Contractile dysfunctions – no longer the therapist's Achilles heel? A clinical review of histopathology, mechanotransduction and management

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Contractile dysfunction, tendinopathy, mechanotransduction, loading strategies

Introduction

Contractile dysfunctions (McKenzie and May 2000) are not uncommon findings in patients with non-spinal musculoskeletal conditions. Contractile dysfunctions appear to account for about a third of mechanical syndrome classifications consistently across a number of patient surveys of non-spinal musculoskeletal conditions (May 2006).

Those of you who were at the 2006 McKenzie Conference of Americas would have heard the exciting presentations by Dr Karim Khan about his and other research groups' work related to tendinopathy. In these he both presented a contemporary understanding of the pathophysiology of tendon problems, but also the possible mechanism by which progressive loading is effective in the management of these conditions. This paper presents a brief summary of some of this work under the following headings, which will include some speculative clinical commentary seeking to explain some of the responses seen in these patients:

- terminology
- aetiology
- pathophysiology
- mechanotransduction
- management
- conclusion

Terminology–'time to abandon the tendonitis myth'

Tendonitis, with the suffix 'itis' denoting inflammation, is clearly a misnomer. No inflammatory cells have been found in affected tendons with chronic symptoms. Animal models have demonstrated some inflammatory cell presence in the first 2 weeks of acute injury only. But histopathological studies have never demonstrated inflammatory cells in persistent tendon problems, nor have studies from a range of sites demonstrated the presence of the inflammatory mediator prostaglandin E2.

Tendon pathologies should instead be referred to as tendinopathy or tendinosis, and clearly fit the definition of structural impairment in contractile dysfunction in the Mechanical Diagnosis and Therapy (MDT) system (Khan et al 1999, Astrom and Rausing 1995, Almekinders and Temple 1998, Kraushaar and Nirschl 1999, Zeisig et al 2006, Rees et al 2006).

At present there appears to be more commonalities between tendinopathy at different sites than differences. It appears likely that the pathophysiology and the most effective management for tendon problems are very similar, whether tennis elbow, rotator cuff lesion, adductor lesion, Achilles tendinopathy, patellar tendon lesion etc. (Chard et al 1994, Khan et al 1999, 2000, Jonsson et al 2006, Rees et al 2006, Zeisig et al 2006, Brukner and Khan 2007).

Aetiology of tendinopathy

Aetiology of tendinopathy is uncertain, but appears to be a complex interaction of mechanical, vascular and other factors; and genetic predisposition has also been proposed. Mechanical factors include questions about the role of 'under use' as well as 'overuse' of a tendon and its insertion, and the failure of a repair mechanism once the tendon integrity becomes compromised by one of these processes. The mechanical theory proposes that tendinopathy occurs with repeated loading, which is within physiological limits but over time leads to tendon fatigue and then failure. This would explain why tendinopathy is commonly found in the tendons of older individuals. However there are certain aspects of tendinopathy that are not explained by the mechanical theory – for instance why are some areas of particular tendons prone to tendinopathy, and why tendinopathy sometimes is painful and sometimes is asymptomatic. Also it seems rather unlikely that loading within the physiological range could actually harm the tendon, and if this is the case then why do exercises also confer a therapeutic benefit (Rees et al 2006)?

The vascular theory asserts that as metabolically active tissue tendons can be susceptible to vascular compromise at certain sites that can lead to degeneration. For instance there is some evidence of a region of reduced vascularity in the Achilles tendon in the area most susceptible to degenerative changes. But again there is controversy over this theory, and it is not completely accepted by all (Rees et al 2006). It does not explain why exercises can heal tendons, nor the recent findings of neovascularisation in symptomatic tendons.

In reality it is likely that the aetiology is a result of some interaction between mechanical, vascular and neural factors, as well as other factors that might have a role. There are other intrinsic and extrinsic factors including age, gender, biomechanics, training errors, and the environment that have been proposed to be involved in causation although the specific literature remains scarce. There is a genetic predisposition to chronic Achilles tendon problems (Mokone 2005), this is supported by research that sustaining an Achilles tendon rupture increases the risk of the other Achilles rupturing by 176 times (Rees et al 2006, Riley 2004).

Pathophysiology

In affected tendons what has been found are: disrupted collagen in disarray, apoptosis (cell death), and primarily proliferation of ground substance and myofibroblasts. In other words what looks like disruption of the collagen structure and failed attempts to repair it. Furthermore tendinopathy has variable amounts of neovascularisation that results in a profusion of abnormal blood vessels and nerves, which can be seen on Doppler US. Some studies have suggested that this vas-

culo-neural in-growth is the source of symptoms, being commonly found in symptomatic tendons, which become pain free after injection of sclerosing substances or disappear over time in patients with positive clinical outcomes, but are not found in normal tendons (Zeisig et al 2006, Ohberg et al 2001, 2004, Weinberg et al 1998, Khan et al 1999, Astrom and Rausing 1995, Almekinders and Temple 1998, Kraushaar and Nirschl 1999, Ohberg et al 2004, Zeisig et al 2006).

The nerves are likely to make the tissue highly sensitive to stress and therefore speculatively might cause a temporary worsening of pain if overloaded too early in the rehabilitation process. Maybe in the past this has been mistaken as an inflammatory response, but is in fact more likely to be a product of peripheral sensitisation. Its lesson is the importance of achieving the right loading strategy during the rehabilitation process.

Mechanotransduction – why loading is the answer?
Loading the tendon appears to be the best clinical solution to tendon problems (see next section), but why is this? Dr Khan hypothesised that this was because the loading targets the affected cells in a positive way, and remarked that to cell biologists all this was patently obvious. The loading and its effects is known as mechanotransduction.

Loading has the following sequential effects:

- mechanical coupling – loading physically stimulates the cells
- biochemical coupling – cells are linked by gap junctions
- transmission of biochemical signal – calcium and protein flow through and between cells
- tendon cell response – nucleus up-regulates protein production including collagen and proteoglycans
- thus repair and remodelling are stimulated

This somewhat hypothetical theory, but based on plenty of applied science from different areas, provides MDT practitioners with the potential science that underpins our management of patients with contractile dysfunctions. It is known that blood flow, oxygen demand and the level of collagen synthesis increase with mechanical loading on human tendons. The proteins of the extra cellular matrix are also modified by exercise; these changes affect the biomechanical and structural properties of the collagen. Mechanical loading thus results in a marked increase in growth factors that stimulate extra cellular proteins (Kjaer et al 2005).

Management
If the pathology is not an inflammatory process then apparently appropriate interventions, such as rest and ice no longer look so relevant. If tendon pathology is related to a failed repair process, or rather a failed remodelling phase of the repair process, it is the remodelling that is most important. This maybe explains the results of some trials in which steroid injections have been used to produce a better quick effect than other interventions, but a poorer or equal long-term effect compared to physiotherapy, naproxen and even a wait-and-see policy (Smidt et al 2002, Hay et al 1999). Perhaps the injection provides pain relief, but the tendon has not been strengthened or remodelled – a return to normal use simply causes a recurrence of symptoms in the still weakened and disrupted tendon.

Furthermore, studies comparing surgical to non-surgical management of tendinopathies clearly demonstrate the value of exploring a loading regime, often eccentric, before considering a surgical option. For instance equal outcomes were demonstrated between surgery and an eccentric training programme in patients with Achilles tendinopathy and patellar tendinopathy (Alfredson et al 1998, Bahr et al 2006), and between surgery and exercise programmes in patients with rotator cuff disease (Brox et al 1993, 1999, Haahr et al 2005). In a pilot study, of 9 patients with 'impingement syndrome' awaiting surgery, 5 improved markedly in pain and function following an eccentric training programme, and withdrew from the surgery waiting list (Jonsson et al 2006). The programme deliberately provoked patient's pain, with an increase in load if the exercise became painless.

There is increasingly good evidence for the use of resistance training in tendinopathy, especially eccentric training. Obviously there is a range of strengthening exercises that could be used, including: isometric, dynamic isotonic, resisted, concentric, eccentric etc. Several research groups are now advocating eccentric loading exercises for the treatment of tendon problems, and clinical research generally supports this approach. Although some of these studies use weak study designs without randomisation or control groups, the results are the same in the randomised controlled trials. Frequently the patients are very chronic and have failed to respond already to a range of conservative treatments. Positive results to resistance training have been demonstrated in Achilles, rotator cuff, adductor, lateral epicondyle, and patellar tendon problems.

(Alfredson et al 1998, Brox et al 1993, 1999, Fyfe and Stanish 1992, Holmich et al 1999, Pienimaki et al 1996, 1998, Stanish et al 1986, Bahr et al 2006, Jonsson et al 2006). However a recent systematic review on the effectiveness of eccentric exercises noted that there was limited evidence that they had a positive effect on outcomes compared to various control interventions, but also that there was a dearth of high quality research on the topic (Woodley et al 2006).

The eccentric studies currently all tend to be modeled on the Alfredson approach of 3 sets of 15 repetitions, two times a day, seven days a week, for 12 weeks, al-

though the exact rationale for this specific regime remains anecdotal. Furthermore, there is no consensus so far in the initial loading that should be used; some advocate loading that provokes pain, but others being unclear about the pain response. It is only MDT (McKenzie and May 2000) that clearly advocates a loading hierarchy based on symptom response in the remodelling of structural impairment in Contractile Dysfunction. From the range of potential exercises the patient should start on one exercise at the intensity that provokes their pain but allows it to fade away within minutes of completing the loading exercise, as has been previously advocated with management of Dysfunction Syndrome in the spine – pain is produced but does not remain worse as a result of the loading strategy.

As this exercise becomes easier or asymptomatic a further progression is incorporated with graduated loading as the intensity of the exercise is increased. Progressions continue as far as they equate with the normal or desired functional requirements of the patients, but should guarantee full and pain free range of movement. This might involve the use of a backpack (for lower limb exercises) or weights during the eccentric loading to increase the intensity to reproduce the patient's symptoms during the exercise. Furthermore, eccentric loading of the patella tendon has been demonstrated to be significantly more effective by using a decline board to increase the load (Bahr et al 2006, Kongsgaard et al 2006).

Rehabilitation may also involve variations in velocity of the exercise, and sport specific functional tasks, particularly if the patients are returning to sport or activities involving high impact or high intensity such as running, jumping, throwing etc

Conclusion

This review has considered some of the background evidence underpinning the management of contractile dysfunction, which is a commonly found mechanical syndrome in extremity patients. The pathophysiology is now understood to be non-inflammatory in nature in most patients, but represents more an attempt at failed repair with an in-growth of blood vessels and nerves into the disrupted collagen. Loading has the effect of stimulating collagen synthesis and other extra cellular matrix. It is hypothesised that loading affects the tendon both bio-chemically and bio-mechanically in such a way that stimulates repair and remodelling so that the structural properties of the tendon is improved. Therefore not surprisingly it has been shown that loading exercises, especially eccentric loading, are an effective management for many patients with tendinopathy.

Clearly there are more studies required to further refine specific exercise prescription and graduated loading strategies.

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References

Alfredson H, Pietila T, Jonsson P, Lorentzon R (1998). Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. Am J Sports Med 26.360-366.

Almekinders LC, Temple JD (1998). Etiology, diagnosis, and treatment of tendonitis: an analysis of the literature. Med Sci Sports Exerc 30.1183-1190.

Astrom M, Rausing A (1995). Chronic Achilles tendinopathy. A survey of surgical and histopathologic findings. Clin Orth Rel Res 316.151-164.

Bahr R, Fossan B, Loken S, Engebretson L (2006) Surgical treatment compared to eccentric training for patellar tendinopathy (Jumpers Knee). Journal of Joint and Bone surgery 88A 8,1689 -1699

Brox JI, Staff PH, Ljunggren AE, Brevik JI (1993). Arthroscopic surgery compared with supervised exercises in patients with rotator cuff disease (stage II impingement syndrome). BMJ 307.899-903.

Brox JI, Gjengedal E, Uppheim G et al (1999). Arthroscopic surgery compared with supervised exercises in patients with rotator cuff disease (stage II impingement syndrome): a prospective, randomised, controlled study in 125 patients with a 2 ½ -year follow-up. J Should Elbow Surg 8.102-111.

Brukner P & Khan K (2007) Clinical Sports Medicine. 3rd edition, McGraw-Hill, Sydney.

Chard MD, Cawston TE, Riley GP, Gresham GA, Hazleman BL (1994). Rotator cuff degeneration and lateral epicondylitis: a comparative histological study. Ann Rheum Dis 53.30-34.

Fahlstrom M, Jonsson P, Lorentzon R & Alfredson H (2003) Chronic Achilles tendon pain treated with eccentric calf-muscle training. Knee Surgery, Sports Traumatology, Arthroscopy 11:327-333

Fyfe I, Stanish WD (1992). The use of eccentric training and stretching in the treatment and prevention of tendon injuries. Clinics in Sports Med 11.601-624.

Haahr JP, Ostergaard S, Dalsgaard J et al (2005). Exercises versus arthroscopic decompression in patients with subacromial impingement: a randomised, controlled study in 90 cases with a one year follow up. Ann Rheum Dis 64.760-764.

Hay EM, Paterson SM, Lewis M, Hosie G, Croft P (1999). Pragmatic randomised controlled trial of local corticosteroid injection and naproxen for treatment of lateral epicondylitis of elbow in primary care. BMJ 319. 964-968.

Holmich P, Uhrskou P, Ulnits L et al (1999). Effectiveness of active physical training as treatment for long-standing adductor-related groin pain in athletes: randomised trial. Lancet.353.439-443.

Jonsson P, Wahlberg P, Ohberg L, Alfredson H (2006) Eccentric training in chronic painful impingement syndrome of the shoulder: results of a pilot study

Knee Surgery, Sports Traumatology, Arthroscopy 14: 76-81

Khan KM, Cook JL, Bonar F, Harcourt P, Astrom M (1999). Histopathology of common tendinoathies. Sports Med 27.393-408.

Khan KM, Cook JL, Taunton JE, Bonar F (2000). Overuse tendinosis, not tendinitis; part 1: A new paradigm for a difficult clinical problem. Physician Sports Med 28.38-45.

Kjaer M, Langberg H, Miller BF et al (2005). Metabolic activity and collagen turnover in human tendon in response to physical activity. J Musculoskeletal Neuronal Interactions 5.41-52.

Kongsgaard M, Aagaard P, Roikjaer S, Olsen D, Jensen M, Langberg H, Magnusson S (2006) Decline eccentric squats increase patella tendon loading compared to standard eccentric squats. Clinical Biomechanics 21, 748-754

Kraushaar BS, Nirschl RP (1999). Tendinosis of the elbow (tennis elbow). JBJS 81A. 259-278.

May S (2006). Classification by McKenzie's Mechanical Syndromes. Report on directional preference and extremity patients. Int J Mech Diag Ther (In Press).

McKenzie RA, May S (2000). The Human Extremities. Mechanical Diagnosis and Therapy. Spinal Publications New Zealand Ltd, Waikanae, New Zealand.

Mokone GG, Schwellnus MP, Noakes TD, Collins M (2006)The COL5A1 gene and Achilles Tendon Pathology Scan J Med Sci Sports 16, 1, 19-26.

Ohberg L, Lorentzon R, Alfredson H (2001). Neovascularisation in Achilles tendons with painful tendinosis but not in normal tendons: an ultrasonographic investigation. Knee Surgery, Sports Traumatology, Arthroscopy 9.233-238.

Ohberg L, Alfredson H (2004). Effects of neovascularisation behind the good results with eccentric training in chronic mid-portion Achilles tendinosis?

Knee Surgery, Sports Traumatology, Arthroscopy 12: 465-470.

Pienimaki TT, Tarvainen TK, Siira PT, Vanharanta H (1996). Progressive strengthening and stretching exercises and ultrasound for chronic lateral epicondylitis. Physiotherapy 82.522-530.

Pienmaki T, Karinen P, Kemila T, Koivukangas P, Vanharanata H.

Long-term follow-up of conservatively treated chronic tennis elbow patients. A prospective and retrospective analysis. Scand J Rehab Med 1998. 30.159-166.

Rees JD, Wilson AM, Wolman RL (2006). Current concepts in the management of tendon disorders. Rheumatology 45.508-521.

Riley G (2004). The pathogenesis of tendinopathy. A molecular perspective. Rheumatology 43,131-142.

Smidt N, van der Windt DAWM, Assendelft WJJ, Deville WLJM, Korthals-de Bos IBC, Bouter LM (2002). Corticosteroid injections, physiotherapy, or a wait-and-see policy for lateral epicondylitis: a randomised controlled trial. Lancet 359. 657-662.

Stanish WD, Rubinovich RM, Curwin S (1986). Eccentric exercise in chronic tendonitis. Clinical Orth & Rel Res 208.65-68.

Weinberg EP, Adams MJ, Hollenberg GM (1998). Color Doppler sonography of patellar tendinosis. Am J Roentgen 171.743-744.

Woodley BL, Newsham-West RJ, Baxter GD (2006). Chronic tendinopathy: effectiveness of eccentric exercise. Br J Sports Med Online 10.1136/ bjsm.2006.029769

Zeisig E, Ohberg L, Alfredson H (2006) Extensor origin vascularity related to patients with tennis elbow. Knee Surgery, Sports Traumatology, Arthroscopy 14: 659-663.