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Combined extracorporeal shockwave therapy and exercise for the treatment of tendinopathy: A Narrative review

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ABSTRACT

Tendinopathy is a chronic degenerative musculoskeletal disorder that is common in both athletes and the general population. Exercise and extracorporeal shockwave therapy (ESWT) are among the most common treatments used to mediate tendon healing and regeneration. The review presents current understanding of mechanisms of action of ESWT and exercise in isolation and briefly synthesises evidence of their effectiveness for various tendinopathies. The

central purpose of the review is to synthesise research findings investigating the combination of ESWT and exercise for five common tendinopathies (plantar heel pain, rotator cuff, lateral elbow, Achilles, and patellar tendinopathy) and provide recommendations on clinical applicability. Collectively, the available evidence indicates that ESWT combined with exercise in the form of eccentric training, tissue specific stretching or heavy slow resistance training are effective for specific tendinopathies and can therefore be recommended in treatment. Whilst there are at present a limited number of studies investigating combined ESWT and exercise approaches, there is evidence to suggest that the combination improves outcomes in treatment of plantar heel pain, Achilles, lateral elbow, and rotator cuff tendinopathy. However, despite overall positive outcomes in patellar tendinopathy, the combined treatment has not been shown at present to offer additional benefit over eccentric exercise alone.

Keywords: Exercise; Muscle Stretching Exercises; High-Energy Shock Waves; Tendinopathy; Resistance Training; Extracorporeal Shockwave Therapy

1. Introduction

Tendinopathy is a degenerative tendon disorder associated with reduced transmission of force from muscle to bone, chronic pain, swelling and impaired physical function [1,2]. Tendons are susceptible to injury as they undergo high forces during loading activities, receive little vascular blood supply, have low elasticity and decreased metabolism [3,4]. Tendinopathy is thought to be caused by repetitive tendon microtrauma and subsequent failed healing responses, characterised by neovascularization, incidence of calcium deposits or calcification and increased tendon thickness or swelling [5]. Inflammatory cells are commonly present; however, tendon cell degeneration rather than inflammation is considered the pathological hallmark of the disorder, leading to the adoption of the term tendinopathy rather than 'tendinitis' [6]. Recent data from Denmark and the Netherlands on lower limb tendinopathies estimate incidence and prevalence ranging from 7.0-11.8 and 10.5-16.6 per 1000 people, respectively [7,8]. Athletes exposed to high musculoskeletal loads are particularly susceptible to developing tendinopathy, particularly if these loads are experienced frequently, which can

lead to repeated tendon stress and overloading [9]. Prevalence of rotator cuff tendinopathy has been reported to be 30% in volleyball players [10], and 13.1% of climbers were reported to have lateral elbow tendinopathy in one study [11]. Studies on patellar tendinopathy have reported a prevalence of 17% in elite basketball players [12] and 5.6% in adolescent athletes [13]. Achilles tendinopathy prevalence has been reported to be 12.5% in adult athletes [14] and 7.8% in adolescent runners [15].

Tendinopathies are considered to have a multifactorial pathogenesis resulting from a range of extrinsic and individual factors [16]. Pain experienced from tendinopathy is not always associated with tissue damage, suggesting other neurophysiological or psychological mechanisms are involved [17,18]. Central nervous system hypersensitivity and the role of pain central sensitisation has recently emerged as a potential contributing factor [19]. Identified risk factors for tendinopathy include altered biomechanics [20], rheumatological and metabolic disorders such as diabetes [21], excess adiposity [22] and medications such as fluoroquinolones [23]. A range of approaches are used in tendinopathy rehabilitation including anti-inflammatory medications, corticosteroid injections, low-level-laser therapy, ultrasound, platelet-rich-plasma injections, prolotherapy, glycerol trinitrate patches, manual therapy, and exercise [24]. Exercise is the most common and recommended treatment option, with specific exercise targeting the injured tendons the most common exercise approach for tendinopathy [25]. In the last decade, there has been a growing body of research investigating the effectiveness of Extracorporeal shockwave therapy (ESWT) as a tendinopathy treatment [26,27]. Musculoskeletal conditions including those involving tendons, ligaments, muscles, joints, and bones can be treated effectively with ESWT [28]. Due to its non-invasive nature, dearth of side effects and patient acceptability, ESWT offers a therapeutic rehabilitation method, when other conservative treatments are ineffective [29]. Although there have been many reviews presenting the evidence on ESWT and exercise in isolation for tendinopathies, there are currently none which have examined a combined approach. The purpose of this review is to synthesize the current available research on exercise and ESWT for five tendinopathies (plantar heel pain, rotator cuff, lateral elbow, patellar, and Achilles), with a focus on the evidence for combined ESWT and exercise

interventions for these tendinopathies. The review will begin with an overview of mechanisms of action for ESWT and exercise in tendinopathy and include a brief summary of the effectiveness of each in isolation, and finally an overview of studies which have combined ESWT and exercise, concluding with clinical recommendations.

2. Methodology

To conduct this narrative review, a systematic literature search was conducted using Medline/PubMed database to identify studies up to March 2020 using a combination of the following search terms: extracorporeal shockwave therapy, shock wave, shockwave therapy, shockwave, ESWT, tendon, tendinopathy, musculoskeletal, plantar, Achilles, patellar, rotator cuff, elbow, epicondylitis, exercise, strengthening, eccentric, resistance training, physical therapy and physiotherapy. Relevant articles were retrieved and used to identify additional sources by cross-referencing and manually checking reference lists. The findings of relevant research investigating combined ESWT and exercise interventions are presented in Table 1.

3. Exercise mechanisms in tendinopathy

Heavy slow resistance training and eccentric strengthening interventions have been shown to be the most evidence-based exercise approach for tendinopathy, having good outcomes for various tendinopathies such as plantar heel pain [30] rotator cuff [31], lateral elbow [32], Achilles [33]; and patellar tendinopathy [34]. The emerging evidence for exercise has resulted in investigations using eccentric training and heavy slow resistance training to treat tendinopathy through utilising the process of mechano-transduction [35]. The high forces and loads produced during slowly performed concentric and eccentric contractions may stimulate tendon remodelling and compliance by stimulating collagen synthesis and reducing neovascularization [36]. Through the process of mechano-transduction,

exercise can influence cell homeostasis and therefore stimulate tendon regeneration [37]. Mechanical stimulus from exercise can upregulate cellular responses which alter structural adaptations in tendinopathy such as disorganized collagen architecture, and increased water content in the extracellular matrix [38]. Structural changes in tendinopathy can alter the capacity of tendons to store and produce kinetic energy, affecting strength and functional performance [39]. Although loading forces applied to tendons during exercise may help stimulate remodelling of abnormal tendon structure, this may not be associated with increased collagen turnover, leading to uncertainties regarding healing mechanisms [40]. Although tendon structure can be altered in those under age 25 with loading exercise, adult tendons have reduced capacity for collagen turnover, therefore tendon changes do not adequately explain the clinical response to loading [41-43]. Clinical improvement from exercise loading interventions may therefore be due to improved tendon mechanical properties, rather than altered tendon structure [44].

4. ESWT mechanisms in tendinopathy

In recent years, ESWT has been shown to have beneficial effects on musculoskeletal disorders and has emerged as an effective tendinopathy treatment [45]. There is now a growing body of evidence indicating the effectiveness of ESWT for both lower limb [46] and upper limb tendinopathies [47]. After first being introduced in urology to treat kidney stones, ESWT is now therapeutically applied to a broad range of medical and musculoskeletal disorders and is considered a significant innovation in regenerative medicine [48]. Two types of ESWT are used to treat musculoskeletal disorders, with focused-ESWT (F-ESWT) targeting deep smaller tissues, and radial-ESWT (R-ESWT) targeting larger superficial tissues [49]. Both types of ESWT generate high pressures which can induce cavitation in human tissues. The cavitation process involves rapid formation, expansion, and forceful collapse of vapor bubbles in liquids due to rapid pressure changes [50]. Cavitation stimulates a plethora of regenerative biological responses in musculoskeletal tissues which activates proteins involved in chondroprotection [51], neovascularization [52], angiogenesis [53], anti-

inflammation [54], anti-apoptosis [55], immunomodulation [56], neurophysiological and analgesic processes [57]. Healing processes are also activated, which induce proliferation, differentiation, and migration of various cells, including mesenchymal stem cells, stromal cells, endothelial cells, osteoblasts, fibroblasts, tenocytes, and collagen [48]. Several other tendon specific responses which stimulate healing have been observed, including reduction in pathological matrix constituents and inflammatory cytokines, upregulation of tendon cells, lubricin expression, anti-inflammatory cytokines and collagen synthesis [58].

5. Combined treatment

In clinical practice, ESWT is rarely used in isolation and is often combined with specific exercises, aimed at loading damaged tendons to stimulate healing [59]. However, studies have generally not adequately addressed this, often comparing ESWT alone with placebo or usual care [60]. Recently a tendon pathology continuum model has been proposed, with tendinopathy presenting in three distinct stages, which would likely respond differently to ESWT and exercise [61]. There is a need to consider comprehensive interventions depending on the type, stage, and characteristics of the tendinopathy [62]. As monotherapy is rarely implemented clinically, there is a need for a comparison of more realistic treatment interventions [63]. Questions regarding combined ESWT and exercise effectiveness applied realistically as polytherapy in tendinopathy are unanswered [60]. There is increasing high quality evidence for the clinical effectiveness of ESWT in tendinopathy, but systematic reviews still suggest a need for higher quality studies [64]. However, the remaining questions are not if ESWT works in isolation, but rather what treatment combinations are most effective for specific tendinopathies. Research needs to follow clinical practice, where tendinopathy treatment is delivered as combined interventions [26]. A recent qualitative study in tendinopathy highlighted that patients felt ESWT alone was inadequate but acceptable as a non-invasive treatment combined with self-management exercise, which they regarded as more important [65]. Current evidence suggests that combined rather than single interventions should be recommended to achieve

decreased pain, improved function, and patient satisfaction in tendinopathy treatment [66,67]. Although combined treatments are recommended there is a dearth of randomised controlled trials (RCTs) assessing their effectiveness with or compared to other efficacious interventions for tendinopathies [68]. Recently studies have begun investigating combined ESWT with exercise for tendinopathies, with an overview of these studies and outcomes for each tendinopathy provided in the following sections.

5.1 Rotator cuff tendinopathy

Despite the aetiology of rotator cuff tendinopathy not being fully understood, a combination of extrinsic and intrinsic mechanisms is thought to be involved [16]. Shoulder impingement is commonly involved, leading to tendon inflammation and eventual degeneration [69]. Symptoms include pain, weakness, and tenderness in the shoulder, especially when lifting overhead or abducting the arm beyond 90 degrees [70]. Some patients can have long-term shoulder impairment, with 42% reporting symptoms after ten years [71]. Calcific rotator cuff tendinopathy is a common cause of shoulder pain in those aged 30-60, with mechanical overloading a key predisposing factor [72]. Calcium hydroxyapatite deposition characterizes calcification, with the supraspinatus tendon being implicated in 80% of cases [73]. Specific exercise strategies focussing on correcting kinematic deficits or eccentric only strengthening can be effective, however there is a lack of evidence showing superiority of any one type of exercise [74-76]. Eccentric exercise was found equally effective as a conventional exercise programme for the rotator cuff and scapular muscles over 12 weeks in one RCT [77]. However, ESWT has emerged as an alternative efficacious and safe treatment option prior to considering surgery [78]. Several systematic reviews have concluded that ESWT is safe and effective in calcific rotator cuff tendinopathy, with ESWT improving shoulder function, reducing pain, and disintegrating calcific deposits, with efficacy maintained at 6-month follow-up [79-80]. Despite compelling evidence and recommendations for calcific rotator cuff tendinopathy, none of these reviews or others recommend ESWT for non-calcific rotator cuff tendinopathy [64]. Supervised exercise has been found equally effective as ESWT for rotator cuff tendinopathy, therefore combining

ESWT and exercise in a comprehensive rehabilitation program may lead to superior outcomes [81].

Three studies have investigated ESWT combined with exercise for rotator cuff tendinopathy, with encouraging results. Kvalvaag et al [82] compared R-ESWT and supervised exercise for 12-weeks with sham R-ESWT and exercise in a RCT with 142 patients. At 24 and 52 weeks, participants in both groups had improved shoulder pain and function, but there were no differences between the groups. Prespecified subgroup analysis of patients with calcification in rotator cuff showed that the R-ESWT plus exercise group had a greater improvement in pain and function after 24 weeks but no difference was found at 52 weeks. Santamato et al. [83] compared three treatment sessions of F-ESWT with the same protocol plus ten supervised sessions of isokinetic exercise in a RCT with 30 patients. At two months follow-up, participants in the F-ESWT plus exercise group showed significantly less pain and greater improvement in function and muscle endurance than the F-ESWT group. The combined group was considered superior in the short to medium term, compared with F-ESWT alone. Carlisi et al. [84] compared F-ESWT plus a supervised eccentric training of the shoulder abductor muscles with F-ESWT only in 22 patients. At 9-weeks follow-up, there was a significant decrease in pain and an improvement in upper limb function in both groups, but no statistically significant differences between groups. However, as a pilot study with small sample size, limited conclusions can be drawn.

5.2 Lateral elbow tendinopathy

Lateral elbow tendinopathy, commonly known as 'tennis elbow', arises from overuse and repetitive microtrauma of the extensor carpi radialis brevis muscle and tendon [85]. The term 'Lateral epicondylitis' refers to an inflammatory condition, however lateral elbow tendinopathy refers to chronic tendon degeneration [86]. Symptoms include lateral elbow pain which can radiate down the arm and weak grip strength [87]. Recreational sports, increased age, smoking, diabetes, repetitive work tasks using the hands or wrists are risk factors [88].

Annual incidence is 1-3% and symptoms typically last 9-12 months, with most cases responding well to targeted exercise and few requiring surgery [89]. Eccentric exercise has been shown to be effective for improving pain and function and is considered the gold standard conservative treatment [90]. However, exercise applied as monotherapy is considered to have lower effectiveness than when combined with other treatments such as ESWT [91]. Although ESWT has been shown to be an efficacious treatment for lateral elbow tendinopathy, it is not without controversy as some studies have provided conflicting results [92]. Despite methodological heterogeneity in many studies, systematic reviews have concluded there is effectiveness of ESWT for lateral elbow tendinopathy, when studies have well-defined restrictive study parameters [93].

Three studies have investigated ESWT combined with exercise for lateral elbow tendinopathy, with all finding positive results. Celik et al. [94] compared photobiomodulation therapy applied three times a week for four weeks with F-ESWT once a week for four weeks in a RCT with 43 patients. Stretching and eccentric strengthening exercises were also given to both groups as a home program. Improvements for elbow extension and shoulder flexion strength and for painful movement were observed only in the photobiomodulation therapy group, whereas improvement of handgrip strength was present in both groups. Five patients in the ESWT group reported no change, and 18 patients reported improvement compared with pre-treatment status. Both treatments were recommended, despite photobiomodulation therapy having better outcomes. Eraslan et al. [95] conducted a RCT with 45 patients randomised to three groups. Group one received 15 physiotherapy sessions including a home exercise programme of stretching and eccentric strengthening exercises. Group two received physiotherapy plus kinesio taping and group three received physiotherapy plus ESWT applied 3 times for 3 weeks. Pain intensity decreased, whereas maximum grip strength and functionality increased in all groups at the end of the treatment. The kinesio taping group and ESWT group yielded better results in improving function than the physiotherapy only group. A case series including 60 patients found that four sessions of F-ESWT combined with eccentric training four times a week for one month was effective for pain and function improvement at one, six and 12 months after treatment [96].

5.3 Patellar tendinopathy

The aetiology of patellar tendinopathy or 'jumpers' knee' involves extrinsic and intrinsic factors, with the pathogenesis related to repetitive microtrauma to the patella tendon leading to an initial inflammatory response progressing to chronic degeneration [59]. Patellar tendinopathy is common in sports such as soccer, basketball, and volleyball, where prevalence has been found to be as high as 30-45% in elite athletes [97]. Prevalence in the general population is thought to be around 14% [98]. Despite being challenging to treat, heavy slow resistance training and eccentric loading exercise can be effective, particularly eccentric decline squats [99,100]. Wang et al. [101] found that ESWT was more effective than stretching and strengthening exercises for the quadriceps and hamstrings. However, the authors did not give details of the type of exercises, so it is unclear if the recommended eccentric training was performed, which limits conclusions. Although studies have found ESWT to have positive results, there are controversies regarding treatment protocols, with published studies using extremely variable parameters [102]. A systematic review including seven studies on ESWT for patellar tendinopathy, concluded that ESWT is an effective short and long-term treatment [26]. However, another systematic review concluded there was low level evidence that ESWT is superior to standard conservative treatment in long-term outcomes [27]. Despite conflicting findings, all RCTs with robust methodological design have found positive effects of ESWT, recommending its use for patellar tendinopathy [98].

Four studies have investigated combined ESWT and exercise interventions for patellar tendinopathy, with the majority finding positive outcomes but not finding additional benefit of ESWT over eccentric exercise. Van Rijn et al. [103] conducted a secondary analysis of the combined databases of three double-blind RCTs, totalling 138 patients. Participants were divided into five groups based on treatment: ESWT, ESWT plus eccentric training, eccentric training, topical glyceryl trinitrate patch plus eccentric training and placebo treatment. Fifty-two patients (37.7%) improved clinically after three months of treatment, with clinical improvement significantly higher in the eccentric training group and the ESWT

plus eccentric training group compared with the other groups. Eccentric training was considered the most effective treatment. Thijs et al. [104] conducted a RCT with 52 patients, randomised to either F-ESWT or sham F-ESWT applied in three sessions at 1-week intervals and all participants were instructed to perform eccentric decline squat exercises daily for three months. No significant differences were found between the groups at six, 12 and 24 weeks, and no additional effect of ESWT to eccentric exercises was found. However, the results should be interpreted with caution due to small sample size and considerable loss to follow-up, particularly in the ESWT group (n=22).

Van der Worp et al. [105] conducted a RCT with 43 patients comparing three sessions of F-ESWT with three sessions of R-ESWT, with both groups receiving an eccentric training programme based on single-leg decline squats. Both groups improved significantly at 14 weeks follow-up, but there was no statistically significant difference between groups. This was also the case for pain during sports activities and the decline squat. The results suggest that the type of ESWT may not be as important a consideration in patellar tendinopathy treatment as the inclusion of eccentric training. Vetrano et al. [106] conducted a RCT with 46 basketball, volleyball and soccer athletes comparing two platelet-rich plasma injections over two weeks, with three sessions of F-ESWT. Both groups received a standardized stretching and strengthening exercise protocol. However, this protocol was only followed for two weeks, whereas recommended patellar tendinopathy strengthening programs are 12 weeks in duration [100]. Patients in both groups showed statistically significant improvement of symptoms at two, six, and 12-month follow-up, with no significant differences between groups at two-month follow-up. However, the platelet-rich plasma group showed significantly better improvement at six and 12-month follow-up compared to the ESWT group in all outcome measures.

5.4 Achilles tendinopathy

Achilles tendinopathy is caused by overuse and repetitive microtrauma of the Achilles tendon and failed healing, leading to chronic degeneration [107]. The term Achilles 'tendinitis' was previously used to describe an acute local inflammatory response, which is histologically absent in chronic Achilles tendinopathy [108]. Clinical risk factors include impaired biomechanics, overtraining, high body mass index and fluoroquinolone use [109]. Chronic diseases and inflammatory conditions are also implicated, responsible for up to 2-30% of cases [110]. Symptoms include pain after activity or on palpation, swelling and stiffness after rest, which can persist for six months, with up to 15% being symptomatic five years after diagnosis [111]. Specific eccentric exercise protocols and heavy slow resistance training protocols have been shown to be effective and are widely recommended [112]. In unresponsive cases surgery may be required, however ESWT has emerged as a potential alternative treatment [113]. Eccentric exercise is considered the gold standard treatment for Achilles tendinopathy, although there is moderate evidence that ESWT may be more effective for insertional Achilles tendinopathy and equally effective for midportion Achilles tendinopathy [27]. Systematic reviews have found that ESWT is an effective short-term intervention for pain and function in Achilles tendinopathy, with low-quality evidence for long-term effectiveness [26]. Another systematic review concluded there was moderate evidence for F-ESWT in midportion and insertional Achilles tendinopathy [64].

Five studies have investigated combined ESWT and exercise interventions for Achilles tendinopathy, with all reporting superior outcomes for pain and function with the combined approach. A RCT with 68 patients by Rompe et al. [114] compared a 12-week eccentric exercise protocol with the same protocol plus R-ESWT for three sessions. At four months from baseline, both groups had significantly improved pain and function, with 19 of 34 patients in group one (56%) and 28 of 34 patients in group two (82%) reporting being completely recovered or much improved. For all outcome measures, groups differed significantly in favour of the combined approach at the four-month follow-up. However, at one year from baseline, there was no significant difference between groups. A prospective cohort study by Mansur et al. [115] with 19 patients investigated a 12-week eccentric strengthening protocol combined with two

sessions of R-ESWT. Fifteen (79%) patients were fully adherent to the exercise protocol, and 13 (68%) patients considered the treatment protocol successful. At 24 weeks follow-up, patients had significantly less pain and improved function, with the combined treatment being considered effective. Wheeler et al. [116] conducted a prospective cohort of 63 patients receiving either three sessions of ESWT or a single high-volume image guided injection. Both groups received a home exercise program based on eccentric strengthening. Statistically significant improvements in pain and function were found in both groups at three months follow-up, with no statistically significant differences between groups.

A case series by Wheeler et al. [117] included 39 patients receiving R-ESWT once per week for three weeks, alongside a home exercise program including stretching, isometric and eccentric strengthening, core stability and proprioception exercises. Statistically significant improvements were seen in insertional Achilles tendinopathy across a range of outcome measures for pain and function, however, these were less apparent for non-insertional tendinopathy. Pavone et al. [118] conducted a case series with 40 patients who were previously unsuccessfully treated with eccentric exercises for three-months. Patients underwent four sessions of F-ESWT with a two-week interval, together with eccentric exercises. At 12-month follow-up, 26 (65.0%) patients did not complain about pain, 11 (27.5%) patients got back to normal activities despite residual pain, and three (7.5%) patients still complained about pain. There had been no significant improvement in patients after previously completing eccentric exercises alone, with the combined ESWT and eccentric exercise intervention being recommended.

5.5 Plantar heel pain

Plantar heel pain (PHP) is one of the most prevalent musculoskeletal disorders, affecting up to 10% of the population, and causing 15% of all clinical foot symptoms [119]. Degenerative shortening of the plantar fascia collagen matrix due to repetitive microtrauma is considered the pathophysiological origin of the condition, which can lead to heel spur formation [120]. Symptoms of PHP include

morning heel pain and functional limitations such as impaired gait and reduced physical activity [121]. The incidence of PHP in running athletes ranges from 4.5 to 10% and prevalence ranges from 5.2% to 17.5% [122]. Prior to the adoption of the clinical term PHP, the condition was previously referred to as 'plantar fasciitis' suggesting an inflammatory cause, and although inflammatory cells are present, degeneration due to repetitive microtrauma is considered the primary cause of the condition [123]. Moreover, the term 'plantar fasciopathy' is considered a more accurate diagnosis describing the chronic degenerative changes of the fascia, with many experts considering the condition to present like a tendinopathy [120].

For many years plantar fascia specific stretching (PFSS) has been the recommended exercise intervention for PHP due to being found effective in earlier RCTs [124]. However, heavy slow resistance training targeting the plantar fascia has been found more effective compared to PFSS for pain and function [30]. A systematic review concluded there is limited evidence for PFSS in isolation and combining other treatments with PFSS such as ESWT is recommended to increase effectiveness [125]. A methodologically robust meta-analysis by Sun et al. [126] included nine high quality RCTs on ESWT and PHP. The review concluded that ESWT is associated with higher success rates and pain reduction compared to placebo in PHP, recommending it when conservative treatment fails. A recent network meta-analysis compared pain relief performance of eight different PHP therapies, and included 41 studies and 2,880 patients. In terms of one-month, three-month and six-month pain outcomes, only ESWT turned out to be of better efficacy than placebo and ranked first for all seven outcomes and was recommended as the optimal treatment [127].

Ten RCTs, and one case series have investigated the effects of combined ESWT and exercise in PHP. All studies have used PFSS as an exercise intervention, with only the case-series also using strengthening exercise. Rompe et al. [128] found that R-ESWT combined with PFSS was more effective than R-ESWT alone for pain in PHP at two and four months, but there was no difference at 24 months. Cinar et al. [68] compared the effectiveness of ESWT, low-level-laser therapy (LLLT)

and control, with each group receiving home PFSS and insoles. There was a significant improvement in pain at three-months in all groups, both ESWT and LLLT were superior to control, with LLLT being superior to ESWT. Grecco et al. [129] found that R-ESWT combined with PFSS was superior for short term pain and function compared to ultrasound and PFSS, however there was no difference at one-year. A three-arm RCT by Chew et al. [130] found that autologous blood injection with PFSS and ESWT with PFSS were both more effective than PFSS alone for pain and function in PHP at six-months.

A three-arm RCT by Ulusoy et al. [131] compared ESWT, ultrasound and LLLT, all combined with PFSS. All three groups significantly improved PHP pain and function at one-month, with treatment success determined as 70.6% for LLLT, 65% for ESWT and 23.5% for ultrasound. Okur et al. [132] compared R-ESWT and daily PFSS with custom fabricated orthotics and PFSS over four weeks. Both groups achieved significant improvements in PHP pain at 24 weeks, with no significant difference between the groups. Eslamian et al. [133] compared ESWT and PFSS with a single corticosteroid injection and PFSS, finding significant PHP pain and function improvement in both groups, although the ESWT group had better outcomes (67.4% versus 47.7%). Good or excellent results in the opinions of patients were achieved in 55% of ESWT and 30% of corticosteroid injection groups. A three-arm RCT by Akinoglu et al. [134] compared R-ESWT combined with PFSS with ultrasound and PFSS and PFSS alone. At one-month all groups had improved PHP pain and function, with both the R-ESWT and ultrasound groups being superior to PFSS alone, and ankle proprioception sense increased only in the R-ESWT group. Vahdatpour et al. [135] compared ESWT combined with PFSS and topical corticosteroid versus ESWT combined with PFSS and sham corticosteroid. Both groups improved pain and function at one and three months, with the topical corticosteroid group being superior at one month, with no difference between groups at three months. The study identified how topical corticosteroid could enhance the short-term effectiveness of combined ESWT and PFSS.

A four-arm RCT by Takla et al. [136] compared ESWT combined with PFSS and LLLT, with each of ESWT and LLLT combined with PFSS, and sham LLLT with PFSS. All groups except the sham LLLT group showed significant pain and function improvement at three-months, with the combined ESWT, PFSS and LLLT group being most effective. Combined ESWT and PFSS was found to be superior to LLLT and sham LLLT combined with PFSS. The study was the first to show that combining LLLT with ESWT and PFSS can lead to improved outcomes in PHP. A recent case series found that ESWT plus a progressive home exercise program including PFSS and strength exercise, led to significantly improved function and pain but not increased activity levels [137]. Specific details of the strength exercise were omitted and despite being a case series with no comparator and only 35 participants, the study demonstrated the feasibility of combined ESWT and multiple types of exercise. A recent RCT found that combining heavy slow resistance training and PFSS with corticosteroid injection, was significantly more effective than corticosteroid injection or the combined exercise program alone for pain and function in PHP [138]. However, no RCTs have investigated the effects of a combined ESWT and heavy slow resistance training intervention for PHP [139].

6. Conclusion

Tendinopathy has a high prevalence in the general population and in athletes, with both exercise and ESWT in isolation being found to be effective treatments in several studies. A limited number of studies have investigated combined exercise and ESWT for common tendinopathies, with further large high-quality RCTs required. The current limited evidence for combined ESWT and exercise interventions is positive for PHP, Achilles, lateral elbow and rotator cuff tendinopathy, especially when calcification exists. Despite overall positive outcomes in patellar tendinopathy, the combined treatment has not been found to offer additional benefit over eccentric training alone. However, studies not showing additional benefit have had methodological limitations and small sample sizes, limiting conclusions. Current evidence recommends combined rather than single modalities in tendinopathy treatment to achieve superior long-term

outcomes. However, there is a dearth of high-quality RCTs investigating combined interventions for tendinopathies, such as ESWT, exercise and other emerging treatments. There is a clear need for further studies comparing combined treatments, such as comprehensive exercise programs which include different types of exercise as opposed to only one type. Detailed description of exercise protocols, adherence and progression parameters are required in future studies, with a lack of information provided in current studies. The current encouraging evidence suggests that combined specific exercise and ESWT interventions should be recommended for PHP, rotator cuff, lateral elbow, and Achilles tendinopathies. Further well-designed RCTs are required to make definitive recommendations on the optimal treatment protocols for tendinopathies, particularly patellar tendinopathy.

7. Key Recommendations

- Eccentric exercise combined with ESWT is feasible and more effective than either alone for Achilles and lateral elbow tendinopathies and may therefore be recommended as combined treatment.
- Isotonic or eccentric exercise combined with ESWT is more effective than either alone for rotator cuff tendinopathy, particularly when calcification exists, and may therefore be recommended.
- ESWT does not provide any additional effect to eccentric exercise for patellar tendinopathy, therefore either treatment in isolation is recommended, with eccentric exercise the most recommended treatment.
- ESWT combined with PFSS can be recommended for treating PHP as it is more effective than either alone. The effectiveness of the combination can be increased further by combining it with LLLT or topical corticosteroid. The effects of combined ESWT and resistance training have not been investigated.
- Overall, tendon specific exercise should be the recommended treatment for tendinopathy in isolation, with combined exercise and ESWT offered when available. Although ESWT can be effective in isolation, combining it with specific exercise will likely be more effective. ESWT should not be

recommended over tendon-specific exercise unless exercise is not appropriate for individual patients.

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Table 1: Studies investigating combined ESWT and exercise interventions for tendinopathies

Study and design	Sample	Interventions	Outcome Measures	Results
Achilles tendinopathy				
Rompe 2009 RCT	N=68	1: 12-week eccentric exercise protocol. 2: eccentric exercise plus R-ESWT for 3 sessions.	VISA-A, VAS.	Combination more effective for pain and function at 4 months, no difference between groups at 1 year.
Mansur 2017 Prospective cohort	N=19	2 sessions of R-ESWT, and 12-week eccentric strengthening protocol.	VAS, AOFAS, VISA-A	Intervention considered effective for pain and function at 24 weeks.
Pavone 2016 Case series	N=40	4 sessions of F-ESWT combined with eccentric exercises.	VAS, AOFAS	Combined intervention effective at 12 months and recommended as superior to eccentric exercise only.
Wheeler 2019 Case series	N=39	3 sessions of R-ESWT and Home exercise: stretching, isometric and eccentric strengthening, core stability and proprioception exercises.	VISA-A	Significant improvements in insertional tendinopathy pain and function at 6 months but not for non-insertional tendinopathy.
Wheeler 2020 Prospective Cohort	N=63	1: 3 sessions of ESWT. 2: High volume image guided injection. Both groups received home eccentric strengthening.	VAS, VISA-A, MOXFQ.	Significant improvements for pain and function in both groups, no significant differences between groups at 3 months.
Patellar tendinopathy				
Thijs et al. 2017 RCT	N=52	1: 3 sessions of F-ESWT. 2: 3 sessions of sham ESWT. Both groups received eccentric squat exercises for 3 months	VISA-P	Both groups effective at 24 weeks, no additional effect of ESWT to eccentric exercises.

Van der worp 2014 RCT	N=43 (57 tendons)	1. 3 sessions of F-ESWT 2. 3 sessions of R-ESWT Both groups received eccentric training based on decline squats.	VISA-P	Both treatments effective at 14 weeks. No statistically significant differences in effectiveness between F-ESWT and R-ESWT.
Van Rijn 2019 Secondary analysis from 3 RCTs	N=138	1. ESWT 2. ESWT plus eccentric training 3. eccentric training 4. topical glyceryl trinitrate patch plus eccentric training 5. Placebo	VISA-P	Clinical improvements were significantly higher in the eccentric training and ESWT plus eccentric training groups compared to other groups.
Vetrano 2013 RCT	N=46: athletes only.	1. 2 PRP injections. 2. 3 sessions of F-ESWT Both groups received stretching and strength exercise for 2 weeks	VAS, VISA-P, Modified Blazina score.	PRP plus exercise had significantly better improvement at 6 and 12 months.
Rotator cuff tendinopathy				
Santamato 2016 RCT	N=30	1: 3 sessions of F-ESWT. 2: F-ESWT plus 10 supervised sessions of isokinetic exercise.	VAS, CMS	Combined group had greater reduction of pain, and superior functional recovery and muscle endurance at 2 months compared with F-ESWT
Kvalvaag 2018 RCT	N=142	1. 4 sessions of Sham R-ESWT 2. 4 sessions of R-ESWT. Both groups received supervised exercise for 12-weeks.	SPADI	Both groups improved at 24 weeks and 1 year but there were no differences between the groups. Patients with calcification had a greater improvement at 24 weeks but not 1 year with R-ESWT plus exercise.
Carlisi 2018 Pilot RCT	N=22	1. F-ESWT plus supervised eccentric training 2. F-ESWT only	p-NRS, DASH	Both groups improved pain and function at 9 weeks with no difference between groups. F-ESWT no benefit to eccentric exercise.
Lateral elbow tendinopathy				
Celik 2019 RCT	N = 43	1. 12 sessions of PBMT 2. 4 sessions of F-ESWT.	VAS, Strength, GRC	Improvements for VAS, elbow extension and shoulder flexion strength were superior in the PBMT group. Handgrip strength improved in both groups. More patients in PBMT group reported improvement

		Both groups received home stretching and eccentric strengthening exercises.		with GRC. Both treatments effective with PBMT superior to ESWT.
Eraslan 2018 RCT	N=45	1: 15 sessions of physiotherapy with home exercise including stretching and eccentric strengthening 2: physiotherapy plus kinesio taping for 3 weeks. 3. physiotherapy plus 3 sessions of ESWT	VAS, Grip strength, PRTEE	Pain and function improved in all groups. The kinesio taping and ESWT groups improved function better than the physiotherapy group.
Testa 2020 Case series	N=60	4 sessions of F-ESWT combined with eccentric exercises 4 times per week for one month.	VAS, PRTEE-1	Combined treatment effective for pain and function at 1, 6 and 12 months.
Plantar heel pain Akinoglu 2017 RCT	N=54 females only.	1. Home exercise including PFSS for 4 weeks 2. 3 sessions of R-ESWT plus exercise 3. 7 sessions of US plus exercise	FFI, AOFAS.	Improved pain and function in all groups with US more effective than other groups. R-ESWT plus exercise superior to exercise alone.
Chew 2013 RCT	N=53	1. Home gastrocnemius stretching and PFSS 2. ACP injection plus stretching 3. 2 sessions of ESWT plus stretching	VAS, AOFAS, VAS, plantar fascia thickness	ACP and ESWT plus stretching more effective for pain and function than stretching at 6 months. No significant difference between ACP and ESWT.
Cinar 2018 RCT	N=66	1. Insoles for 3 months and stretching. 2. 3 sessions of R-ESWT, insoles and stretching. 3. 10 sessions LLLT, insoles and stretching	FFI-p, NRS-p.	All groups effective, LLLT and ESWT more effective than usual care, LLLT more effective than ESWT in reducing pain at 3 months.
Vahdatpour 2018 RCT	N=80	1. 4 sessions of ESWT plus topical corticosteroid and home stretching 2. 4 sessions of ESWT plus Vaseline and stretching	VAS, RMS.	Both groups effective, combined group more effective than control at 1 month for pain and function, no difference at 3 months.

Takla 2019 RCT	N=120	1. sham-PBMT plus stretching for 3 weeks 2. 9 sessions of PBMT plus stretching 3. 3 sessions of ESWT plus stretching 4. 3 sessions ESWT, 9 sessions of PBMT and stretching.	VAS, FFI-d, PPT.	Both ESWT and PBMT were effective for pain and function at 12 weeks. PBMT with ESWT was superior to ESWT and PBMT alone, and ESWT was superior to PBMT.
Grecco 2013 RCT	N=40	1. 10 sessions of US plus home stretching 2. 3 sessions of R-ESWT plus home stretching.	VAS, PPT	Both treatments effective for pain and function. R-ESWT superior at 3 months, no difference between groups at 12 months.
Eslamian 2016 RCT	N=40	1. 5 sessions of R-ESWT and home stretching 2. Single CSI and stretching	VAS, FFI	Both groups effective for pain and function at 8 weeks, ESWT superior to CSI.
Rompe 2015 RCT	N=152, PHP 12 months	1. 3 sessions of ESWT plus PFSS 2. 3 sessions of ESWT	FFI, Morning pain	Combined group more effective for pain and function at 4 months, no difference between groups at 24 months.
Ulusoy 2017 RCT	N=60, PHP 6 months or longer	1. 15 sessions of LLLT and home stretching 2. 15 sessions of US and home stretching 3. 3 sessions of ESWT and home stretching	VAS, AOFAS.	All groups effective for pain and function. LLLT and ESWT resulted in similar outcomes and were more successful than US.
Okur 2019 RCT	N=83	1. 3 sessions of R-ESWT plus home stretching for 4 weeks. 2. Custom orthotics plus home stretching for 4 weeks	VAS	Both groups effective in reducing pain with neither group superior at 24 nor 48 weeks.
Wheeler 2018 Case series	N=35, PHP duration 24 months	3 sessions of R-ESWT and home exercise: stretching, foot and calf strengthening, balance exercises for 3 weeks.	VAS, FFI, MOXFQ	Intervention effective for pain and function at 3 months, but not in overall markers of health, anxiety/depression scores, or activity levels.

Abbreviations: AOFAS = American Orthopaedic Foot and Ankle Society; CMS = Constant-Murley score; CSI = Corticosteroid injection; DASH = disabilities of the arm, shoulder, and hand; ESWT = extracorporeal shockwave therapy; F-ESWT = focused extracorporeal shockwave therapy; FFI = Foot function index; GRC = Global Rating of Change; LLLT = low level laser therapy; MOXFQ = The Manchester-Oxford Foot Questionnaire; N = number; PBMT = photobiomodulation therapy; PRP = Platelet-rich plasma; PRTEE-1 =

Patient Rated Tennis Elbow Evaluation Test; PHP = Plantar heel pain; p-NRS = pain numeric rating scale; PPT = Pain pressure threshold; RCT = randomised controlled trial; R-ESWT = radial extracorporeal shockwave therapy; RMS = Roles and Maudsley score; SPADI = The Shoulder Pain and Disability Index; US = ultrasound; VAS = Visual Analogue Scale; VISA-A = Victorian Institute of Sport Assessment-Achilles score; VISA-P = Victorian Institute of Sport Assessment-Patella score.

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