Eccentric training as a new approach for rotator cuff tendinopathy: Review and perspectives

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Eccentric training as a new approach for rotator cuff tendinopathy: Review and perspectives

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Abstract

Excessive mechanical loading is considered the major cause of rotator cuff tendinopathy. Although tendon problems are very common, they are not always easy to treat. Eccentric training has been proposed as an effective conservative treatment for the Achilles and patellar tendinopathies, but less evidence exists about its effectiveness for the rotator cuff tendinopathy. The mechanotransduction process associated with an adequate dose of mechanical load might explain the beneficial results of applying the eccentric training to the tendons. An adequate load increases healing and an inadequate (over or underuse) load can deteriorate the tendon structure. Different eccentric training protocols have been used in the few studies conducted for people with rotator cuff tendinopathy. Further, the effects of the eccentric training for rotator cuff tendinopathy were only evaluated on pain, function and strength. Future studies should assess the effects of the eccentric training also on shoulder kinematics and muscle activity. Individualization of the exercise prescription, comprehension and motivation of the patients, and the establishment of specific goals, practice and efforts should all be considered when prescribing the eccentric training. In conclusion, eccentric training should be used aiming improvement of the tendon degeneration, but more evidence is necessary to establish the adequate dose-response and to determine long-term follow-up effects.

Key words: Cellular; Mechanotransduction; Rehabilitation; Shoulder Impingement; Supraspinatus; Tendon injuries

Core tip: Eccentric training can be considered a new and ambitious treatment approach for several tendinopathies. The paper establishes the basic principles for explaining the effects on the tendon of an intense mechanical load, as the eccentric training. Further, the authors bring other possible explanations of the success of this training for tendinopathies, as the individualization of the exercise programs and the motivation of the patients who reach specific goals. Negative and side effects are also identified. Finally, the main evidence afforded by original articles is commented and future research purposes are defined.

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INTRODUCTION

Tendon injuries in the shoulder account for overuse injuries in sports as well as in jobs that require repetitive activity[1-4]. Excessive mechanical loading is considered the major causation factor. Although tendon problems are very frequent, they are not always easy to manage.

Rehabilitation of shoulder tendinopathy can take several months and conservative treatment is usually used as it can help the healing of the tendon by changing its metabolism and their structural and mechanical properties[5]. The use of eccentric exercise in rehabilitation has increasingly gained attention in the literature as a specific training modality. The eccentric exercise is an overall lengthening of a muscle as it develops tension and contracts to control motion. This kind of training differs from conventional training regimen because the tension in muscle fibers when lengthening is considerably greater than when muscle fibers are shortening[6]. There is some evidence that eccentric training may be effective in the management of tendinopathy of the Achilles and patellar tendons[7-9]. Histological changes in the supraspinatus tendinosis have been found to have similarities with those of the Achilles and patellar tendinosis[10,11]. Collagenous changes, extracellular matrix changes, increased cellularity and increased vascularity are among the histological and molecular changes observed in rotator cuff tendinosis[12]. As such, few studies were done evaluating the effectiveness of eccentric training in subjects with this condition[13-16].

The purpose of this paper is to review the studies that used eccentric training program in the treatment of rotator cuff tendinopathy as well as the tendon structure, the healing process and the possible mechanisms for why eccentric exercises can be effective in treating tendinopathy.

TENDON STRUCTURE

Tendons are mechanically responsible for transmitting muscle forces to bone as they connect bone to muscle belly at their ends. Consequently, motion is allowed and joint stability is enhanced.

As a type of connective tissue, tendon properties are determined primarily by the amount, type and arrangement of an abundant extracellular matrix[17]. Thus, the tendon has a multi-unit hierarchical structure composed of collagen molecules, fibrils, fiber bundles, fascicles and tendon units that run parallel to the tendon's long axis[5,18]. The fibril is the smallest tendon structural unit consisted of collagen molecules[5], which slide performing up to 50% of the longitudinal deformation of a tendon[19]. Fibers form the next level of tendon structure and are composed of collagen fibrils and are bound by endotenons, a thin layer of connective tissue[20,21]. They are responsible for the ability of the fascicles (fiber bundles) to slide independently against each other, transmitting tension despite the changing angles of a joint as it moves, and allowing tendons to change shape as their muscles contract[22]. Bundles of fascicles are enclosed by the epitenon, which is a fine, loose connective-tissue sheath[5]. More superficially, a third layer of connective tissue called the paratenon surrounds the tendon. Together, the epitenon and paratenon can also be called as the peritendon, which reduce friction with the adjacent tissue[23]. Vascular and nerve supply derive from all layers of the tendon and also from the myotendinous and osteotendinous junctions[24]. In general, tendons have a less vascular supply than that of the muscles with which they are associated[25].

The rotator cuff is composed of four tendons (supraspinatus, infraspinatus, teres minor and subscapularis) that blend into a single structure. First, the supraspinatus and infraspinatus bind 1.5 cm before insertion. Second, the infraspinatus and teres minor merge near its myotendinous union. Finally, the supraspinatus and subscapularis tendons also intertwine to form a sheath around the tendon of the biceps[26]. This sheath and the superior glenohumeral ligament and the coracohumeral ligament form the biceps pulley[27]. The supraspinatus, infraspinatus, subscapularis and the adjacent structures are strongly associated and form a capsule-cuff complex. The tendon proper acts with the capsule to transmit tensional force from the muscle to the bone[26].

Specifically, the supraspinatus consists morphologically of two different sub-regions. Anterior muscle fiber bundles were found to be bipennate, while posterior fiber bundles demonstrated a more parallel disposition[28]. Further, the anterior sub-region tendon is thick and tubular while the posterior tendon is thin and strap-like. These sub-regions have shown different mechanical properties[29]. In fact, anterior tendon stress is significantly greater than posterior tendon stress[28]. Each of the two sub-regions could also be divided into superficial, middle, and deep parts. This division has been associated to the initiation and progression of supraspinatus tendon tears[30].

Other authors have described four functional structurally independent parts in the supraspinatus tendon. The first part, also called the proper tendon, is extended from the musculotendinous junction to approximately 2.0 cm medial to the humerus insertion and it is composed of parallel collagen fascicles oriented along the tensional axis and separated by a prominent endotenon region. The second part is the attachment fibrocartilage that extends from the first part of the tendon to the greater tuberosity and it consists of a complex basket-weave of collagen fibers. The densely packed unidirectional collagen fibers of the rotator cable extend from the coracohumeral ligament posteriorly to the infraspinatus to form the third part, coursing both superficial and deep to the first part. Finally, the capsule is composed of thin uniform collagen sheets each, whose alignment differs slightly between sheets. This structure allows the tendon to adapt to tensional load dispersion and resistance to compression[22].

The upper fibers of the subscapularis tendon interdigitate with the anterior fibers of the supraspinatus tendon and the other structures of the rotator cuff, such as the coracohumeral ligament and the superior glenohumeral ligament[29].

The vascular anatomy of the healthy rotator cuff tendon has been controversial, with authors who have described a reduction in the number of capillaries[31], while others support the absence of hypovascularity. However, the changes in blood supply could be a secondary phenomenon, instead of an etiologic phenomenon, in the

rotator cuff lesions[26].

TENDON COMPOSITION

Tendons are consisted of collagens, proteoglycans, glycoproteins, glycosaminoglycans, water and cells[5]. The predominant elements of the tendon are the fibrillar collagen molecules. Type I collagen (more rigid) constitutes about 95% of the total collagen and the remaining 5% consists of types Ⅲ and V collagens[5,32]. Type Ⅲ forms smaller and less organized fibrils, which may result in decreased mechanical strength. This type of collagen was found in highly stressed tendons such as the supraspinatus[33]. The principal role of the collagen fibers is to resist tension, although they still allow for a certain degree of compliance (*i.e.*, reversible longitudinal deformation). Such apparently conflicting demands are probably resolved because of the hierarchical architecture of tendons[25]. Proteoglycans, as highly hydrophilic molecules, are primarily responsible for the viscoelastic behavior of tendons, but do not make any major contribution to their tensile strength[34]. Aging can cause a decrease in mean collagen fibril diameter, which is possibly regulated by type V collagen. The size shift may be related to the reduced mechanical strength of older tendons[35].

Fibroblasts are the dominant cell type in the tendon[5]. Tendon fibroblasts are responsible for the secretion of the extracellular matrix (*i.e.*, collagen orientation, assembly and turnover)[25], being considered a key player in tendon maintenance, adaptation to changes in homeostasis and remodeling in case of minor or more severe disturbances to tendon tissues. These cells are aligned in rows between collagen fibers bundles. Fibroblasts surrounded by biglycan and fibromodulin within the tendon ("niched" fibroblasts) exhibit stem-cell-like properties[36]. They are scarce in tendon tissue and decrease with age, but their prolongations create a large net in healthy status[10]. Tenocytes, the tendon fibroblasts, are increasingly recognized as a defined cell population that is functionally and phenotypically distinct from other fibroblast-like cells[25].

The supraspinatus tendon is a highly specialized inhomogeneous structure that is subjected to tension and compression[12]. The extracellular matrix composition of the insertion anatomy of the supraspinatus tendon has been categorized in four transition zones[37]. The first one is made up of largely type I collagen and small amounts of decorin, and could be considered as proper tendon. The second zone consists of largely types II and III collagen, with small amounts of types I , IX and X collagen forming a fibrocartilage. A mineralized fibrocartilage defines the third zone composed of type II and type X collagen and aggrecan. Finally, the fourth zone is bone with mineralised type I collagen. The mineral content and collagen fiber orientation define the effective bone-tendon attachment and are important in the appearance of rotator cuff tears[12].

Histological analysis of the rotator cuff tendon shows layers of loosely organized glycosaminoglycans between the longitudinal collagen fiber fascicles, which are usually undetectable in other tendons. These molecules, incorporated into collagen fibrils during the early, lateral assembly of fibrils[38], may be necessary to allow transmission of inhomogeneous strains during glenohumeral stabilization. Further, the increased amount of glycosaminoglycans in the supraspinatus may serve to resist compression and to separate and lubricate collagen bundles as they move relative to each other (shear) during normal shoulder motion[39]. In fact, the kinematics of the shoulder joint and shape of the supraspinatus tendon dictate that different regions of the supraspinatus tendon move independently in relation to each other, providing a mechanism of compensation[22]. It should also be stated that the total collagen content of the normal supraspinatus tendon does not change significantly with age and was similar to other shoulder tendons as the biceps tendon[40], for example.

ETIOLOGY AND PATHOLOGIC PROCESSES OF TENDINOPATHIES

The supraspinatus tendon is the most common injured tendon of the shoulder due to its location just under the coracoacromial ligament[41]. Shoulder impingement is one of the most common causes of shoulder tendinopathy[42,43] and refers to the compression of the subacromial structures against the coracoacromial ligament during elevation of the arm[44]. Apoptosis[45], vascular changes[26,31], tears[46] and calcifications[47] of the supraspinatus tendon have already been described in subjects who were treated with subacromial decompression.

Tendinopathy is a term usually used to cover all pain conditions both in and around the tendon. Although the knowledge of the causes of the tendinopathies continues to evolve[48], different intrinsic (anatomical variants and alterations, muscle tightness/imbalance/weakness, nutrition, age, joint laxity, systemic disease, vascular perfusion, overweight and all conditions linked to apoptosis[49]) and extrinsic factors (occupation, physical load and overuse, technical errors, inadequate equipment and environmental conditions) contributing to the pathologic processes have been identified. It is now recognized that most tendinopathies are rarely associated with any single factor, and the degenerative process that precedes tendon rupture may result from a variety of different pathways and etiology factors[50].

Classically, pain in tendinopathy has been attributed to inflammatory processes and the patient would be diagnosed as having "tendinitis"[18]. However, there are evidences that tendinopathy could be considered a non-inflammatory injury of the tendon at the cellular level[51,52], with absence of inflammatory precursors and cells in the tendon[48]. This condition is labeled as "tendinosis" and is defined from histopathologic findings involving widening of the tendon, disturbed collagen distribution, neovascularization and increased cellularity[53]. In fact, tendinopathies represent several degenerative processes mixed and, sometimes, overlapped. Tendinosis can lead to rupture of the tendon for vascular and/or mechanic reasons[50].

Among the most common sites of tendinopathy are the Achilles tendon, the patellar tendon, the wrist extensors tendon and the supraspinatus tendon[7,13,54,55]. The degenerative changes found in these tendons are associated with old age and with the high physical demands (strain, compression or shear forces) at the neighboring joints[6,56] with high rates of matrix turnover[50].

TENOCYTES BIOLOGY: MECHANOTRANSDUCTION IN EXERCISE

Tendons are metabolically active[57], but the mechanisms in transmitting/absorbing tensional forces within the tendon, and how tension affects the tendon, are not completely understood[58]. Nevertheless, tendons as a whole exhibit distinct structure-function relationships geared to the changing mechanical stresses to which they are subject[25].

The activity and microscopy architecture of the tenocytes could be modified by mechanical factors[5,59]. Further, the local stimulation of the tenocytes, which depends on the load, is the main fact associated to the tendinosis apparition[50], instead of apoptosis, that appears in more advanced stages[60]. In other words, the mechanical stress changes the cellular activity, and these changes alter the tendon structure[50] with a final negative balance of collagen[57]. However, different stress patterns provoke different cellular reactions depending on the amount and duration of the tensional stress applied[25].

The tenocytes are also responsible for producing an organized collagen and remodeling it during tendon healing[5]. Tenocyte strain regulates the collagen protein synthesis response. The increase in collagen formation peaks around 24 h after exercise and remains elevated for about 3 d, which produces a positive balance of collagen formation[57].

Kjaer *et al*[61] have suggested that gender difference exists in collagen formation where females respond less than males with regard to an increase in collagen formation after exercise. Also, the adaptation time to chronic loading is longer in tendon when compared to contractile elements of skeletal muscle, and only very prolonged loading can change the gross dimensions of the tendon[61].

In conclusion, the role of the tenocytes is relevant in both degeneration and healing processes of the tendon depending on the mechanical load applied[62]. The response of tendon cells to load is both frequency and amplitude dependent, and tendon cells appear to be "programmed" to sense a certain level of stress[62]. An adequate dose of mechanical load could improve the repairing, but an insufficient of inadequate stimulation could inhibit or prevent it.

TENDON LESION AND HEALING PROCESSES

The tendon is submitted to a constant process of synthesis and proteolysis (matrix turnover). The main actions of this cycle activity occur in the tendon matrix. Proteoglycan and glycoprotein activities are involved in the organization of the collagen fibers, and all their activities are mediated by the tenocytes. The changes in cellular activity in the extracellular matrix have been identified as a precursor of tendon lesion[61]. These changes include loss of matrix organization, high number of mechanoreceptors and fatty infiltration[12].

Lesions of the rotator cuff typically start where the loads are presumably the greatest: at the deep surface of the anterior insertion of the supraspinatus[63]. In absence of a total tear, when the repetitive load exceeds the healing capacity of the tenocyte (overuse), the tendinopathy appears[60]. Although the precise mechanism of injury that leads to tendinopathy remains unknown, the proposed mechanisms imply that there are one or more "weak link" in the tendon structure that result in the pathological response of the tenocyte[57].

Poor blood supply has also been implicated as a factor contributing to tendon injuries because it could delay the regeneration process, but tendon vascularization appears ample both around and inside the tendon in patients with tendinopathy[23,64]. Thus, tendinopathy itself is often associated with neovascularization and elevated intratendinous blood flow that seems to normalize during the course of exercise-based conservative treatment[65].

Although other degenerative features are associated with tendinopathy, including glycosaminoglycan accumulation, calcification and lipid accumulation, many of these features are found in normal tendons and are not necessarily pathological[66,67].

The role of each of the anatomical structures (*i.e.*, the supraspinatus tendon, the subacromial bursa and the glenohumeral joint capsule) are not completely known[12], but the progressive histological changes in rotator cuff disease include a characteristic pattern, which includes thinning of the collagen fibres, a loss of collagen structure, myxoid degeneration, hyaline degeneration, chrondroid metaplasia and fatty infiltration[68]. Total collagen content decreases, with a significant increase in the proportion of type Ⅱ and Ⅲ collagen relative to type Ⅰ collagen, decreasing the mechanical tendon properties. As previously commented, the tendon matrix also changes, and its attempt to heal, leads to a mechanical weak scar tissue as part of this failing remodelling process[12]. The histopathology shows that severity of tendon matrix degeneration increased with age and that more severe degeneration is associated with the development of tendinopathy[67].

For the supraspinatus tendon, extracellular matrix shows an increase of the concentrations of hyaluronan, chondroitin, and dermatan sulfate in chronic rotator cuff ruptures, that could represent an adaptation to an alteration in the types of loading (tension *vs* compression *vs* shear)[40]. Other pathologic factors such as low oxygen tension or the autocrine and paracrine influence of growth factors may also be important in the altered matrix following rupture[62]. In conclusion, higher rates of turnover in the nonruptured supraspinatus may be

part of an adaptive response to the mechanical demands on the tendon and to an imbalance in matrix synthesis and degradation. An increase in type Ⅲ collagen in some "normal" cadaver supraspinatus tendons is evidence that changes in collagen synthesis and turnover may precede tendon rupture[40].

The most common form of tendon healing is by scarring, which is inferior to healing by regeneration[6]. The contraction of tenocytes and the processes associated to its transformation in myofibroblasts seem to facilitate wound closure while minimizing scar tissue formation, playing an important role in tissue scarring[5].

Tendon healing can be divided into 3 overlapping phases: the inflammatory, repairing and remodeling phases[69]. The inflammatory phase lasts from 1 to 7 d with the phagocytosis as the main activity in this phase[70]. The repairing phase starts a few days after the injury and may last a few weeks[5]. The tenocytes starts the synthesis of large amounts of collagen after the 5th day until 5th week at least[70]. Type Ⅲ collagen is synthesized and then is gradually replaced by collagen type I with increase in tensile strength[71]. After about 6 wk the remodeling phase starts. This phase is characterized by decreased cellularity and decreased collagen. During this phase, the tissue becomes more fibrous and the fibrils become aligned in the direction of mechanical stress[72]. The final maturation stage occurs after 10 wk when there is an increase in crosslinking of the collagen fibrils, which causes the tissue to become stiffer. Gradually, over a time period of about one year, the tissue will turn from fibrous to scar-like[5].

Although the injured tendon tends to heal, there is evidence that the healing tendon does not reach the biochemical and mechanical properties of the tendon prior to injury[6]. In fact, collagen fibrils can be reduced as a result of injury[73]. A specific treatment approach, which takes into account each healing phase, has been recommended for improving these results[74].

The ability of the rotator cuff tendon to regenerate instead of repair is controversial, although the tendon heals better when good conditions are preserved. The functions of the subacromial bursa in healing include the gliding between two layers of tissue, the blood supply to the cuff tendons and the contribution of cells and vessels after surgical repair[12]. The changes in collagen composition in rotator cuff tendinopathy are consistent with new matrix synthesis, tissue remodelling and wound healing, attempting to repair the tendon defect even though when there is no visible evidence of a tendon fiber rupture. These changes may be the result of repeated minor injury and microscopic fiber damage or factors such as reduced vascular perfusion, tissue hypoxia, altered mechanical forces and the influence of cytokines, that could lead to tendon rupture[40].

Sometimes, in the last period of the remodeling and maturation of the healing, calcium apatite crystals are deposited in the damaged tissues. The location of this is close to the greater tubercule of the humerus where is the supraspinatus insertion[75].

When surgical treatment is necessary, the aim is to provide a better mechanical environment for tendon healing. Despite a normal response healing, the resultant tendon healing does not regenerate the tendon-bone architecture initially formed during prenatal development. Instead, a mechanically weaker, fibrovascular scar is formed, leading to suboptimal healing rates[76].

CLINICAL ASSESSMENT OF SHOULDER TENDINOPATHY

To diagnose tendinopathy, the anamnesis should include questions that allow the clinician to recognize if there is increase in inactivity and to identify which are the aggravating activities and also the relieving factors. The use of self-report questionnaires focused on the shoulder and upper extremity can be useful to quantify the patient's level of function in the shoulder, contributing for clinical decision-making process. Some of the commonly used questionnaires are the Disabilities of the Arm, Shoulder and Hand Questionnaire[77], the Western Ontario Rotator Cuff Index[78], the Shoulder Pain and Disability Index[79] and the Penn Shoulder Score[80]. Careful palpation helps in the search of points of tenderness that reproduce the pain of the patient. The clinician should use provocation tests that load the tendon to reproduce pain during the physical examination and other loading tests that load alternative structures[18]. The literature recommends that a combination of 3 positive of 5 tests (Neer, Hawkins-Kennedy, painful arc, empty can, and external rotation resistance tests)[81] can confirm the diagnosis of rotator cuff tendinopathy. Tendon pain itself usually does not radiate[18], although referred pain can contribute to the development of a secondary muscle problem as occurs with myofascial pain[82,83]. Imaging assessment (ultrasound and magnetic resonance imaging) improves the diagnosis of tendinopathy as it provides morphological information[84] about the tendon leading to a better clinician's make-decision. The ultrasound may provide an appropriate quantitative measure of the thickness of supraspinatus tendon that is important for determining improvement or deterioration in muscle function[85]. Fatty infiltration and tear can be better analyzed in magnetic resonance imaging. The presence and severity of fatty infiltration have been associated with increasing age, tear size, degree of tendon retraction, number of tendons involved and traumatic tears[86].

CONSERVATIVE TREATMENT OF SHOULDER TENDINOPATHY

Treatment of any organic medical condition must be based on understanding of pathophysiology. In fact, the knowledge of connective tissue properties, mechanotransduction, types of lesions, and tissue healing are important aspects for the correct and safe development of an exercise program[87]. However, this guide has not always been attended, and nowadays more questions than

answers remain around tendon injury treatment[10]. For example, although there are no established rules about the magnitude of the tear and the treatment options, the presence and the size of the rotator cuff tears could limit the therapeutic capacity of the exercises that underline the necessity of a correct diagnostic[9,88]. Massive chronic rotator cuff tears are often associated to restricted or loss of active shoulder range of motion[89]. Further, size of the tears could be related to joint inflammation and tissue remodeling, both of which are important for the advancement of rotator cuff treatment[90], but more research is necessary.

The common modalities used to treat a painful tendon include the use of anti-inflammatory drugs, rest and stretching and strengthening exercises[10]. It is important to highlight that the rest and anti-inflammatory are mainly used for the symptomatic relief with no direct effect in the tendinopathy as chronic tendon disorders are predominantly degenerative. Further, both non steroidal anti-inflammatory drugs[91] and corticosteroid drugs[92,93] could have deleterious effects on long-term tendon healing.

Another interesting point associated to rehabilitation process is the deterioration of the tendon after immobilization. A decrease of protein synthesis[94] and an increase of collagenase activity in damaged and not damaged fascicles[95] degenerate the immobilized tendon. Curiously, these deleterious processes have been stopped through cyclic stretching in *in vitro* studies[96,97].

As such, stretching techniques must be applied in the correct dose because its capacity of turnover the collagen synthesis[10]. Stretching techniques can consist of 3 repetitions of 30 s with a 30-s rest between the repetitions[1,98], 2 to 3 times per week[99].

Ultrasound, laser and electrical stimulation improve biomechanical and biochemical factors of the tendons and could help to reverse the tendinosis by stimulating fibrosis and repair[10]. However, there is lack of randomized trials that confirm the efficacy of these therapeutic approaches.

An effective treatment strategy that stimulates a healing response of the injured tendon need to be developed. So, exercises with mechanical loading should be started as soon as the pain "allows". The mechanical loading stimulates the healing response of the tendon as it accelerates tenocytes metabolism and may speed repair[5,71,100].

ECCENTRIC TRAINING

The eccentric training consists of the contraction of a muscle for controlling or decelerating a load while the muscle and the tendon are stretching or remain stretched. This technique has been advocated as a treatment of tendinopathy, such as chronic Achilles, patellar, lateral humeral epicondylagia and rotator cuff tendinopathies[18]. Good clinical results were already demontrated[7,13,55,101], although some controversies of this success also appears in the literature[102]. More evidence is necessary to support those results[103]. Currently, the eccentric training is included in algorithms of treatment[104] and has been considered a guiding principal of the rehabilitation[87,105].

The high forces produced eccentrically seem to induce remodeling response when applied chronically and progressively[100]. However, the specific mechanisms as to why eccentric training seems to optimize the rehabilitation of painful tendons are not totally known.

Three basic principles in an eccentric loading regime have been proposed, but the use of them still requires confirmation[70]: (1) length of tendon: the tendon length increases when the tendon is pre-stretched, and less strain will happen on that tendon during movement; (2) load: the strength of the tendon should increase by progressively increasing the load exerted on the tendon; and (3) speed: by increasing the speed of contraction, a greater force will be developed.

It has been suggested that eccentric exercises expose the tendon to a greater load than concentric exercises[106]. So, the prescription of an eccentric exercise program could be the best mechanism for strengthening the tendon[107]. Nevertheless, Rees *et al*[8] reported that peak tendon forces in eccentric loading are of the same magnitude as those seen in concentric loading suggesting that the tendon force magnitude alone cannot be responsible for the therapeutic benefit seen in eccentric loading. Thus, another possible mechanism that might explain the efficacy of eccentric loading is the high-frequency oscillations in tendon force produced by eccentric contractions. It was proposed that these fluctuations in force may provide an important stimulus for the remodeling of the tendon[8].

Other possible mechanisms may be related to the increase in fibroblast activity, acceleration of collagen formation, increase in type I collagen, collagen organization/alignment (remodeling of the tendon)[107,108] by muscular lengthening (stretching)[99,109] and increase in the number of sarcomeres in series[110]. Ohberg *et al*[84] have showed a localized decrease in tendon thickness and a normalized tendon structure in patients with chronic Achilles tendinosis after treatment with eccentric training. All these beneficial adaptations could allow proposing the eccentric training as a "tendon-strengthening" program[9].

Finally, another explanation of the eccentric training effectiveness is the traction and consequent disappearance of neovessels[65] that could lead to a lack of perfusion produced by the tendinosis. Although the decreased capillary tendon blood associated with increasing age might imply a consecutive bad perfusion and leads to tendinopathy and finally to tendon rupture, it was found that neovascularisation is associated with a significantly increased capillary blood flow at the point of pain in symptomatic tendinopathy.

In fact, it has been hypothesized that the resolution of the tendinosis neovascularisation by eccentric training, closely associated with new nerve endings, will be disturbed or even destroyed due to a lack of perfusion by their nutrient neovessels[53]. These studies speculate that some of the good clinical effects of the eccentric training may be mediated through decreasing pathological increased capillary tendon flow without deterioration of

local tendon microcirculation, but more evidence is necessary.

Another mechanism of the well tolerated reactions of the patients under eccentric training treatment includes neuromuscular benefits through central adaptations[8] and pain habituation, but there are not high quality trials to support this[103].

One of the most important aspects for the success of an exercise program is the individualization of the prescription. The exercise program should be as similar as possible to the usual mechanical stressors identified in each patient[87]. The comprehension and motivation of the patients, and the establishment of specific goals, practice and efforts could make easy the motor learning[111]. The more exhaustive process of the information (explanations, knowledge, motivation, attention), the deeper learning[112]. All these aspects, clearly linked to the eccentric training, could partially explain the effectiveness of this treatment approach.

It is well documented that the first bout of eccentric training could result in damage, including muscle pain, inflammation, cellular and subcellular alterations, force loss, blood markers of muscle damage[113]. The damage of eccentric contractions is related to a "mechanical insult", because as muscle lengthens, the ability to generate tension increases and a higher load is distributed among the same number of fibers, resulting in a higher load per fiber ratio and, curiously, a lower muscle activity[114]. However, this fact is still controversial[115].

Hypoxia has been described as a mechanism of tenocyte changes and death[76]. As previously commented, this is another controversial point because the intermittent capillary flow interruptions associated to eccentric training have been proposed as a benefic effect, but it could also produce tissue hypoxia and damage in capillaries[116].

Nevertheless, these adverse effects are mainly associated to the first bout of eccentric exercise. In fact, the following bouts of eccentric exercises do not produce the same muscle soreness or alteration in blood markers, and the recovery of the strength is faster when compared to the first bout[113].

In summary, eccentric training effects could be compared with the mechanical effects in tenocyte biology, where an adequate load increases healing and an inadequate (over or underuse) load can deteriorate the tendon structure.

Rotator cuff tendons attach the humerus very close to the glenohumeral joint, blending imperceptibly with the joint capsule. This increases the speed with which they can move the joint, producing a most effective moment arm[117]. The tendons "compete" with the glenohumeral capsule for bony anchorage, multiplying their functions. The conflict may be resolved by the fusion of the two structures[25].

Although the literature supports the use of strengthening and stretching exercises to reduce pain and functional loss in subjects with shoulder impingement[1,118], few studies have evaluated the effects of the eccentric training in subjects with this condition. Further, the literature supporting the beneficial effects of eccentric training in Achilles and patellar tendinopathy is abundant, but these effects are less known in rotator cuff tendon disorders[9].

Jonsson *et al*[13] have shown good clinical results of eccentric training for the supraspinatus and deltoid muscles in chronic painful subjects. The authors completed the study in 9 subjects that were on the waiting list for surgery. All subjects had to perform painful eccentric training for the supraspinatus and deltoid muscles for 12 wk, 7 d a week, 3 sets of 15 repetitions, twice a day. After this period of training and at 52-wk follow-up, 5 out of 9 subjects were satisfied with the result of the treatment and withdrew from the waiting list for surgical treatment.

Bernhardsson *et al*[14] have evaluated the effects of an exercise focusing on specific eccentric training for the rotator cuff on pain intensity and function in subjects with shoulder impingement. The training programme comprised 5 exercises, of which 2 were warm-up and scapular control (shoulder shrug and scapular retraction) exercises and stretching for the upper trapezius. The 2 main exercises were eccentric strengthening exercises for the supraspinatus and infraspinatus performed in a side-lying position and using dumbells. The frequency of the protocol was the same as proposed by Jonsson *et al*[11]. The training was effective to decrease pain and increase function.

Camargo *et al*[15] had their patients with shoulder impingement to perform eccentric isokinetic training at 60°/s for shoulder abductors during 6 wk (3 sets of 10 reps, 2 d a week). Subjects improved pain and function, but isokinetic variables were only moderately changed after the intervention. This type of training may be difficult to be incorporated in a clinical setting, as it requires an isokinetic device.

The main limitation of the previous studies is that none of them included a control group. They all had one group performing the same exercises. The lack of control group does not allow us to completely rule out that the natural maturation of the condition may have influenced the results.

Based on this, Maenhout *et al*[16] investigated if adding heavy load eccentric training to rehabilitation of patients with shoulder impingement would result in better outcome. One group of patients performed the traditional rotator cuff training and the other group performed the same exercises combined with heavy load of eccentric training. The protocol consisted of 3 sets of ten reps, daily, for 12 wk. The eccentric exercises were performed twice a day. Adding heavy load of eccentric training resulted in higher gain in isometric strength, but was not superior for decreasing pain and improving shoulder function.

It is important to highlight that different doses of eccentric training were used in the previous studies. The lack of understanding about the basic pathophysiology of tendinopathy makes determining the optimal dosage of intervention difficult. Because the studies in this area have not used an underlying rationale to determine load-

ing parameters, progressions and frequency of treatment, further research needs to be undertaken before an optimal dosage can be determined.

Other studies have also incorporated the use of eccentric exercises along with other exercises in the rehabilitation protocol for subjects with shoulder impingement[119-121], but they didn't intend to evaluate the effects of the eccentric training. The cited studies on eccentric training[13-16] only evaluated the effects of the eccentric training on shoulder pain, function and strength. None of the studies assessed the effects on the shoulder kinematics and muscle activity.

It is known that subjects with shoulder impingement present increased retraction and elevation of the clavicle, increased internal rotation and decreased upward rotation and posterior tilting of the scapula[122], and increased anterior and superior translations of the humerus during elevation of the arm as compared to healthy subjects[123]. The literature also brings that these alterations are commonly associated with increased activity of the upper trapezius, decreased activity of the lower trapezius, serratus anterior and rotator cuff muscles[124]. Based on the alterations above, many protocols are proposed in an attempt to restore kinematics and muscle activity in these individuals. Most of the protocols include stretching exercises for the anterior and posterior shoulder, strengthening exercises for the lower trapezius, serratus anterior and rotator cuff muscles, relaxation for the upper trapezius and techniques of manual therapy[1,118,125-127]. Good clinical results were observed in these investigations.

Further clinical trials should be done to evaluate the effects of eccentric training programs on scapular and humeral kinematics and shoulder muscles activity[104]. Future investigations should include long-term follow-up of large groups, and the comparison of different eccentric training protocols. Imaging evaluation before and after the period of treatment is also necessary to check on possible improvements of the injured tendon.

Finally, there is still lack of evidence of the really benefits that the eccentric exercises may bring to subjects with shoulder tendinopathy. In the treatment of shoulder impingement, the approach should not only focus on decreasing the impingement, but should additionally address the tendon degeneration. As such, eccentric training should be used aiming improvement of the tendon degeneration, and usual stretching and strengthening exercises associated with manual therapy techniques to restore kinematics and muscle activity.

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