The plantaris tendon in relation to the Achilles tendon in midportion Achilles tendinopathy

Studies on morphology, innervation and signalling substances

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i sal BiA201, Biologihuset, fredagen den 12 juni, kl. 09:00. Avhandlingen kommer att försvaras på engelska.

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Abstract
Midportion Achilles tendinopathy (tendinosis) is a troublesome painful condition, often characterised by pain, local swelling, tenderness and functional disability. Despite extensive research, the pathogenesis is poorly understood and treatment remains challenging. Features related to the peritendinous connective tissue can be of importance. Recently it has been suggested that the plantaris tendon might be involved in this condition. Furthermore, it has been hypothesised that tendon pain and the tendinosis-related tissue changes in tendinopathy might be mediated by signalling substances such as glutamate and acetylcholine. A clinical observation, not scientifically evaluated, has been that unilateral treatment for bilateral Achilles tendinosis can lead to an effect on the contralateral side.

The aim of this work was to examine the morphology and innervation patterns in the plantaris tendon and the peritendinous connective tissue in between the Achilles and plantaris tendons in midportion Achilles tendinopathy, and to evaluate if plantaris tendon removal has an effect on Achilles tendon structure. Another aim was to determine if unilateral treatment for Achilles tendinopathy targeting the peritendinous connective tissue can result in bilateral recovery. Furthermore the presence of non-neuronal cholinergic and glutamate systems was examined.

Sections of plantaris tendons with adjacent peritendinous connective tissue from patients with midportion Achilles tendinopathy were stained for morphology (H&E), and innervation patterns were evaluated using antibodies against general nerve marker (PGP9.5), sensory (CGRP) and sympathetic (TH) nerve fibres and Schwann cells (S-100β). Furthermore immunostainings against non-neuronal acetylcholine (ChAT) and glutamate signalling components (glutamate, VGluT2, NMDAR1) were performed. Plantaris tendon cells were cultured and also stained for glutamate signalling components, and were stimulated with glutamate and glutamate receptor agonist NMDA. Furthermore, Ultrasound Tissue Characterisation (UTC) was used to monitor the integrity of the Achilles tendon collagen structure after plantaris tendon removal.

Plantar tendon exhibited tendinosis-like tissue patterns such as hypercellularity, collagen disorganisation and large numbers of blood vessels. The peritendinous connective tissue between the plantaris and Achilles tendons contained large numbers of fibroblasts and blood vessels and to some extent macrophages and mast cells. A marked innervation was found in the peritendinous connective tissue and there were also nerve fibres in the loose connective tissue spaces within the tendon tissue proper. Most nerve fibres were identified as sensory fibres. Some nerve fascicles in the peritendinous connective tissue showed absence of axons but homogenous reactions for Schwann cell marker. Tenocytes and cells in the peritendinous connective tissue expressed ChAT, glutamate, VGluT2 and NMDAR1. Tendon cells in vitro expressed VGluT2, NMDAR1 and glutamate. UTC showed significant improvement of Achilles tendon integrity 6 months after surgical plantaris tendon removal and scraping procedure. Eleven out of thirteen patients reported of a bilateral recovery after unilateral surgical treatment. The results of this work show that plantaris tendons exhibit tendinosis-like tissue changes, internal innervation and features that suggest occurrence of glutamate and acetylcholine production and signalling. Plantaris removal improves Achilles tendon structure suggesting possible compressive/shearing interference between the Achilles and plantaris tendons in tendinopathy. The peritendinous connective tissue shows marked innervation, which thus might transmit pain when being compressed. The partial absence of axons indicates a possible nerve degeneration. On the whole, the study gives new evidence favouring that the plantaris tendon and the peritendinous connective tissue might be of importance for pain and Achilles tendon structure in midportion Achilles tendinopathy.

Keywords
Plantaris tendon, Achilles tendon, midportion Achilles tendinopathy, innervation, nerve degeneration, bilateral effects, glutamate, acetylcholine

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