REVIEW ARTICLE

Continuum model of tendon pathology – where are we now?

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SUMMARY

Chronic tendon pathology is a common and often disabling condition, the causes of which remain poorly understood. The continuum model of tendon pathology was proposed to provide a model for the staging of tendon pathology and to assist clinicians in managing this often complex condition (*Br. J. Sports Med.*, **43**, 2009, 409). The model presents clinical, histological and imaging evidence for the progression of tendon pathology as a three-stage continuum: reactive tendinopathy, tendon disrepair and degenerative tendinopathy. It also provides clinical information to assist in identifying the stage of pathology, in addition to proposed treatment approaches for each stage. The usefulness of such a model is determined by its ability to incorporate and inform new and emerging research. This review examines the degree to which recent research supports or refutes the continuum model and proposes future directions for clinical and research application of the model.

Introduction

Chronic tendon pathology, or tendinopathy, is a highly prevalent musculoskeletal condition affecting both athletes and non-athletes, with the most commonly affected tendons being the Achilles, patella, rotator cuff and elbow extensor tendons. Clinical management of tendinopathy can be challenging, and clinical trials have failed to provide robust evidence for many of the commonly used interventions (Woodley *et al.* 2007; Coombes *et al.* 2010; Krogh *et al.* 2012). However, because it is broadly agreed that there is much yet to be understood about the causes of tendinopathy (Riley 2008), it is perhaps unsurprising that clinical trials including patients with a range of degrees of tendinopathy report equivocal results (Bennell *et al.* 2010).

This review focuses on the continuum model of tendon pathology, as proposed by Cook and Purdam (2009), which provides a model for the staging of tendon pathology. Historically, research, assessment and treatment of tendon pathology were focused around an inflammatory model of pathology, which progressed to a perspective of the pathology as 'failed healing', followed by the more recent view of

a primarily degenerative pathology with minimal inflammatory influence (Maffulli *et al.* 1998). A number of authors have provided theoretical models to explain the basis for development of tendon pathology or to assist clinicians in managing this condition. Neer (1972) and Blazina *et al.* (1973) proposed what are essentially classification systems for the rotator cuff and patellar tendon respectively. Nirschl (1992) went a step further and proposed a 5-stage model to describe the progression of tendon pathology using tennis elbow as an example. This model integrated pathological, histological and clinical findings and described a range of tendon states from healthy, through acute and chronic tendonitis, to tendinosis and rupture. Coombes *et al.* (2009) advanced the modelling of lateral epicondylalgia with a framework that incorporated local changes in the muscle and tendon, along with changes in the wider pain system. The EdUReP model was developed by Davenport *et al.* (2005) and is a theoretical framework for the conservative management of tendinopathy, with emphasis on the importance of patient education and controlled loading. However, this model did not consider the staging of tendon pathology or incorporate the growing area of tendon imaging.

In response to the need for a model that would provide an explanation for the diverse presentations of tendinopathy while also providing a useful tool for clinicians, Cook and Purdam (2009) proposed a generic model of tendon pathology based around a continuum model, incorporating clinical, histological and imaging information. The model describes the early stages of reactive tendon pathology as a non-inflammatory proliferative tissue reaction, usually in response to acute overload or compression. The tendon thickens due to the up-regulation of large proteoglycans and an increase in bound water, with minimal collagen damage or separation. Tendon disrepair is characterized by greater tissue matrix breakdown, with collagen separation, proliferation of abnormal tenocytes and some increase in tendon neovascularity. These two stages are considered to have some degree of reversibility, with the appropriate healing environment. The final stage of degenerative tendinopathy sees a further disruption of collagen, widespread cell death and extensive ingrowth of neovessels and nerves into the tendon substance, leading to an essentially irreversible stage of pathology. The model is highly clinically applicable, with a framework describing how treatments might be best aligned with the stage of tendinopathy, along with descriptions of the clinical presentation of each stage. This model has the potential to provide a basis for more targeted assessment and treatment approaches in tendinopathy; however, it was primarily based on lower limb tendinopathy. Lewis (2010) subsequently applied the model to rotator cuff tendinopathy, incorporating bursal pathology and further emphasizing the importance of optimal loading in maintaining normal tendon function and health. Cook and Purdam (2009) stated that the usefulness of this new continuum model will be evidenced in how successfully it can incorporate new and emerging research from pathology, clinical and imaging perspectives. Its applicability to practice will be proven by its uptake by clinicians for the assessment and management of tendinopathy. This review aims to evaluate the degree to explore recent tendon research in the context of the continuum model and propose future directions for clinical and research application of the model.

Ethical approval

No ethical approval was required.

Pathology studies

Recent studies of rotator cuff tendinopathy have provided further histochemical evidence for the idea of tendinopathy as a continuum. Longo *et al.* (2011) showed that smaller tears had more cell proliferation and greater inflammatory cell infiltrate than larger tears, where collagen degeneration was predominant, and few cells were present. Similarly, Murphy *et al.* (2012) examined tissue biopsy specimens from 45 patients with varying degrees of imaging or arthroscopically diagnosed rotator cuff pathology. There was significant reduction in vascularity and cell proliferation as pathology progressed towards the most degenerative stage. The results provide evidence of an early inflammatory component in those with tendinopathy but no tendon tears, that is, reactive or early disrepair stage, while in the later degenerative stages of pathology (patients requiring arthroscopic surgery), there is reduced proliferative and vascular activity within the pathological tendon tissue.

A comprehensive review of the pathophysiology of tendinopathy was provided by Abate *et al.* (2009) describing a 'pathogenetic cascade' in which inflammation and degeneration are often concurrent processes. They describe how inflammatory, regenerative and degenerative changes proceed in parallel across early- to late-stage tendinopathies, resulting in a continuum ranging from healthy tendon to overt painful tendinopathy. Using an 'iceberg model', they propose that asymptomatic tendinopathy converts to symptomatic when higher levels of neural and vascular proliferative change have occurred. Determining the source of pain in tendinopathy remains a significant challenge for researchers. Current theories suggest that the pain arises from biochemical irritants (Fredberg & Stengaard-Pedersen 2008), peritendinous tissues (Van Sterkenburg & Niek van Dijk 2011) or neurovascular ingrowth (Lian *et al.* 2006). However, none of these factors have yet been correlated with a subjective measure of pain, and for example, neovascularization has been widely shown to have little correlation with symptoms or clinical outcome despite the widespread use of injection therapies aimed at reducing it (Wilde *et al.* 2011; Tol *et al.* 2012). Therefore, while the pathological basis for the continuum model remains well supported, the process of transition towards pain in the structurally abnormal tendon is yet to be elucidated.

Healthy tendons are 'plastic' structures, capable of adapting to the load environment through alterations in their structural and mechanical properties (Killian *et al.* 2012). The continuum model is strongly based around the effects of loading or unloading on tendon. The response of tendon to loading has been evaluated experimentally in a variety of animal models (Edelstein *et al.* 2011). While the application of this research has been perhaps primarily targeted towards developing surgical techniques for tendon tears, there is wide potential for such research to inform both the pathological basis for and clinical application of the continuum model. For example, studies of fatigue loading in rats have demonstrated distinctly different tendon responses to different levels of strain. Sun *et al.* (2008) demonstrated a dose–response effect in rat patellar tendon *in vivo* when undergoing cyclic loading, where lower strain levels produced a more favourable tissue deformation pattern than moderate or high strain, along with suppression of the activity of pro-inflammatory mediators, *vs.* an increase in these substances in the tendons loaded to higher fatigue levels. Such an *in vivo* model offers potential to provide further histopathological and biochemical evidence to support choosing different exercise interventions for various stages of tendinopathy in humans.

In additional to exposure to loading, there is a multitude of extrinsic and intrinsic factors that may influence the

development of tendinopathy (Lewis 2010). Extrinsic factors include local anatomical factors, posture and biomechanical factors, and occupational and sporting activities. Intrinsic and personal factors are also important in the predisposition of certain individuals to tendinopathy. Genetic factors have been identified as a predisposing factor in rotator cuff (Chaudhury & Carr 2012) and Achilles tendinopathy (Posthumus *et al.* 2010; Legerlotz *et al.* 2012). Metabolic factors also play a role in tendinopathy, with diabetes being a well-known risk factor (De Oliveira *et al.* 2011), and associations between adiposity and tendinopathy noted in both Achilles (Gaida *et al.* 2010) and gluteal tendinopathy (Fearon *et al.* 2012). Other than age, none of the tendinopathy models have incorporated intrinsic factors, perhaps due to their limited modifiability. However, such factors may be important in prognosis setting, with poorer capacity for recovery in affected individuals.

Knowledge about pain physiology in relation to musculoskeletal pathologies has advanced greatly in recent years, with a strong emphasis now being placed on the consideration of central sensitization mechanisms, as well as psychosocial factors, in spinal pain in particular (Moseley 2003). There has been limited investigation of the role of these mechanisms in the development of chronic tendon pain. Studies of common elbow extensor tendinopathy have demonstrated the presence of mechanical hyperalgesia, both locally at the tendon site and contralaterally, which has been proposed to be an indicator of sensitization of the central nervous system (Coombes *et al.* 2009). Similarly, lowered mechanical pain thresholds have been demonstrated in patellar and shoulder tendinopathy (Hidalgo-Lozano *et al.* 2010; Van Wilgen *et al.* 2013). Studies of risk factors for rotator cuff dysfunction in occupational populations have generally emphasized the role of mechanical and work-related factors in the development of the disorder (Van Rijn *et al.* 2010); however, psychosocial factors may be important in prognosis and development of chronicity (Horsley 2011). While this is an area that requires further research, with findings that may differ according to the site of tendinopathy and population, it appears important that the relative contribution of local *vs.* central dysfunction to the individual's pain presentation is considered to provide the most appropriate treatment.

Therefore, the continuum model continues to be supported by pathological research, with the possibility for animal studies to further reinforce the recommendations for load progression in tendinopathy rehabilitation. Ongoing developments in the understanding of how genetic and metabolic factors, as well as pain physiology, may affect tendinopathy may be important to incorporate as the continuum model evolves.

Clinical studies

It is difficult to apply the continuum model to clinical studies, as no published clinical studies have attempted to subgroup or analyse tendinopathy participants according to stage or degree of pathology. In fact, most studies include a heterogenous population of people with pathology of varying duration and severity. However, in an attempt to apply the continuum approach to existing studies, two studies of rotator cuff tendinopathy with conflicting results will be discussed. Holmgren *et al.* (2012) carried out a randomized clinical trial involving rotator cuff tendinopathy patients who were on a waiting list for subacromial decompression. It is probable that this group of patients were from a relatively homogenous population that may have corresponded with the disrepair or degenerative subcategories. The trial compared specific loading exercises, including an eccentric component, to a simple range of motion exercise programme (control). The specific exercise group had significantly better improvement in their functional scores at 12-week follow-up, and only 20% of this group went on to have surgery, *vs.* 63% of the control group. In a study with contrasting results, Bennell *et al.* (2010) recruited people with shoulder pain from primary care and community settings and randomized them to receive an exercise and manual therapy intervention or a placebo ultrasound treatment. At the 11-week follow-up, there was no difference between groups in pain and disability scores, and although the active exercise group showed better improvement in functional scores at 22 weeks, there was no significant between-group difference in pain at this time point. It is likely that the recruitment strategy used by Bennell *et al.* (2010) resulted in quite a heterogenous group of participants, across the spectrum of rotator cuff tendon pathology. Because the continuum model suggests that reactive tendinopathy may benefit from reduced loading, it is possible that participants within the reactive subcategory would have done better in the placebo group, as ultrasound is a form of passive unloading and active exercise may have exacerbated any reactivity present. The only directly comparable outcome measure at baseline between the two studies was the visual analogue scale for pain. Mean resting pain was similar in the two studies (1.7 in the Holmgren study and 2.2 in the Bennell *et al.* study); however, activity-related pain was higher in the Holmgren *et al.* study (6.4 compared with 4.9 in the Bennell *et al.* study), possibly supporting the greater degree of tendon pathology in the Holmgren study. As these studies were not designed in line with the continuum model, this discussion remains speculative. To further investigate this, future research investigations in tendinopathy could be designed to assess outcome against targeted interventions, according to the subcategories of the continuum model.

Corticosteroid (CS) injection has been shown to be successful in treating pain in the short term in both patellar and rotator cuff tendinopathy; however, this benefit diminishes in the long term or with more chronic presentations (Smidt *et al.* 2002; Kongsgaard *et al.* 2009). van Ark *et al.* (2011), in a recent systematic review of injections for patellar tendinopathy, suggest that different injections may be suitable for different stages of disease. For example, for reactive or early-stage pathology, corticosteroid may be suitable to address the inflammatory and proliferative

mechanisms involved, while for disrepair/degenerative stage, other types of injection such as platelet-rich plasma may be more suitable, in conjunction with a loading programme, as it may have a more regenerative mechanism of effect. Matthews *et al.* (2006), in a histological study of rotator cuff tears, suggest that the use of CS injection for small rotator cuff tears may in fact be detrimental, reducing their ability to heal and directing the tissue into a more degenerative, metabolically inert state. Injections provide another example of a treatment, which could be optimized by targeting to the appropriate stage of tendon pathology.

Imaging studies

There have been a number of imaging-based studies involving athletic populations that have provided evidence for the continuum model. Malliaras and Cook (2011) examined the patellar tendons of 58 volleyball players on a monthly basis using ultrasound imaging and demonstrated that tendons transitioned between different stages of pathology, for example, normal to diffuse thickening or hypoechoic to diffuse thickening. There was also a significant association between greyscale ultrasound changes and the presence of pain, with pain most likely if the tendon contained a hypoechoic region. Fredberg and Bolvig (2002) studied previously asymptomatic football players found that only players with sonographically abnormal patellar tendons at the beginning of the season went on to develop painful tendons, with no occurrence of pain in players who were sonographically normal in the preseason. In a recent longitudinal study of asymptomatic ballet dancers, the presence of moderate or severe hypoechoic defects in the patellar and Achilles tendons on ultrasound was a weak predictor of the development of tendon-related pain and disability (Comin *et al.* 2013).

In contrast, imaging has not provided a good basis for determining the outcome of treatment for tendinopathy. Ekeberg *et al.* (2010) described a prognostic study examining factors associated with the success of corticosteroid injections in RC disease and found that imaging findings (MRI and US) were not good predictors of patient outcome. Drew *et al.* (2012) systematically reviewed the evidence for the relationship between structural changes in tendon and the outcome of treatment and made a strong argument against the use of structural changes to explain the effect of therapeutic interventions for tendinopathy. However, they suggest that imaging could perhaps be used to identify diagnostic subtypes within tendinopathy populations to better target treatment.

One of the biggest challenges in terms of the use of imaging in tendinopathy is the high degree of prevalence of asymptomatic structural changes – it is not possible as yet to differentiate between symptomatic and asymptomatic tendon pathology on any form of imaging (Moosmayer *et al.* 2009). Similar issues in diagnostic radiology for spinal and knee pain have caused some authors to call for more judicious use of imaging in the clinical setting and a need for better

integration with clinical findings (Englund *et al.* 2008; Chou *et al.* 2009). Ultrasound has traditionally been the preserve of radiologists, but in recent years has been increasingly adopted as a 'point of care' imaging modality by rheumatologists, sports medicine physicians and physiotherapists (Yim & Corrado 2012). This development could be a positive step towards better integration of imaging findings as part of the full clinical examination, which aligns well within the framework presented in the continuum model. Tendinopathy is often associated with 'latent' symptoms, developing subsequent to aggravating activity. The development of imaging protocols to assess changes in tendon properties (e.g. vascularity, thickness) in response to loading, may be another method that could help identify tendons in the reactive stage of pathology (Shalabi *et al.* 2004).

Newer protocols have opened up the possibilities for ultrasound imaging to contribute to knowledge regarding the structural properties of tendons. Ultrasound tissue characterization (UTC) is a method that quantifies echo patterns in the greyscale US image and provides a 3D reconstruction, which has been shown to be related to tendon histopathology (van Schie *et al.* 2003). A small study in chronic Achilles tendinopathy found that UTC could reliably distinguish between symptomatic and asymptomatic tendons (van Schie *et al.* 2010). Arya and Kulig (2010) used dynamic ultrasound imaging and dynamometry to assess the stiffness, stress and strain of the Achilles tendon during isometric activity in men with Achilles tendinopathy and matched controls. Tendinopathic tendons exhibited a loss of stiffness and a reduced Young's modulus (stiffness normalized to tendon geometry), potentially related to the loss of collagen structure in the pathological tendons and giving some explanation for the loss of functional performance. Similar imaging methods were used by Morrissey *et al.* (2011) to demonstrate a greater increase in Achilles tendon stiffness in response to an eccentric exercise programme in healthy individuals, compared with a similar group undergoing a concentric programme. Notwithstanding the potential limitations of this 2D method in assessing what is a 3D phenomenon (Magnusson *et al.* 2008), it offers at least some increased capacity to model tendon properties dynamically *in vivo* and in response to therapeutic interventions. Sonoelastography is another ultrasound-based method that provides an estimation of tissue elasticity or 'hardness', with pathological areas of tendon exhibiting a softer tissue spectrum. De Zordo *et al.* (2009) showed that sonoelastography is highly sensitive and specific in identifying regions of pathology in the common extensor tendons of patients with clinical signs of lateral epicondylar pain. Further refinement of this technique is likely to provide useful information in staging and treatment planning in tendinopathy (Klauser *et al.* 2010).

Scott and Khan (2010) discuss how a preventive treatment model for tendinopathy using imaging may be a way forward, where susceptible patients could be identified early on using ultrasound imaging and suitable rehabilitative measures instigated. Fredburg *et al.* (2008) undertook a preventive

study aimed at preventing the onset of patellar tendinopathy in soccer players, where players with sonographically abnormal tendons undertook a prophylactic strengthening and stretching programme. This programme failed to prevent development of symptoms and may in fact have increased the risk in some players. As such, the content of any preventive or early-stage programme remains to be determined; however, an effective programme could have widespread benefit in reducing the personal and economic cost of chronic tendinopathies.

Summary

It is clear that the continuum model continues to be supported by pathological research; however, clinical research has continued to favour a heterogeneous model of tendon pathology, with the result that the optimal intervention for each stage of pathology is still unknown. While imaging has failed to provide a mechanism for this staging process to date, suggestions have been made as to how new developments in imaging technology may be able to further develop this process. The continuum model could be supplemented with prognostic information in terms of patient-based factors, both physical and psychosocial, to optimize its use in terms of treatment choice for the individual patient.

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We can confirm that both listed authors meet ICMJE authorship criteria, and nobody who qualifies for authorship has been excluded.

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Conflict of interest

We certify that no actual or potential conflict of interest in relation to this article exists for either author.

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