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Feature

Current understanding of the diagnosis and management of the tendinopathy: An update from the lab to the clinical practice ☆

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ABSTRACT

Tendinopathy is labeled by many authors as a troublesome, common pathology, present in up to 30% medical care consultations involving musculoskeletal conditions. Despite the lasting interest for addressing tendon pathology, current researchers agree that even the exact definition of the term tendinopathy is unclear. Tendinopathy is currently diagnosed as a clinical hypothesis based on the patient symptoms and physical context. One of the main goals of current clinical management is to personalize treatment approaches to adapt them to the many different needs of the population.

Tendons are complex structures that unite muscles and bones with two main objectives: to transmit forces and storage and release energy. Regarding the tensile properties of the tendons, several authors argued that tendons have higher

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tensile strength compared with muscles, however, are considered less flexible.
Tendinopathy is an accepted term which is used to indicated a variety of tissue conditions that appear in injured tendons and describes a non-rupture damage in the tendon or paratendon, which is intensified with mechanical loading Even when the pathoetiology of tendinopathy is unclear, there is a wide array of treatments available to treat and manage tendinopathy. Although tendinitis usually debuts with an inflammatory response, the majority of chronic tendinopathies do not present inflammation and so the choosing of treatment should vary depending on severity, compliance, pain and duration of symptoms.
The purpose of this article is to review and provide an overview about the currently research of the tendon diagnosis, management and etiology.

Background

Introduction

Tendinopathy is labeled by many authors as a troublesome, common pathology present in up to 30% medical care consultations involving musculoskeletal conditions.[1] Symptoms may vary in intensity but can potentially affect the patients' perceived life quality. In some cases, activities and professions involving physical activity have to be interrupted.[2] Despite the lasting interest for addressing tendon pathology, current researchers agree that even the exact definition of the term tendinopathy is unclear.[3] Tendinopathy condition is usually related to a disorganization within the tendon structure, but several authors have stablished a discrepancy between imaging findings and clinical symptoms.[4] Therefore, in clinical practice, pain or disfunction observed in clinical testing can be unrelated to imaging tests findings; such as magnetic resonance imaging (MRI) or ultrasound imaging (USI).[5] Frequently, asymptomatic subjects present tendon disorganization signs when explored through MRI or US, whereas subjects with tendon pain present an image of apparently healthy tendons.[6] It is possible to observe changes in the clinical symptoms of the patients (e.g. improvement or aggravation of the pain perception) that are not in line with the changes on the US image of the structure.[7]

Therefore, tendinopathy is currently diagnosed as a clinical hypothesis based on the patient symptoms and physical context. There is not a defined model of patient regarding the level of activity, tendon loading, pain symptoms or functional capability.[8] Patients may range from elderly populations to young athletes, so one of the main goals of current clinical management is to personalize treatment approaches to adapt them to the many different needs of those populations.[1]

Epidemiology

This wide range of conditions under the label of tendinopathy, makes their epidemiology an important study topic.

Regarding age, children are less susceptible to tendon pathology, due to the specific features of the infant's musculoskeletal system, being the growth plate and the tendon insertion more

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susceptible to injuries that the body of the tendon, which is, in comparison, stronger and more elastic.[9] Due to this fact, the most common tendinopathies reported in children are the Osgood-Schlatter[10] and Sever's disease.[11]

Osgood Schlatter disease is a traction apophysitis and/or tendonitis on the tibial tubercle. It has prevalence of 10% over all sport overuse injuries and is considered a common cause of anterior knee pain in young athletic population. This condition is usually related with jumping sports, for example: basketball or volleyball.[10] The prevalence of Sever apophysitis is estimated around 8% amongst overuse injuries in teenagers. Obesity and high levels of physical activity had been identified as primary risk factors, as well as high-impact sports (e.g., soccer, gymnastics, running or ballet).[9]

Currently research showed that gender can be considered as a risk factor in some types of tendinopathies, such as Achilles tendinopathy. However, this tendence is changing, probably due to the increase of women's participation in sports and physical activities compared to the past decades.[9]

Regarding the tendinopathy etiology and diagnosis, global data of incidence or prevalence of this condition are not available. Nevertheless, it is possible to categorize the epidemiology of tendon conditions into several subgroups.

Rotator cuff tendinopathy (RCT) has been described to be the most common responsible for shoulder pain (80% prevalence). Moreover, half of the patients with RCT are still symptomatic after a year, presenting limitations in their daily live activities.[12] Calcific tendinopathy is reported in 2.5–7.5% of general population, especially in women (70% of cases), with no correlation with physical activity.[13]

Lateral epicondylitis (LE), also known as "Tennis Elbow" is estimated to affect between 1–3% of adults,[14] and 40% of tennis players.[15] The prevalence of LE in subjects over 40 years seem to be 2 to 3.5 times higher than in subjects under that age, and higher among tennis players that practice more than 2 h/day.[9]

Medial epicondylitis (ME), also known as "Golfer's elbow", it is to be found mainly in golf, baseball and javelin throwing athletes, but has also a prevalence of around 1% in general population,[16] affecting both gender in their 40–60 years in a similar proportion.[17]

Hand and wrist tendinopathies have a particularly high prevalence amongst stick and racquet sports practitioners.[18] De Quervain Tenosinovitys, that involves the first dorsal extensor, shows a higher prevalence in women (2.8 per 1000) with an increase of symptomatic cases over 40 years of age.[19] Among athletes, volleyball players are a risk group for De Quervain Tenosinovitys due to repetitive microtrauma.[20] In other sports, such as tennis, rowing or golf, the risk factors seem to be more associated to the type of grip.[18] Other less prevalent hand and wrist tendinopathies would be Intersection Syndrome, Extensor Pollicis Longus Entrapment, Flexor Carpi Radialis Tendinopathy, Flexor carpi Ulnaris Tendinopathy, and Extensor Carpi Ulnaris Conditions. This last tendinopathy is mainly related to racquet or stick sports.[21]

Lower limb tendinopathies are commonly found in sport practitioners. Hamstring tendinopathy (HT) especially affects the proximal insertion, and is typically associated with long-distance running and hurdling.[22] In non-sports related cases, hormonal changes associated to menopause and genetic predisposition are possible causes of HT.[23] Tendons of the semimembranosus, semitendinosus and biceps femoris can be affected separately or as a complex triad.[24]

Gluteal tendinopathy (GT) is considered to be responsible for most cases of lateral hip pain (62.5%).[25] This frequent condition has an important impact in patients' participation in daily living activities. The prevalence is higher in population over 40 years of age, and it is also more frequent in women.[26] In the population between 50 and 79 years, the ratio is of 23.5% of women and 8.5% of men, mainly in sedentary individuals, but also in athletes. Current evidence correlates GT with mechanical factors, such as increased hip adduction.[27]

A common sport-related injury is the Patellar tendinopathy (PT). Prevalence among elite jumping athletes and recreational jumping athletes is of 45% and 14% respectively. It also has a high prevalence in elite basketball players (45%) and volleyball players (32%) .[28] Some authors report that only 46% of sport practitioners affected with PT are able to return to previous activity with no symptoms.[29] Due to the morphologic characteristics of the quadriceps tendon,

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Quadriceps tendinopathy (QT) is less prevalent than PT. The main clinical symptom is pain in the superior border of the patella. It is associated to chronic adaptations of the tendon to repetitive stress.[30] Several authors label QT and PT together as "Jumper's knee", without diagnostical differentiation between the two of them. "Jumper's knee" is mostly prevalent in athletes, but it can also be found in non-athlete patients, showing a high statistical correlation with obesity and subject's height (increased height correlates with increased risk of tendinopathy).[31]

Achilles tendinopathy (AT) is commonly found amongst runners, specially middle-distance runners, who report an 83% prevalence of signals of AT.[32] Track and field athletes have also a high prevalence (43%), reporting pain and performance decrease. Recovery time is described to last over a year, and recurrent injuries are common.[33] AT is not necessarily sport-related, but can also be found in general population. In these last cases, body weight and diabetes seem to play a role as factor risks.[34,35]

Iliotibial Band Syndrome (IBS), is a lower limb tendinopathy that affects mainly runners. (62% women, 38% men). Several authors report IBS as a frequent cause of knee pain in cyclist (24%), soccer and hockey players.[36]

In conclusion, epidemiology of tendon injuries is necessarily divided and categorized by the affected structure, as global numbers do not represent a clear picture of this miscellaneous conditions that affect athletic and sedentary population equally.

Biomechanics and pathophysiology of the tendon injuries

Tendon structure

Tendons are complex structures that connect muscles and bones with two main objectives: to transfer forces and storage and release energy.[37] All body tendons have a similar histological organization, that is, a soft tissue structure mainly composed by connective cells.[38] This connective tissue includes an extracellular matrix (ECM) described as a macromolecular network with structural and changing functions.[39] ECM is basically composed of collagen and tenocytes.[40] According to currently research, collagen conforms 65–80% of dry mass in healthy people.[41] In addition, this collagen proteins are well organized and separated according to their features and properties.[42] Tendon has a hierarchical structure, well-observed in the ECM, which is high organized with collagen molecules connecting into filamentous collagen fibrils. These groups of fibrils are known as collagen fibers, the main structural element of the tendon.[43] Fibrils are ordered in fibrils packs, fascicles and fiber packs that are aligned in the same direction to the axis of the tendon, named primary, secondary and tertiary bundles.[44]

Regarding the tensile properties of the tendons, several authors argued that tendons have higher tensile strength compared to muscles; however, they are considered less flexible. Those characteristics allow to support higher and time-maintaining loads with a lower rate of deformation due to the force that a muscle can produce is maintained without losing any power.[45] The myotendinous junction (the area where the tendon converges with the muscle) has collagen fibrils that make connections with muscles cells shaping into folds. This area extends the contact zone between tendon and muscle, facilitating a decrease in the force applied during muscle contraction.[46]

From a structural point of view, the tendon structure is constituted by a great number of collagen bands, which are externally protected by the peritenon. Inside this cover, the secondary and sub-fascicular band can both be found wrapped and divided by the endotendon.[47]

Biomechanics of the tendon

Regarding tendon biomechanics, these structures achieve a mechanical advantage, increasing the force generated by the muscle by the pulley or lengthening systems. In addition, viscoelastic material properties allows to maintain and release energy, which is a main mechanism for

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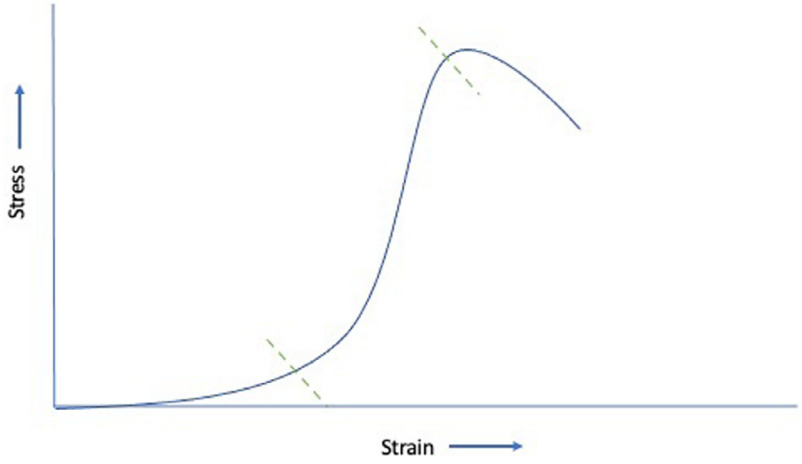

Fig. 1. Load-elongation curve.

injury prevention.[48] Knowledge about the tendon function, its morphology and biomechanics is considered essential to achieving maximum efficiency of their functions and healing response.[49]

Collagen fibrils form an undulation configuration (like a wave) present in all tendons, which is known as "crimp". This tissue structure can be viewed using a microscope and it is relevant for the early loading stages, due to the tendon mechanical properties.[50] At the first loading stages, tendons suffer an initial stiffness expansion directly proportional to the received load. Tendon biomechanics, due to this nonlinear characteristic shows two separate zone in the load-elongation curve.[49] The next Fig. 1 shows the behavior of tendon tissue in response to load activity. On the left side of the curve, when the load is starting, a low deformation can be observed in the stress-strain curve. After that, there is a cut point where a load increase providing greater tissue deformity. In this context, the collagen fascicle itself is straightened and the crimp vanishes. As deformation increases, there is a second cut point where tendon experience irreversible injury and, if sustained, could suffer a tear or rupture.[51]

In this line, it must be pointed that the crimp formation and the collagen structure of the ECM facilitates viscoelastic properties of the tendons, which are essential for the understanding of the biomechanical characteristic of the tendons.

Pathophysiology

From a historical point of view an extent number of different terminologies has been described to identify tendon injury, such as *tendinitis* or *tendinosis*.[52] Before the nineties, tendons that suffered a pain process were diagnosed as tendinitis, because it was thought that the inflammatory response was the key point of the pathological course.[53]

Maffuli et al. were considered one of the first researchers to promote a change in the clinical terminology from tendinitis to tendinopathy. Currently, tendinopathy is an accepted term which is used to indicated a variety of tissue conditions that appear in injured tendons and describes a non-rupture damage in the tendon or paratendon, which is intensified with mechanical loading.[52]

This shift in the nomenclature has been related with new advances in the understanding of tendon pathophysiology, implying: 1) a further description of the overuse cycle and the following structural and functional damage in tendons with chronic pain; 2) increased knowledge about the biomechanical disturbances which provoke chronic tendon pathology; and 3) a better picture about the importance of intrinsic and extrinsic factors related to lifestyle.[54]

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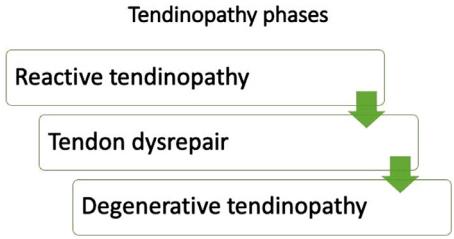

Fig. 2. Tendinopathy phases[8].

Tendinosis has been usually employed to name chronic midportion tendon injury, focusing off from the inflammatory process. If the damage is localized in the synovial sheath -for example in the finger extensors/flexors- the appropriated term is *tenosynovitis*.[55] Moreover, if the injured zone is the paratendon, the chosen descriptor is *paratendonitis* or *peritendinitis*.[54]

Inflammatory action is considered in the current scientific literature, as one factor in the onset of the tendinopathy; nevertheless, this process alone cannot explain the development of the ailment.[56] A large amount of research showed disruption without the presence of an inflammatory cell infiltrate, separation or thinning in collagen fibrils.[57]

In 21st century, degenerative theories have been reconsidered in order to explain the tendon tissue injury process. The "cumulative injure" and "vascular failed model" are two of these approaches. These theories are focus on irreversible, degenerative cell transformations and separation of the matrix.[58] Other studies have pointed that damage of the tendon appears in a healing phase when there is a disorganization of the matrix with an increase of protein production and cell activation.[59]

Cook and Purdam developed a model that proposes that there is a continuum of the tendon pathology. This model presents three different stages of tendinopathy: reactive tendinopathy, tendon disrepair (failed healing) and degenerative tendinopathy.[8] From the pedagogical point of view, this model is presented and divided in three stages, in which there is a progression between levels. In the early stages, increasing or reducing loading is the first stimulus that causes the tendon to go forward or backward in the continuum model.[60]

Reactive tendinopathy is the result of an acute compressive and/or tensile load which provokes a non-inflammatory proliferative cell and matrix response. This situation occurs after an acute overload such as an excessive physical activity periods (Fig. 2).

Also it can be observed after a direct traumatism such as falling onto the tendon.[61] It is noticed that damaged tendons suffered structural changes observed through ultrasound.[62] In previous research, it was thought that a thickened tendon was a symptom of a maladaptive response. Nowadays, some studies show that this adaptive response can be explain as an effort to maintain an available amount of aligned fibrillar structured to avoid overloading in the damaged area.[63] This enlargement of the tendon surface can decrease stress and increase stiffness. If there is enough time between loads or the overload is reverted, the tendon structure can return to normal.[8]

Second stage is defined as tendon disrepair, which is determined for the development of fibrillar disorganization. This phase is observed as the attempt at tendon healing, also known before as "failed healing".[64] Changes in the matrix level are more noticeable and could be caused by an increase of the vascularization of the tendon due to neuronal maturity.[65]

The last stage is known as degenerative tendinopathy. In this phase, a variety of changes can be observed within the matrix and cells. During this period, the possibility of natural recovery decreases. Several areas of cells will die related to trauma or tenocyte apoptosis.[66] As a result, large zones of acellularity can be observed and the disordered zones of the matrix will appear filled with vessels.[60]

Several authors argued that it is essential to review the intrinsic and extrinsic factors that may contribute to a successful management of the continuum model of tendon pathophysiology

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and that they may have an important role in the response to intervention in tendinopathy. Intrinsic risk factors can be labeled as: unmodifiable or modifiable, some of them are related to lifestyle or general health status, while others are linked to personal body characteristics.[47]

In this line, the individual factors that should be considered are genes, age, sex, biomechanics, and body composition. Obesity, illnesses associated with obesity and systematic diseases can provoke tendinopathy.[67] Extrinsic factors could vary in each tendon; while weight bearing is highly related to lower limbs tendinopathies, upper limbs tendons injuries can be observed in overload movements. Health care professionals must understand load management and take it into account as a part of their assessment and intervention.[68]

Rotator cuff tendinopathy

Introduction

The rotator cuff tendon is formed by the contribution of scapular muscle tendon in the anterior aspect of humeral head, the supraspinatus in the superior aspect and the infraspinatus and teres minor in the posterior margin of the humeral head. The confluence of these components in a surrounding tendon of the humeral head, provides to the glenohumeral joint of movement, stability for humeral head translations as well as sensory and proprioceptive information for motor control.[69] Rotator cuff tendons attach to the humeral head through a wide and multilayered insertion in the greater and minor humerous tuberosity and firmly connected to the glenohumeral capsule.[69] Posteriorly, the infraspinatus and teres minor muscles merge in a tendon to form the posterior edge of the cuff. Superior and laterally, the infraspinatus and supraspinatus tendon forms an interdigitation of theis fibers 15mm before its attachment in the greater tuberosity.[70] Subescapularis tendon inserts onto the minor tuberosity of humeral head and supraspinatus tendon attach to the anterior aspect of the greater tuberosity. Both components of the rotator cuff fuse at the end of the bicipital groove forming a fibrous tunnel for the long head tendon of the brachial biceps commonly referred as a rotator cuff interval (RCI).[71,72] This triangular shape region is formed by the humeral head and slightly medially the superior glenohumeral ligament as the base of the region, the coracohumeral ligament in the superior aspect, the subescapularis tendon medially and the supraspinatus laterally.[72] The RCI plays a complex role in function and stability of the shoulder and glenohumeral joint, supporting the long head of the biceps tendon preventing from antero-medially and antero-inferior luxation in rotator cuff and capsular injuries, in addition to participation in dynamic conflict syndromes which affects glenohumeral rotations (anterior internal impingements, external coracoid impingements, etc.).[72–74]

Rotator cuff tendinopathy is considered a degenerative condition, which involves pain and reduction of function in shoulder movements such as elevation and rotations, characterized by the presence of structural abnormalities in tendon microstructure, cellular composition and protein fiber arrangement.[75] Tendon degeneration involves a sequence of events that progress to the fragmentation of collagen fibers and extracellular matrix disorganization, increasing the deposit of matrix protein fibers and substances, such as glycosaminoglycans, replacing the matrix components as protective response.[75]

Traditionally referred as a subacromial impingement syndrome, this term has been recommended to be avoided due to the general lower consensus between structural alterations in acromion morphology and the development of rotator cuff symptoms.[76]

Rotator cuff tendon structure and biomechanics

The rotator cuff is made up by the interdigitation of various tendons, forming a particular structure where fascicles are separated by endontendon connective tissue, which contains

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amounts of proteoglycans, such as hyaluronic acid, that plays a role in matrix and bundle lubrication. From a microscopic point of view, five layers where described near the insertion of the supraspinatus and infraspinatus in the medial lateral facets of the greater tuberosity. The first most superficial layer is described as the coracohumeral ligament, directly superimposed on the fourth layer that corresponds to the tendinous fibers of the rotator cuff. Immediately below, a thicker third layer of tendon fibers is described with smaller fascicles, to give way to a fourth layer of loose connective tissue that presents fibers from the coracohumeral ligament forming the rotator cable. The fifth, deeper layer corresponds to the fibers of the glenohumeral joint capsule with a multiaxial orientation.[77] Thereby, mechanical forces applied to the rotator cuff through multiaxial joint movements of the glenohumeral joint, will subject tendon such us supraspinatus and its different layers to internal shear stress, which becomes important in functionality of the complex.

The objective of the biomechanics of the shoulder is to achieve 180° of mobility by incorporating all the joint elements that participate in this joint complex. In normal shoulder kinetics, the humeral head moves around the scapular glenoid fossa through the glenohumeral joint (GHJ) in a coordinated manner incorporating the participation of all rotator cuff elements. Above 120°, the scapula will rotate around the clavicle through the acromioclavicular joint (ACJ) and it will rotate around the sternum through the sternocostoclavicular joint (SCCJ). Moreover, humeral head displacement must be integrated during normal physiological movements of the glenohumeral joint and shoulder function. Superior translation of 0.35 mm of the humeral head relative to the glenoid fossa has been described in the cranio-caudal direction during shoulder elevation movements.[78] Furthermore, anterior translations of the humeral head of 3.8 mm were describe during flexion movement of the shoulder, and posterior humeral head translations of 4.9 mm during extension movements of the shoulder.[79] Humeral head translations may be associated with capsular stiffness and connective tissue tightening, which it has been proposed as a primary mechanism of glenohumeral internal rotation deficit (GIRD).[80–82]

Rotator cuff muscles and tendons are accurately involved in GHJ stability and function, throughout couples forces between paired muscles generating moment forces around an axis of movement. Integrated and coordinated patterns of muscle activation coordinate migrational translations forces and displacements of humeral head during shoulder movements. Functional tasks in coronal plane that incorporates shoulder abduction, will require forces couples between deltoid and supraspinatus in order to increase humeral head compression onto the glenoid fossa, avoiding superior translations and compression of the soft tissue of the subacromial space. Infraspinatus and subscapular coordinates in the axial plane during rotational movements such as internal or external rotations during throwing activities increasing horizontal forces against the glenoid fossa of the scapula. Hereby, this couples force will increase compression joint reaction forces against the concave glenoid fossa, known as concavity compression,[83,84] which is a mechanism to improve dynamic stability of the glenohumeral joint by the scapular tilt modification and humeral head and neck retroversion. For example, the subscapularis and the infraspinatus couple forces stabilize the GHJ in abduction from 0° to 150°, while in the last degrees the infraspinatus becomes the main stabilizer in isolation.[85]

Pathoethiology of rotator cuff tendons

Tendinopathy encompasses a broad concept that affects the tendon through a series of mechanisms that lead to the degeneration of the tendon structure, its cellular and molecular components, resulting in decreased function and the appearance of pain.[75]

Microscopic lesions in the fibrillar collagen network through loads or repetitive mechanical stress have been considered the main trigger for the onset of tendon degeneration and subsequent stages such as the appearance of partial or complete tears. In healthy conditions, damage to the tendon matrix triggers effective repair responses, but the combination of extrinsic factors such as mechanical overstimulation of the tendon or morphological variants as well as intrinsic factors such as low repair potential can tip the balance towards structural degeneration. In

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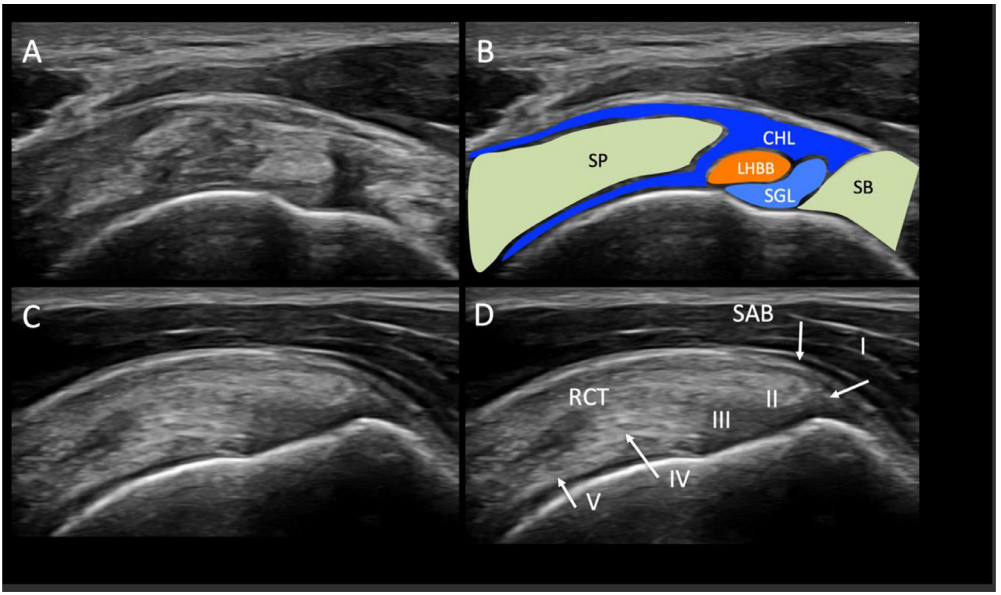

Fig. 3. Rotator cuff structures in a longitudinal ultrasound view. CHL, coracohumeral ligament; LHBB, long head of biceps brachialis tendon; SB, subscapularis; SGL, superior glenohumeral ligament; SP, supraspinatus; RCT, rotator cuff tendon.

this context, the initial phases of degeneration remain clinically silent, but the accumulation of cytokines, chemokines, vascular and neuro-inflammatory peptides unleash a cascade of nociceptive events and signals that manifest the appearance of symptoms in patients, leading to loss of function and appearance of pain.[75,86]

Rotator cuff dysfunction is frequently associated with extrinsic and intrinsic tendon factors. Extrinsic factors such as the coracoacromial arch or the bony acromion morphology may play a role as potential structures which compress soft tissues immediately below in the subacromial space, such as the subacromial bursa (SAB) or rotator cuff. The subacromial bursa formed by fibrous, areolar, fat and synovial cells have an important function diminishing humeral head frictions against the coracoromial arch during shoulder movement. Moreover, it has been correlated strongly the presence of pro-inflammatory peptides in the subacromial bursa and pain symptoms during shoulder elevations, which support the hypothesis of the bursa participation in the detection of increasing compressive forces in subacromial space.[69] Bone morphology variations of the acromion has been traditionally argued in the irritation of rotator cuff. Despite this, recent evidence support the avoidance of this pathoethiology hypothesis which has been mentioned as "Subacromial impingement syndrome", due to the poor level of association between symptoms and structural deformation.[87,88] Tissue impingement between humeral head and coracoacromial arch also could be associated to muscle imbalance or weakness during shoulder movements, developing motor control disturbances such as muscle activity inhibition delayed onset patterns of muscle activation of rotator cuff or scapula, leading to the appearance of pain symptoms.[89–91] In this sense, scapular dysfunction due to postural, motor control or muscle imbalance has been proposed as an extrinsic mechanism of tendinopathy development, where individualize assessment protocols are emerging aiming improvement due to broadly variations between posture and symptoms presentations.[92]

Chiefly, extrinsic factors such as tendon overloading or overuse, suddenly increases of training loads or intensities, incorporations of new tasks or exercise during trainings, reduction of resting periods, highly repetitive movements during overthrowing activities or poor technique or posture control, have been considered the main causative factor in tendinopathy development.[75,93]

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Otherwise, intrinsic factors for tendon degeneration consider factors such as aging, genetics, inflammatory conditions or metabolic diseases like diabetes meillitus or obesity, tendon vascularization in main areas of degeneration, ligaments laxity and glenohumeral hypermobility or mobility restrictions, muscle weakness or neuromuscular disorders.[75]

Despite this, the combination of intrinsic and extrinsic factors should be considered as a mixed pattern in the development of rotator cuff tendinopathy. For example, the reduction of acromiohumeral distance has been evidenced in muscle fatigue conditions of rotator cuff muscles, specifically in supraspinatus tendon.[94,95] In this way, a loading exercise program until rotator cuff fatigue, was compared between shoulder controls and rotator cuff tendinopathy group measuring the acromiohumeral distance and the supraspinatus thickness by ultrasound. Both groups showed similar findings related to the increase in the thickness of the supraspinatus and the reduction of the acromiohumeral space, but differences were observed in the reduction of the recovery time of normal values in the control group respectively the tendinopathy group.[96] Studies in this direction would improve the understanding of the interaction of extrinsic factors such as mechanical overuse and repetitive exposure to high loads, as well as intrinsic factors such as recovery capacity and vascularization of rotator cuff degeneration.[97]

Besides, central sensitization changes have been observed in patients with rotator cuff tendinopathy showing hyperalgesia and hypersensitivity in local shoulder regions and referred areas, which is a very typical symptom in shoulder clinical patterns presentation of rotator cuff tendinopathy. Central sensitization is being related with chronic states of pain experience in patients and usually associated with central motor disturbances such as corticospinal inhibition or reduction of excitability in some muscles such as infraspinatus, that assume an accurate role in glenohumeral joint reaction forces, shoulder function and stability.[98] Corticospinal disturbances have been described in deltoid muscle exhibiting an hyperexcitability during resting tasks and hipoexcitability during movements, supporting the hypothesis of how neuromuscular disruption may be directly linked with tendinopathy disorders.[99]

Assessment of the rotator cuff tendinopathy

Physical therapy evaluation of the shoulder in tendinopathy conditions requires numerous steps to better identify and understand the most reliable approach for each patient due to the general variables that may be related to tendon degeneration or, at least, the presence of pain and loss of function in the rotator cuff.

Firstly, an extensive and detailed subjective interview of the patient will allow to recognize the description and behavior of the symptoms as well as the functional restrictions of the shoulder. Questionnaires such as the Shoulder Pain and Disability Index (SPADI) or the Western Ontario Rotator Cuff Index (WORC) will allow these variables to be objectively analyzed.[100]

Secondly, the physical examination should focus specifically on the reproduction of the patient's symptoms, quantity and quality of movement during the analysis of active and passive mobility, the evaluation of the accessory movements of the humeral head with respect to the glenoid fossa, the diagnosis of scapular dysfunction, the exploration of the extensibility of the posterior capsule of the shoulder and glenohumeral internal rotation range of motion, muscle function in terms of strength and endurance, as well as neurodynamic test for neural mechanosensitivity and orthopedic tests for the diagnosis of impingement or rotator cuff tendinopathy.[101] Approaches based on symptom modification such as the Shoulder Symptom Modification Procedure (SSMP)[92] explore the interaction of thoracic spine, scapular different positions and humeral translations in patient's shoulder symptoms. This Manual Therapy approach based on the reproduction of symptoms arises because of the gaps related to the association of symptoms based on a specific structural diagnosis. In this way, the relief and reproduction of symptoms associated with the identification of postures, combined physiological movements, directions of joint accessory movements and neighboring joints, serve as an approach guide to the therapist.[92,100]

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Additionally, whole-body screening for functional or technical gesture evaluation may play a determinant role in overhead athletes with shoulder complaints. In this sense, the concept of kinetic chain emerges referring to the transfer of energy through interconnected segments from the lower limb, passing through the trunk and shoulder, being very illustrative in technical gestures such as tennis serve or throwing in handball.[102] Functional or mobility restrictions in segments of the lower limb responsible for generating energy, can reduce the transfer of energy to the shoulder, increasing the mechanical and functional demands on it, which could have a potential impact on pain, weakness, motor control or muscle imbalance.[103,104]

Orthopedic test in rotator cuff tendinopathy

The performance of orthopedic tests based on the identification of structures responsible for shoulder dysfunction, is based on the reproduction of symptoms such as pain or weakness. Currently, there is controversy about the reliability of these tests to isolate the components of the rotator cuff as a source of reproduction of the patient's symptoms.[105] Due to the complex anatomy of the glenohumeral joint, as well as the indivisible relationship between structural components such as the joint capsule and the interdigitated rotator cuff tendons, or biomechanically in relation to coupling forces and scapular orientation, they seem to question the clinical validity for the diagnosis of structures involved in the patient's symptoms.[92]

Despite the existing controversy, numerous studies have analyzed the orthopedic tests that provocation of the rotator cuff is related to the symptoms of impingement, in primary impingement (the inflammation or injury of the tendon directly causes the reduction of the space between the humeral head and the scapula) or secondary impingement (migration of the humeral head in different directions as a consequence of the impact of structures). Cools[74] proposed a clinical assessment algorithm for impingement symptoms including tests such as Jobe, Neer or Hawking; for rotator cuff pathology such as *full and empty can* test or for scapular dysfunction identification such as The Scapular Assistance Test (SAT) and The Scapular Retraction Test (SRT) in order to identifiy the dominant pattern of symptoms in athletes in presence of shoulder pain. In this line, Kibler and Sciascia[106] also proposed a clinical algorithm for shoulder pain or dysfunction in presence of scapular dysfunction in order to identify the causative factor of symptoms.

Imaging tools in rotator cuff tendinopathy

Diagnostic imaging tools such as ultrasound or magnetic resonance imaging (MRI) in rotator cuff tendinopathy has been used traditionally as a "gold standard test" in structural diagnosis and in clinical validation of orthopedic test. The main criteria to confirm the diagnosis is the presence of structural abnormality in imaging in order to rule out true positive test results. For this reason, imaging tests associated with the diagnosis of rotator cuff tendinopathy are controversial in the recent literature due to the presence of studies that showed findings of structural shoulder alterations in participants who do not present symptoms.[107,108] Other studies have reported associations between MRI findings and SPADI scores in patients diagnosed with subacromial syndrome of at least 3 months of evolution at the beginning of the study and after one year of evolution, but with a poor level of correlation in patients who received treatment and who presented major degenerative changes, tendinosis or bursitis in the imaging test.[109]

Despite the improvements in the image quality of imaging tools, the outbreak of tests such as ultrasound, that are more accessible and with less associated economic cost, and the high reliability in the detection of degenerative signs in structures of the shoulder joint and the rotator cuff, more studies are needed to assess the efficacy between the determination of structural changes by imaging tests and the presentation of the patient's symptoms[110,111] (Fig. 3).

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Conservative management of rotator cuff tendinopathy

Treatment of rotator cuff tendinopathy by the conservative point of view is integrated by different approaches. Most of the approaches agrees in the importance of exercise therapy as the main and useful therapeutic option for management of this patients independently of concomitant conditions presented such as rotator cuff partial tears, bursitis, etc. Different exercises combinations and strategies focusing on pain control and relief, as well as increase of function and decrease of weakness during progression have been proposed.[100] Exercise options may be based on motor control exercise for glenohumeral rotator cuff muscles, scapular exercise related to retraction position and mobility, shoulder self-stretches in order to restore glenohumeral internal rotation deficit (GIRD) in those patients which interact as a causative or risk factor,[112] restoration of normal values of range of motion,[113] strength improvement and endurance of the rotator cuff muscles and scapula stabilizers as well as including functional and kinetic chain based exercises in order to improve scapular and lumbopelvic muscle activation.[102–104,114] Ellenbecker and Cools[115] have proposed an algorithm for rotator cuff injuries based on a integrated approach focused in the detection of lack of tissue mobility of direct or indirect structures attached to the shoulder such as capsular restrictions or scapular muscles shortening, or muscle performance in terms of muscle control or strength. Progressions are stablished combining manual therapy and exercise to restore the lack of these elements and including stretching exercise programs, neuromuscular techniques and strength training.

However, active therapeutic approaches may also be related to reducing exercises or activities that increase the patient's symptoms in tendinopathy. Irritable rotator cuff tendinopathy conditions associated with a nightly increase in pain symptoms, persistent and highly irritated conditions, can benefit from relative rest and activity restriction of those that increase pattern irritability. In this context, exercise will focus on pain control strategies such as isometric exercises, movement in pain-free ranges, load management, and gesture modification.[100] Ultrasound-guided injections of the subacromial bursa with analgesics or corticosteroids should be a potentially effective option in reducing pain from irritative clinical pattern conditions, but are also recommended in combination with an exercise program. Finally, the evidence supports the importance of focusing on patient education on pain, concepts and biomechanics of the shoulder rotator cuff, the importance of the exercise program and personal involvement, activity restrictions or adaptation especially in athletes who are exposed daily to complex mobility exercises or high doses of repetitions.[100]

Hamstring tendinopathy

Introduction

Regarding the prevalence of proximal hamstring tendinopathy, specific numbers still not reported, however literature shows a high prevalence in speed runners.[116,117] In the same line of other tendinopathies, proximal hamstring tendinopathies muscles are due to overload during training or recreational activity.[118] Population shows 45% of gluteal tendinopathy in more advanced countries and is not related to a specific exercise.[117,119] Therefore, is less prevalent than others, gluteal tendinopathy in subjects with low exercise activities and can be related to overload of the gluteus maximus and medius, or both.[119]

Assessment and treatment

Diagnosis of hamstring and gluteus tendinopathy

Proximal hamstring tendinopathy reported a similar phenotype to general tendinopathy with similar features and symptoms that common tendinopathies. Pain located at the gluteal region is considered one of the main features, which could be irradiate along the hamstrings area.[116,120]

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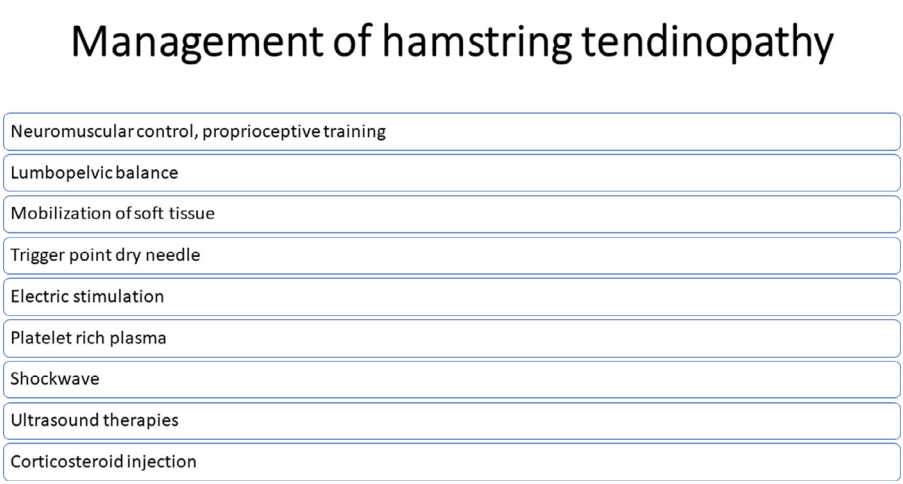

Fig. 4. Management of hamstring tendinopathy.

In this context, symptoms are presented at the beginning of the exercise and disappear after warming up and usually return when the activity is finished. Pain can progress without improvement with warm up activities or even in case of continued effort, and remain after the exercise, frequently with activities of daily living,[121] or in case of resting seated down or driving. In addition, sitting down or driving was also related with proximal hamstring tendinopathy.[116]

Gluteus tendinopathy is the most frequent lower limb tendinopathy.[122] Degenerative tendinosis is the first clinical manifestation and could produce greater trochanter pain syndrome or trochanteric bursitis.[123].

Prevalence of gluteal tendinopathy is increasing in sportsmen as a result to the popularity of amateur sport practise, such as running or football.[122] Regarding the biomechanical features, anatomic differences could be a risk factor to predispose the development of this pathology, for example: an increased acetabular anteversion, decreased gluteus medius insertion at the surface, shorter gluteal abductor moment arm, and higher adiposity tissue. Lower femoral neck shaft angle (coxa vara) is associated with gluteal tendinopathy[124] with a gluteus medius activation during dynamic single-leg activity as a result of the increased hip adduction moment.[122] Considering the muscle tissue, hip abductors tension disturbances may contribute to increase the risk of development gluteal tendinopathy. In this line, hip abductors during monopodal support influences the direction of the resultant hip joint reaction force, which lies in line with femoral neck and produce distribution of compressive force on the joint area.[122]

Gluteus medius weakness is related to a higher reaction force vector on the hip in the vertical plane and the flexion moment at the crural neck with balance disturbances; this outcomes as a result of force concentration on the superior surface of crural head, as the case of higher tensile forces along the superior femoral neck.

Management of hamstring tendinopathy

Usual care for hamstring tendinopathy are similar to the rest of tendinopathies: including ice and load management based on physical exercise and soft tissue mobilization[120] (Fig. 4).

Several authors estimate the time to heal around one to three months. Regarding previous sport activity levels there are different results, meanwhile a little pain could persist more weeks.[120,125] Other therapies have employed motor control for the lumbopelvic balance, trigger point dry needling or muscle electric stimulation.[126] Moreover, a neuromuscular approach using proprioceptive training was showed as a good treatment.[120]

Regarding the pathogenic cells tissue histology, low stretching could improve cell differentiation in tenocytes which contribute to increase level of tendon homeostasis.[127] Otherwise, large

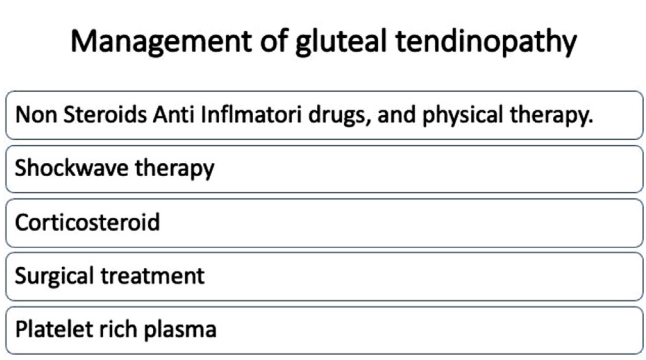

Fig. 5. Management of gluteal tendinopathy.

loading stretch could produce adverse effects, with degenerative symptoms as the case of calcification, or similar disorders.[120]

Different approaches have been described in recalcitrant tendon pathology, for example, shockwave and ultrasound therapies, or ultrasound- guided corticosteroid injection, and platelet rich plasma injection.[120,128,129] Comparing a combination of non-steroid anti-inflammatory drugs with physiotherapy and specific exercises and shockwaves had significantly increase time to resolve the disability with a time range from ten months..[128] However, ultrasound-guided corticosteroid could produce inhibition of collagen fibres, which could produce a difficult healing process and recurrent pathology associated.[130] Besides symptoms reappears after good short-term results.[131]

Platelet rich plasma as a new biological therapy has limited scientific evidence. For this reason the needing of clinical trials to check efficacy and safety have been developed during last years, however several limitations in method does not clarify the clinical significance.[132,133]

Management of gluteal tendinopathy

Gluteus tendinopathy have been managed in a conservative approach with exercise programs, non-steroid anti-inflammatory drugs, and physical therapy[129] (Fig. 5).

Also there are evidence of the efficacy of shockwave therapy conservative treatment for greater trochanteric pain.[128,134]

Corticosteroids injections have been employed to treat greater trochanteric pain. But even when patients reduce their pain around to 55%, the effect does not remain one year compared to patients who does not receive injection.[135,136] In addition, there are scientific literature that corticosteroids could harm musculoskeletal tissues with worse results in epicondylitis conditions.[137,138] Surgical treatment is employed in case of gluteal tendinopathies which not respond to conservative therapies. In this line, a decrease on pain intensity and functional results have been showed with endoscopic and open abductor tendon repair. However, these techniques have been related with other complications, for example: tendon re-tear, greater trochanter fracture, or infection.[139]

There are some researchers who have reported positive outcomes of platelet rich plasma in gluteal tendinopathy. Fitzpatrick et al.[140,141] carried out a randomized controlled trial comparing ultrasound-guided platelet rich plasma injection with a corticosteroid injection, and results highlighted that pain and function were improved for the platelet rich plasma group with respect to corticosteroid group. However, Jacobson et al[142] developed a single-blinded prospective clinical trial which not showed significative differences between 30 chronic gluteus tendinopathy subjects treated with either percutaneous needle puncture or platelet rich plasma infiltration. Moreover, a significant pain score decrease was showed with a fifty-day follow-up that in both groups.

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As mentioned above, the prevalence of tendinopathy is related with aging; however, subjects who received surgical treatment for hamstring tendinopathy are frequently young and usually physically active individuals.[120] Differences between sport activity stress and age regarding to tendon degeneration is not clearly defined yet, Ruzzini et al. demonstrated that tendon cells in older hamstring tendons had weaker potential related to mechanical tissue characterises which could suggest a possible biological basis for age-related differences.[143]

The aetiology of hamstring tendinopathy still not clear and could be the same as in other tendinopathies. In this line, similarities to other tendons tissues must be addressed with caution due to the different anatomy and fascial strains architecture. Despite platelet rich plasma as new therapy could be an interesting treatment, the first conservative option should be a conservative approach based on a load management exercise program to decrease pain symptoms and increasing functionality.

Knee tendinopathy

Definition and epidemiology

Patellar tendinopathy (PT) is an injury often described as “jumper’s knee”. It is caused by functional overload, which is related to an excessive and intense use of the patellar tendon.[144] This pathomechanic is caused by an inability to adapt to the forceful and repetitive loading of the quadriceps, especially if there is a high volume of training.[145]

PT has been described as a very limiting condition; sports involving explosive jumps or explosive starts and stops are considered risk factors for the development of this overuse injury.[146] Although this injury can be suffered by the entire population,[147] physically active people were more predisposed to develop this musculoskeletal condition. The prevalence is reported as lower in amateur athletes, who train fewer hours per week and less intensively than elite athletes.[148,149] It is mainly suffered by subjects who need to jump in their sports practice, such as volleyball and basketball players, but it is also found in a lower percentage in athletes who practice athletics (long-distance runners) due to repeated micro-traumas and soccer, as a result of quick starts and repeated changes of direction.[150,151]

Pain associated to PT usually appears at the beginning and at the end of physical activity, whit a decreasing of symptoms during the physical activity. If the symptoms persists, PT could be develop a continuous pain, even after the end of the exercise and at rest.[152]

Multiple causes could overlap in the development of PT. Intrinsic factors have been described such as genetics, gender (with a higher incidence in men than in women), metabolic diseases, altered flexibility, collagen metabolic disorders, hypercholesterolemia, diabetes, age (with a higher incidence rate in young people than in adults), high uric acid levels and rheumatoid diseases, among others. Extrinsic factors include all the training variables, the level of participation (with a higher incidence in elite athletes versus recreational level), drug use and the administration of some medications.[153–158]

Regarding biomechanical factors and anatomical alterations, it is known that patients with PT have a greater degree of lateral patellar mobility compared to healthy subjects without PT.[159] Patellar mobility can be measured using a manual mobility test, however this tool reported low reliability due to lack of accuracy during the assessment procedure.[160] In this context, an alternative device who reported good validity is a patellofemoral arthrometer, showing a high reliability if we compare its results with images taken by magnetic resonance.[161]

There are multiple lower extremity injuries that are related to excessive hip adduction, such as iliotibial band syndrome,[162] tibial stress fractures,[163] patellofemoral pain[164] and also in patients with PT.[159] Increased hip adduction may lead to altered quadriceps loads, which could lead to increased patellar tendon strain.[159]

Jumping sports, such as basketball or volleyball, shared two biomechanical features directly related with patellar conditions: the lack of strength and increased lateral mobility of the patella

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and the lack of control of the hip due to an increased adduction, can lead to increased traction and tension in the proximal portion of the patellar tendon during the landing phase after a jump with an associated increase on the traction and tension in the proximal portion of the patellar tendon.[159] Ground reaction forces and the force of gravity could also be taken into account in the development of the TP.[165,166]

Several studies reported biomechanical factors as contributors to PT, such as increased knee and ankle flexion and increased internal tibial rotation during initial contact in jump reception or running.[166–168] Therefore, dynamic tests performed in patients with PT founded biomechanical alterations in the hip and/or in the ankle joint because of interdependence of the knee with its surrounding joints. Those findings could be interpreted as a prevention strategy and should be considered for the diagnosis and the management of this musculoskeletal condition. Regarding the biomechanics disturbances, osteoarthritis disease located in the hip, which causes limited internal rotation, can lead to increased external rotation of the hip during flexion, resulting in lateral knee pain associated with excessive traction force on the proximal insertion of the patellar tendon.[169] In the same context, a misalignment of the knee flexion-extension axis, such as increased physiological varus or valgus, presence of recurvatum or alteration of the Q angle, can increase the loading forces and traction on the patellar tendon, which is related to patellar tendinopathies.[152] It has also been described how a reduced flexibility of the hamstrings or a previous knee injury can favor the development of patellar tendinopathy.[170]

Diagnostic tests

It is necessary the employment of validated tests to detect PT, and it is suggested to combine all the results to understand the multifactorial presentation of tendinopathy. Individual participation should be measured, and the degree of disability at work, in daily activities and in sports. It is also necessary to quantify pain intensity at rest, during the performance of different activities and under functional load, such as performing a one-legged squat on a declined plane.[171] Psychological factors and functional capabilities have been considered very important added to an anamnesis, static and dynamic visual examination, palpation, and range of motion assessment for a complete PT assessment.[172–174] The most widely employed questionnaire for assessing symptom severity is the Victorian Institute of Sports Assessment for patellar tendinopathy (VISA-P), a validated tool consisting of eight items, six of which rate pain during functional tests and activities and the other two provide information on the impact of PT on sports participation or physical activity.[172,175]

Ultrasound imaging and MRI can be used as diagnostic imaging tests for the detection of abnormalities or disorders of the patellar tendon along its entire length, from the inferior pole of the patella to its insertion on the tibial tuberosity[176–178] (Fig. 6). Finding histopathological changes is not always related to symptoms, on the contrary, there is evidence that the presence of abnormalities increases the probability of developing PT with symptoms.[179]

In injuries of less than eight weeks of duration, which are considered acute, the presence of neovessels can be observed in the ultrasound and Doppler and could be justified with the increase of vascularization of the tendon that occurs during the repair phase, this is a natural and expected process. If the angiogenesis process persists beyond the first eight months (considered as a pathological finding) it may be related to an incorrect tendon repair. To neovascularization assessment, ultrasound doppler can be used with the modified Öhberg scoring scale, which scores over four grades and has been shown to be a reliable and reproducible assessment tool.[180] The presence of neovessels in tendons with pathology is associated with a higher degree of pain than in pathological tendons where neovascularization is not observed.[181,182] Therefore, the blood flow evaluation by ultrasound imaging could be beneficial for the diagnosis and management of tendon conditions.

In this line, ultrasound imaging has been described as a valid and reliable tool to evaluate quantitative data of the tendon and peritendinous structures. Pathological tendons compared with healthy tendons show differences for the architecture (thickness and CSA) and the pixel

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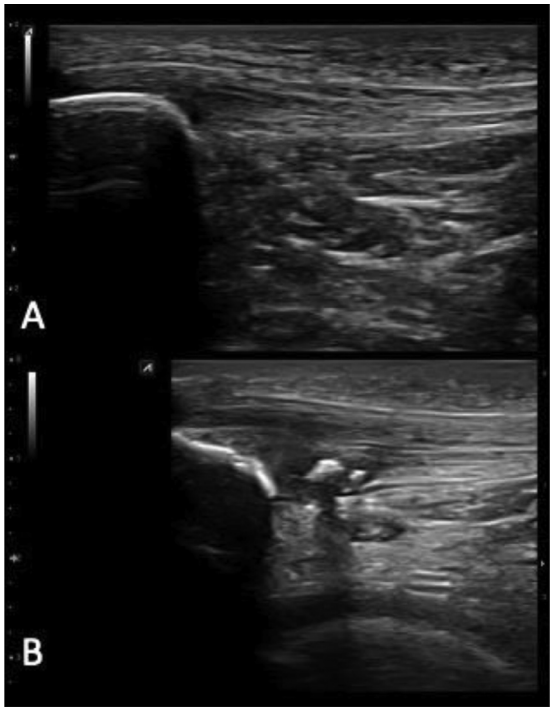

Fig. 6. Ultrasound imaging in a longitudinal view of a healthy tendon (A) and a intrasubstance calcification tendon (B).

gray-scale. These changes may suggest different stages for the PT development. Hypoechoic areas should be associated with pain locations and usually present blood flow signals assessed with the doppler tool from an ultrasonography tool.[183] These imaging findings should be taken into account carefully due to the PT was considered a clinical condition, based on the clinical findings founded in the anamnesis. Therefore, the imaging findings were important always related with the clinical test values and symptoms.[184,185]

In this line, physical examination combined with imaging evaluation could be used with tools such as the VISA-P questionnaire. Results reported by all the physical test, tools and questionnaires could be used to validate the efficacy and progress of treatment, as well as for early identification of risk factors with good reliability.[147]

The Oslo Trauma Research Center developed the OSTRC questionnaire to quantify the prevalence and severity of repetitive trauma in sports injuries. PT cases can be identified through this questionnaire whit the adaptation of OSTRC test based on symptoms and features of the injury. Therefore, the specific PT questionnaire now called OSTRC-P was described also as a low-cost tool that could be used on the one hand to perform a diagnostic self-report, which examines the severity of the injury, and on the other hand to follow up the tendinopathy.[186]

Treatment

Injury location within the tendon define the tendinopathy approach, when the injury is located in the deep interface (near the Hoffaś fat pad), tensile forces are transmitted more during flexion movement, than in the superficial interface where extension is responsible for this force. Moreover, the peritendon area was defined as the most reactive area subject to mechanical changes that could be related on the development of patellar tendon pathology.[152]

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During the first eight weeks from the appearance of the injury, a great cellular and chemical activity triggers the physiological healing process. If this process is prolonged in time and the symptoms are persistent, the reactive tendinopathy enters into a degenerative processes and therefore the tissue recovery become more difficult.[187]

Evidence-based literature support the classification of tendon condition as an overuse injury, so an optimal training load management plays an important role in the first stages of tendon rehabilitation.[188] In this line, exercise and load management were considered the first non-invasive option for PT.[189–193] An individualized approach including pain intensity assessment during activity, via a visual analog pain scale (VAS), may be an appropriate for managing the training load program.

Regarding the therapeutic exercise program that should be prescribed, there are also multiple options, several studies reported a decrease in pain intensity and improvement in function by performing a program for twelve weeks of unilateral squatting on a board with a decline of 25 degrees to reduce pain.[194–198] According to the literature, treatment with eccentric exercises improves functionality and reduces pain in the early stages of the disease, and also has the ability to increase tendon remodeling due to the stimulation of collagen fibers.[199]

Although the literature is much more extensive and there is sufficient evidence to implement eccentric contraction exercises for patellar tendinopathy, there are other therapeutic exercise alternatives such as isometric contraction.[151,191,200,201] In a study by Rio et al. it was shown that a single isometric contraction in athletes in competition season resulted in immediate pain relief that extended for 45 min, this finding is important as this pain latency period can be used to increase load and performance.[201]

Other studies found clinical improvement in function and pain that could be related to normalization of tendon fibril morphology following slow and heavy strength training (HSR) work. The HRS consisted of a strength program performed bilaterally and for twelve weeks, including squats, leg presses, and machine squats (hack squats).[191,202].

Therefore, we could use isometric exercises, eccentric exercises or HSR exercises, the first ones would be more indicated during the competition phases, since it gives us that short-term analgesia. Eccentric and HSR exercises seem more effective and adequate to improve functionality and pain in the long term.[193] Another option is to perform an isometric exercise and benefit from the period of analgesia to implement the treatment with eccentric exercises or HSR.

In this line, currently research show that loading seems to be necessary for tendon remodeling, there are athletes who present pain during therapeutic exercise programs, and this may justify the lack of improvement after completing such programs. A previously described proposal for these cases is to perform the activity under pain monitoring. An alternative approach found in the literature is the use of blood flow restriction therapy (BFR), an inflatable cuff that is placed on the proximal thigh as a tourniquet with the intention of occluding blood flow during exercise. In patients who do not support high load exercises, this training with BFR achieves the benefits of high intensity such as increased strength and increased cross section of the quadriceps and patellar tendon with the advantage of suffering less stress on the tendon and joint.[203–205]

If the subject presents hip adduction, which we know is directly associated with patients with PT, we should include hip abduction work in our therapeutic exercise program to improve the movement pattern.[159] The correlation between increased patellar mobility and the presence of PT is also described, although more studies are needed, it would be interesting to investigate the use of stabilizing supports to reduce the lateral displacement of the patella in the flexion movement and how this could improve the symptoms in patients with PT.[159]

Extracorporeal shock waves therapy (ESWT) has been described as an alternative option, which could reactivate the tendon repair process and reducing the surgery intervention. It is a therapy that uses mechanical loading to try to reactivate the tissue regeneration of the patellar tendon.[206] The use of ESWT is becoming more and more widespread in lower limb tendinopathies, although there is no clear guideline regarding the dosage of the technique and further studies focused on the treatment of PT would be necessary. The use of ESWT is attributed to a decrease in pain due to the suppressive effect of nociceptors, a decrease in edema and swelling, a decrease in inflammatory cells in the tendon, a proliferation of tenocytes and

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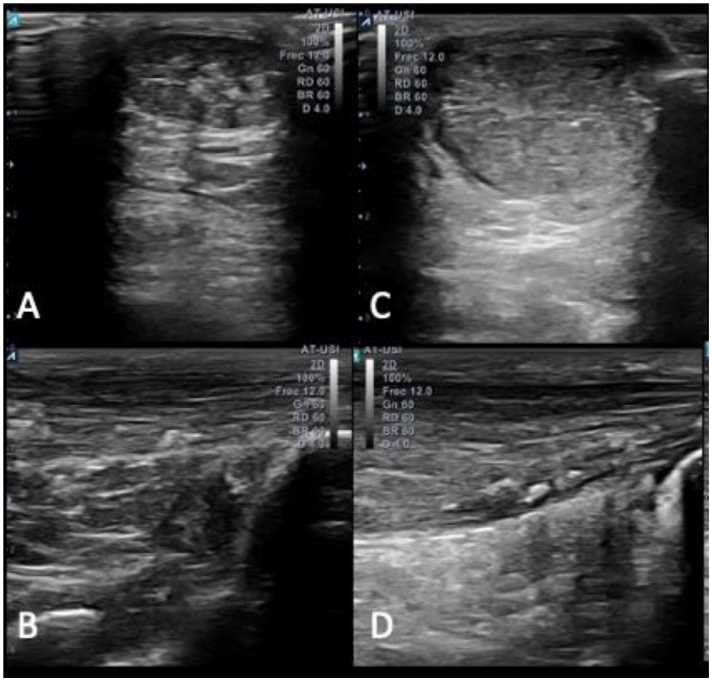

Fig. 7. Ultrasound imaging of a healthy Achilles tendon -transversal (A) and a longitudinal view (B) – and an Achilles tendinopathy tendon – transversal (C) and longitudinal view (D).

neovascularization that will facilitate the arrival of oxygen and nutrients to the injured area, and a stimulation of healing to help the progressive regeneration of the tendon.[207–210]

Invasive treatments have been reported benefits, and there is an increasing range of possibilities among which we find, among other therapies, treatment with ultrasound-guided elecrolysis, percutaneous neuromodulation (PNM), the use of adipose tissue stem cell injections (ASC), hyaluronic acid (HA), and platelet-rich plasma (PRP), although these last two options are not included as physiotherapy techniques and must be performed by specialized physicians.

Ultrasound-guided electrolysis produce the rupture of fibrotic and necrotic tissue, thereby creating new blood vessels that ensure the supply of oxygen and nutrients to the area to allow the tendon to regenerate.[211] In this line, repeated puncture of the damaged tendon area stimulates an inflammatory response, which induces the creation of new granulation tissue, thus reinforcing the tendon.[212]

Ultrasound-guided electrolysis could be considered one alternative and/or a complement of physical therapy programs for the treatment of PT.[212–215] It has been shown that there is a relationship between the healing process and the increase of growth factors.[216,217] Although this statement is promising, more studies are needed to determine a standard protocol for the number of sessions and the interval between electrolysis intervention.[218,219]

Regarding the use of ultrasound-guided, HA injections around the patellar tendon, several studies have shown a decrease in pain, decreased pain on palpation, decreased neovascularization, reduced swelling and decreased tendon thickness. It could therefore be considered an alternative to a physical therapy programs without adverse effects for the treatment of PT.[209,220,221]

Regarding the tissue regeneration, mesenchymal cells could differentiate and activate the proliferation of tissue-specific cells where they are injected with ASC. Several authors support an activation of the repair pathways of damaged tissue, regulate inflammation by their immunoregulatory action and secrete growth factors and neovascularization. Therefore, the use of autologous

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ASC is considered an useful treatment for the manageament of chronic patellar tendinopathy, achieving a decrease in pain and an improvement in functionality and performance in the short term. However, further studies are needed to define the role of this therapy in the treatment of PT and to specify the dosage of the technique.[222–224]

If all conservative treatments fail, surgery might be indicated in chronic and recalcitrant cases of PT.[225] However, some subjects remain symptomatic or even worsen after surgery.[226]

Achilles tendinopathy and plantar fasciitis

Introduction

Achilles tendinopathy is a degenerative pathology that is caused by a failure in healing due to an imbalance between the load and the rest of the tendon, which causes an affectation of the tenocytes, a disorganization of the collagen fibers, and a proliferation of non-collagenous matrix. In addition, it also increases type III collagen, which has poorer biomechanical properties, due to its lower extensibility. Structurally, in these patients, an increase in the cross-sectional area of the tendon can be observed by ultrasound imaging.[227,228] Achilles tendinopathy can be insertional, proximal, or more frequently, affect the central part of the tendon. In insertional tendinopathy, other conditions such as intratendinous calcifications may also appear.[227,229]

Epidemiology

Achilles tendinopathy is common among athletes, especially in runners, where this pathology represents 6–17% of all injuries. While 43% of elite track and field athletes have suffered from this pathology at some point, among medium-distance runners the prevalence is 83%.[33] Most athletes who develop Achilles tendinopathy describe that at some point during their training program there has been a sudden increase in load, as well as inadequate rest. Therefore, the planning of sports training is very important in the prevention of this pathology.[230]

Diagnostic

The diagnosis of Achilles tendinopathy is clinical, and should be based mainly on the medical history of the patient and the physical examination.[231] The most frequent symptoms are morning stiffness, stiffness after a period of inactivity, and a progressive appearance of pain associated with sports activity. When this foot disorder is established, initially the pain appears only at the beginning and at the end of sports activity. If the pathology does not remit and becomes chronic, the pain can appear progressively in most daily living activities, even in low intensity tasks. In addition to pain, swelling often occurs around the tendon, and athletes experience a decline in athletic performance.[227] On physical examination, mid-tendon tenderness is considered a highly sensitive and specific test to diagnose Achilles tendinopathy.[232] This test can be completed with the Royal London Hospital test, which is more specific.[231]

In addition to clinical diagnosis, ultrasound tissue characterization has recently been established as a valid method to quantitatively assess tendon structure[233] (Fig. 7).

In cases where the ultrasound diagnosis is unclear, magnetic resonance imaging (MRI) can be used, which gives very extensive information on the internal morphology of the tendon, as well as other structures that surround it. In fact, in the event of surgery, MRI makes it possible to differentiate between tendinopathy and para-tendinopathy, in addition to quantifying the amount of tissue affected. However, MRI data should be interpreted with caution, and should always be checked against the patient's symptoms to be relevant.[227]

To assess the evolution of the patient affected by Achilles tendinopathy, the Victorian Institute of Sport Assessment –Achilles questionnaire can be used, with a difference of 10 points being considered clinically significant.[234]

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Risk factors

The following risk factors must be taken into account and addressed when designing the treatment of the Achilles tendinopathy: a decrease in plantar flexion strength, lack of motor control in the hip muscles, lack of range of motion in dorsiflexion of the ankle, excessive pronation of the foot, or being overweight.[235] Other factors should not be ignored, such as the use of fluoroquinolone antibiotics, which have been related to the onset of Achilles tendinopathy or even tendon rupture one week after being used.[236] Regarding other risk factors such as the influence of footwear or sports surfaces, there is little scientific evidence to date about their relationship with the development of the Achilles tendinopathy.[32,235]

Scientific evidence of Achilles tendinopathy treatments

To date, in 24–45.5% of patients suffering from this pathology, conservative treatment fails. According to several authors, complete recovery from this pathology following conservative treatment can last up to a year, so it is recommended to wait for this period before considering surgical treatment. If conservative treatment is started as soon as the first symptoms of stiffness and pain appear, the prognosis is more favorable.[32] When considering surgical treatment, the options are wide, ranging from percutaneous tenotomy to open surgeries.[227] As intermediate therapy between conservative and surgical treatment, percutaneous therapies can be carried out. Among them, the less aggressive options are platelet-rich plasma injection and dry needling in the tendon. According to observational studies, both therapies achieve effective benefits in terms of pain and function, with similar results.[237] These treatments appear to have a positive impact on neovascularization and tissue remodeling. Although the results are promising the level of scientific evidence today is very weak.[238]

Regarding conservative treatments, cryotherapy, to which analgesic and anti-inflammatory properties are attributed, has not proven to be an effective technique for the management of this pathology. However, some randomized clinical trials that analyzed the use of thermotherapy suggest that this therapy could stimulate repair processes, relieve pain, and increase tendon extensibility.[227]

Eccentric exercises are one of the main conservative therapies for Achilles tendinopathy. It is attributed to them that they facilitate the remodeling of the tendon through the stimulation of collagen formation.[239] Even though in randomized clinical trials of high methodological quality with eccentric exercises the results in the clinical manifestations of patients affected by Achilles tendinopathy are very favorable,[240,241] the mechanisms that explain why pain decreases, or the histological changes produced in the tendon are unclear.[227] Eccentric exercises could be included within exercise rehabilitation, which is the conservative therapy with the most scientific evidence for Achilles tendinopathy.[235] This therapy aims to provide a mechanical load to the tendon by stimulating the remodeling of collagen fibers, in addition to increasing the strength and endurance of the calf muscles.[242] The ideal dose of exercises is not well established, although it seems that high loads with slow contractions are more effective than low loads at high speeds.[230]

In rehabilitation through exercise, it has recently been proposed that isometric exercises should be performed in the initial stages due to their analgesic effect, in addition to eccentric exercises.[243] In this initial phase, the load on the tendon should also be reduced, by changing the type of activity, or by reducing the volume or intensity of the exercise. It is important not to fall into the error of setting a complete rest since it is counterproductive and it would imply a deconditioning of the muscles and other structures. The reduction of the training load must be agreed upon with the patient, and also with the coaches if the patient is an athlete.[243]

As the patient's symptoms improve, progressively exercises such as heel rise standing on a step should be incorporated, gradually increasing the intensity, the number of repetitions, the speed of movement, or the range of motion, always without causing pain. However, in patients with insertional tendinopathy, the degree of dorsiflexion will be limited when performing these exercises to avoid compressing the tendon. Specific strengthening exercises for the intrinsic muscles of the foot, and exercises to improve hip muscles function should also be added since they are key aspects of running biomechanics. Later, plyometric training should be incorporated,

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which will overlap with the return-to-sport phase. In this last phase, pain should be monitored as a criterion to continue progressing towards returning to training, and functional tests are also very useful to assess symmetry in terms of strength and motor control between limbs.[242] Finally, when returning to training, the sessions should be scheduled with enough space to allow rest the tendon and avoid relapses, especially when performing high load activities.[32]

Regarding other conservative therapies, according to a recent meta-analysis published by Fan et al. in 2020, low-energy shock waves are effective in reducing pain and improving the Victorian Institute of Sports Assessment –Achilles questionnaire score in patients with Achilles tendinopathy, which may be because the shock waves can stimulate soft tissue healing and inhibit pain receptors. However, more studies are needed to determine the optimal energy level.[244] According to another recent systematic review, low-energy shock waves combined with eccentric exercises are more effective than therapy based exclusively on eccentric exercises.[245]

Finally, other therapies such as ultrasound or orthoses have not demonstrated their efficacy to recommend their use to treat this pathology.[227]

Conclusions

In conclusion, patients affected by Achilles tendinopathy must understand that treatment is not easy, that it can last many months, and that even after recovering, their symptoms may relapse, or even require surgery if conservative approach fails after one year of treatment. Priority should be given to a therapy based on rehabilitation through exercise, taking great care in the progression between stages, and perhaps in combination with a low-energy shock-wave treatment. On the other hand, in addition to thinking about a total cure of this pathology, it can be very useful to teach patients to control symptoms by dosing training loads.[32,227]

Plantar fasciitis

Introduction

Plantar fasciitis, also known as plantar heel pain or plantar fasciopathy, is a degenerative pathology of the foot characterized by degenerative changes in the collagen fibers in the plantar fascia, and histologically by micro-tears, without inflammatory signs. These degenerative changes are generally due to overuse or repetitive microtraumas with stretching of the plantar fascia, which exceed its ability to recover.[246]

Often, patients affected by this condition have tightness of the calf muscle and the Achilles tendon, in addition to painful ankle dorsiflexion. The most characteristic sign is post-static dyskinesia: Patients describe a stabbing pain at the origin of the plantar medial tubercle of calcaneal tuberosity when taking the first steps in the morning after the plantar fascia has not been stretched for several hours during sleeping.[247]

Epidemiology

Plantar fasciitis is one of the most common foot pathologies, accounting for 10% of the injuries of runners, and 11–15% of consultations for foot pain in the adult population, having its peak incidence in the range 40–60 years old.[248]

Diagnostic

The diagnosis of plantar fasciitis is clinical (Fig. 8). Patients often present with hypersensitivity to the plantar fascia at the origin of the plantar medial tubercle of calcaneal tuberosity, limited dorsiflexion, and contractures of the gastrocnemius. The use of radiography allows making a differential diagnosis with a calcaneal stress fracture or with a calcification,[249] while ultrasonography allows seeing the plantar fascia thickness, in addition to fascial tears.[250,251] On the other hand, the use of MRI is not necessary to diagnose plantar fasciitis. What is complicated about this pathology is not its diagnosis but rather finding a cost-effective treatment.[252]

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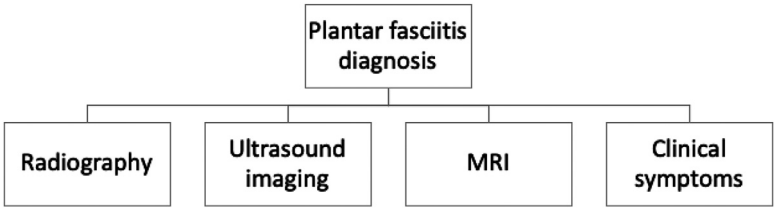

Fig. 8. Plantar fasciitis diagnosis.

Risk factors

Some of the risk factors that have been associated with the development of plantar fasciitis are limb length discrepancy, limitation of dorsiflexion, and biomechanical factors of the foot such as excessive pronation or supination of the foot, pes planus, and pes cavus,[253] as well as being obese/overweight.[254] In addition, posterior leg muscles thickness is usually found in these patients, possibly affecting their normal gait biomechanics.[255] Regarding gait deviations, according to a systematic review carried out in 2017 in which 19 studies were included, the stance phase during gait was not modified in patients affected by plantar fasciitis, while other parameters such as pressure in the center of the rearfoot or the maximum vertical reaction force of the ground at loading response were significantly lower. This implied, among other aspects, a longer contact time of the midfoot and forefoot. Although more studies are needed to analyze the gait in patients affected by plantar fasciitis, it seems clear that an inadequate gait is a risk factor for developing this pathology.[256]

Scientific evidence of plantar fasciitis treatments

Commonly, plantar fasciitis treatment is conservative, and includes dosing the training load to reduce pain and promote tissue regeneration,[257] taping therapy to relieve tension in the plantar fascia,[258] and soleus and gastrocnemius stretching.[259] It should be noted that the symptoms can remain for weeks or months despite having a well-focused treatment. If the patient's symptoms do not improve with conservative approach, techniques such as extracorporeal low-energy shock-wave therapy or platelet-rich plasma injections can be used. Only in 5% of cases is surgery necessary, when there has been no improvement after 12 months, the most common surgical options being total or partial fasciotomy, although to date the results are not satisfactory.[253]

Regarding stretching, a recent meta-analysis compared the efficacy of calf stretching versus plantar fascia-specific stretching, the latter being more effective in reducing pain, with moderate-quality evidence. To avoid long-term recurrences in this pathology, isolated stretching is not effective, but it is a valid short-term solution for pain.[260]

The mobilization of the soft tissues of the plantar arch has been shown to be effective in reducing pain caused by plantar fasciitis regardless of whether or not it is combined with stretching or joint mobilizations, according to a systematic review carried out in 2018, in which six high- methodological quality randomized controlled trials were included, so it should be performed in the earlier stages of the plantar fasciitis.[261]

According to a meta-analysis carried out by Li et al. in 2018, in which 19 studies were included, extracorporeal low-energy shock-wave therapy is effective in reducing pain in patients affected by plantar fasciitis, especially in the first six weeks of evolution. There is no scientific evidence about the effectiveness of ultrasound therapy, low-level laser therapy, or pulsed radiofrequency, in improving the symptoms these patients.[262]

Regarding other conservative therapies, according to a systematic review carried out by Lewis et al., orthotics are effective in reducing pain and increasing functionality in patients affected by plantar fasciitis in its acute phase, used alone or in combination with conventional therapy, with a level of evidence A.[263]

As for platelet-rich plasma injections, according to a recent meta-analysis, they allow the plantar fascia to be regenerated through growth factors. These injections have been shown to be

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more effective than corticosteroid injections in relieving pain and improving function in patients with plantar fasciitis in the short, medium, and long term.[264]

To reduce recurrences in plantar fasciitis, it has been suggested that specific physical exercise consisting in strengthening the intrinsic muscles of the foot, could be effective by providing more stability to the ankle, the foot joints, and the plantar arch. However, there is no scientific evidence in this regard, according to a systematic review carried out by Huffer et al., due to the wide heterogeneity of exercise programs and measurement tools, which is why more studies are needed about this topic. However, it is believed that specific strengthening of the intrinsic muscles of the foot could help relieve pain and increase function in patients.[265] A recent randomized controlled trial compared the effect of a muscle strengthening program versus stretching in patients with plantar fasciitis, finding a reduction in pain and a gait improvement in both groups, with no significant differences between the two groups.[266]

Conclusions

In the management of plantar fasciitis, conservative treatment should be considered at first with specific stretching of the plantar fascia, taping in the plantar fascia, use of orthotics, low-energy shock-wave therapy, in addition to dosing the training load. If the patient does not progress favorably, platelet-rich plasma injections could be performed. Regarding the strengthening of the intrinsic muscles of the foot, it is believed that it can be very useful to prevent the appearance or recurrences of this pathology, but more studies should be carried out on this treatment.

Other lower limb tendinopathies

Concerning other lower limb tendinopathies, some of the most common are the posterior tibial tendinopathy and the iliotibial band syndrome, which are developed next.

Posterior tibial tendinopathy

Definition/epidemiology

Posterior tibial tendinopathy is an underdiagnosed condition, most common in women aged more than 40 years, and its most frequent presentation in the initial stages is a tenosynovitis of the distal part of the tendon. The posterior tibial tendon is the main stabilizer of the medial longitudinal arch of the foot,[267] so if this pathology is not treated correctly, it can cause a flattening of the foot due to the fall of the medial longitudinal plantar arch, as well as abnormal foot alignment, and an affectation of the ambulatory function.[268]

Risk factors

Some of the risk factors that predispose to developing this pathology are obesity and previous trauma in the area.[267] On the other hand, to date, there is no evidence that hip muscle performance is a risk factor for developing posterior tibial tendinopathy, but rather seems to be a consequence.[269]

According to a recent meta-analysis, there is very limited evidence that a higher peak rearfoot eversion is associated with a higher probability of developing this pathology in runners.[270] Likewise, according to another recent meta-analysis, patients affected by posterior tibial tendinopathy present alterations in gait function, such as increased dorsiflexion and abduction of the forefoot, as well as increased plantarflexion and eversion of hindfoot during stance of walking, compared with healthy controls.[271]

Diagnostics

Initially, the patient reports tenderness in the area, and swelling and warmth along the tendon can be observed. In this initial stage, the use of ultrasonographic ultrasound can be useful.

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If this keeps evolving, an increase in the hindfoot valgus and a collapse of the arch upon standing can be observed, and this can progress to a rigid forefoot abduction, with involvement of the subtalar joint. Finally, this pathology can progress to the ankle joint. In these final stages, deformities in different joints of the foot can be observed by radiography imaging.[272]

Scientific evidence of posterior tibial tendinopathy treatments

The classical approach to treating patients with posterior tibial tendinopathy consists in bracing, stretching the gastrocnemius, and strengthening the posterior tibialis. When this approach is not effective after six months, surgical intervention is indicated to correct the alignment of the foot.[271]

According to a meta-analysis carried out in 2018, only three randomized controlled trials have been published to date that analyze the effect of exercise strengthening in patients with posterior tibial tendinopathy. Eccentric exercises have been shown to be effective in reducing pain and disability, with moderate effect size, compared to the traditional therapies such as stretching, orthoses, and concentric exercises. In these clinical trials, some exercise prescription parameters are missing, to be able to reproduce these treatments.[273]

Conclusions

The causes of the posterior tibial tendinopathy are still unclear, although recent studies show biomechanical alterations that may be related to this pathology. Regarding treatments, it appears that eccentric exercises are an effective treatment option, although there is still a lack of studies about this topic that fully detail the parameters of the exercises.

Iliotibial band syndrome

Definition, epidemiology, and diagnosis

Iliotibial Band Syndrome is a common cause of knee pain, especially in runners and cyclists, because they perform repetitive flexion-extension of the knee joint.[274] Iliotibial band syndrome accounts for 10% of running-related injuries. Also, the prevalence is higher in women. The pain usually appears at 30° of knee flexion during the stance phase of running.[274,275]

The diagnosis of this pathology is mainly through clinical symptoms, although the inflammation symptoms can also be assessed by MRI. However, there is no uniform diagnostic criterion.[276]

Risk factors

Regarding the biomechanical risk factors that contribute to iliotibial band syndrome development in runners, according to a recent systematic review, the main factors are an exaggerated internal knee rotation during the stance phase, a decrease in rearfoot eversion at heel strike[275,277] and weakness of the hip abductors that causes an increase in hip adduction, and an over-tension of the iliotibial band during knee flexion-extension.[278]

However, in a study carried out in 2020 with sonographic elastography, they concluded that the tension in the iliotibial band was not related to the iliotibial band syndrome, while the strength deficit of the hip abductors was a key factor.[269]

Scientific evidence of iliotibial band syndrome treatments

According to a systematic review carried out in 2020 by Bolia et al.[274] which included six randomized controlled trials of moderate quality about non-operative treatment, multiple conservative therapies such as low-energy shock wave therapy, stretching of the gluteal muscles, or hip abductors strengthening have been performed for the management of iliotibial band syndrome, mostly in runners. All these conservative therapies were effective in reducing pain, although the follow-up time was short. There are no conclusive data about other variables, nor a long-term follow-up, and there is a high heterogeneity of the treatments, so the scientific evidence available about this topic is limited.[274] Nine randomized controlled trials about operative

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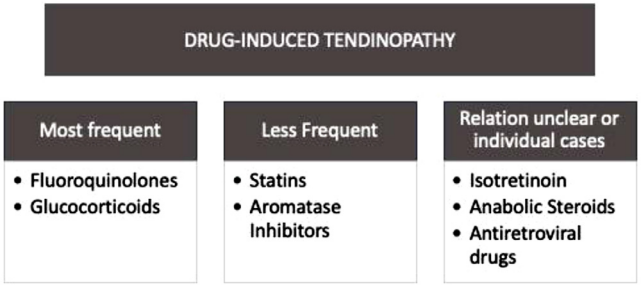

Fig. 9. Drug-induced tendinopathy.

treatment were included. This type of therapy is indicated if conservative treatments are not effective after six months. Multiple surgical options such as bursectomy and iliotibial band partial release have been proposed, with an 81–100% reported return-to-sport rate, which was the main outcome reported.[274]

According to a systematic review carried out by Baker et al. in 2016, after an acute phase in which stretching and myofascial treatment of the gluteal muscles should be carried out as analgesic measures, a program of progressive strengthening of the hip abductors should be started, with exercises such as the single-leg step-down, the single-leg pelvic drop, or the single-leg deadlift. Complementarily, doing a specific running technique training could also be very useful.[279]

Conclusions

It seems that the iliotibial band syndrome, which occurs mainly in athletes who practice sports with repetitive knee flexion-extension gestures, is closely related to a deficit of strength of the hip abductors among other factors, and it seems that a treatment based on strengthening these muscles, along with adequate training load dosing, is an effective treatment strategy. However, there is a lack of scientific evidence available about the iliotibial band syndrome management, so more randomized controlled trials about this topic are needed.

Drug-induced tendinopathy

Drug-induced tendinopathy or toxic tendinopathy is a rare complication that has been associated with the administration of several medications (Fig. 9).

Primarily it has been linked to aromatase inhibitors, fluoroquinolone antibiotics, glucocorticoids and statins, being the fluoroquinolones the most commonly related to tendon disorders.[280–282]

Toxic tendinopathy has also been associated with metalloproteinase inhibitors, anabolic steroids, Isotretinoin and antiretroviral agents (mainly protease inhibitors).[280,281]

The most frequent presentations associated with toxic tendinopathy are tendinosis, tendon rupture and tenosynovitis.[281–283]

Fluoroquinolones

Fluoroquinolones (FQs) are broad-spectrum antibiotics used to treat bacterial infections. FQs are frequently prescribed for urological, gastrointestinal, respiratory, sexually transmitted, skin and soft tissue infections.[283,284]

All fluoroquinolones had been associated with tendinopathy and tendon rupture (284) In 1995, the US Food and Drug Administration (US FDA) included a warning about the possibil-

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ity of tendon rupture in relation to the use of FQs. This and other serious side effects led the US FDA to add a "black box" warning to fluoroquinolones in 2008.[283,285]

It has been recently recommended restricting the use of fluoroquinolones only to complicated infections and patients for whom there is no other appropriate alternative.[284]

Fluoroquinolone tendon toxicity can be observed with all members of this class of antibiotics regardless of the administration route or the dosage; however the risk is incremented by the concomitant use of corticosteroids; so much that 50% of tendon rupture patients had had recent use of corticosteroids.[286–289]

Half of ruptures occurred within the first week of FQs administration, and symptoms appear in 85% of cases in less than one month when FQ was administered in association with oral corticosteroid.[287]

The most frequently reported FQs causing tendon disorders are ciprofloxacin and pefloxacin. However, all regularly used FQs (levofloxacin, ofloxacin, norfloxacin) have been reported although its incidence appears to be much lower that ciprofloxacin induced tendinitis.[284,288,290]

Achilles tendinopathy is the most common presentation for tendon disorders caused by fluoroquinolones, accounting for nearly 90% of the reported cases with 27% of patients suffering from bilateral involvement. Other affected tendons include quadriceps, peroneus brevis and rotator cuff; two episodes of epicondylitis have also been reported.[287,291]

Given the evidence available, clinicians should be suspicious of unexplained changes in recovery trajectory in patients and tendon disorders without a history of overuse or past tendinopathy.[284–286,288]

Statins

Statins are lipid-lowering drugs that work by competitively inhibiting 3-hydroxy-3-methylglutaryl-coenzyme (HMGCR) and thus limiting cholesterol biosynthesis.[292] Statins are used to lower blood cholesterol levels, which helps prevent cardiovascular disease.[293] Statins have increasingly been a mainstay treatment for hyperlipidemia since 1987.[294]

Statins are administered daily for primary and secondary prevention of coronary heart disease, stroke and peripheral arterial disease. They are also used in patients with coronary heart disease with LDL cholesterol elevations and in previously healthy patients with high/normal baseline LDL cholesterol values.[295] Commonly used statins are rosuvastatin, atorvastatin, fluvastatin, lovastatin, simvastatin, pravastatin and pitavastatin.[292] Although they are largely believed to be safe, muscle toxicity is not rare.[293]

Statins have been associated with tendonitis and tendon rupture and have been reported in the FDA adverse event database.[296] Its more common side effects are myopathy, tendinopathy, hepatotoxicity, type 2 diabetes, cataract, polyneuropathy, memory loss and behavioural changes.

Rosuvastatin and fluvastatin had the most adverse effect cases reported while atorvastatin and simvastatin showed intermediate risks and pravastatin and lovastatin had the lowest rate of side effects.[292,297]

The data available suggest an increased risk of tendon disorders between statin users although this data is inconclusive.[293] The side effects associated with statins are dose independent and appear approximately 8 to 10 months after the beginning of the treatment with an estimated incidence of 2%.[298]

The Achilles tendon was the most reported type of tendinopathy. Other case reports showed tendon disorders in rotator cuff, biceps brachii, extensor carpi radialis brevis, gluteus medius, quadriceps, patellar tendon, tibialis anterior, supraspinatus, scapularis terrea, infraspinatus and finger extensor and flexor tendons.[292,295]

Statins could predispose tendons to damage and even rupture; they can deteriorate the integrity of tendons by reducing the cholesterol content in cell membranes and thus promoting its apoptosis.[299,300] Statins affect tenocyte migration and also the functional network which is a potential mechanism for statin related tendinopathy.[294]

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We can associate statin use and tendinopathy based in the available studies that shows temporal relationship between symptomatology debut and the beginning of statin use, the disappearance or improvement of symptoms after the disruption of statins and the reappearance of symptoms when statins therapy was reinstituted.[295]

In some studies the rate of tendon rupture among statin users was similar to the background rate in the general population.[301] This may be understood because patients suffering from diabetes, chronic kidney disease and hyperuricemia are more likely to suffer from tendinopathy[292,299] and the of use of statins by this group of patients is higher than the common population[299,300] therefore no conclusion can be made related whether the statin use is linked directly to tendon disorders.[301] tendon disorders are due to overuse conditions and so, degenerative process are detected rather than inflammatory; consequently, corticosteroid or anti-inflammatory therapy is mostly ineffective.[302]

Various studies suggest that corticosteroids are associated with a higher risk of tendon rupture.[303] There is also strong evidence that even though corticosteroid could have some short-term effect on pain in some tendinopathy, their long-term use would not be more effective than other treatment options and their effect was reversed at long and intermediate –terms.[302–306] Long-term corticosteroid is a well-documented source of iatrogenic tendon rupture regardless of the administration route.[307,308]

Aromatase inhibitors

Aromatase inhibitors (AIs) are an antihormonal therapy in the treatment of breast cancer in postmenopausal women. AI-associated tendinopathy and muscle tendon rupture is extraordinarily rare.[309] The most common reported symptom was severe early morning stiffness, hand/wrist pain and trigger finger.[307,310]

Currently, the particular range of syndromes induced by aromatase inhibitors has still to be determined.[311]

Other drugs with potential tendon toxicity

Isotretinoin

It has been linked with tendinopathy and enthesopathy, to this day the pathophysiological mechanism remains unknown. To our knowledge no case of rupture tendon has been reported.[280,307]

Anabolic steroids

Some studies have found a relation between the use of anabolic steroids in animal models and an alteration of the mechanical properties of the tendon but there is no certainty that it increases risk of tendon rupture in humans.[307] According to some reports, risk of tendinopathy associated with steroids use may be linked to a difference between the increase of muscle strength due to anabolic steroids use and slower changes in tendon strength.[312]

Antiretroviral drugs

They have been linked to tenosynovitis and capsulitis of some joints. The data available has only shown a few cases of bilateral ankle tenosynovitis and adhesive capsulitis of the shoulder.[130,131,307]

Clinical applications

Even when the pathoetiology of tendinopathy is unclear, there is a wide array of treatments available to treat and manage tendinopathy.[313] Although tendinitis usually debuts with an in-

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flammatory response, the majority of chronic tendinopathies do not present inflammation. One plausible explanation for tendinopathy is the mechanical theory, which suggests a failed healing process because of overloading, and thus the generation of multiple micro-injuries to the tendon.[314]

There are a number of risk factors for the development of tendinopathy such as age, gender, heavy physical work, type of training surface and high training volume[314] Several of these risk factors are modifiable and preventable through appropriate physiotherapy programs and should be assessed as such.

The choosing of treatment should vary depending on severity, compliance, pain and duration of symptoms.[313]

Nowadays, the consensus is still that eccentric exercise and other exercise programs are the gold standard for conservative tendinopathy management[314, .315] Strong, consistent findings supports this, particularly heavy eccentrics based in Alfredson eccentric protocol.[313,316]

However, there is not enough evidence that eccentric exercise is better than any other kind of exercise in order to improve pain and function in tendinopathies.[314] For instance, some evidence showed that eccentric exercises were not effective in athletes during a competitive season.[193] Isometric and heavy slow resistance (HSR) exercises have also shown potential in pain reduction and functional improvement. A vastly shared study by Rio in 2015 showed isometric as a better option to reduce pain in tendinopathies. Nevertheless, it remains unclear if isometric exercise provides a greater pain relief when compared to other types of exercise.[193]

Exercise-induced hypoalgesia (EIH) is a response to exercise in healthy populations however EIH is not present in some patients usually due to central sensitization.[314] The EIH response is independent of the type of exercise and so it would make irrelevant the differentiation between isometric or eccentric exercise to alleviate pain during tendinopathies.[314,317]

The great majority of available evidence is based on one type of tendon only, commonly the patellar tendon, the Achilles tendon and the rotator cuff complex. Further research including comparison between different types of tendinopathy should be considered in order to develop more accurate clinical guidance.

Progressive tendon loading seems to be crucial in the management of tendinopathy[314] The rule of 10% appears to be the method of choosing for progression for most clinicians. This rule is based on control between the loads applied every week and the average load applied in the previous week. If this progression happens to be higher than a 10% the risk of injury would increase significantly.[314,315]

Generally, the progression criterion is symptomatology based and not driven by physical or structural capacity.[314] There is still a too heterogeneous criterion for progression in load and a lack of consensus leading to an uncertain assessment in a central matter for tendinopathy management; on that account, following investigations should be directed to the unification of this criterion.

Other treatments are usually combined with exercise protocols in order to accelerate and guarantee a better outcome in tendinopathy management. Previous reviews showed low quality evidence supporting Non-steroidal anti-inflammatory drugs or extra corporeal shockwave therapy for tendinopathy related shoulder pain.[316] There is also no consensus in the use of platelet rich plasma or corticoid injections in rotator cuff tendinopathy[193,316] however exercise and manual therapy were widely recommended.[316]

For patellar tendinopathy extra corporeal shockwave therapy has shown positive results just as static stretches were also found useful.[317] For the management of Achilles tendinopathy, traditional physiotherapy, based in ultrasound and deep friction massage provided good outcomes for tendinopathy.[318] Achilles tendinopathy is presented typically in two different forms depending of the portion affected. The results may vary depending whether it is the mid portion affected or the insertional part. Either way, extra corporeal shockwave therapy reported successful results; the mechanical stimulus provided by ESWT is believed to help initiate tendon regeneration in tendon disorders.[319]

In treating Achilles tendinopathy, all injection therapies were found unhelpful and with insufficient evidence to recommend its clinical use.[320]

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The use of corticosteroids or NSAIDs is not supported based on the high risk of tendon rupture and toxic tendinopathy and the lack of inflammation in most tendinopathy presentations.[306]

Surgical approaches may be justified for more complex or advanced tendinopathies but only should they be considered after a failure in conservative approach, as they were unsuccessful in improving both function and/or pain.[313]

Nowadays, some renowned experts in tendinopathy management proposed the continuum model based on the changes within the tendon tissue with the purpose of helping clinicians understand the different presentation of tendinopathies and allowing for better interventions.[321] Despite the great progress in tendon research, to date the management of tendinopathies is still mostly restricted to symptomatic therapy and further investigation should address this issue in order to improve the management of tendon disorders.[322]

Conclusions

Current advances and research in tendinopathy shows that even though there is still a lot we do not know, conservative treatment through exercise and load management should be the first source of treatment, aided by other conservative treatments like ESWT. Surgical approach should only be used as a last resource once the conservative options have failed after six to twelve months of treatment. Future research lines are necessary in order to achieve a consensus of exercises dosage, intensity and type.

Conflicts of Interest

There are no conflicts of interest.

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