CHAPTER **14**

INSIGHTS INTO ACHILLES TENDINOPATHY

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TERMINOLOGY

The terminology used to describe Achilles tendon pathology can be misleading and sometimes confusing. Often we use the term tendinitis, when in reality there are very few inflammatory cells, and no significant increase in the biochemical mediators of inflammation (e.g., prostaglandin E2) in chronic Achilles tendon lesions. A better term is tendinosis, which implies that there has been a process of tendon degeneration without the typical histologic signs of classic inflammation. Paratenonitis involves acute edema and hyperemia of the paratenon, accompanied by the infiltration of inflammatory cells and sometimes the presence of a fibrinous exudate filling the tendon sheath. Clinically, one can sometimes appreciate this condition on palpation as crepitus along the Achilles tendon sheath. The presentation of Achilles tendinopathy usually involves the gradual onset of pain and dysfunction secondary to a chronic overuse injury. There are however, many patients with sedentary lifestyles that present with significant symptoms but no associated history of overuse.

ANATOMY

The Achilles tendon is made up of proteins (type I collagen and elastin) and proteoglycans. Proteoglycans are glycoproteins found in connective tissue and are a major component of the extracellular matrix, the "filler" substance existing between cells. Proteoglycans form large complexes, both to other proteoglycans, to hyaluronan and to fibrous matrix proteins (such as collagen). The crural fascia separates the subcutaneous tissue from the paratenon. The epitenon surrounds the tendon itself and the endotenon surrounds the individual collagen fibers/bundles.

TENDON HISTOPATHOLOGY

The four components of tendon histopathology are cellular activation and increase in cell numbers, increase in ground substance, collagen disorganization, and neovascularization, (the formation of functional microvascular networks with red blood cell perfusion). Neovascularization differs from angiogenesis in that angiogenesis is mainly characterized by the protrusion and outgrowth of capillary buds and sprouts from pre-existing blood vessels. The process of Achilles tendinopathy does not follow a classic inflammatory process. Microscopic evaluation of Achilles tendon biopsies, as well as other sophisticated molecular biology techniques (cDNA-arrays, real-time quantitative PCR) have all failed to show evidence of the prostaglandin-mediated inflammation.

Interestingly, there are signs of neurogenic inflammation, a process different from the classic prostaglandin-mediated inflammatory process. Neurogenic inflammation is mediated by the release of certain factors such as substance P and calcitonin gene-related peptide from afferent neurons. In classic prostaglandin mediated inflammation, it is the cell membrane that releases the chemical substances responsible for the response. Neurogenic inflammation appears to play a role in the pathogenesis of a number of diseases such as asthma, fibromyalgia, eczema, and psoriasis. Neuropeptides such as substance P and calcitonin gene-related peptide are found in increased levels in chronically inflamed tendons.

WHERE DOES THE PAIN COME FROM?

It is well known that the chronic painful Achilles tendon is difficult to treat, and furthermore, the pain mechanism associated with the condition is not completely understood. Methods such as microdialysis, cDNA-array, PCR, and ultrasonography combined with color Doppler, are providing potentially important information about the chronic painful Achilles tendon. Glutamate, a well known neurotransmitter and very potent modulator of pain in the central nervous system, is found in high levels in painful tendons but not in normal tendons. In conjunction with the findings of a local neurovascular in-growth and results of pilot studies with sclerosing injections, there is some evidence that the neural pathways associated with tendinopathy could be associated with the process of neovascularization. Biopsies taken from an area with tendinosis with neovascularization showed nerve structures in close relationship with the vessels. Studies have also shown substance P nerves in the vascular wall and calcitonin gene-related peptide nerves close to the vascular wall. Also, the neurokinin-1 receptor, which is known to have a high affinity for substance P, has been found in the vascular wall. The findings suggest an explanation for the pain associated

with tendinosis. This is the basis for the use of sclerotherapy, which produces an interference with this neurovascular in-growth that has been shown to decrease pain.

The source of pain in tendinopathy could be related to the neurovascular in-growth seen in the tendon's response to injury. Overuse is considered to induce the condition, but the etiology and pathogenesis have not been scientifically clarified. A study on chronic Achilles tendinopathy (342 tendons) showed that physical activity was not correlated with the extent of histopathology, suggesting that physical activity could be more important in provoking the symptoms than being the root cause of pathology. The lack of association between activity, pain and structural abnormality has also been reported in other tendons, and pathological changes are seen on imaging in physically active asymptomatic individuals.

TENDON HEALING PROCESS

Normal tendon healing can be largely divided into 3 overlapping phases, inflammatory, repair, and remodeling phases. This description is primarily associated with acute tendon injuries. The initial inflammatory phase lasts about 24 hours. Erythrocytes, platelets and inflammatory cells (e.g., neutrophils, monocytes, and macrophages) migrate to the wound site and clean the site of necrotic materials by phagocytosis. These cells release vasoactive and chemotactic factors that recruit tendon fibroblasts to begin collagen synthesis and deposition.

A few days after the injury, the repair phase begins and will continue for several weeks. Tendon fibroblasts produce abundant collagen and other extra cellular matrix components such as proteoglycans and deposit them at the site of injury. After about 6 weeks, the remodeling phase begins. This phase is characterized by decreased cellularity and decreased collagen and glycosaminoglycan synthesis. During this period, the immature repair tissue changes to fibrous tissue. After approximately 10 weeks, the fibrous tissue begins to transform into scar-like tendon tissue. At this point, however, the collagen fibers are not well organized. During the late remodeling phase, covalent bonding between the collagen fibers increases, resulting in higher tensile strength of the repaired tissue. Also, during this phase, the number of tenocytes and tendon vascularity decline.

During tissue healing, growth factors play an important role in this process. Platelet derived growth factor is produced shortly after tendon injury and stimulates the production of other growth factors. TGF-beta is active during the inflammatory and repair phases of tendon healing. TGF-beta plays a major role in the repair of injured tendons and aids in extracellular matrix deposition; however, its over expression results in tissue fibrosis. TGF-beta 2 functions similarly to TGF-beta 1 and has been shown to improve tissue scarring. Peak levels of TGF-beta receptor expression occur at day 14 post injury and decrease until day 56 post injury. Vascular endothelial growth factor (VEGF) stimulates endothelial cell proliferation, enhances angiogenesis and increases capillary permeability. VEGF RNA expression is detected at the repair site 7 days post injury with peak levels at 10 days post injury. Nitric oxide synthase isoforms are expressed with differential expression patterns during the 3 phases of tendon healing. It should be noted that, except for degenerative tendons (tendinosis), injured tendons tend to heal. However, the healing tendon does not reach the biomechanical properties of the tendon prior to injury.

ETIOLOGY OF ACHILLES TENDINOPATHY

Modern ultrasound-based imaging technology shows that chronic painful Achilles tendons are characterized by increased blood flow and perfusion (called neovascularization) intratendinously and peritendinously. This new vascularization is most likely an attempt to repair degenerative lesions on the tendon. Such lesions may be due to tissue hypoxia or repetitive microtrauma, frequently described as overuse injuries. Tissue hypoxia may result from increasing age, vascular degeneration, physical disuse, or trauma. In 60% of patients with Achilles tendinopathy, malalignment has been found, most often limited mobility of the subtalar joint and limited range of motion in the ankle joint.

In addition, various deformities of the forefoot and increased foot pronation have been found to be associated with Achilles tendinopathy. Other reported contributory factors are leg length discrepancy, muscle weakness and imbalance, and training errors. Several diseases have been associated with increased risk of tendinopathy such as diabetes mellitus, renal disease, as well as various rheumatologic diseases.

Overuse injury has been associated with Achilles tendinopathy. Kujala et al showed a 10-fold increase in Achilles injuries in runners compared with age-matched controls. Another study reported the incidence of Achilles tendinopathy in top-level runners as 7-9%.

Biomechanical deficits have also been shown to be associated. Clement et al studied 109 runners and reported that besides overtraining, the most common factors contributing to Achilles tendinopathy were functional overpronation (61 cases) and gastrocnemius/soleus insufficiency (41 cases). They surmised that runners may be especially prone to Achilles tendinopathy due to

microtrauma of the tendon caused by eccentric loading of fatigued muscle, increased pronation necessitating whipping action of the Achilles tendon, and concomitant pronation and knee extension that impart opposing internal and external rotatory forces on the tibia. A study by Kaufman et al showed that rearfoot varus deformity and limited ankle dorsiflexion with the knee in extension was associated with Achilles tendinopathy. Finally, in a study of 455 athletes with Achilles tendon overuse injuries, Kvist reported biomechanical deficits in 60% of the athletes, including forefoot varus deformity and markedly limited passive subtalar joint mobility and ankle joint dorsiflexion with the knee in an extended position.

Additional factors leading to Achilles tendinopathy are male gender, increased height/weight, older age, fluroquinolone exposure, impaired arterial blood supply within the tendon leading to local hypoxia, impaired metabolic activity, and poor nutrition. Quantitative analysis of the cross sections of the Achilles tendon showed an area of diminished blood supply in the mid-section of the tendon.

Other theories of degeneration imply production of cytokines by an overloaded matrix that fails to adapt to excessive loads. There is also a tendinosis cycle when the tendon is disrupted by the repetitive strain causing the collagen fibers to slide past each other, breaking the cross links.

IMAGING

On occasion special studies may be considered to help delineate the degree of pathology in the Achilles tendon. Achilles tendinopathy is associated with areas of increased signal on magnetic resonance imaging (MRI) and regions of hypoechogenicity on ultrasound. Radiologic abnormalities of the Achilles tendon generally correspond to histopathologic findings of tendinosis, specifically increased interfibrillar glycosaminoglycans disrupting collagen fiber structure, which is termed mucoid degeneration. In addition, other studies can even demonstrate pathology in tendons that appear normal with standard ultrasound and MRI imaging. These studies use color and power Doppler ultrasound tendon imaging that demonstrates blood flow in tissues. In the Achilles tendon, blood flow is not detectable in normal tendons but color Doppler often reveals blood flow in pathological tendons. Such blood flow has been linked to greater pain scores, poorer function and longer symptoms in the Achilles tendon, compared with control participants who have no visible flow. The association, however, has not been proven to be absolute.

CONSERVATIVE TREATMENT

Many treatments are offered to patients with a painful Achilles tendon, but the scientific evidence measuring the effectiveness of most of the conservative and even surgical treatments is sparse. Treatments that have some evidential basis and have been investigated with randomized controlled trials include eccentric exercise, glyceryl trinitrate patches, electrotherapy (microcurrent and microwave), sclerosing injections and nonsteroidal anti-inflammatory drugs (NSAIDs). There are no randomized or prospective studies that compare different conservative and surgical treatment regimens.

Some investigators believe that Achilles tendon damage likely exists before the onset of symptoms, so even patients who present acutely with Achilles tendinopathy may already have significant tendon degeneration.

NSAID's

Treatment should begin with relative rest to allow time for the tendon to heal. The use of NSAIDs can and often are considered initially; however, their role in the treatment of Achilles tendinopathy is unclear because many believe anti-inflammatory medications do not benefit the condition of tendinosis, which is classically non-inflammatory. A study by Anstom and Westlin found no beneficial effects of NSAIDs in the treatment of patients with Achilles tendinopathy.

Cortisone

The role of corticosteroid injections in the treatment of Achilles tendon injuries is uncertain. There is insufficient published data to determine the comparative risks and benefits of corticosteroid injections in Achilles tendinopathy. There are reports in animal studies of decreased Achilles tendon strength associated with intratendinous injections and subsequently suggest that tendon rupture may be a potential complication for several weeks after Achilles tendon injection. Peritendinous injections have fewer effects on the tendon and can be a worthwhile adjunct to a conservative management program. Steroid injections may be most beneficial when used to relieve pain while undergoing a monitored physical therapy program.

Ultrasound

Therapeutic ultrasound seems to be helpful in the promotion of local tendon healing. In animal studies, ultrasound has been shown to stimulate collagen synthesis in injured Achilles tendons and increase tendon tensile strength. The role, however of electrophysical agents in the treatment of tendinopathy in humans remains poorly

investigated. Although, therapeutic ultrasound does increase protein synthesis in tendons, there is already an oversupply of poor-quality protein in tendons suffering from overuse. Therefore, increasing further protein production may not improve clinical outcome.

Extracorporeal Shockwave Treatment (ESWT)

ESWT has been shown to offer some positive benefit as a supplemental form of treatment in the management of chronic Achilles tendinopathy. However, it can require multiple treatments which at this point can be cost prohibitive.

Sclerosing Injections

As earlier stated, there is an established relationship between the number of blood vessels and tendon thickness. The role of the neovascularization in tendon pain has been further examined in a pilot study where a vascular sclerosant (Polidocanol) was injected in the area with neovascularization anterior to the tendon. Short-term (6 months) evaluation of this treatment has shown a positive benefit.

Heel Lift

Other measures hypothesized to support healing include manual mobilization of the Achilles tendon and short-term use of a 12–15-mm heel lift, which helps reduce tensile loading. The heel lift should be eliminated, however, after calf flexibility improves because of the possibility of perpetuating calf inflexibility.

Cryotherapy

Cryotherapy has been shown to be effective in minimizing pain, decreasing the flow of blood and protein from capillaries, and lowering the metabolic rate in tendinopathy.

Night Splint

A night splint has been shown to be an effective intervention for Achilles tendinopathy. A greater reduction in pain was seen when the night splint was combined with a 12-week eccentric exercise program.

Topical Glyceryl Trinitrate

This medication has been studied in randomized controlled trials in the Achilles, elbow, and supraspinatus tendons as an adjunct to an eccentric exercise program. The topical glyceryl trinitrate was applied to the skin superficial to the tendon as a patch, and was renewed each day for 6 months. The treatment was compared with a placebo patch, and pain and function were measured over 6 months. In the Achilles tendon group, activity pain in the glyceryl trinitrate group was reduced at 12 and 24 weeks compared with placebo, and it also improved outcomes at 6 months. This study also supports the use of just an eccentric exercise program, as 49% of the placebo group still reported excellent outcomes.

REHABILITATION

Eccentric Musculotendinous Training

Eccentric training essentially involves aggressive stretching of the Achilles tendon (Table 1) using the patient's body weight to produce the load. The forefoot is supported on the edge of a stool or step, while the heel is lowered. These exercises involve no concentric loading and emphasize the need for patients to complete the exercise protocol despite pain in the tendon. If patients experience no tendon pain doing this program, the load should be increased (by wearing a small backpack loaded with weight) until the exercises provoke pain. It is typically a 12-week program and can be effective in conjuction with other conventional treatments (rest, NSAIDs, change of shoes, orthoses, physical therapy, and ordinary training programs). Alfredson reports that the program is successful in approximately 90% of those with mid-tendon pain and pathology. Insertional Achilles tendon pain is not as responsive, and good clinical

Table 1

PATIENT INSTRUCTIONS STRETCHING EXERCISES FOR ACHILLES TENDINITIS

1. Stand on the edge of a stair-step or a small step ladder with only the toes and ball of each foot touching the step. The heels should not be touching the step.
2. Hold on to the hand railing for balance and support.
3. Slightly raise the painful foot off of the step, so that it is not touching the step at all.
4. Now go up on the toes and ball of the non-painful foot so that the heel is in a raised position.
5. At this point the painful foot is gently placed onto the step with the toes and ball of the foot touching the step, with the heel in a raised position.
6. Gently start lowering both heels to the point where moderate pain is experienced or the heels are well below the level of the step.
7. Now only using the non-painful foot raise back up onto the ball of the foot.
8. Gently replace the painful foot in the raised position and repeat the lowering of the heels.
9. Do 3 sets of 15 repetitions with the knee on the painful side in a straight position, then do 3 sets of 15 repetitions with the knee on the painful side in a slightly bent position.
10. The course generally lasts for 10-12 weeks.
11. If at some point the exercises can be done pain-free, put on a small backpack and add some weight until some mild discomfort is experienced.

results are achieved in only approximately 30% of tendons.

The question has been asked: Why does eccentric exercise reduce pain in tendinopathy? Although there are several possible explanations for the effectiveness of eccentric exercise, none have been fully investigated. Eccentric exercise has been shown to alter tendon pathology in both the short term and the long term. In the short term, eccentric exercise increases tendon volume by its effect on type I collagen production and, in the absence of further injury, may increase the tendon volume over the longer term. The net effect is that an eccentric exercise program may increase tensile strength in the tendon over time. In addition, repetitive stretching can produce a lengthening of the muscle–tendon unit, which may have an impact on capacity of the musculotendinous unit to effectively absorb load.

Another possible benefit of eccentric stretching exercises relates to mechanical destruction of pain-producing nerves. A unique feature of the eccentric training program is that the patient is encouraged to perform heel-drop exercises until pain is experienced. The nerve structures found in painful tendons lie in close proximity to the tendon vessels. As these vessels disappear with muscle contraction and stretch, fewer nerves are noted as well. Therefore, good clinical effects demonstrated with eccentric training could be due to this alteration of the neovascularization and accompanying nerves. The number of repetitions (180 repetitions/day) may also damage the vessels and accompanying nerves as they traverse the soft tissue outside the tendon into the dense tendinosis tissue. The finding that patients satisfied with the result of the eccentric training program had no neovascularisation remaining, and all patients with a poor clinical result continued to have neovascularization, is consistent with this hypothesis.

Rehabilitation of Achilles Tendinopathy

The rehabilitation of Achilles tendinopathy can be divided into 3, often overlapping phases: the acute phase, the recovery phase, and the functional phase.

During the acute phase, focus should be placed on controlling pain and preventing progression of tendon degeneration. Limitation of activities, use of pain medications, therapeutic ultrasound, manual mobilization, heel lifts, and application of ice are commonly used measures in this stage. When the pain is controlled, an eccentric strengthening program for the gastrocnemius-soleus complex, the second phase of rehabilitation, can begin.

In the recovery phase, the goal is to correct various biomechanical deficits. Manual mobilization is employed to improve foot and ankle range of motion, as well as medial and lateral stretching of the Achilles tendon. Multiplanar stretching and eccentric strengthening exercises of the gastrocnemius and soleus muscles are important components of rehabilitation during this stage. Several studies have shown that eccentric training of the gastrocnemius-soleus complex is superior to concentric training with regard to decreasing pain and improving function. At the core of physical therapy for Achilles tendinopathy is the heel drop, performed with the knee flexed (to strengthen the soleus) (Figures 1, 2) and extended (to strengthen the gastrocnemius) (Figures 3, 4) with progression of weight on the injured leg. As pain subsides and flexibility and strength improve, the final rehabilitation phase can begin.

Figure 1.

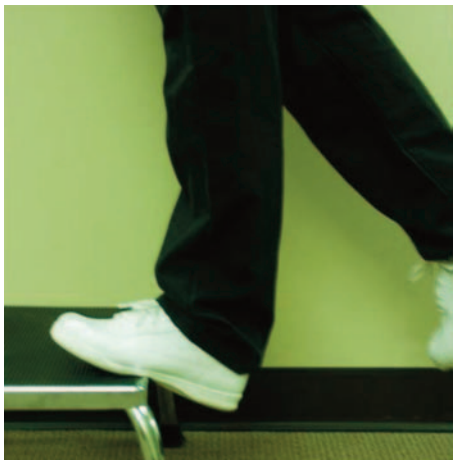

Figure 2.

Figure 3.

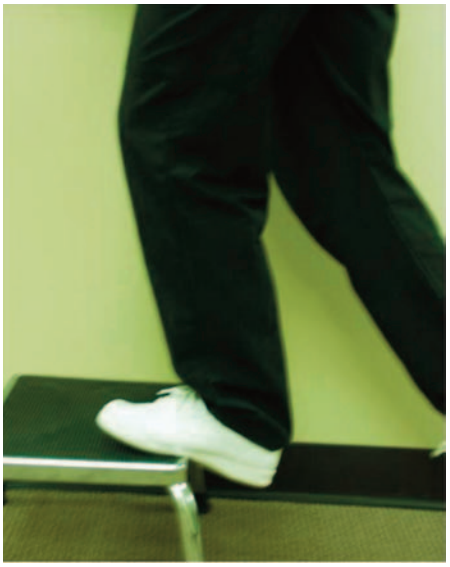

Figure 4.

During the functional phase, exercises should progress to being performed in multiple planes and with single-leg stance to promote normal motor patterns and control of the entire lower extremity. If after 6 months, proper medical management and rehabilitation are unsuccessful, surgery can be considered.

SURGICAL TREATMENT

Surgery typically consists of releasing the paratenon and debriding the necrotic intratendinous tissue if present. However, no prospective randomized studies have been performed comparing surgical versus nonsurgical management. The results of uncontrolled studies have been favorable, but it is not clear whether the beneficial results were due to the surgery or to the prolonged convalescence and rehabilitation. Many of the surgical procedures are designed to irritate the tendon and initiate a chemically mediated healing response.

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