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Chapter 8

Midportion Achilles tendinopathy: why painful? An Evidence-based philosophy

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ABSTRACT

Chronic midportion Achilles tendinopathy is generally difficult to treat as the background to the pain mechanisms has not yet been clarified. A wide range of conservative and surgical treatment options are available. Most address intratendinous degenerative changes when present, as it is believed that these changes are found responsible for the symptoms. Since up to 34% of asymptomatic tendons show histopathological changes, we believe that the tendon proper is not the cause of pain in the majority of patients. Chronic painful tendons show ingrowth of sensory- and sympathetic nerves from the paratenon with release of nociceptive substances. Denervating the Achilles tendon by release of the paratenon, is sufficient to cause pain relief in the majority of patients. This type of treatment has the additional advantage that it is associated with a shorter recovery time when compared to treatment options that address the tendon itself. An evidence- based philosophy on the cause of pain in chronic midportion Achilles tendinopathy is presented.

INTRODUCTION

Chronic Achilles tendon pathology is one of the most frequent injuries in sports involving running and jumping. In elite long-distance runners there is a lifetime risk of 52% for sustaining an Achilles tendon injury³⁹. Thirty percent of patients have a sedentary lifestyle⁷.

Chronic midportion Achilles tendinopathy⁷⁸ is characterized by impaired performance due to Achilles tendon pain and swelling located typically at 2-7 cm from the insertion onto the calcaneus⁴⁸. The source of pain and the background to the pain mechanisms associated with midportion Achilles tendinopathy have not yet been clarified⁴⁹. Many different explanations have been raised. Consequently, a wide range of conservative and surgical treatment options are available. Most of them address the intratendinous degenerative changes when present. Surgical measures include open excision of degenerative tendon. This means that the intratendinous changes are found responsible for the symptoms. But does the origin of the pain in these patients indeed rise from the Achilles tendon itself? It is known that the tendon itself is relatively aneuronal. It is also recognized that intratendinous degenerative changes often occur without symptoms.

It is hypothesized that the main cause of the pain in patients with symptomatic midportion Achilles tendinopathy does not arise from the tendon proper but is generated by its surrounding tissues. In this paper, a premise on the cause of pain based on existing knowledge and personal research is presented.

ANATOMY

The Achilles tendon is the combination of tendons of soleus and gastrocnemius muscles, inserting approximately halfway the calcaneus. The gastrocnemius muscle crosses the knee, subtalar and ankle joints; originating from the posterior medial and lateral femoral condyles and inserting onto the calcaneus. The soleus muscle lies anterior to the gastrocnemius muscle and originates from the proximal tibia, fibula and interosseous membrane and crosses the ankle and subtalar joints. Distally, both the gastrocnemius and soleus muscles form an aponeurosis, from each of which a tendon originates. At about the level where the soleus contributes fibres to the Achilles tendon, rotation of the tendon begins and becomes more marked 2-7 cm proximal to the insertion onto the calcaneus. The gastrocnemius fibres rotate to lateral and the soleus fibres are positioned medial to the insertion^{9,21,57}. Medial to the Achilles tendon the plantaris tendon is located, originating from the lateral femoral condyle and inserting onto the medial calcaneus. The Achilles tendon is involved in plantarflexion, whereas according to its anatomical course, the tri-articular plantaris tendon also contributes to ankle inversion.

The Achilles and plantaris tendon are collectively surrounded by a paratenon, which lies on an inner layer of endotenon, and exists of a layer of mesotenon and an outer layer of epitenon.

Tendon consists predominantly of extracellular tissue with low metabolic requirements, and therefore appears white on macroscopic inspection. This relatively bradytrophic character enables the tendon to remain under tension for a long period, without the risk of necrosis or ischemia. The Achilles tendon has 3 sources of vascular supply, which are (1) the perimyseal vessels at the musculotendinous junction; (2) periosteal vessels at the osteotendinous junction; and (3) vessels around the tendon within the paratenon, forming a capillary loop system. This last system is the main vascular supply for the Achilles tendon. The neural supply to the Achilles tendon and the surrounding paratenon is provided by nerves from the attaching muscles and by small fasciculi from cutaneous nerves, in particular the sural nerve^{9,71}. The number of nerves and nerve endings is relatively low, and the tendon proper is relatively aneuronal^{43,65}.

AETIOLOGY

A distinction is made between the aetiology of intratendinous degenerative changes and the aetiology of complaints in patients with midportion Achilles tendinopathy. Causes of intratendinous changes can be divided into extrinsic and intrinsic factors, but most commonly will be a combination of both. Malalignment of the foot, hyperpronation^{63,68}, age⁴⁵ and chronic disease like diabetes mellitus, obesity and hypertension²⁸ have been described. Malalignment and hyperpronation impose excessive strain on the Achilles tendon. The aging tendon loses its elastic properties causing the muscle to work more, resulting in a local rise in temperature with subsequent tendon changes⁶⁸.

Inappropriate physical training may also be an important issue^{37,46} causing degenerative Achilles tendon changes. Tendons transmit muscle forces to bone, allowing locomotion and enhancing joint stability. They respond to mechanical forces by changing their metabolism and their structural and mechanical properties. Appropriate training increases the diameter and tensile strength of tendons, with tendon fibroblasts increasing the production of collagen type I^{42,53,72,75}. Training also induces biochemical changes in tendons. Strenuous endurance training increases collagen turnover and decreases collagen maturation in tendons; excessive mechanical loading is considered a major concern. Repetitive strains below the failure threshold of the tendon cause tendon micro-injuries^{38,61}. Quality of foot gear and training surface influencing the alignment and statics of the ankle are also often mentioned as a cause of intratendinous pathology.

The aetiology of the pain in a patient with midportion Achilles tendinopathy has not yet been entirely clarified. Pain was believed to be caused by expansion of the Achilles tendon proper due to increased ground substance and an increased concentration of

glucosaminoglycans (GAGs). A few years ago the presence of neovascularisation around symptomatic tendons was raised as the cause of pain; now accompanying nerves with high concentrations of nociceptive substances (glutamate, substance P, calcitonin gene related peptide (CGRP)) are also supposed to play a role^{5,8}.

CLINICAL PRESENTATION

Symptoms of a patient with midportion Achilles tendinopathy include painful swelling typically 2-7 cm proximal to the insertion, and stiffness especially when getting up after a period of rest. Pain is the main symptom in Achilles tendinopathy that leads a patient to seek medical help. It is often most prominent 2-7 cm from the insertion onto the calcaneus on the medial side⁶⁷. Tendinopathy and paratendinopathy often co-exist⁶⁴. Intratendinous changes most often remain asymptomatic³⁵. In these cases a painless swelling at 2-7 cm proximal to the insertion is the only finding⁵⁸. In isolated paratendinopathy, there is local thickening of the paratenon. The area of swelling does not move with dorsiflexion and plantarflexion of the ankle, where it does in isolated tendinopathy^{50,69,82}. Paratendinopathy can be acute or chronic. *Acute* isolated paratendinopathy manifests itself as painful peritendinous crepitus as the tendon glides within the inflamed covering. Areas of increased erythema, local heat, and asymptomatic palpable tendon nodules or defects may also be present at clinical examination. In *chronic* paratendinopathy, exercise-induced pain is the main symptom while crepitation and swelling diminish.

HISTOPATHOLOGY

Normal situation

Morphologically, healthy tendon is a complex composite material consisting of collagen fibrils embedded in a matrix of proteoglycans, with a relative small number of cells. Between the parallel collagen bundles, fibroblasts are arranged, which are the predominant cells within tendons¹⁰. The matrix has tight bundles of long strands of type I collagen, which give the tendon its inherent strength. Between the collagen is the ground substance, made up of mainly small proteoglycans and glycosaminoglycan (GAG) chains. In normal tendon, there is minimal ground substance¹⁴.

The paratenon consists of straight bundles of type I and type III collagen fibrils with straight microfibrillar arrangement and variable diameter^{23,41}. This peritendinous tissue is lined on its inner surface by synovial cells^{31,82} and acts as an elastic sleeve permitting the movement of tendon against the surrounding tissues³⁴. The paratenon serves to carry blood vessels, lymphatics and nerves.

Pathological situation

In contrast with the white appearance of healthy tendon, in tendinopathy they macroscopically appear grey or yellow-brown and amorphous. *Microscopically* the tendon shows disrupted collagen, a decrease in the amount of type I collagen and an increase of the amount of the weak type III collagen which is produced in response to injury and is less able to bundle. The classical hierarchical structure is lost, there is increased ground substance with a high concentration of GAGs, more prominent and numerous tenocytes without their normal fine spindle shape and with more rounded nuclei^{14,24}. Some areas of tendinopathy become acellular³⁶ or have decreased cell numbers and function^{14,33}.

In the *peritendinous* tissue in the chronic phase of Achilles tendinopathy 2 types of cells have been identified: fibroblasts and myofibroblasts⁴¹. During biological processes that include extensive tissue remodelling, fibroblasts may acquire morphological and biochemical features of contractile cells which have been named myofibroblasts²⁰. The myofibroblasts have stress fibers composed of α -smooth muscle actin in their cytoplasm and thus are capable of creating forces required for wound contraction²⁰. In chronic Achilles tendinopathy, these cells are especially well established at the sites of scar formation, and it is estimated that about 20% of peritendinous cells are myofibroblasts⁴¹. The myofibroblasts synthesize abundant amounts of collagen and are believed to be responsible for the formation of permanent scarring and the shrinkage of peritendinous tissue around the tendon^{30,41}. They can induce and maintain a prolonged contracted state in the peritendinous adhesions around the tendon and thus influence the development of a contracture^{30,41}. This, in turn may lead to constriction of vascular channels and to impaired circulation and further contribute to the pathogenesis of Achilles tendinopathy. The proliferating connective tissue around the Achilles tendon causes increased intratendinous tension and pressure resulting in increased friction between the tendon, paratenon, crural fascia, and the skin³⁰.

Vascularity seems increased in tendinopathy, as neovascularisation with thick walls, a tortuous appearance and small lumen ventral from the Achilles tendon and in the paratenon is found in 50-88% of symptomatic tendons but not in pain-free tendons^{18,59,60,80,83}.

The healthy Achilles tendon proper is superficially innervated by the paratenon, but does not have a rich nervous supply itself⁸. It is normally aneuronal; conversely chronic painful tendons have been shown to exhibit new ingrowth of nerve fibers accompanying the peritendinous neovascularisation from the paratenon into the tendon proper^{43,65}. Sensory nerve ingrowth has been observed as a reaction to repetitive loading⁵² and also as a response to injury^{2,4}. With this nerve ingrowth, levels of glutamate, calcitonin gene-related peptide (CGRP) and substance P rise^{4,8,43,65}. These substances are all linked with increased nociception. Substance P is also associated with vasodilation and stimulates proliferation of fibroblasts⁷⁰, possibly causing some of the morphologic changes in Achilles tendinopathy.

CAUSE OF PAIN

Several factors play a role in the cause of pain in a patient with Achilles tendinopathy.

The process starts with localized tendon micro-injury and degeneration which are caused by ageing and repetitive strain below the failure threshold of the tendon. The most hypovascular region is in the midportion area (2-7 cm from the insertion), where the tendon makes a marked twist. This is the location where the degeneration and micro-injury most often occur. Blood flow further declines with ageing and mechanical loading. When the demands of the tendon are higher than can be managed, micro-injuries develop¹. The body reacts with a repair process, which is adequate in most cases, but inadequate in patients developing tendinopathy. This inadequate repair causes a repetitive cycle of inadequate collagen and matrix production, tenocyte disruption, a further decrease of collagen and matrix and an increased vulnerability to further micro-injuries. Due to the lack of bloodvessels within the tendon, instead of a chemical- a neurogenic inflammatory process is activated to repair these microruptures. This neurogenic inflammation occurs in the tissue surrounding the Achilles tendon. Matrix metalloproteinases (MMPs) responsible for the degradation of extracellular matrix, cytokines (vascular endothelial growth- factor (VEGF), epidermal growth factor (EGF), and platelet- derived growth factor (PDGF)) are over- expressed. VEGF promotes angiogenesis, upregulates the expression of MMPs and down-regulates tissue inhibitors of metalloproteinases (TIMP-3), altering the properties of tendon. Invasion of vessels derived from the paratenon into a normally hypovascular intratendinous region weakens the normal tendon structure. When the repair of tendon is inadequate, e.g. due to submission to further loads without adequate recovery time or a declined blood flow due to ageing, the healing process fails and the pathogenic cascade leading to symptomatic tendinopathy occurs. The transition to *symptomatic* tendinopathy is marked by nerve proliferation accompanying the neovessels. Vascular ingrowth to repair the defect arises from the paratenon. These bloodvessels are accompanied by sensory neones^{11,22} (Figure 1), causing an increase in pain signalling by

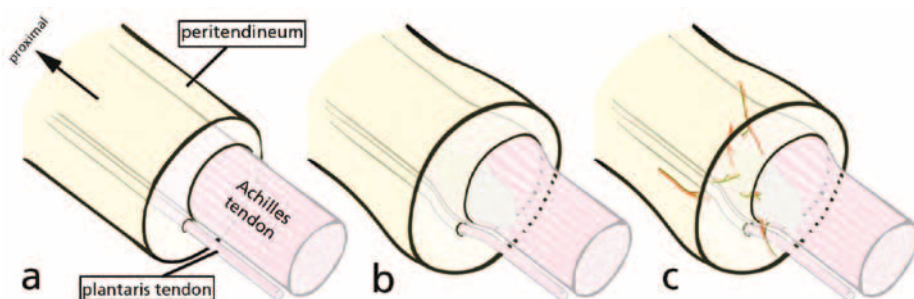


Figure 1A-C. (A) Schematic depiction of normal tendon. (B) Pathological tendon proper. (C) Vasculoneuronal ingrowth from the paratenon into the tendon proper

producing nociceptive substances (glutamate, substance P, calcitonin gene related peptide (CGRP)) past the critical threshold^{5,8}. Neovascularisation has indeed been found to correlate with the location of pain in patients with symptomatic tendinopathy¹⁹. The upregulated nociceptive substances further damage the tendon by inducing vasodilation, tendon cell apoptosis and the vicious circle of neurogenic inflammation^{1,5,8,22,54}.

Myofibroblasts proliferate and are transported by the peritendinous blood vessels and neovascularisation into the peritendineum and the tendon proper. Myofibroblasts synthesize abundant amounts of collagen to repair the tendon proper, but also cause the formation of scar tissue around the tendon and consequently adhesions of the paratenon onto the Achilles tendon at the location of the neurovascular ingrowth. Scarring in turn may lead to constriction of vascular channels and to impaired circulation and further contribute to the pathogenesis of Achilles tendinopathy, meaning that there is no further action towards repair.

Vasoconstriction and scarring with mechanical constriction will lead to obliteration of neovessels. In 20-50% of long lasting tendinopathy patients no neovascularisation is

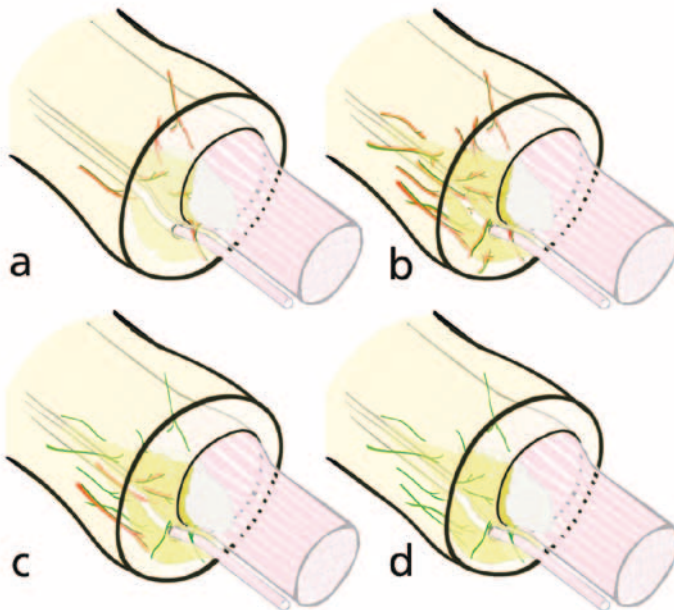


Figure 2A-D. (A) Adhesion of the paratenon onto the Achilles tendon due to myofibroblast proliferation and consequently formation of scar tissue. (B) Continuing ingrowth of vessels and nerves and augmented adhesion (C) Obliteration of neovessels due to constriction. (D) The painful end situation in which neovascularisation has been mostly obliterated but nerve endings persist

found^{18,59,60,80,83}. Nerves however will survive (Figure 2), secreting glutamate and substance P causing pain on activity as described earlier.

Reduction of blood flow may also be explained by the fact that pathological tendons exhibit a decreased occurrence of *sympathetic* nerve fibres. This reduction in vasoregulatory nor-adrenalin causes vasoconstriction³.

It has been described that the location of the pain in patients with Achilles tendinopathy is most often located on the medial side^{67,69}. During Achilles tendoscopy in patients with Achilles tendinopathy, it has been observed that at the level of complaints the plantaris tendon is affixed onto the Achilles tendon on the medial side⁶⁹ (Figure 3). Some authors describe a higher medial stress onto the Achilles tendon due to hyperpronation. This is supported by the finding that most ultrasonographic midportion disorders (91%) are found in the (postero)-medial segment of the tendon^{26,79}.

In patients with a painful nodular thickening in the Achilles tendon, the pain is often most prominent on the medial side of the midportion Achilles tendon. At this level the plantaris tendon runs closely with- and parallel to the Achilles tendon.

The plantaris tendon originally is a knee -and ankle flexor. In primates it attaches to the plantar aspect of the proximal interphalangeal joints of the toes in primates, explaining its functionality for grasping with their feet. Darwinists suggest that through evolution in humans

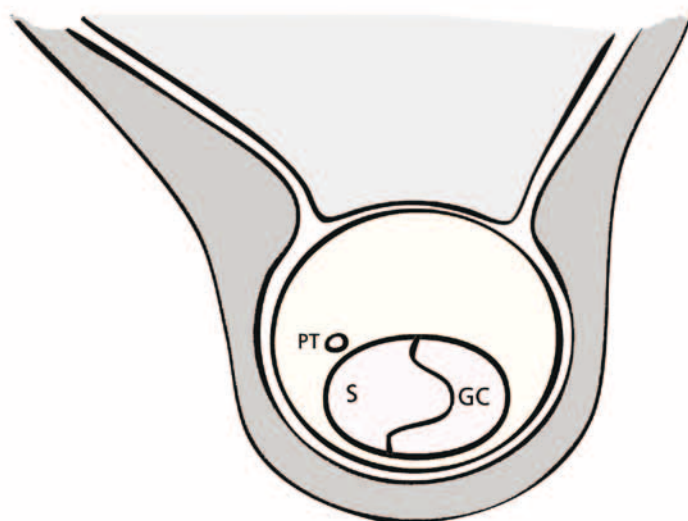


Figure 3. The most common position (52%) of the gastrocnemius-soleus complex at the midportion of the Achilles tendon ¹⁵ (PT= plantaris tendon, S= Soleus, GC= Gastrocnemius)

the plantaris tendon is rudimental since human beings do not grasp with feet nor swing from trees any longer. Absence in 7-20% human lower limbs has been reported^{16,17,25,55,66}.

In humans the plantaris muscle is triangularly shaped and lies posterior to the knee joint, originating from the inferior part of the lateral supracondylar line of the femur. Its tendon travels inferomedially, posterior to the soleus muscle and anterior to the medial gastrocnemius muscle. The tendon crosses the calf relatively proximal, running medial from, and parallel with the Achilles tendon from the midportion of the calf; in the majority of cases ultimately inserting medially onto the calcaneus^{17,27}. The plantaris muscle-tendon complex nowadays is a weak ankle- and knee flexor and ankle invertor.

The medial portion of the Achilles tendon consists solely of the soleus tendon since at about the level where the soleus contributes fibers to the Achilles tendon (3-11 cm), rotation of the tendon begins and becomes more marked in the distal 5-6 cm. Gastrocnemius fibers are therefore positioned lateral- and the soleus fibers on the medial side of the insertion (Figure 4). The soleus is biarticular (ankle- and subtalar joints). The plantaris tendon runs anteromedial to it. It is believed that in a healthy situation the plantaris tendon can move freely in relation to the Achilles tendon. Adhesions between plantaris- and Achilles tendon can be the results of an inflammatory response of the paratenon, which is located around the Achilles- and plantaris tendons.

The plantaris muscle-tendon complex not only causes flexion but also inversion, whereas the triceps surae is a flexor only. Adhesions between both tendons obstruct the opposite forces of these two bi- and tri-articular muscle groups. Although the movement between the two will be limited, traction onto the surrounding paratenon will take place with every step

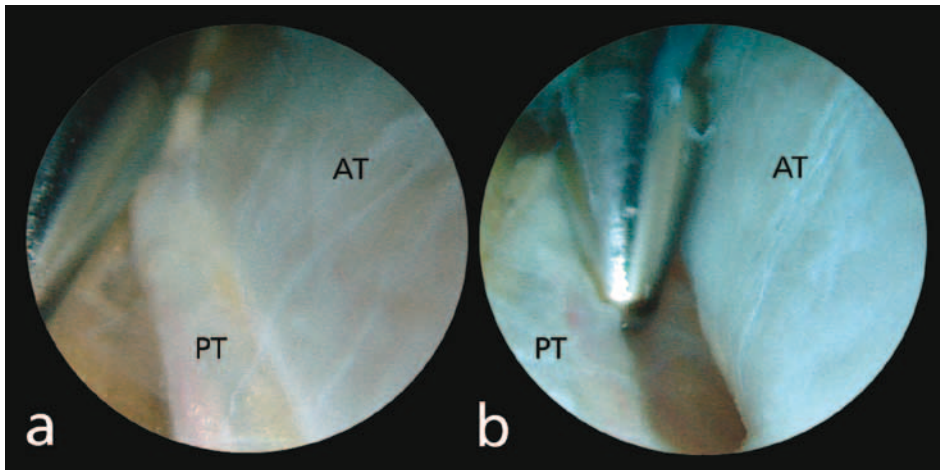


Figure 4A-B. Endoscopic image of a patient with medial pain of his right Achilles tendon due to mid-portion Achilles tendinopathy. On Achilles tendoscopy the paratenon is released from the Achilles tendon and in this image the plantaris tendon is identified. **(A)** The plantaris tendon is attached to the Achilles tendon. **(B)** With a trocar (in this case) the plantaris tendon is released from the Achilles tendon

with a mean of 5,000 - 12,500 steps/ day in people with a low active to active lifestyle^{76,77}. Chronic painful tendons have been shown to exhibit new ingrowth of sensory nerve fibers from the paratenon^{43,65}. Repetitive traction onto this richly innervated area might contribute to the medially located pain and stiffness during and after walking.

SURGICAL TREATMENT

Most surgical procedures aim at debridement or tenotomy of the tendon itself. In all these procedures the paratenon is incised, released or removed as well. In open surgical debridement of the tendon proper the paratenon has to be opened^{32,40,47,62}, and during minimally invasive tenotomy the paratenon is also addressed. It is therefore uncertain which part of the procedure is responsible for a possible favourable outcome of such an approach. Paratendinopathy and tendinopathy often co-exist. In some procedures only peritendinous structures are addressed, such as in open or minimally invasive paratenectomy^{44,56} and Achilles tendoscopy where the paratenon is released and the plantaris tendon cut to relieve symptoms (Figure 5)^{51,69}. These procedures render good results not in all, but in 75-100% of patients. Aftertreatment most often is functional and recovery time, although not often

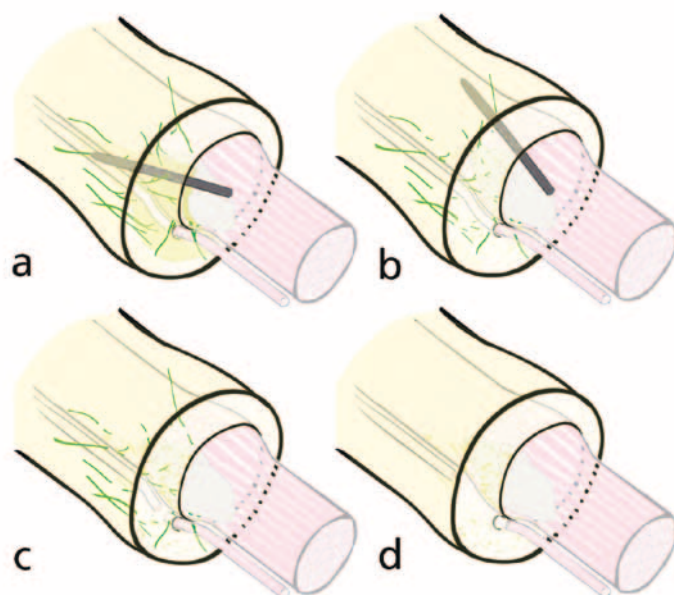


Figure 5A-D. The rationale of Achilles tendoscopy. **(A)** With a blunt trocar the paratenon is released from the Achilles tendon. **(B)** Thereby the nerves are destroyed. **(C)** The plantaris tendon is cut at the level of complaints. **(D)** In the weeks postoperative, remnants of nerves obliterate and the proximal end of the plantaris tendon retracts

described, is 6 weeks to 6 months^{44,51,69,74}. With surgery of the tendon proper, including minimally invasive tenotomy, the tendon is temporarily weakened. Recovery time until sport resumption therefore can be extensive and takes 3-18 months^{12,73,81}.

How can the favourable results of addressing the paratenon only in patients with symptomatic Achilles tendinopathy be explained? Pain relief could be explained by destruction of the sensory nerves running from the paratenon into the Achilles tendon proper in these chronic patients: *denervation* of the Achilles tendon by releasing the paratenon may be the most important part of all these procedures.

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Positive results obtained from the more invasive conservative treatments may also be contributable to the destruction of nerve fibres. For example sclerosing injections with Polidocanol and High Volume Image Guided Injections (HVIGI) aim at obliterating neovessels and the accompanying nerve fibres^{6,13,29}.

If pain can be relieved with denervation, extensive surgery of the tendon proper becomes redundant.

CONCLUSION

The goal of treatment of patients with chronic complaints of midportion Achilles tendinopathy is to relieve pain. Many surgical procedures focus on the debridement of alterations in the tendon proper. Since up to 34% of asymptomatic tendons show histopathological changes, it is now believed that the tendon proper is not the cause of pain in the majority of patients with symptomatic midportion Achilles tendinopathy. Chronic painful tendons show ingrowth of sensory- and sympathetic nerves from the paratenon with release of nociceptive substances. Denervating the Achilles tendon by release of the paratenon, is sufficient to cause pain relief in the majority of patients. This type of treatment has the additional advantage that it is associated with a shorter recovery time when compared to treatment options that address the tendon itself.

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