Systematic Review Protocol

Biomedical risk factors of Achilles tendinopathy in physically active people: systematic review

Background

Achilles tendinopathy has been identified as one of the most prevalent overuse tendon injuries associated with physical loads such as running and jumping \(^1\). Achilles tendinopathy is the most common clinical diagnosis of Achilles tendon disorders and accounts for 55-65% of these injuries, with the highest incidence among runners, track and field athletes, volleyball, tennis and soccer players \(^2\). The term ‘tendinopathy’ was coined by Maffuli et al in 1998 and has become an umbrella term for the description of tendon pathology \(^3\). Clinically, Achilles tendinopathy develops as a result of strenuous physical activity with continuous overloads of the tendon. It is typically characterised by pain and swelling around the tendon and morning stiffness. At the histological level this leads to a failed healing response and non-inflammatory degeneration and disruption of collagen fibres \(^3\).

Conservative treatment of Achilles tendinopathy shows debatable results and some clinicians argue that conservative management of chronic Achilles tendinopathy is time consuming and unsatisfactory \(^4\). Surgery is recommended after exhaustion of conservative treatments, however, the recovery process in tendon is slow due to poor blood flow and slow synthesis of collagen \(^4\).

Aetiological factors of Achilles tendinopathy are divided into intrinsic and extrinsic, with the interaction between these leading to the symptoms and further progress of the tendinopathy. Intrinsic risk factors include demographic factors (sex, age, weight, and height) and genetic polymorphisms; and local anatomic factors: leg length discrepancy, malalignment and decreased flexibility. Extrinsic factors comprise therapeutic agents (corticosteroids, antibiotics), environmental conditions, and sport-related factors, involving training patterns, technique and equipment \(^2\,^3\).

The majority of the studies published over the last two decades are dedicated to the investigation of anatomical features and biomechanical faults as possible causes of the Achilles tendinopathy. Kvist et al (1991, 1994) demonstrated that several foot malalignments and particularly ankle joint overpronation were predisposing factors to the Achilles tendinopathy \(^5\,^6\). In addition to malalignment, limited range of motion in the ankle joints was more frequent among athletes with Achilles tendinopathy \(^5\,^6\). A recent systematic review of biomechanical risk factors for Achilles tendinopathy in runners identified a high arch in the foot as a protective factor against Achilles tendinopathy \(^7\). Reduced eccentric and concentric muscle strength and maximum pronation were found to be risk factors of Achilles tendinopathy. Large peak braking force was the variable with the most negative effect on tendon health \(^7\). A systematic review on running-related musculoskeletal injuries concluded that excessive loading generated in the gastrocnemius and soleus muscles was
the main stimulus for the development of Achilles tendinopathy\textsuperscript{8}. Mechanisms of the contribution of biomechanical risk factors to the development of Achilles tendinopathy remains debatable.

Imaging and histopathological analysis of the degenerative and recovery processes in tendon have provided better understanding of the molecular processes associated with the tendon structure and metabolism. In terms of biochemical and metabolic processes, tendon tissue is relatively inert, with new collagen fibres requiring a long time to synthesise\textsuperscript{4}. The opportunity to look at the genetic components may lead to a better understanding of the underlying processes. Several genetic association studies have demonstrated that genetic polymorphisms play a role in the collagen tissue structure, its turnover, degradation processes and therefore susceptibility to tendon injuries.

Biomedical risk factors may include medical comorbidities and physiological, biochemical and genetic factors. There is relatively little research focusing on potential biomedical risk factors for Achilles tendinopathy. The current priority of injury management in relation to Achilles tendinopathy is prevention of the injury, therefore the systematisation of the current known biomedical risk factors will improve the understanding of Achilles tendinopathy development and possible preventative measures.

Review questions
The purpose of this systematic review is to identify studies that investigated biomedical risk factors of Achilles tendinopathy in physically active people, and determine which of these factors are associated with the development of Achilles tendinopathy.

Inclusion criteria

Types of participants
This review will consider all studies that involve human subjects performing any type of regular physical activity. Age, sex and age of the Achilles tendinopathy manifestation are not selection criteria, but will be described in the review.

Types of intervention
Interventions of interest include biomedical risk factors: genetic polymorphisms, medical comorbidities, physiological and biochemical factors.

Types of outcome measure
The primary outcome is Achilles tendinopathy, however, studies that investigated Achilles tendinopathy and the consequences of Achilles tendinopathy and its development into partial and complete ruptures will also be considered.

**Types of studies**
The review will consider all studies investigating risk factors of Achilles tendinopathy through the statistical analysis of data pertaining to case and control groups. Large cohort studies will be considered if they present incidence of the measured outcome and evaluate interventions and their contribution to the investigated outcome.

**Search strategy**
The search strategy will be designed to find all published materials relating to Achilles tendinopathy and biomedical risk factors. The following keywords and their combinations will be used to search in four databases: “risk OR predisposition OR genetic* OR aetiology OR etiology OR overuse OR pathogenesis” AND “Achilles OR Achilles Tendon” AND “tendinopath* OR tendinitis OR tendonitis OR tendinosis OR injury OR pain AND “exercise OR physical activity OR sport* OR run*”. The search will be limited by English language, but not the year of publication. The following databases will be searched:

- CINAHL
- EMBASE
- PubMed
- SPORTDiscus

Full texts of the identified studies will be saved in the electronic library EndNote for consideration in relation to the inclusion criteria based on their title, abstract, studied subjects and outcome. After deleting duplicates two reviewers will independently select articles against the inclusion criteria. Discrepancies in the selection will be resolved through discussion between the reviewers.

**Critical appraisal**
The quality of the selected studies will be evaluated using Newcastle-Ottawa Quality Assessment Scale for case-control and cohort studies as one of the recommended instruments in the Cochrane Handbook for Systematic Reviews of Interventions 9 10.
Data extraction

Results of the studies will be described separately, for quantitative data, odds ratio and confidence intervals or relative risks of developing Achilles tendinopathy will be reported. Other results will be presented in a narrative form.