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Tendinopathy and Doppler activity: the vascular response of the achilles tendon to exercise

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Background: **Intratendinous Doppler activity has been interpreted as an equivalent of neovessels in the Achilles tendon and as a sign of tendinosis (AT).** ***Aim:*** **To evaluate the vascular response as indicated by color Doppler activity after repeated loading of both symptomatic and non-symptomatic Achilles tendons.** ***Material and methods:*** **Ten non-trained, healthy subjects ran 5 km. Ultrasound (US) Doppler activity was determined before and after the exercise. Eleven patients with chronic AT performed 3×15 heavy-load eccentric exercise. The Achilles tendons were scanned before and immediately after the exercise.** ***Results:*** **Non-symptomatic: six Achilles tendons in five subjects had intratendinous Doppler activity before the exercise. All but two subjects (80%) had intratendinous Doppler activity after running. Symptomatic: all patients had Doppler activity in the tendons, with a median color fraction before eccentric exercise of 0.05 (range 0.01–0.33). The Doppler activity did not disappear after exercise. Tendons with a color fraction below the median at baseline increased significantly after the exercise ($P = 0.02$).** ***Conclusion:*** **The mere presence of Doppler in the Achilles tendon does not** ***per se*** **indicate disease. Eccentric exercise does not extinguish the flow during or after one training session in patients with chronic AT.**

Ultrasound (US) with the Doppler technique is an emerging diagnostic tool for the diagnosis of the hypervascularization found in e.g. rheumatoid arthritis (Qvistgaard et al., 2001; Terslev et al., 2003) and tenosynovitis (Newman et al., 1994, 1996). Intratendinous Doppler activity has been described in both the patellar and Achilles tendons (Ohberg et al., 2001; Terslev et al., 2001; Koenig et al., 2004). In normal resting musculo-skeletal tissues, flow is seen with color or power Doppler in muscles and connective tissue, seldom in joints and reportedly never in tendons (Ohberg et al., 2001). In tendons, the presence of intratendinous Doppler activity is interpreted as a sign of pathology and in patients with clinical signs of tendinosis, Doppler activity is regularly present (Ohberg et al., 2001; Richards et al., 2001; Koenig et al., 2004; Reiter et al., 2004). Color Doppler has been reported as an important tool both for the diagnosis and follow-up of Achilles tendinosis (Ohberg & Alfredson, 2004).

In chronic Achilles tendinosis, various treatment strategies have been suggested. An initial non-operative (conservative) treatment is recommended by most authors (Clement et al., 1984; Kvist, 1994; Archambault et al., 1995; Jozsa & Kannus, 1997; Alfredson & Lorentzon, 2000) with identification and if possible correction of eliciting factors. Most commonly, a multioriented approach is recommended, with rehabilitation as the key factor and supplementary modalities like heat and cold therapy (Clement et al., 1984), massage, US, electric stimulation (Rivenburgh, 1992) and laser therapy (Siebert et al., 1987). Most of these therapies are based on circumstantial evidence and have not been subjected to controlled trials. Eccentric calf muscle training as treatment of painful mid-portion chronic Achilles tendinosis has been demonstrated to give good clinical short-term results (Alfredson et al., 1998, 1999a; Mafi et al., 2001; Fahlstrom et al., 2003; Ohberg et al., 2004), and such exercises have in general been accepted in the rehabilitation of tendinosis. However, the mechanism behind the supposed effect remains to be clarified. Long-term studies on the effect of eccentric exercise have reported both normalized tendon volume and disappearance of intratendinous hyperemia (Ohberg et al., 2004).

The aim of the present study was to evaluate the vascular response as indicated by color Doppler activity after repeated loading of both symptomatic and non-symptomatic Achilles tendons. In the non-symptomatic subjects, this was obtained by a – for them – strenuous running exercise, while the patients with chronic Achilles tendinosis were examined before and after eccentric exercise of the gastrocnemius–soleus complex.

Material and methods

Study 1: The non-symptomatic subjects

Ten healthy non-trained subjects were recruited. The mean age was 28 years (18–49 years), and the mean body mass index (BMI) was 21 (SD 2). An inclusion criterion was absence from regular training for at least 2 years.

Running exercise: The subjects were asked to run 5 km as fast as possible. The maximum heart rate, average heart rate, and running time were recorded. In each subject, both Achilles tendons were scanned before and after the exercise. Pain was determined before and after the exercise on a visual analogue scale (VAS) and by a telephone interview 2 days later.

Study 2: The symptomatic patients

A total of 11 patients (eight males) with clinical and US diagnosis of chronic Achilles tendinosis were included in the study. The mean age was 34 years (25–56 years). Two patients had bilateral symptoms, so their color fractions were pooled to obtain one (assumed) relevant estimate per patient.

Patients were referred by general practitioners or by sports clinics. All patients had pain, some degree of swelling, and local tenderness at palpation of the Achilles tendon. Clinical signs of tendinopathy were found in the mid-tendinous area in eight patients and in the insertion area in the remaining three patients.

Eccentric exercise

The symptomatic tendon(s) underwent two times of three sets with 15 repetitions of heavy-loaded eccentric training with the knee in a straight and slightly bent position – identical to the rehabilitation program proposed by Fahlstrom et al. (2003). The Achilles tendons were scanned before and immediately after the exercise.

Evaluation

The end point was the presence, amount, and distribution of Doppler activity.

The same experienced investigator performed scanning and evaluation of the examination.

US

US was performed with an Acuson Sequoia (Mountainview, California, USA) equipped with a 14 MHz linear array transducer. The color Doppler was optimized for low flow, and the Nyquist limit was ± 0.014 m/s. The Doppler frequency was 7 MHz and the gain was set just below the level that produced random noise. The Doppler settings were the same for all exams. The Achilles tendon was scanned in longitudinal and transverse planes with the patient lying prone and the feet relaxed in a resting position at the end of the couch. The tendon and peritendinous tissues were evaluated with color Doppler and gray scale UL. To minimize the pressure on the tendons when scanned for Doppler activity, we aimed at having a discernible thin layer of gel seen on the screen between the transducer sole and the skin. A longitudinal image with maximum flow on color Doppler was obtained to calculate the percentage of color pixels. The digitally stored image was exported as a DICOM file, and the color fraction was calculated with a β-version of DataPro (Noesis, Courtaboeuf, France). The Achilles tendon was traced inside the color box whereupon the software reported the total number of pixels inside the trace as well as the number of color pixels inside the trace. The color fraction was calculated as color pixels/total pixels.

Statistics

The mean and median values ± standard deviations and independent samples t-tests were calculated by the computerized SPSS system (version 12.0, SPSS Inc., Chicago, Illinois, USA). A P-value less than 0.05 was considered significant.

Ethics

The study was approved by the local committee on ethics, Copenhagen, and informed consent was obtained from all patients.

Results

All participants completed the exercises as prescribed.

Part 1: Non-symptomatic, non-trained subjects.

The subjects' (four males, six females) demographic parameters and physiologic results after exercise are listed in Table 1. The development of pain after the run on a VAS is listed in Table 2. All subjects had a VAS of 0 before running. The tendon structure on gray-scale US was normal in all tendons both before and after exercise. Six Achilles tendons in five subjects had intratendinous Doppler activity before the exercise.

After the exercise, three subjects developed pain on VAS. All but two subjects (80%) had intratendinous Doppler activity after running.

The mean VAS after running was four (0–35) in the Achilles tendon. Three subjects (30%) with intratendinous Doppler activity before running showed increased (Fig. 1) or sustained activity inside the Achilles tendon, and in two subjects (numbers 8 and 10) the Doppler activity disappeared after the run. No subjects complained of pain at the telephone interview 2 days later. Appearance of Doppler activity in the Achilles tendons after the run was statistically significant ($P = 0.005$). Doppler activity as color fraction before and after the run is listed is Table 2.

There was no significant correlation between color fraction (Doppler activity) and VAS before (right Achilles: $r = -0.154$; $P = 0.671$; $n = 10$ and left Achilles: $r = -0.307$; $P = 0.388$; $n = 10$) and after the run (right Achilles: $r = 0.257$; $P = 0.473$; $n = 10$ and left Achilles: $r = -0.192$; $P = 0.594$; $n = 10$).

Table 1. Demographic data and physiological results after exercise (a 5 km run)

Subject	Time	Age (year)	Height (cm)	Weight (kg)	BMI	HR-max	HR-av	Theoretical load (% max pulse)
1	28.27	29	179	75	23.4	186	153	80.1
2	31.57	19	178	65	20.5	195	187	93.0
3	36.34	38	170	60	20.8	147	143	78.6
4	29.13	23	170	58	20.1	191	183	92.9
5	42,29	41	170	60	20.8	159	143	79.9
6	39	49	160	60	23.4	172	168	98.2
7	24.56	21	180	72	22.2	191	179	89.9
8	26.58	22	188	68	19.2	192	180	90.9
9	42.36	18	172	66	22.3	190	173	85.6
10	36.23	20	173	55	18.4	179	157	78.5
Mean	34	28	174	64	21	180	167	87
SD	6	11	8	6	2	16	17	7

BMI, body mass index; HR-max, maximum heart rate; HR-av, average heart rate.

Table 2. Color fraction in percent before and after the run and VAS after the run

Subject	Location					
	Pre		Post		Post-VAS	
	Ac dx	Ac sin	Ac dx	Ac sin	Ac dx	Ac sin
1			1.2	0.6	0	0
2				2.7	6	0
3			3.6	2.2	33	33
4			4.6	6.3	0	0
5	4.3				0	11
6		1.3		10.2	0	0
7			4.6	3.1	0	0
8	0.7	1.7	3	2.3	0	0
9		0.3	1.5		0	0
10		1.2		2.2	0	0

VAS, visual analogue scale; Ac dx, right Achilles tendon; Ac sin, left Achilles tendon.

Part 2: Chronic Achilles tendinosis

The subjects' demographic parameters are listed in Table 3.

All patients had Doppler activity in the tendons, with a median color fraction before eccentric exercise of 0.05 (range 0.01–0.33). The Doppler activity did not disappear after exercise. In all but three tendons, the Doppler activity increased after the exercise to a mean of 0.14 (range 0.01–0.33) (Fig. 1). Tendons with a color fraction below the median at baseline increased significantly after the exercise (t-test, $P = 0.02$), whereas in individuals above the median, no significant increase in color fraction was observed. The development in color fraction is shown in Fig. 2.

Discussion

Color/power Doppler US is an established technique for measuring blood flow and has been used successfully in evaluating local hyperemia such as tendinosis (Newman et al., 1994, 1996). The amount of color pixels in a region reflects the amount of flowing blood in the investigated area (Rubin et al., 1997), which makes it possible to obtain an estimate of the blood flow in a particular area as an estimate of disease activity (Qvistgaard et al., 2001; Terslev et al., 2001, 2003). There is a good correlation between Doppler activity and tendon disorders (Weinberg et al., 1998; Torp-Pedersen et al., 2002). Other groups have shown similar results and conclude that the color/power Doppler technique is a good way to visualize soft-tissue hyperemia as a sign of tendinosis (Ohberg et al., 2001; Terslev et al., 2001; Alfredson et al., 2003) and that the technique may be used to quantify disease activity in treatment.

Doppler activity cannot be interpreted as a sign of pathology in all cases as shown in the present material of healthy volunteers even before exercise. This is in contrast to a previous study on 14 healthy volunteers where no Doppler activity was found in normal Achilles tendons (Ohberg et al., 2001). The difference may be because of different machine settings as the same equipment was used in the two studies. The possibility of artifacts in these cases was excluded by varying the angulation of the transducer and, as far as possible, by further spectral Doppler test of the vessels (data not shown).

To our knowledge, this is the first study to show some intratendinous Doppler activity as a normal finding in Achilles tendons from non-symptomatic, sedentary individuals. As a further sign of the physiological importance of these vessels, an increase in Doppler activity was demonstrated after repetitive load. In the symptomatic group, the pathology was localized in two different regions (the mid-portion and the insertional areas). The necessity of a subclassification for e.g. in therapeutic studies must be taken into account, but in this study we only looked at the Doppler response in the tendons and therefore they are in the same group.

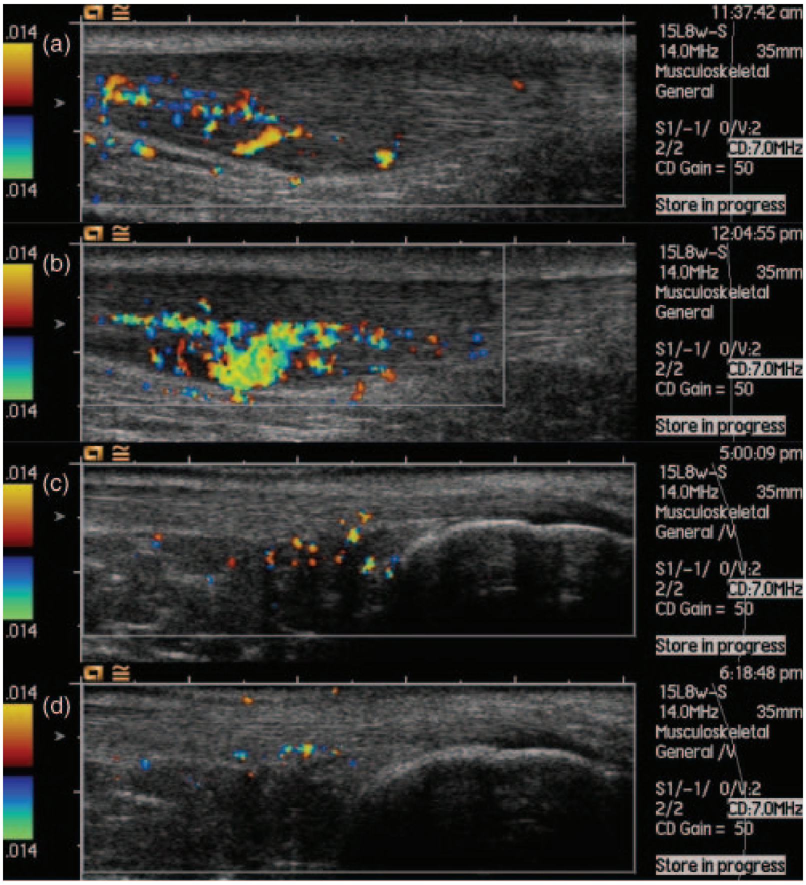

Fig. 1. Intratendinous Doppler activity before and after exercise. (a)Before and (b)After eccentric exercise in a patient with chronic Achilles tendinosis. The scan planes are not identical but represent the scan plane with the maximum Doppler activity. Proximal is oriented left and posterior is oriented up. There is clearly more intratendinous Doppler activity in (b). The sharp posterior demarcation of the color pixels is because the Doppler activity is in the soleus part of the tendon. (c)Before and (d)after a 5 km run in a normal subject. Proximal is oriented left and posterior is oriented up. Before the run there is a slight intratendinous Doppler activity – only the two most posterior color foci are with absolute certainty inside the tendon. Most of the Doppler activity is anterior to the tendon. After the run, there is more intratendinous flow. Most of the Doppler activity in (d) is inside the tendon. *Comment*: Please notice that the images were recorded with focus on the Doppler findings, and image plane and insonation angle were not optimized for gray-scale evaluation.

Table 3. Demographic data and location of injury in the symptomatic patients

Number	Age (year)	Height (cm)	Weight (kg)	BMI	Side	Location
1	36	165	55	20.2	L+R	M
2	27	178	69	21.8	L	M
3	27	196	102	26.6	L	M
4	25	199	90	22.7	R	M
5	38	180	75	23.1	L	I
6	41	172	126	42.6	R	M
7	56	176	83	26.8	L	M
8	32	184	80	23.6	L	M
9	31	175	70	22.9	L+R	I
10	34	175	81	26.4	L	M
11	31	168	72	25.5	R	I
Mean	34.36	178.91	82.09	25.66		
SD	8.67	10.6	18.97	6.01		

L, left; R, right; M, Mid-tendinous; I, insertional.

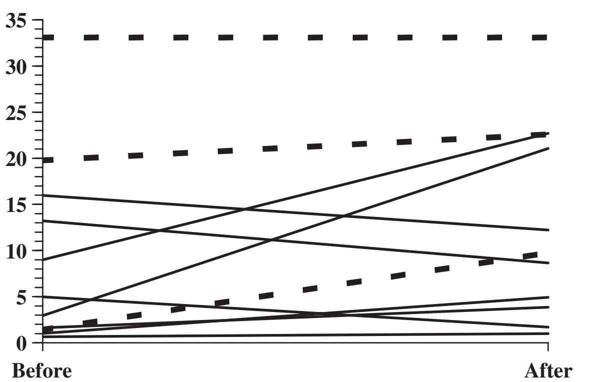

Fig. 2. Intratendinous Doppler activity and eccentric exercise. The graph shows the color fraction before and immediately after eccentric exercise in 11 patients with chronic Achilles tendinosis. The color fraction increased in seven cases, was sustained in one and decreased in three. The decrease was present in tendons where the color fraction was above or equal to the median color faction of the whole group before exercise. The three dotted lines indicate patients with insertional tendinopathy.

Although the amount of Doppler activity in non-symptomatic, healthy subjects was minute compared with chronic tendinosis cases, a threshold would be useful to distinguish normal intratendinous Doppler activity from pathological. This threshold will be machine dependent.

After repetitive loading, we observed Doppler activity in nine of 10 subjects. We believe that the relative hyperemia seen after exercise is a physiological response. Another indication of the physiological nature of the vascular response was the lack of correlation to symptoms documented on the VAS in the running study. In two of the three subjects who complained of pain on the VAS immediately after the run, there was no detectable Doppler activity in the painful tendons.

Furthermore, previous studies have shown that blood flow, oxygen demand and the level of collagen synthesis and matrix metalloproteinases increase with mechanical loading of the tendon (Boushel et al., 2000; Kjaer et al., 2005).

In patients with chronic tendinosis, Doppler activity was present in all cases at rest and increased in seven of 11 subjects when recorded immediately after an eccentric exercise. The acute findings are in contrast to the proposed long-term hypothetical action of this type of eccentric exercise, which leads to disappearance of hyperemia (Ohberg & Alfredson, 2004). Similarly, signs of an increased tendon volumen and intratendinous signal immediately after eccentric training have recently been shown with magnetic resosnance imaging (MRI) (Shalabi et al., 2004). They explained this increase by a higher water content and/or hyperemia in the Achilles tendon. The acute findings should be followed by long-term follow-up studies on MR to see whether the MRI results are similar to the long-term US results.

It has been proposed that eccentric exercise affects neovessels and the accompanying nerves because of the environment created by repeated stretching of the tendon fibers eventually leading to a termination of the hyperemia of the tendon (Alfredson, 2003; Ohberg & Alfredson, 2004). Our study measured the immediate response (increase in hyperemia) and it is possible that the long-term effect is indeed the model proposed by Ohberg and Alfredson (Alfredson, 2003). In our material, the Doppler activity increased significantly in the tendons with the smallest degree of Doppler activity before exercise, indicating that a vascular supply in this range may be invoked by eccentric training, while tendons with the largest vascular supply before exercise did not show a similar increase. A possible explanation is that all tendons, both healthy and diseased, have a certain amount of vascularization, which may be manifested on demand up to a certain maximum.

The etiology and pathogenesis of tendinosis remain to be clarified. Overuse and repetitive loading appear to play a significant role (Archambault et al., 1995). Tendinosis, however, is also seen in physically non-active individuals (Alfredson & Lorentzon, 2000). Other suggested factors include aging with a decreased blood supply and decreased tensile strength, muscle weakness and imbalance and insufficient flexibility (Clement et al., 1984; Galloway et al., 1992). So far, inflammatory cells in possible tendinosis have only been shown in one study (Cetti et al., 2003), while most biopsies have been negative (Jarvinen et al., 1997; Khan et al., 1999).

However, the study by Cetti et al. dealt with patients with ruptured Achilles tendons and the biopsies were taken from ruptured and the contralateral side. In recent studies on patients with chronic mid-portion Achilles tendinosis, Alfredson et al. used intratendinous microdialysis techniques and gene analysis on biopsies and found no significant differences in prostaglandin (PGE2) from normal tendons. Therefore, they concluded that there was no sign of a chemical prostaglandin-mediated inflammation (Alfredson et al., 1999b). Instead, they found higher concentrations of glutamate and the presence of glutamate NMDA receptors (Alfredson et al., 2001). Glutamate, being a pain mediator in the central nervous system, and now shown in Achilles tendinopathy, rises the question about a possible neurogenic inflammation. Future studies must clarify this. The terms "tendonitis" (inflammation) and tendinosis (degeneration) are still used to describe the same condition, indicating the different views on the etiology. Some authors advocate that the "tendonitis myth" be completely abandoned (Khan et al., 2002). The intratendinous hyperemia found in chronic Achilles tendinosis has been interpreted as the presence of neovessels (Ohberg et al., 2001). This may be true but it may also indicate the increased flow in a pre-existing vascular bed. This is indicated by the induced hyperemia in the normals in this study (presumably no neovessels) and by the immediate increase in hyperemia after eccentric exercise (increased flow in already existing vessels). In parallel, in patients with knee joint synovitis, Schmidt et al. (2000) found that the number of color pixels did not correspond to the number of vessels found by histology but rather to the area of these vessels. In both groups (normal subjects and patients), the trend was an increase in Doppler activity after exercise. In both groups, however, some of the tendons reacted with a decrease in color fraction. We have no explanation for this.

Nevertheless, a precise diagnosis is important, and the clinical examination may be supplemented by US (Astrom et al., 1996), magnetic resonance imaging (MRI) (Astrom et al., 1996; Paavola et al., 1998) and, in some cases, biopsy (Movin et al., 1997).

Perspectives

One conclusion of our findings is that the mere presence of Doppler in the Achilles tendon does not *per se* indicate disease. Thus, without defined thresholds for the amount of Doppler activity, pathologic and physiologic perfusion cannot be distinguished in all cases. At present, this is only an issue with high-end equipment correctly tuned to low-flow sensitivity. However, with the on-going improvement in Doppler sensitivity, it may also be foreseen that less-expensive equipment will allow for the detection of normal intratendinous flow and that thresholds must be defined. These thresholds will be machine and settings dependent.

Another important aspect raised by this study is the necessity of a standardization of the physical activity before an US-Doppler examination, when Doppler is used to evaluate the extent of disease or effect of treatment. The tendon should not be evaluated immediately after strenuous activity or eccentric exercise, which may generate a physiological response. Future studies must extend the knowledge of this physiological response both in healthy subjects and in patients, which might be influenced by other factors as temperature (skin temperature), time of day, smoking, BMI (subclinical tendinosis), diabetes, etc.

Key words: Achilles tendon, color fraction, Doppler, eccentric exercise, hyperemia, tendinosis.

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