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Effects on neovascularisation behind the good results with eccentric training in chronic mid-portion Achilles tendinosis?

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Abstract The background to the good clinical results reported using painful eccentric calf-muscle training as treatment for chronic painful mid-portion Achilles tendinosis is not known. Recently, using ultrasound and colour Doppler technique, we showed that painful tendinosis was associated with a local neovascularisation. Furthermore, in a pilot study, destroying these neovessels by sclerosing therapy cured the pain in most patients. Dynamic ultrasound and colour Doppler examination has shown that the flow in the neovessels stops during dorsiflexion in the ankle joint. Therefore, it was of interest to study the occurrence of neovascularisation before and after eccentric training. Forty-one tendons in 30 patients (22 men and 8 women, mean age 48 years) with chronic painful mid-portion Achilles tendinosis were examined with ultrasonography and colour Doppler, before and after 12 weeks of eccentric calf-muscle training. Before treatment, there was a local neovascularisation in the area with tendon changes (hypo-echoic areas, irregular fibre structure) in all tendons. At follow-up after treatment (mean 28 months), there was a good clinical result (no tendon pain during activity) in 36/41 tendons, and a poor result in 5/41 tendons. In 34/36 tendons with a good clinical result of treatment there was a more normal tendon structure, and in 32/36 tendons there was no remaining neovascularisation. In 5/5 tendons with a poor clinical result there was a remaining neovascularisation in the tendon, and in 2/5 tendons there were remaining structural abnormalities. In conclusion, in patients with chronic painful mid-portion Achilles tendinosis, a good clinical result after eccentric training seems to be associated with a more normal tendon structure and no remaining neovascularisation. Action on the area with neovessels during the eccentric training regimen might possibly be responsible for the good clinical results.

Keywords Achilles tendinosis · Pain · Ultrasonography and colour Doppler · Neovascularisation · Eccentric training

Introduction

Influenced by the theory put forward by Curwin and Stanish [7] that eccentric training should be included in the rehabilitation of tendon injuries, we designed in 1996 a special type of eccentric-training regimen to be used on patients with chronic painful mid-portion Achilles tendinosis. In a pilot study on recreational athletes [1], in a larger project containing also non-physically active individuals [8], and in a randomized study comparing the effects of eccentric training with the effects of concentric training [12] we have shown very good short-term clinical results with eccentric calf muscle training. However, the background to the good clinical results achieved with this method is unknown.

There are many theories, but the source of pain and the background to the pain mechanisms associated with chronic Achilles tendinosis have not been scientifically clarified [3, 5, 10].

The occurrence of a neovascularisation in the area with tendon changes, demonstrated with colour Doppler examination simultaneously with ultrasonography, has been shown to possibly be correlated with pain in chronic mid-portion Achilles tendinosis[13]. In that study, it was demonstrated that passive dorsiflexion of the ankle stopped the flow in these vessels (area with neo-vascularisation) (Fig. 1a, b).

Ultrasound is an established technique for examining tendons [16, 6], and the colour Doppler technique is a method to study flows, and directions of flows, like blood flow in blood vessels[18]. Only flows with high flow rates can be recorded; therefore the normal blood flow in the Achilles tendon cannot be demonstrated.

In a recent pilot study on patients with chronic mid-portion Achilles tendinosis, sclerosing the area with neovascularisation outside the ventral part of the tendon cured the pain in the majority of patients [14]. The results of this study indicate that the area with neovascularisation (neovessels and accompanying nerves) might be the source of pain in the chronic stage of this condition.

The aim with this investigation was to study the occurrence of neovascularisation before and after treatment with eccentric training, and to relate the findings to the results of treatment in patients with chronic painful mid-portion Achilles tendinosis.

Material and methods

When the eccentric calf-muscle training regimen was started as a treatment model for chronic mid-portion Achilles tendinosis at our clinic, all patients were examined with grey-scale ultrasonography. During the last years, ultrasonography has been combined with colour Doppler examination.

Thirty-four patients with painful mid-portion Achilles tendinosis in a total of 45 tendons, who had been examined with ultrasonography and colour Doppler before treatment was instituted, were asked to participate in this follow-up. All tendons had neovessels in the area with tendon changes, demonstrated by ultrasound and colour Doppler before treatment was instituted.

Drop outs

Four patients (four tendons) stated that they were pain-free and satisfied with treatment, but didn't want to participate in the follow-up.

Follow-up

Forty-one tendons in 30 patients (22 men and 8 women, mean age 48 years) with chronic painful mid-portion Achilles tendinosis were examined with ultrasonography and colour Doppler before and after the eccentric calf muscle training regimen.

Eccentric training model

All patients were instructed how to perform the eccentric training by one of two physiotherapists (T.P. or P.J.). They were given practice instruction and a written manual on how to progress. A control on how the patients did their exercises was carried out by the physiotherapist after 6 weeks. The patients were instructed to do their eccentric exercises twice daily, 7 days/week, for 12 weeks.

Two types of eccentric exercises were used. The calf-muscle was eccentrically loaded both with the knee straight and – to max-

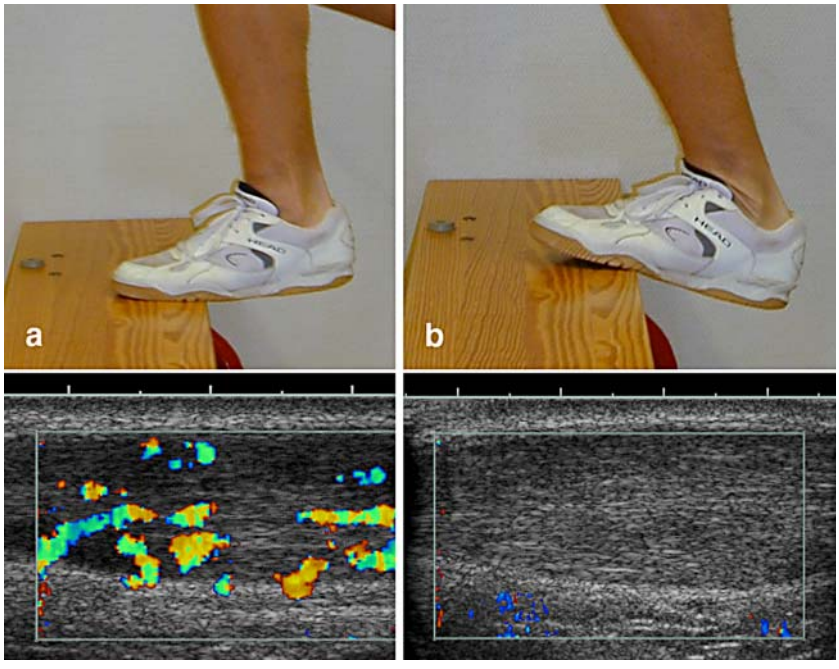

Fig. 1a, b Ultrasound and colour Doppler examination of a patient with chronic painful mid-portion Achilles tendinosis. **a** "Resting position"-no dorsiflexion in the ankle joint. Longitudinal view, showing a thickening of the tendon, structural abnormalities with hypoechoic areas, and neovascularisation (*coloured structures*) inside and outside the ventral part of the tendon. **b** During dorsiflexion in the ankle joint. Longitudinal view, showing a thickening of the tendon, structural abnormalities with hypoechoic areas, but no flow in the neovessels

imize the activation of the soleus muscle – also with the knee bent. Each of the two exercises included fifteen repetitions done in three sets (3×15 reps). The patients were told that muscle soreness during the first 1 to 2 weeks of training was to be expected.

In the beginning the loading consisted of the bodyweight, and the patients were standing with all their body weight on their injured leg. From an upright body position and standing with all body weight on the "forefoot", with the ankle joint in slight plantar flexion, the calf-muscle was loaded by having the patient lower the heel beneath the lever. They were only loading the calf-muscle eccentrically, no following concentric loading was done. Instead, the noninjured leg was used to get back to the start position. The patients were told that the exercises should be painful, and when there was no pain in the tendon during training the load should be elevated to reach a new level of "painful training". However, no training through disabling pain was encouraged. Increasing the load could easily be done by using a backpack that was successively loaded with weight. If very high weights were needed, the patients where told to use a weight-machine.

The patients were allowed to gradually go back to their previous (before injury) tendon loading activity level during the last 4 weeks of the 12 week training regimen.

After the 12 weeks of training, the patients were instructed to continue to do their exercises once or twice per week.

Table 1 Clinical results, ultrasonography and colour Doppler findings before and after treatment, in patients with chronic painful mid-portion Achilles tendinosis treated with eccentric calf-muscle training

Patient	Ultrasonography structure		Colour Doppler neovessels [0,(+),+]		Follow-up (months)	Result/activity
Age/sex	Before	After	Before	After		
40/M	changes	normal	+	0	48	Good/jogging
41/M[a]	changes	normal	+	0	48	Good/basketball
41/M[a]	changes	normal	+	0	48	Good/basketball
37/M[a]	changes	normal	+	0	47	Good/jogging
37/M[a]	changes	normal	+	0	47	Good/jogging
47/M[a]	changes	normal	(+)	0	46	Good/jogging
47/M[a]	changes	normal	+	(+)	46	Good/jogging
40/F	changes	changes	+	0	42	Good/walking
36/M	changes	normal	+	0	41	Good/jogging
51/M[a]	changes	normal	+	0	37	Good/running
51/M[a]	changes	normal	+	0	37	Good/running
55/M[a]	changes	normal	+	0	36	Good/walking
55/M[a]	changes	normal	+	0	36	Good/walking
59/F	changes	normal	+	(+)	36	Good/walking
53/M	changes	normal	+	(+)	36	Good/walking
66/M	changes	normal	+	0	36	Good/walking
52/F[a]	changes	normal	+	0	35	Good/walking
52/F[a]	changes	normal	+	0	35	Good/walking
36/M[a]	changes	normal	+	0	34	Good/floorball
36/M[a]	changes	normal	+	+	34	Pain/floorball
62/F[a]	changes	normal	+	(+)	32	Pain/walking
62/F[a]	changes	normal	+	0	32	Good/walking
66/M	changes	normal	+	0	29	Good/walking
51/M	changes	normal	+	(+)	26	Good/jogging
39/F[a]	changes	normal	+	0	26	Good/aerobics
39/F[a]	changes	normal	+	0	26	Good/aerobics
43/M[a]	changes	normal	(+)	0	26	Good/running
43/M[a]	changes	normal	+	0	26	Good/running
29/M[a]	changes	normal	+	0	24	Good/soccer
29/M[a]	changes	normal	(+)	+	24	Pain/soccer
63/M	changes	normal	+	0	24	Good/walking
55/M	changes	normal	+	0	23	Good/jogging
44/M	changes	normal	+	0	22	Good/jogging
37/M	changes	normal	+	0	21	Good/jogging
63/M	changes	changes	+	+	21	Pain/walking
74/M	changes	normal	+	0	21	Good/walking
57/M	changes	changes	+	0	19	Good/walking
26/F	changes	normal	+	0	18	Good/walking
45/M	changes	normal	+	0	14	Good/jogging
40/F	changes	changes	+	+	10	Pain/jogging
49/F	changes	normal	+	0	6	Good/jogging

[a]Bilateral

Ultrasonography and colour Doppler examination

Ultrasound was performed with a linear transducer (Acuson Sequoia 512) with 8–13 MHz frequency, before and after the eccentric training regimen. The examinations were carried out in prone position with both feet free from the examination table to enable movements of the feet. The Achilles tendons were examined in longitudinal and transverse plane. It was important to examine the tendons parallel with the fibres in the longitudinal plane and perpendicular in the transversal plane to minimise artefacts. Both tendons were always examined in the same manner. The pathological changes in the painful thickened Achilles tendon were registered.

Colour Doppler was used to diagnose the neovascularisation and to find the entrance of the vessels into the tendon.

All ultrasonography and colour Doppler examinations were performed by the same experienced radiologist (L.Ö). The test-to-test reliability for the observer (L.Ö.) was evaluated by examining one tendon ten times over a short period of time, with repositioning between investigations. The coefficient of variation (CV) was estimated to be 1.1%.

There is no established technique for quantitatively measuring the amount of neovascularisation in tendons.

At study entry and at follow-ups, the same experienced radiologist (L.Ö.) estimated neovascularisation in the Achilles tendon as (0), (+) or +, according to the appearance of vessels inside the tendons. When there were no visible vessels the estimation was (0). When there were one or two small vessels mostly in the anterior part of the tendons the estimation was (+). When there were several irregular vessels throughout the tendon, the estimation was +.

Questionnaire

At the follow-up for ultrasound and colour Doppler examination, the patients were asked about their satisfaction with the treatment and about their current Achilles tendon loading activity level (recreational or sport activity).

Results

Data on each patient participating in the follow-up are presented in Table 1.

Before treatment, all patients had Achilles tendon pain during loading, and there was a local neovascularisation in the area with structural tendon changes (hypoechoic areas, irregular fibre structure), and outside the ventral part of the tendon, in all 45 tendons.

Four patients (four tendons) did not wanted to participate in the follow-up.

At follow-up after treatment (mean 28 months, range 3–48), there was a good clinical result (no tendon pain during loading) in 36/41 tendons, and a poor result in 5/41 tendons.

In 34/36 tendons with a good clinical result of treatment there was an ultrasonographically more normal tendon structure, and in 32/36 tendons there was no remaining neovascularisation (Fig. 2a, b). In 4/36 tendons with a good clinical result from treatment a minor neovascularisation remained, and in 2/36 tendons there were remaining structural abnormalities. In 5/5 tendons with a poor clinical result there was a remaining neovascularisation in the tendon, and in 2/5 tendons there were remaining structural abnormalities.

Discussion

Eccentric calf-muscle training has in different studies been shown to be a good treatment model for patients with chronic mid-portion Achilles tendinosis [1, 8, 12]. However, the background to the good clinical results achieved with this method is largely unknown.

In a recent prospective study we demonstrated that successful treatment with eccentric calf-muscle training in patients with chronic painful mid-portion Achilles tendinosis was associated with a significantly-decreased tendon thickness and in most tendons also an ultrasonographi-

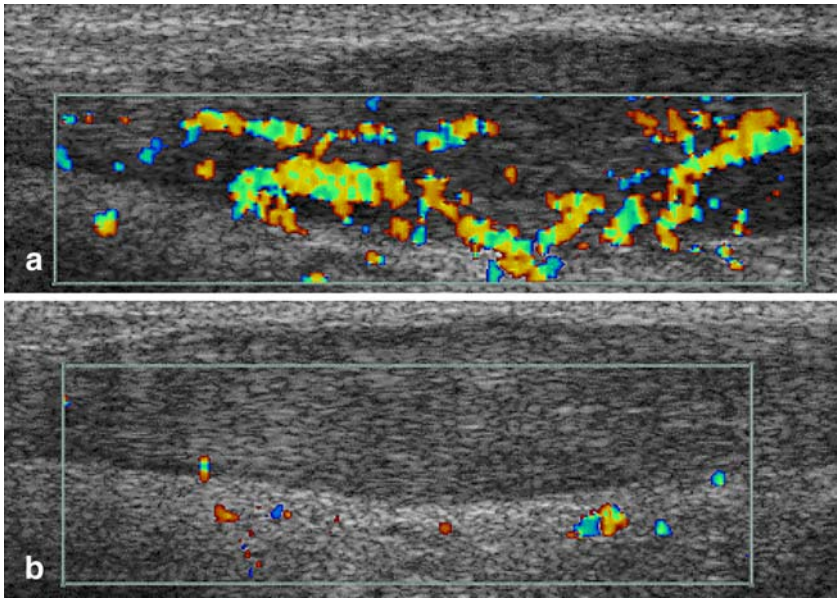

Fig. 2a, b Ultrasound and colour Doppler examination of a patient with chronic painful mid-portion Achilles tendinosis. **a** Before treatment with eccentric training. Longitudinal view, showing a thickening of the tendon, structural abnormalities with hypo-echoic areas, and neovascularisation (*coloured structures*) inside and outside the ventral part of the tendon. **b** After treatment with eccentric training. Longitudinal view, showing a more normal tendon structure and no remaining neovascularisation in the tendon

cally normalized tendon structure[15]. At the time of that study, we didn't have the possibility of using the colour Doppler technique, and consequently we couldn't get any information about neovascularisation. However, after introduction of the colour Doppler technique the results of a recent study indicated a possible relationship between the occurrence of a neovascularisation in the area with tendon changes and tendon pain during activity[13]. Furthermore, destroying these neovessels by sclerosing therapy, in a small pilot study, cured the pain in most patients [14]. Consequently, it was of interest to study the occurrence of neovessels before and after treatment with eccentric training, in relation to pain during tendon-loading activity.

The results of this study showed that in the majority of the tendons with a good result after eccentric training, the neovessels demonstrated in all tendons before treatment had disappeared at follow-up. In the five tendons with a poor result of treatment there was remaining neovascularisation. From another study on biopsies from Achilles tendinosis tissue, we know that there are nerve structures in close relation to the vascular wall [4]; consequently, the area with neovascularisation should be considered as an area with neovessels and accompanying nerves. These findings, together with the findings from treatment with sclerosing therapy [14] and from an investigation combining ultrasound and colour Doppler, immunohistochemical analyses of tendon biopsies, and diagnostic injections [2], indicate that the area with neovascularisation is very probably of major importance for the pain in this condition.

In all but two tendons with a good clinical result, the tendon structure was ultrasonographically more normal after treatment. This could indicate that a "normalized" structure is the background to the absence of pain, but with the results from sclerosing therapy in mind – where the pain disappeared despite remaining structural tendon changes – it is most likely to be the area with neovascularisation that is responsible for the pain. However, it might very well be something in the area with structural tendon changes that is triggering the neovascularisation. The high levels of glutamate [3] and lactate [5] that previously have been demonstrated might alone, or together, stimulate neovascularisation. The high lactate concentrations could indicate ischaemic conditions in the tendon, possibly triggering neovascularisation. A possible "hypoxic tendinopathy" was discussed already in 1997 by Jozsa and Kannus [9].

In three recent studies, colour or power Doppler has been used to study chronic painful conditions in the Achilles tendon [11, 17, 19]. Power Doppler varies from colour Doppler in that the imaging is independent of the angle of incident beam [19]. The findings by Peers et al. [17] that there was a neovascularisation in 22/25 chronic painful Achilles tendons are in line with our findings. However, Khan et al. [11] and Zanetti et al. [19] did not find any correlation between neovessels and pain in in their studies on patients presenting with Achilles tendinopathy and Achillodynia. The reason for the discrepancy between the findings in their studies and our findings cannot be definitely clarified. However, it seems that there are major differences between the criteria for inclusion in the studies. All patients in our study had structural tendon changes on ultrasound corresponding to a painful swelling localised in the mid-portion of the Achilles tendon, while only 37/57 tendons in the study by Khan et al., and 35/55 tendons in the study by Zanetti et al. had structural changes in the tendons. To be included in our studies on chronic pain in the mid-portion of the Achilles tendon it is not enough to have pain in the Achilles tendon (tendinopathy, Achillodynia), there have also to be structural tendon changes on ultrasound corresponding to the painful area in the mid-portion of the tendon. It might be that the patients with "tendinopathy" and "Achillodynia" where no structural tendon changes were found on ultrasound had other diagnoses such as tibial or peroneal tendon problems, os trigonum, lumbar nerve root pain etc. Furthermore, in the study by Khan et al. MRI was also used, and showed that there were structural tendon changes in only 19/34 symptomatic tendons.

The results from the current study indicate that there might be something in the eccentric training regimen that affects the area with neovascularisation. It is difficult to explain exactly how the eccentric exercises have influence on the area with neovessels, but using dynamic ultrasound and colour Doppler examination we have demonstrated that during the heel-drop the flow in the neovessels is stopped, whilst in the resting position there is flow again (Fig. 1a, b). Theoretically, if the flow is stopped 180 times/day (the eccentric program consists of 180 repetitions/day), this might, directly or indirectly, hurt the neovessels and accompanying nerves. Also, the neovessels and nerves travel from the soft tissue outside the ventral part of the tendon, into the area with tendinosis where the tissue is more dense and hard, possibly increasing the risk for injury. It is tempting to believe that the frequently severe pain these patients experience, especially during the first 2 weeks of treatment, might be a result of nerve damage.

The limitation of this study is that it is non-controlled. However, the patients in this study had had a long duration of pain symptoms, and all had tried rest as a treatment, and therefore it was not ethically correct to have a control group that were resting. Furthermore, at the time for the study, there was no other active treatment model designed for ultrasonographically and clinically-verified mid-portion Achilles tendinosis, and showing good clinical results, that could have been used as a comparative treatment model.

In conclusion, we would like to raise the theory that the good clinical effects demonstrated with painful eccentric calf-muscle training, on the pain in chronic mid-portion Achilles tendinosis, might be mediated through action on the area with neovascularisation.

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