

The Long-Term Effects of Eccentric Exercise Vs. Extracorporeal Shockwave Therapy in Athletes Aged 18-50 with Lower Extremity Tendinopathy: A Meta-Analysis and Systematic Review

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Abstract

Background: Establishing the most effective treatments for patellar tendinopathy (PaT) is critical because of its high prevalence in as an orthopedic condition, particularly in jumping athletes. Two increasingly popular and researched therapy interventions are extracorporeal shockwave therapy (ESWT) and eccentric exercise (EE). Yet it has not been established how the two compare to each other.

Objective: The purpose of this study was to compare via meta-analysis the long-term effects of EE on both pain and function to those of ESWT in athletes with PaT and to also compare with a systematic review the same PICO components with the addition of Achilles Tendonopathy (AT).

Data Sources: Search procedures followed PRISA guidelines using the PubMed, CINAHL, and Cochrane Library databases.

Study Selection: Athletes ages 18-50 years, PaT for >3 months, EE, ESWT, Visual Analog Scale (VAS) measuring pain, Victorian Institute of Sport Australia – Patella (VISA-P) measuring function.

Results: A fixed effects model was used to compare the interventions. Eccentric Exercise was found to have very large effect sizes of 2.363 (1.075, 3.651) and 18.790 (8.604, 28.977) for improving pain and function respectively when compared with extracorporeal shockwave therapy.

Conclusion: Eccentric exercise is the treatment of choice for athletes with patellar tendinopathy, while extracorporeal shockwave therapy is a viable secondary option for patients that fail to respond to eccentrics alone.

Keywords: Eccentric Exercise; Extracorporeal Shockwave Therapy; Athlete; Patellar Tendinopathy

Abbreviations: PaT: Patellar Tendinopathy; ESWT: Extracorporeal Shockwave Therapy; EE: Eccentric Exercise; AT: Achilles Tendonopathy; VAS: Visual Analog Scale; VISA-P: Victorian Institute of Sport Australia-Patella; DPaT: Degenerative Patellar Tendinopathy.

Introduction

Tendinopathies are among the most prevalent type of overuse injuries to occur in sports. [1]. Common sites for tendinopathy include the Achilles tendon (AT), extensor tendon of the forearm, rotator cuff tendon, and patellar tendon [2]. Patellar Tendinopathy (PaT) is a prevalent orthopedic condition for recreational and elite athletes [3]. Athlete overall prevalence of PaT is 14.2% [4,5] and is particularly high in jumping sports such as basketball, volleyball, and soccer, which involve excessive running, jumping, and directional changes [5,6]. Prevalence rates for tendinopathies as a whole are as high 45% in some sports [5]. Patellar tendinopathy leads to impairment of functional activities such as stairs, squats, stand to sit, and prolonged sitting⁷ and it can impact an athlete as much as an acute knee injury [5].

Causative factors for the condition are hard playing surfaces, high frequency of training sessions with repetitive eccentric movement, and decreased hamstring and quadriceps flexibility [6-9]. Additional proposed risk factors include: increased weight, increased BMI, increased waist-to-hip ratio, leg-length discrepancy, lower arch height of the foot, and decreased quadriceps strength [10]. Patellar tendinopathy is commonly characterized by chronic load-dependent pain at the inferior pole created by fibril degeneration and mechanical failure [3].

There are 2 types of PaT, reactive (RPaT) and degenerative patellar tendinopathy (DPaT). Neither involve an inflammatory process. However, RPaT, is the patellar tendon's response to a rapid increase in loading or training frequency with swelling and subsequent pain, and it can progress to DPaT [11].

Degenerative patellar tendinopathy occurs over several months and the structure becomes tangled and disorganized, leading to advanced matrix breakdown and increased risk of rupture [11,12]. Mucoïd degeneration is a loss of structural integrity within the tendon in which healthy tissue is replaced by gelatinous mucoïd ground substance [13]. In addition, fibrocartilaginous metaplasia takes place [14-16].

Another feature seen in DPaT is an increased amount of fibroblasts, which leads to increased cellularity [14,15].

The new cells do not lay down as tight parallel collagen bundles, but are separated by the increased amounts of mucoïd ground substance. Collagen appears disorganized and discontinuous, which leads to the tendon becoming less capable of absorbing and transducing forces [12,17]. Theories suggest that mechanical and biochemical factors play a role in the pain that is created. Tendon degeneration involving mechanical collagen breakdown and chemical irritants such as lactate, glutamate, and substance P have all been identified as potential causes of pain [18,19].

Because of multifactorial etiology and lack of quality longitudinal studies on treatment effect, patellar tendinopathy is poorly understood [10] and therefore there is no consensus on the best conservative treatment approach [7,20]. Current conservative interventions include: eccentric exercise (EE), soft tissue mobilization, manual therapy, range of motion, and modalities. A recent clinical review recommended EE, STM, strengthening of the hip musculature, and stretching throughout the course of PaT [21]. The most popular nonoperative treatment for PaT is EE [22].

Eccentric Exercise for Patellar Tendinopathy

The exact effect of EE on tendinopathies is not completely understood, however, evidence support both increased rate of collagen synthesis and improved tendon microcirculation [23-26]. Studies however do not propose an optimal duration and frequency of exercise, or whether drop squats verses slow eccentric movement, use of a decline board, or exercising into pain, should be incorporated [22]. A systematic review reported that 5 of 7 EE studies, reported significant improvement and concluded that EE training appears to be the treatment of choice [24,25]. Some evidence also indicates that the Alfredson model for EE training many be optimal [27-33].

Extracorporeal Shockwave Therapy for Patellar Tendinopathy

Recently, extracorporeal shockwave therapy (ESWT) is a treatment option for lower limb tendinopathies that is growing in popularity and studies show approximately a 90% success rate in the treatment of shoulder, elbow, and heel tendinopathies, with only a 5-7% recurrence rate [34-42]. There is also a trend toward success with PaT where EE has failed [43-54]. Shockwaves are rapid, short and distinct single fluctuations of acoustic energy that propagate quickly through a medium [35,47] and attenuation of the shockwave is highly dependent on the medium type [35].

Several different mechanisms of action on tendinous tissue are described including direct stimulation of healing, neovascularization, direct suppressive effects on nociceptors, and a hyperstimulation effect that blocks the gate-control mechanism [54-60]. ESWT causes fibrinoid necrosis, paratenon fibrosis, inflammatory cell infiltration [48], and impaired tensile strength in tendons [36] and it can elicit release of growth factors and other active substances [38] which increase the number of neovessels at the normal tendon-bone junction [37]. However, similar to EE there is not a consensus on optimal treatment parameters or use of anesthesia [34-49].

Purpose

The purpose of this meta-analysis and systematic review was to determine the long-term effects of EE on pain and function compared to ESWT in athletes aged 18-50 with PaT. The systematic review was extended to the additional lower extremity tendinopathy of AT because of its similar prevalence. It is hypothesized that EE will result in a significant difference, in reducing pain and improving function in athletes with PaT, compared to ESWT. The purpose of the systematic review was to define qualitatively, via PICO parameters, which treatment (ESWT or EE) was more supported for LE tendonopathy.

Methods

Search Strategy

The study design and protocol were in accordance with the Systematic Reviews and Meta-Analysis (PRISMA) guidelines [50]. A systematic review was conducted by one reviewer from September 2016 to October 2016 in PubMed, CINAHL, and Cochrane Library databases and reference lists from resulting articles were reviewed. The following search terms included: eccentric exercise OR eccentrics AND patellar tendinopathy OR jumper's knee; extracorporeal shockwave therapy OR shockwave therapy AND patellar tendinopathy OR jumper's knee; and tendinopathy (which included AT for the systematic review). The systematic review articles include the same PICO requirements (athletic population with tendinopathy (but specifically AT), EE (I), ESWT (C) and VISA-P and VAS, outcomes.

Eligibility Criteria

Inclusion criteria consisted of the following: subjects over 18 years of age, a history of exercise-related patellar tendon pain for at least 3 months, RCTs, published in the

peer-reviewed journals in the year 2003 or later, published in English, use of the Victorian Institute of Sport Australia - Patella (VISA-P) and/or the Visual Analog Scale (VAS) outcome measures, use of the Alfredson protocol, 12-week follow-up data available with both means and standard deviations. Exclusion criteria consist of the following: concurrent corticosteroid or NSAID use during the study period, use of local anesthesia prior to ESWT treatment, pregnancy, subjects with a history of knee surgery, inflammatory or degenerative joint conditions, and symptoms for less than 3 months. For the systematic review search extended to AT

Outcome Measures

The VISA-P scale is a subjective measure used to quantify functional deficits experienced by athletes with PaT [51]. The outcome measure is a self-administered 8-item scale that provides information about pain during functional activities and sports participation [52]. The VISA-P is currently the most widely used outcome measure for athletes with PaT, but the minimum clinically important difference is unknown. The VAS is validated for its accuracy in recording changes in both acute and chronic pain [53-54].

Operational Definitions

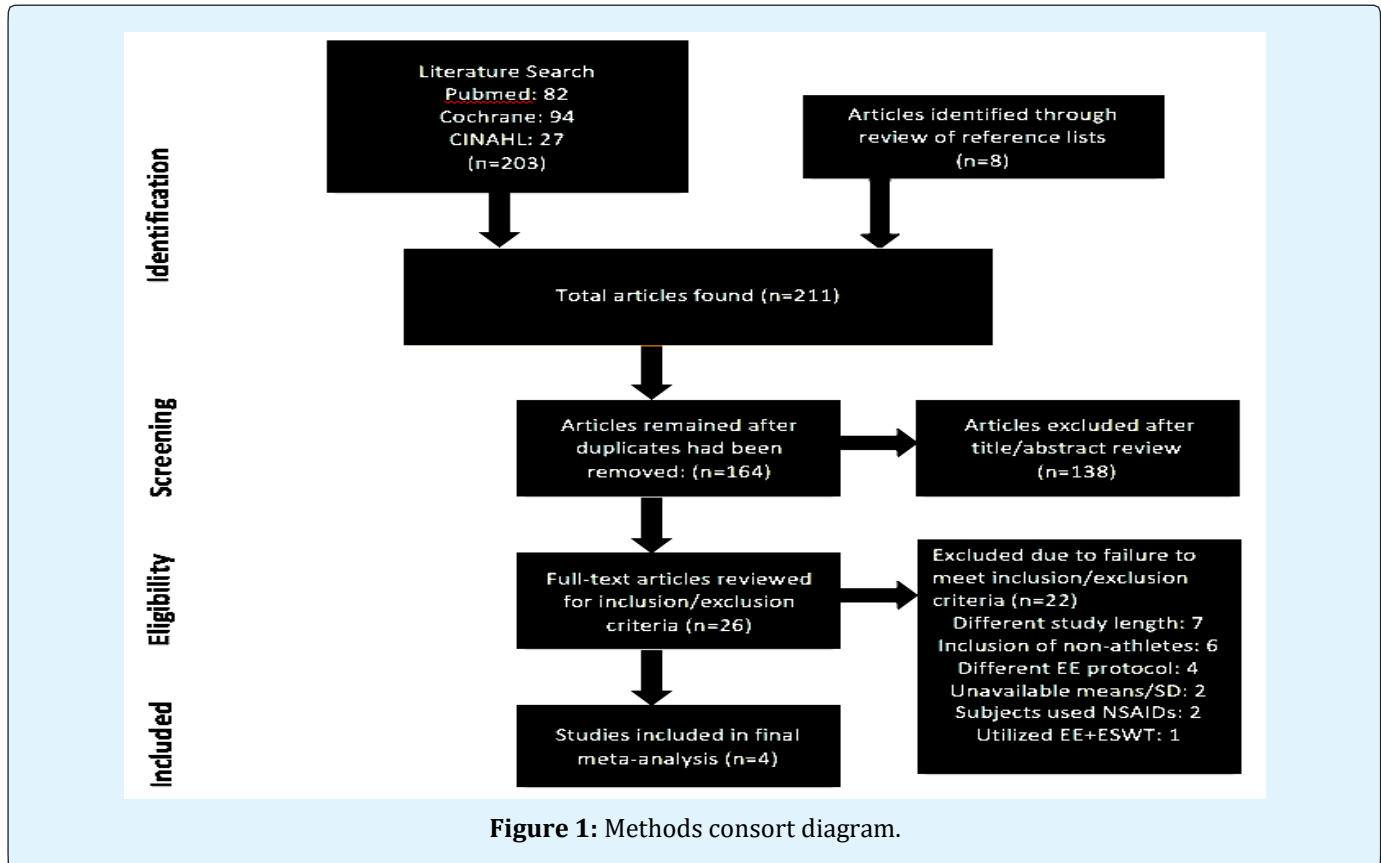
Athletes were defined as those regularly active in a sport or exercise-based activity at either elite or recreational levels. Eccentric exercise was defined by Purdam, et al. [30] adaptation of Alfredson's [55] protocol to the patellar tendon. Knee flexion at the bottom of the squat was required to be at least 70°. Extracorporeal shockwave therapy was defined as 3 sessions provided, without local anesthesia as Roope, et al. [59] showed better effect without local anesthesia and intervals were between 48 hours to 1 week because best parameters for PaT are unknown, ESWT treatment was broadened to any protocol

The 11-point PEDro served as the primary evaluation measure for studies included in both the meta-analysis and systematic review [56]. Because none of the included studies analyzed both EE and ESWT, it was necessary to combine studies to generate comparisons. Studies were matched based on population size, symptom duration, type of athletes included, and mean baseline VISA-P and VAS scores. Means and standard deviations were used to determine effect size, confidence interval, Q statistic, and p-value for analysis. Cohen's categorization of ES was used [57] and forest plots were used for visual representation of ES.

Study Selection

See consort Figure 1. for included studies for the Meta-analysis. For the systematic review the effects of both EE and ESWT were reviewed however, articles also included the lower extremity tendinopathy AT along with PaT, the two most common tendinopathies in athletes

[58,59]. For both reviews the PICO, inclusion and exclusion criteria were observed however for the systematic review an extended age, additional research designs and an expansion of outcome were permitted provided the study also used one of the meta-analysis measurements.



Results

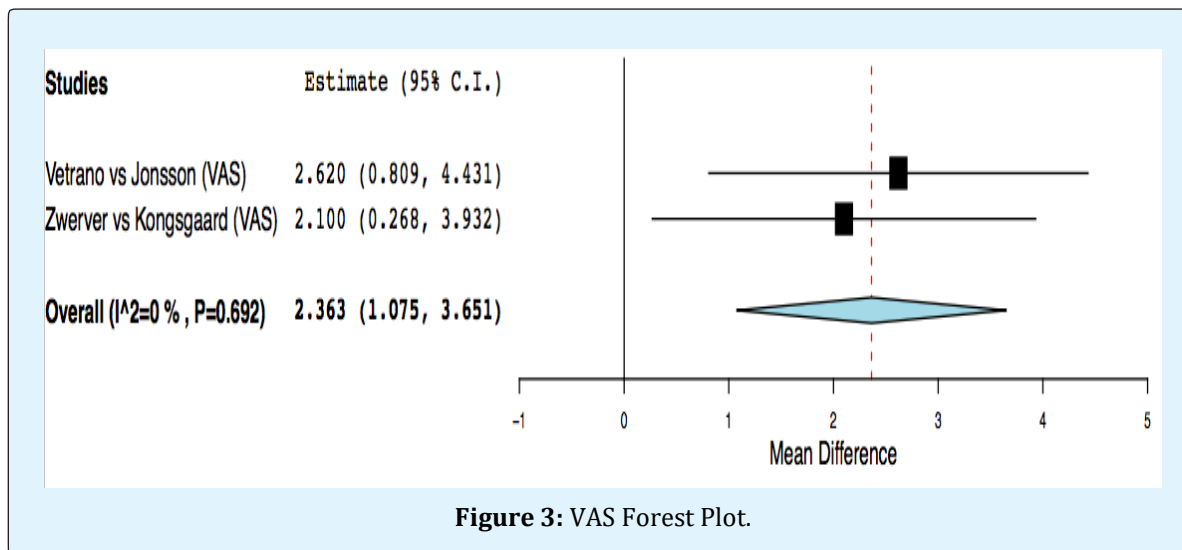
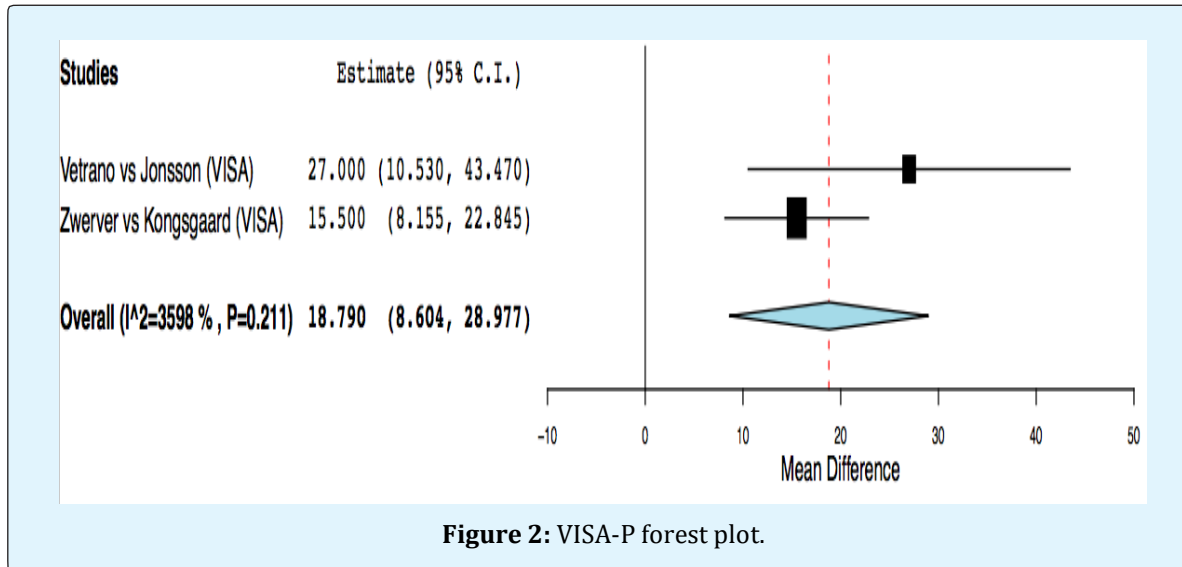
Meta-Analysis Study Characteristics

Among the 4 included studies, PEDro scores ranged from a low of 4 to as high as 9 out of 10. All 4 were level 1 RCTs with the most prominent threat being blinding of therapists. All of the studies lasted 12 weeks, except for Vetrano, et al. which ran for 8 weeks Both Jonsson, et al. and Kongsgaard, et al. [60-63]. used the same EE protocol [30] however, ESWT differed by device and treatment parameters. There were a broad range of symptom durations the meta-analysis studies (range from 3 months to 3 years with mean average of 18.8 ± 13 months) [64]. The majority of studies included were all level 1 RCT's

with the exception of one level four observational study [65].

Meta-analysis-Synthesis of Results

The alternative hypothesis of this meta-analysis that EE would result in a greater treatment effect in reducing pain and improving function than ESWT was accepted for both the VISA-P and VAS measures. The grand effect size for the VISA-P analysis was 18.790 (8.604, 28.977) (Figure 2) and for the VAS the grand effect was 2.363 (1.075, 3.651) (Figure 3). The VISA-P and VAS measures were homogenous at ($Q = 1.56, p = 0.21$) and ($Q = .15$ and $p = 0.692$), respectively.



Systematic Review-Study Characteristics

A total of 11 studies qualified for inclusion; 5 studies looked at athletes with AT, and 6 looked at athletes with PaT. Because of issues such as missing data or lack of follow-up reassessment the PaT studies could not be used in the meta-analysis [31-82]. The study by Purdam, et al. met all meta-analysis inclusion criteria, but was excluded due to a shortage of ESWT studies for comparison.

Achilles Tendinopathy: Eccentric Exercise

A full description of the data for the systematic review studies is included in Tables 2 and 3. The studies were

mostly RCT's. Age ranges varied with patients between the ages of 29-60 years of age and most subjects fell in the 40-50 range. All 4 of the studies looked at recreational athletes with chronic mid-portion AT, which consisted of symptoms 2-7 cm proximal to the Achilles tendon insertion point on the calcaneus and an EE only group using the Alfredson protocol for AT with a 12-week intervention periods [32,67-69]. The Victorian Institute of Sport Australia – Achilles (VISA-A) Scale [32-68], was the most common functional outcome measure. See Table 1 for details by studies compiled.

Study	Study design	Sample size (n) and characteristics	Intervention	Outcome Measures	Treatment Parameters/ Study Length
Jonsson (2005)	RCT	N=10 soccer, running, and floorball athletes Average age=25.7±9.9 years Duration of symptoms=15.4±6.0 months (range:10-24)	EE: Single limb squat on 25° decline board	VISA, VAS	3x15; 2x/day for 12 weeks
Kongsgaard (2009)	RCT	N=12 recreational male athletes Average age= 31.3±8.3 years Duration of symptoms=18.8±13.0 months (range:3-36)	EE: Single limb squat on 25° decline board	VISA, VAS	3x15; 2x/day for 12 weeks
Zwerver (2011)	RCT	N=31 volleyball, basketball, and handball athletes Average age= 24.2±5.2 years Duration of symptoms=7.3±3.6 months (no range provided)	ESWT: using a Piezoelectric device Parameters: 2000 impulses at a frequency of 4Hz; Intensity of 0.58 mJ/mm ²	VISA, VAS	3 sessions at 1 week intervals; outcomes assessed at 12 weeks
Vetrano (2013)	RCT	N=23 elite and non-elite basketball, volleyball, and soccer athletes Average age= 26.8±8.5 years Duration of symptoms=17.6±20.2 months (no range provided)	ESWT: using an electromagnetic device Parameters: 2400 impulses; no frequency listed; Intensity of 0.17-0.25 mJ/mm ²	VISA, VAS	3 sessions at 48-72 hour intervals; outcomes assessed at 8 weeks

Table 1: Summary of Meta-Analysis Study Characteristics.

Study	Study Design	Population size (n) and characteristics	Intervention	Comparison	Outcome measures	Treatment parameters/ Study Length
Beyer [41]	RCT	N=10 Average age=44.6 years Duration of symptoms=19±6.0 months (range:3-120)	EE: Single limb squat on 25° decline board	Alfredson EE protocol to those of the Stanish and Curwin method	VISA-A, VAS	3x15; 2x/day for 12 weeks; outcomes assessed @ 12 & 52 weeks
DeJonge [51]	RCT	N=34 Average age= 48±2 years Duration of symptoms=30.7 months	EE: Single limb squat on 25° decline board	EE in addition to the use of a night splint	VISA-A	3x15; 2x/day for 12 weeks; outcomes assessed @ 12 weeks & 1 year
Petersen [52]	RCT	N=37 Average age= 42.1±11 years Duration of symptoms=7.1±2.6 months	EE: Single limb squat on 25° decline board		AOFAS, SF-36, VAS	3x15; 3x/day for 12 weeks; outcomes assessed @ 6, 12 & 54 weeks
Stasinopoulos[18]	RCT	N=20 Average age=48.2±5.1 years	EE: Single limb squat on 25° decline board		VISA-A	3x15; 2x/day for 12 weeks; outcomes assessed @ 12 weeks & 6 months
Vulpiani [44]	Observational Study	N=127 Average age=47.8±11 years Duration of symptoms=7.1±12.8 months	ESWT: Electromagnetic device; Parameters: 1,500-2,500 impulses; 0.08-0.40 mJ/mm ²		VAS	3-5 sessions at 48 hr intervals; outcomes assessed @ 2, 6-12, & 13-24 months

Table 2: Systematic Review Study Characteristics: Achilles Tendinopathy.

Study	Design	Population size (n) and characteristics	Intervention	Outcome measure	Treatment parameters/Study Length
Purdam [19]	RCT	N=8 Athletes (8 male and 3 female) Average age=28 years	EE: Single limb squat on 25° decline board Control group with standard squats	VAS (EE significant over control (74.2 to 28.5) 6 of 8 returned to sport	3x15; 2x/day for 12 weeks; outcomes assessed @12 weeks & 15 months
Young [20]	RCT	N=17 13 males 4 females; Elite volleyball players Average age=27.3±1.8 years	EE: Single limb squat on 25° decline board vs. EE on a 10-cm step Significant within group difference; no between group difference Both EE decline and step group showed improves up to a year EE: Single limb squat on 25° decline board	VISA-P, VAS	3x15; 2x/day for 12 weeks; outcomes assessed @ 12 weeks & 1 year
Visnes [24]	RCT	N=13 Elite volleyball players; 19 males and 10 females Average age=26.8±4.6 years Duration of symptoms=67±44 months	Control performing sports training as usual	VISA-P No significant between group difference Both significant within group difference	3x15; 2x/day for 12 weeks; outcomes assessed @ 6 weeks & 6 months
Vulpiani [45]	Observational	N=73 54 male and 19 female Duration of symptoms=>3 months	ESWT: Electromagnetic device; Parameters: 1,500-2,500 impulses; 0.08-0.44 mJ/mm ² 2-7 day interval period between treatments depending on pain and presence of calcifications	VAS changes with ADL's Significant change in VAS	3-5 sessions @ 2-7-day intervals; outcomes assessed at 1, 6-12, 13-24, and >24 months Attrition of subjects @later follow-ups
Taunton [46]	RCT	N=20; 10 male; 10 female Duration of symptoms=>3 months	ESWT: Electromagnetic device; Parameters: 2,000 impulses; 0.17 mJ/mm ² ; frequency not known	VISA-P, Vertical jump Control Significant VISA-P within group for ESWT; Significant between group vertical jump over control	3-5 sessions @ 1 week intervals; outcomes assessed at 5 & 12 weeks
Van der Worp [47]	RCT	N=43 with bilateral involvement 57 tendons; 32 male; 11 female Average age=31.1±10.7 years Duration of symptoms=35.2±43.5	3 treatments; ESWT- Electromagnetic device; FSWT Parameters: 2,000 impulses; frequency of 4Hz; Intensity of 0.12 mJ/mm ² RSWT 2.4 intensity (comparable to .12 mJ/mm ² at 8 Hz Radial to focused shockwave)	VISA-P, VAS during ADL's and decline squat Significant changes in VISA-P @ 14 wk for both ESWTs no between group difference	3 sessions @ 1 week intervals; outcomes assessed at 1, 4, 7, & 14 weeks

Table 3: Systematic Review Study Characteristics: Patellar Tendinopathy.

Each of the 4 studies demonstrated a statistically significant within-group improvement on the part of the pure EE group for the VISA-A [32,67-69]. Of the studies that used pain as an outcome measure, both reported statistically significant within-group improvement for the VAS [67-69]. Additionally, Petersen demonstrated improvement on the pain subscale of the SF-36 in the EE. However this study showed no significant difference between subjects treated with EE and those receiving an AirHeel brace [69]. Likewise, Beyer's study failed to show

a significant difference between EE and heavy slow resistance training [67].

Achilles Tendinopathy: Extracorporeal Shockwave Therapy

A single study by Vulpiani et al. [70] utilized ESWT as an intervention for AT and met all other inclusion criteria for the systematic review. This level 4 observational study examined a mixed population of 105 professional and recreational athletes (89 males and 16 females) with both

insertional and midportion AT. Subjects had a mean age of 47.8 ± 12.8 . The majority (60%) of subjects were amateur athletes, 30.5% practiced sports at least once per week, and 10.5% competed at the professional level. Symptoms were required to be present for longer than 6 months to qualify as a subject [70].

All patients received an average of 4 sessions (between 3-5) of ESWT. An average 2-day rest period was used between sessions. Settings are specified in table 2. Evaluation of the outcome measures were reassessed at short-term (defined as 2-months), medium-term, (6-12 months) and long-term (13-24 months) [70].

The mean VAS significantly decreased from 7.49 ± 1.6 to 4.75 ± 2.9 at the 2-month follow-up point. The mean score further decreased to 2.88 ± 3.1 and 2.6 ± 3.3 at medium and long-term follow-ups respectively. The authors concluded that ESWT appears to be a viable treatment option for athletes with AT, leading to long-lasting improvement in pain without collateral damage [70].

Patellar Tendinopathy: Eccentric Exercise

Three studies all used the Alfredson protocol adapted to the Patellar tendon for a 12 week intervention period. Subjects were a mix of males and female, and all were athletes. In the three studies subject ages ranged between 18 to 35 and the VAS and VISA-P were measured [30-33]. Two studies found not significant difference compared to a control group and although Young, M et al. [31] found significant within group differences for the both groups (Traditional Alfredson protocol and EE performed on a 10 cm step), there was not between group differences for a superior approach of EE. Young, et al.'s significance was found at both 12 weeks and 1 year post [30-33].

Patellar Tendinopathy: Extracorporeal Shockwave Therapy

Three studies also examined the effect of ESWT on PaT [65-70]. Subjects ranged from 15 to 69 with an approximate mean age of 31.1 ± 10.7 . Mean symptom duration was 35.2 ± 43.5 with all subjects having symptoms for at least 3 months and subject were male and female. Studies included VAS and VISA-P and change in vertical jump [65,66]. Study protocols ranged from 4Hz to 8Hz, 0.08 to 0.44 mJ/mm², and 1,500 to 2,500 impulses. There was not a difference between focal versus radial shockwave but both showed and significant within group improvement. ESWT should significant improvement in VISA-P and vertical jump over controls and ESWT was effective with eccentric drop squat protocol [70].

Discussion

The purpose of this meta-analysis and systematic review was to evaluate the current literature for both EE and ESWT in the treatment of PaT. Most studies have demonstrated improvement using both interventions, however the results of this meta-analysis show that EE is more effective than ESWT at both reducing pain and improving function in athletes with PaT.

Eccentric Exercise and Pain Reduction

The efficacy of EE in reducing PaT pain is shown in several studies [30-71] possibly due to a stimulatory effect of EE on collagen synthesis with an increase in peritendinous type I collagen, which is primary seen in non-pathological tendons. There is also an inverse correlational between increased type I collagen and decreased pain levels [24]. In AT, EE also causes a temporary decrease in blood flow of peritendinous vessels and it is believed this disruption of flow cause changes in nerve signaling which may influence pain perception [72].

Eccentric exercise may have appeared more effect because more jumping athletes were included in the ESWT studies and PaT is more aggravated by jumping sports^{5,73}, and thus would negatively affected the VAS score. Another threat affecting ESWTs success on pain, such as the case with Zwerver et al. [12] was not placing activity restrictions on subjects during the 12-week treatment period [62]. Other studies such as Jonsson and Kongsgaard placed some activity restrictions on athletes. Continued training could have led to the accumulation of microtrauma over time due to overloading pathological tendons. Continuous microtrauma, in turn, may lead to a failed healing response associated with collagen fibril degeneration, tendon disrepair, and mechanical failure of the tendon [11,13]. It stands to reason that this difference may explains the 2.1-point difference in effect size.

Finally, EE may have been superior for pain reduction because some of the EE groups such as subjects in Zwerver's study, had the lowest mean baseline VAS score, meaning they were less symptomatic than the others [62].

Eccentric Exercise and Improved Function

This study is not the first to demonstrate improved functional performance following EE treatment. Several others studies have also found that EE improved VISA-P scores in both athletic and non-athletic subjects with PaT [31,75-93] and these studies suggests that treatment effect may be due to a mechanical load-induced reversal

of the degenerative process where tensile loading can have an effect on tenocyte production of growth factor release and protein synthesis [24,78,79]. These anabolic components may help repair the extracellular matrix, leading to a normalization of both tendon structure and vascularity [72-80].

The positive effects of EE may be accentuated by placing limitations on sports participation during the treatment period. Several studies that instituted activity restrictions reported favorable results [60-85]. Additionally, Liu et al noted that avoidance of painful sports activity plays a crucial role in the healing process of PaT [76]. Visnes, et al. [33] allowed athletes to resume normal training and competition, and found no functional improvement following a 12-week EE training program. Like those by Zwerver and Vetrano, this study also included elite volleyball athletes. This variable alone could have contributed to the poor outcome, due to the high impact nature of the sport.

Another explanation for the poor results in the study by Visnes, et al. [33] is that they are due to poor compliance rates among the subjects. reported an overall compliance rate of only 58%, compared to the 72% and 89% reported by Young, et al. [31] and Kongsgaard, et al. respectively [77]. The findings of Young et al. [31] directly contradicted those of Visnes et al. [33] Young studied elite volleyball players who were given no activity limitations during a 12-week EE training regimen, and found significant improvement in VISA-P scores, indicating improved functional ability [31].

Systematic Review on Common Lower Extremity Tendinopathies

Four studies examined the effects of EE on subjects with AT [32,67-69]. All 4 reported significant increase in functional ability. Both Beyer, et al. and Petersen et al. [67,69] demonstrated significant improvement in pain. A single study by Vulpiani, et al. 2009 examined the effects of ESWT on AT at 2, 6-12, and 13-24 months. The results demonstrated a significant decrease in VAS score at 2 months with further improvements at the subsequent follow-ups [70].

Three studies, Visnes, et al. [33], Young, et al. [31], and Purdam, et al. [30], studied the effects of EE on athletes with PaT. Each conducted a 12-week EE intervention with differing follow-up periods. Young demonstrated significant improvement in both VISA-P and VAS scores [31], Purdam found a significant decrease in VAS scores [30], and Visnes reported no treatment effect [33]. The

final 3 studies, Taunton, et al. [65], Van der Worp, et al. [82], and Vulpiani, et al. [64] examined the effects of ESWT on athletes with PaT. Both Taunton and Van der Worp demonstrated significant improvement in VISA-P score measured at 12 and 14 weeks respectively. Taunton also showed significant improvement in vertical jump [65]. Van der Worp and Vulpiani demonstrated significant improvement in VAS score as measured at varying follow-up times ranging from 1 month to 2 year [64-66].

For the systematic review, overwhelmingly positive results were found for the use of both EE and ESWT in treatment of athletes with lower extremity tendinopathies. There is strong evidence to support the use of EE for athletes with AT. Additionally, there is moderate evidence to support the efficacy of ESWT in both PaT and AT. Low-quality evidence was found in support of ESWT for AT. From these results, it is not possible to clearly ascertain which intervention is superior, though both EE and ESWT have support for effectiveness at reducing pain and improving function in both LE tendinopathies. Overall, there is a lack of research on athletes with tendinopathies, especially in combination with ESWT.

Clinical Implications of Meta-Analysis Combined with Systematic Review: Achilles Tendinopathy

Given the fact that the systematic review on AT included only 1 ESWT study, no definitive conclusions can be drawn in regards to effectiveness of ESWT for this condition. However, the study by Vulpiani, et al. did produce a statistically significant change in VAS score in favor of the experimental group. These findings suggest that ESWT is effective in reducing pain for athletes with AT. This theory has been validated at both 4 months [44] and 1 year in the general population. However, more RCTs are necessary to confirm this finding in athletic populations.

Each of the 4 studies that examined the effect of EE on AT, compared the intervention to another treatment strategy. None included a pure control group that took part in traditional conservative treatments alone including soft tissue mobilization, manual therapy, range of motion, and modalities. Each of these 4 studies found significant improvement in favor of the EE group. However, in the absence of a pure control group, it is impossible to conclude from this review alone that EE alone is more effective than conservative management for athletes with AT. It is necessary to interpret the results in the context of the broader scope of literature.

Numerous studies that did not meet inclusion criteria for the systematic review have demonstrated the effectiveness of EE among mixed samples of athletic and non-athletic populations with varying types of chronic AT [25,28,86,87]. Further, the results of multiple studies suggest that athletes receive greater benefit from EE than sedentary subjects [44-88].

Clinically, these findings indicate that EE is a highly effective treatment for athletes with AT, and should be a key component of the rehabilitation program. Athletes should be dosed according to the Alfredson protocol for the Achilles tendon. Overall, there is a limited evidence to support the use of ESWT in this population and more research is necessary before this intervention can be recommended as an evidence-based treatment option for athletes with AT.

Patellar Tendinopathy

No studies currently exist that compare EE to ESWT in a population of athletes with PaT. The findings of the present study help to fill this gap in the current literature. This meta-analysis and systematic review found that both EE and ESWT effectively improve pain and functional status relative to baseline in athletes with PaT. In the present study, eccentric exercise was effective compared to a control group in 3 studies [31,60-77]. However, as with AT, there was a lack of quality studies examining ESWT in athletes with PaT. Therefore, the results support that EE is currently the most effective physical therapy treatment option to address an athlete's PaT [30,31,60,61] and it also significantly improves function associated with this condition [31,60,61]. For these reasons, EE should be the first-option treatment for PaT and this is supported by a recent systematic review by Larsson, et al. [81]. It is also superior because it is cost-effective, non-invasive, time-efficient, and appropriate for a home exercise program [61].

Results of this meta-analysis show that EE is more effective than ESWT at reducing pain and improving function in athletic individuals with PaT. The within group sub-analyses for ESWT however, revealed that while it is effective at improving function in this population, it may not be as effective at reducing pain. Clinically, the results indicate that EE should be introduced first, and if ineffective, ESWT can then be tried. This recommendation agrees with the conclusion of Muffulli, et al. [90].

This systematic review was inconclusive regarding ESWT's effect at improving pain and function. Taunton, et

al. [62] and Zwerver, et al. [65] were the only studies that compared an ESWT group to a pure control group, but produced conflicting results [62,65]. Multiple studies on subjects with AT, that directly compared EE and ESWT for change in pain and function, have demonstrated equal or better results in the ESWT group [44-91]. However, these findings have not yet been replicated in populations with PaT.

In a long-term RCT by Wang, et al. subject with PaT were treated with a single-application of ESWT, while the control group received standard conservative treatment. At 2-3 year follow up the ESWT group achieve significantly better functional outcomes which is also supported by Van der Worp, et al.'s study that supports ESWT for improved functional performance.

Clinically, ESWT should be incorporated into a more comprehensive treatment program for tendinopathies [28,92]. There is some evidence to suggest that the concurrent use of ESWT and EE may have a synergistic effect, but research on this topic is scarce. Existing studies have shown promising results [66,83,93,94] and each of these studies found significant improvement in groups treated with both interventions. The efficacy of this combined treatment may be due to the healing effects of EE and ESWT at the cellular level that increases circulation to tendinous tissue which increased rate of collagen synthesis, and release of growth factor can combine to promote increased rates of tendon repair, decreased pain, and improved functional outcomes. Furthermore, the clear majority of studies have shown ESWT to be effective for both PaT and AT [34-96]. These studies however, included subjects from the general population rather than athletes.

Rationale for use of ESWT

Currently, the mechanism of ESWT is not fully understood [95]. It is suggested that ESWT may lead to long-term improvement in tendon function through biochemical signaling where shockwaves activate a biochemical signaling cascade. This results in the release of growth factors TGF- β 1 and IGF-1. These growth factors cause an anabolic effect within the damaged tendon tissue by promoting extracellular matrix biosynthesis by tenocytes [97,98]. There is also the release of TGF- β 1, proliferating cell nuclear antigen, and nitric oxide which lead to tenocyte proliferation and collagen synthesis [99]. This stimulating effect may accelerate healing within injured tendon. Fibroblast cells treated by ESWT may also increase proliferation [100] which may lead to an increase in collagen synthesis, and therefore rebuilding of

damaged tendon. The protein TGF- β 1 may also be an inhibitor of macrophage-induced extracellular matrix degradation as well as play a key role in mRNA expression for both collagen types 1 and 3, which make up tenocytes [100]. Collectively, these findings seem to confirm that the activation of primary connective tissue repair processes occur following the administration of ESWT.

Limitations

There were several limitations in this study, the most prominent being the lack of research on athletes with either PaT or AT. Some studies also had lower PEDro scores and there was a shortage of studies that directly compare EE to ESWT which necessitated the pairing of studies. Both of the EE Studies in the meta-analysis had small sample sizes skewed in favor of EE. Lack of parameter consistency of ESWT is another concern and finally, the treatment windows and follow-up times differed greatly for both interventions.

According to Wang, et al. the most important parameters when using an ESWT application for treatment of musculoskeletal disorders are pressure distribution, energy flux density, and total acoustic energy [95]. Different variations of each of these factors should be further investigated as well as delineating the optimal number of treatments, length of rest period between treatments, and most effective type of application for tendinopathies. Additionally, future studies should differentiate between subjects that are in different stages of PaT.

Conclusion

This meta-analysis demonstrated a greater decrease in pain and improvement in function using EE in athletic populations with PaT. Given the differences in study characteristics and protocols, these results should be interpreted with caution. However, it does seem safe to conclude that both EE and ESWT can safely and effectively be incorporated into a patient's plan of care. The systematic review further revealed that both interventions were effective for PaT and AT. Collectively, this means that EE should be the first choice for treatment of PaT, while ESWT is a viable option for individuals that do not respond to EE alone. In these cases, a combination of EE and ESWT seems promising, but further research is necessary to confirm the efficacy of this approach.

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