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NARRATIVE REVIEW

Platelet-Rich Plasma for Patellar Tendinopathy: A Comprehensive Review of Current Literature

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Abstract

Background: Patellar tendinopathy is frequently seen among athletes, particularly those involved in sports that heavily utilize the extensor mechanisms of the leg (i.e., basketball and volleyball). Symptoms are commonly exacerbated by load-related activities (i.e., jumping) due to the storage and distribution of stress forces through the patellar tendon potentiating small tears.

Methods: A comprehensive narrative review of PubMed and Medline was conducted using a combination of key words and MeSH terms. Key words included platelet-rich plasma (PRP), patellar tendinopathy, patellar tendon, jumper's knee, patella, physiotherapy, conservative management, and extracted information was independently reviewed by two co-authors.

Review: The current mainstay of treatment for patellar tendinopathy remains physical therapy, with a good body of evidence supporting eccentric training programs with decline squats. In recent years, PRP has emerged as a promising treatment modality for a variety of musculoskeletal injuries, due to its role in accelerated healing and ability to shorten overall recovery time. However, currently there is a lack of consistent clinical evidence to support the routine use of PRP in the treatment of patellar tendinopathy.

Conclusion: Patellar tendinopathy is a common condition, particularly among athletes in sports with repetitive jumping activities. While PRP is a promising therapy for both symptom resolution and regenerative healing, physical therapy remains the mainstay of conservative treatment at this time. This review highlights the need for further standardized and high-power randomized, controlled trials (RCTs) to fully elucidate the potential efficacy of PRP and its role in the treatment of patellar tendinopathy.

Keywords

Patellar tendinopathy, Platelet-rich plasma, Jumper's knee, Physical therapy

Abbreviations

MRI: Magnetic Resonance Imaging; PRP: Platelet-Rich Plasma; MeSH; Medical Subject Headings; ESWT: Extracorporeal Shockwave Therapy; VISA-P: Victorian Institute of Sport Assessment for Patellar Tendinopathy; VAS: Visual Analogue Scale of Pain; BFR: Blood Flow Restriction; LL-BFR: Low-load Resistance Training with BFR; RCT: Randomized Controlled Trial; PDGF: Platelet Derived Growth Factor; VEGF: Vascular Endothelial Growth Factor; TGF-beta: Transforming Growth Factor-beta; FGF: Fibroblast Growth Factor; EGF: Epidermal Growth Factor; IGF-1: Insulin-like Growth Factor-1; LP-PRP: Leukocyte Poor-PRP; LR-PRP: Leukocyte Rich-PRP

Introduction

Patellar tendinopathy is a degenerative tendon disease characterized by pain frequently localized to the inferior pole of the patella, which worsens with increased load and demand on the knee extensors [1]. In addition to the inferior pole of the patella, symptoms may also develop at the distal insertion of the patellar tendon at the tibial tuberosity [1,2]. Frequently a clinical diagnosis, patellar tendinopathy is corroborated by a comprehensive patient history and physical examination. Imaging, such as ultrasound and magnetic resonance imaging (MRI), may be utilized to further

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aid in diagnosis [3]. Traditionally, initial management involves activity modification and targeted reduction of impact loading through the affected knee. Following symptom resolution, conservative measures such as physical therapy, load management, and biomechanical interventions may be employed to gradually facilitate return to play [1,4,5]. Alternative therapies, such as extracorporeal shock wave therapy (ESWT), hyperthermia thermotherapy, infrapatellar taping/straps, topical agents (i.e., glyceryl trinitrate), and local injections (corticosteroids, sclerotherapy, proliferation therapy) have also been proposed as novel treatment options, however evidence-based support for their use is inconsistent at this time [6-15].

Given the high incidence of refractory symptoms and chronic degeneration of the patellar tendon, there has been growing interest in evaluating the regenerative potential of autologous platelet-rich plasma (PRP) as a treatment for patellar tendinopathy. This review will summarize the current understanding of the pathogenesis of patellar tendinopathy, highlight treatment techniques described in literature, and provide an evidence-based evaluation of the role and utility of PRP in clinical practice today.

Methods

We conducted a narrative review by performing a comprehensive literature search of PubMed and Medline using both key words and Medical Subject Heading (MeSH) terms. Keywords included PRP, patellar tendinopathy, patellar tendon, jumper's knee, patella, physiotherapy, conservative management. Two co-authors independently reviewed and extracted information from the articles of interest on PRP and management of patellar tendinopathy. Non-English sources or those with incomplete results were excluded. All questions on source inclusion were directed and addressed by the senior author.

Review

Epidemiology

Colloquially, patellar tendinopathy is referred to as "jumper's knee" due to its prevalence in athletes engaging in high stress and repetitive jumping sports - such as volleyball (44%), basketball (32%), and track and field (28%) [16-18]. Studies have shown that symptoms present more commonly in males and frequently affect both elite and nonelite, recreational athletes [17-20]. Symptoms most commonly occur in adolescence, but may even present as late as the third decade of life and on [17,21].

The associated pain can be substantial and may lead to decline in sports performance, an inability to perform activities of daily living and, in severe cases, cause long-term disability due to irreversible degeneration [22,23]. In an observational study, Bahr, et al. identified that even after completing a 12-month rehabilitation program, only 46% of athletes in high-impact, jumping sports were able to return to their previous level of activity [24]. Given the persistence of symptoms in daily activities, longitudinal studies have even demonstrated that up to 50% of athletes may be forced to retire from their athletic career altogether [25,26].

Pathophysiology

Currently, a host of factors have been identified that predispose to the development of patellar tendinopathy, including body mass index, waist-to-hip ratio, leg length discrepancies, arch height of the foot, quadriceps/hamstring flexibility and strength, and vertical jump performance [27]. Although an exact pathogenesis of patellar tendinopathy has yet to be identified, several models have been proposed that relate to mechanical imbalances, anatomic impingement, vascular insufficiencies and neurodevelopmental factors. Most commonly, the tears associated with patellar tendinopathy are attributed to an overloading injury caused by a mismatch between the functional demand and the adaptational rate of tendinous tissue [28]. Furthermore, the viscoelastic properties of the tendon may be altered by the proliferation of hydrophilic macromolecules, changes of type I toward type III collagen, crosslinking concentrations, and fibril density [14,29-31].

The progression of load-induced tendinopathies has recently been presented on a continuum with phases that include reactive tendinopathy, tendon disrepair, and tendon degeneration [32,33]. Reactive tendinopathy occurs with acute tensile or compressive stress and may also be seen in the setting of trauma. Repeated microtrauma during this reactive phase leads to hypertrophy of the tendon and allows for better compensation of stress forces over a greater cross-sectional area. Continued loading of the tendon fibroblasts increases prostaglandin E2 and leukotriene B4, both of which further contribute to tendinopathy [34]. Following this adaptive phase, the tendon may progress to a state of disrepair characterized by matrix disorganization from the proliferation of chondrocytes, myofibroblasts, and increased proteoglycan production [32]. These alterations at the cellular level gradually compromise the mechanical properties of the tendon. Ultimately, the tendon progresses to tendinosis and/or degeneration, which stands as the pathophysiologic hallmark of end-stage patellar tendinopathy [32,33,35]. Tendinosis and/or partial-thickness tears typically occur in the posterior or posteromedial portion of the proximal end of the patellar tendon, adjacent to the inferior patellar pole [34-36].

Clinical signs and diagnosis

Patellar tendinopathy presents as anterior knee pain that worsens with load-related demand on the knee

extensors, such as walking down stairs or performing decline squats [1,35]. Physical examination may reveal pain localized at the proximal patellar tendon when palpated and at the distal pole of the patella when the leg is fully extended [35]. A detailed history and physical examination are key to differentiating patellar tendinopathy from other differential diagnoses such as patellofemoral pain syndrome, Osgood-Schlatter (eg. tibial tubercle apophysitis), pathologies of the plica or fat pad, and abnormal patellar tracking [19]. In 1973, Blazina, et al. classified the progression of the pathology into 4 stages. In the initial Stage I, pain or discomfort develops after physical activity. Subsequently, pain in Stage II may present at the beginning of physical activity but may resolve or dissipate with continued use. As the tendinopathy worsens, pain in Stage III may gradually appear during rest and with activity - possibly interfering with activities of daily living. Finally, the pathology may progress to the fourth and final stage, which is patellar tendon rupture [37].

A critical assessment for patellar tendinopathy includes an evaluation of the strength and endurance of the patellar tendon-quadriceps unit. The decline squat test requires the patient to perform a single leg squat with 30° knee flexion resulting in a substantial load being placed on the patellar tendon, which may result in anterior knee pain localized to the inferior pole of the patella [38]. Ultrasound or magnetic resonance imaging may reveal tendon thickening, irregularity of the paratenon, and/or tendinosis at the inferior pole of the patella. However, these findings may also be observed in asymptomatic patients [1]. Imaging of the patellar tendon can be particularly helpful in excluding other diagnoses of anterior knee pain when the clinical presentation is unclear [3,17]. Notably, previous studies have identified that 60% of elite sports players with painful tendinopathy were found to have neovascularization in the tendon as identified by the Doppler ultrasound [39,40]. While more studies are needed to establish a definitive correlation, preliminary evidence suggests that the presence of neovascularization in the patellar tendon may be associated with greater pain and lower functional scores in early, acute stages of patellar tendinopathy [39,41]. Additionally, an MRI-based classification system has been proposed as a predictor of patellar tendinopathy severity by correlating the ratio of tear thickness to the relative thickness of the patellar tendon. A retrospective review of patients with symptomatic patellar tendinopathy found that increasing ratios were indicators of higher grades of disease with: grade 1 indicating no tear, with tendinosis/edema on MRI (classic patellar tendinitis; Blazina grade 1) grade 2 showing minor, partial tears, with percentage tear thickness ratio < 25% (Blazina grade 1-2); grade 3 signifying moderate, partial tears, with thickness tear percentage ratio between 25% and 50% (Blazina grade 2-3); and grade 4 representing severe partial tears, with tear percentage ratio > 50% (Blazina grade 2-3) [36]. At this time, however, more directed outcomes-based research will be required to link imaging characteristics of patellar tendon tears to the optimal nonsurgical and surgical interventions.

Current clinical practices

Currently, numerous strategies have been employed to treat patellar tendinopathy; however, no consensus has been reached regarding the most effective treatment modality. Techniques that have been utilized include eccentric training, ESWT, various local injections, and open/arthroscopic surgery.

Nonoperative: Conservative treatment may be burdensome for patients and may include physical therapy and load management which ultimately may not prevent the eventual need for surgery [1,4,5]. To date, eccentric exercise has been one of the most investigated interventions and is accepted as the first-line approach for managing patellar tendinopathy [42]. In a study performed by Bahr, et al., [43] 55% of sub-elite athletes receiving eccentric training had improved knee function based on self-reported Victorian Institute of Sport Assessment for patellar tendinopathy (VISA-P) score, versus 45% of those receiving open tendonectomy. When comparing eccentric exercises to corticosteroid injections, patients that underwent eccentric decline squat training had greater VISA-P and visual analogue scale of pain (VAS) improvements at 6 months (76 vs. 64; $p < 0.05$) [14]. Furthermore, when compared to concentric quadriceps training, eccentric training has demonstrated a significant improvement in function and reduction in pain [42,44]. However, given the significant variability in published exercise programs, there is currently no definitive consensus on the optimal form of physical therapy.

Additional noninvasive treatments, such as ESWT, low-intensity pulsed ultrasound, patellar straps, blood flow restriction (BFR), and topical glyceryl trinitrate, have largely demonstrated unclear benefits for alleviating symptoms [6-9]. Early investigations suggest that BFR may be a potential treatment option in combination with low-load resistance training (LL-BFR). In an available case series, patients undergoing a 3-week rehabilitation with LL-BFR exhibited a clinically significant improvement in pain scores versus conventional therapy, however further research will be required to establish its true efficacy as a potential rehabilitation tool [45]. Importantly, ESWT has been identified to produce superior results compared to traditional conservative treatments in patients with patellar tendinopathy. Specifically, Wang, et al. demonstrated clinically significant differences in mean Victorian Institute of Sports Assessment scores (92.0 vs. 41.0; $p < 0.001$) and self-reported patient satisfaction (90% vs. 50%; $p < 0.001$) when comparing patients who were randomized into a shockwave therapy versus a control cohort receiving

NSAIDs, physiotherapy, and an exercise program. While the mechanism of ESWT is not fully understood, studies have speculated that shockwave therapy relieves pain through hyperstimulation analgesia, reduction of substance P, induction of peripheral nerve dysfunction and improvement in blood supply to promote tissue regeneration in late stage, chronic patellar tendinopathy [46].

Given the refractory response to many conservative approaches, local injections requiring tendon penetration have been proposed as therapeutic alternatives for treatment. Studies found that injections of polidocanol resulted in moderate improvement in knee function and reduced pain as described by VISA-P in elite athletes with patellar tendinopathy. However, despite its effectiveness in some patient populations, the majority of patients still had reduced function and substantial pain in long-term follow-up at 24 months and 44 months [12,13]. Ultrasound-guided sclerosing injections became increasingly popular since Öhberg, et al. reported it as an effective treatment for Achilles tendinopathy [47]. However, for use in patellar tendinopathy, a systematic review identified very weak evidence supporting use of injectable sclerotherapy (i.e., polidocanol, sodium tetradecyl, or sodium morrhuate) and prolotherapy (i.e., hypertonic dextrose solution) due the limited number of high quality, randomized, controlled trials (RCTs) that have been performed to date [10-13]. Similarly, a single RCT found that aprotinin (bovine derived, broad spectrum inhibitor of matrix metalloproteinases) appeared superior to both corticosteroid and saline injections for patellar tendinopathy [48]. However, a more recent large, retrospective case series of 97 patients showed less promising results and concluded that Level 1-2 evidence supporting use of aprotinin in tendinopathy is largely incomplete at this time [49]. Finally, while local injections of corticosteroids have been shown to be more effective than placebo for pain relief, rebound symptoms are expected and the theoretical risk of patellar rupture remains [14].

Operative: Most patellar tendinopathy cases are resolved through nonoperative management, but operative treatment may be necessary in refractory and unresponsive cases - especially when symptoms escalate to Blazina stage III. Classically, surgical treatment involves the debridement of degenerative areas of the inferior pole of the patella and tendon. Depending on the degree of degeneration or presence of tears, surgeons may perform a tendon release and later use tensioning sutures or suture anchors to recreate the native anatomy of the knee.

Both arthroscopic and open surgery have been used, with the success of each being 87% and 91%, respectively [50].The return to sport time is lengthy, with recovery estimated to be approximately 8.3 months and 3.9 months following open procedures and arthroscopic approaches, respectively [50]. Importantly, Ferreti, et al. [51] reported that for competitive athletes receiving an open surgical treatment, 82% of these patients were able to perform their respective activity at their preinjury level, but only 63% were symptom free. Thus, while surgery may be indicated in select patients to return function, long-term outcomes indicate that substantial pain may continue to persist despite the extended recovery period.

Platelet-rich plasma

Since the early 1900s, PRP has been recognized as a rich source of autologous growth factors [52]. In the field of orthopedics, PRP has been noted to aid in recovery from joint replacement [53], fracture healing [53], spine surgery [53], anterior cruciate ligament reconstruction [54,55], muscle strains, and tendinopathies [56-58]. PRP has been shown to not only promote cell recruitment, proliferation, and angiogenesis, but has also been suggested to induce transient inflammatory events that trigger a regenerative response [59,60]. Additionally, PRP injections for musculoskeletal soft tissue injuries, including patellar tendinopathy, are generally considered a relatively safe treatment option, with minimal adverse events or side effects being reported in available literature [61-63]. Given that tendinopathies are among the most common musculoskeletal complaints in patients seeking medical care, there has been a growing body of evidence investigating PRP's biological and biomechanical impact.

Generally, the process of creating the PRP solution begins with the collection of whole blood in the presence of an anticoagulant such as citrate dextrose-A or citrate phosphate dextrose that binds to calcium and prevents the initiation of the clotting cascade. The citrated whole blood is then centrifuged. The resulting plasma supernatant is either harvested for use or subjected to another round of centrifugation to further separate the mixture into platelet-poor plasma and platelet-rich plasma. Once injected, platelets within PRP preparations are theorized to form a fibrin matrix, which serves as a repair scaffold at the site of injury. Additionally, platelets are responsible for the local release of a host of growth factors, including platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF-beta), fibroblast growth factor (FGF), epidermal growth factor (EGF), and insulin-like growth factor-1 (IGF-1) (Table 1). These growth factors are speculated to augment the healing process through cell signaling and paracrine effects localized to the injected, injury site.

PRP can be classified into three groups according to cellular component concentrations, including: leukocyte-poor PRP (LP-PRP), leukocyte-rich PRP (LR-PRP), and platelet-rich fibrin [64]. Given the inclusion of

Table 1: Function of relevant growth factors.

Growth Factor	Function
PDGF	Stimulates cell proliferation, chemotaxis, and differentiation; stimulates angiogenesis
TGF-Beta	Stimulates collagen type I and type III production, angiogenesis, re-epithelialization, and synthesis of protease inhibitors to inhibit collagen breakdown
VEGF	Regulates endothelial cell proliferation and migration
EGF	Modulates cell proliferation and cytoprotection, accelerates re-epithelialization, increases tensile strength in wounds, facilitates organization of granulation tissue
FGF	Stimulates angiogenesis, promotes stem cell differentiation and cell proliferation, promotes collagen production and tissue repair
IGF-1	Modulates cell proliferation and differentiation, influences matrix secretion from osteoblasts and production of proteoglycan, collagen, and other non-collagen proteins

white blood cell fraction, LR-PRP has been suggested to induce a greater short-term inflammatory and fibrotic response than LP-PRP. It is important to note, however, that while LR-PRP may increase the growth factor yield at the injury site, animal studies have shown that the induction of a greater inflammatory response may ultimately delay healing [65]. While existing literature has attempted to assess the utility of LR-PRP and LP-PRP for use in patellar tendinopathy, variability among study design and leukocyte fraction have ultimately led to a lack of consensus on the efficacy of PRP [58,65-67]. For example, when assessing pain scores, a meta-analysis performed by Fitzpatrick, et al. [68] found good evidence to support the use of single injections of LR-PRP for tendinopathy. Rodas, et al. [69] also noted a clinically significant reduction in pain and improvement in activity levels but utilized LP-PRP in combination with a structured rehabilitation protocol. Conversely, when directly comparing a single injection of LR-PRP and LP-PRP in athletes, Scott, et al. reported that neither PRP preparation was more effective than saline in improving symptoms when combined with an exercise-based rehabilitation program [70]. Thus, the current literature does not appear clear in delineating the inclusion or appropriate concentration of leukocytes (LR-PRP versus LP-PRP) in current PRP preparations.

Going further, numerous studies have reported outcomes following treatment with PRP for patellar tendinopathy, however, nearly all publications to date are limited by sample size (Table 2). When compared to a cohort of subjects receiving dry-needling alone, Dragoo, et al. (n = 23) identified that patients who received an injection of LR-PRP with dry-needling had significant improvements in symptoms at 12 weeks; however, this difference was not significant through long-term follow-up, at > 26 weeks [71]. Another study (n = 46) demonstrated that PRP may have significant long-term benefits for athletes when compared to ESWT at 6-month and 12-month follow-up [64]. Specifically, at 12-month follow-up, 91.3% of PRP patients reported a higher level of satisfaction and the ability to pursue sports at their preinjury level compared to 60.8% of patients in the ESWT cohort. Kaux, et al. (n = 33) identified that PRP and hyaluronic acid combination injections could alleviate symptoms in the midterm (3 months), with only the PRP cohort reporting decreases in pain and improvements in quadriceps strength [72]. Charousset, et al. (n = 28) utilized 3 ultrasound-guided injections of PRP in athletes that failed 4 months of nonoperative treatments. Of the athletes included in the study, 75% were able to return to their pre-symptom sporting level after 3 months with 57% showing a complete repair of the tendon confirmed by MRI [73]. Similarly, Filardo, et al. (n = 43) and Kon, et al. (n = 20) reported promising results as 81% and 80% of study subjects, respectively, returned to their pre-symptom level of sporting activity after receiving PRP injections [61,74]. Gosens, et al. (n = 36) reported that only 22% of their patients were able to return to exercise without pain at 6 months, yet found a statistically significant improvement in pain scores when compared to pre-injection status [75]. Even with studies reporting promising outcomes with the use of PRP in patellar tendinopathy, the full potential of this treatment largely remains unknown due to the current lack of generalizable, large-scale, RCTs.

Additionally, determining the efficacy of PRP is further confounded by a lack of standardization pertaining to the origin, composition, and preparation of samples [64]. At the commercial level, there are various preparation profiles of PRP kits available for use [76]. A recent systematic review done by Chahla, et al. found that of the 105 studies utilizing PRP in orthopedics, only 11 provided enough transparency in their protocol to allow for subsequent investigators to accurately reproduce preparations [77]. Therefore, variations in PRP preparation related to the initial blood volume sample, inclusion/exclusion of white blood cells, and patient-specific factors related to platelet/growth factor concentrations have contributed to a current body of literature that highlights a need to standardize use in future RCTs to allow for comparability [78].

Finally, given the limited lifespan of growth factors available within platelets, the number and timing of PRP injections is crucial to optimize tendon healing. Several published studies have suggested that weekly

Table 2: Evidence for PRP in patellar tendinopathy.

Study (y)	Study Design	Intervention	Inclusion	Outcomes
Rodas, et al. (2021) [69]	II	1) 2 injections of LP-PRP 23 days apart and standardized rehabilitation protocol (n = 10) 2) BM-MSC injection and standardized rehabilitation protocol (n = 10)	Athletes with chronic patellar tendinopathy with pain for > 4 months (mean, 23.6 months) and unresponsive to nonoperative treatments. Intratendinous lesion > 3mm at the proximal insertion.	• Significant reduction in VAS pain scores in daily life and sports activities at 6 months, but no statistically significant difference between the two groups at 6 months. • Statistically significant improvement in VISA-P scores in both groups at 6 months. Scores were > 60 (suitable for intense athletic activity) in both groups with no significant difference in scores between groups. • Statistically significant improvements in tendon structure on 2-D ultrasound, UTC, and MRI for BM-MSC group only.
Lee, et al. (2020)	Case series	1) PRP injection and a 2-week period of rest from physical lower body activity, no anti-inflammatory medication, and no treatment with cooling or ice (n = 15)	Elite athletes with refractory chronic patellar tendinopathy	• 12 athletes were eventually able to fully return to sport after the PRP injection (range 3 weeks to 16 weeks). • 3 of the athletes required surgical debridement and repair of the patellar tendon.
Kaux, et al. (2019) [72]	II	1) Single LP-PRP injection and standardized eccentric training protocol (n = 18) 2) 2 HA injections 1 week apart and standardized eccentric training protocol (n = 15)	Sportsmen with chronic patellar tendinopathy unresponsive to classical conservative treatments (painkillers, NSAIDs, eccentric training, ESWT)	• Significant improvement in VAS, VISA-P, and IKDC for both groups at 6- and 12-week follow-ups. No statistically significant differences in these scores between the two intervention groups.
Scott, et al. (2019) [70]	I	1) 15% hematocrit in 3.5 mL PRP and standardized rehabilitation program (n = 19) 2) 2% hematocrit in 3.5 mL PRP and standardized rehabilitation program (n = 19) 3) 3.5 mL saline and standardized rehabilitation program (n = 19)	Recreational/elite athletes with patellar tendinopathy symptoms for at least 6 months that were not resolved with exercise-based rehabilitation for a minimum of 6 weeks	• No significant difference in mean change of VISA-P scores, NPRS scores, nor GROC scores at 6-, 12-, 24-, and 52-weeks following treatment. A nonsignificant trend for poorer outcomes was noted in the LR-PRP group.
Manfreda, et al. (2019) [79]	Prospective study	1) 3 PRP injections in 15 days, for all patients followed by rehabilitation (n = 23)	Athletes who did not want to undergo surgery and who are non-responders to other conservative treatments for the chronic patellar tendinopathy	• Both for VAS and for VISA-P, there was no significant difference in results at 4 and 12 months compared to baseline ($p > 0.05$).

Zayni, et al. (2015) [5]	Randomized prospective consecutive series	1) Single PRP injection and physical therapy (n = 20) 2) Two PRP injections (2 weeks apart) and physical therapy (n = 20)	Elite/competitive non-elite athletes with chronic anterior knee pain with focal tenderness at the proximal insertion of patellar tendon on clinical examination	• 23% of PRP patients had failed PRP treatment and needed surgery. • Patients that received 2 PRP injections had significantly better clinical scores than those who received a single PRP injection with VAS, Tegner score, and VISA-P.
Dragoo, et al. (2014) [71]	Double-blind, randomized controlled trial	1) Dry-needling and standardized eccentric exercises (n = 13) 2) Single injection of ultrasound-guided LR-PRP, dry-needling, and standardized eccentric exercises (n = 10)	Patellar tendinopathy which had failed nonoperative treatment	• At 12 weeks the PRP group showed a statistically significant improvement in VISA scores compared to the dry-needling group ($p = 0.02$). • At 12 weeks the difference in improvement in Lysholm scores was not significant ($p > 0.05$). • At > 26 weeks, the dry-needling group showed significant improvement in Lysholm scores compared to the PRP group ($P = 0.006$). • At > 26 weeks, the difference between VISA score improvement was not significant ($p > 0.05$).
Charousset, et al. (2014) [73]	Prospective Study	1) Athletes with chronic patellar tendinopathy refractory to nonoperative management and received PRP injections (3 consecutive injections 1 week apart: n = 28)	Professional/semi-professional athletes with chronic anterior knee pain, tenderness at the inferior pole of the patella, or pain during provocative tests of the knee extensors and morphological signs of chronic patellar tendinopathy	• The VISA-P, VAS, and Lysholm scores all significantly improved at the 2-year follow-up. • 21 of the 28 athletes returned to their pre-symptom sporting level at 3 months. • MRI assessment showed improved structural integrity of the tendon at 3 months after the procedure and complete return to normal structural integrity of the tendon in 16 patients. • 7 patients did not recover their pre-symptom sporting level, 3 patients returned to sport at a lesser level, 1 patient changed his sport activity, and 3 needed surgical intervention.
Filardo, et al. (2013) [74]	Prospective study	1) 3 intratendinous injections of PRP (2 weeks apart). After the second injection the patients were instructed to start a rehabilitation program based on eccentric exercises to be carried out for about 12 weeks (n = 43)	Chronic patellar proximal tendinopathy that has undergone unsuccessful conservative or surgical management	• Significantly poorer results were obtained in patients with a longer history of symptoms, and poor results were also observed in bilateral lesions. • VISA-P score significantly increased from baseline to two months, to six months, and to four years. • EQ-VAS score significantly increased from baseline to two months and to six months.

Vetrano, et al. (2013) [62]	Randomized controlled trial	1) 3 sessions of ESWT at 48- to 72-hour intervals and standardized stretching and muscle strengthening protocol for 2 weeks (n = 23) 2) 2 ultrasound guided PRP injections over 2 weeks (1 per week) and standardized stretching and muscle strengthening protocol for 2 weeks (n = 23)	Athletes who had chronic patellar tendinopathy for at least 6 months before treatment and failure of nonoperative treatment	• Both treatments led to improvement from baseline VISA-P and VAS scores at 2, 6, and 12 month follow-ups ($P < 0.005$ for all). • At 6 and 12 months, the PRP group significantly improved in VISA-P and VAS scores when compared to the ESWT group.
Gosens, et al. (2012) [75]	Prospective Study	1) Patients that had been treated with cortisone, ethoxysclerol and/or surgical treatment before PRP injection (n = 14) 2) Patients had not received an injection or surgical treatment before their PRP injection (n = 22) **All patients had visited a physiotherapist and eccentric exercises had been performed exhaustively before being treated with PRP.	Chronic patellar tendinopathy	· VISA-P significantly improved in group 2 from baseline to follow-up (average 18 months). · Group 1 did not show significant improvement on VISA-P. · VAS ADL scores, VAS sport scores, and VAS work scores significantly improved in both groups.
Fildaro, et al. (2010)	Prospective study	1) Patients affected by chronic jumper's knee, who had failed previous nonsurgical or surgical treatments, with multiple PRP injections (3 occasions over 2 weeks) and physiotherapy (n = 15) 2) Patients who had not undergone any treatment (for at least two months) and were primarily treated with the physiotherapy protocol alone (n = 16)	Athletes with >3 months of exercise-associated pain and failed to respond to other nonsurgical treatments	· PRP group experienced a significant improvement in the EQ VAS and pain level was identified from baseline evaluation to the end of the injection cycle, and at six-month follow-up. · When comparing the two groups, no statistically significant differences were obtained with the EQ VAS and pain level evaluation, as with time-to-recover and patient satisfaction ($p > 0.05$). · When compared to the control group, the PRP group had a statistically significant improvement in sport activity level.
Kon, et al. (2009) [61]	Prospective Study	1) 3 PRP injections (injections were administered every 15 days). Rest between 1st and 2nd injection, mild activities after 2nd injection, stretching exercises and mild activities after 3rd injection (n = 20)	Athletes with > 3 months of exercise-associated pain and failed to respond to other nonsurgical treatments	· At 6 months, the patients reported significantly improved Tegner, EQ VAS, and SF 36 Q scores.

Abbreviations: EQ VAS: EuroQol-Visual Analogue Scales; ESWT: Extracorporeal Shock Wave Therapy; GROC scores: Global Rating of Change Scale; HA: Hyaluronic Acid; IKDC: International Knee Documentation Committee Form Score; Lysholm Score: Lysholm Knee Scoring Scale; NPRS scores: Numerical Pain Rating Scale; BM-MSC; Single Bone Marrow-Derived Mesenchymal Stem Cell; SF 36 Q Scores: 36-Item Short Form Health Survey; Tegner Score: Tegner Activity Score; UTC: Ultrasound Tissue Characteristics; VAS: Visual Analog Scale; VAS-ADL: Visual Analog Scale-Activities of Daily Living; VISA-P: Victorian Institute of Sport Assessment-Patellar Tendinopathy

PRP injections or receiving 3 intratendinous injections 15 days apart demonstrated clinically significant improvement in outcomes [61,74,75]. Charousset, et al. demonstrated that the application of 3 consecutive US-guided PRP injections administered 1 week apart significantly improved the symptoms and facilitated quicker return to play [73]. Similarly, Zayni, et al. [5] reported that athletes receiving 2 PRP injections administered 2 weeks apart had significantly greater clinical outcomes compared to individuals that received a single PRP injection. However, Manfreda, et al. [79] reported that receiving 3 PRP injections within a 15-day time span did not significantly improve clinical outcomes compared to baseline. Given the conflicting evidence available in current literature, more targeted randomized, controlled studies will be needed to best elucidate the ideal timing and quantity of PRP therapies.

Discussion

With up to 40% of athletes reporting patellar tendon pain at some point in their career, it is imperative to create a standard of care protocol that facilitates a safe timeline to return to play [80,81]. Since tendon and ligament pathology may significantly impact sports performance and quality of life, it is critical to identify and optimize the ideal treatment modality. NSAIDs and corticosteroids can be utilized to manage acute tendinopathy symptoms, but their use provides little benefit in the long-term resolution of the pathology [82]. Additionally, while surgical intervention may be indicated for refractory patellar tendinopathy, outcomes remain unpredictable regarding refractory pain and discomfort in the post-operative period [83].

Given the varying approaches to conservative management, PRP has gained noteworthy attention as a treatment strategy for patients with patellar tendinopathy [82,84,85]. A systematic review and meta-analysis completed by Miller, et al. [86] concluded that injections of PRP were more efficacious than control injections for patients with symptomatic tendinopathy. However, it is important to mention that only a single study in this analysis specifically addressed patellar tendinopathy and variable methods of PRP preparation could not be controlled for. Such results should be interpreted with extreme caution as the number of high-quality studies is sparse, and generalizability is limited due to significant differences in methodologies. Specifically, the basic characteristics of the solution such as volume and the concentration of platelets may confound current reporting of clinical outcomes [78]. Moreover, PRP contains varying levels of leukocytes (monocytes, basophils, eosinophils, and neutrophils) that may either positively or negatively affect the repair process, which makes their inclusion a major point of controversy [87].

Additionally, it must be noted that treatment effectiveness is not synonymous with observed improvement over time. Even patients with recalcitrant tendinopathies may exhibit some degree of improvement with time, regardless of treatment. Readers should interpret the results of clinical trials with an understanding that biases (i.e., placebo responses, Hawthorne effect, etc.) related to research may confound results, especially when available RCTs are largely underpowered [70].

Going further, value-based healthcare has been a growing enterprise in the United States and the cost-effectiveness of PRP injections has yet to be shown. Although it has received FDA-clearance for off-label use in a variety of musculoskeletal pathologies, PRP is regarded as an autologous biologic and is not subject to the formal FDA-approval process [88]. As a result, PRP injections are not covered by insurance companies, and this limits the ability to conduct thorough cost-benefit or value-based analyses to justify its use. Prices for PRP injections are largely set arbitrarily by individual medical practices and previous literature has reported a mean cost per injection to be $714 with a standard deviation of $144 [89]. Thus, current literature indicates that PRP injections may be socioeconomically restrictive, as production, personnel, and equipment drive the out-of-pocket price beyond that of most alternative treatments [88,90].

The conclusions that can be drawn from this review are largely limited by the paucity of available RCTs and unstandardized techniques relating to the preparation and timing of PRP injections. Currently, the mainstay of treatment for patellar tendinopathy remains physical therapy, with a good body of evidence supporting eccentric training programs with decline squats [14,91]. While PRP shows promise as a safe and effective future treatment for patellar tendinopathy, there is currently insufficient evidence to support its widespread use.

Conclusion

Patellar tendinopathy is a common condition, particularly among athletes in sports with repetitive jumping activities. While PRP is a promising therapy for both symptom resolution and regenerative healing, physical therapy remains the mainstay of conservative treatment at this time. This review highlights the need for further standardized and high-power RCTs to fully elucidate the potential efficacy of PRP and its role in the treatment of patellar tendinopathy.

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