



REVIEW

Potential risk factors leading to tendinopathy



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Abstract Tendinopathy has a multifactorial etiology that is not well understood. Risk factors are often separated into extrinsic (those acting on the body) and intrinsic groups (those acting from within the body). In this narrative review, we will separate potential risk factors into 1) load-related (extrinsic); 2) biomechanical factors (intrinsic); and 3) other individual factors such as systemic variations (intrinsic). Too much load is clearly linked to tendinopathy, but there appears to be large variation in how much load individuals can endure before developing tendinopathy. Less active people also suffer tendinopathy, suggesting that the effect of load is likely to be moderated by intrinsic factors. These individual intrinsic factors are likely to reduce tolerance or capacity to withstand load. This narrative review will provide a brief overview of key potential risk factors and mechanisms, as well as limitations in the current literature.

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PALABRAS CLAVE

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Factores potenciales de riesgo que conducen a la tendinopatía

Resumen La tendinopatía tiene una etiología multifactorial que no es bien conocida. Los factores de riesgo a menudo se dividen en extrínsecos (los que actúan sobre el cuerpo) e intrínsecos (los que actúan desde dentro del cuerpo). En esta revisión descriptiva clasificamos los factores de riesgo potenciales en: 1) factores relacionados con la carga (extrínsecos); 2) factores biomecánicos (intrínsecos), y 3) otros factores individuales, como los factores sistémicos (intrínsecos). Una carga excesiva está claramente relacionada con la tendinopatía, pero parece que existe una gran diferencia en la cantidad de carga que los individuos pueden soportar antes de desarrollar una tendinopatía. Las personas menos activas también sufren tendinopatía, lo que sugiere que es probable que el efecto de la carga esté mediado por factores intrínsecos. Es

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probable que estos factores intrínsecos individuales reduzcan la tolerancia o la capacidad de soportar la carga. Esta revisión descriptiva ofrece un breve resumen de los principales factores de riesgo y mecanismos, así como las limitaciones en la literatura actual.

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Load

Stretch shorten cycle loads

In the lower limb, repetitive stretch-shortening cycles (SSC) of the muscle-tendon unit (e.g. walking and running for Achilles tendinopathy or jumping for patellar tendinopathy)^{1,2} is associated with tendinopathy. During SSC there is energy storage through elastic lengthening of the tendon and subsequent release of some of the stored energy to reduce the energy cost of locomotion.^{3,4} In the Achilles-calf there is energy storage in terminal midstance and subsequently this energy contributes to positive work in toe off of walking and running.²

The magnitude of tendon load can be quite high during SSC activities. For example, Achilles tendon load is reported to be 6–8 times bodyweight in running^{5,6} and as high as 8–10 times bodyweight in submaximal hopping.⁷ The magnitude of tendon load is often lower with slow and heavy contractions that are commonly used in rehabilitation (e.g. heavy slow resistance training or eccentric training). Even during a maximal isometric plantar flexion contraction load is about a third to half (3.5 times bodyweight) of that during hopping.⁸ Although it seems that higher load is not always a distinguishing feature between SSC and slow and heavy loads. Patellar tendon load during loaded squatting (4.78 bodyweights) is similar to load during a stop jump such as a spike jump take off (5.17 bodyweights).^{9,10} However, the tendon strain rate is much lower during the squatting task (1–2 bodyweights/second) than during the stop jump task (almost 40 bodyweights per second). The tendon strain rate may explain why tendinopathy is associated with repetitive SSC rather than slow and heavy loads.¹¹

Compression

Compression has been suggested to play a part in most insertional tendinopathies, or enthesopathies.¹² Benjamin et al.¹³ described a specialized tendon–bone junction, 'the enthesis organ', that functions to reduce load concentration at the enthesis. A bony prominence, and at some sites bursa adjacent to the enthesis, have a role in absorbing and dispersing enthesis loads thereby limiting stress concentration at the tendon–bone junction. Tendons adapt to the increased compressive loads at the enthesis with increased fibrocartilage, larger water-binding proteoglycans and type II collagen.¹⁴ Ground substance accumulation is a feature of insertional tendinopathy which has been suggested to be a response to compressive load.¹² The pathology has been localized to the side of the tendon adjacent to the bone, which also suggests compressive loads may be implicated.¹⁴

Soslowsky et al.¹⁵ investigated the effect of compressive and tensile loads in isolation or combination (downhill running) on rat supraspinatus tendons. Their conclusions were that a compressive load alone did not lead to reduced mechanical properties, but a combination of compressive and tensile load was more damaging than tensile load alone. For insertional tendinopathies reducing enthesal compression is suggested to be an important aspect of prevention and management.¹² For example, in the case of the Achilles this can be achieved by using a heel wedge/lift.

Intratendinous loading patterns

Tensile stress may not be uniform throughout a tendon. Studies investigating cadavers,¹⁶ optic fibres in vivo¹⁷ and mathematical modeling¹⁸ have found greater tensile strain in the posterior compared with the anterior side of the patellar tendon. This contrasts to Almekinders et al.¹⁹ who found reduced strain in the posterior tendon in a cadaver study. Despite inconsistencies, these studies demonstrate different strain gradients or 'stress shielding' of part of the tendon may have a role in the development of patellar tendinopathy.²⁰ Similarly, in the Achilles tendon, there is emerging evidence from imaging studies using speckle tracking that the tendon does not strain uniformly under load.²¹ The implications for the development of tendinopathy and rehabilitation (e.g. specific loading for certain parts of the tendon) are so far unknown.

Change in load

The most common cause for tendinopathy is described as 'training errors'. This is an ambiguous term, but is normally considered to encompass any alterations in physical load on the tendon.²² Primarily, this involves fluctuations in intensity, frequency or duration of exercise, although it may be components of all three. Returning to training after a short break, e.g. after a holiday, is an example of a training error involving sudden change in load. The break in exercise is thought to lead to deconditioning, resulting in tendinopathy on a return to normal load. This is often evidenced in patients who misguidedly go through periods of rest to settle the tendon and then return to normal loading immediately, inevitably re-triggering symptoms.

Load management has recently been extensively investigated by Gabbett and colleagues.²³ They have demonstrated a relationship between chronic workload rates (exercise levels over the preceding 4 week period) and the acute rates (that week, although, to date, this ratio has not been extensively investigated in relation to tendinopathy).²⁴ Clinically, it is important to ask about change in energy storage type

loads that may contribute to tendinopathy and reduce these in the short term (load management) if pain is significant and worsening for more than 24 h after performing these types of activities.¹¹

Load parameters

Training hours per week is associated with patellar tendon pain (e.g. 25, 26) and greater running volume with Achilles tendinopathy,²⁷ suggesting excessive duration or volume is associated with tendon injury. McCrory et al.²⁸ found that a higher training pace (intensity) was associated with Achilles tendinopathy in endurance runners. Repeating loading too often (frequency) may also be important. Four or more volleyball sessions per week was associated with a doubling of the prevalence of patellar tendon pain.^{29,30} This fits with evidence that intense loading (e.g. 3 h run, 1 h of repetitive kicking) results in net collagen degradation for up to 36 h.³¹ Repeated intense loading (i.e. repeated stretch shorten cycle) without sufficient recovery time (i.e. at least a rest day between sessions) may be a risk factor for tendon pathology. It should be made clear, however, that factors such as training hours per week and sessions per week are not consistently associated with tendinopathy in the literature. This may be explained by confounders, including change in load.

How does load lead to pathology?

How energy storage and compressive loads may lead to tendon pathology is largely unknown. The current body of evidence suggests the pathogenesis of tendinopathy involves a change in tissue homeostasis. Homeostasis is normally maintained by the tendon cells (tenocytes), which control tendon protein synthesis through various chemical messengers. Tendon matrix is directly influenced by the activity of tenocytes. In a normal Achilles tendon we expect to find a change in the collagen structure to fibrocartilage at zones that undergo high compressive loads, this is an example of the capacity of tenocytes to respond to different loads.³² Tendinopathy is likely to involve a loss of homeostasis within the tendon due to excessive loading (e.g. intensity, frequency, duration) and insufficient recovery/repair of the tendon.³¹ Changes in signaling of cytokines, inflammatory factors, matrix regulator and the stress-activated factors (e.g. TGF β -1, IGF, VEGF, substance P, TNF α , MMP's, nitric oxide) may be involved in loss of tendon homeostasis.^{33,34} Various systemic factors may influence repair rates whilst extrinsic factors and biomechanical factors are likely to influence the stress on the tissue.

Biomechanics

Individual biomechanics, including movement kinetics and kinematics, foot posture, flexibility, neuromuscular capacity and structural anatomy may influence tendinopathy risk. Horizontal or 'stop' jump landing is associated with greater patellar tendon force than vertical landing.³⁵ Further, participants with asymptomatic patellar tendon pathology

landed in greater knee flexion and had a stiffer knee strategy in stop jump landing than their counterparts with normal patellar tendons.³⁶ Asymptomatic pathology is considered a useful model to investigate movement patterns that may increase risk of pain. Given patellar tendon forces were similar between the groups, the authors suggest that the landing strategy of the pathology group may involve greater patellar tendon shear forces. Azevedo et al.³⁷ demonstrated a stiffer knee strategy (reduced knee flexion from initial contact to heel strike) among runners with Achilles tendon pain. It is possible that this kinematic pattern is a protective compensation to reduce Achilles tendon load. This example highlights the limitations of cross sectional research design where associated factors may develop secondary to pain.

Foot posture and function (dynamic pronation) has been proposed as a risk factor for lower limb tendinopathy,²⁷ although there is conflicting literature.³⁸ Patellar tendinopathy has been associated with both a higher³⁹ and lower²⁶ static arch height. There is also limited or conflicting evidence linking plantar heel pain with static and dynamic foot posture.⁴⁰ A recent systematic review identified limited evidence for a change in plantar pressures in Achilles tendon pain during running gait, indicating a more lateral foot roll over following heel strike.^{41,42} A lateral foot roll over may indicate compromised windlass action but may also be a secondary adaptation to reduce Achilles load. Murley et al.⁴³ found that a pronated foot posture was associated reduced Achilles tendon cross sectional area among participants without pain, indicating that foot posture may impact on tissue loading and development throughout life, potentially increasing injury risk.

Muscle flexibility (e.g. hamstring) and joint range of motion (e.g. ankle dorsiflexion) has received much interest, results are so than any other factors. Unfortunately, the results are often conflicting, which leaves the clinician with a dilemma in attempting to manage and prevent injury. For example, both increased⁴⁴ and decreased ankle dorsiflexion^{45,46} range of motion have been associated with the development of Achilles tendinopathy in prospective studies. Patellar tendinopathy has been associated with both increased²⁶ and decreased⁴⁷ hamstring flexibility. Clinically, it may be important to consider addressing extremes of range of motions of these joints/muscles where this is possible.

Although suggested to be a common risk factor, few studies have investigated the link between neuromuscular capacity and tendinopathy.⁴⁸⁻⁵⁰ Both cross-sectional^{47,51} and prospective work has found that greater jump height is associated with patellar tendinopathy and this is thought to relate to greater thigh strength.⁵² Seemingly in contrast, Crossley et al.²⁶ found that patellar tendinopathy was associated with reduced thigh strength, which may be explained by change in neuromuscular function secondary to pain (long or short term). Plantarflexor muscle weakness has been associated with Achilles tendinopathy in cross-sectional studies^{28,53} this has often been thought to be a direct consequence of the pain. However, more recently Mahieu et al.⁴⁴ found that plantarflexor torque was 85% sensitive at predicting those who went on to develop Achilles tendinopathy, suggesting muscle weakness may be a causative factor.

Other individual factors

Multiple systemic factors have been linked with tendinopathy including: age, lipid levels, adiposity and genetics. These have been extensively reviewed elsewhere.³⁴ Systemic factors are thought to reduce the capacity of the tissue to tolerate load, gradually altering tendon capacity so that an extra walk, a quick dash across the road, or a day spent gardening may be sufficient to overload the tendon triggering symptoms. Therefore, these factors may be particularly relevant among patients who are not performing regular high intensity SSC loads. They may also explain, along with biomechanical factors, why not all athletes exposed to the same loads develop tendinopathy. Systemic factors need to be considered in clinical practice, as this population may be more difficult to manage, respond less favorable to load-based interventions and benefit from additional adjunct interventions (e.g. aerobic exercise).

The exact mechanism by which systemic factors influence tendinopathy risk is largely unknown. For example, increased age may be associated with change in tendon cellular activity, mechanical properties (through glycation) as well as muscle function,⁵⁴ all of which may influence tendinopathy risk. Adiposity is thought to increase the level of pro-inflammatory cytokines in circulation and these chemical messengers are thought to influence the tendon matrix through various effects on tenocytes.⁵⁵ An alternate mechanism is that adiposity is associated with greater bodyweight (which has also been linked to tendinopathy) and increased tendon load. Malliaras et al.⁵⁶ found that waist girth was a stronger predictor of patellar tendinopathy than body mass in a multivariate model. This highlights that the link between anthropometry and tendinopathy is more complex than purely increased tendon load and the importance of multivariate models delineating confounding factors.

We know that previous injury appears to be an important predictor of tendinopathy. The reason for this has not been established, but is thought to link to changes in tissue resilience and/or the neuromuscular system²² reducing the ability to withstand the demands of physical activity.^{48,57} These adaptations reduce the coping ability of the muscle tendon unit. In such cases, continued loading can take the tissue past the point of homeostasis, leading to tissue breakdown and symptom onset.⁵⁸ Obviously, we cannot alter the fact that the patient has sustained a previous injury or tendinopathy, but we can reduce the likelihood of such issues in the first place. A recent meta-analysis pooled data from 26,610 participants and showed that strength training reduced overuse injuries by 50% and acute injuries such as sprains and tears by 33%.⁵⁹ This suggests that our best approach is to ensure that all subjects at high risk of tendinopathy include strength training regularly in order to reduce risk. For example, in Achilles tendinopathy, targeting those with poor plantarflexor strength is likely to reduce the risk of tendinopathy.

Limitations of the literature

A major limitation of the literature is that most studies use a cross-sectional design which does not allow a temporal

sequence between exposure to the risk factor and development of tendinopathy to be established. Thereby, no causal inferences can be made. It is likely that changes in kinematics and neuromuscular function may be secondary to pain.⁶⁰ In managing tendinopathy, it may still be necessary to address these changes that may be secondary to pain in order to restore optimal function and tendon loading.

Another consideration is that most studies investigate the relationship between potential risk factors and the onset or presence of pain (e.g. 26, 45). Pathology is thought to precede pain and a recent systemic review concluded that pathology is a risk factor for the onset of tendon pain in Achilles and patellar tendinopathy.⁶¹ Many factors such as load may influence the risk of both pathology and pain. Some factors may increase the risk of developing pain among people with asymptomatic tendinopathy. These may include cognitive and emotional factors such as anxiety and maladaptive beliefs about pain that lead to fear-avoidance behaviors.⁶² Understanding factors that influence pain is important in order to prevent and manage painful tendinopathy.

Some authors have suggested that unilateral and bilateral tendinopathy have a different etiology.⁶³ For example, Crossley et al.²⁶ found that hamstring flexibility was increased in unilateral but not bilateral patellar tendinopathy. What is becoming increasingly clear is that bilateral tendinopathy is common. There may be several explanations for this, including biomechanical load affecting both sides of the body, systemic factors that are described above, or even bilateral nervous system involvement.⁶⁴⁻⁶⁶ More evidence is needed to understand the potentially different etiology of unilateral and bilateral tendinopathy.

Implications for prevention

There are four stages to injury prevention outlined by van Mechelen et al.⁶⁷ These include 1) establishing the extent of the injury problem; 2) establishing the etiology and mechanisms of injury; 3) introducing preventative measures; and 4) assessing the effectiveness of these measures by re-assessing the extent of the problem. There are several studies that investigate potential risk factors for tendinopathy (stage 2) as outlined in this review, but very few that evaluate preventative interventions (stage 3). In any case, targeting preventive interventions toward individuals deemed to be at greater risk of injury based on screening to identify risk factors has been challenged.⁶⁸ Most risk factors are not strongly associated with injury so do not clearly delineate individuals who will develop injury from those who do not. Therefore, preventative interventions may be more effective if applied across an entire cohort rather than solely among individuals deemed to be at greater risk of injury. In summary, risk factor knowledge is important and may inform injury prevention interventions (e.g. calf weakness may be a risk factor for Achilles pain suggesting calf loading may be an effective preventative intervention). However, it is important to progress to stage three of the injury prevention model and evaluate whether changing risk factors influences injury risk.

Only two randomized trials have evaluated preventative exercise interventions for tendinopathy. Kraemer et al.⁶⁹

found that a neuromuscular conditioning program reduced the risk of Achilles and patellar tendinopathy development among female soccer players. However, Fredberg et al.⁵³ investigated whether eccentric training for the Achilles and patellar tendons performed during the season reduced injury risk among soccer players. There was no change in Achilles tendinopathy risk but an increase in patellar tendon pain among those with asymptomatic patellar tendon pathology at baseline. This suggests the addition of rehabilitation loads to sporting load for people with existing asymptomatic patellar tendon pathology may increase the risk of pain. We need to know more about effective rehabilitation strategies to prevent tendinopathy and in the meantime load monitoring (e.g. acute to chronic workload) is critical.

Conclusion

Understanding risk factors and mechanisms is critical for prevention and management of tendinopathy. Change in SSC loads seem to be related to the onset of tendinopathy, particularly in the lower limb and monitoring change in these loads is important for tendinopathy prevention. Multiple biomechanical and neuromuscular factors have been identified but the literature is limited and many neuromuscular changes from cross-sectional studies may have arisen after the onset of pain. The current challenge to researchers is to identify prospective risk factors and then investigate whether modifying these factors reduces injury risk in cohorts of individuals at risk of tendinopathy.⁶⁷

Conflicts of interest

Authors declare that they don't have any conflict of interests.

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