow-up between the 2 groups.

According to the evidence of possibly different results attributable to injection cycles, the quantitative analysis in the present article was performed by dividing the PRP treatment groups according to the number of infiltrations received.

Other Biological Agents. Five studies reported the use of different biological therapies: injections of autologous plasma; laboratory-prepared, amplified, collagen-producing cells derived from dermal fibroblasts and suspended in autologous plasma; and bone marrow– and abdominal fat–derived stem cells.

Three studies investigated injections of autologous plasma. One prospective case series[43] reported clinical improvement and only 3 failures in 44 patients treated with dry needling and injections of autologous plasma. An RCT compared saline injections and autologous plasma injections,[71] reporting a good improvement of symptoms with both treatments and no significant differences between the 2 groups. Another RCT[17] compared autologous plasma injections and laboratory-prepared, amplified, collagen-producing cells derived from dermal fibroblasts and suspended in autologous plasma injection. The results showed a significant improvement of VISA in both groups but a faster and higher improvement for the cell group at 6 months' follow-up; furthermore, 29 of 33 patients in the cell group were satisfied versus 19 of 27 patients in the autologous plasma group. A prospective case series[67] investigated autologous bone marrow stem cell injection: 7 of 8 patients were fully satisfied with the procedure and 1 patient was somewhat satisfied at 60 months of follow-up. Finally, a case report[11] described the use of injection of PRP plus abdominal fat cells, reporting moderate clinical improvement at 18 months' follow-up.

Hyaluronic Acid. Two studies analyzed the outcome of hyaluronic acid injections. One prospective case series[53] investigated the efficacy of a single injection of high-molecular-weight hyaluronic acid at 1-week follow-up, reporting an improvement in pain. A retrospective case series[64] showed good results at a mean follow-up of 25.7 months for multiple hyaluronan injections, reporting 54% excellent results and 40% good results.

Corticosteroids. Two RCTs reported the use of corticosteroid injections. One RCT[32] compared 3 injections of triamcinolone with placebo, reporting better improvement in pain in the corticosteroid group after 6 months; reversible atrophy was seen in 9 of 24 tendons, and none of the athletes reported problems caused by atrophy. The other RCT[51] compared multiple injections of methylprednisolone with eccentric exercise and heavy slow resistance training, showing good improvements in VISA and pain in all groups but a worsening of VISA after 12-week follow-up in the corticosteroid group and better results for eccentric training and heavy slow resistance training after 6 months; no deleterious effects on the tendons were experienced because the treatments were given by peritendinous injection.

Sclerosing Polidocanol Injection. Five studies investigated the use of sclerosing polidocanol injections. One prospective case series[5] reported that all 15 patients returned to their previous activity level and experienced a reduction of pain at 6 months' follow-up. Two prospective case series[39,41] showed clinical improvement at 44 and 24 months' follow-up, respectively; however, the study with longer follow-up[39] reported 12 failures out of 29 patients.

Two RCTs compared polidocanol injections with other treatments. One RCT[40] compared injections of polidocanol and injections of lidocaine-epinephrine, reporting an improvement of clinical scores and training volume at 12 months' follow-up for polidocanol and no improvement for injections of lidocaine-epinephrine. Furthermore, when patients receiving injections of lidocaine-epinephrine crossed to the active treatment after 4 months, they showed a significant improvement. Finally, at 12 months' follow-up, an RCT[99] reported better improvement of pain and a higher rate of satisfaction in patients treated with arthroscopic shaving than patients treated with injections of polidocanol.

Other Injections. A retrospective case series of 97 patients[66] investigated the use of injections of matrix metalloproteinase inhibitor aprotinin, reporting that 7% of patients subjectively felt completely cured, 34% felt much better, 31% felt slightly better, 28% felt similar, 3% felt slightly worse, and 0% felt much worse after a mean follow-up of 11.7 months. Two studies investigated a high-volume, image-guided injection. In particular, a prospective case series[57] administered an ultrasound-guided tendon injection of a mixture of 10 mL of 0.5% bupivacaine hydrochloride, 62,500 IU of aprotinin, and 40 mL of normal saline solution; the authors reported a significant improvement of VISA and pain and good results in terms of return to sport (72% of patients returned to sport at the same level as before the onset of the symptoms) and satisfaction (80% of the patients rated their condition as good or excellent) at a follow-up of 15 months. The other study was a combined retrospective and prospective case series[63] that showed a significant improvement of VISA in both prospective and retrospective groups for an ultrasound-guided tendon injection of 10 mL of 0.5% bupivacaine, 25 mg of hydrocortisone, and 30 mL of normal saline solution at a follow-up of 9 months for the retrospective group and 12 weeks for the prospective group.

Meta-analysis

Among the 70 studies included in the qualitative synthesis, according to inclusion criteria, 5 case reports and 26 studies not reporting both pretreatment and postoperative VISA-P scores were excluded. Moreover, 17 articles were excluded because they reported results of treatments described in fewer than 5 studies. Thus, a total of 22 studies reporting on 591 patients were included in the quantitative synthesis (Table 1).

Four major treatment groups were identified and included in the meta-analysis, as follows:

1. Eccentric exercise: 7 studies[8,24,33,46,51,85,101] reporting on 10 treatment groups at short-term follow-up and 7 study groups at long-term follow-up
2. ESWT: 7 studies[34,85,89,90,95,103,104] reporting on 7 treatment groups at short-term follow-up and 5 study groups at long-term follow-up
3. Single injection of PRP: 6 studies[25,36,47,48,88,102] reporting on 4 treatment groups at short-term follow-up and 7 study groups at long-term follow-up
4. Multiple injections of PRP: 6 studies[16,27,31,48,90,102] reporting on 4 treatment groups at short-term follow-up and 6 study groups at long-term follow-up

Results at Short-Term Follow-up

The results at short-term follow-up (<6 months, mean 2.7 ± 0.7 months) were reported for 470 patients. Eccentric exercise protocols in 150 patients showed a mean improvement of 25.6 points (95% CI, 18.3-32.9 points), with the

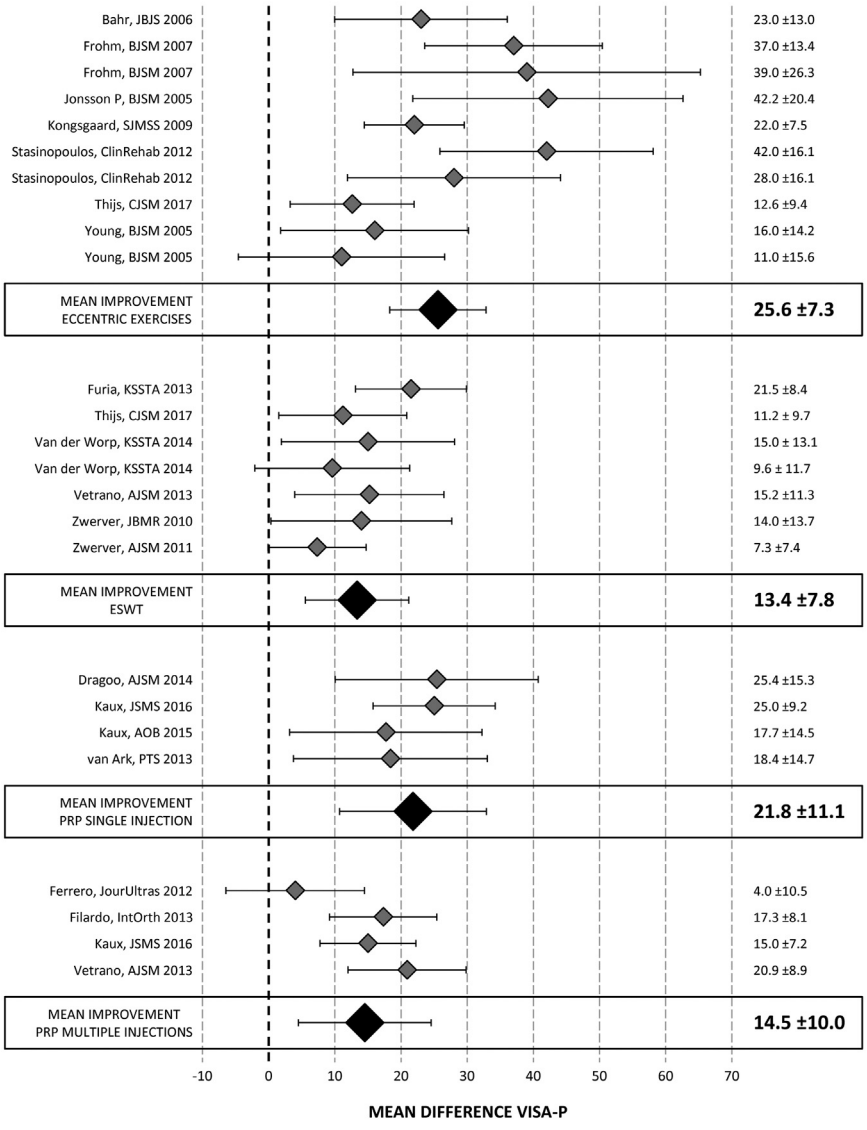

Figure 2. Forest plot of mean improvement of VISA-P (Victorian Institute of Sport Assessment scale for patellar tendinopathy) at short-term follow-up (<6 months). ESWT, extracorporeal shockwave therapy; PRP, platelet-rich plasma.

pretreatment VISA-P score of 49.0 (95% CI, 43.4-54.5) to a posttreament mean of 75.3 (95% CI, 70.1-80.5). ESWT in 175 patients showed a mean improvement of 13.4 points (95% CI, 5.5-21.2 points), with the pretreatment VISA-P mean of 50.8 (95% CI, 45.0-56.6) to a posttreament mean of 64.4 (95% CI, 58.3-70.5). A single infiltration PRP in 45 patients showed a mean improvement of 21.8 points (95% CI, 10.8-32.9 points), with the pretreatment VISA-P mean of 46.7 (95% CI, 38.3-55.0) to a posttreament mean of 68.9 (95% CI, 60.7-77.0). Multiple infiltrations of PRP in 100 patients showed a mean improvement of 14.5 points (95% CI, 4.7-24.4 points), with the pretreatment VISA-P mean of 50.1 (95% CI, 42.7-57.5) to a posttreament mean of 64.7 (95% CI, 57.0-72.3). All treatments reached an improvement higher than the MCID.

The comparison among treatments showed that eccentric therapies obtained the best results in terms of improvement ($P < .05$) at short-term, followed by the single PRP infiltration group compared with multiple PRP ($P < .05$) and ESWT groups ($P < .05$), which reached a similar improvement at short-term follow-up (P not significant) (Figure 2). However, none of the mean differences comparing the different treatments reached the MCID.

Results at Long-Term Follow-up

The results at long-term follow-up (≥6 months, mean 15.1 ± 11.3 months) were reported for 501 patients. Eccentric exercise protocols in 122 patients showed a mean improvement of 28.3 points (95% CI, 18.9-37.8 points), with the pretreatment VISA-P mean of 49.6 (95% CI, 40.4-58.9) to

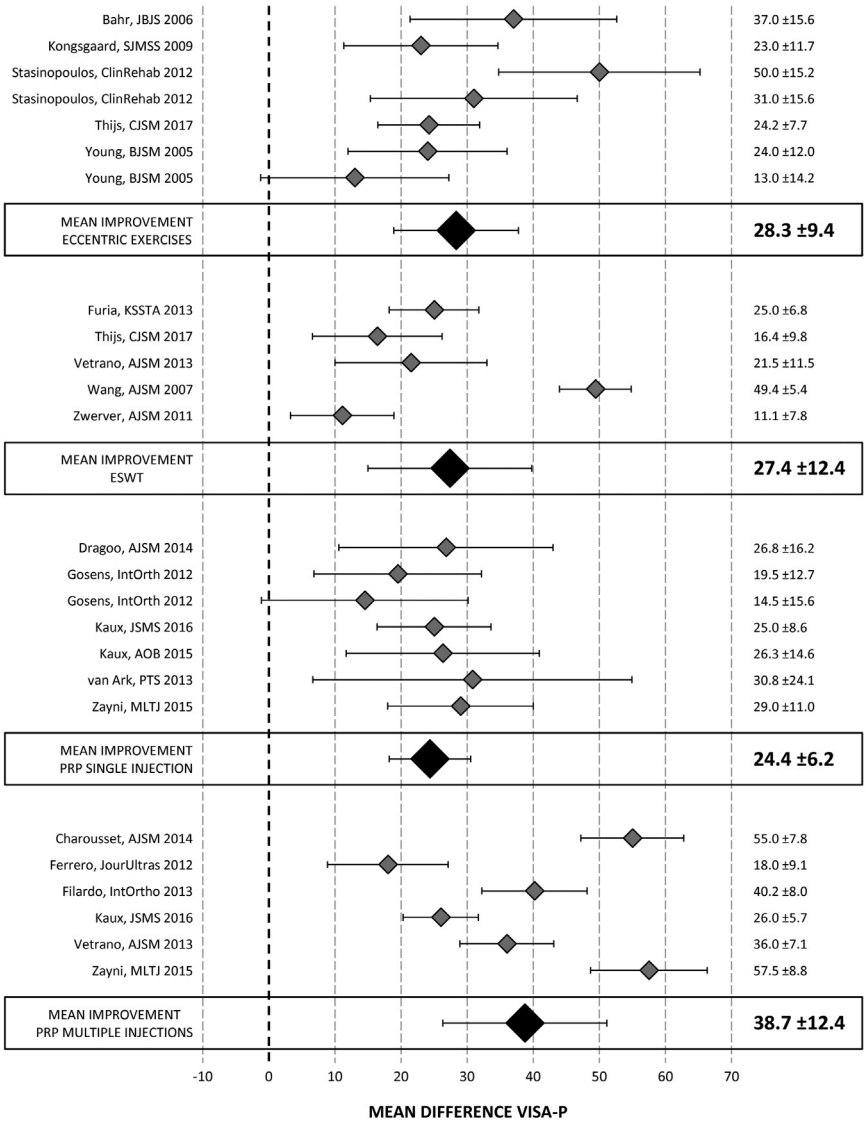

Figure 3. Forest plot of mean improvement of VISA-P (Victorian Institute of Sport Assessment scale for patellar tendinopathy) at long-term follow-up (≥6 months). ESWT, extracorporeal shockwave therapy; PRP, platelet-rich plasma.

a posttreament mean of 79.3 (95% CI, 72.4-86.1). ESWT in 140 patients showed a mean improvement of 27.4 points (95% CI, 10.0-39.8 points), with the pretreatment VISA-P mean of 52.2 (95% CI, 45.4-59.0) to a posttreament mean of 77.3 (95% CI, 67.5-87.0). A single infiltration of PRP in 97 patients showed a mean improvement of 24.3 points (95% CI, 18.2-30.5 points), with the pretreatment VISA-P mean of 42.6 (95% CI, 38.6-46.7) to a posttreament mean of 68.0 (95% CI, 61.9-74.0). Multiple infiltrations of PRP in 142 patients showed a mean improvement of 38.7 points (95% CI, 26.3-51.2 points), with the pretreatment VISA-P mean of 45.8 (95% CI, 39.8-51.7) to a posttreament mean of 84.7 (95% CI, 76.3-93.1). All treatments reached an improvement higher than the MCID.

The comparison among treatments showed that multiple injections of PRP obtained the best results in terms of improvement ($P < .05$), followed by ESWT and eccentric exercise, which offered a similar improvement (P not significant), and both obtained a greater improvement compared with the single PRP injection group ($P < .05$) at long-term follow-up (Figure 3). Only the difference between single and multiple PRP injection reached the MCID.

DISCUSSION

The main finding of this study is that several nonsurgical treatments have been documented in the literature with

an overall positive outcome, although a relatively poor quality of evidence. The meta-analysis demonstrated that eccentric exercise is an effective strategy to obtain the best short-term results, but multiple PRP injections offer better results after 6-months follow-up, which remain stable at long-term follow-up.

The literature analysis found 70 articles reporting results of different nonsurgical treatments of patellar tendinopathy, which can be schematically divided into categories of rehabilitation, physical instrumental therapies, oral therapies, and injective treatments. Among the different treatment categories, the most extensively studied treatment approaches were eccentric exercises, ESWT, and PRP.

Eccentric exercises for patellar tendinopathy have been widely reported, and isolated eccentric loading regimens for tendinopathy are commonly accepted as first-line treatment,[21] even though the potential mechanisms behind this intervention remain unclear. The fact that muscles can produce greater maximal force eccentrically than concentrically would suggest a potential for greater mechanical stimulation from eccentric than from concentric exercise.[21,26,42] Accordingly, it has been suggested that the tendon may stretch more during eccentric than concentric loading,[21,81] with more efficacious interactions between collagen fibers and the induction of mechanotransduction, leading to a greater number of blood vessels, larger quantity of collagen, and, in the end, better mechanical properties of the healing tendon.[49] A minimum of 20 training sessions appears to be necessary to ensure that the treatment is effective, with series typically performed at a 15-repetition maximum.[33,101] Numerous clinical studies have shown the need for a prolonged program of submaximal eccentric contractions, from 6 weeks to 1 year, depending on the severity of the condition, to significantly reduce symptoms of tendinopathy.[49,78,101]

ESWT works through a mechanism addressing the failed tendon healing response. Studies have shown that mechanical stimulation increases the expression of several growth factors and cytokines, such as insulinlike growth factor 1, transforming growth factor β1, and interleukin,[97] and recent studies have demonstrated that ESWT can increase the number of neo-vessels at the normal bone-tendon junction[54] and promote cell growth and collagen synthesis[54,90,91] through the release of growth factors and other active substances. Decision making about whether to use ESWT and the energy levels, number of treatment sessions, and number of impulses to choose is hindered by the diversity of published works. The benefits of using a local anesthetic are also disputed.[60] In this review, ESWT was shown to achieve good results especially at long-term follow-up, and thus its use provides an alternative to multiple injections of PRP.

PRP has recently gained increasing interest, its rationale being the promotion of tendon healing through the delivery of platelet-derived growth factors and bioactive molecules in hyperphysiologic doses, which should enhance tissue repair mechanisms.[90] Numerous studies have investigated the effects of PRP in vitro and in vivo, demonstrating benefits that include improved cellular remodeling and decreased healing time.[6,30,36,77,90] Many aspects regarding the optimal preparation and administration of PRP remain unclear, such as the best PRP formulation, the activation method, and combination with other rehabilitation regimens. Since some evidence[102] suggested different results between single and multiple infiltrations of PRP, perhaps because most growth factors contained in platelets are short-lived, in this review the 2 groups were considered separately to investigate the added benefit of multiple injections. Interestingly, a single injection of PRP was shown to provide better short-term results, whereas multiple injections demonstrated higher improvements at longer follow-up times. This may be due to a faster effect of a single infiltration compared with a cycle, which implies more protracted injection-related discomfort and requires a delay in resuming physical activities. In contrast, a single infiltration of PRP may be less efficient in obtaining the desired biological benefits, since most growth factors contained in platelets are short-lived and the benefit of PRP may dissipate over time.[102] Accordingly, while the meta-analysis comparing the different nonoperative treatments showed a larger improvement of eccentric exercises at short-term, multiple injections of PRP resulted in the best outcome at longer follow-up times.

Other aspects are important in terms of treatment indication, such as invasiveness and practical considerations. In this regard, eccentric exercises are often used as first-line treatment, given their lack of invasiveness and their low cost. The current study found that PRP groups started from a lower score level, probably indicating that studies investigating PRP treatment involved complex cases with patients with more serious symptoms. Nonetheless, multiple PRP injections offered a significant benefit at long-term follow-up, with patients gaining greater improvements. Thus, in complex cases (patients with more serious, longer lasting symptoms or failure of other therapeutic strategies), it seems advisable to combine PRP treatment with rehabilitation (worse results have been shown for patients not following a postprocedure rehabilitation protocol)[50] and specifically eccentric protocols due to their benefit documented by the literature.[‖] A single infiltration of PRP might provide short-term relief but not optimal long-term results. Thus, until further evidence emerges regarding patient and lesion characteristics requiring more injections, 2 or 3 consecutive infiltrations should be considered when administering PRP.

Many other treatments were identified in the literature: treatment involved complex cases with patients with more serious symptoms (1) various rehabilitative treatments, (2) physical instrumental therapies (such as intratissue electrolysis, laser therapy CO_2, cryo-ultrasound therapy, TECAR therapy, pulsed ultrasound, wired iontophoresis, wireless iontophoresis patch, topical glyceryl trinitrate), and (3) multiple substances for intra-articular injection. Intra-articular injections included biologics, such as autologous plasma and bone marrow concentrate; medicinal products, such as hyaluronic acid and corticosteroid; and high-volume ultrasound-guided injections of bupivacaine hydrochloride, aprotinin, and saline solution or of bupivacaine, hydrocortisone,

[‖]References 33, 46, 47, 51, 52, 70, 78, 82, 83, 85, 100.

and saline solution. Although results in most of the studies appear to be promising, the majority of articles present a poor level of evidence and report the results of a small number of patients. Future studies are needed to examine the results of these treatments, as currently available studies do not present enough evidence for a clear indication.

The current literature presents some limitations about the most studied treatments (ie, eccentric exercise, ESWT, and PRP), which reflect the limitations of this review. The quality analysis of the included studies evaluated with the CMS showed an overall poor quality. This confirms the results of a recent Cochrane review on application of PRP to treat tendons, ligaments, and muscles, which included only 1 study about the use of PRP for patellar tendinopathy.[62] Even though treatments were grouped together for study purposes, every treatment has been applied in the literature with different methods. For example, eccentric rehabilitation was used for different periods and different frequencies, with or without the use of a decline board and with or without limitations in other training activities. In turn, ESWT was used with different timing and different rates and doses of impulses, applying radial or focused shockwave. The use of PRP also differed among the studies, in terms of platelet count, presence of leukocytes, activation, storage procedures, number of infiltrations, and interval between infiltrations. Thus, it was not possible to recommend a precise PRP injective treatment protocol supported by literature's evidence. Another limitation is presented by the association between rehabilitation protocols and other treatments, which makes it difficult to quantify the real effect of the treatment itself. This meta-analysis showed a significant difference between single and multiple infiltration protocols for PRP, and likewise it is possible that differences in protocols for eccentric exercises and ESWT could affect the results, which could be optimized by improving the administration protocol of each treatment approach. Unfortunately, the limitations of the literature do not allow such evaluation, and future studies should be performed not only to compare different treatment approaches but also to determine the ideal administration protocol of each treatment, the benefits of combinations of treatments, and the indications in terms of patient and lesion characteristics to develop a targeted treatment approach and optimize results in patients affected by patellar tendinopathy.

CONCLUSION

The literature documents several nonsurgical approaches for the treatment of patellar tendinopathy. The overall outcome is positive, but some differences have been identified. Eccentric exercises may seem the strategy of choice in the short-term, but multiple PRP injections may offer better and more stable results at long-term follow-up and can be therefore considered a suitable option for the treatment of patellar tendinopathy. However, the literature has important limitations, such as the small number of high-level studies and the heterogeneity of treatment strategies, as well as different application modalities for each procedure. Until further research of higher quality is available to describe the potential and indications of available nonoperative treatments, the results of the available literature suggest that multiple PRP injections may be considered a suitable option for complex cases with patients with more serious symptoms or when conservative rehabilitative approaches fail to treat chronic patellar tendinopathy.

ACKNOWLEDGMENT

The authors thank Elettra Pignotti for the assistance in the statistical analysis and Lucia Mancini for English editing.

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