Efficacy of eccentric exercise for lower limb tendinopathies in athletes

Article *in* The Journal of sports medicine and physical fitness · November 2015

6 authors, including:


Antonio Frizziero
University-Hospital of Padova
54 PUBLICATIONS **443** CITATIONS


Augusto Fusco
Foundation Santa Lucia
46 PUBLICATIONS **315** CITATIONS

Arrigo Giombini
Università degli Studi di Roma Foro Italico
85 PUBLICATIONS **669** CITATIONS

Stefano Masiero
University of Padova
81 PUBLICATIONS **1,033** CITATIONS

THE JOURNAL OF SPORTS MEDICINE AND PHYSICAL FITNESS
EDIZIONI MINERVA MEDICA

Efficacy of Eccentric Exercise for lower limb tendinopathies in athletes.

Antonio FRIZZIERO, filippo VITTADINI, Augusto FUSCO, Arrigo GIOMBINI, Giuseppe GASPARRE, Stefano MASIERO

J Sports Med Phys Fitness 2015 Nov 26 [Epub ahead of print]

THE JOURNAL OF SPORTS MEDICINE AND PHYSICAL FITNESS
Rivista di Medicina, Traumatologia e Psicologia dello Sport
pISSN 0022-4707 - eISSN 1827-1928
Article type: Review Article

The online version of this article is located at http://www.minervamedica.it

Manuscript without highlighted corrections

TITLE

Efficacy of Eccentric Exercise for lower limb tendinopathies in athletes.

Authors

Frizziero A,[1] Vittadini F,[1] Fusco A,[2,3] Giombini A,[2,4] Gasparre G,[1] Masiero S.[1]

[1] Department of Physical and Rehabilitation Medicine, University of Padua, Padua, Italy

[2] Institute of Sport Medicine and Science, Italian Olympic National Committee, Rome, Italy

[3] Clinical Laboratory of Experimental Neurorehabilitation, IRCCS Fondazione Santa Lucia, Rome, Italy

[4] Department of Health Science and Medicine, University of Molise, Campobasso, Italy

Corresponding Author:

Augusto Fusco, M.D.

Via Aredatina, 306

00179 Rome - Italy

tel. +39 0651501077

fax +39 0651501004

a.fusco@hsantalucia.it

Abstract

Tendinopathies represent one of the most frequent sport injuries and their correct treatment is a crucial issue in sport medicine practice. In most of the cases, these multifactorial conditions are related to overuse and it is characterized by activity-induced pain, local tenderness and swelling. Although tendinopathies are common, their treatment is not easy. Currently, it is generally accepted that the management of tendinopathies should include early functional exercises. Eccentric Exercise (EE) is considered a fundamental therapeutic resource, especially for the treatment of Achilles and patellar tendinopathy. In our review we analyze the use of EE for the treatment and prevention of the lower limb tendinopathies, evaluating the adopted programs and efficacy, the possible mechanisms of the healing process and the action of EE on tendon structure. Treatments with EE are useful to improve symptoms and function in lower limb tendinopathies, but more evidences are necessary to establish the adequate dose-response and to determine long-term effects.

Keyword: Rehabilitation, Achilles tendinopathy, Patellar tendinopathy, conservative treatments, outcomes

Tendinopathies in athletes

Tendinopathies are multifactorial clinical conditions affecting tendons, in most of the cases related to an overuse of tendon structures. It is characterized by activity-induced pain, local tenderness and swelling [1]. The term "tendinopathy'' indicates both the tendinosis and tendonitis [2]. To identify the tendinosis, an histopathological assessment is mandatory, contemplating degenerative modifications with lack of inflammatory features. Changes in tendon tissue are consequent to a failed healing response and consist in ipercellularity, disarrangement of collagen fibers with following increase in type III collagen and proteoglycans, and neoangiogenesis in surrounding tissue (paratenon) and on the tendinopathic areas [3,4,5]. On the contrary, tendonitis are related to an inflammatory process. Inflammation seems to be evident exclusively in the initial phase of the tendinopathies whereas in chronic stage of disease, inflammation is absent or minimal [6].

Tendinopathies typically arise in athletes, due to the mismatch between the tendons' loading capacity and the load on the tendon, commonly for consistent or abrupt load variations [7]. This may happen with a full return to sport activity after a sudden detraining. In this period it has been noted a disorganization in collagen fibers arrangement as demonstrated in patellar tendons of rats [8]. Because the capacity of tendons to react to the load is very slow, a pathological response is triggered when magnitude or temporal distribution of loading exceeds the tendons' threshold of load. At the same time, the underload could be also a predisposing factor for histopathological modification, particularly for the patellar and Achilles tendons in which the store and release of energy is continuously repeated [9]. Finally, a great interest on the role of metabolic and endocrine disorders is emerging, especially in thyroid and oestrogen hormones deficiencies, diabetes and hypercholesterolemia [10-12]. In particular, it was demonstrated that before menopause the risk of developing tendon pathology in women is lower than in men, in contrast with the findings for older women for whom the incidence of tendinopathy and tendon rupture is similar to males [13, 14].

Therapies for tendinopathies are changing with the progression of the research and the growing evidences on this topic. Currently, it is generally indicated as the clinical management should include early functional treatments, rather than rest and immobilization [15]. Several therapeutic options are allowed as conservative treatments: eccentric and concentric exercise, extracorporeal shock wave therapy, therapeutic ultrasound, low level laser therapy, hyperthermia, splintingbracing and orthoses, deep transverse friction and topical glycerine [16,17]. Recently, Platelet-Rich Plasma and hyaluronic acid injections have been also proposed for different tendinopathies, resulting to be effective in preclinical and clinical studies [18-21].

Eccentric Exercise (EE) is considered a fundamental rehabilitative phase of conservative management of the tendinopathies, especially for the Achilles tendinopathy (AT) and for the patellar tendinopathy (PT), representing also a promising and feasible tool for other sites of tendinopathies in athletes.

This review aims to describe the proposed eccentric training programs in the treatment of the tendinopathies, focusing on AT and PT. We investigate the possible mechanisms of efficacy, the healing process and the action of EE on tendon structure.

Eccentric Exercise in tendinopathies

Eccentric muscle contractions applied as a regular training program over months are considered the gold standard for managing AT and PT [22]. Even if little is known about the mechanisms of efficacy, EE has been demonstrated to improve tendon structure and muscle strength also modulating genes' expression for myotendinous junction proteins [23-25]. Although the lack of a general consensus, it has been noted that EE reduces the tendency of tendon to degenerate by increasing collagen content and reducing neovascularization both in animal and human studies [26-28]. In a study on elite male soccer players, Langberg and colleagues have observed as a 12-weeks eccentric training program stimulates the production of collagen type I, with a significant pain reduction during loading [28].

Neovascularisation plays an important role, especially in AT. Capillary blood flow is quantitatively increased at the point of pain in both insertional and mid-portion of the Achilles tendon [27]. Although not fully elucidated yet, the reduction in neovascularization after EE may be related to the direct action on microvascular circulation determined by shear forces between paratenon-fascial-tendon layers [27]. However, the presence of neovascularization in absence of pain is not necessarily pathological, and, in athletes, it can just indicate a physiological response to physical training [29].

Although the ability to adapt to training seems to be gender-specific [30], it is not clear whether the adaptation to eccentric training differs between male and female patients. Hicks and colleagues observed a gender-specific difference in fascicle behavior during eccentric contractions may be partially attributed to the differences in patellar tendon compliance between males and females [31].

Most of the studies on EE have been carried out on the Achilles tendon. Acute and chronic AT represent 50% of all sports-related injuries and the 75% of Achilles tendon ruptures had an history of AT [32,33]. The AT is often observed in long-distance runners with an incidence of 7-9% per year. However, it frequently occurs in middle-aged males during a large amount of sport activities [34]. Some athletes (i.e. jump high or agile athletes) frequently suffer this condition, maybe due to the peculiar athletic gesture. These could be associated to the expression of definite genotypes. Brown and colleagues have showed as better endurance runners are more frequent to be TT genotype of the COL5A1 gene, that is correlated to an higher frequency of tendinopathies [35].

Other frequent district of tendinopathies is patellar tendon. The prevalence of PT is dependent by sport characteristics, competitive level and gender. It is higher in repetitive jumping disciplines. In fact, elite athletes are affected up to 35% for basketball players and up to 45% volleyball players, while it is 8.5% in non-elite athletes population and 14.4% in volleyball amateur players [36,37].

Even if EE has been showed to be effective, programs are not yet well established, neither for dose, velocity and number of contractions or for period of treatment. Kjaer and Heinemeier have also claimed that it is not clear which type (eccentric or concentric) and which modality (slow or fast) of exercise determines the remodeling of tendon structure of exercise [38].

Firstly, it was speculated as tendons could be exposed to higher forces during eccentric than concentric exercise [39]. While other studies have not reported any differences in peak Achilles tendon force during the two types of exercises [40,41], Rees and his collaborators found that fluctuations in tendon forces were more pronounced during EE, probably for the intrinsic difficulty in controlling a dynamic movement during elongation [42]. Frequencies of the force loading were found to be in a 8-12 Hz range. This range could represent in part the stimulus for remodeling stimulation [43]. Chaudhry and colleagues have shown that this frequency is not related to tendons' stiffness even if the magnitude of 10 Hz is inversely correlated to it. Because of tendinopathies lead to a stiffness reduction, it was argued that the magnitude of perturbations is greater in these conditions [44]. It was consequently proposed as a training program with 8-12 Hz magnitude and frequency bandwidth could increase successful repetition sets with less fatigue and beneficial effect in tendon of healthy adults [45,46].

Is eccentric exercise effective for Achilles Tendinopathy?

The efficacy of EE in athletes is difficult to evaluate due to the wide heterogeneity of the involved populations, outcome measures and inadequate sample sizes for most of the studies. Moreover, rehabilitative protocols with EE differ for frequency of administration, number and velocity of repetitions, load parameters, presence of pain, interruption with sport activities.

In a pioneering study, Stanish, Rubinovich and Curwin evaluated 200 patients affected by AT, in absence of a control group [39]. In their study, they proposed a treatment program including specific eccentric and strength exercises for the healing process of tendons affected by tendinopathy. Afterward, Alfredson and colleagues showed a significant superiority of 12-week training program with EE for the return to sport-activity in a controlled study on 15 athletes [47]. The Alfredson's protocol is still used widely. It consists of 3 sets of 15 repetitions performed twice in a day for 12 weeks with progressive loading until to pain threshold.

Rompe and colleagues demonstrated that EE was more effective with respect to wait and see strategy and comparable to low energy shock wave therapy (ESWT) at 4-month follow-up in Achilles midportion tendinopathy [48]. Then, the same authors have also showed that outcomes could be improved with a combined therapy based on eccentric loading and repetitive ESWT in comparison than EE alone [49].

de Jonge and collaborators have observed as EE, with or without a night splint, improved the functional outcome after one-year follow-up in patients with chronic AT, without any difference in terms of splinting use [50]. In a study based on patients' point of view, Mafi, Lorentzon and Alfredson showed as patients resumed the sport activity level before injury with a high level of satisfaction, more than those treated with a training based on concentric exercise [51]. Then, Nørregaard and colleagues have found significant improvements in terms of impairments and pain both in the eccentric training group and in the stretching group after 3 weeks and 1 year follow-up in a mixed population [52].

In terms of long-term outcomes, contrasting results were showed. Van der plas and collaborators evaluated a 3-months period Alfredson's EE protocol at 5-year follow-up, concluding that use of EE is effective in increasing function and controlling pain symptoms [53]. In another study, it was reported a recurrence of symptoms (15%) after 5 years, even if the majority of the patients (80%) fully recovered from the injury [54]. In this study, the rehabilitative program was performed under the supervision of a physiotherapist and lasted from 12 weeks to 6 months. Exercises consisted of eccentric-concentric progression until to eccentric loading of two-legged and one-legged concentric–eccentric toe-raises. Intensity was gradually increased by raising the range of motion, number of repetitions, load and speed of loading. In a previous study, Silbernagel indicated as an EE program did not ensure the full recovery of muscle-tendon function in AT, encouraging to continue their rehabilitation protocol [55]. A discrepancy in long-term outcomes may be partially explained by the differences of adopted program.

The EE has been shown to be more effective for patients with mid-portion AT with respect to patients with insertional AT. In chronic tendinosis of insertional AT, pain was reduced in only 32% of patients [57]. In reason of that, a modified EE treatment was introduced. This program avoided the ankle dorsiflexion and the consequent mechanical impingement between the prominent calcaneus and the tendon and bursa that may be responsible for the lack of efficacy. This protocol consists of 45 repetitions of the exercise, twice a day, 7 days a week, for 12 weeks in 27 patients, resulting in significant reduction of pain also for patients who were not satisfied [57]. At the moment, this pilot study remains the only one adopting this treatment regimen.

Is eccentric exercise effective for Patellar Tendinopathy?

Most of the studies that have investigated EE in PT were performed on a decline board, whereas only few studies adopted eccentric drop squats or heavy slow resistance training [58-61]. Cannell and colleagues recruited 19 athletes from different sports affected by unilateral or bilateral PT [59]. Patients were randomized in two groups: one group was treated with eccentric drop squats program; the other group was treated with concentric leg extension/curl exercises. Both trainings lasted 12 weeks. Even if any significant difference between groups was found, a larger number of athletes fully returned to sport activity within 12 weeks after the eccentric drop squats program. Authors noted as the lack of statistical significant differences could be partly due to the small sample and the short period of observation (12 weeks).

The EE performed on decline board was found to be more effective in the management of pain for PT [62]. Young and colleagues compared the decline board protocol versus drop squats in elite volleyball players throughout competitive season [63]. Both programs were effective to improve pain and sport function, although the group treated with decline board displayed a significant improvement in function, pain, and ability to perform sport at the end of the sport season (Victorian Institute of Sport Assessment, VISA). These findings may be related to the fact that squats performed on a 25˚ decline board are targeted for the knee extensor mechanism more specifically than the drop squat, in which the load applied on the knee may be altered by other factors such as calf tension or trunk flexion.

In a prospective randomized trial, Jonsson and Alfredson treated a PT of jumper's knee comparing a program of eccentric versus concentric exercises of the quadriceps on a decline board, enhancing gradually load by means of weights [64]. At the 12 week follow up, the EE group presented significantly lower VAS score and higher VISA scores. In the group of the concentric exercises, more patients dropped out the rehabilitative program and they were unable to return to previous sporting activity after treatment. Moreover, at long-term follow-up, patients in concentric group needed to be treated with sclerosing injections or surgery, while patients treated with eccentric protocol were fully recovered to sport at the same level before injury.

One of the focus point is related to the interruption from the sport activity during the management of PT. A program of EE on decline board performed at home has been shown to be ineffective during a competitive season (VISA scores unchanged during the intervention period, and at 6 weeks and 6 months follow-up evaluations) [65].The treated athletes did not significantly differ with respect to those who continued to train and compete as usual during the treatment period [65]. On the contrary, a recent study performing a EE without interruption of the training during the competitive season has shown promising results [66]. In volleyball players between 16 and 19 years-old suffering PT, the experimental group performed daily EE once a day on the left and on the right leg. In the match days or when athletes had intense trainings, they were educated to not perform the eccentric squats. In the fourth week, an unstable surface was added to the protocol, in order to increase the body stabilization. Use of this protocol allowed to avoid detraining risks, maintain muscle strength, maximal power and jumping ability. These results confirmed similar outcomes, obtained in previous studies both for AT and PT [56,57,60], indicating the possibility to continue the sport activity during the clinical management of tendinopathies [67].

To enhance the effects of EE, static stretching exercises of quadriceps and hamstrings have been proposed [68]. In a study involving non-athletes affected by chronic PT (symptoms lasting for more than 3 months), the program associating EE and static stretching was found to be more effective in respect to EE alone for improving function and relief pain until 6 months follow-up.

Finally, EE have been tested also as rehabilitation program after open patellar tenotomy [69]. Post-operative rehabilitation consisted of a gradual increase in the number of training sessions and repetitions with progression to eccentric training. This treatment was compared with a conservative management based on EE training. This program consisted of squats on a 25° decline board performed twice daily for 12 weeks. During the first 8 weeks of treatment, athletes were allowed to gradually return to their sport whether pain was absent or minimal. Even if treatment options resulted in a definite improvement in knee function and symptoms relief, only half of all patients were able to return to sport within one year after treatment with each option, and fewer with complete symptoms relief. No advantage for the surgical treatment was demonstrated. Consequently, authors suggested to perform a conservative rehabilitation before to consider surgery for the treatment of PT [69].

Is it useful to perform eccentric exercise as preventive treatment in tendinopathy?

The role of EE as a preventive treatment has to be deeper investigated.

In muscle injuries, EE are effective in preventing hamstrings muscular injuries in soccer and rugby players [70-72]. A study on pre-season training has shown as EE could decrease hamstring injury risk during competitive season [73]. The rationale of using EE is thought to be linked to the enhancement of the hamstrings angle to the optimal torque. In fact, the mechanism of injury is related to the activity of flexor muscles, stretched beyond optimal torque threshold during rapid eccentric contraction [74].

In tendinopathies, prevention with EE should be directed to athletes with structural modifications of their tendons even if clinically asymptomatic. Morphological changes are detectable with the ultrasonographic investigation and consist of hypoecogenic areas, tendon thickening, neovascularization and, in case of Achilles tendon, paratenon blurring [75]. It was observed a significant correlation between mid-portion Achilles thickening and increased risk of tendinopathies' onset in football players at 1 year follow-up [76]. Fredberg and Bolving have estimated that up to 40% of football players with Achilles tendon abnormalities and 17% with patellar tendon abnormalities develop symptomatic tendinopathies [77].

To the best of our knowledge, only one study has investigated the possible role of a combined treatment (EE and stretching) in the prevention of tendinopathies, with contrasting results [78]. In a randomized controlled trial involved 209 professional soccer players, the authors found that EE and stretching significantly reduced the risk of developing structural modifications and symptoms of PT for asymptomatic athletes with normal patellar tendons. This was not revealed for AT. On the contrary, in asymptomatic players with ultrasonographically morphological abnormalities of patellar tendons, prophylactic EE and stretching increased the injury risk. One of the reason of the failure of this prevention program based on EE has been associated to the low dosage of training, insufficient to achieve the proposed aim [79]. In fact, the total number of the EE repetition was about one-third of the total amount of the training in Alfredson's protocol. Moreover, this prevention training lasted a whole competitive season (about 36 weeks) versus a program of treatment lasting 12 weeks. Despite the existing difficulties to recommend an intensive program to professional athletes as preventive treatment, it may be interesting to define whether results may be different modifying parameters related to dosage and time.

Conclusions

Although EE is widely used in the rehabilitation of midportion AT e PT in athletes, many points need to be clarified. It remains unclear how exactly EE works and what dosage of the training is necessary. Then, there is still lack of evidences about a possible efficacy of EE in the prevention of the onset of tendinopathies. Further clinical trials should be done to assess the effects of eccentric training programs. Future studies need longer-term follow-up in wider sample sizes. To verify protocols, different eccentric training program should be compared. Imaging assessments are also necessary before and after the period of treatment, in order to check on morphological modification of the treated tendons.

Enhancing clinical research on AT and PT is crucial for sport medicine, considering how these conditions affect sport participation, compromise the athletic performances and may even cause career ending. Despite all methodological limits, current findings support the extensive use of eccentric exercise in the management of Achilles and patellar tendinopathies, alone and also with stretching exercises, both for pain and function. It is recommended to perform programs lasting 12 weeks at least, with an high number of repetitions, to sustain positive outcomes in longer periods.

References

1. Maffulli N, Longo UG, Loppini M. Current treatment options for tendinopathy. Expert Opin Pharmacol Ther 2010;11:2177‑86.
2. Maffulli N, Khan KM, Puddu G. Overuse tendon conditions: time to change a confusing terminology. Arthroscopy 1998; 14:840-843.
3. Frizziero A, Bonsangue V, Trevisan M, Ames PR, Masiero S. Foot tendinopathies in rheumatic diseases: etiopathogenesis, clinical manifestations and therapeutic options. Clin Rheumatol. 2013 May;32(5):547-55.
4. Cook JL, Purdam CR. Is tendonpathology a continuum? A pathology model to explain the clinical presentation of load induced tendinopathy. Br J Sports Med 2009; 43: 409–16.
5. Kubo K. Effects of Repeated Concentric and Eccentric Contractions on Tendon Blood Circulation. Int J Sports Med 2015; 36: 481–484
6. Maffulli N, Loppini M. Conservative management of tendinopathy: an evidence-based approach. MLTJ 2011; 1 (4): 134-137.
7. Cook JR, Purdam CR. The challenge of managing tendinopathy in competing athletes. Br J Sports Med 2014; 48:506–509.
8. Frizziero A, Fini M, Salamanna F, et al. Effect of training and sudden detraining on the patellar tendon and its enthesis in rats. BMC Musculoskelet Disord 2011; 12:20.
9. Arnoczky SP, Lavagnino M Egerbacher M. The mechanobiological aetiopathogenesis of tendinopathy: is it the over-stimulation or the under-stimulation of tendon cells? Int J Exp Path 2007; 88:217–226.
10. Abate M, Schiavone C, Salini V, Andia I. Occurrence of tendon pathologies in metabolic disorders. Rheumatology 2013; 52:599-608.
11. Torricelli P, Veronesi F, Pagani S, et al. In vitro tenocyte metabolism in aging and oestrogen deficiency. Age (Dordr) 2013; 35:2125-36.
12. Frizziero A, Vittadini F, Gasparre G, Masiero S. Impact of oestrogen deficiency and aging on tendon: concise review. MLTJ 2014; 4 (3): 324-328.
13. Maffulli N, Waterston SW, Squair J, Reaper J, Douglas AS. Changing incidence of Achilles tendon rupture in Scotland: a 15-year study. Clin J Sport Med. 1999;9(3):157-160.
14. Tauton J, Ryan M, Clement D. A retrospective case-control analysis of 2002 running injuries. Br J Sport Med. 2002;36:95-101.

15. Frizziero A, Trainito S, Oliva F, Nicoli Aldini N, Masiero S, Maffulli N. The role of eccentric exercise in sport injuries. Rehabilitation. Br Med Bull 2014; 110:47-75.
16. Rowe V, Hemmings S, Barton C, et al. Conservative management of midportion Achilles tendinopathy: a mixed methods study, integrating systematic review and clinical reasoning. Sports Med 2012; 42:941–67.
17. Giombini A, Di Cesare A, Safran MR, Ciatti R, Maffulli N. Short-term effectiveness of hyperthermia for supraspinatus tendinopathy in athletes: a short-term randomized controlled study. Am J Sports Med 2006; 34:1247-53.
18. Charousset C, Zaoui A, Bellaiche L, Bouyer B. Are multiple platelet-rich plasma injections useful for treatment of chronic patellar tendinopathy in athletes? a prospective study. Am J Sports Med 2014; 42:906-11.
19. Muneta T, Koga H, Ju YJ, Mochizuki T, Sekiya I. Hyaluronan injection therapy for athletic patients with patellar tendinopathy. J Orthop Sci 2012;17:425-31.
20. Frizziero A, Salamanna F, Giavaresi G, et al. Hyaluronic acid injections protect patellar tendon from detraining-associated damage. Histol Histopathol. 2015 Mar 13:11605. [Epub ahead of print]
21. Salamanna F, Frizziero A, Pagani S, et al. Metabolic and cytoprotective effects of in vivo peri-patellar hyaluronic acid injections in cultured tenocytes. Connect Tissue Res 2015; 56:35-43.
22. Malliaras P, Barton CJ, Reeves ND, Langberg H. Achilles and Patellar Tendinopathy Loading Programmes. A systematic review comparing clinical outcomes and identifying potential mechanisms for effectiveness. Sports Med 2013; 43:267–286
23. Ohberg L, Lorentzon R, Alfredson H. Eccentric training in patients with chronic Achilles tendinosis: normalized tendon structure and decreased thickness at follow up. Br J Sports Med 2004; 38:8–11.
24. Frenette J, Côté CH. Modulation of structural protein content of the myotendinous junction following eccentric contractions. Int J Sports Med 2000; 21:313-20.
25. Curzi D, Baldassarri V, De Matteis R, et al. Morphological adaptation and protein modulation of myotendinous junction following moderate aerobic training. Histol Histopathol. 2015 Apr;30(4):465-72.
26. Kjaer M, Langberg H, Heinemeier K, et al. From mechanical loading to collagen synthesis, structural changes and function in human tendon. Scand J Med Sci Sports 2009; 19:500–10.

27. Ohberg L, Alfredson H. Effects on neovascularization behind the good results with eccentric training in chronic mid-portion Achilles tendinosis? Knee Surg Sports Traumatol Arthrosc 2004; 12:465–70.

28. Langberg H, Ellinsgaard H, Madsen T, et al. Eccentric rehabilitation exercise increases peritendinous type I collagen synthesis in humans with Achilles tendinosis. Scand J Med Sci Sports 2007; 17:61–66.

29. Tol J, de Jonge S, Weir A, De Vos R, Verhaar J. Relationship between neovascularization and clinical severity in achilles tendinopathy: A prospective analysis of 556 paired measurements. Knee Surg Sports Traumatol Arthrosc. 2013;30.

30. Magnusson SP, Hansen M, Langberg H, et al. The adaptability of tendon to loading differs in men and women. Int J Exp Pathol. 2007; 88:237-240.

31. Hicks KM, Onambele-Pearson GL, Winwood K, Morse CI. Gender differences in fascicular lengthening during eccentric contractions: the role of the patella tendon stiffness. Acta Physiol (Oxf). 2013 Nov;209(3):235-44. doi: 10.1111/apha.12159. Epub 2013 Sep 19

32. Jarvinen TA, Kannus P, Maffulli N, Khan KM. Achilles tendon disorders: etiology and epidemiology. Foot Ankle Clin 2005; 10:255-66.

33. Raikin SM, Garras DN, Krapchev PV. Achilles tendon injuries in a United States population. Foot Ankle Int 2013; 34:475-80.

34. Haglund-Akerlind Y, Eriksson E. Range of motion, muscle torque and training habits in runners with and without Achilles tendon problems. Knee Surg Sports Traumatol Arthrosc 1993; 1:195–9.

35. Brown JC, Posthumus M, Schwellnus MP, et al. The COL5A1 gene, ultra-marathon running performance, and range of motion. Int J Sports Physiol Perform 2011; 6:485–96.

36. Lian OB, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports: a cross-sectional study. Am J Sports Med 2005; 33:561–7.

37. Zwerver J, Bredeweg SW, van den Akker-ScheekI. Prevalence of jumper's knee among non elite athletes from different sports: a cross-sectional survey. Am J Sports Med 2011; 39:1984-8.

38. Kjaer M, Heinemeier KM. Eccentric exercise: acute and chronic effects on healthy and diseased tendons. J Appl Physiol 2014; 116:1435-8.

39. Stanish WD, Rubinovich RM, Curwin S. Eccentric exercise in chronic tendinitis. Clin Orthop Relat Res 1986; 208:65-8.

40. Rutherford OM, Purcell C, Newham DI. The human force: velocity relationship; activity in the knee flexor and extensor muscles before and after eccentric practice. Eur J Appl Physiol 2001; 84:133–40.
41. Rees JD, Wolman RL, Wilson A. Eccentric exercises; why do they work, what are the problems and how can we improve them?. Br J Sports Med 2009; 43:242-6.
42. Rees JD, Lichtwark GA, Wolman RL, Wilson AM. The mechanism for efficacy of eccentric loading in Achilles tendon injury; an in vivo study in humans. Rheumatology 2008; 47:1493-7.
43. Henriksen M, Aaboe J, Bliddal H, Langberg H. Biomechanical characteristics of the eccentric Achilles tendon exercise. J Biomech 2009; 42:2702-7.
44. Chaudhry S, Morrissey D, Woledge RC, Bader DL, Screen H RC. Eccentric and Concentric Loading of the Triceps Surae: An In vivo Study of Dynamic Muscle and Tendon Biomechanical Parameters. J Appl Biomech. 2014 Oct 16. [Epub ahead of print].
45. Huang CT, Hwang IS, Huang CC, et al. Exertion dependent alternations in force fluctuation and limb acceleration during sustained fatiguing contraction. Eur J Appl Physiol 2006; 97:362–71.
46. Grigg NL, Wearing SC, O'Toole JM, Smeathers JE. The effect of exercise repetition on the frequency characteristics of motor output force: implications for Achilles tendinopathy rehabilitation. J Sci Med Sport 2014; 17:13-7.
47. Alfredson H, Pietila T, Jonsson P, Lorentzon R. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. Am J Sports Med 1998; 26:360-6.
48. Rompe JD, Nafe B, Furia JP, Maffulli N. Eccentric loading, shock-wave treatment, or a wait-and-see policy for tendinopathy of the main body of tendon Achillis: a randomized controlled trial. Am J Sports Med 2007; 35:374-83.
49. Rompe JD, Furia J, Maffulli N. Eccentric loading versus eccentric loading plus shock-wave treatment for midportion achilles tendinopathy: a randomized controlled trial. Am J Sports Med 2009; 37:463-70.
50. de Jonge S, de Vos RJ, Van Schie HT, Verhaar JA, Weir A, Tol JL. One-year follow-up of a randomised controlled trial on added splinting to eccentric exercises in chronic midportion Achilles tendinopathy. Br J Sports Med 2010; 44:673-7.
51. Mafi N, Lorentzon R, Alfredson H. Superior short-term results with eccentric calf muscle training compared to concentric training in a randomized prospective multicenter study on

patients with chronic Achilles tendinosis. Knee Surg Sports Traumatol Arthrosc 2001; 9:42-7.

52. Nørregaard J, Larsen CC, Bieler T, Langberg H. Eccentric exercise in treatment of Achilles tendinopathy. Scand J Med Sci Sports 2007; 17:133-8.
53. van der Plas A, de Jonge S, de Vos RJ, van der Heide HJ, Verhaar JA, Weir A, Tol JL. A 5-year follow-up study of Alfredson's heel-drop exercise programme in chronic midportion Achilles tendinopathy. Br J Sports Med 2012; 46:214-8.
54. Silbernagel KG, Brorsson A, Lundberg M. The majority of patients with Achilles tendinopathy recover fully when treated with exercise alone: a 5-year follow-up. Am J Sports Med 2011; 39:607-13.
55. Silbernagel KG, Thomeé R, Eriksson BI, Karlsson J. Full symptomatic recovery does not ensure full recovery of muscle-tendon function in patients with Achilles tendinopathy. Br J Sports Med 2007; 41:276-80.
56. Fahlström M, Jonsson P, Lorentzon R, et al. Chronic Achilles tendon pain treated with eccentric calf-muscle training. Knee Surg Sports Traumatol Arthrosc 2003;11:327–33.
57. Jonsson P, Alfredson H, Sunding K, Fahlström M, Cook J. New regimen for eccentric calf-muscle training in patients with chronic insertional Achilles tendinopathy: results of a pilot study. Br J Sports Med 2008; 42:746-9.
58. Couppé C, Svensson RB, Silbernagel KG, Langberg H, Magnusson SP. Eccentric or Concentric Exercises for the Treatment of Tendinopathies? J Orthop Sports Phys Ther. 2015 Oct 15:1-25.
59. Cannell LJ, Taunton JE, Clement DB, Smith C, Khan KM. A randomized clinical trial of the efficacy of drop squats or leg extension/leg curl exercises to treat clinically diagnosed jumper's knee in athletes: pilot study. Br J Sports Med 2001; 35:60–4.
60. Kongsgaard M, Kovanen V, Aagaard P, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. Scand J Med Sci Sports 2009; 19:790–802.
61. Kongsgaard M, Qvortrup K, Larsen J, et al. Fibril morphology and tendon mechanical properties in patellar tendinopathy: effects of heavy slow resistance training. Am J Sports Med 2010; 38:749-56.

62. Purdam CR, Jonsson P, Alfredson H, Lorentzon R, Cook JL, Khan KM. A pilot study of the eccentric decline squat in the management of painful chronic patellar tendinopathy. Br J Sports Med 2004; 38:395-7.
63. Young MA, Cook JL, Purdam CR, Kiss ZS, Alfredson H. Eccentric decline squat protocol offers superior results at 12 months compared with traditional eccentric protocol for patellar tendinopathy in volleyball players. Br J Sports Med 2005; 39:102-5.
64. Jonsson P, Alfredson H. Superior results with eccentric compared to concentric quadriceps training in patients with jumper's knee: a prospective randomised study. Br J Sports Med 2005; 39:847-50.
65. Visnes H, Hoksrud A, Cook J, Bahr R. No effect of eccentric training on jumper's knee in volleyball players during the competitive season: a randomized clinical trial. Clin J Sport Med 2005; 15:227-34.
66. Biernat R, Trzaskoma Z, Trzaskoma L, Czaprowski D. Rehabilitation protocol for patellar tendinopathy applied among 16- to 19-year old volleyball players. J Strength Cond Res 2014; 28:43-52.
67. Saithna A, Gogna R, Baraza N, Modi C, Spencer S. Eccentric Exercise Protocols for Patella Tendinopathy: Should we Really be Withdrawing Athletes from Sport? A Systematic Review. Open Orthop J 2012; 6:553-7.
68. Dimitrios S, Pantelis M, Kalliopi S. Comparing the effects of eccentric training with eccentric training and static stretching exercises in the treatment of patellar tendinopathy. A controlled clinical trial. Clin Rehabil 2012; 26:423-30.
69. Bahr R, Fossan B, Løken S, Engebretsen L. Surgical treatment compared with eccentric training for patellar tendinopathy (Jumper's Knee). A randomized, controlled trial. J Bone Joint Surg Am 2006; 88:1689-98.
70. Brooks JHM, Fuller CW, Kemp SPT, Reddin DB. Incidence, risk, and prevention of hamstring muscle injuries in professional rugby union. Am J Sports Med 2006; 34:1297–306.
71. Petersen J, Thorborg K, Nielsen MB, Budtz-Jorgensen E, Holmich P. Preventive effect of eccentric training on acute hamstring injuries in men's soccer: a cluster-randomized controlled trial. Am J Sports Med. 2011; 39(11):2296–303.
72. van der Horst N, Smits DW, Petersen J, Goedhart EA, Backx FJ. The preventive effect of the Nordic Hamstring Exercise on hamstring injuries in amateur soccer players: a randomized

controlled trial. Am J Sports Med 2015 Mar 20. pii: 0363546515574057. [Epub ahead of print].

73. Askling C, Karlsson J, Thorstensson A. Hamstring injury occurrence in elite soccer players after preseason strength training with eccentric overload. Scand J Med Sci Sports. 2003; 13(4):244–50.
74. Porter T, Rushton A. The efficacy of exercise in preventing injury in adult male football: a systematic review of randomised controlled trials. Sports Medicine - Open 2015; 1:4.
75. Ohberg L, Lorentzon R, Alfredson H. Neovascularisation in Achilles tendons with painful tendinosis but not in normal tendons: an ultrasonographic investigation. Knee Surg Sports Traumatol Arthrosc 2001; 9:233-8.
76. Jhingan S, Perry M, O'Driscoll G, Lewin C, Teatino R, Malliaras P, Maffulli N, Morrissey D. Thicker Achilles tendons are a risk factor to develop Achilles tendinopathy in elite professional soccer players. Muscles Ligaments Tendons J 2011; 1:51-6.
77. Fredberg U, Bolvig L. Significance of ultrasonographically detected asymptomatic tendinosis in the patellar and achilles tendons of elite soccer players: a longitudinal study. Am J Sports Med 2002; 30:488-91.
78. Fredberg U, Bolvig L, Andersen NT. Prophylactic training in asymptomatic soccer players with ultrasonographic abnormalities in Achilles and patellar tendons: the Danish Super League Study. Am J Sports Med 2008; 36:451-60.
79. Knobloch K. Re: Prophylactic training in asymptomatic soccer players with ultrasonographic abnormalities in Achilles and patellar tendons: the Danish Super League Study. Am J Sports Med 2008; 36:e1-2.

Declaration of Interest

All authors state that any financial and personal interest have influenced this work. No funding for research has been used.