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Real-time sonoelastography and ultrasound evaluation of the Achilles tendon in patients with diabetes with or without foot ulcers: a cross sectional study

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ABSTRACT

Background: Diabetes mellitus (DM) is an endocrine disease characterized by metabolic abnormalities and long-term complications. The Achilles tendon (AT) plays an important role in foot biomechanics. We aimed to investigate the effect of DM on the Achilles tendon, which may contribute to long-term complications in the foot–ankle complex.
Methods: Seventy-eight patients with diabetes, with (35 patients, group I) or without (43 patients, group II) foot ulcers were recruited from the endocrinology clinic. Thirty-three age-, gender-, and BMI-matched healthy individuals were selected as controls. All participants underwent ultrasonography and sonoelastography of their AT in order to evaluate Achilles tendon thickness (ATT) and stiffness (ATS). Each patient was also tested for fasting plasma glucose (FPG) and glycosylated hemoglobin (HbA1C) as a measure of diabetes control. Other chronic complications were also evaluated in all patients with diabetes.
Results: The AT was significantly thicker in group I compared to group II and the controls. HbA1C, FPG, and duration of diabetes were higher in group I. We observed that ATT was positively correlated with neuropathy, retinopathy, nephropathy, peripheral arterial disease and coronary arterial disease in group II while this correlation was not detected in group I. ATS was reduced in group I more than group II and control groups.
Conclusion: Changes in the structure of the AT may precede foot ankle disorders in patients with diabetes. This is the first study that reported the results of sonoelastosonography of AT in patients with diabetes and revealed the correlation between ATT and other chronic complications of diabetes.
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1. Introduction

Diabetes mellitus (DM) is a diffuse endocrine disease characterized by metabolic abnormalities and long-term complications. Non-enzymatic glycation of proteins plays an important role in the development of complications in DM (Mentink, Hendriks, Levels, & Wolffenbuttel, 2002).

The Achilles tendon (AT) is the strongest, largest, and thickest tendon in the human body (Schweitzer & Karasick, 2000), and plays an important role in foot biomechanics. It absorbs mechanical shock, stabilizes the longitudinal arch during propulsion, and prevents its collapse during landing. There is increasing evidence that static stiffness of the Achilles tendon may be in part responsible for the increased forefoot loading that might initiate the pathologic process which causes foot ulcers (Rao, Saltzman, Wilken, & Yak, 2006; Salsich et al., 2005; Trevino, Buford, Nakamura, John Wright, & Patterson, 2004). Nonenzymatic glycation of proteins provided by hyperglycemia results in accumulation of glycosylated end-products in most human tissues, containing muscles, cartilage, tendons and ligaments (Mentink et al., 2002). AT thickness is increased in subjects of type 1 and type 2 diabetes, mainly in those with peripheral neuropathy (Akturk, Ozdemir, Maral, Yetkin, & Arslan, 2007; Batista et al., 2008; Papanas et al., 2009). Foot disease of diabetes is a combination of neuropathy, deformity, ischemia and increased susceptibility to infection.

Determining changes of the Achilles tendon is relatively easy due to its size and location, where there may be early manifestation of some long-term complications in the foot–ankle complex of patients with diabetes. Sonoelastography (SE) is a relatively new ultrasound-based imaging technique that provides information on the elastic properties and stiffness of various tissues and lesions (Garra, 2011). It has found numerous clinical applications and widespread use in the diagnosis and assessment of thyroid nodules; mass lesions of breast,

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and lymph nodes; liver diseases; and many other disorders (Alam et al., 2008; Bojunga et al., 2010; Carstensen, Parker, & Lerner, 2008; Gong et al., 2011). However, the clinical utility of this method has been infrequently studied in musculoskeletal disorders and has not been studied in diabetic patients (McNally, 2011). Achilles tendon's superficial location makes it attainable to many types of ultrasound examinations (Dong & Fessell, 2009). Real-time SE provides useful information concerning the consistency of the tendons and can complete the information obtained on B-mode ultrasound (Drakonaki, Allen, & Wilson, 2009; Palle, Reddy, Reddy, & Kumari, 2011). In the color-coded images of the SE method normal tendon architecture appears hard and is pointed by shades of blue and green, whereas pathological alterations decrease the stiffness of the tendon and are pointed by shades of yellow or red for moderate or severe softening respectively (Drakonaki et al., 2009).

Here we evaluated Achilles tendon thickness and stiffness in patients with type 2 diabetes mellitus with or without foot disease and investigated the factors that influence these.

2. Material and methods

This study was conducted in the endocrinology and the radiology departments of our university hospital. Patients with diabetes admitted to diabetes clinics between July 2012 and December 2014 were enrolled. Thirty-five diabetic patients with foot ulcers applied to our clinic in this time period. Informed written consent was obtained from all subjects prior to their enrollment, and our local ethical committee approved the study protocol.

Seventy-eight patients with type 2 diabetes recruited from the outpatient clinics served as the study group and were divided in two subgroups according to presence of foot ulcers. Those with ulcers were defined as group I (35 cases), and those without ulcers were defined as group II (43 cases). Thirty-three age-, gender-, and body mass index (BMI)-matched healthy individuals were selected among hospital staff and served as controls. History of rheumatic disease, acromegaly, trauma, and tendinitis in the Achilles tendon were the exclusion criteria.

The diagnosis of diabetes was based on medical history and current treatment. In all subjects, demographic data (age, sex), anthropometric measures (height, weight, and BMI), duration of diabetes, and drugs that were being used were recorded. In the study group, fasting blood glucose (FBG) and glycosylated hemoglobin (HbA1c) were determined. Drugs that patients with diabetes used are grouped as: no drug for new diagnosis, oral anti diabetics (OAD), insulin, and insulin plus OAD.

Urinary albumin excretion over 30 mg/day was accepted as a clinical evidence of nephropathy (Molitch et al., 2004). Evaluation of micro-albuminuria was performed by measurement of the albumin-to-creatinine ratio in random spot urine collection on three different days. If the first two microalbumin measurements were below or higher than 30-mg/g creatinine, then the third determination was not conducted. If two out of three measurements were higher than 30-mg/g creatinine, then this was accepted as evidence of nephropathy.

An ophthalmologist evaluated each patient for presence of retinopathy of diabetes with fundoscopic examination. We questioned for complaints to assess the existence of peripheral neuropathy in addition to using the Semmes–Weinstein 5.07 (10 g) monofilament test. All participants were questioned for hypertension, peripheral arterial disease, and coronary artery disease. Resting blood pressure of normotensive subjects was measured using a sphygmomanometer for confirmation. We assessed peripheral arterial disease by Doppler ultrasonography for group I. In group II and the control group, Doppler ultrasonography was performed only in patients with a positive symptom for or history of peripheral artery disease. We categorized the other patients as having no peripheral arterial diseases. Osteomyelitis was investigated for group I by magnetic resonance imaging.

All sonographic examinations were performed with a real-time sonoelastographic scanner (HI Vision Avius, Hitachi Medical, Japan) and a linear-array transducer with a frequency of 5–13 MHz by one experienced radiologist.

Each Achilles tendon was examined in axial and longitudinal planes in prone position with the foot hanging over the examination bed in a relaxed position. The Achilles tendon was divided into the following three parts: proximal third (musculotendinous junction), middle third (2–6 cm above from insertion of calcaneus) and distal third (insertion at the calcaneus) (De Zordo et al., 2009). The anteroposterior diameters of each third were measured in transverse scans. Real-time sonoelastographic images of the tendon were obtained in the longitudinal plane while the transducer was perpendicular to the tendon in order to avoid tissue shifting. Local strain was calculated under slight compression and decompression applied using a free-hand technique. The optimal strain was assessed according to the visual indicator for compression seen on the video screen, which indicates the average strain in the region of interest between two frames. The tissue elasticity distribution was calculated in real-time, and the results were represented on a color map superimposed on the B-mod image. The spectrum of color ranged from blue (hard) to red (soft) and represented the relative stiffness of the tissue. The reliability of this technique was shown in previous studies mentioned above. At least three real-time sonoelastography images of each tendon third were recorded to the hard disc of sonoelastography scanner. After all data of the individuals were collected, the images were assessed, and the most representative one was chosen for image interpretation; the definition of elastographic patterns were then assessed by two radiologists in consensus who were blind to the group of participants.

The elasticity of tendons was divided into two main types: type 1 blue/green (hard tissue) and type 2 yellow/red within green (intermediate-soft tissue). In addition, two subtypes of these types were defined: type 1a blue predominance, type 1b green predominance, type 2a small yellow/red areas within green predominance, and type 2b small green areas within yellow-red predominance. According to the definition, the elasticity of the tissue was in a spectrum ranging from hard to soft as the type progresses from 1a to 2b (Fig. 1).

2.1. Statistical analysis

Statistical analysis was performed using the SPSS 20 software package. Normal distribution of data was evaluated by the Kolmogorov–Smirnov test. Kruskall–Wallis H test, chi square test, Fisher's chi square test, and analysis of variance (ANOVA) were performed, and the results were expressed as mean ± standard deviation. The significant level was determined as $p < 0.05$.

3. Results

All demographic characteristics of groups are demonstrated in Table 1. There was no statistically significant difference between the groups in terms of gender (M:F ratio), age, BMI, height, and weight ($p > 0.05$). Insulin usage was higher in group I than in group II. In 34.3% of the patients, foot ulcers were present in the right foot, and in 42.9%, the left foot was involved. Bilateral involvement was present in 22.9% of all subjects. Osteomyelitis was detected 42.9% of the patients in group I. An antibiotic (penicillin or cephalosporin and ciprofloxacin) was used in 80% of the cases in group I, while there was no antibiotic use in group II or the control group. Retinopathy, nephropathy, and neuropathy were higher in group I than group II ($p < 0.001$). Hypertension frequency was similar in two subgroups of diabetes ($p = 0.487$). Coronary arterial disease ($p = 0.037$) and peripheral arterial disease ($p < 0.001$) were more common, and HbA1c and FPG were higher in group I.

There was no statistically significant difference in the average values of the left and right ATT and ATS between group I, group II, and the control group ($p > 0.05$) (Tables 2–3). For this reason, the average

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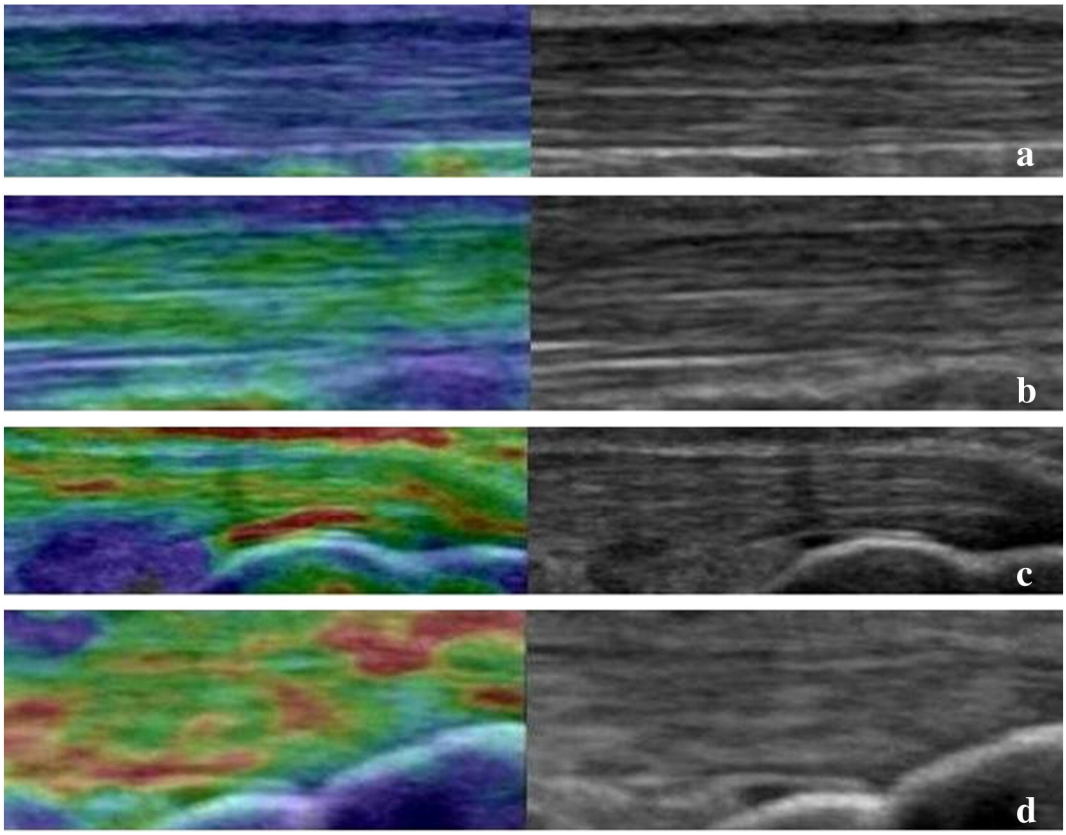


Fig. 1. The elasticity of tendons by sonoelastography. (a) Type 1a blue predominance; (b) type 1b green predominance; (c) type 2a small yellow/red areas within green predominance; (d) type 2b small green areas within yellow–red predominance. The elasticity of the tissue was in a spectrum ranging from hard to soft as the type progresses from 1a to 2b.

Table 1
Patients' baseline characteristics.

	Control	Group II	Group I	p-value
Age	57.1 ± 11.4	55.7 ± 9.3	59.3 ± 10	0.895
Gender				
F	23 (69.7)	24 (55.8)	17 (48.6)	
M	10 (30.3)	19 (44.2)	18 (51.4)	0.190
Height	162.0 ± 7.1	163.8 ± 10.1	164.1 ± 8.4	0.653
Weight	69.9 ± 10.4	70.4 ± 15.8	69.1 ± 16	0.503
BMI	26.6 ± 3.3	26.5 ± 6.6	25.7 ± 6.1	0.611
Diabetes duration		6 (0.3–30)	15 (0.3–40)	0.004*
Treatment				
No drug	33 (100)	4 (9.3)	2 (5.7)	
OAD	0 (0)	24 (55.8)	7 (20)	
Insulin	0 (0)	7 (16.3)	23 (65.7)	<0.001*
Insulin + OAD	0 (0)	8 (18.6)	3 (8.6)	
Foot ulcers				
Right	–	–	12 (34.3)	
Left	–	–	15 (42.9)	
Bilateral	–	–	8 (22.9)	
Osteomyelitis	–	–	15 (42.9)	
Antibiotic	–	0 (0)	28 (80)	<0.001*
HbA1C	–	7.9 ± 1.9	10.4 ± 2.1	<0.001*
FPG	–	164 ± 56.9	263.8 ± 92.5	<0.001*
Retinopathy	–	13 (30.2)	27 (77.1)	<0.001*
Nephropathy	–	4 (9.3)	21 (60)	<0.001*
Neuropathy	–	12 (27.9)	33 (94.3)	<0.001*
Hypertension	–	26 (60.5)	24 (68.6)	0.487
CAD	–	9 (20.9)	15 (42.9)	0.037*
PAD	–	1 (2.3)	18 (51.4)	<0.001*

* $p < 0.05$, group II, patients with diabetes without foot ulcer; group I, patients with diabetes with foot ulcers; BMI, body mass index; F, female; M, male; OAD, oral antidiabetic drugs; HbA1C, glycated hemoglobin; FPG, fasting plasma glucose; CAD, coronary arterial disease; PAD, peripheral arterial disease.

thickness and stiffness of the left and right Achilles tendon measurements were conducted to measure a possible difference (or any correlation) in between those groups.

Proximal, medial, and distal third of ATT values were significantly higher in group I than in group II and the control group ($p = 0.029$, $p < 0.001$, $p < 0.001$ respectively) (Table 4). In group II, the values were higher than the control group, but the difference was not significant.

Stiffness of proximal third of the Achilles did not differ between the groups. Stiffness of medial and distal third of the Achilles reduced significantly in group I; namely, it was softer (Fig. 2). Medial and distal thirds of the Achilles in group II and the control group were similar and harder than group I (Table 4).

Site of the foot ulcers did not affect ATT and ATS (Table 5). Medial and distal third of ATT values were increased by age ($r = 0.419$, $p = 0.001$; $r = 0.417$, $p = 0.001$ respectively) and BMI ($r = 0.224$, $p = 0.04$; $r = 0.253$, $p = 0.016$ respectively) in the control group, while the

Table 2
Left and right ATT measurements in group I, group II and control groups.

ATT	Side	Control		Group II		Group I	
		Value	p	Value	p	Value	p
Medial	Right	4.2 ± 0.6	0.066	4.5 ± 0.7	0.217	5.2 ± 0.8	0.999
	Left	4.5 ± 0.7		4.7 ± 0.6		5.2 ± 0.6	
Distal	Right	4.1 ± 0.6	0.442	4.5 ± 0.8	0.539	5.4 ± 1.9	0.519
	Left	4.2 ± 0.6		4.6 ± 0.7		5.2 ± 0.7	
Proximal	Right	1.8 ± 0.3	0.999	1.8 ± 0.3	0.241	1.9 ± 0.3	0.491
	Left	1.8 ± 0.2		1.9 ± 0.4		2.0 ± 0.8	

Group II, patients with diabetes without foot ulcer; group I, patients with diabetes with foot ulcers; ATT, Achilles tendon thickness.

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Table 3
Left and right ATS measurements in group I, group II and control groups.

ATS	Side	Control			Group II			Group I		
		1a–b	2a–b	p	1a–b	2a–b	p	1a–b	2a–b	p
Medial	Right	26 (78.8)	7 (21.2)	0.997	29 (67.4)	14 (32.6)	0.215	14 (40.0)	21 (60.0)	0.987
	Left	25 (75.8)	8 (24.2)		35 (81.4)	8 (18.6)		13 (37.1)	22 (62.9)	
Distal	Right	12 (36.4)	21 (63.6)	0.173	15 (34.9)	28 (65.1)	0.999	6 (17.1)	29 (82.9)	0.596
	Left	6 (18.2)	27 (81.8)		15 (34.9)	28 (65.1)		4 (11.4)	31 (88.6)	
Proximal	Right	32 (97.0)	1 (3.0)	0.992	42 (97.7)	1 (2.3)	0.991	32 (91.4)	3 (8.6)	0.999
	Left	33 (100)	0		43 (100)	0		32 (91.4)	3 (8.6)	

Group II, patients with diabetes without foot ulcer; group I, patients with diabetes with foot ulcers; ATS, Achilles tendon stiffness.

proximal third did not change. In group II, age, existence of nephropathy, retinopathy, neuropathy, higher FPG and HbA1C values, and prevalence of CAD and PAD were correlated with medial and distal third ATT. In group I, those variables were not correlated with ATT. Existence of osteomyelitis and antibiotic usage did not affect ATT and ATS measurements. Variables did not affect the proximal third of the Achilles tendon thickness and stiffness. Medial third of the Achilles tendon was softer in patients with longer duration of diabetes, use of insulin rather than OAD, and presence of foot ulcers regardless of the site, with neuropathy or PAD. Only the existence of neuropathy made the distal third of Achilles tendon softer.

4. Discussion

Some studies have proposed a relationship between tendinopathy and diabetes mellitus. Tendinopathy is characterized by a thickening of peritendinous tissue and expression of fibrinous exudate, prominent and widespread proliferation of fibroblasts and composition of new connective tissue and adhesions. These changes increase tendons' thickness, making the measurement of thickness an important indicator of tendinopathy (Paavola et al., 2002). Increased thickness of ligaments of the most distal parts of the body has long been observed in patients with diabetes. This study is programmed to assess the thickness and stiffness of Achilles tendons of diabetic patients. Giacomozzi et al. demonstrated that the Achilles tendon was thicker in patients with diabetes than in controls (Giacomozzi, D'Ambrogi, Uccioli, & Macellari, 2005). Thickening of the Achilles tendon became statistically significant for patients with neuropathy and with previous neuropathic ulcers compared to the control group. Cheing et al. showed that patients with diabetes with or without neuropathy had a thicker Achilles tendon than the healthy controls (Cheing, Chau, Kwan, Choi, & Zheng, 2013). The studies by Akturk et al. and Papanas et al. also demonstrated increased thickness of the Achilles tendon, under the condition that this difference was found only among women (Akturk et al., 2007; Papanas et al., 2009). The results provided by Batista et al. did not support the studies presented above; they demonstrated thinning of the tendons of the diabetic group (Batista et al., 2008). In our study, the results were similar to the study of Giocomozzi et al. However, in contrast to the study by Giocomozzi et al., our patients had current foot ulcers, while patients of their study had previous neuropathic ulcers. Patients with diabetes and previous history of ulceration occupy the highest category of risk for reulceration (Miller, Salloum, Button, Giovinco, & Armstrong, 2014). Because of the similarity between our study group with current ulcers and the group of patients with diabetes with previous neuropathic ulcers involved in Giocomozzi et al.'s study, the results may not be accidental. It has been hypothesized that the non-enzymatic glycation of the collagenous component due to the hyperglycemia contributes to this thickening (Palastanga, Field, & Soames, 1989; Sarrafian, 1993), as well as the increase in the mechanical load on the foot resulting from the higher body mass commonly noted in people with DM (Cheing et al., 2013; Duffin, Lam, Kidd, Chan, & Donaghue, 2002). In our study, BMI of the groups were similar. BMI and ATT was correlated only in the control group, while in other groups, this significance was lost. Abate et al. showed that the pathogenic role of diabetes was independent from body weight (Abate, Salini, Antinolfi, & Schiavone, 2014). Indeed, an increased prevalence of asymptomatic sonographic abnormalities was found in subjects with higher BMI (both patients and controls), but only in patients with diabetes with BMI values in the normal range (Abate, Schiavone, & Salini, 2010).

Table 4
Comparison of ATT and ATS measurements in group I, group II and control groups.

		Controls	Group II	Group I	p
ATT	Proximal	1.8 ± 0.2	1.9 ± 0.3	2.1 ± 0.8	0.029*
	Medial	4.5 ± 0.7	4.7 ± 0.6	5.2 ± 0.6	<0.001*
	Distal	4.2 ± 0.6	4.6 ± 0.7	5.2 ± 0.7	<0.001*
	Proximal				
ATS[1]	2a–b	1 (3)	1 (2.3)	3 (8.6)	0.37
	1a–b	32 (97)	42 (97.7)	32 (91.4)	
	Medial				
	2a–b	8 (24.2)	8 (18.6)	22 (62.9)	<0.001*
	1a–b	25 (75.8)	35 (81.4)	13 (37.1)	
	Distal				
	2a–b	21 (63.6)	28 (65.1)	29 (82.9)	0.027*
	1a–b	12 (36.4)	15 (34.9)	6 (17.1)	

* $p < 0.05$; group II, patients with diabetes without foot ulcer; group I, patients with diabetes with foot ulcers; ATT, Achilles tendon thickness; ATS, Achilles tendon stiffness.
[1] According to the definition, the elasticity of the tissue was in a spectrum ranging from hard to soft as the type progresses from 1a to 2b.

The differences in results among the articles can be associated with the lack of a standardized assessment protocol, because the studies did not standardize the location for measurement of the thickness of tendon (de Oliveira, Lemos, de Castro Silveira, da Silva, & de Moraes, 2011). In most of the studies about ATT, thickness was measured at the insertion part of the posterior calcaneus (distal third) (Akturk et al., 2007; Cheung, Zhang, & An, 2006; D'Ambrogi, Giacomozzi, Macellari, & Uccioli, 2005; de Jonge et al., 2015; Giacomozzi et al., 2005). In some studies, only the medial third of the Achilles tendon was assessed (Abate, Schiavone, Di Carlo, & Salini, 2012). In our study, we measured the medial, distal, and also proximal third of the Achilles tendon. There is only one study that evaluates asymptomatic sonographic abnormalities along the full length of Achilles tendon (Abate et al., 2014). To the best of our knowledge, this is the first study in which all three thirds of the Achilles tendon thickness in patients with diabetes was measured. ATT of all three parts increased in the group of patients with foot ulcers more than the ones without ulcers and the control group.

D'Ambrogi et al. showed that thickening of Achilles tendon was more evident in the presence of neuropathy but already detectable in patients with diabetes without neuropathy (D'Ambrogi et al., 2005). Akturk et al. observed that the ATT levels of male DM patients with retinopathy or neuropathy were significantly higher than male DM patients without retinopathy or neuropathy (Akturk et al., 2007). However such a statistically significant relationship was not demonstrated between the ATT and nephropathy or carotid plaque neither

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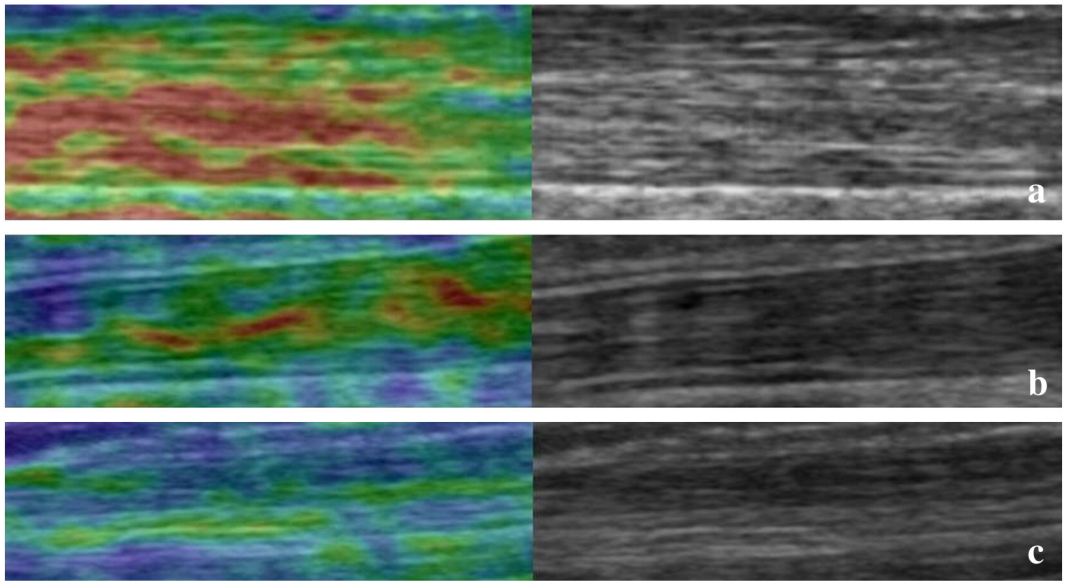


Fig. 2. Sonoelastography and ultrasound images of medial third of the Achilles tendon. (a) Images of a patient from group I, Achilles tendon thickness is 5.5 mm, the elasticity of tendon is 2b (b) images of a patient from group II, Achilles tendon thickness is 4.3 mm, the elasticity of tendon is 2a (c) images of an individual from control group, Achilles tendon thickness is 3.6 mm, and the elasticity of tendon is 1b.

for male nor female diabetic patients. Kiortsis et al. showed that Achilles tendon thickening was associated with peripheric atherosclerosis (Kiortsis, Argyropoulou, Xydis, Tsouli, & Elisaf, 2006). Nomura et al. observed that Achilles tendon thickness was correlated with coronary arterial disease in a patient with diabetes (Nomura et al., 1992). Hirobe et al. showed that the Achilles tendon was thicker in patients with CAD than in those without CAD, both for males and females (Hirobe et al., 1982). In our study, existence of nephropathy, retinopathy, neuropathy, CAD, and PAD were positively correlated with medial and distal third of Achilles tendon thickness in those without foot ulcers, while thickness of proximal third of Achilles tendon was not correlated with those parameters. Any of these correlations were not detected in patients with diabetes with foot ulcers. We are not aware of any pathological mechanisms that could affect the ATT and these complications at the same time and also which one occurred first. For now we cannot explain why there is no relation between complications and ATT of diabetic patients with foot ulcers while there is a positive correlation for the other diabetic patients. Therefore, this study could lead to other prospective studies on this particular relation.

Table 5
Site of the foot ulcers and right, left ATT and ATS.

		Patients with diabetes with foot ulcers			p
		Right	Left	Bilateral	
Right ATT	Proximal	2.0 ± 0.4	1.9 ± 0.3	1.9 ± 0.3	0.441
	Medial	5.2 ± 0.7	5.3 ± 0.8	5.1 ± 0.8	0.848
	Distal	5.1 ± 0.8	5.2 ± 0.7	5.1 ± 0.7	0.950
Left ATT	Proximal	2.4 ± 0.4	1.9 ± 0.3	2.1 ± 0.5	0.205
	Medial	5.3 ± 0.4	5.3 ± 0.7	4.9 ± 0.5	0.274
	Distal	5.2 ± 0.8	5.1 ± 0.7	5.3 ± 0.7	0.915
Right ATS	Proximal				
	2b	0 (0)	1 (6.7)	1 (12.5)	0.126
	2a	1 (8.3)	0 (0)	0 (0)	
	1b	2 (16.7)	6 (40.0)	5 (62.5)	
	1a	9 (75.0)	8 (53.3)	2 (25.0)	
	Medial				
	2b	0 (0.0)	1 (7.1)	1 (14.3)	0.473
	2a	6 (50.0)	9 (64.3)	2 (28.6)	
	1b	5 (41.7)	4 (28.6)	3 (42.9)	
	1a	1 (8.3)	0 (0.0)	1 (14.3)	
	Distal				
	2b	2 (16.7)	0 (0)	2 (28.6)	0.094
	2a	6 (50.0)	12 (85.7)	5 (71.4)	
	1b	4 (33.3)	2 (14.3)	0 (0)	
	1a	0 (0)	0 (0)	0 (0)	
Left ATS	Proximal				
	2b	0 (0)	0 (0)	0 (0)	0.197
	2a	0 (0)	0 (0)	1 (14.3)	
	1b	1 (8.3)	4 (28.6)	2 (28.6)	
	1a	11 (91.7)	10 (71.4)	4 (57.1)	
	Medial				
	2b	0 (0.0)	2 (14.3)	1 (14.3)	0.36
	2a	5 (41.7)	8 (57.1)	4 (57.1)	
	1b	4 (33.3)	4 (28.6)	2 (28.6)	
	1a	3 (25.0)	0 (0.0)	0 (0.0)	
	Distal				
	2b	3 (25.0)	1 (7.1)	2 (28.6)	0.571
	2a	7 (58.3)	11 (78.6)	5 (71.4)	
	1b	2 (16.7)	2 (14.3)	0 (0)	
	1a	0 (0)	0 (0)	0 (0)	

ATT, Achilles tendon thickness; ATS, Achilles tendon stiffness.

Batista et al. showed that patients with a disorganized Achilles tendon pattern had an 11.5 ± 1-year duration of disease, while those with an organized pattern had a 6.3 ± 2-year duration of disease (Batista et al., 2008). But this difference was not significant. Cronin et al. observed that Achilles tendon length changes during walking were attenuated in long-term diabetic patients compared to control subjects. Stretch distribution between muscle and tendon during walking is altered in diabetic patients, which could decrease walking efficiency, a factor that may be exacerbated with increasing diabetes duration (Cronin et al., 2010). In our study duration of diabetes of group I and II was different. But the effect of diabetes duration was not significant on ATT. Only medial third of the Achilles tendon was softer in patients with longer duration of diabetes. Our results may demonstrate a possible effect of diabetes duration on ATS. There is a need for further studies to investigate this relationship.

This is the first study that the stiffness of Achilles tendons of patients with diabetes is evaluated by elastosonography. Guney et al. evaluated biochemical parameters of diabetic and non-diabetic Achilles tendons and observed decreasing of the stiffness and elasticity of diabetic tendons (Guney et al., 2015). In this study, medial third of the Achilles tendon was softer in patients with longer duration of diabetes, or patients using insulin instead of OAD, having foot ulcers regardless of the site, or having neuropathy or PAD. Only neuropathy made the distal third of the Achilles tendon softer, while no variants affected the proximal third. Stiffness of the proximal third

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did not differ between groups as it did in the study performed by Turan et al. (De Zordo et al., 2010; Turan et al., 2013). As showed by Tan et al., the proximal third of the tendon was more likely to have a stiff pattern as compared to middle and distal portions (Tan et al., 2012). There is no study that evaluates the relationship between PAD, neuropathy and Achilles tendon stiffness.

Sonoelastography is ultrason-based, so it has methodological limitations as found in any other ultrason-based techniques. We did our best to avoid potential problems by performing standard recommendations, including extensive training, before commencing the study (Havre et al., 2008). Two highly experienced sonoelastography examiners practiced the elastography. Finally the histological verification of SE findings was lacking. However we do not think that it is a major limitation, since as previously shown, SE has perfect correlation with histological examination (Klauser et al., 2013).

In conclusion, patients with diabetes with foot ulcers have a softer and thicker AT than the other patients with diabetes and healthy controls. This is the first reported study researching sonoelastosonography of Achilles tendon of patients with diabetes. These changes may be important on the development and progression of foot ulcers. Further studies are warranted to investigate diabetes mellitus and Achilles tendon stiffness.

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