

# Tendinopathies

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Tendinopathy is an umbrella term used to identify a complex clinical condition characterized by molecular, cellular, and histological changes occurring in affected tendons that leads to persistent pain, swelling, and impaired physical performance. Several pathogenic mechanisms are involved in the occurrence of this condition. High load demands and repetitive mechanical exposure during exercise act as *primum movens* of tendinopathy.

Keywords: tendinopathy ; hyaluronic acid ; athletes ; return to sport ; conservative treatment

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## 1. Introduction

Tendinopathy is an umbrella term used to identify a complex clinical condition characterized by molecular, cellular, and histological changes occurring in affected tendons that leads to persistent pain, swelling, and impaired physical performance <sup>[1][2]</sup>. Several pathogenic mechanisms are involved in the occurrence of this condition. High load demands and repetitive mechanical exposure during exercise act as *primum movens* of tendinopathy. A persistent failed healing response leads to the progressive accumulation of matrix damage with microruptures of collagen fibrils in tendons. Moreover, tendon injury triggers the release of cytokines, chemokines, and other inflammatory molecules, responsible of the symptoms reported by affected patients <sup>[1]</sup>.

Both prevalence and incidence of tendinopathy are increasing worldwide in the last decades, particularly in sport practice, where accounts for up to ~30% of total injuries <sup>[3]</sup>. In the general population, common sites of tendinopathy involve rotator cuff and extensor carpi radialis brevis tendons for the upper limb and gluteal, patellar, and Achilles' tendons for the lower limb <sup>[4]</sup>. On the other side, in athletes, Achilles' tendinopathy affects up to 30% of all runners, while patellar tendinopathy mostly affects volleyball and basketball player, with an incidence of 14% and 12%, respectively <sup>[5]</sup>. Several risk factors contribute to the development of tendinopathy including genetic susceptibility (i.e., polymorphisms in collagen type V alpha 1 chain- COL5A1, Tenascin C-TNC, Matrix Metalloproteinase 3-MMP3 and Estrogen Related Receptor Alpha-ESRR), chronic diseases (i.e., diabetes), or specific pharmacological therapies (i.e., quinolone antibiotics) <sup>[1]</sup>.

Recovery of an adequate tendon load-bearing capacity is mandatory among athletes, particularly due to the high risk of recurrence of tendinopathy observed after early return to sport <sup>[6]</sup>. Currently, recommended treatment strategies are extremely variable <sup>[1]</sup>. Exercise remains the most effective approach <sup>[7][8]</sup> and may be associated with the use of the local therapies as adjunctive treatment <sup>[2]</sup>. For several years, glucocorticoids (GC) have been used as the main injection treatment in patients with tendinopathy. Despite their large use in this population, the safety of GC is still debated <sup>[9][10][11]</sup>. Indeed, GC alter tendon homeostasis by inducing collagen disorganization and necrosis. Moreover, GC reduce tenocytes' viability, promoting the cell senescence and consequently tendon ruptures <sup>[9][12]</sup>.

## 2. The Rationale of HA Use in the Management of Tendinopathies

Hyaluronic acid, also known as hyaluronan or hyaluronate, is a fascinating biologically active molecule, composed of repeating disaccharides of  $\beta$ -1,4-D-glucuronic acid, and  $\beta$ -1,3-N-acetylglucosamine units <sup>[13]</sup>. This compound is largely present in the extracellular matrix (ECM) of articular cartilage and in synovial fluid and is secreted by synovial cells of the tendon sheath. Rheological characteristics of HA contribute to lubrication, viscoelasticity, and hydration balance, acting as a shock absorber and a structure stabilizer in different tissues, including tendons <sup>[14]</sup>. Furthermore, HA seems to be involved in the regulation of the tissue repair process, modulating the main phases of tendon healing (i.e., inflammation, cellular migration, and angiogenesis) <sup>[15]</sup>. All these properties supported HA use as a conservative treatment for several musculoskeletal disorders, including tendinopathy <sup>[16][17]</sup>.

### 3. Clinical Implications of HA Injections in Sport-Related Tendinopathies

Tendinopathies may occur in both elite and recreational athletes, with the contribution of several factors including intrinsic (i.e., reduced muscle flexibility) and extrinsic (i.e., increased training volume, eccentric exercises, hard surfaces) conditions [18]. The pathophysiological changes of tendon injured are well known, encompassing neurovascular in-growth, abnormal tendon density and degeneration of ECM, all induced by overuse and high load demand of tendon [19]. Nevertheless, current treatment strategies are limited, particularly among athletes, that are often tempted to return prematurely to play, with an inadequate recovery and high risk of reinjury [5].

In this scenario, HA injections seem a reliable option for the management of this disease. HA administration has demonstrated anti-inflammatory, proliferative, repairing and analgesic effects during tendinopathy, playing a role also on stiffness and tone of the tendon, identified as markers of this disease [20]. Moreover, HA seems to promote a significant and prompt clinical and functional improvements that encourage its use in athletes.

In a recent systematic review, Habets et al. defined 8 criteria to be filled, used to support the RTS decision after Achilles tendinopathy, commonly observed among elite soccer players with short recovery periods [21]. In our opinion, these criteria ( **Table 1** ) might be adaptable to both upper and lower limb tendinopathies that occurred in athletes. Taking into account all the biological actions modulated by HA on the tendon, HA injections might influence several aspects of the RTS considered by these criteria: level of pain and functional recovery as well as muscular strenght, range of motion, endurance, and anatomical properties of tendon may be positively affect by HA, although well-designed studies are needed to provide evidence for this hypothesis.

**Table 1.** Proposal of RTS criteria after Achilles tendinopathy [21].

level of pain
level of functional recovery
muscular strength
range of motion
endurance
medical advice
psychosocial factors
anatomical/physiological properties

### 4. Conclusions

Tendinopathy is a common sport-related injury, due to overuse and repetitive loading, with a progressive accumulation of damage in tendon tissue.

Emerging therapeutic options include the use of HA, although current recommendations still not consider this intervention among the approved treatment strategies for the management of tendinopathies, also in athletes.

Further research with more rigorous methods, adequate sample size, long-term follow up and instrumental assessment of tendon damage are needed to improve the biological and clinical knowledge about HA as a viable therapeutic option in the management of sport-related tendinopathies.

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