Orthobiologics: Diagnosis and Treatment of Common Tendinopathies

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Abstract

Orthobiologics, including platelet-rich plasma, prolotherapy, and mesenchymal stem cells, are seeing increasing use in the treatment of osteoarthritis (OA), muscle injury, and tendinopathy. This article reviews the biology and applications of orthobiologics in tendons, muscles, and joints, and focuses on platelet-rich plasma (PRP). Clinical evidence-based literature related to the use of PRP in the treatment of rotator cuff injury, lateral epicondylosis, Achilles tendinopathy, plantar fasciitis, knee OA, and acute muscle injury are discussed.

Keywords
- orthobiologics
- platelet-rich plasma
- tendinopathy
- ultrasonography

Orthobiologics: An Overview

The term *orthobiologics* describes biological agents applied to musculoskeletal (MSK) injuries, most frequently in the form of ultrasonography (US)-guided injection, to reduce pain and to facilitate healing.[1,2] Such agents include bone grafts, platelet-rich plasma (PRP) (both leukocyte-rich [LR] plasma and leukocyte-poor [LP] plasma), autologous blood, and stem cells (mesenchymal and embryonic). These substances are used to treat a variety of MSK problems, such as tendinopathies, osteoarthritis (OA), and acute muscle injuries, and their use is becoming increasingly relevant for both young and older age groups. MSK pathologies, including arthritis, joint complaints, and traumatic injuries, are rising in prevalence in the United States, especially as the population ages. The most recent edition of the *United States Bone and Joint Initiative: The Burden of Musculoskeletal Diseases in the United State*s estimates that, for MSK disorders, "expenditures in 2014 dollars increased from $381.4 billion in 1996–1998 to $882.5 billion in 2012–2014, an increase of more than 130%. . . . In 1996–1998, aggregate all-cause expenditures for persons with a musculoskeletal disease . . . represented 3.2% of the GDP [gross domestic product]. By 2012–2014, the proportion had grown to 5.2% of the GDP."[3] Orthobiologics are especially important in pain management as patients and providers alike seek long-term solutions that avoid opiate-based therapies.

The initial theoretical foundation for the use of orthobiologics derived from recognition of the limited regenerative capabilities of the MSK system. It was hypothesized that the injection of growth factors, typically derived from a patient's own blood, would enhance regeneration and repair. Since initial studies in the 1990s demonstrating that platelet-rich plasma (PRP) could hasten the consolidation of mandibular bone grafts,[4] the use and applications of orthobiologics generally, and PRP particularly, have only continued to expand. This review article focuses on PRP, including its biology and practical applications, with special attention given to the role of the radiologist in the use of this expanding therapy.

Platelet-rich Plasma: Biology and Classification Systems

PRP, as the name suggests, is a preparation of autologous blood enhanced with an increased concentration of platelets. It is obtained through the centrifugation of anticoagulated whole blood, yielding a plasma layer that is platelet poor, a leukocyte layer that is platelet rich, and a red blood cell (RBC) layer.[5–8]

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Table 1 Platelet-rich plasma classification by Ehrenfest et al[7]

Type	Constituents
P-PRP, also called leukocyte-poor platelet-rich plasma	Without leukocytes and with low-density fibrin network after activation
L-PRP	With leukocytes and with low-density fibrin network after activation
P-PRF, also called leukocyte-poor platelet-rich fibrin	Without leukocytes, with high-density fibrin network
L-PRF	With leukocytes, with high-density fibrin network

Abbreviations: L-PRF, leukocyte- and platelet-rich fibrin; L-PRP, leukocyte- and platelet-rich plasma; P-PRF, pure platelet-rich fibrin; P-PRP, pure platelet-rich plasma.

Platelets, the namesake component of PRP and an important element of the clotting cascade, also play a significant role in tissue healing, a process that is relatively compromised in ligaments, tendons, and joints, given their relatively poor blood supply.[8] When tissue incurs trauma, a three-phase process of wound healing begins. With the formation of a hematoma in the *inflammatory phase*, recruited platelets release the growth factors stored in their α granules, including basic fibroblast growth factor, epidermal growth factor, insulinlike growth factor-1, platelet-derived growth factor, transforming growth factor-β, and vascular endothelial growth factor.[5,6,9] These factors have a variety of functions, including mitogenesis of fibroblasts, osteoblasts, other growth factors, smooth muscle cells, mesenchymal cells, chondrocytes, and osteoblasts. In the *proliferative phase* that occurs a few days later, these elements contribute to collagen deposition, angiogenesis, granulation tissue formation, and ultimately wound contraction. The final *remodeling phase*, during which collagen matures and excess cells undergo apoptosis, can last for months.

In addition to platelets, PRP also contains leukocytes and RBCs. Although leukocytes (including neutrophils, macrophages, and monocytes) are essential for the inflammatory phase of wound healing and help prevent infection, the increased inflammation they promote can counteract the benefits provided by PRP.[10–13] Recent research has indicated that reducing leukocyte concentrations in PRP, rather than increasing platelet concentrations, may be a crucial aspect of enhancing therapeutic efficacy.[10] In general, LR-PRP is used to promote inflammation and healing for tendinopathies, whereas LP-PRP is preferred for treating knee OA. Similarly, RBCs are also believed to compromise the efficacy of PRP preparations through the release of cytotoxic oxygen-free radicals in the setting of oxidative stress.[14] Differing concentrations of each of these components in PRP preparations can make comparisons across research trials challenging.[6] Still further variability can be introduced into PRP preparations through activation with mixtures of thrombin and calcium that facilitate rapid delivery of growth factors. However, less is known regarding possible benefits of rapid versus gradual delivery of growth factors, with some studies suggesting that rapid delivery enhances bony regeneration but slows fibroblast differentiation.[6,15,16]

The broad term *platelet-rich plasma*, therefore, can often gloss over differences between subcategories of this substance, which are important to maintain in light of growing evidence that certain concentrations of platelets and growth factors are more suitable for some conditions than others.[2] Multiple classification systems have been used, each placing variable emphasis upon, for example, concentrations of constituents in the centrifugate, fibrin levels, and/or use of activation techniques, such as adding calcium to promote degranulation of platelets to release growth factors.[17]

The 2014 classification by Ehrenfest et al is widely cited (summarized in ►**Table 1**) and uses the presence or absence of leukocytes, and high- versus low-density fibrin networks, as the basis for categorization.[7] The 2012 classification system by Mishra et al, also divided into four groups, is based on relative leukocyte levels (increased over baseline versus minimal to no leukocytes) and whether or not the preparation is activated. Each group is subclassified into "A" (more than five times the baseline level of platelets) or "B" (less than five times the baseline level of platelets).[18] DeLong et al proposed the platelet-activation-white blood cell (PAW) system, dividing platelet levels into four groups, total white blood cells (WBCs) into two groups, and neutrophil levels into two groups, and providing an additional marker to indicate whether the preparation has undergone activation (►**Table 2**).[19] The 2015 platelet count, leukocyte content including percentage of neutrophils if applicable, RBC content, and activation (PLRA) system devised by Mautner et al is both a means of classification and a proposed mechanism for standardized reporting in methodological descriptions.[17]

Such diversity of preparation, description, and reporting creates challenges for the interpretation of PRP studies and

Table 2 PAW classification system by DeLong et al[19]

Platelets	Concentration, platelets/μL	Label
	Baseline or lower	P1
	Above baseline to 750,000	P2
	> 750,000–1,250,000	P3
	> 1,250,000	P4
Activation	Exogenous activation applied	X
White blood cells	WBCs above baseline	A
	WBCs below or equal to baseline	B
	Neutrophils above baseline	α
	Neutrophils below baseline	β

Abbreviations: PAW, platelet-activation white blood cell; WBCs, white blood cells.

therefore the standardization of PRP therapy. In this review, evidence related to the use of variable preparations is discussed further within each anatomically focused subsection.

Platelet-rich Plasma and Radiology

Imaging is an essential component in the administration of PRP therapy and in the assessment of its efficacy. Because US guidance is often used in the acquisition of PRP, and nearly always used in its application, radiologists are at the forefront of PRP-based therapies.[8,20] US also makes PRP therapies portable: because basic preparation of PRP only requires a small tabletop centrifuge and the patient's own blood, injections can occur in operating rooms, radiology suites, sports medicine clinics, or even at sporting events.[8] ►**Table 1** Le et al summarize specifications related to commercially available PRP centrifuge systems.[21] For most systems, ~ 50 mL of venous blood is required (up to a maximum of 54 mL), which can yield an increase in platelets up to 10 times above baseline for LR preparations and up to 7 times above baseline for LP preparations.[22]

For the radiologist performing a PRP injection, the preprocedure protocol is similar to the protocol for other US-guided procedures. Before the procedure, the radiologist or practitioner should obtain informed consent from the patient, which involves a discussion of the benefits and the risks that include hemorrhage, tissue injury, and infection (minimized using a sterile technique). Because PRP is considered experimental and therefore often not reimbursed by insurance, a detailed discussion on alternative reimbursable treatments (such as dry needling) should also be considered. Indications for PRP include pain at least 4 of 10 on the visual analog scale (VAS), for at least 3 months, that has not responded to conservative measures such as nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy (PT); clinical and imaging findings consistent with tendinopathy, OA, or MSK injuries for which PRP is recommended; ability to follow through with postprocedural restrictions and rehabilitation protocols; and a desire to defer or avoid more invasive therapies.[23] Contraindications to PRP therapy include the presence of a joint prosthesis, active infection, immunocompromised individual, coagulopathy (including medical anticoagulation), an international normalized ratio >2.5, tendon tear, and severely advanced OA.[6] If the patient is an athlete, she or he must be able to refrain from play for at least 4 to 8 weeks following treatment.

After the blood is obtained and prepared according to the protocols most relevant to the injection site and related pathology, it is injected, typically under US guidance, via a 10-mL closed-system syringe and a 20G or 22G needle. After the injection, patients can expect inflammation that may be associated with an initial increase in pain or discomfort that typically subsides within 24 to 48 hours. NSAIDs should be avoided 2 weeks before and after the injection because their anti-inflammatory properties may compromise the healing benefits provided by the platelets and their associated growth factors. Steroids, too, should be avoided during this time.[8] Detailed descriptions of, and timelines associated with, postprocedural restrictions and rehabilitation protocols were published by Emory University and the University of Wisconsin Health and are summarized in Wu et al.[6,24,25]

Magnetic resonance imaging (MRI) is used before the procedure to assess candidates' appropriateness for treatment and afterward to evaluate treatment response. MRI assessment before injection enables detailed anatomical characterization of the affected area and can assist with confirming the clinical diagnosis.[6] Preprocedural imaging also provides a baseline that can be used to evaluate response to therapy. US or computed tomography may also be used in the initial diagnostic work-up, but regardless of the initial modality used, the radiologist will play a central role in preprocedural planning and determination of the suitability of PRP therapy for a given patient. MRI can also be an important component of postprocedural imaging.[26–28] Post-PRP injection MRI at 3 to 6 months may show improvement, with decreased tendon thickening, as well as decreased T2-weighted signal abnormality and surrounding soft tissue edema typically seen with tendinopathy. Normalization of the tendon structure may also be seen on MRI. Postprocedure US at 3 to 6 months may also show decreased tendon thickening, as well as improvement in the tendon fibrillar pattern, including decreased hypoechogenicity and hyperemia. An innovative US-based technology called shear wave elastography shows promise as a quantitative measure using shear wave speed (meters per second) as a biomarker for tendon healing.

Tendinopathies Commonly Treated with PRP

As previously described, PRP and its many formulations have demonstrated variable efficacy in different anatomical areas and in the treatment of different pathologies. This section focuses on four of the most common and extensively researched uses of PRP in the treatment of tendinopathy, listed anatomically from upper to lower extremity.

Rotator Cuff Tendinopathy

Studies of PRP injection for the treatment of rotator cuff tendinopathy have suggested that PRP provides some benefit for up to 1 year (►**Fig. 1**). A 2020 meta-analysis of five randomized controlled trials (RCTs),[29–34] comparing PRP injection with sham injection, no injection, or PT alone, found that patients with PRP experienced a reduction in their pain after 24 weeks, although no significant differences in pain between the PRP and other treatment groups was observed at the short (3 weeks) or medium (12 weeks) postprocedural time points. Maximum follow-up was 1 year for three studies[29,31,33] and 6 months for the other two.[30,32] Standardized mean difference analysis indicated no significant difference between PRP injection groups and other treatment groups with respect to functional improvement at any postprocedural time point. It should be noted that, in four of these studies, more than one PRP injection was given during the study duration.[29,30,32,33] Little is known about the number of PRP injections required for optimal tendon treatment, but typically only one PRP injection is

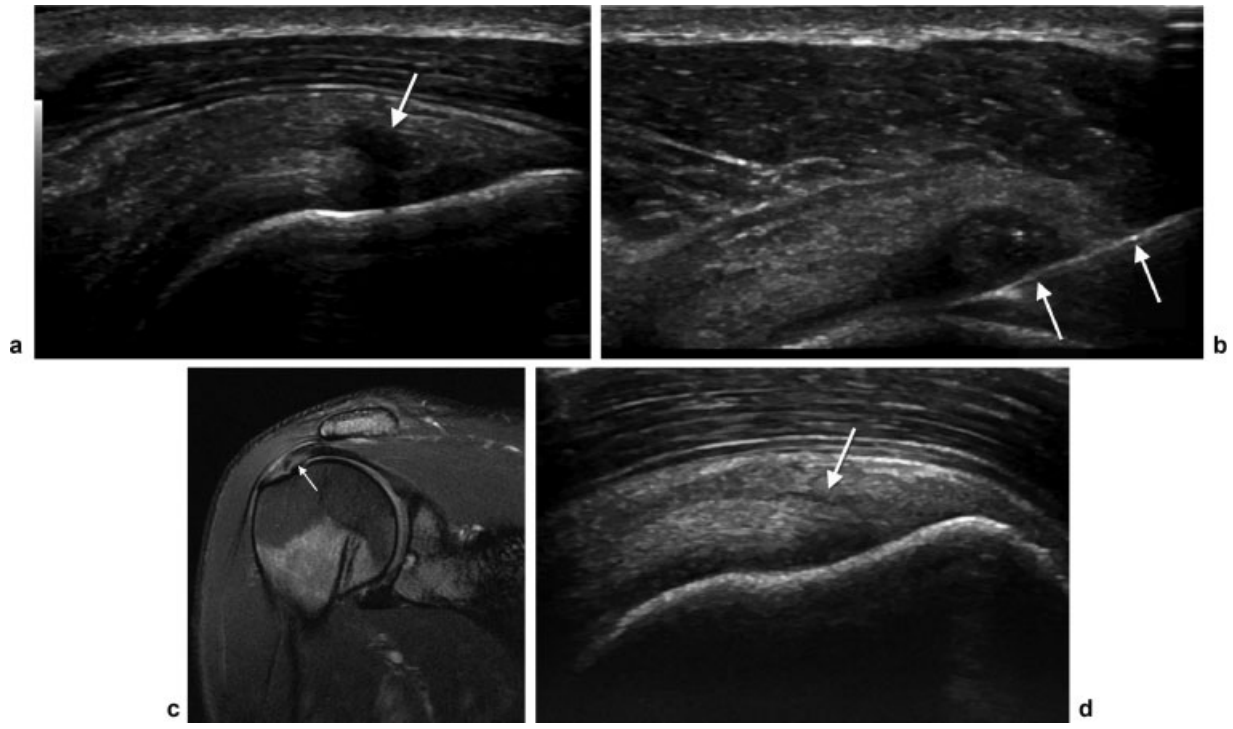

Fig. 1 (**a**) A 37-year-old woman with shoulder pain. Longitudinal sonogram of the supraspinatus shows focal area of intrasubstance hypoechogenicity suggestive of an interstitial tear (arrow). (**b**) A 37-year-old woman with shoulder pain. Longitudinal sonogram of the supraspinatus shows a 22G needle (arrows) placed within the focal area of intrasubstance hypoechogenicity during platelet-rich plasma (PRP) treatment. (**c**) A 37-year-old woman with shoulder pain. Coronal T2-weighted fat-saturated magnetic resonance imaging of the shoulder demonstrates small area of intrasubstance high signal (arrow) corresponding to the ultrasound abnormality seen. (**d**) A 37-year-old woman 4 months after PRP treatment. Longitudinal sonogram of the supraspinatus shows near-complete resolution of the focal area of intrasubstance hypoechogenicity (arrow) suggestive of healing. Patient's pain and function improved.

performed. Of particular relevance for the radiologist is that four studies used US-guided injection[29–32] and that US[30] or MRI was an integral part of the initial diagnostic work-up and/or follow-up assessment.[29,31,32]

Two RCTs published since this 2020 meta-analysis also showed reductions in pain with administration of PRP injection. A double-blind RCT comparing PRP with corticosteroid injection in 99 patients showed statistically significant improvement in VAS pain scores, American Shoulder and Elbow Surgeon Index scores, and Western Ontario Rotator Cuff Index scores for the PRP group at 3 months after the procedure. However, no differences were observed between the PRP and corticosteroid groups at 12 months.[35] US or MRI was used to establish preprocedural diagnoses of tendinopathy, and US guidance was used for the injections. A RCT comparing US-guided PRP and PT in 64 patients with clinically diagnosed adhesive capsulitis showed no difference in VAS pain scores or in passive range of shoulder motion at 1, 3, and 6 weeks posttreatment. The number of patients taking acetaminophen at each time point was lower for the PRP group.[36]

Although all of these studies described the commercial system used to prepare the PRP and the volume of PRP injected, only Nejati et al described the plasma in detail, noting the platelet concentration ($900{,}000 \pm 15{,}000$ platelets/mm^3), its magnitude above baseline blood platelet count, and leukocyte concentration ($5{,}000–10{,}000/mm^3$). Kwong et al described their preparation as leukocyte poor, with "80% platelets at 1.6× concentration," and noted the manufacturer's reported filtration rates for RBCs, WBCs, mononuclear cells, and granulocytes. Inconsistences in the preparation, administration, and published description of PRP were also noted in a 2018 meta-analysis of six studies assessing PRP for rotator cuff pathologies. This additional meta-analysis showed decreased pain scores for PRP-treated patients at 6.5 months and beyond.[37] In sum, it is difficult to reproduce these studies and to interpret their results, given the lack of detailed information about the preparation of the PRP that was ultimately administered.

PRP has also been studied as an adjunct to surgical rotator cuff repair. A 2020 meta-analysis of 13 RCTs compared the effect of arthroscopic rotator cuff repair with either LR- or LP-PRP on rates of retear, healing, and pain scores.[38] LP-PRP reduced rates of retear and/or incomplete tendon healing after fixation for both small and medium to large tears. In addition, patients with this treatment experienced reduced pain, as measured by multiple pain scales. However, post hoc analyses showed that LR-PRP did not lead to significant improvements over the control group with respect to any outcome metric.[38] Durability of therapeutic benefit is not well characterized, with some studies showing lower rates of re-tears at 1 year.[39–41] Others suggest that improvements in pain and functionality wane after 1 year.[41–44]

Lateral Epicondylosis

Literature assessing the role of PRP in the treatment of lateral epicondylosis showed clear reductions in pain, especially in

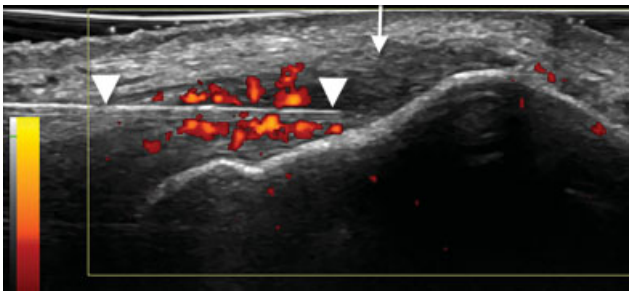

Fig. 2 A 55-year-old man with lateral elbow pain. Longitudinal sonogram of the common extensor tendon (arrow) of the lateral elbow shows thickening and hypoechogenicity. Power Doppler shows hyperemia in red. A 22G needle (arrowheads) is inserted into the tendon during platelet-rich plasma treatment.

comparison with corticosteroids (►**Fig. 2**). A 2018 literature review and meta-analysis including 11 articles examining PRP in the treatment of lateral epicondylosis showed no differences in pain scores between PRP and control groups at 2 to 6.5 months postprocedure, but significant reductions in pain scores for the PRP-treated groups at $\geq$ 6.5 months postprocedure.[37,45–54] A prominent and consistent finding in studies examining PRP in the treatment of lateral epicondylosis has been the relatively extended duration of pain reduction,[55,56] with at least one study demonstrating persistent pain reduction up to 2 years.[53] PRP was also shown to improve function, as evaluated by both subjective (Disabilities of the Arm, Shoulder, and Hand questionnaire) and objective scales (Mayo Clinic performance index for the elbow).[48,49,53,56] Comparison between PRP and whole-blood injections revealed improved scores on the Patient-related Tennis Elbow Evaluation (assessment of both pain and subjective function) at both PRP and whole blood.[52]

Some studies focused on lateral epicondylosis showed that PRP injections are not superior to other treatment strategies. For example, a smaller double-blind RCT comparing PRP and saline found decreased pain scores at 6 months for both groups but no statistically significant differences in pain scores between the PRP and control groups.[46] Another study, which compared PRP, saline, and glucocorticoid injections, found that glucocorticoids reduced color Doppler activity and tendon thickness relative to PRP and saline, and that saline showed better pain reduction at 3 months compared with PRP and glucocorticoids.[51] A RCT comparing PRP and whole blood found improved pain scores for PRP at only 6 weeks.[54] A second RCT also comparing PRP and whole blood showed improvements in pain and functionality scores at 1, 2, 6, and 12 months but no statistically significant difference between the two injection types.[50]

Imaging is an essential component of the preprocedural diagnostic work-up and the assessment of treatment efficacy for lateral epicondylosis. US was frequently used for preprocedural imaging, injection guidance, and follow-up assessments.[49] Although MRI was used less frequently in lateral epicondylosis studies, some investigators still employed it in both preprocedural assessments and follow-up evaluations.[57] In one study, PRP was used as an adjuvant to tenotomy, with improvements in both pain scales and functionality for at least 6 months.[56] A retrospective case review showed that PRP injections reduced the number of patients needing surgery, with an absolute risk reduction of 0.773 and a number needed to treat of 1.3. This study also showed improvement in symptoms with PRP.[57]

Most studies did not characterize the constituents of the PRP injected, aside from mentioning manufacturer details for the separation system. Those that did characterize PRP used preparations without leukocytes and with moderate enrichment of platelets.[48,50,56] At least one study mentioned platelet concentration but did not discuss leukocyte concentration.[51] These gaps in reporting the precise features of the PRP used in the studies, a persistent issue for PRP research, regardless of the anatomical site involved, also make research about the role of PRP in the treatment of lateral epicondylosis difficult to interpret.

Patellar Tendinopathy

Studies regarding the use of PRP in the treatment of patellar tendinopathy have also yielded mixed results. One study showed functional improvements lasting up to 4 years (►**Fig. 3** shows a sonogram of PRP injection into the patellar tendon).[58] A 2015 review and meta-analysis evaluated 11 studies, of which only two were RCTs.[59] Among the eight noncomparative studies, four reported on patients' ability to return to activity: rates for pain-free return to activity ranged from 22%[60] to 81%.[58] Comparative studies investigated PRP versus dry needling and exercise (23 patients total)[61]; PRP plus PT versus shock wave therapy plus PT (46 patients total)[62]; or PRP versus PT alone (15 patients in the PRP group).[58] Compared with dry needling, PRP patients had greater improvements in pain at 12 weeks, but the pain returned at 6 months.[61] In comparison with shock wave therapy, PRP provided greater improvements in pain at 2, 6, and 12 months. PRP versus PT alone showed no significant difference in pain scores. Increased number of injections may contribute to improved outcomes,[63] but the precise number and chronological pacing of the injections is still poorly characterized. Typically, a single injection of PRP is performed.

Simultaneous injection of PRP and high volumes of saline, which may improve symptoms of patellar tendinopathy by disrupting neurovascular structures and lysing adhesions,[64] may have more prolonged benefits than injection of saline

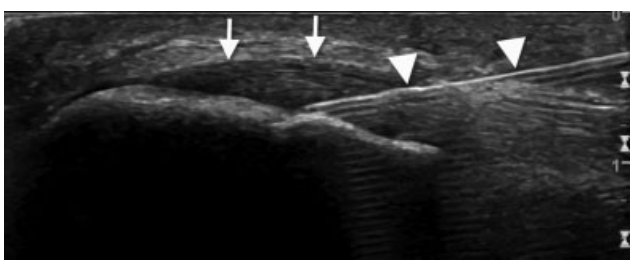

Fig. 3 A 20-year-old man with anterior knee pain below his patella. Longitudinal sonogram of the patellar tendon shows thickening of the proximal patellar tendon (arrows). A 22G needle (arrowheads) is inserted into the tendon from an inferior to superior approach during platelet-rich plasma treatment.

alone.[65] Intraoperative PRP, applied in the setting of bone-patellar tendon-bone autograft anterior cruciate ligament reconstruction, provided no significant difference with respect to reductions in pain or functionality when compared with controls. Both groups showed similarly improved symptoms at the same time points, as well as similar MRI findings.[66] Authors noted that they used LP-PRP with a platelet concentration 2 to 3 times above baseline.

Imaging was discussed less frequently in articles describing PRP therapy for patellar tendinopathy. Diagnosis of patellar tendinopathy was more frequently made clinically, with relatively limited use of diagnostic or postprocedural US. MRI was used to assess postprocedural healing in a few studies,[61] particularly those using intraoperative PRP.[66] US guidance was still often used for injection, although its use was described in research articles less frequently for patellar tendon injections than for those in the upper extremity. For example, at least three studies did not use US guidance in PRP injections but instead performed blindly by palpation.[58,60,67] Consistent with much of the PRP research that has been discussed, most studies only provided details regarding the manufacturer of the PRP preparation system; few, if any, metrics were provided regarding plasma characteristics.

Achilles Tendinopathy

The compartmentalized nature of the Achilles tendon creates additional challenges in the interpretation of the therapeutic efficacy of PRP studies because injection into the mid-substance or insertional region can yield different results for functional benefit and pain management. Moreover, as observed in patellar tendinopathy studies, the use of saline as a negative control may be misguided. Injection of saline itself appears to yield therapeutic benefit by the mechanical disruption of tendon fibers and scar tissue with the needle and volume of injectant. Although smaller studies have pointed toward improved functionality,[68–71] even up to 4 years after the procedure,[58] RCTs and meta-analyses have been less conclusive (►**Fig. 4** shows a sonogram of the Achilles tendon during PRP treatment).

A recent comprehensive systematic review with network meta-analysis of 29 RCTs evaluated multiple therapies for Achilles tendinopathy, including wait-and-see, placebo injections, high-volume injections, whole-blood injections, prolotherapy injections, PRP injections, shock wave therapy, acupuncture, night splinting, mucopolysaccharide supplements, and multiple combinations of these therapies.[72] All of the included studies were at moderate to high risk for bias. Overall, 86% of the trials included patients with mid-substance tendinopathy. One-year follow-up showed that injection therapy, exercise alone, exercise and injections, and exercise and night splinting were all comparable in terms of symptom remediation, as measured by the Victorian Institute of Sport Assessment-Achilles score. The authors ultimately concluded that the studies' elevated risk of bias and the large uncertainties in comparative estimates preclude recommendation of a specific treatment. However, the analysis grouped multiple different therapies (e.g., saline injection, prolotherapy, whole-blood injections, and PRP injections) into one intervention group, simply termed "injection therapy," reducing the ability to detect differences in efficacy among these subgroups. Another meta-analysis of five RCTs in 2019 comparing PRP with placebo injections also found that the quality of evidence supplied by these studies was low to moderate.[73] Statistical analysis of these studies suggested that PRP injection is not superior to saline injections[74–77] or PT.[69]

US guidance was common for injection protocols, as was the use of both US and MRI to assess the postprocedural appearance of the tendon.[68,71,76,78]

Plantar Fasciitis

Limited cohort studies have shown promising results for the use of PRP in the setting of plantar fasciitis, with improvement noted in pain,[79] functionality,[80] and tissue integrity (►**Fig. 5**).[81] Comparisons with corticosteroid injections suggest that PRP is at least as effective as corticosteroids and more effective than saline at pain reduction, 3 months after the injection.[82] More extended comparative studies demonstrated improvements in pain and functionality up to 2 years.[83,84] A recent systematic review and meta-analysis included 10 prospective trials and found that PRP therapy provides greater pain relief, compared with corticosteroids, at 3 and 6 months after the injection.[85] Additional comparisons between PRP and shock wave therapy,[86] and PRP and prolotherapy,[87] showed equivalent efficacy regarding pain reduction and improved patient functionality for patients

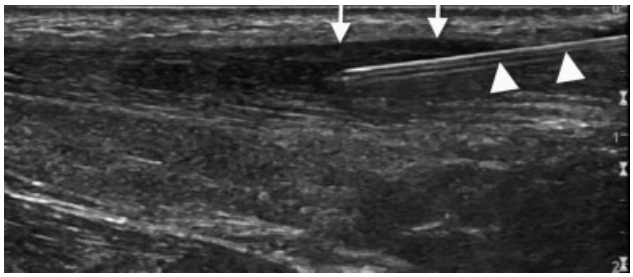

Fig. 4 A 68-year-old woman with posterior ankle pain. Longitudinal sonogram of the Achilles tendon shows thickening (arrows) and hypoechogenicity of the mid-substance Achilles tendon. A 22G needle (arrowheads) is shown from an inferior to superior approach during platelet-rich plasma treatment.

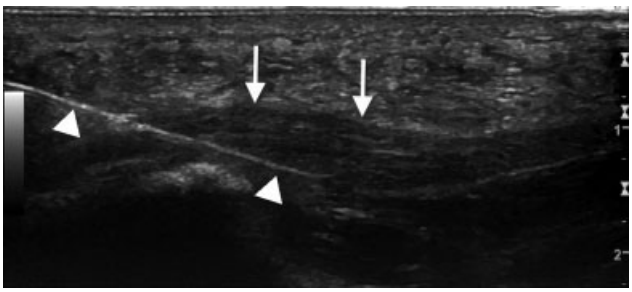

Fig. 5 A 56-year-old man with inferior heel pain. Longitudinal sonogram of the plantar fascia demonstrates thickening (arrows) and hypoechogenicity. A 22G needle (arrowheads) is inserted from a proximal to distal approach inside the plantar fascia during platelet-rich plasma treatment.

who receive PRP over these other treatments. Imaging (both US and MRI) were used in a few studies for preprocedural evaluation and postprocedural assessment. US-guided injection was used in most studies. PRP preparations were again rarely discussed in detail.

Treatment of Arthritis with PRP: A Brief Note

PRP is also used to treat other MSK pathologies, including OA. The most extensive research in this area has involved the knee joint. A 2017 systematic review and meta-analysis of 14 RCTs investigating PRP therapy for knee OA yielded equivocal evidence.[88–101] Four studies were deemed to be of moderate risk for bias and 10 of high risk for bias.[102] Controls were varied and included saline, hyaluronic acid, ozone, and corticosteroids. PRP was shown to reduce Western Ontario and McMaster Universities Arthritis (WOMAC) pain scores relative to hyaluronic acid and ozone at 6 and 12 months,[95] and relative to saline at 3, 6, and 12 months,[98] and to improve WOMAC function scores, at 3, 6, and 12 months, postprocedure. However, in a 1-year RCT comparing PRP with viscosupplementation, PRP was not shown to be superior, with diminishing benefit after 9 months.[103]

Reporting of PRP formulations was also rare in these studies, severely limiting evaluation of treatment efficacy and duration.

Conclusions

In summary, PRP, particularly in its low-leukocyte formulations, has shown promise in the treatment of tendinopathy, especially with respect to lateral epicondylosis. Other studies have shown more limited benefits in rotator cuff, knee, and Achilles tendinopathies. However, recommendations regarding the generation, administration, and assessment of PRP are challenging to make because of substantial heterogeneity in PRP preparations. Future research endeavors should focus on ensuring standardized reporting of PRP components, ideally using one of the classification schemata listed here, to facilitate comparisons across studies.

Conflict of Interest
None declared.

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