The role of eccentric exercise in sport injuries rehabilitation

Antonio Frizziero[†], Sabina Trainito[†], Francesco Oliva[‡], Nicolò Nicoli Aldini[§], Stefano Masiero[†], and Nicola Maffulli[¶,‖,#,*]

[†]Department of Physical and Rehabilitation Medicine, University of Padova, Italy, [‡]Department of Orthopaedics and Traumatology, University of Rome 'Tor Vergata' School of Medicine, Rome, Italy, [§]Department Rizzoli RIT, Laboratory of Biocompatibility, Technological Innovations and Advanced Therapies, Rizzoli Orthopedic Institute, Bologna, Italy, [¶]Department of Physical and Rehabilitation Medicine, University of Salerno, Italy, [‖]Centre for Sports and Exercise Medicine, Queen Mary University of London, Mile End Hospital Mann Ward, 275 Bancroft Road, London E1 4DG, UK, and [#]Barts and The London School of Medicine and Dentistry, Mile End Hospital, London, UK

*Correspondence address. Department of Musculoskeletal Disorders, Faculty of Medicine and Surgery, University of Salerno, Salerno, Italy. E-mail: n.maffulli@qmul.ac.uk

Abstract

Introduction: Sports injuries frequently involve tendons, muscles and ligaments. The variable outcome of surgery and medical treatment support early functional treatments. Eccentric exercise (EE) showed effectiveness in the management of Achilles tendinopathy (AT), patellar tendinopathy (PT) and lateral epicondyle tendinopathy (LET). Preliminary results of EE in other tendinopathies and sports injuries suggest its wide prescription in the sport rehabilitation field.

Sources of data: A comprehensive search of PubMed, Web of Science, the Cochrane Collaboration Database, Physiotherapy Evidence Database (PEDro), Evidence Based Medicine (EBM) Search review, National Guidelines, Scopus and Google Scholar was performed using keywords such as '*eccentric exercise*', '*sports injuries rehabilitation*', '*tendinopathy*', '*hamstrings strain*' '*adductor injuries*' and '*ACL reconstruction rehabilitation*'.

Areas of agreement: EE, alone or associated with other therapies, represents a feasible, cost-effective and successful tool in the treatment of well-known targets and might be promising in shoulder tendinopathy, adductor-related groin pain, hamstring strains, and ACL rehabilitation.

Area of controversy: The lack of standardization of protocols, the variable amount, quality and follow-up of studies, the different anatomy and

pathophysiology of the therapeutic targets limit the evidence of applicability of EE to sports injuries.

Growing points: The role of pathology and biomechanics in the response to EE should be further investigated.

Areas timely for developing research: New randomized controlled trials should test the effectiveness of standardized EE regimens to various sites of sports injuries.

Key words: eccentric exercise, rehabilitation, sport injuries, tendinopathy, ligament injuries

Introduction

Although they can affect all the musculoskeletal system, overuse and trauma injuries frequently involve tendons. Tendinopathy is a common work- and sport-related condition and a major cause of disability. Overuse injuries, including tendinopathies, represent ~7% of all primary care physician visits in the USA.[1] More than 30% of injuries related to sports activity arise from or have an element of tendinopathy. On the other hand, tendinopathy is not restricted to athletes, affecting also sedentary population.[2]

The management of tendinopathies is challenging, since medical treatment is generally unsatisfactory and the outcome of surgical procedures unpredictable.[3] The term tendinopathy refers to a general primary disorder of a tendon, associated with overuse in and around it, in the absence of histopathological data. The main characteristics of tendinopathies are a failed healing response and a weaker tendon structure, determined by tenocyte disarrangement and increased extracellular matrix. Since inflammation is absent or minimal in biopsy specimens, the descriptive term 'tendinitis' (implying an inflammatory process) should be used only when a histological confirmation is available,[4,5]

In patients with rheumatic disease, for instance, foot tendinopathies can emerge both in an inflammatory and in a non-inflammatory context.[6] Although tendinopathy is a major concern for athletes, it is also associated with risk factors for microvascular disease (obesity, increased waist circumference, older age, diabetes, hypertension, dyslipidaemia).[2]

Together with aging, postmenopausal oestrogen deficiency negatively affects tendon metabolism and healing, thus predisposing to tendon injuries.[7]

According to the current evidence, the management of tendinopathies should include early functional treatments, rather than rest and immobilization. Sudden detraining resulted harmful to patellar tendon and its enthesis in rats, while moderate exercise has a positive effect on tendons, suggesting that complete interruption of physical activity after a tendon injury should be minimized.[8] There is little support to the use of NSAIDs and corticosteroid injections in chronic tendinopathy. Conservative management of tendinopathies involves many therapeutic options, ranging from eccentric exercise (EE) to extracorporeal shock wave therapy (ESWT), splinting-bracing, active rest, low level laser therapy (LLLT), concentric exercise (CE), orthoses, therapeutic ultrasound (US), deep transverse friction (DTF) and topical glycerine.[9,10] Despite the large amount of therapeutic possibilities, only a few randomized controlled trials (RCTs) have been performed providing clinical evidence supporting their use; thus, the ideal treatment for tendinopathy remains unclear.[1,5,11,12] Eccentric training has shown efficacy in tendinopathies of the Achilles, patellar, supraspinatus and in lateral epicondylitis. Also, eccentric training has been successfully employed in muscle strains and ACL rehabilitation.[3]

However, whether EE is the most effective therapeutic exercise remains questionable.[13] Many eccentric training programmes are based on the early work of Alfredson *et al.*[14] and Mafi *et al.*[15] Due to the dearth of compliance data, the relative effectiveness of

various dosages of EE is still unknown. A few RCTs are available and most are of low methodological level.[16] In the last few years, many RCTs have been performed to evaluate the efficacy of EE not only in different sites of tendinopathies, but also in other injuries, such as adductor-related groin pain, hamstring strains and ACL ruptures. This review updates the evidence in support to the prescription of EE in various sports injuries, such as Achilles, patellar and supraspinatus tendinopathies, lateral epicondylitis, adductor related groin pain, ACL and hamstring strains.

Methods

Literature search

A comprehensive literature search was performed in February 2014 using PubMed, Web of Science, the Cochrane Collaboration Database, Physiotherapy Evidence Database (PEDro), Evidence Based Medicine (EBM) Search review, National Guidelines, Scopus and Google Scholar. The keywords used included *eccentric exercise, sports injuries rehabilitation, tendon, tendinopathy, supraspinatus, hamstrings strain, groin strain rehabilitation, hamstring injuries, adductor injuries, ACL reconstruction rehabilitation*, and *adductor-related groin pain*. The search results and the relative selection process are shown in the quality of reporting of meta-analyses (QUORUM) flow diagram in Fig. 1.

Study selection

The selection criteria were (i) language of publications (English or Italian); (ii) study design (RCT); (iii) sample, including adult patients with a diagnosis of Achilles, patella or supraspinatus tendinopathy, lateral epicondylitis, adductor related groin pain, ACL tear or hamstring strains; (iv) outcome measures, including pain and functional improvement, patient satisfaction or return to sport; (v) treatment, consisting in EE, alone or associated with other therapies. Using the above-mentioned criteria, relevant studies were selected after reading the title and/or abstract, while publications that did not meet the
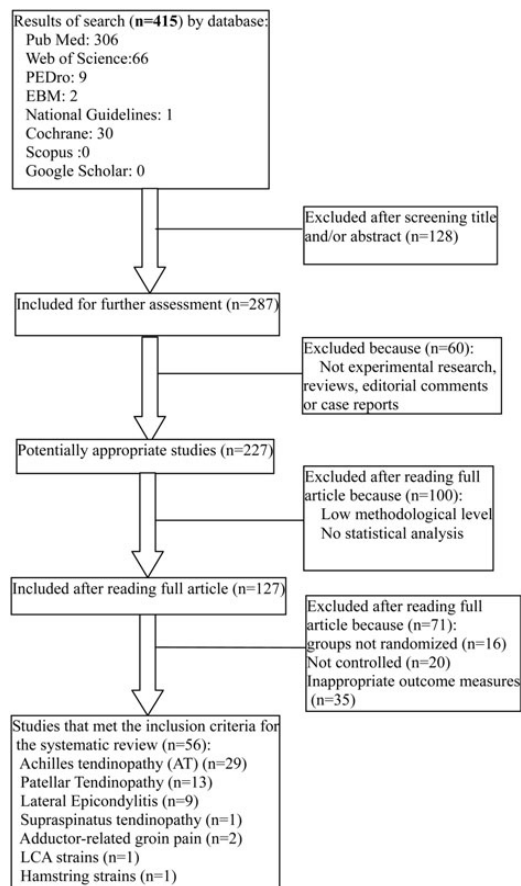

Figure 1 Selection of relevant articles to be included in the review according to the PRISMA protocol

criteria were excluded. Full text from articles selected for inclusion in the review was read, and the bibliographies were hand searched for further relevant publications. As a result, some studies were withdrawn after reading the full text, whereas others were retrieved from the bibliography of the selected articles. When available, a PEDro score was retrieved from the PEDro database online to rate the methodological quality of the studies.

Eccentric exercise

Several studies addressed the mechanism of action of EE. Alfredson *et al.* hypothesized that Achilles tendon injuries in runners may result from repetitive

micro-trauma, advocating a possible role of eccentric training in inducing tendon remodelling. Tenocytes are mechanosensitive cells, since they are able to reprogram their phenotype (gene expression, metabolism, structural properties) in response to mechanical stimuli.[17,18] However, the velocity-specific effect of eccentric training was not extensively analysed and supported by their studies.[14] In an experimental study of human Achilles tendons *in vivo*, Arampatzis *et al.* demonstrated that mechanical load induces mechanical and morphological changes with a threshold of activation.[18] However, the appropriate loading pattern is still unclear, since the threshold between healing stimulus and damage is not clearly defined. Injured tendons contain high levels of glutamate,[19] substance P and chondroitin sulphate[20] and such neurotransmitters and cartilage molecules has been implicated in the aetiology of pain arising in chronic tendinopathies. However, microdialysis performed on chronically injured Achilles tendons from six patients treated with an EE training programme failed to detect a significant decrease of glutamate after treatment.[21] Another mechanism advocated yet not demonstrated for the effectiveness of EE is the temporary compression of new vessels, accounting for the interruption of blood flow to the injured tendon.[22] Ultrasound studies have reported a positive effect of EE on tendon structure, but these results were not confirmed by independent research.[23] Moreover, aggressive eccentric stretching producing moderate pain may modulate the neurological stretch response, impaired in Achilles tendinopathy (AT).[24,25] EE protocols differ between studies, not only for frequency of administration and number of repetitions, but also for speed and load parameters, and indication to continue exercise through pain, or to interrupt the activity in case it arises. Furthermore, inconsistency between studies was present regarding allowance of concomitant physical activity, possible association with other treatments (e.g. ESWT, splinting, laser-therapy) or additional forms of therapeutic exercise (e.g. CE, stretching).[13,16,26,27] In a recent pilot study Alfredson protocol have shown superior outcomes in term of Victorian Institute of Sport Assessment-Achilles score (VISA-A) compared with Stanish protocol in

patients with AT.[28] EE seems to be effective in mid-portion AT, but not in insertional AT. Since clinical efficacy should result from a combination between loading profile and range of motion during loading, this might explain why insertional pain responds poorly to standard eccentric loading programmes.[4,29] A modified protocol of painful eccentric calf-muscle training seems more promising in this field.[30] The effectiveness of EE in AT could result from the unique interaction between ankle biomechanics and Achilles tendon loading profile; thus, further investigations are needed to validate the use of EE at other tendinopathy sites.[25]

EE versus CE

When examining the superior effectiveness of EE compared with CE in AT, Stanish *et al.* attributed this finding to the higher magnitude of force that the tendons are subjected to under eccentric training, inducing a greater remodelling stimulus.[31] It seems that eccentric loading induces a greater decrease in tendon thickness immediately after the training programme, but with a similar recovery to that of CE.[32] Rees *et al.* measured tendon force and length changes in EE compared with CE; unexpectedly, consistent differences were not found in these parameters, but EE showed a particular pattern of high-frequency oscillations that could be responsible for its greater effectiveness. The authors attributed this finding also to the higher speed adopted in the EE protocol and hypothesized that increased velocity might induce a greater remodelling stimulus on tendon.[3] The role of speed in exercise represents an open question between physicians and deserves further research. A recent study has pointed out that load and speed parameters might influence tendon healing more than exercise type itself (e.g. concentric versus eccentric).[33] The number of repetitions in Alfredson protocol is related to changes in magnitude and frequency of ground reaction force, with possible implications on effectiveness of the EE programme.[32] Allison and Purdam stated that EE should not be considered an optimal strengthening programme, since it specifically avoids the concentric–eccentric coupling that is proper of the stretch-shortening cycle

(SSC).[25] Along with speed, also frequency of exercise sessions is an open field of discussion between researchers. EE is usually prescribed twice daily every day, while the typical muscle strengthening protocol recommends training one time per day every other day. This different posology seems related to a lower integrated electrical activity in EE. However, greater muscle tension has been observed after 7 weeks of EE than after CE.[34] In this perspective, eccentric training for tendinopathy has been defined a 'tendon-strengthening' programme.[2] Since collagen synthesis has a maximum peak at 24 h and a maximum decrease at 72 h after exercise, some authors have proposed to increase the interval between sessions respect with the most adopted twice-daily programme.[2] A pilot study found effectiveness of a twice weekly high load eccentric training in patellar tendinopathy (PT).[35]

Results

As shown in the study selection flow diagram, of the original database search, identifying 415 citations, 287 citations were selected for further assessment, while the other were excluded after reading title and/or abstract. Of the remaining, 160 were excluded because they were not experimental studies or case reports. Of the remaining 127, 71 were excluded because of low methodological level, or lacking of statistical data or randomization. As a result of this process, 56 studies were selected for the systematic review. Ten studies, although not available as full text, were included in the review after screening the abstract, because meeting the selection criteria.

Achilles tendinopathy

The estimated prevalence of AT in runners ranges between 11 and 29%, while an incidence rate of symptomatic midportion AT of 2.35 per 1000 was detected in the general population aged between 21 and 60 years.[2]

The aforementioned study by Alfredson *et al.* established the EE programme based on 12 weeks of 3 sets × 15 repetitions, twice daily, showing safety, effectiveness and feasibility in a group of recreational athletes.[14] In their following study of 2002, the authors tested the level of intratendinous glutamate before and after an EE programme, finding a significant decrease of VAS after treatment, independently from the glutamate variation, which was not statistically significant. These and other studies who were initially selected[29,31,36,37] were excluded from the review because of the lack of randomization or of a control group. The follow-up study by van Der Plas *et al.*[38] was also not included, as we considered only the original work. The study by Nillson–Helander *et al.*, comparing the effect of surgical versus non-surgical treatment in Achilles tendon rupture, was excluded because conservative treatment consisted in CEs (e.g. heel raises), and did not comprise eccentric training.[39] Eventually, 29 articles about AT fulfilling the selection criteria were recruited. The characteristics of these studies are presented in Table 1.

EE versus CE or other forms of therapeutic exercise

Silbernagel *et al.* compared several outcome measures (a specific questionnaire, ankle ROM test, jumping, toe raise test, toe-raises and rest, pain during jumping and on palpation,) between a group treated with an eccentric–concentric progressing to eccentric protocol and the control group treated with a non-specific concentric–eccentric programme and stretching of the calf muscle. No significant differences between the two groups were retrieved, except for the jumping test (worse in the specific EE group). However, the EE group showed statistically significant pain reduction with palpation at 3 and 6 months' follow-up, and pain reduction during walking at 6 weeks' and 6 months' follow-up in comparison with the baseline. Moreover, the study group showed a statistically significant increase of asymptomatic periods at the 6-month evaluation compared with the time before treatment, and a statistically significant decrease in tendon swelling at the 3- and 6-month evaluations compared with the baseline. At 1-year follow-up, absence of pain and satisfaction with physical activity were significantly superior in the experimental group, compared with

Table 1 Eccentric exercise in Achilles Tendinopathy

Study ID	Number of patients (tendons)	Participants' characteristics	EE protocol	Work through pain (Y = yes/N = no)	Physical activity (A = allowed, NA = not allowed)	Additional therapy (CE, ESWT, splint, laser therapy	PEDro score	Follow-up	Outcomes
Bell et al. (2013)	53	Inclusion criteria: duration symptoms >3 months, unilateral midportion AT, US changes; exclusion criteria: previous rupture/ surgery, previous therapy	Alfredson protocol	Y (until 4/10 in the NRS scale)	Not available	Two unguided peritendinous autologous blood injections one month apart + EE (study group); EE only (+ dry needling) (control group)	NA	1, 2, 3, 6 months	No statistically significant difference in VISA-A, perceived rehabilitation and return to activity
Brown et al. (2006)	26 (33)	Clinical finding of non-insertional tenderness of the Achilles tendon, Achilles pain activity related and with gradual onset	Alfredson protocol	Not available	Not available	Aprotinin (protease inhibitor) + anaesthetic injection + EE (study group); Saline (0.9%) + anaesthetic injection + EE (placebo group)	6	2, 4, 12, 52 weeks	No statistically significant difference in VISA-A and secondary outcomes between groups
De Jonge et al. (2010)	58 (70)	Not available	Not available (12 weeks)	Not available	Not available	Night splint (Group 1: only EE; Group 2: EE + added splinting)	6	1 year	Increase of VISA-A score and subjective patient satisfaction in both groups with no additional value of splinting; neovascularization score measured with PDU has no prognostic value
De Jonge et al. (2011)	54	See De Vos et al. (2010)	See De Vos et al. (2010)	See De Vos et al. (2010)	See De Vos et al. (2010)	PRP	NA	1 year	No clinical neither US statistically significant superiority between PRP and placebo group
De Vos et al. (2007)	58 (70)	age 18–70 years, active participation in sports, midportion AT	Alfredson protocol (knee straight and knee bent, 3 × 15, twice daily × 12 weeks; progressive load increase with a backpack or a weight machine)	Y (stop when unbearable)	Weight bearing activities not allowed for the first 4 weeks	Night splint (Group 1: only EE; Group 2: EE + added splinting)	7	None	Increase of VISA-A score in both groups; patient satisfaction 63% in the EE only group compared with 48% in the EE + splint group (not significant); no additional value of splinting
De Vos et al. (2010)	54	Age 18–70 years, symptoms of midportion AT ≥2 months; exclusion criteria: other musculoskeletal disease, medications, previous EE protocol or inability to perform it, previous PRP injection	Heel drops on a step for 12 weeks	Only mild pain (3/10)	Patient were provided with detailed instructions about rehabilitation programme sport activity (stop for 4 weeks, after 4 weeks gradual return to sports) and stratified for activity level.	US-guided PRP injection	NA	6, 12, 24 weeks	No statistically significant difference between PRP group and placebo in term of VISA-A improvement. at 24-week follow-up
Herrington and McCulloch (2007)	25	Age 20–55 years, duration symptoms >3 months, midportion AT, negative squeeze test	Combined Alfredson et al. (1998) and Stanish et al. (1986) protocol with increasing speed	Only slight pain/ discomfort	A (only without pain)	US, DTF (conventional treatment)	6	None	Increase of VISA-A significantly higher in the group treated with EE

Horstmann et al. (2013)	58	Not available	Not available	Not available	Not available	Whole body vibration, eccentric training or wait-and-see	NA	None	Significantly greater pain improvement in tendon midsection in the EE group; significantly greater pain improvement at the musculo-tendinous junction in the body vibration group compared with the other groups
Hunte and Lloyd-Smith (2005)	65 (84)	Age >18 years, history of insidious onset of Achilles tendon pain, a tender nodule localized to the region of the calcaneal insertion, ultrasound examination that excluding tendon tear. Exclusion criteria Achilles tendinopathy of <3 months' duration, previous operation on, or dislocation of, the affected ankle or leg, distal neurologic signs, a local corticosteroid injection in the previous 3 months, pregnancy	Not available	Not available	rest from aggravating activities	Topical glyceril trinitrate	NA	2, 6, 12, and 24-week	Statistically significant superiority in pain reduction for the topical glyceril trinitrate group compared with the placebo at 12 and 24 weeks follow-up; stat. sign. less pain on the 10-hop test in the glyceryl trinitrate group than in the placebo group at 24 weeks
Kearney et al. (2013)	20	Inclusion criteria: duration symptoms >3 months, midportion AT, US changes; exclusion criteria: underlying causes (trauma in the last 12 months, diabetes, RA, previous rupture/surgery)	Alfredson protocol	Not specified (exercise intensity could be progressed as pain allowed)	A (only without pain)	Platelet Rich Plasma (PRP) injection	NA	6 weeks, 3, 6 months	No statistically significant difference in VISA-A between groups
Knobloch et al. (2008)	116 (116)	Not available	Not available	Not available	Not available	AirHeel Brace®	4	None	Significant reduction of FAOS score and VAS score from preoperative to postoperative in both groups (no improvement of clinical outcome with the AirHeel Brace®)
Mafi et al. (2001)	44 (44)	22 M, 20 F, mean age 48 years, chronic severe midportion AT, referred to surgery, mean duration of symptoms 21 months	Alfredson protocol	Y	Only with slight pain/discomfort	CE (control group)	5	none	Satisfaction and return to activity significantly greater after treatment in the EE group (82%) than in the CE group (36%)

Continued

53

Table 1 Continued

Study ID	Number of patients (tendons)	Participants' characteristics	EE protocol	Work through pain (Y = yes/N = no)	Physical activity (A = allowed, NA = not allowed)	Additional therapy (CE, ESWT, splint, laser therapy	PEDro score	Follow-up	Outcomes
Mayer et al. (2007)	28	Only men, 18–50 years, mileage >32 km/week, unilateral chronic tendon problems during exercise, untreated for at least 6 months	Alfredson exercise, drop-jumps and countermovement jumps (n of repetitions not specified)	Y	Y	DTF, US, sensory motor training + EE (first group), insoles (second group) versus control group (no treatment)	5	none	Statistically significant PDI (pain disability index) reduction in first and second group in relation with baseline and with control group
Norregaard et al. (2007)	45	18–70 years, pain and tenderness or US changes to the AT	Alfredson protocol with gradual increase of repetitions (from 1 × 10 to 3 × 15) and load	Y, but decreasing intensity in case of morning stiffness	Y, only pain-free and not new activities or with increasing amount of exercise	Stretching (control group)	4	3, 6, 9, 12 weeks and 1 year	Significant improvement of pain score (modified KOOS score), US findings, patients global assessment, manually assessed tenderness score in both groups
Notarnicola et al. (2013)	60	18–80 years, diagnosis based on clinical symptoms ≥6 months/ instrumental tests, VAS score >4; Exclusion criteria: contraindications to CHELT or ESWT, previous Achilles tendon surgery, peritendinous injections	Eccentric Thera-band exercises (3 sets × 10 reps) for 2 months	Not available	Not available	CHELT + EE + stretching (Study group); ESWT + EE + stretching (control group)	NA	End of treatment, 2 and 6 months	Statistically significant superior VAS improvement in the CHELT group at all follow-up. Significantly superior improvement in Ankle–Hindfoot Scale at 2 and 6 months and in Roles and Maudsley Score at 2 months follow-up in the CHELT group.
Paoloni et al. (2004)	65 (84)	>18 years, insidious onset Achilles tendon pain, a tender nodule 2–6 cm from the calcaneal insertion, and an US examination excluding a frank tendon tear	Not available (12 weeks)	Not available	rest from aggravating activities in the early stages	Exercise (including EE and stretching), topical tinitrate glyceril (study group); exercise only placebo administration (control group)	NA	2, 6, 12, 24 weeks	Significant improvement in pain with activity, night pain, pain after hop test tenderness, number of asymptomatic with activities of daily living, in the study group compared with the control group, increase in ankle plantar flexor mean total work compared with the baseline. I
Pearson et al.	33 (40)	Clinical symptom of midportion AT ≥3 months; exclusion criteria: insertional pain, anticoagulant therapy, systemic disease, elite athletes, previous injection in the tendon ≤3 months	Alfredson protocol	Mild to moderate pain	Active lifestyle, rest from aggravating activities,	Peritendinous autologous blood injections	NA	none	Statistically significant higher improvement in VISA-A in the blood injection group at the end of treatment.
Petersen et al. (2007)	100	Mean age 42.5 years, 60 M, 40 F	Alfredson protocol	Y (stop when disabling)	Y, only with mild discomfort and pain	EE (Group 1) vs Air Heel Brace® (Group 2), Air Heel Brace® + EE (Group 3)	5	6, 12, 54 weeks	VAS score, AOFAS score and SF-36 improvement in all treatment groups, no synergistic effect of bracing and EE

Rompe et al. (2009)	68	18–70 years, 38 F, 30 M, Chronic (≥ 6 months) midportion AT treated with unsuccessful non-operative management	Alfredson protocol with gradual increase of repetitions and load	Y (stop only when unbearable)	Y (only without pain)	Low-energy ESWT associated with EE (control group)	8	4 months, 1 year	Significant difference in VISA-A increase, pain rating and Likert Scale decrease between the two groups with better outcome of the eccentric loading + ESWT group compared with the ESWT only group
Rompe et al. (2008)	50	Chronic (≥6 months) insertional AT treated with unsuccessful non-operative management	Not available	Not available	Not available	ESWT (control group)	8	4 months, afterward patients allowed to cross over; 1 year	For all outcome measures (pain, function and activity) better results with ESWT compared with EE
Rompe et al. (2007)	75	Chronic (≥ 6 months) midportion AT treated with unsuccessful non-operative management	Alfredson protocol with gradual increase of repetitions and load)	Not available	Not available	EE (Group 1), ESWT (Group 2), wait-and-see policy (Group 3)	8	4 months	Significantly higher improvement of all outcomes measures (VISA-A increase, pain rating and Likert Scale decrease)in Groups 1 and 2 compared with Group 3. No significant difference between Groups 1 and 2.
Roos et al. (2004)	45	20–60 years, 23 F, 22 M, 65% active in sports	Alfredson protocol with gradual increase of repetitions and load	Not available	Not available	EE group (Group 1), night splint (Group 2), combination of the two (Group 3)	6	6, 12, 26 weeks, òpp1 year	FAOS improvement in all groups, less pain reduction in Groups 2 and 3 compared with Group 1
Silbernagel et al. (2001)	32(44)	Mean age 45 years, 31 M, 11 F, chronic (>6 months) proximal achillodinia	Gradually increasing concentric- eccentric progressing to eccentric exercise + stretching of the calf muscles	Y (stop only when disabling)	Pain allowed according to a pain monitoring model	Other therapeutic exercise (CE-EE, stretching): control group (included toe raises on a step)	5/6	6, 12 weeks, 6 months, 1 year	No statistically significant differences between groups, however higher satisfaction, improvement in plantar flexion,, lower symptoms were found in the EE group
Stergioulas et al. (2008)	52	Recreational athletes with unilateral symptoms of midportion AT activity related ≥6 months, US changes, ROM restriction (<10° active dorsiflexion). Exclusion criteria: oral or injected steroids ≤26 weeks, arthritis or hypercholesterolemia	Alfredson exercise, with gradually increasing frequency from 1 set of 5 reps, to 12 sets of 12 reps with 1 min rest btw sets, 4 day/week × 8 weeks	Mild-moderate (≤50/100 mm in VAS scale)	Not available	Stretching and EE (both groups). LLLT (study group) vs sham-LLLT (placebo group)	7	4, 8, 12 weeks	Significantly higher improvement in VAS-pain and all the secondary outcomes in the LLLT group than in the placebo group at all follow-up. Similar results in the placebo group at 12 weeks and in LLLT group at 4 weeks.
Stevens and Tan (2013)	28	Nonathletic patients with midportion AT	Alfredson protocol	Y (unspecified)	Not available	'do-as-tolerated' protocol	NA	none	No statistically significant difference in VISA-A and VAS-pain between the standard and the do-as-tolerated group at the end of treatment
Tumilty et al. (2012)	40	18–65 years, midportion AT	Alfredson protocol	Not available	Not available	LLLT	10	4, 12, 52 weeks	No statistically significant difference in VISA-A between the EE only group and the EE + LLLT group.
Yelland et al. (2011)	43	Painful mid-portion AT	Not available	Not available	Not available	Prolotherapy vs EE vs combined therapy	7	12 months	Prolotherapy in association with EE associated with quicker improvement than EE alone, but with similar long-term VISA-A scores

Continued

Table 1 Continued

Study ID	Number of patients (tendons)	Participants' characteristics	EE protocol	Work through pain (Y = yes/N = no)	Physical activity (A = allowed, NA = not allowed)	Additional therapy (CE, ESWT, splint, laser therapy	PEDro score	Follow-up	Outcomes
Yu *et al.* (2013)	32	Male, age 20–30 years, diagnosis of chronic (≥6 months) unilateral Achilles tendinopathy after ultrasonography, at least a 6-months incidence period of Achilles tendinopathy, compliance with outpatient follow-up, ability to walk independently	Combination of Alfredson and Curwin and Stanish protocols; 3 × 15, twice daily × 12 weeks, 50 min/day, 3 days/week × 8 weeks	Y (stop only when disabling)	Not available	CE (control group)	7	none	Statistically significant improvement in pain, ankle dorsiflexion endurance, total balance index and agility after the intervention in the experimental group compared with the control group, showed; no significant difference in dexterity between the two groups
Zhang *et al.*	64	Clinical diagnosis of midportion AT with symptoms for ≥2 months	Alfredson protocol	Y (stop only when disabling)	Not available	acupuncture	NA	8, 16, 24 weeks	Statistically significant superior improvement in VISA-A and VAS at all follow-up considered in the study group compared with the control group

the control group.[40] Mafi *et al.* demonstrated the superior effectiveness of an EE regimen compared with CE in a prospective multicentre RCT.[15] Patient satisfaction and return to previous activity were significantly superior after treatment in the experimental group than in the control group. The VAS score decreased significantly in both groups after the 12-week regimen, but the reduction resulted significantly higher in the EE group than in the CE group. This study, however, is of limited evidence because of the absence of follow-up. The study by Norregaard *et al.*, assigning patients randomly either to a stretching (control group) or to an EE regimen (study group), failed to demonstrate a greater effectiveness of EE. A marked improvement of symptoms was found after 1 year follow-up with both therapeutic exercises. A negative prognosis was associated with female gender and insertional pain. These findings could probably result from the inclusion of an older and sedentary population of patients. The absence of evidence of superiority of the EE regimen compared with the previous studies might be due to the indication of performing only pain-free exercise, probably leading to a low-intensity training.[41] In the study by Yu *et al.*, 32 patients with chronic AT were randomized to a study group (*n* = 16), performing EE and a control group (*n* = 16), treated with concentric training. At the end of the training period (8 weeks), VAS for pain was reduced more significantly in the study group. In the experimental group, knee extension and calf muscle strength increased significantly after the intervention. Ankle dorsiflexion endurance increased more significantly in the study group than in the control group, whereas ankle plantarflexion endurance increased significantly only in the EE group. The total balance index improved more significantly in the experimental group than in the control group. Dexterity and agility increased significantly in both groups after the intervention, but agility after the exercise compared with the baseline was significantly superior in the experimental group. The medial–lateral balance index decreased significantly in both groups. The absence of follow-up limits the validity of the results of this study.[42] Stevens and Tan compared two groups of patients with midportion AT treated respectively with the

standard Alfredson protocol and with a do-as-tolerated EE protocol. At the end of treatment (6 weeks) a statistically significant improvement in VISA-A, VAS pain from the baseline was detected for both groups, with no statistically significant difference between them. No follow-up was performed.[43]

EE versus ESWT

In their first RCT, Rompe et al. found a statistically significant progress of all the outcomes considered (Victorian Institute of Sport Assessment, VISA-A score, pain rating and Likert scale) in 75 patients with midportion AT treated with EE or ESWT, compared with a wait-and-see policy. No significant difference was found between EE and ESWT. The follow-up evaluation was performed at 4 months.[44] A later RCT found greater effectiveness of an association between EE and ESWT than EE alone. At 4-month follow-up, the improvement in all outcomes considered (VISA-A score, pain rating and Likert scale) was significantly higher in the combined approach group. At 1 year from the baseline, 15 failed patients from Group 1 were recruited for the crossover study and received combined therapy, while only 6 patients from Group 2 were referred to surgery.[45] On the other hand, significantly better and long lasting results in the VISA-A score, pain rating and Likert scale were found at both first (4 months) and last (1 year) follow-up after treatment with ESWT than with an EE regimen in 50 patients with chronic insertional AT. At four months, 18 of 25 patients from EE-group opted to crossover, compared with 8 of 25 patients from ESWT-group.[46] Cold air and high-energy laser therapy (CHELT) was compared with ESWT in two groups of patients with insertional AT both treated with EE and stretching for two months. At all the follow-up considered (end of treatment, 2 and 6 months), a statistically significant difference in VAS improvement was found in favour of the CHELT group. This group was significantly superior also for Ankle-Hindfoot Scale at 2 and 6 months' follow-up and for Roles and Maudsley Score at 2 months' follow-up. There was no untreated control group, thus the valuation of effectiveness of EE itself was not possible.[47]

Other treatments

Herrington and McCulloch treated 25 patients with midportion AT either with EE in association with DTF and US (study group) or with DTF and US alone (control group). All participants demonstrated a significant increase in VISA-A scores over the 12-week treatment period compared with the baseline, but the study group showed statistically significant greater VISA-A scores compared with the control group. No follow-up was performed for this pilot study, limiting the evidence of its results.[48] The study of Paoloni et al. aimed to detect any benefit of the topical application of glyceryl trinitrate in addition to exercise (including EE, but also stretching) in patients with AT. Compared with the placebo–control group, treated only with exercise, the glyceryl trinitrate group showed a statistically significant decrease in pain with activity, night pain and tenderness at 12 weeks' follow-up. At 24 weeks' follow-up, pain during activity and after the hop test were significantly decreased in the study group compared with the control group, while ankle plantar flexor mean total work increased compared with the baseline. In addition, at this time point, a significantly higher number of patients from the glyceryl trinitrate group were asymptomatic with activities of daily living, compared with the placebo group. This study is limited by the lack of an untreated control group and the missing description of the exercise protocol.[49] In another study, topical glyceril trinitrate in association with EE and stretching retrieved statistically significant superior achievements in terms of pain decrease (pain with activity, night pain and local tenderness and after the 10-hop test) compared with the placebo group.[50] Compared with EE alone, acupuncture in association with EE has been associated with superior results in terms of VISA-A and VAS improvement after a follow-up of 24 weeks.[51]

When compared with EE and a wait-and-see policy, whole-body vibration provided a statistically significant higher improvement of pain at the musculo-tendinous junction, while a significantly greater pain improvement in tendon midsection was observed in the EE group compared with the other groups.[52]

In the study by Pearson *et al.*, patients with AT were randomized to receive EE alone for 12 weeks, or in addition to blinded peritendinous autologous blood injections. Six weeks after the start of the programme, statistically significant improvements in VISA-A from the baseline were present in both groups, with no statistically significant difference between them, while at the end of the programme there was a statistically significant higher improvement in the blood-injection group. No follow-up was performed, as patients were evaluated only at the end of treatment.[53]

In another study, peritendinous autologous blood injections in combination with the Alfredson protocol failed to demonstrate any statistically significant additional benefit in terms of VISA-A and secondary outcomes (perceived improvement and return to sport) at all the follow-up considered (1,2,3,6 months).[54] De Vos *et al.* studied the effect of one Platelet Rich Plasma (PRP) injection in addition with EE in a double-blind RCT. Patients were stratified for activity level, a possible confounding factor, and provided with detailed information about the timing of rehabilitation protocol and sport activity allowance. At 24-week follow-up, no statistically significant difference was detected between the PRP group and the placebo.[55] These observations were confirmed by a 1-year follow-up study, which failed to detect any clinical and ultrasonographic superiority of PRP over placebo in chronic AT, combined with a standard EE programme.[56] More recently, Kearney *et al.* did not detect a statistically significant difference in VISA-A between two groups of patients with midportion AT treated respectively with EE and PRP injections at all the follow-up evaluations (6 weeks, 3 and 6 months), although little evidence can be drawn from this pilot RCT.[57]

Night splinting was proposed for its possible action of elongation of the musculotendinous unit and reduction of tendon strain. The 1 year-follow up study by De Jonge *et al.* evidenced no significant differences in the VISA-A score between a group of patients with chronic midportion AT treated with EE only and a group of patients treated with night splint in association with EE, although both groups had a significant increase of the VISA score from the

baseline after 1-year follow-up.[58] In the study by de Vos, splinting was associated with lower satisfaction and poorer compliance, although the trend observed was not statistically significant and there was no follow-up.[59] In the study by Roos *et al.*, 44 patients with midportion AT were recruited and randomized into three treatment groups: EE only, night splint only and EE plus night splint. All groups improved significantly in the Foot and Ankle Function Scale (FAOS). Night splint was associated with significant improvement from 26 to 52 weeks; on the other hand, at 52 weeks, similar pain reduction was reported in all groups. However, the eccentric group reported significantly earlier and higher pain reduction from the baseline and a significantly lower difficulty during sporting activities compared with the other groups.[60] At 12 months, 50% of the patients treated only with splint and 15% of patients performing EEs were found having tried other treatments. Knobloch *et al.* randomized 116 patients with midportion AT were in two groups, one receiving only EE and the other performing the EE associated with Air Heel bracing. At the end of treatment, FAOS and VAS score were significantly improved from pre-intervention values in both groups, without critical difference between groups. In the group treated with both EE and bracing, oxygen saturation in the main body of the tendon significant increased and post-capillary venous filling pressures decreased from the baseline. The association with the Air Heel Brace® can improve tendon microcirculation, although these changes are not related to a superior effectiveness compared with EE alone. No follow-up was available for this study.[61] The prospective RCT by Petersen *et al.* compared the effectiveness of EE against Air Heel bracing and the combination of the two in 100 patients with midportion AT at the three follow-up evaluations (6, 12 and 54 weeks). SF-36, AOFAS and VAS score for pain improved significantly in all the three groups at all the follow-up examinations. No significant difference between groups was detected for all the outcomes considered, including tendon thickness after treatment. According to these results, Air heel Bracing and EE are equally effective and bracing could represent an alternative treatment option, with no synergistic

effect to EE.[62] Mayer *et al.* showed a statistically significant improvement in PDI (Pain Disability Index) both after a complex physiotherapy programme (EE, DTF, US and sensory–motor training) and after an insoles-only treatment compared with the baseline and to a control group. Insoles might reduce pain improving muscular-regulated joint stability. Their application could be more time and cost-effective than complex physiotherapy programs and, obviously than surgical and medical treatment. However, this study appears not conclusive because the only outcome measure evaluated was pain, and did not analyse the additional benefit of EE to the physiotherapy programme. Furthermore, no follow-up was performed.[63]

In the study by Stergioulas *et al.* 52 recreational athletes with chronic AT were randomized to receive either blinded LLLT or placebo in addition to EE and stretching performed for 8 weeks. The primary outcome, VAS-pain and all the secondary outcomes (morning stiffness, active dorsiflexion, palpation tenderness and crepitation during physical activity) were significantly better in the LLLT group than in the placebo LLLT group at all follow-up considered (4, 8 and 12 weeks). At 12 weeks' follow-up the placebo group got similar results to those reached at 4 weeks by the LLLT group.[64] Tumilty *et al.* randomized 40 patients with AT in two groups, treated either with EE and LLLT or with EE alone and placebo laser therapy administration. At the first follow-up evaluation, no statistically significant difference in VISA-A scores was found between groups. At the 4-week follow-up, VISA-A was significantly better in the placebo group. The other outcome scores were not significantly different between the groups.[65] Yelland *et al.* randomized 43 patients with painful midportion AT to EE ($n = 15$), prolotherapy with lignocaine ($n = 14$) or a combination of the two ($n = 14$). At 6 weeks and 12 months follow-up VISA-A was significantly better after the combination treatment than after the EE only programme. However, at 12 months the scores were similar in the two groups.[66] Aprotinin, a protease inhibitor, has been proposed in association with EE and anaesthetic injection, but no statistically significant difference between the study group and the placebo group was detected in VISA-A and secondary outcomes at

all the follow-up considered (2, 4, 12, 52 weeks). Since also the control group received an eccentric training, the effect of EE itself cannot be evaluated by this study.[67]

Effectiveness of EE in AT

The quality of studies was variable; 19/29 studies were rated in the PEDro database, with a mean PEDro score of 6/10. Eight of 29 studies were available only in abstract form. Nine of 29 studies did not perform a follow-up and evaluated patients only at the end of the treatment.

When compared with other therapeutic exercise, EE appears more effective in terms of VAS pain and tendon swelling reduction, increase in patient satisfaction, ankle dorsiflexion endurance, total balance index, agility and return to previous activity.[15,40,42] An eccentric–concentric progressing to eccentric protocol (Silbernagel combined) seem also promising compared with an unspecific eccentric–concentric exercise.[40,68] The indication to work through pain was given in 16/29 studies, with unspecified pain intensity in 1 study,[43] slight pain permitted in 3/29,[48,55,56] pain allowance until 4/10 according to the Numeric Rating Scale (NRS) in one study,[54] and moderate–severe pain allowed in 11/29 studies. On the basis of the current studies, no evidence about the role of pain during exercise exists, although in no case it was harmful. The comparison between the Alfredson and a 'do-as-tolerated' EE programme did not detect a lower effectiveness of the customized regimen, although no follow-up was performed.[43] EE combined with ESWT is more effective than EE alone in midportion AT,[46] while in insertional tendinopathy ESWT leads to better and longer results in VISA-A score, pain rating and Likert scale compared with EE.[46] In insertional pain, CHELT therapy seem even more effective in terms of functional recovery and satisfaction, compared with ESWT.[47] Whole-body vibration might represent a treatment alternative option to EE, especially in insertional AT.[52] EE appears more effective than the association DTF/US.[48] Topical glyceryl trinitrate showed promising results in AT treatment in association with a composite exercise programme, including EE and stretching,

but further RCT including an untreated group are needed to strengthen these observations.[49,50] Autologous blood injections provided little or no advantage in addition to a standard EE programme and larger studies are needed to compare PRP injections to EE alone and to an untreated control group.[53–57] Aprotinin did not provide any additional benefit in association with EE.[67] Acupuncture seem promising in association with EE in patients with midportion AT, although more RCTs are needed to confirm this observation.[51]

Night splints did not show additional benefits relative to treatment with EE only and the EE regimen is more effective than splint-only treatment, reducing pain at 12 weeks' follow-up and accelerating return to sport.[58–60] Air Heel bracing is as equally effective as EE, representing a possible alternative treatment option, with no synergistic effect to EE.[61,62] Insoles have been proposed as a valid alternative to complex physiotherapy regimens including EE with promising results, although the only outcome measure evaluated was pain.[63] The role of LLLT remains controversial and more studies are needed to establish if it could provide additional benefit to the EE regimen.[64,65] Prolotherapy in addition to EE has shown to speed clinical remission and to be cost-effective, reducing the incremental cost per additional responder when compared with EE. However, the long-term VISA-A scores associated with the combination were similar to those recorded in the EE-only group.[66]

Patellar tendinopathy

PT is a common condition, in particular in sports implying frequent jumps (jumper's knee). The prevalence of PT reported in the literature is 45% in volleyball players and 32% in basketball players.[2]

The main characteristics of the studies included about EE in PT are summarized in Table 2. Most of the studies (10 of 13) employed EE performed on a decline board, a painful, slow EE training derived from the AT Alfredson protocol, whereas only one study adopted the eccentric drop squats (Stanish and Curwin) programme[69] and one study applied also heavy slow resistance (HSR) training.[70] For two studies description of the EE protocol adopted was

not available.[71,72] In all the 13 studies selected, EE groups were compared with control groups treated either with other therapeutic exercise protocols or with physical therapies different from exercise.

EE versus other forms of therapeutic exercise

Frohm *et al.* compared overload bilateral EE performed on the Brosman device with the eccentric protocol on a decline board, finding a significant improvement in VISA-score, functional parameters (extensor torque, one-leg triple hop) and VAS in both groups, without any statistically significant difference between them. At the end of the 12 weeks' trial, most patients from both groups returned to sports. No follow-up was performed apart from the 3 months' evaluation at the end of treatment.[73] When comparing the decline board protocol with drop squats, significant improvement in VISA-score and VAS were found in both groups. At 12 months the decline group reported a more favourable VISA scores, which was statistically significant.[74] However, when this EE programme was administered to volleyball players during the competitive season, no statistically significant improvement of VISA-P score was found.[74] Cannell *et al.*, comparing a CE protocol (leg extension and curl exercises) to EE, found improvement in pain and return to sport, quadriceps and hamstrings moment of force in both groups without statistically significant differences between them. No follow-up was available to evaluate long-term results.[69] Jonsson and Alfredson found striking superiority of EE compared with CE (both performed on a decline board) in terms of patient satisfaction, VAS and VISA score. At follow-up, satisfaction and return to sport were still present in the eccentric group, while all the concentric group had underwent surgery or sclerosing injections.[75]

EE performed with or without pain

Pain experience during exercise was considered in all the selected studies. In particular, all the studies but one recommended to work through pain.[69] The RCT by Alves da Cunha *et al.* compared the effect of a decline squat regimen performed with or without pain. An improvement in VISA-P e VAS scores from

Table 2 Eccentric exercise in Patellar Tendinopathy

Study ID	N patients (tendons)	Participants' characteristics	EE protocol	Work through pain (Y = yes/ N = no)	Physical activity (A = allowed, NA = not allowed)	Control group or additional therapy (CE, ESWT, splint, laser therapy)	PEDro score	Follow-up	Outcomes
Alves da Cunha *et al.* (2012)	17	Athletes	Squats on a 25° decline board (3 sets × 15 repetitions twice daily × 12 weeks)	Y (control group)	Not available	Performing the same exercise through pain	NA	None	Improvement of outcomes (VISA and VAS)in both groups with no significant difference between them
Bahr *et al.* (2006)	35(40)	Grade III-B PT referred for surgical treatment	Squats on a 25°decline board (3 sets × 15 repetitions twice daily × 12 weeks)	Y	NA for first 4 weeks (withdrawn from sports)	Surgical treatment followed by structured rehabilitation with gradual progression to EE	7	3, 6, 12 months	improvement in both groups; no difference between the 2 groups in return to sport and VISA score
Cannell *et al.* (2001)	19(19)	Athletes recruited from different sports	Eccentric drop squats (3 sets × 20)once a day 5 days/week	N	A	Leg extension/curl (CE)	NA	None	improvement in both groups; no statistically significant difference in VAS
Dragoo *et al.* (2014)	23	Patients from sport medicine clinic with persistence of symptoms of PT after 6 weeks of EE	5-phase programme outpatient twice week and home-based (posology is not specified)	Not available	Not available	PRP + EE (study group); PRP + dry needling (control group)	NA	3, 6, 9, 12, ≥26 weeks	Statistically significant VISA-P improvement only in the PRP group at 12 weeks, no statistically significant difference between groups at ≥26 weeks. Statistically significant Lysholm score improvement in the control group compared with the PRP group.
Frohm *et al.*(2007)	20	Athletes	EE with Brosman device, 4 sets × 4 reps, twice/ week × 12 weeks vs decline squats (25°, 3 sets × 15 reps, twice daily) × 12 weeks	Y	NA for first 6 weeks (withdrawn from sports)	EE with Brosman device, 4 sets × 4 reps, twice/ week × 12 weeks vs decline squats (25°, 3 sets × 15 reps, twice daily) × 12 weeks	6	None	Significant VISA-A improvement in both groups with no statistically significant difference between them
Jonsson *et al.* (2005)	15(19)	Recreational athletes recruited from a sports clinic performing different sports	Squats on a 25°decline board (3 sets × 15 repetitions twice daily × 12 weeks)	Y	NA for first 6 weeks (withdrawn from sports)	CE on a decline board	NA	Mean 32.6 months	Statistically significant difference in VAS and VISA score

Continued

Table 2 Continued

Study ID	N patients (tendons)	Participants' characteristics	EE protocol	Work through pain (Y = yes/ N = no)	Physical activity (A = allowed, NA = not allowed)	Control group or additional therapy (CE, ESWT, splint, laser therapy)	PEDro score	Follow-up	Outcomes
Konsgaard et al. (2009)	39()	Recreational athletes	Squats on a 25° decline board (3 sets × 15 repetitions twice daily × 12 weeks)	Y	A	Peritendinous corticosteroid injections vs EE vs HSR (Heavy Slow Resistance training	6	6 months	Comparable short-term VISA-P improvement; exercise groups had a better long-term outcome, with best clinical and collagen production gains in the HSR group, (no statistical analysis)
Stasinopoulos and Stasinopoulos (2004)	30(10)	Patients recruited from a rehabilitation and rheumatology clinic	EE (no decline board) + stretching, 3 sets × 15 repetitions 3 days per week	Y (stop when disabling)	Not available	Pulsed US, Transverse friction	5	4, 8, 16 weeks	Significant difference in patient satisfaction on pain in EE group
Steunebrink et al. (2013)	33	Clinical diagnosis of chronic PT <3 months, age 18–40 years,. Exclusion criteria: previous EE protocol ≤ last 2 years, VISA-P > 80, previous surgery or steroids, pregnancy	EE on a 15–30°decline board in a home setting (3 sets × 15 repetitions twice daily × 12 weeks)	<5 of VAS	Avoid weight bearing during the first 4 weeks, gradual return after 4 weeks	Topical Glyceril trinitrate (GTN)	NA	6, 12, 24 weeks	No statistically significant clinical improvement in GTN group compared with placebo group
Van der Worp et al. (2013)	43 (57)	Patients from sport medicine clinic	Squats on a 25° decline board (3 sets × 15 repetitions twice daily × 12 weeks)	Y (around 4 on VAS)	Reduce sport activities during the treatment and the first weeks after treatment	21 patients (31 tendons): FSWT; 22 (26): RSWT.	NA	None	Statistically significant improvement in VISA-P and secondary outcomes in both groups, with no statistically significant difference between them.
Visnes et al. (2005)	29(29)	Elite athletes recruited from high-level volleyball, intervention during the season	Squats on a 25° decline board (3 sets × 15 repetitions twice daily × 12 weeks)	Y	A	Regular sports training, no special programme	7	6 weeks, 6 months	No significant difference in VISA score
Warden et al. (2008)	37	Patients with clinical or radiological diagnosis of PT	Daily EE programme based on the best practice (description not available) × 12 weeks	Not available	Not available	LIPUS vs sham-LIPUS	NA	None	LIPUS did not provide any statistically significant advantage compared with inactive-LIPUS
Young et al. (2005)	17	Elite athletes recruited from high-level volleyball, intervention out of season	Squats on a 25° decline board (3 sets × 15 repetitions twice daily × 12 weeks)	Y	A	Decline squats vs EE drop squats onto a step (3 sets × 15 repetitions twice daily × 12 weeks	6	Throughout the 12 weeks, 12 months	Improvement in both groups, no significant difference in VISA score

baseline was reported in both groups, with no statistically significant difference between them. No follow-up was available, thus the interpretation of these results is controversial.[76]

EE versus surgery

In the RCT by Bahr *et al.,* 35 patients with severe PT (40 tendons) were randomized to a group of patients undergoing surgery (20 tendons) and a group receiving an EE programme (20 tendons). At 20 months' follow-up, both groups had an improvement in VISA-P, without any statistically significant difference between the groups, suggesting that the EE regimen should be tried for 12 weeks before referring the patient for surgery.[77]

Other treatments

Stasinopoulos and Stasinopoulos found striking superiority of EE performed for 4 weeks, compared with pulsed US and DTF, with 100% success in the EE group. The limitations of this study are the non-validated outcome measure (subjective evaluation of pain) and the lack of an untreated control group, necessary to rate the absolute effectiveness of the three treatments.[78] Konsgaard *et al.* randomized 39 patients with chronic PT in three distinct groups treated with EE, HSR exercise and ultrasound-guided peritendinous steroid injections. All the three groups showed significant short-term (12 weeks) VISA-P improvement from the baseline. However, at 6 months' follow-up, only the exercise groups maintained this result. The group treated with corticosteroid injections and the HSR group had a statistically significant decrease of tendon swelling and vascularization at 12 weeks. The HSR group had both relevant short term results, and the best long-term outcome, with an elevated collagen turnover and the best clinical outcome in terms of patient satisfaction, although small numbers precluded statistical analysis.[70] Platelet-rich plasma was proposed in association with EE for the treatment of PT, retrieving significantly superior results in term of VISA-P at short term (12 weeks), but not at long term (≥26 weeks) follow-up. In addition, the control group (receiving EE and US-guided dried needle) retrieved statistically significant superior

results in the Lysholm knee scale compared with the PRP group.[72] Three patients from the control group and no patient from the PRP group failed treatment and crossed over. These results suggest that PRP may provide additional benefit to an EE programme in patients with PT, but this effect is not long lasting. This study is limited by the absence of an untreated control group and by the poor description of the EE protocol.[72] Low-intensity pulsed ultrasound (LIPUS) in association with EE in a group of patients with PT did not show any additional benefit compared with the placebo group, although patients were evaluated for outcome measures only at the end of treatment.[71] Topical glyceril trinitrate did not provide statistically superior clinical improvements compared with placebo in patients with PT treated with an EE programme on a decline board at any of the follow-up evaluations (6, 12 and 24 weeks).[79]

Extracorporeal-focused shockwave therapy (FSWT) was compared with radial shockwave therapy (RSWT) in two groups of patients with PT both treated with an EE training programme. No statistically significant difference in VISA-P and in the secondary outcome measures (pain during ADL, sport and EE) was detected between FSWT and RSWT and all the outcome measures improved significantly from the baseline in both groups. No follow-up was available because the last assessment was performed at the end of the EE programme.[80]

Effectiveness of EE in PT

In conclusion, when compared with other therapies, EE alone was associated with significantly better outcome in only 2 of 11 studies about PT. However, in 11 of 13 studies EE determined an improvement from the baseline and in no case was it harmful. In 2 studies, EE is associated with other treatments, and a comparison with an untreated control group is missing.[72,80]

The quality of studies was variable and 7 of 13 studies were not rated in the PEDro database; the mean PEDro score was 7.6/10. Two of 13 studies were available only in abstract form. Five of 13 studies only evaluated patients at the end of the EE protocol. The bilateral training performed through the Brosman device has comparable results of those

obtained using a decline board.[73] The decline squat protocol seems more promising than the step squat protocol in athletes who need to continue training and physical activity. Both EE and CE (leg extension/curl exercises) seem equally effective in terms of pain reduction and return to sport in jumper's knee.[69] Jonsson and Alfredson found a dramatic superiority of an EE regimen compared with a CE programme, both performed on a decline surface.[75] In 2[74,75] of 10 studies of EE performed on a decline board, this protocol showed superior effectiveness in terms of VISA score, VAS and/or patient satisfaction or return to activity. Pain during exercise should not be regarded as a positive prognostic factor.[76] When comparing EE with HSR training and corticosteroid injections, HSR training was the most successful, while EE was effective only on VISA-P and VAS; corticosteroid treatment was effective on VISA, VAS-P, tendon swelling and vascularization. The positive clinical outcomes of this study are associated with improved neuromuscolar performance on one hand, reduced Doppler area, anteroposterior diameter and increased collagen turnover on the other hand.[68,70] Shock wave therapy (SWT) has limited evidence of prescription in PT, and no statistically significant difference has been found between FSWT and RSWT and between EE and SWT versus EE alone.[80] Neither LIPUS,[71] nor topical glyceril trinitrate[79] seem useful for treatment of PT in association with EE. Most of the studies considered adopted sport cessation during the EE programme, as recommended by recent reviews.[81,82] However, other authors stated that sport withdrawal should not be a dogma,[83] since only one study showed a probable negative effect of continuing sport during the rehabilitation protocol.[84] The 3 RCTs considered for this review in which concomitant sport was allowed, did not report any disadvantage due to sport activity.[69,70,74] Compared with surgery, EE in severe PT did not show statistically significant differences in VISA score and pain;[77] thus, an EE protocol should always be tried before surgery.

Lateral Epicondyle Tendinopathy

Lateral epicondyle tendinopathy (LET), also known as lateral epicondylosis or tennis elbow represents up to 40% of all elbow injuries in tennis players. The prevalence of LET is noteworthy (up to 15%) also in workers performing repetitive movements of the hand and upper limb.[2] This condition is usually located in the dominant arm in association with quick, repetitive eccentric contractions and gripping movements of the wrist. Although no ideal treatment exists, EE and other types of therapeutic exercise are often employed. A recent systematic review has demonstrated the effectiveness of resistance exercise in LET, but that search was confined to studies published before December 2010.[85] Nine RCTs in total comparing EE with other treatment options for LET were retrieved, and the results reported in Table 3. Slater *et al.* found that EE, with or without association with CE, leads to a decrease of the pressure pain threshold, recorded at three sites (the common extensor origin at the lateral epicondyle, the musculo-tendinous junction of extensor carpi radialis brevis muscle and the radial head as a control site), but has no effect on muscle strength and endurance compared with baseline.[86] This study supports the role of EE in LET, but was not included in the review because the outcome of treatment was measured on healthy subjects.

EE versus no treatment

In the RCT by Peterson *et al.*, 81 patients with chronic LET were randomized to two groups (study group performing EE and control group represented by the waiting list to the same protocol). During the 3 months' trial period, a statistically significant decrease of pain (Cozen's test and modified empty-can test) was detected in the exercise group compared with the baseline and to the control group; no statistically significant difference between the exercise and the untreated group in muscle strength, DASH score and in quality of life was found. The maintenance of these promising results was not verified, as no follow-up was performed.[87] When an EE protocol was associated with a forearm band, significantly higher pain-free hand-grip and wrist-extensor strength were found at the end of the EE regimen, compared with the forearm band only treatment. No follow-up was performed.[88]

Table 3 Eccentric Exercise in Lateral Elbow Tendinopathy

Study ID	N patients (tendons)	Participants' characteristics	EE protocol	Work through pain (Y = yes/N = no)	Physical activity (A = allowed, NA = not allowed)	Additional therapy (CE, ESWT, splint, laser therapy,	PEDro score	Follow-up	Outcomes
Martinez-Silvestrini et al. (2005)	94	50 M, 44 F, age 44.5 symptom duration >3 months	Slow wrist flexion starting from a prone, full extension wrist position using an elastic band held by a handle and fixed on the floor with the ispilateral foot, lengthening the band with the opposite hand to avoid resistance concentric contraction; 3 sets × 10 reps, once daily, with 2–5 min rest between sets	N	Avoidance of aggravating activities	Stretching (first group) vs stretching + EE (second) vs stretching + CE (third group). All subjects received also icing.	6	none	No significant differences btw 3 groups in terms of pain-free grip strength, Patient-rated Forearm Evaluation Questionnaire, Disabilities of the Arm, Shoulder and Hand Questionnaire (DASH), SF-36 and VAS.
Nagrale et al. (1996)	60	Age 30–60 years, epicondylalgia >1 months	Seated position, full elbow extension, forearm pronation: from maximum wrist extension slow flexion for a count of 30, using contralateral hand to return to maximum extension; progressive load increasing using free weights; 3 sets × 10 reps; 1 min rest btw sets	Y (stop when disabling)	Remain as active as possible, avoiding symptom provoking activities	Supervised exercise (stretching + EE) + phonophoresis with diclofenac gel vs Cyriax physiotherapy (DTF + Mill's manipulation)	6	none	Superior outcome (Vas, pain-free grip strength, Tennis Elbow Function Scale) of Cyriax physiotherapy

Continued

Table 3 Continued

Study ID	N patients (tendons)	Participants' characteristics	EE protocol	Work through pain (Y = yes/N = no)	Physical activity (A = allowed, NA = not allowed)	Additional therapy (CE, ESWT, splint, laser therapy,	PEDro score	Follow-up	Outcomes
Peterson et al.(2011)	81	Almost 40% F, mean age 48 years, epycondilalgia lasting for >3 months	Seated on armchair with forearm support, lifting and lowering a liquid container (with variable weight in it), 3 sets × 15 reps, twice daily × 12 weeks.	Not available	A (ordinary daily activities)	Exercise (CE + EE) vs wait-list	7	none	Greater regression of pain during maximum voluntary contraction (Cozen's test) and during maximum elongation with a load (modified Empty-can test) in the exercise group; no significant difference in muscle strength and no difference in DASH score and Gothenburg Quality of Life Questionnaire
Soderberg et al. (2011)	37	Pain around the lateral epicondyle ≥1 month, pain at palpation of the lateral epicondyle and positive results in ≥2/3 pain-provocation tests;	Eccentric training of the forearm using a bucket of water as a resisted weight for 6 weeks. 8–12 reps once/day during first week, twice/ day the following 2 weeks, at third week 3 × 8–12 reps twice/ day	N	Not available	Forearm band	6	none	Significantly higher pain-free hand-grip and wrist-extensor strength at the end of the EE regimen, compared with the forearm band only treatment
Svernlov et al.(2001) (pilot study)	31	13 M, 2 F, mean age 46.3, mean symptom duration 14.2 weeks	Wrist flexion from a complete extension starting position, flexed elbow with a fillable dumb-bell in the hand (3 sets × 5 reps × 12 weeks)	N	Patients were encouraged to use the affected arm in the usual activities as much as the pain allowed	EE vs stretching programme (both groups were given also a forearm support and wrist bands)	4	6 months	Reduced VAS in both groups, improved grip strength and patient self-rating was more significant in the EE compared with the stretching group

Svernlov et al.(2001) (clinical study)	129	57 M, 72 F, mean age 46 years, symptom duration 19.4 (patients were divided into 2 groups Group 1 with symptoms <1 year, Group 2 with symptoms >1 year)	Wrist flexion from a complete extension starting position, flexed elbow with a fillable dumb-bell in the hand (3 sets × 5 reps × 12 weeks)	N	Patients were encouraged to use the affected arm in the usual activities as much as the pain allowed	Same EE protocol in the 2 groups	4	3.4 years	Improvement in VAS and grip strength in both groups without statistical significant difference
Tyler et al. (2010)	21 (21)	Chronic unilateral lateral epicondylosis	Isolated eccentric training obtained with an inexpensive rubber bar which is twisted during flexion of the uninvolved wrist and untwisted with affected wrist eccentric extension (duration: 4 s), 3 sets × 15 reps, 30′rest periods btw sets, twice daily; duration of treatment individualized on the patient symptoms	Not available	Not available	EE vs standard treatment (isotonic wrist extensor strengthening). Both groups had also stretching, US, cross friction massage, heat and ice	5	none	Major improvement of all outcome measures (DASH, VAS, tenderness, strength) in EE group compared with standard treatment
Viswas et al. (2012)	20	Lateral epicondylitis	Seated position, full elbow extension, forearm pronation: from maximum wrist extension slow flexion for a count of 30, using contralateral hand to return to maximum extension; progressive load increasing using free weights; 3 sets × 10 reps; 1 min rest btw sets; 3 times/week × 4 weeks	Y (stop when disabling)	Activity modification to avoid aggravation of symptoms	Supervised exercise programme (stretching + EE) vs Cyriax physiotherapy	6	none	Major improvement of VAS and Tennis Elbow Function Scale (TEFS) improvement in EE vs Cyriax group
Wen et al. (2011)	28	Age older than 18 years; lateral elbow pain for at least 4 weeks; physical examination evidence of lateral epicondylosis,	Extension of the involved wrist under resistance for 6 to 8″ (3 sets × 5 reps × 12 weeks)	The participants were warned that the exercises would be quite painful.	Not available	Control group: local treatment as iontophoresis ultrasound or other modalities, wrist extensor stretching	3	4, 8, 12, 16, 20 weeks	Both groups improved their pain scores from baseline to the 4-week time point, with no statistically significant differences between groups at any follow-up time point

EE versus other forms of therapeutic exercise

Martinez-Silvestrini *et al.* found no superiority of treatment with EE when compared with concentric strengthening and stretching in all the outcomes considered (pain-free grip strength, patient-rated forearm evaluation questionnaire, DASH, SF-36 and VAS, evaluated only at 2 weeks and at the end of the 6 weeks' trial). In fact, all the three protocols determined a statistically significant improvement, without any statistically significant difference between them.[88] Svernlov and Adolfsson published a pilot study indicating the superiority of EE over a stretching regimen. An improvement of pain and grip strength compared with the baseline was seen in both treatment groups, but in the intergroup comparison, patient's self-rating and grip strength were significantly higher at 6 months in the EE than in the CE group. In a larger population, the authors compared the effectiveness of EE in patients with symptoms of LET lasting for more and less than one year respectively. EE produced a statistically significant effectiveness in terms of patient self-rating, VAS and grip-strength irrespective of duration of symptoms, even after a long follow-up (3.4 years).[89] Tyler *et al.* showed a statistically superior improvement of DASH, VAS, tenderness and strength after a novel isolated eccentric wrist exercise obtained with the use of an inexpensive rubber bar than after an isotonic strengthening standard programme. The non-homogeneous duration of treatment and the absence of follow-up limit the interpretation of the results.[90] Wen *et al.* randomized 28 patients with LET to a group performing eccentric strengthening and to a stretching programme group. At the 4 weeks follow-up, both groups had improved their pain scores from the baseline. At all the follow-up considered, no statistically significant difference was found between the two groups. The wide variability in the control treatment limits the interpretation of this trial.[91]

EE versus Cyriax physiotherapy

Nagrale *et al.* found a statistically significant superiority in the outcomes considered (VAS, pain-free grip strength and Tennis Elbow Function Scale) of Cyriax physiotherapy, a protocol for lateral epycondialgia based on DTF combined with Mill's manipulation, compared with an association between supervised EE and phonophoresis. Both treatment groups, however, showed a statistically significant improvement in the outcome measures examined from baseline.[92] Conversely, Viswas *et al.* found a better outcome for a supervised exercise programme consisting in EE and stretching compared with the Cyriax regimen. Although both groups showed significant reduction in pain and improvement of function from the baseline, intergroup comparison showed a higher reduction in VAS and TEFS scores in the EE group than in the Cyriax group, which was statistically significant.[93] The absence of a follow-up limits the evidence of the two studies about Cyriax physiotherapy included in this review.

Effectiveness of EE in LET

According to the PEDro database, the mean rating score was 5.2/10. There was large variation in posology of EE, treatment duration, clinical or home setting and pain experience during training between studies. One of nine studies was available only in abstract form. Six of nine studies did not perform a follow-up, evaluating patients only at the end of the treatment. In all studies, EE produced an improvement of LET from the baseline. When compared with other therapies, EE was associated with a significantly better outcome in only two of nine studies. In particular, EE in LET seems more effective than isotonic strengthening, while the superiority of EE against wrist extensor stretching is controversial.[89,90] Whether supervised EE is more effective than Cyriax programme, it is still not clear,[92,93] but EE should be adopted as first-line choice for LET. In conclusion, the evidence of effectiveness of EE in LET in comparison with other treatments is low. There was large inconsistency about pain prescription during exercise and no indication in this sense can be provided. These results, in contrast with those reported for AT, might be attributed to the different functional and anatomic characteristics of the therapeutic targets, as above mentioned. Nevertheless, the superiority of EE versus no treatment[87,88] and the absence of

worsening induced by this regimen should encourage physicians to experiment it also in this field.[94]

Other tendinopathies and sports injuries

Shoulder tendinopathy

The review by Zandt et al. suggested that EE may act a promising role when applied to upper extremities, although the frequent involvement of soft tissues surrounding the tendon might limit the effectiveness of this technique.[95] Only one RCT supports the role of EE in supraspinatus tendinopathy. In this study, 104 patients with subacromial impingement were randomized to two groups. The study group was treated with rotator cuff strengthening EEs and concentric/eccentric exercises for the scapula stabilizers, with increased external load performed in 5 or 6 sessions during 12 weeks. Patients were expected to work through pain, but without exceeding a grade of 5/10 on the VAS pain scale. The control group performed non-specific exercises for the neck and shoulder without loading and without any intensification during the training period. Statistically significant greater improvement was observed in the study group compared with the control group for Constant-Murley Score, DASH score, VAS scores for pain during the night, health-related quality of life, patient global assessment and refer to surgery. No statistically significant difference was found between the two groups concerning VAS scores for pain, pain during activity or at rest, or for EQ-VAS.[96]

Adductor tendinopathy and groin pain

The etiologic diagnosis of groin pain is both challenging and mandatory for a correct treatment.[97] Therapeutic options range from conservative treatment, based on strengthening exercise programs, to surgical procedures (adductor tenotomy, abdominal wall repair, neurotomy of the ilioinguinal and/or iliohypogastric nerve).[98] Most adductor strains are incomplete tears close to the musculotendinous junction occurring especially in male soccer and ice hockey players and often evolving in chronic tendinopathy; their diagnosis and treatment should be initiated early. For biomechanical reasons, the adductor longus is the most commonly affected tendon accounting for up to 62% of groin strains. Groin strains represent ~10% of all injuries in professional ice hockey players throughout the world, and 13% of all injuries in soccer players in Scandinavia, with an incidence between 10 and 18 injuries per 100 soccer players.[98–101] Eccentric strengthening of the adductor muscles is well-established in the prevention of groin injuries in soccer players.[102,103] However, only two RCTs support EE in the rehabilitation of adductor strains. Holmich et al. compared an active training programme, including eccentric strengthening and core stability, with a passive treatment programme, based on laser therapy, transverse friction massage, stretching and TENS. The treatment group showed significantly superior results compared with the passive regimen in terms of distribution of outcomes (pain at palpation, pain during adduction against resistance; groin pain in connection with sport performed at the same level as before injury; pain-free ad successful return to sport), subjective global assessment and adduction strength. In particular, return to activity without pain was obtained in 79% of the athletes in the active group compared with 14% in the passive regimen. This study was rated 8/10 in the PEDro score system.[104] In a 8–12 year' follow-up study (PEDro score 5/10),[105] the authors detected a significant long lasting effect of active training especially in the subgroup of soccer players. The eccentric programme included one-foot exercises on sliding board, with parallel and 90° angle feet, leg abduction and adduction exercises lying on side and standing, coordination exercises swinging arms and flexing and extending knee. The group analysed was homogeneous for age, sports activity, reasons for activity reduction, or time to follow-up. Weir et al. compared the exercise treatment proposed by Holmich et al. to a multi-modal treatment (MMT), including heat, manual therapy, stretching and return to running programme. The MMT showed a statistically significant superiority in timing of return to sports. However, there was no statistically significant difference between the two groups in terms of objective treatment outcome and VAS pain score. This study was rated 7/10 in the PEDro score system. In conclusion, the two RCTs available about EE in long-standing

groin pain reported a beneficial effect of both an eccentric training programme, associated with core stability and of a multi-modal approach.[106]

The beneficial effects of the active training programme might be attributed not necessarily to a direct effect on the tendon or the entheses, but rather to eccentric and core strengthening, which leads to increased ability to control and stabilize, a quality crucial to production, transfer, and control of force and motion in physical activity.[105] According to Weir *et al.*, however, neither treatment was very effective, and a combination of both protocols might be more successful and should be investigated in future RCTs.[106]

ACL strains

EE plays an important role in rehabilitation after ACL reconstruction. Also after surgical treatment of meniscal tears,[107] a specific rehabilitation protocol is essential to recover quadriceps function and prevent degenerative conditions. Only one RCT was found in the literature about eccentric training in rehabilitation of ACL injuries, with a PEDro score rating of 5/10.[108] In this trial, 40 patients who underwent ACL reconstruction were randomized to a study group receiving early progressive EE and to a control group treated with standard rehabilitation, for a trial period of 12 weeks. At 12 months' follow-up, 32 patients completed the whole assessment. Quadriceps femoris muscle volume and strength, gluteus maximus volume and hopping distance increased significantly from the baseline in both groups, but the improvement was significantly superior in the study group compared with the control group. Although an eccentric training programme seems more effective than CE for developing quadriceps strength, an association between EE and neuromuscular training has been proposed to improve the outcomes.[109]

Hamstrings strains

Hamstring strains occur during sharp turns or cutting in ball sports, or when running at full speed in sprinting.[109] As well as for the adductor muscles, eccentric strengthening is considered effective in the prevention of hamstrings injuries, since they are associated with an eccentric strength deficit of the

hamstrings and weakness during concentric action of the hip extensors in elite sprinters.[110–113]

Despite these considerations, only one randomized clinical trial was found about eccentric training in hamstrings injuries rehabilitation, with a PEDro score rating 4/10. In this trial, 29 patients with a history of hamstring injury within the prior ten days were evaluated with MRI and physical examination, and then randomized to a group receiving progressive agility and trunk stabilization, and a control group performing progressive running and eccentric strengthening. During the trial period and in the following 6 months, the rate of re-injury was low (4/29 patients), and 25 patients completed the whole assessment. At the time of return to sport (individualized on the recovery of function, improvement of pain and self-perception of each patient), all patients gained a nearly complete resolution of pain and recovery of isometric muscle strength, although no subject exhibited a complete morphological resolution of injury (evaluated with MRI). No statistically significant difference in the outcome measures was found between the two groups.[114]

Conclusion

To our knowledge, only one review has systematically analysed the effectiveness of EE in various sites of tendinopathies to date.[10] However, this study did not specifically address the effectiveness of EE in supraspinatus, hamstring strain and adductor-related groin pain. The review by Wasielewski and Kotsko[13] was restricted to AT and PT. Moreover, since 2006 several new studies tested the validity of EE at the traditional sites of application, but also in other less well-known therapeutic targets. The latest reviews available do not summarize their results systematically.[2,68,115] This review presents a comprehensive insight in the most up-to-date evidence in support of EE in sports injuries, intended as traditional targets and possible emerging fields of application. The conclusions of our review are limited by the volume and quality of the literature available. In many cases, the literature reviewed is affected by large variability and lack of high-level evidence. Association of EE with other treatments in absence

of an untreated control group limited the analysis of effectiveness of EE in many studies. Therefore, research about tendinopathies could be improved by adoption of strict and homogeneous diagnostic criteria based on clinical and ultrasound evaluation, which should be performed before referring patients to any treatment protocol. On the other hand, we did not include a statistic analysis to support the evidence of our review. Our results can be summarized in two key messages: first, EE programs are widely used in the rehabilitation of midportion Achilles and patellar tendon injuries with a successful outcome. Second, although little evidence is available, EE seems promising also in the management of other sites of sports-related tendinopathies (lateral epicondyle, supraspinatus) and lower limb muscle and ligament strains. Regarding the first point, more RCTs are needed to compare the existing protocols and establish the possible relative effectiveness of different dosages, in terms of load, speed, amount of repetitions and pain experience. For PT, along with the eccentric decline squat training, HSR protocol performed with some degree of discomfort and without suspending sport activity, seem associated to a good short- and long-term clinical outcome and to regression of tendinopathic changes and increase in collagen turnover.[68,70] For chronic midportion AT, evidence supports the association between EE and ESWT.[45] According to a recent review, isolated eccentric muscle training and the Silbernagel combined protocol seem equally effective for AT treatment.[40,68] There was large inconsistency about the indication of working through pain between studies. Exercise for PT is usually prescribed through pain, although the only RCT comparing exercise with or without pain to date appears not conclusive. No indication can be provided about pain allowance during EE in the other sites of tendinopathies. Concerning the second point, given the lack of RCTs, there is a need for high quality studies, investigating whether EE protocols can be successfully applied to other sites of tendinopathies, ligaments and muscle strains, or if their effectiveness is restricted, to the above-mentioned well-known targets. This restriction could be based on biomechanical and loading characteristics, which could be exclusive of patellar and Achilles muscular–tendon unit.

Preliminary studies suggest that EE might be promising also in other fields, but no conclusive evidence can be extrapolated when EE is administrated together with other forms of therapeutic exercise. EE is a fundamental therapeutic resource for the treatment of AT and PT and may represent a promising and feasible tool for the conservative management of other sites of tendinopathies, ligaments and muscle strains.

References

1. Skjong CC, Meininger AK, Ho SS. Tendinopathy treatment: where is the evidence?. *Clin Sports Med* 2012;31:329–50.
2. Murtaugh B, Ihm JM. Eccentric training for the treatment of tendinopathies. *Curr Sports Med Rep* 2013;12:175–82.
3. Rees JD, Lichtwark GA, Wolman RL, et al. The mechanism for efficacy of eccentric loading in Achilles tendon injury; an in vivo study in humans. *Rheumatology (Oxford)* 2008;47:1493–7.
4. 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.
5. Maffulli N, Longo UG, Loppini M, et al. Current treatment options for tendinopathy. *Expert Opin Pharmacother* 2010;11:2177–86.
6. Frizziero A, Bonsangue V, Trevisan M, et al. Foot tendinopathies in rheumatic diseases: etiopathogenesis, clinical manifestations and therapeutic options. *Clin Rheumatol* 2013;32:547–55.
7. Torricelli P, Veronesi F, Pagani S, et al. In vitro tenocyte metabolism in aging and oestrogen deficiency. *Age (Dordr)* 2013;35:2125–36.
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, 2474–12–20.
9. 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.
10. Woodley BL, Newsham-West RJ, Baxter GD. Chronic tendinopathy: effectiveness of eccentric exercise. *Br J Sports Med* 2007;41: 188–99.
11. Maffulli N, Longo UG, Denaro V. Novel approaches for the management of tendinopathy. *J Bone Joint Surg Am* 2010;92:2604–13.
12. Andres BM, Murrell GA. Treatment of tendinopathy: what works, what does not, and what is on the horizon. *Clin Orthop Relat Res* 2008;466:1539–54.

13. Wasielewski NJ, Kotsko KM. Does eccentric exercise reduce pain and improve strength in physically active adults with symptomatic lower extremity tendinosis? A systematic review. *J Athl Train* 2007;42:409–21.

14. Alfredson H, Pietila T, Jonsson P, et al. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. *Am J Sports Med* 1998;26:360–6.

15. Mafi N, Lorentzon R, Alfredson H. Superior short-term results with eccentric calf muscle training compared to concentric training in a randomized prospective multi-center study on patients with chronic Achilles tendinosis. *Knee Surg Sports Traumatol Arthrosc* 2001;9:42–7.

16. Meyer A, Tumilty S, Baxter GD. Eccentric exercise protocols for chronic non-insertional Achilles tendinopathy: how much is enough?. *Scand J Med Sci Sports* 2009;19:609–15.

17. Maffulli N, Longo UG. How do eccentric exercises work in tendinopathy? *Rheumatology (Oxford)* 2008;47:1444–5.

18. Arampatzis A, Karamanidis K, Albracht K. Adaptational responses of the human Achilles tendon by modulation of the applied cyclic strain magnitude. *J Exp Biol* 2007;210(Pt 15):2743–53.

19. Scott A, Alfredson H, Forsgren S. VGluT2 expression in painful Achilles and patellar tendinosis: evidence of local glutamate release by tenocytes. *J Orthop Res* 2008;26:685–92.

20. Andersson G, Danielson P, Alfredson H, et al. Presence of substance P and the neurokinin-1 receptor in tenocytes of the human Achilles tendon. *Regul Pept* 2008;150:81–7.

21. Alfredson H, Lorentzon R. Intratendinous glutamate levels and eccentric training in chronic Achilles tendinosis: a prospective study using microdialysis technique. *Knee Surg Sports Traumatol Arthrosc* 2003;11:196–9.

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

23. Ohberg L, Lorentzon R, Alfredson H. Eccentric training in patients with chronic Achilles tendinosis: normalised tendon structure and decreased thickness at follow up. *Br J Sports Med* 2004;38:8–11.

24. Alfredson H. Conservative management of Achilles tendinopathy: new ideas. *Foot Ankle Clin* 2005;10:321–9.

25. Allison GT, Purdam C. Eccentric loading for Achilles tendinopathy--strengthening or stretching? *Br J Sports Med* 2009;43:276–9.

26. Kramer R, Lorenzen J, Vogt PM, et al. Systematic review about eccentric training in chronic achilles tendinopathy. *Sportverletz Sportschaden* 2010;24:204–11.

27. Silbernagel KG. Does one size fit all when it comes to exercise treatment for achilles tendinopathy? *J Orthop Sports Phys Ther* 2014;44:42–4.

28. Stasinopoulos D, Manias P. Comparing two eccentric exercise programmes for the management of Achilles tendinopathy. A pilot trial. *J Bodyw Mov Ther* 2013;17:309–15.

29. Fahlstrom 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.

30. Jonsson P, Alfredson H, Sunding K, et al. 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.

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

32. Grigg NL, Wearing SC, Smeathers JE. Eccentric calf muscle exercise produces a greater acute reduction in Achilles tendon thickness than concentric exercise. *Br J Sports Med* 2009;43:280–3.

33. Kjaer M, Heinemeier KM. 4. Eccentric exercise: Acute and chronic effects on healthy and diseased tendons. *J Appl Physiol (1985)* 2014; Jan 16.

34. Komi PV, Buskirk ER. Effect of eccentric and concentric muscle conditioning on tension and electrical activity of human muscle. *Ergonomics* 1972;15:417–34.

35. Frohm A, Saartok T, Halvorsen K, et al. Eccentric treatment for patellar tendinopathy: a prospective randomised short-term pilot study of two rehabilitation protocols. *Br J Sports Med* 2007;41:e7.

36. Deans VM, Miller A, Ramos J. A prospective series of patients with chronic Achilles tendinopathy treated with autologous-conditioned plasma injections combined with exercise and therapeutic ultrasonography. *J Foot Ankle Surg* 2012;51:706–10.

37. Shalabi A, Kristoffersen-Wilberg M, Svensson L, et al. Eccentric training of the gastrocnemius-soleus complex in chronic Achilles tendinopathy results in decreased tendon volume and intratendinous signal as evaluated by MRI. *Am J Sports Med* 2004;32:1286–96.

38. van der Plas A, de Jonge S, de Vos RJ, et al. 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.

39. Nilsson-Helander K, Silbernagel KG, Thomee R, et al. Acute achilles tendon rupture: a randomized, controlled study comparing surgical and nonsurgical treatments using validated outcome measures. *Am J Sports Med* 2010;38:2186–93.

40. Silbernagel KG, Thomee R, Thomee P, et al. Eccentric overload training for patients with chronic Achilles tendon pain–a randomised controlled study with reliability testing of the evaluation methods. *Scand J Med Sci Sports* 2001;11:197–206.

41. Norregaard J, Larsen CC, Bieler T, et al. Eccentric exercise in treatment of Achilles tendinopathy. *Scand J Med Sci Sports* 2007;17:133–8.

42. Yu J, Park D, Lee G. Effect of eccentric strengthening on pain, muscle strength, endurance, and functional fitness factors in male patients with Achilles tendinopathy. *Am J Phys Med Rehabil* 2013;92:68–76.

43. Stevens M, Tan CW. Effectiveness of the alfredson protocol compared with a lower repetition-volume protocol for midportion Achilles tendinopathy: a randomized controlled trial. *J Orthop Sports Phys Ther* 2014;44:59–67.

44. Rompe JD, Nafe B, Furia JP, et al. Eccentric loading, shock-wave treatment, or a wait-and-see policy for tendinopathy of the main body of tendo Achillis: a randomized controlled trial. *Am J Sports Med* 2007;35:374–83.

45. Rompe JD, Furia J, Maffulli N. Eccentric loading versus eccentric loading plus shock-wave treatment for mid-portion Achilles tendinopathy: a randomized controlled trial. *Am J Sports Med* 2009;37:463–70.

46. Rompe JD, Furia J, Maffulli N. Eccentric loading compared with shock wave treatment for chronic insertional Achilles tendinopathy. A randomized, controlled trial. *J Bone Joint Surg Am* 2008;90:52–61.

47. Notarnicola A, Maccagnano G, Tafuri S, et al. CHELT therapy in the treatment of chronic insertional Achilles tendinopathy. *Lasers Med Sci* 2013; Dec 19.

48. Herrington L, McCulloch R. The role of eccentric training in the management of Achilles tendinopathy: A pilot study. *Physical Therapy in Sport* 2007;8:191–6.

49. Paoloni JA, Appleyard RC, Nelson J, et al. Topical glyceryl trinitrate treatment of chronic noninsertional achilles tendinopathy. A randomized, double-blind, placebo-controlled trial. *J Bone Joint Surg Am* 2004;86-A: 916–22.

50. Hunte G, Lloyd-Smith R. Topical glyceryl trinitrate for chronic Achilles tendinopathy. *Clin J Sport Med* 2005;15:116–7.

51. Zhang BM, Zhong LW, Xu SW, et al. Acupuncture for chronic Achilles tendnopathy: a randomized controlled study. *Chin J Integr Med* 2013;19:900–4.

52. Horstmann T, Jud HM, Frohlich V, et al. Whole-body vibration versus eccentric training or a wait-and-see approach for chronic Achilles tendinopathy: a randomized clinical trial. *J Orthop Sports Phys Ther* 2013;43:794–803.

53. Pearson J, Rowlands D, Highet R. Autologous blood injection to treat Achilles tendinopathy? A randomized controlled trial. *J Sport Rehabil* 2012;21:218–24.

54. Bell KJ, Fulcher ML, Rowlands DS, et al. Impact of autologous blood injections in treatment of mid-portion Achilles tendinopathy: double blind randomised controlled trial. *Bmj* 2013;346:f2310.

55. de Vos RJ, Weir A, van Schie HT, et al. Platelet-rich plasma injection for chronic Achilles tendinopathy: a randomized controlled trial. *Jama* 2010;303:144–9.

56. de Jonge S, de Vos RJ, Weir A, et al. One-year follow-up of platelet-rich plasma treatment in chronic Achilles tendinopathy: a double-blind randomized placebo-controlled trial. *Am J Sports Med* 2011;39:1623–9.

57. Kearney RS, Parsons N, Costa ML. Achilles tendinopathy management: A pilot randomised controlled trial comparing platelet-richplasma injection with an eccentric loading programme. *Bone Joint Res* 2013;2:227–32.

58. de Jonge S, de Vos RJ, Van Schie HT, et al. 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.

59. de Vos RJ, Weir A, Visser RJ, et al. The additional value of a night splint to eccentric exercises in chronic midportion Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2007;41:e5.

60. Roos EM, Engstrom M, Lagerquist A, et al. Clinical improvement after 6 weeks of eccentric exercise in patients with mid-portion Achilles tendinopathy—a randomized trial with 1-year follow-up. *Scand J Med Sci Sports* 2004;14:286–95.

61. Knobloch K, Schreibmueller L, Longo UG, et al. Eccentric exercises for the management of tendinopathy of the main body of the Achilles tendon with or without an AirHeel Brace. A randomized controlled trial. B: Effects of compliance. *Disabil Rehabil* 2008;30:1692–6.

62. Petersen W, Welp R, Rosenbaum D. Chronic Achilles tendinopathy: a prospective randomized study comparing the therapeutic effect of eccentric training, the AirHeel brace, and a combination of both. *Am J Sports Med* 2007;35:1659–67.

63. Mayer F, Hirschmuller A, Muller S, et al. Effects of short-term treatment strategies over 4 weeks in Achilles tendinopathy. *Br J Sports Med* 2007;41:e6.

64. Stergioulas A, Stergioula M, Aarskog R, et al. Effects of low-level laser therapy and eccentric exercises in the treatment of recreational athletes with chronic achilles tendinopathy. *Am J Sports Med* 2008;36:881–7.

65. Tumilty S, McDonough S, Hurley DA, et al. Clinical effectiveness of low-level laser therapy as an adjunct to

eccentric exercise for the treatment of Achilles' tendino-pathy: a randomized controlled trial. *Arch Phys Med Rehabil* 2012;93:733–9.

66. Yelland MJ, Sweeting KR, Lyftogt JA, et al. Prolother-apy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. *Br J Sports Med* 2011;45:421–8.

67. Brown R, Orchard J, Kinchington M, et al. Aprotinin in the management of Achilles tendinopathy: a rando-mised controlled trial. *Br J Sports Med* 2006;40:275–9.

68. Malliaras P, Barton CJ, Reeves ND, et al. Achilles and patellar tendinopathy loading programmes: a systematic review comparing clinical outcomes and identifying potential mechanisms for effectiveness. *Sports Med* 2013;43:267–86.

69. Cannell LJ, Taunton JE, Clement DB, et al. A rando-mised 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.

70. Kongsgaard M, Kovanen V, Aagaard P, et al. Corticoste-roid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. *Scand J Med Sci Sports* 2009;19:790–802.

71. Warden SJ, Metcalf BR, Kiss ZS, et al. Low-intensity pulsed ultrasound for chronic patellar tendinopathy: a randomized, double-blind, placebo-controlled trial. *Rheumatology (Oxford)* 2008;47:467–71.

72. Dragoo JL, Wasterlain AS, Braun HJ, et al. Platelet-Rich Plasma as a Treatment for Patellar Tendi-nopathy: A Double-Blind, Randomized Controlled Trial. *Am J Sports Med* 2014;42:610–8.

73. Frohm A, Halvorsen K, Thorstensson A. Patellar tendon load in different types of eccentric squats. *Clin Biomech (Bristol, Avon)* 2007;22:704–11.

74. Young MA, Cook JL, Purdam CR, et al. 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.

75. 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.

76. da Cunha RA, Dias AN, Santos MB, et al. Comparative Study of Two Protocols of Eccentric Exercise on Knee Pain and Function in Athletes with Patellar Tendi-nopathy: Randomized Controlled Study. *Revista Brasileira De Medicina do Esporte* 2012;18:167–70.

77. Bahr R, Fossan B, Loken S, et al. Surgical treatment com-pared with eccentric training for patellar tendinopathy (Jumper's Knee). A randomized, controlled trial. *J Bone Joint Surg Am* 2006;88:1689–98.

78. Stasinopoulos D, Stasinopoulos I. Comparison of effects of exercise programme, pulsed ultrasound and transverse friction in the treatment of chronic patellar tendinopathy. *Clin Rehabil* 2004;18:347–52.

79. Steunebrink M, Zwerver J, Brandsema R, et al. Topical glyceryl trinitrate treatment of chronic patellar tendino-pathy: a randomised, double-blind, placebo-controlled clinical trial. *Br J Sports Med* 2013;47:34–9.

80. van der Worp H, Zwerver J, Hamstra M, et al. No dif-ference in effectiveness between focused and radial shockwave therapy for treating patellar tendinopathy: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2013; May 12.

81. Lorenzen J, Kramer R, Vogt PM, et al. Systematic review about eccentric training in chronic patella tendi-nopathy. *Sportverletz Sportschaden* 2010;24:198–203.

82. Visnes H, Bahr R. The evolution of eccentric training as treatment for patellar tendinopathy (jumper's knee): a critical review of exercise programmes. *Br J Sports Med* 2007;41:217–23.

83. Saithna A, Gogna R, Baraza N, et al. Eccentric Exercise Protocols for Patella Tendinopathy: Should we Really be Withdrawing Athletes from Sport? A Systematic Review. *Open Orthop J* 2012;6:553–7.

84. Visnes H, Hoksrud A, Cook J, et al. No effect of eccen-tric training on jumper's knee in volleyball players during the competitive season: a randomized clinical trial. *Clin J Sport Med* 2005;15:227–34.

85. Raman J, MacDermid JC, Grewal R. Effectiveness of Different Methods of Resistance Exercises in Lateral Epicondylosis-A Systematic Review. *Journal of Hand Therapy* 2012;25:5–26.

86. Slater H, Theriault E, Ronningen BO, et al. Exercise-induced mechanical hypoalgesia in musculotendinous tissues of the lateral elbow. *Man Ther* 2010;15:66–73.

87. Peterson M, Butler S, Eriksson M, et al. A randomized controlled trial of exercise versus wait-list in chronic tennis elbow (lateral epicondylosis). *Ups J Med Sci* 2011;116:269–79.

88. Soderberg J, Grooten WJ, Ang BO. Effects of eccentric training on hand strength in subjects with lateral epi-condylalgia: a randomized-controlled trial. *Scand J Med Sci Sports* 2012;22:797–803.

89. Svernlov B, Adolfsson L. Non-operative treatment regime including eccentric training for lateral humeral epicondylalgia. *Scand J Med Sci Sports* 2001;11:328–34.

90. Tyler TF, Thomas GC, Nicholas SJ, et al. Addition of isolated wrist extensor eccentric exercise to standard treatment for chronic lateral epicondylosis: a prospective

randomized trial. *J Shoulder Elbow Surg* 2010;19: 917–22.

91. Wen DY, Schultz BJ, Schaal B, et al. Eccentric strengthening for chronic lateral epicondylosis: a prospective randomized study. *Sports Health* 2011;3:500–3.

92. Nagrale AV, Herd CR, Ganvir S, et al. Cyriax physiotherapy versus phonophoresis with supervised exercise in subjects with lateral epicondylalgia: a randomized clinical trial. *J Man Manip Ther* 2009;17:171–8.

93. Viswas R, Ramachandran R, Korde Anantkumar P. Comparison of effectiveness of supervised exercise program and Cyriax physiotherapy in patients with tennis elbow (lateral epicondylitis): a randomized clinical trial. *Scientificworldjournal* 2012;2012:939645.

94. Martinez-Silvestrini JA, Newcomer KL, Gay RE, et al. Chronic lateral epicondylitis: comparative effectiveness of a home exercise program including stretching alone versus stretching supplemented with eccentric or concentric strengthening. *J Hand Ther* 2005;18:411–9.

95. Zandt JF, Hahn D, Buchmann S, et al. May eccentric training be effective in the conservative treatment of chronic supraspinatus tendinopathies? A review of the current literature. *Sportverletz Sportschaden* 2010; 24:190–7.

96. Holmgren T, Hallgren HB, Oberg B, et al. Effect of specific exercise strategy on need for surgery in patients with subacromial impingement syndrome: randomised controlled study. *Br Med J* 2012;344:e787.

97. Ekstrand J. A common symptom among athletes and persons who exercise. Correct treatment of groin pain requires a meticulous diagnosis. *Lakartidningen* 1999;96:480–3.

98. Nicholas SJ, Tyler TF. Adductor muscle strains in sport. *Sports Med* 2002;32:339–44.

99. Valent A, Frizziero A, Bressan S, et al. Insertional tendinopathy of the adductors and rectus abdominis in athletes: a review. *Muscles Ligaments Tendons J* 2012;2:142–8.

100. Maffulli N, Loppini M, Longo UG, et al. Bilateral mini-invasive adductor tenotomy for the management of chronic unilateral adductor longus tendinopathy in athletes. *Am J Sports Med* 2012;40:1880–6.

101. Lynch SA, Renstrom PA. Groin injuries in sport: treatment strategies. *Sports Med* 1999;28:137–44.

102. Jensen J, Holmich P, Bandholm T, et al. Eccentric strengthening effect of hip-adductor training with elastic bands in soccer players: a randomised controlled trial. *Br J Sports Med* 2014;48:332–8.

103. Holmich P, Larsen K, Krogsgaard K, et al. Exercise program for prevention of groin pain in football players: a cluster-randomized trial. *Scand J Med Sci Sports* 2010;20:814–21.

104. Holmich P, Uhrskou P, Ulnits L, et al. Effectiveness of active physical training as treatment for long-standing adductor-related groin pain in athletes: randomised trial. *Lancet* 1999;353:439–43.

105. Holmich P, Nyvold P, Larsen K. Continued significant effect of physical training as treatment for overuse injury: 8- to 12-year outcome of a randomized clinical trial. *Am J Sports Med* 2011;39:2447–51.

106. Weir A, Jansen JA, van de Port IG, et al. Manual or exercise therapy for long-standing adductor-related groin pain: a randomised controlled clinical trial. *Man Ther* 2011;16:148–54.

107. Frizziero A, Ferrari R, Giannotti E, et al. The meniscus tear. State of the art of rehabilitation protocols related to surgical procedures. *Muscles Ligaments Tendons J* 2013;2:295–301.

108. Gerber JP, Marcus RL, Dibble LE, et al. Effects of early progressive eccentric exercise on muscle size and function after anterior cruciate ligament reconstruction: a 1-year follow-up study of a randomized clinical trial. *Phys Ther* 2009;89:51–9.

109. Gokeler A, Bisschop M, Benjaminse A, et al. Quadriceps function following ACL reconstruction and rehabilitation: implications for optimisation of current practices. *Knee Surg Sports Traumatol Arthrosc* 2013; Jun 28.

110. Sugiura Y, Saito T, Sakuraba K, et al. Strength deficits identified with concentric action of the hip extensors and eccentric action of the hamstrings predispose to hamstring injury in elite sprinters. *J Orthop Sports Phys Ther* 2008;38:457–64.

111. Ahmad CS, Redler LH, Ciccotti MG, et al. Evaluation and Management of Hamstring Injuries. *Am J Sports Med* 2013;41:2933–47.

112. Schache A. Eccentric hamstring muscle training can prevent hamstring injuries in soccer players. *J Physiother* 2012;58:58.

113. Jonhagen S, Nemeth G, Eriksson E. Hamstring injuries in sprinters. The role of concentric and eccentric hamstring muscle strength and flexibility. *Am J Sports Med* 1994;22:262–6.

114. Silder A, Sherry MA, Sanfilippo J, et al. Clinical and morphological changes following 2 rehabilitation programs for acute hamstring strain injuries: a randomized clinical trial. *J Orthop Sports Phys Ther* 2013;43: 284–99.

115. Childress MA, Beutler A. Management of chronic tendon injuries. *Am Fam Physician* 2013;87:486–90.