

New options in the management of tendinopathy

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Abstract: Tendon injuries can be acute or chronic, and caused by intrinsic or extrinsic factors, either alone or in combination. Tendinopathies are a common cause of disability in occupational medicine and account for a substantial proportion of overuse injuries in sports. Tendinopathy is essentially a failed healing response, with haphazard proliferation of tenocytes, abnormalities in tenocytes, with disruption of collagen fibres and subsequent increase in noncollagenous matrix. The scientific evidence base for managing tendinopathies is limited. What may appear clinically as an “acute tendinopathy” is actually a well advanced failure of a chronic healing response in which there is neither histologic nor biochemical evidence of inflammation. In this review we report the new options for the management of tendinopathy, including eccentric exercises, extracorporeal shockwave therapy, injections (intratendinous injections of corticosteroids, aprotinin, polidocanol platelet-rich plasma, autologous blood injection, high-volume injections) and surgery. Open surgery aims to excise fibrotic adhesions, remove areas of failed healing and make multiple longitudinal incisions in the tendon to detect intratendinous lesions, and to restore vascularity and possibly stimulate the remaining viable cells to initiate cell matrix response and healing. New surgical techniques aim to disrupt the abnormal neoinnervation to interfere with the pain sensation caused by tendinopathy. These procedures are intrinsically different from the classical ones in present use, because they do not attempt to address directly the pathologic lesion, but act only to denervate them. They include endoscopy, electrocoagulation, and minimally invasive stripping. Further randomized controlled trials are necessary to clarify better the best therapeutic options for the management of tendinopathy.

Keywords: tendon, tendinopathy, management, injections, surgery, sports

Introduction

Tendon injuries can be acute or chronic, and caused by intrinsic or extrinsic factors, either alone or in combination. Tendinopathies are a common cause of disability in occupational medicine,¹ and account for a substantial proportion of overuse injuries in sports.²⁻⁴ We advocated the use of the term tendinopathy as a generic descriptor of the clinical conditions (both pain and pathology) arising from overuse in and around tendons.⁵ We challenged the common wisdom, intrinsic in the suffix “-itis”, that overuse tendinopathies are attributable to inflammation. Such terms as paratenonitis, tenosynovitis, tendovaginitis, peritendinitis, and partial rupture have been used to describe the noninsertional pain problems of tendons.

The histologic descriptions “tendinosis” (a degenerative pathology with a lack of inflammatory change) and “tendonitis” or “tendinitis” (implying an inflammatory process) should only be used after histopathologic confirmation.⁵ Tendinopathy

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is essentially a failed healing response, with haphazard proliferation of tenocytes, abnormalities in tenocytes cells, and disruption of collagen fibres, and subsequent increase in noncollagenous matrix.⁶ Tendinopathic tendons have an increased rate of matrix remodeling, leading to a mechanically less stable tendon which is probably more susceptible to damage.⁷ Surgical specimens of patients with established tendinopathy consistently showed either absent or minimal inflammation at histopathologic examination.⁸⁻¹⁰ They generally also show hypercellularity, a loss of the tightly bundled collagen appearance, an increase in proteoglycan content and, commonly, neovascularisation.^{11,12} Inflammation seems to play a role only in the initiation, but not propagation and progression, of the disease process.¹³ Several theories have been proposed to explain the pathogenesis of tendon pathology at specific stages and presentations of the condition.¹⁴⁻¹⁹

The scientific evidence base for managing tendinopathies is limited. Despite an abundance of therapeutic options, very few randomised prospective, placebo-controlled trials exist to assist in choosing the best evidence-based management.^{20,21} What may appear clinically as an “acute tendinopathy” is actually a well advanced failure of a chronic healing response in which there is neither histologic nor biochemical evidence of inflammation. Evidence for the effectiveness of any available drug management regimen is at best controversial when tested in randomized controlled trials.²² The available literature suggests that, in the absence of an overt inflammatory process, there is no rational basis for the use of nonsteroidal anti-inflammatory drugs in chronic tendinopathy; they are unlikely to change its still ill-defined natural history.²³

There are no randomized or prospective studies that compare different conservative and surgical management regimens. Surgery should be reserved for patients in whom conservative management has proved ineffective for at least six months.²⁴

The aim of this review is to report the new options for management of tendinopathy.

Eccentric exercises

Stanish et al first suggested eccentric strength training for the rehabilitation of tendon injuries in 1986.²⁵ Eccentric exercises have been proposed to promote collagen fibre cross-link formation within the tendon, thereby facilitating tendon remodeling.²¹ Evidence of histologic changes following a program of eccentric exercise are lacking, and the mechanisms by which eccentric exercises may

help to resolve the pain of tendinopathy remain unclear.²⁶ A systematic review of eccentric training concluded that no definite answer can be given to the question of whether eccentric overload training in patients with chronic Achilles tendinopathy has a beneficial effect on pain and function, because of the methodologic shortcomings of the studies. The effect of such training on function and sports participation cannot be established definitely at the moment. Large, methodologically sound studies from multiple sites in which functional outcome measures are included are warranted.²⁷ The concept of eccentric exercises is based on the structural adaptation of the musculotendinous units to protect it from increased stresses and thus prevent reinjury. The basic principles in an eccentric loading regime are length of tendon, load, and speed. If the tendon is pre-stretched, its resting length is increased, and there will be less strain on that tendon during movement. By progressively increasing the load exerted on the tendon, there should be a resultant increase in the inherent strength of the tendon itself. By increasing the speed of contraction, greater force will be developed. Colour Doppler sonography demonstrated decreased neovascularisation following eccentric training intervention.²⁸ Evidence for the effectiveness of this management regimen is at best controversial when tested in randomized controlled trials. The results observed from our group in athletic²⁹ and nonathletic³⁰ patients were less convincing than those reported from Scandinavia.^{31,32} However, in general, the overall trend suggest a positive effect of eccentric exercises, with no reported adverse effects.^{21,29,31-42} Combining eccentric training and shock wave therapy (SWT) produces higher success rates compared with eccentric loading alone or SWT alone.⁴³

Extracorporeal shock wave therapy

Extracorporeal SWT is a noninvasive procedure which uses single pulsed acoustic or sonic waves generated outside the body and focused at a specific site within the body. The shock waves dissipate energy at the interface of two substances with different acoustic impedance, such as the bone-tendon interface, resulting in the release of kinetic energy at the junctions that can cause tissue alterations.⁴⁴ Experimentally, low-energy SWT stimulates soft tissue healing and inhibits pain receptors. Effects after repetitive application were significantly greater than after single application.⁴⁵ Low-energy SWT also enhances angiogenesis.^{26,46} The rationale for its clinical use is stimulation of soft tissue healing and inhibition of pain receptors. Hence, SWT has been investigated clinically during the past decade.⁴⁷⁻⁶⁵

There is no consensus on the use of repetitive low-energy SWT, which does not require local anesthesia, and on the use of high-energy SWT, which requires local or regional anesthesia.⁴⁴

Low-energy SWT in tendinopathy has been proposed to stimulate soft tissue healing and inhibit pain receptors.^{43,44,66,67} Low-energy SWT or eccentric training for the management of Achilles tendinopathy produced comparable results in a randomized controlled trial,²⁶ and both management modalities showed outcomes superior to the wait-and-see policy.²⁶ The combined use of low-energy SWT and eccentric exercises is beneficial.⁶⁸ However, when low energy SWT is used outside the indications and modalities outlined in the above trials, the results can be disappointing.⁶⁹ Eccentric training or SWT should be offered to patients with chronic recalcitrant tendinopathy of the main body of tendo Achillis as an alternative to surgery.

Injections

Corticosteroids

Corticosteroid injections have been used as a standard management option for tendinopathy for several years. Today, the use of corticosteroid injections is highly contentious.¹³ There is a lack of good quality research data to support the widespread use of these drugs. In humans, there are numerous case reports of tendon rupture after corticosteroid injections.^{70,71} Generally, steroid injection is associated with an increase in reported pain for the first 24 hours of treatment, but the therapeutic benefits are evident three to four days after the start of treatment. Animal studies have suggested that local corticosteroid injections may lead to a reduction in tendon strength,⁷² but this finding is not universal.⁷³ At present, there is not significant evidence from which to draw firm conclusions on the utility of local steroid treatments for Achilles tendinopathy. Three randomized controlled trials^{74–76} showed a mixed picture of the effect of local steroids on healing, with two studies reporting some benefit^{74,75} and the other detecting none.⁷⁶ A meta-analysis of the effects of corticosteroid injections has shown little benefit.⁷⁷ The safety of using corticosteroid injections can be enhanced with the use of imaging as a guide to enter the peritendinous space.⁷⁸

Corticosteroid injections appear to be effective at providing pain relief from tendinopathy in the short term, which may arise from inhibition of prostaglandins. The role of steroids in management of tendinopathy is still debated. Meta-analysis of the effects of corticosteroid has shown that published data are insufficient to determine the risk of rupture

following corticosteroid injections,⁷⁷ and we do not advocate their intratendinous injection.⁷⁹

Aprotinin

Aprotinin has been used to prevent blood loss during major surgery, which is its major indication.^{80–82} Aprotinin is an 85 amino-acid, 65 kD basic polypeptide extracted from bovine lungs. It is a broad-spectrum serine protease inhibitor, with particular inhibition of plasmin (along with trypsin and kallikrein),^{81,83,84} forming reversible competitive bonds with these enzymes, inhibiting their proteolytic action and their vasoactive effect in the first stages of inflammation.^{83,84} It may block matrix metalloproteinases (MMPs), including MMP-1, MMP-8 and MMP-13 (collagenases) and MMP-2 and MMP-9 (gelatinases), either directly or via inhibition of plasminogen and plasmin.^{83,84} The major side effect is anaphylaxis, which is particularly seen after repeated use of the drug.^{85,86} The rate of allergic reaction when using repeat injections of aprotinin (bovine-derived) is higher than for most medications and this represents a major factor to consider when choosing this drug.^{81,86}

Aprotinin was popularized by Maffulli as an off-label injection for management of tendinopathy.^{87–93} If aprotinin works simply as a form of prolotherapy, it would be a better choice to use dextrose or autologous blood for treatment of tendinopathy. However, if aprotinin works specifically as a collagenase inhibitor, then it may have advantages over more inert substances. This is an important question, with mixed results demonstrated to date in the randomised controlled trials.^{91,94}

Brown et al⁹⁴ conducted a randomised controlled trial to compare aprotinin and exercises with placebo and exercises. They found no statistically significant improvement in the aprotinin group over placebo at any followup visit for either the primary or secondary outcome measures. However, the authors stated that the lack of statistical significance could reflect the small sample size.

Polidocanol

Polidocanol (Aetoxisclerol[®], Kreussler, Germany) is a sclerosing substance, which shows the potential to reduce tendon pain during activity in patients with chronic tendinopathy.^{95–109} In Achilles and patellar tendinopathy, there is evidence of neural ingrowth in conjunction with neo-vascularisation. Scandinavian researchers have shown good results by injecting polidocanol into and around the neovessels. Injections of sclerosing substances close to the tendon seem to be remarkably safe.

Of 150 patients managed with sclerosing injections for Achilles tendinopathy, two complications were experienced. One patient who had insertional Achilles tendinopathy sustained a total rupture in the proximal part of the tendon at the end of an 800 m running race, and one patient sustained a partial rupture in a midportion of the tendon where he previously had also received four intratendinous corticosteroid injections.¹¹⁰

Platelet-rich plasma

Platelet-rich plasma (PRP) is now being widely tested in different fields of medicine for its possibilities in aiding the regeneration of tissue with low healing potential.^{111–118} The unique combination and concentration of bioactive molecules that exist within PRP have profound effects on the inflammatory, proliferative, and remodeling phases of wound healing. Its use in orthopedic surgery began during this decade especially for augmentation of bone grafting, even though to date no definitive evidence is available for its use to improve bone healing. The use of PRP to favor tendon healing has been advocated only recently.^{116,119,120} The specific elements of PRP have not been uniformly defined in the literature.¹¹⁹ PRP, in general, has a higher concentration of platelets compared with baseline blood.^{121,122}

Clinically valuable PRP preparations typically contain one million platelets or more per microliter.¹²³ PRP has been defined as only platelets or as increased concentrations of white blood cells.¹¹⁹ Tendon healing occurs through three overlapping phases (inflammation, proliferation, and remodeling), which are controlled by a variety of growth factors.^{119,124–126} The rationale for the use of PRP to promote tendon healing is the high content of these cytokines and cells in hyperphysiologic doses of PRP. Several studies are ongoing worldwide on the application of PRP for tendon healing, even though the exact mechanisms by which PRP promotes tendon healing are not yet clarified. One of the main advantages is that PRP is autologous and is prepared at the point of care, and therefore it has an excellent safety profile. Researchers worldwide are evaluating PRP with increasing interest.

Autologous blood

Autologous blood injection has been also used for the management of tendinopathy¹²⁷ to provide cellular and humoral mediators and to induce healing in areas of failed healing response. Use of autologous blood injection may lead to tendon healing through collagen regeneration

and the stimulation of well-ordered angiogenesis.¹²² It is hypothesized that transforming growth factor- β and basic fibroblast growth factor carried in the blood will act as humoral mediators to induce the healing cascade.^{128,129} Laboratory studies are encouraging. However, they always use healthy tendons or surgically induced lesions, given the lack of a good experimental model for tendinopathy. At present, it is unclear whether these results can be extrapolated to tendinopathic tendons.¹²²

Various studies seem to describe autologous blood injections after repeated needling of the relevant tendon. In this respect, therefore, it could be difficult to distinguish between the effects of needling and the effects of autologous blood injection.¹²⁹

High-volume injections

Neovascularisation only occurs in patients with tendinopathy, and is accompanied by nerve ingrowth. The ingrowth of new vessels and associated nerves from the ventral side of the tendon may be a source of pain. The hypothesised rationale behind this management modality was that the high-volume injection would produce local mechanical effects, causing neovessels to stretch, break, or occlude. By occluding and possibly breaking these neovessels, the accompanying nerve supply would also be damaged either by trauma or ischemia, therefore decreasing the pain in patients with resistant Achilles tendinopathy.

Preliminary studies showed that high-volume injection significantly reduces pain and improves short- and long-term function in patients with Achilles and patellar tendinopathy, regardless of their level of symptoms. High-volume injection is safe and relatively inexpensive, with the potential to offer an alternative management option before surgery, aiding a quicker return to sport.⁷⁹ We used hydrocortisone acetate in the high-volume injections, primarily to prevent an inevitable acute mechanical inflammatory reaction produced by the large amount of fluid injected in the proximity of the tendon. The injection is performed under ultrasound guidance, so the steroid has no direct action on the tendon itself.

Surgery

Surgery aims to excise fibrotic adhesions, remove areas of failed healing and make multiple longitudinal incisions in the tendon to detect intratendinous lesions and to restore vascularity, and possibly stimulate the remaining viable cells to initiate cell matrix response and healing.^{12,130} Recent studies show that multiple longitudinal tenotomies trigger neoangiogenesis at the tendo Achillis, with increased

blood flow.¹³¹ This would result in improved nutrition and a more favorable environment for healing. Multiple percutaneous longitudinal tenotomies can be performed when conservative management has failed in patients with isolated tendinopathy with no involvement of the paratenon and a well-defined nodular lesion less than 2.5 cm long,¹³² possibly ultrasound-guided to confirm the precise location of the area of tendinopathy.^{132–134} It is a simple procedure and can be performed in the clinic under local anesthesia without a tourniquet, but attention to detail is necessary, given that even in minimally invasive procedures complications are possible. Percutaneous longitudinal ultrasound-guided internal tenotomy of the tendo Achillis is simple and can be performed on an outpatient basis. However, it requires the use of high-resolution ultrasound to locate properly the tendinopathic area and to place the initial stab wound. Also, with this technique, it is not possible to collect samples of tendon material for biopsy, even though histopathologic work has shown that symptomatic intratendinous areas that are hypoechoic at ultrasound show tendinosis.¹³⁵ Complications were minimal and led to no long-term morbidity. In our hands, it is an intervention in the management of chronic Achilles tendinopathy when conservative treatment has failed. The technique is not as effective in patients with pantendinopathy. Good results can also be achieved by arthroscopic management of patellar^{136–138} and Achilles tendinopathy.¹³⁹

Radiofrequency microtenotomy

Radiofrequency microtenotomy is a safe and effective procedure to manage patients with chronic tendinopathy. Microtenotomy is a technically simple procedure to perform and has been proposed to produce a rapid and uncomplicated recovery. It is hypothesized that the mechanism of action may be the acute degeneration and/or ablation of sensory nerve fibers. Early degeneration followed by later regeneration of nerve fibers after bipolar radiofrequency treatment may explain long-term postoperative pain relief after microtenotomy for tendinopathy.^{139–142}

Neovessel destruction

Pathologic nerve ingrowth accompanies pathological neovascularization in the tendon, and it has been considered as a possible cause of the pain experienced with tendinopathy. Some authors have attempted to disrupt the abnormal neoinnervation to interfere with the pain sensation caused by tendinopathy. These procedures are intrinsically different from the classical ones in present use, because they do not

attempt to directly address the pathologic lesion, but act only to denervate them. Endoscopy,^{143–148} electrocoagulation,¹⁴⁹ and minimally invasive stripping^{150–152} have been described to this aim.

Minimally invasive stripping

We have developed a novel minimally invasive technique of stripping of neovessels from the Kager's triangle anterior to the Achilles tendon.¹⁵¹ This achieves safe and secure breaking of neovessels and the accompanying nerve supply. The patient undergoes local or general anesthesia, according to surgeon or patient preference. The patient is positioned prone with a calf tourniquet which is inflated to 250 mmHg after exsanguination. Skin preparation is performed in the usual fashion. Four skin incisions are made. The first two are 0.5 cm longitudinal incisions at the proximal origin of the Achilles tendon, just medial and lateral to the origin of the tendon. The other two are also 0.5 cm longitudinal incisions, but 1 cm distal to the distal end of the tendon insertion on the calcaneus.

A mosquito is inserted in the proximal incisions, and the Achilles tendon is freed of peritendinous adhesions. A Number 1 unmounted Ethibond (Ethicon, Somerville, NJ) suture thread is inserted proximally, passing through the two proximal incisions, anterior to the Achilles tendon at the border between the Achilles tendon and the Kager's triangle. The Ethibond is retrieved from the distal incisions. Using a gentle see-saw motion, similar to using a Gigli saw, the Ethibond suture thread is made to slide posterior to the tendon, which is stripped and freed from the fat of Kager's triangle. If necessary, using an 11 blade, longitudinal percutaneous tenotomies parallel to the tendon fibres are made.^{41,132,133}

The subcutaneous and subcuticular tissues are closed in a routine fashion, and Mepore (Molnlycke Health Care, Gothenburg, Sweden) dressings are applied to the skin. A removable scotch cast support with Velcro straps can be applied if deemed necessary.

Conclusions

Musculoskeletal physicians attempt to give their patients the best available management at their disposal. Recently, the concept of "evidence-based medicine" has come to the forefront, attempting to recognise and define the best scientific observation which might influence clinical practice. Further randomized controlled trials are necessary to clarify better the best therapeutic options for the management of tendinopathy.

A genetic component has been implicated in tendinopathies, but investigations into the genetic factors involved in their etiology are still in their infancy.^{153–155} In the equine model, good results have been achieved, but these are preliminary results,¹⁵⁶ and tissue engineering, though stimulating, is still far from clinical application.^{156,157} An enhanced understanding of these factors holds the promise of new approaches to the prevention and management of these common conditions.

Disclosures

The authors report no conflicts of interest in this work.

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