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Platelet-Rich Plasma in Management of Tendinopathy

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Abstract

Tendons are vital component of our musculoskeletal system that link between the dynamic and the static part transmitting the forces generated by muscles to bony attachments producing joint motion and stabilize joints. Chronic painful tendon disorders are common in athletic and sedentary individuals. Tendon degeneration may occur when tissue breakdown exceeds the rate of tissue healing due to extrinsic factors such as tendon overload, excessive mechanical stimulation, training errors, fatigue or chemical stresses. Choices of treatment often change in parallel with physiopathological discoveries regarding tendinopathy. Platelets Riched plasma (PRP) is defined as a volume of the plasma fraction of autologous blood having a platelet concentration of 5 times more than base line. Injection of platelet-rich plasma (PRP) is considered a promising new treatment in management of tendinopathy. Platelet-rich plasma (PRP) injections are widely accepted by patients because the injection is produced from the patient's own blood and the risk of adverse effects is minimal. The aim of this Syistimic Review is to highlight on the recent trends in management of tendinopathy, especially platelet rich plasma.

Keywords: Musculotendinous unit, Tendinopathy, Platelet rich plasma.

1. Introduction

Tendon disorders are a class of pathology that includes traumatic injuries as well as chronic diseases, such as tendinopathy. They represent some of the most frequent orthopedic diagnosis, accounting for over 30% of all musculoskeletal consultations [1].

Beyond sport activity, other modifiable and not modifiable risk factors are involved in developing tendinopathy, like age and gender. Adolescents seem to be less affected by tendinopathy compared to adults, since there is evidence that age influences tendinopathy [2].

Although there is no clear trend in the prevalence or incidence between male and female athletes, specific tendinopathies have sex as a risk factor. Even occupational exposure, especially that characterized by highly repetitive movements and poor workplace ergonomics, can predispose one to the risk of tendinopathy. In this case, tendinopathy involves almost exclusively the upper extremity, the most common of which is lateral epicondylitis. Obviously, the type of work influences the prevalence of tendinopathy [3].

Tendon pathologies can represent the first clinical presentation of various metabolic diseases. In chronic gouty arthritis and hypercholesterolemia, monosodium urate crystal and cholesterol deposition in the tendons can determine low-grade inflammation, which is responsible for tendon degeneration. In patients affected by diabetes, glycation products deteriorate the biological and mechanical functions of tendons and ligaments [4].

Platelet-rich plasma is defined as a plasma fraction of autologous blood having platelet concentration above baseline, and prepared from blood drawn from the patient. The application of PRP has been documented in many fields; orthopedics, sports medicine, dentistry, otolaryngology, neurosurgery, ophthalmology, urology, wound healing, cosmetic, cardiothoracic and maxillofacial surgery [5].

Crescibene et al. [6] selected 14 patients affected by Achilles tendinopathy and 7 patients affected by patellar tendinopathy, with a two-year final follow-up. The patients showed a clear pain reduction. From ultrasound scans, reduction in tissue irregularity in 86% of infiltrated tendons was noticed. PRP infiltration is a valid option to patients with chronic tendinopathy who did not benefit from other treatments.

The use of PRP for musculoskeletal injuries has increased significantly during the past few years, given its safety and availability for outpatient preparation and delivery. However, PRP still is a controversial area in orthopedics and Sports medicine. So, the aim of this essay is to highlight on the recent trends in management of tendinopathy, especially platelet rich plasma.

Tendinopathy

The tendons are "mechanical bridges". They are strong fibrous structures of pearly color that connect the muscles to the bones and have the main function of transforming the force generated by muscle contraction into movement. In addition to this, they are able to absorb external forces in order to limit muscle overloads and act as temporary energy storage devices. Thanks to their proprioceptive properties, the tendons are also of primary importance in postural adjustments [7].



Fig (1) Structural changes in chronic human Achilles tendinopathy⁽⁸⁾

Tendon disorders are a class of pathology that includes traumatic injuries as well as chronic diseases, such as tendinopathy. The rotator cuff, the long head of the brachial biceps, the extensors and flexors of the wrist, the thigh adductors, the posterior tibial tendon, the patellar tendon, and the Achilles tendon are the most frequently involved anatomical sites. However, any anatomical district may be interested depending on the type of sport. For instance, dancers show higher prevalence of Achilles tendinopathy, while rotator cuff tendinopathy or epicondylitis are common in rowers [9].

Achilles tendinopathy affects approximately 30% of all runners, with an annual incidence of 7–9%. Patellar tendinopathy is common in volleyball (14%), team handball (13%), basketball (12%), and it is a common condition in football/soccer players (2.5%). Sports such as tennis and baseball show 4 times greater risk of shoulder tendinopathy before the age of 45 years compared with controls [10].

Different pharmacological molecules can play a negative role on tendon tissue biology and represent a risk factor for developing tendinopathy. Among them, corticosteroids, quinolone antibiotics, aromatase inhibitors, and statins as β -Hydroxy β -methylglutaryl-CoA (HMG-CoA) reductase inhibitors are the drugs most frequently associated with alteration of tendon properties [11].

Even adiposity may be a risk factor for tendon disorders because of the increased weight on the loadbearing tendons and systemic dysmetabolic factors [12]. Moreover, Pantazis et al. [13] have shown a relationship between dysthyroidism and tendon disorders such as rotator cuff tears and spontaneous rupture of the long head of the biceps tendon.

Mechanism of injury

The mechanism of injury for a given tendinopathy can vary from region to region, and from patient to patient. Tendons and their insertions are rarely loaded purely in tension; although tensile overload may be the dominant mechanism for many tendinopathies, there is often compression of the tendon as well, either internally (eg, one fascicle or bundle of fibers against another) or against external structures (paratendon, retinacula, bone). The combination of tension and compression results in shearing and friction. For example, the rotator cuff may experience substantial shearing forces when coming in contact with the acromion and subacromial bursa, particularly if the tendon and/or bursa are thickened, or against the glenoid labrum in positions of extreme external rotation. The common extensor tendons of the wrist and fingers at the elbow may be injured not only by repetitive tensile loading, but also by shearing forces against the capitellum with rotation [14].

In the Achilles region, shearing and torsional forces could result from the differential displacement of gastrocnemius and soleus tendon components, the "whipping/wringing" effect of excessive pronation, or friction against the adjacent plantaris tendon [15].

Another aspect of pathomechanics that may be clinically relevant is that of tendon "stress shielding," as

well as de-adaptation ("use it or lose it"). Stress shielding refers to the existence of a zone within a tissue that receives less load compared to surrounding areas due to the microinjury of collagen fibers or to the uneven distribution of forces (eg, it has been proposed that there may be differential force distribution through the patellar tendon) [16].

Reduction of load through tendons (eg, bed rest or relative inactivity) can lead to a large and rapid loss of structural organization and mechanical properties. Thus, a period of relative inactivity followed by a sudden increase in loading may precipitate a tendon injury. Once symptoms and pain develop, ensuing movement dysfunction may contribute to the chronicity of symptoms. Tendon pain causes widespread motor inhibition in the affected region. evidenced by decreased muscular activity as assessed with electromyography. Individuals with tendinopathy also tend to use movement patterns that place excessive or abnormal load on their tendons: the faulty movement may represent either a root cause or a reason for chronicity or slow resolution. For example, the results of several studies focusing on the relationship between jump biomechanics and patellar tendinopathy suggest that individuals with patellar tendinopathy have a less upright position (more hip and knee flexion) at initial contact in landing [17].

In individuals with rotator cuff tendinopathy or tear, scapular dyskinesia is a common finding. More prospective studies are needed, but normalizing movement patterns with the goal of optimizing the loading environment of the tendon seems to be a reasonable approach [18]

Extrinsic and intrinsic factors associated with tendinopathy:

Józsa and Kannus [19] summarized a number of clinical features that place tendons at risk of overuse injury. As each patient may present with a unique cluster of relevant risk factors, the clinician must decide which of these to emphasize in assessment and treatment. Extrinsic factors include excessive volume, magnitude, or speed of loading; training errors such as the use of poor-quality equipment and abrupt or acute changes in amount or type of load (eg, sudden change to a different shoe type); and environmental conditions such as temperature (eg, cold weather, which makes the tendon stiffer and reduces its circulation) and running surface. Intrinsic factors include individual biomechanics (malalignments, muscle weakness or imbalance, decreased flexibility), age, and adiposity. At the highest level of activity, tendinopathy is nearly universally prevalent in some sports (eg, radiologically diagnosed rotator cuff tendinopathy in elite swimmers).

Rehabilitation programs emphasizing individualized biomechanics and overall movement/function underlined, the potential importance of biomechanics in the etiology of tendinopathy. With regard to adiposity as a risk factor for tendinopathy, an association between elevated body mass index and increased risk of tendinopathy appears to hold true both for lower extremity tendons (Achilles, patellar) and upper extremity tendons (rotator cuff, common wrist extensor tendon at the elbow) [20]. Individuals with tendinopathy who have a body mass index or waist girth above healthy reference values could be informed that their diet or their weight may be contributing to their tendon condition, and an appropriate exercise prescription made (and perhaps a lipid profile should be suggested if it has not been done recently). Generalized exercise targeted at weight loss, for example, for the overweight individual with rotator cuff tendinopathy or golfer's elbow, may also address concomitant features of chronic musculoskeletal pain syndromes, such as decreased pain threshold and emotional depression. Smoking is also associated with worse tendon histology than that seen in nonsmokers [21].

Management of tendinopathy

The clinical scenario is quite uniform for all TPs. Patients complain of pain at the site of the tendon affected, which sometimes arises insidiously during a heavy training session or from one specific athletic movement and may ease completely while exercising; with time and continued activity, however, the pain worsens and limits sporting performance. Eventually, pain can develop during light activities and can even be present at rest. A common complaint is a feeling of stiffness in the morning or after rest. Physical examination may reveal local tenderness, swelling and reduced articular range of motion, which are signs of inflammation [22].

It is worth noting that there is no evident relationship between the extent of the anatomical damage, as shown by ultrasound or magnetic resonance imaging, and symptoms: such variations in symptoms and, more specifically, why some patients have pain and others do not is a question that remains to be answered. Tendons are also subjected to sudden ruptures after a single bout of heavy activity; in some cases this happens in individuals with a known clinical picture of chronic TP, but otherwise may be unexpected. This means that TP may develop asymptomatically [23].

Ultrasound imaging can be used to evaluate tissue strain, as well as other mechanical properties. Ultrasoundbased techniques are becoming more popular because of its affordability, safety, and speed. Ultrasound can be used for imaging tissues, and the sound waves can also provide information about the mechanical state of the tissue [24].

A number of medical conditions are associated with tendinopathies and ought to be considered relevant when conducting the history and clinical examination. Some patients present with multiple tendon injuries, with or without a family history. Despite the fact that a number of gene variants associated with increased risk of tendon injury or tendinopathy have been identified, there is no clinically useful genetic test for these; however, a positive family history or tendinopathies at multiple locations could signal elevated risk [25].

Numerous treatment options are proposed in the treatment of patients affected by tendinopathies. Usually, they can be grouped in pharmacological therapies, physical therapies, and therapeutic exercise [26].

Pharmacological therapies:

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Pharmacological treatment of tendinopathies is difficult. Anatomically, these structures suffer from a reduced vascularization and therefore drug availability in the target tissue is low. Moreover, while the effectiveness of drugs on other components of the musculoskeletal system has been proved, such as bisphosphonates in bone, myorelaxants in muscle, and anticonvulsants in peripheral nerve diseases, no specific tendon-target drugs have been developed. For these reasons, painkillers administrated orally and/or parenterally are often used in the treatment of tendinopathies. NSAIDs (non-steroidal anti-inflammatory drugs), SAIDs (steroidal anti-inflammatory drugs), and other alternative injective approaches have been used [26].

Physical therapies

Several physical therapy approaches have been developed during the last years:

- Extra-corporeal shock wave therapy.
- Pulsed electromagnetic fields⁽²⁷⁾.

Therapeutic exercise

A cornerstone in the treatment of tendinopathy is represented by therapeutic exercise. Several protocols of exercise have been proposed and investigated. Although the exact mechanism is not still completely understood, eccentric exercise with lengthening of muscle during contraction has had a major role in the treatment of tendinopathy. Indeed, it seems to be very effective, especially in the management of patients affected by tendinopathies of the Achilles and patellar tendon. These exercises have been shown to promote cross-linking of collagen fibers and facilitate tendon remodeling and cause an upregulation of insulin-like growth factor (IGF) that promotes cellular proliferation and matrix remodeling. Mechanical proprieties of physical exercises are able to affect tendon's fibers reorganization and healing [28].

Some protocols include eccentric exercise alone, such as Alfredson protocol for Achilleous tendinopathy [29]. Other protocols like Stanish et al. [30] permitted concentric contraction and stretching also.

Some other approaches, like heavy slow resistance training required the application of specific instrumentations to enhance the load on tendinous structures. No single protocols have shown a definite superiority versus other protocols and the adoption of several protocols of exercise, including eccentric exercise, seems to guide the rehabilitation process, as load is able to stimulate tissue regeneration and reorganization [31].

Many other types of treatment for tendinopathies have been described but no single therapy has been shown to be more effective than others and often the same technique has shown ambiguous results. The common denominator of the different approaches proposed in the literature is to promote a regenerative response of the tendinous tissue. In fact, due to new initiatives in the pathophysiology of tendon injuries, the use of therapies with antiinflammatory effect should be abandoned in favor of strategies that promote tissue regeneration [32].

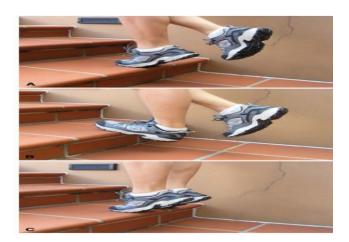


Fig (2) An eccentric training protocol for the treatment of Achilles tendinopathy is demonstrated.

Operative management

Surgery should be reserved to patients in whom conservative management has proved ineffective. Once the diagnosis is made, the patient's general health and comorbidities should be assessed. Although the procedure generally may be performed with the patient under local anesthesia, in some patients general anesthesia may be necessary, and appropriate preparation should be made for those individuals. Valid informed consent should be obtained, and the patient should be aware of the risks of infection, bleeding, wound and scar problems, the operation's failure to relieve symptoms, and that further surgery may be required [33].

percutaneous The ultrasound-guided tenotomy procedure was offered as an alternative to surgical Intervention. Seng et al. [34] published case series study about ultrasonic percutaneous tenotomy for recalcitrant lateral elbow tendinopathy. They documented the 3-year surveillance of the entire initially reported cohort undergoing a novel definitive intervention for chronic refractory lateral tendinopathy. This includes documented continued improvement and maintenance of satisfactory outcomes in pain reduction and improved activity. This procedure offers the advantages of surgery that cuts and removes diseased tissue, under local anesthesia in an office setting, with an efficacy that compares favorably with traditional surgical measures. This is achieved without the morbidity, complications, or cost of traditional definitive intervention. With no further need for adjunct interventions and a high satisfaction rate, this novel treatment modality is a promising option for the treatment of recalcitrant elbow tendinopathy as an alternative to surgical intervention.

Platelet-rich plasma in specific tendinopathies

Platelet-rich plasma, also referred to as plateletenriched plasma, platelet-rich concentrate and autologous platelet gel is defined as a plasma fraction of autologous blood having platelet concentration above baseline, and prepared from blood drawn from the patient. Platelet count in PRP has not been yet optimized, but for therapeutic effectiveness, platelet count of 4-5 times above the baseline should be present in the concentrate This is a therapeutic modality that contains abundant autologous growth factors and proteins, which on activation are involved in different phases of the tissue healing like collagen synthesis, tissue granulation and angiogenesis [35].

Sheth et al. [36] noted that randomized clinical trials of PRP injection studies for Achilles tendinopathy and lateral epicondylitis and nonrandomized clinical trial studies for chronic elbow tendinosis and chronic refractory patellar tendinopathy were of very low quality. Evidence for the use of autologous whole-blood injections in plantar fasciopathy was of very low quality.

Sandrey [37] reported mixed results regarding the effectiveness of PRP treatment. Currently, more evidence is available to support the use of PRP in treating lateral elbow tendinosis than in treating Achilles and patellar tendinopathy and plantar fasciopathy. These findings may require athletic trainers to be cautious about recommending these injections but do not justify dismissal of these injections as an ineffective treatment.

Achilles tendinopathy

Filardo et al. [38] prospectively evaluated 27 patients with chronic mid-portion tendinopathy refractory to previous treatment. Patients were treated with three ultrasound-guided intratendinous injection of PRP. Repeated intra-tendinous injections of autologous PRP produced good results in the treatment of chronic recalcitrant Achilles tendinopathy, with a stable clinical improvement maintained up to a mid-term follow-up.

Guelfi et al. [39] evaluated the long-term clinical outcome in patients affected by mid-portion chronic recalcitrant achilles tendinopathies treated with administration of single platelet-rich plasma (PRP) in a retrospective study. Seventy-three patients of 85 treated were assessed in the study for a total of 83 tendons (10 treated bilaterally). They concluded that one injection of autologous leukocyte-rich PRP safely provides mid–longterm clinical benefits within treatment of chronic recalcitrant achilles tendinopathies. The symptoms showing improvement and functional recovery are experienced over time in mid–long-term follow-up.

Salini et al. [40] retrospectively evaluated the efficacy of PRP therapy in young and elderly subjects suffering for Achilles tendinopathy. They show that PRP treatment provides satisfactory results in young subjects with Achilles recalcitrant non-insertional tendinopathy reducing pain and improving function. These findings are in agreement with previous literature data in patients suffering from Achilles, patellar, and elbow tendinopathies, but PRP is less effective in aged people. This finding can be ascribed to several biochemical and biomechanical differences documented in tendons of young and elderly subjects (reduced number and functionality of tenocytes and tenoblasts), which becomes more evident in the long-term tissue healing.

Matteo et al. [41] conducted a systematic review regarding the application of PRP in the management of patellar and Achilles tendinopathy. Twenty-two studies were included in the present analysis. Nine studies focused specifically on patellar tendinopathy, 9 on Achilles tendinopathy whereas 4 papers reported data on both the aforementioned tendon disorders. they suggest considering PRP as an option for the management of both patellar and Achilles tendinopathies. PRP seems useful for tendinopathies not responsive to other conservative treatments and, therefore, at the moment, it can be considered as a second-line approach for such conditions.

Kearney et al. [42] in their pilot randomised controlled trial comparing platelet-rich plasma injection with an eccentric loading programme, concluded that there is no definitive answer regarding the superiority of PRP injections for patients with mid-substance Achilles tendinopathy.

Patellar tendinopathy:

Charousset et al. [43] evaluated the efficacy of multiple Platelet-Rich Plasma injections for treatment of chronic patellar tendinopathy in athletes in a prospective study. They evaluated a total of 28 athletes (17 professional, 11 semiprofessional) with chronic patellar tendon refractory to non-operative management were prospectively included for US-guided pure PRP injections into the site of the tendinopathy. They concluded that application of three consecutive US-guided PRP injections significantly improved symptoms and function in athletes with chronic PT and allowed fast recovery to their pre-symptom sporting level. The PRP treatment permitted a return to a normal architecture of the tendon as assessed by MRI.

Dragoo et al. [44] had a double-blind, randomized controlled trial evaluating Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy. A total of 23 patients with patellar tendinopathy on examination and MRI who had failed non-operative treatment were enrolled and randomized to receive ultrasound-guided dry needling alone or with injection of leukocyte-rich PRP, along with standardized eccentric exercises. A therapeutic regimen of standardized eccentric exercise and ultrasound-guided leukocyte-rich PRP injection with dry needling accelerates the recovery from patellar tendinopathy relative to exercise and ultrasound-guided dry needling alone, but the apparent benefit of PRP dissipates over time.

Zayni et al. [45] had a randomized prospective study for comparison of a single versus two consecutive injections of Platelet-rich plasma as a treatment for chronic patellar tendinopathy. At a 34 month mean follow-up, patients suffering from chronic patellar tendinopathy who underwent two consecutive ultrasound-guided intratendinous PRP injections showed a better improvement in their outcomes when compared to a single injection. PRP injection improved clinical outcomes in almost 77% of patients and allowed them to return to their pre-symptom activity level in 86% of cases.

Liddle and Merchán [46] had a systematic review to determine the safety and effectiveness of PRP in the treatment of PT and to quantify its effectiveness relative to other therapies for PT. They concluded that Platelet-rich plasma is a safe and promising therapy in the treatment of recalcitrant PT. However, its superiority over other treatments such as physical therapy remains unproven. PRP can be recommended as the gold standard treatment for the large group of patients who suffer significant morbidity and activity restriction as a result of PT.

Lateral elbow tendinopathy:

Schwetlik and Strempel [47] reviewed systemically the effect of platelet rich plasma in lateral epicondylar tendinopathy. There is no gold standard lateral elbow tendinopathy. They concluded that there was insufficient evidence to recommend PRP injection over other recent modalities for lateral elbow tendinopathy. Use of PRP may beneficial for pain and function. However they suggested PRP efficacy over corticosteroids injection but all blood injection have the same effect like PRP.

De Vo et al. [48] systematically presented literature on the efficacy of PRP injections for chronic lateral epicondylar tendinopathy. They concluded that PRP injections are not efficacious in the treatment of chronic lateral epicondylar tendinopathy and there is no significant benefit of PRP at the final follow-up measurement.

Mishra et al. [49] published a double-blind, prospective, multicenter, randomized controlled trial of 230 patients with chronic lateral epicondylar tendinopathy were treated at 12 centers over 5 years to evaluate the efficacy of platelet-rich plasma for chronic tennis elbow. There is more than a decade of experience using PRP to effectively treat chronic tennis elbow with a safe biological protocol at the point of care. Based on these data, it is not possible to recommend treating patients with un-activated, leukocyte-enriched PRP (type 1 PRP) before considering surgical intervention primarily because it provides a similar rate of success with lower cost and less risk [49].

Lebiedziński et al. [50] presented a randomized study of autologous conditioned plasma and steroid injections in the treatment of lateral epicondylitis. They concluded that autologous conditioned plasma therapy of lateral epicondylitis allows better results to be obtained at 12 months. Betamethasone injections give more rapid improvement, but the therapeutic effect is not as permanent as in the autologous conditioned plasma group. Rotator cuff tendinopathy:

Kesikburun et al. [52] published a randomized controlled trial with 1-year follow-up evaluating plateletrich plasma injections in the treatment of chronic rotator cuff tendinopathy. Following-up, a PRP injection was found to be no more effective in improving quality of life, pain, disability, and shoulder range of motion than placebo in patients with chronic RCT who were treated with an exercise program.

Scarpone et al. [53] evaluated the effectiveness of US guided platelet-rich plasma Injection for rotator cuff tendinopathy. A single ultrasound-guided, intralesional injection of PRP resulted in safe, significant, sustained improvement of pain, function, and MRI outcomes in participants with refractory chronic rotator cuff tendinopathy. This suggests that PRP has the potential to heal the muscle-tendon unit of the rotator cuff at the level of degenerative tissue and may be a primary nonsurgical treatment for refractory RCT.

Factor and Dale [54] provided evidence that PRP treatment in vivo may enhance tendon healing by increasing tenocyte number and production of collagen (types 1 and 3), which makes up a major portion of the tendon. However, there is only limited clinical support for PRP when used for RC repair and cartilage healing, although it is safe for clinical use.

Carr et al. [55] compared both the clinical and tissue effects of the application of PRP injection with arthroscopic acromioplasty in patients with chronic rotator cuff tendinopathy. They showed that arthroscopic acromioplasty with and without PRP injection significantly improves clinical outcomes up to 2 years. The study comprised 60 randomized patients diagnosed with rotator cuff tendinopathy (55% women) aged between 35 and 75 years. Patients were randomized to arthroscopic acromioplasty alone or in combination with an injection of autologous PRP into the sub-acromial bursa. Efficacy of treatment was assessed by analysis of patient-reported outcomes up to 2 years after treatment and by analysis of tendon biopsy specimens taken 12 weeks after treatment. However, there was no evidence that the application of PRP has any additional effect on clinical outcomes. Importantly, the tissue effects of PRP included reduced cellularity and vascularity and an increase in a marker of apoptosis. These tissue findings revealed a potentially detrimental effect of PRP to the long-term structural properties of the tendon.

Zumstein et al. [56] investigated the effect of the biologic augmentation with L-PRF on the clinical outcome at a mean follow-up of 14 months postoperatively. The secondary end point was to investigate the radiologic outcome of this treatment. They did not support the use of autologous L-PRF for augmentation of a double-row repair of a rotator cuff. Arthroscopic rotator cuff repair with application of L-PRF yields no beneficial effect in clinical outcome, anatomic healing rate, mean postoperative defect size, and tendon quality at 12months of follow-up. Compared with the significantly shorter and technically less demanding double-row repair without augmentation, they did not find an improved clinical or structural outcome.

2. Conclusion

There are many pathways through which nutrition can positively or negatively affect tendon homeostasis.

Injection of platelet-rich plasma (PRP) is considered a promising new treatment in management of tendinopathy. PRP is created from an autologous whole-blood sample through a platelet separation process, which results in an increased platelet concentration compared with the original whole-blood sample.It is theorized that when PRP is injected into an area of tendinopathy, the platelets release a multitude of growth factors and stimulate a healing response.

Platelet-rich plasma (PRP) injections are widely accepted by patients because the injection is produced from the patient's own blood and the risk of adverse effects is minimal. In addition, in a study on the antibacterial effect of platelet-rich gel in vitro, investigators found that the gel inhibited the growth of Staphylococcus aureus and Escherichia coli. The risk of acquiring a transmitted blood-borne infection or experiencing an anaphylactic reaction is virtually nonexistent. Finally, PRP has a lower cost and shorter recovery time when compared with surgical management. Surgery has been considered the final option for recalcitrant tendinopathies despite highly variable clinical outcomes.

References

- N.Andarawis-Puri, E.L.Flatow, L.J.Soslowsky. Tendon Basic Science: Development, Repair, Regeneration, and Healing. J. Orthop. Res, Vol.33, PP.780,2015.
- [2] I.S.Albers, J.Zwerver, R.L.Diercks. J.H.Dekker. Incidence and prevalence of lower extremity tendinopathy in a Dutch general practice population: A cross sectional study. BMC Musculoskelet Disord., Vol.17, PP.16, 2016.
- [3] S.Morton, S.Williams, X.Valle, D.Diaz-Cueli. Patellar Tendinopathy and Potential Risk Factors. Clin. J. Sport Med., Vol.27, PP.468–474, 2017.
- [4] M.Abate, C.Schiavone, V.Salini. Occurrence of tendon pathologies in metabolic disorders. Rheumatology., Vol.52, PP.599–608, 2017.
- [5] N.N.Knezevic, K.D.Candido, R.Desai. Is Platelet-Rich Plasma a Future Therapy in Pain Management? Medical Clinics of North America., Vol.100(1), PP.199-217, 2016.
- [6] A.Crescibene, M.Napolitano, R.Sbano. Infiltration of Autologous Growth Factors in Chronic

- [7] C.T.Thorpe, H.R.C. Screen. Tendon Structure and Composition. Adv. Exp. Med. Biol., Vol.920, PP.3– 10,2016.
- [8] P.Brukner, K.Khan. Clinical Sports Medicine. 3rd ed. Sydney, Australia: McGraw-Hill, 2006.
- [9] C.Hopkins, S.-C.Fu, E.Chua. Critical Review on the Socio-Economic Impact of Tendinopathy. Asia-Pac. J. Sport. Med. Arthrosc. Rehabil. Technol, , Vol.4, PP.9–20,2016.
- [10] P.W.Ackermann, P.Renström. Tendinopathy in Sport: multidisciplinary approach. Sports Health., Vol.4 (3), PP.193-201, 2012.
- [11] K.Knobloch. Drug-Induced Tendon Disorders. Adv. Exp. Med. Biol, Vol.920, PP.229–238,2016.
- [12] M.Abate, K.Gravare-Silbernagel, C.Siljeholm. Pathogenesis of Tendinopathies: Inflammation or Degeneration? Arthritis Res. Ther, Vol.11, PP.235, 2009.
- [13] K.Pantazis, N.D. Roupas, A.Panagopoulos. Spontaneous Rupture of the Long Head of the Biceps Tendon in a Woman with Hypothyroidism: A Case Report. J. Med. Case Rep., Vol.10, PP.2,2016.
- [14] A.Scott, J.Zwerver, N.Grewal. Lipids, adiposity and tendinopathy: is there a mechanistic link? Critical review. Br J Sports Med, Vol.49, PP.984-988,2015.
- [15] B.Almohimeed, L.Backman, G.Anderson, P.Danielson. Evolving inflammatory cell populations in the overused rabbit Achilles tendon [abstract]. Br J Sports Med, , Vol.48, PP.A60-A61,2014.
- [16] J.Boudreault, F.Desmeules, J.S.Roy. The efficacy of oral non-steroidal anti-inflammatory drugs for rotator cuff tendinopathy: a systematic review and metaanalysis. J Rehabil Med., Vol.46, PP.294-306,2014.
- [17] E.M.Spiesz, C.T.Thorpe, S.Chaudhry. Early inflammatory response of tenocytes to overload. Br J Sports Med, , Vol.48, PP.A63-A64, 2014.
- [18] C.Harris-Adamson, D.You, E.A.Eisen. The impact of posture on wrist tendinosis among blue-collar workers: the San Francisco study. Hum Factors., Vol.56, PP.143-150, 2014.
- [19] L.G.Józsa, P.Kannus. Human Tendons: Anatomy, Physiology, and Pathology. Champaign, IL: Human Kinetics, 1997.
- [20] G.Vallone, T.Vittorio. Complete Achilles tendon rupture after local infiltration of corticosteroids in the treatment of deep retrocalcaneal bursitis. J Ultrasound., Vol.17, PP.165-167, 2014.
- [21] K.Lundgreen, O.B.Lian, A.Scott, P.Nassab. Rotator cuff tear degeneration and cell apoptosis in smokers versus nonsmokers. Arthroscopy., Vol.30, PP.936-941,2014.
- [22] N.Maffulli, P.Sharma, K.L.Luscombe. Achilles tendinopathy: aetiology and management. J R Soc Med, , Vol.97, PP.472-476,2004.
- [23] M.Paavola, P.Kannus, T.A.Jarvinen. Achilles tendinopathy. J Bone Joint Surg Am, Vol.84-A,PP.2062- 2076,2002.

- [24] S.Duenwald-Kuehl, R.Lakes, R.Vanderby. Straininduced damage reduces echo intensity changes in tendon during loading. J Biomech., Vol.45 (9), PP.1607–11, 2012.
- [25] A.V.September, M.Posthumus, M.Collins. Application of genomics in the prevention, treatment and management of Achilles tendinopathy and anterior cruciate ligament ruptures. Recent Pat DNA Gene Seq, , Vol.6, PP.216-223, 2012.
- [26] K.Zhang, S.Zhang, Q.Li, J.Yang. Effects of Celecoxib on Proliferation and Tenocytic Differentiation of Tendon-Derived Stem Cells. Biochem. Biophys. Res. Commun, , Vol.450, PP.762–766,2014.
- [27] L.Leone, S.Raffa, M.Vetrano. Extracorporeal Shock Wave Treatment (ESWT) Enhances the in Vitro-Induced Differentiation of Human Tendon-Derived Stem/Progenitor Cells (HTSPCs). Oncotarget., Vol.7, PP.6410–6423,2016.
- [28] E.I.E.Massoud. Healing of Subcutaneous Tendons: Influence of the Mechanical Environment at the Suture Line on the Healing Process. World J. Orthop., Vol.4, PP.229–240,2013.
- [29] H.Alfredson, T.Pietilä, P.Jonsson. Heavy-Load Eccentric Calf Muscle Training For the Treatment of Chronic Achilles Tendinosis. Am. J. Sports Med, , Vol.26, PP.360–366, 1998.
- [30] W.D.Stanish, S.Curwin, S.Mandel. Tendinitis: Its Etiology and Treatment; Oxford University Press: Oxford, UK, 2000.
- [31] R.Beyer, M.Kongsgaard, B.Hougs Kjær. Heavy Slow Resistance Versus Eccentric Training as Treatment for Achilles Tendinopathy. Am. J. Sports Med, , Vol.43, PP.1704–1711,2015.
- [32] C.Loiacono, S.Palermi, I.Massa B,Belviso. Tendinopathy: Pathophysiology, therapeutic options, and role of nutraceutics: A narrative literature review. Medicina, , Vol.55, PP.447,2019.
- [33] N.Maffulli, N.G.Longo. Conservative management for tendinopathy: is there enough scientific evidence? Rheumatology, Vol.47, PP.390–391,2008.
- [34] C.Seng, P.C.Mohan, S.B.J.Koh. Ultrasonic Percutaneous Tenotomy for Recalcitrant Lateral Elbow Tendinopathy: Sustainability and Sonographic Progression at 3 Years. The American Journal of Sports Medicine., Vol.20, PP.3-6,2015.
- [35] D.M.Dohan, L.Rasmusson, T.Albrektsson. Classification of platelet concentrates: from pure platelet rich plasma (P-PRP) to leucocyte-and plateletrich fibrin(L- PRF). Trends Biotechnol., Vol.27, PP.158-167,2009.
- [36] U.Sheth, N.Simunovic, G.Klein. Efficacy of autologous platelet-rich plasma use for orthopaedic indications: a meta-analysis. J Bone Joint Surg Am, , Vol.94(4), PP.298–307, 2012.
- [37] M.A.Sandrey. Autologous Growth Factor Injections in Chronic Tendinopathy. Journal of Athletic Training, , Vol.49(3), PP.428–430,2014.
- [38] G.Filardo, E.Kon, B.D.Matteo. Platelet-rich plasma injections for the treatment of refractory Achilles

tendinopathy: results at 4 years. Blood Transfus., Vol.12, PP.533-540,2014.

- [39] M.Guelfi, A.Pantalone, D.Vanni. Long-term beneficial effects of platelet-rich plasma for noninsertional Achilles tendinopathy. Foot and Ankle Surgery., Vol.21, PP.178-181, 2015.
- [40] V.Salini, D.Vanni, A.Pantalone. Platelet Rich Plasma Therapy in Non insertional Achilles Tendinopathy: The Efficacy is Reduced in 60-years Old People Compared to Young and Middle-Age Individuals. Frontiers in Aging. Neuroscience, , Vol.7 (228), PP.1-7, 2015.
- [41] B.D.Matteo, G.Filardo, E.Kon. Platelet-rich plasma; evidence for the treatment of patellar and Achilles tendinopathy: A systematic review. Musculoskelet Surg, , Vol.99, PP.1–9, 2015.
- [42] R.S. Kearney, N.Parsons, D.Metcalfe . Injection therapies for Achilles tendinopathy (Review). The Cochrane Collaboration, 2016.
- [43] C.Charousset, A.Zaoui, L.Bellaiche . Are Multiple Platelet-Rich Plasma Injections Useful for Treatment of Chronic Patellar Tendinopathy in Athletes?: A Prospective Study. Am J Sports Med, , Vol.42(4), PP.906-911,2014.
- [44] J.L.Dragoo, A.S.Wasterlain, H.J.Braun . Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy: A Double-Blind, Randomized Controlled Trial. Am J Sports Med., Vol.20, PP.42- 61, 2014.
- [45] R.Zayni, M.Thaunat, J.M.Fayard, J.P.Hager. Plateletrich plasma as a treatment for chronic patellar tendinopathy: comparison of a single versus two consecutive injections. Muscles, Ligaments and Tendons Journal., Vol.5(2), PP.92-98,2015.
- [46] A.D.Liddle , E.C.R.Merchán. Platelet-Rich Plasma in the Treatment of Patellar Tendinopathy: A Systematic Review. Am J Sports Med, , Vol.43, PP.2583-2590,2015.
- [47] S.Schwetlik , L.Strempel. The Effect of Platelet-Rich Plasma on Elbow Tendinopathies. The Internet Journal of Allied Health Sciences and Practice, Vol.11(3), PP.1-110,2013.

- [48] R.J.De Vo, J.Windet, A.Weir. Strong evidence against platelet rich plasma injection for chronic lateral epicondylartendinopathy. Br J Sports Med., Vol.48(12), PP.952-956, 2014.
- [49] A.K.Mishra, N.V.Skrepnik, S.G.Edwards, G.L.Jones. Efficacy of Platelet-Rich Plasma for Chronic Tennis Elbow: A Double-Blind, Prospective, Multicenter, Randomized Controlled Trial of 230 Patients. Am J Sports Med., Vol.42, PP.463-471, 2014.
- [50] R.Lebiedziński, M.Synde, P.Buchcic. A randomized study of autologous conditioned plasma and steroid injections in the treatment of lateral epicondylitis. International Orthopaedics (SICOT), Vol.39, PP.2199– 2203, 2015.
- [51]C.A.Kahlenberg, M.Knesek , M.A.Terry. New Developments in the Use of Biologics and Other Modalities in the Management of Lateral Epicondylitis. BioMed Research International., Vol.Article ID.pp, 439309,2015.
- [52] S.Kesikburun, A.K.Tan, B.Yilmaz. Platelet-Rich Plasma Injections in the Treatment of Chronic Rotator Cuff Tendinopathy: A Randomized Controlled Trial with 1-Year Follow-up. Am J Sports Med, , Vol.41, PP.2609-2616, 2013.
- [53] M.Scarpone, D.Rabago, E.Snell, P.DeMeo. Effectiveness of Platelet-rich Plasma Injection for Rotator Cuff Tendinopathy. Global Adv Health Med., Vol.2(2), PP.26-31, 2013.
- [54] D.Factor, B.Dale. Current Concepts of Rotator CuffTendinopathy. The International Journal of Sports Physical Therapy., Vol.9(2), PP.275-288, 2014.
- [55] A.J.Carr, R.Murphy, S.G.Dakin. Platelet-Rich Plasma Injection With Arthroscopic Acromioplasty for Chronic Rotator Cuff Tendinopathy: A Randomized Controlled Trial. Am J Sports Med, Vol.43, PP.2891-2897,2015.
- [56] M.A.Zumstein, A.Rumian, C.A.Thelu. Use of plateletand leucocyte-rich fibrin (L-PRF) does not affect late rotator cuff tendon healing: a prospective randomized controlled study. J Shoulder Elbow Surg, Vol.25, PP.2-11, 2016.