ORIGINAL ARTICLE

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Correlates of the Ultrasonographic and Elastosonographic Parameters of the Plantar Fascia in Patients with Type 2 Diabetes

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SUMMARY

Background. Prevalence of plantar fasciitis is increased in type 2 diabetes. This study was aimed at assessing the correlates of ultrasonographic and elastosonographic parameters in plantar fascia (PF) individuals with type 2 diabetes encompassing various degrees of complications.

Methods. This cross-sectional study included 98 patients with type 2 diabetes. Thickness of PF was assessed by ultrasonography, whereas elasticity of hard tissue (Elx-Hrd) at PF insertion and course and the subcutaneous-to-insertional strain ratio (Elx 2/1) were determined by elastosonography.

Results. No significant differences were detected according to age category, sex, physical activity, and presence of complications, except for higher Elx-Hrd insertion and Elx 1/2 in participants with cardiac autonomic neuropathy (CAN). Thickness of PF, Elx-Hrd insertion and Elx 1/2 correlated significantly with BMI, waist circumference, fat-free mass, and parameters of peripheral neuropathy and CAN; BMI, waist circumference, fat mass, fat-free mass, and CAN were independently associated with PF thickness, Elx-Hrd insertion, and Elx 1/2.

Conclusions. Adiposity, body composition and presence of CAN are the main correlates of PF ultrasonographic and elastosonographic parameters, suggesting that body weight reduction, maintenance of muscle mass, and prevention of neuropathic complications may result in a decreased incidence of plantar fasciitis in individuals with type 2 diabetes.

Study registration. Study registered with ClinicalTrial.gov, NCT01600924 at https://clinicaltrials.gov/ct2/show/NCT01600924.

KEY WORDS

Body mass index; cardiac autonomic neuropathy; elastosonography; plantar fasciitis; ultrasonography.

INTRODUCTION

Diabetes mellitus is associated with multiple long-term complications, including musculoskeletal disorders (1), the most common of which are the frozen shoulder, rotator cuff tears, Dupuytren's contracture, trigger finger, and cheiroarthropathy for the upper limbs and the Achilles' tendinopathy, heel spurs, and plantar fasciitis for the lower limbs (2). In particular, the prevalence of plantar fasciitis was found to be significantly higher in patients with type 2 diabetes (1.31%) than in those with type 1 diabetes (0.92%) or in non-diabetic controls (0.80%) (3). The predisposing effect of diabetes toward the development of plantar fasciitis may be related to the increased formation of advanced glycation end-products (AGEs) that induce collagen crosslinking, leading to altered collagen structure and secondary mechanical dysfunction (4). Moreover, neuropathic complications cause pathological distribution of plantar pressure on the foot, which is associated with an increased incidence of foot ulcers and might also favor the development of plantar fasciitis (5). However, as diabetes and plantar fasciitis share common comorbidities and risk factors such as obesity and sedentary lifestyle, it is unclear whether there is a cause-effect relationship between the two (3).

Diagnostic procedures for plantar fasciitis include magnetic resonance imaging and ultrasound evaluation (6). Ultrasonography has been shown to be effective for differentiating normal *versus* diseased plantar fascia (PF) (7) on the basis of higher thickness (usually > 4.0 mm), lower echogenicity, and perifascial edema (8), which reflect the morphological changes of the PF (9), though these findings are not invariably detected and are not apparently correlated with pain (10). Real-time elastonography is a recently developed non-invasive ultrasound technique with higher sensitivity and specificity than ultrasonography in detecting plantar fasciitis (11, 12) and other conditions such as degenerative Achilles' tendinopathy (13, 14) and lateral epicondylitis (15), and plantar fasciitis (12). It uses ultrasound to qualitatively and quantitatively assess structural and biomechanical features of PF, such as "elasticity" (16), and could therefore be useful for detecting PF tissue change induced by diabetes through the above mechanisms.

This study aimed at assessing the correlates of PF ultrasononographic and elastosonographic parameters in individuals with type 2 diabetes encompassing various degrees of micro and macrovascular complications.

MATERIALS AND METHODS

Patients

Ninety-eight consecutive Caucasian patients with type 2 diabetes (39 females, 59 males, aged 69.3 ± 9.7 years) attending the yearly follow-up visit for the Study on the Assessment of determinants of Muscle and Bone strength Abnormalities in diabetes (SAMBA) between January 2021 and December 2021 were considered for this cross-sectional analysis. The SAMBA is an observational, prospective, cohort study, aimed at assessing the independent correlates of impaired muscle and bone strength in diabetic patients with and without micro and macrovascular complications. The study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments and meets the ethical standards of the journal. The research protocol was approved by the locally appointed ethics committee and participants gave written informed consent (Protocol n. 784/2012 - Date of approval: September 24, 2012).

According to the SAMBA protocol, traditional cardiovascular risk factors and a variety of measures of complications were assessed in study participants by the use methods that were previously described (17) and are partly reproduced here; in addition, for the purpose of the current analysis, patients underwent also an ultrasonographic and elastosonographic evaluation of PF.

Measurements

Ultrasonography and elastosonography of PF

Conventional B-mode ultrasonographic evaluation of the PF was performed by a physiatrist with a > 3-year experience using a high-resolution 4-15 MHz linear-array transducer (MyLabOmega; Esaote, Genoa, Italy), according to the European Society of Musculoskeletal Radiology guidelines (18). The PF was evaluated at the insertional region and along its course and the operator measured the maximum thickness at the calcaneal enthesis.

Real-time elastosonographic images were then obtained by applying light rhythmic pressure with the probe and recorded on the ultrasonographic machine (12). Transducer pressure was applied horizontally, keeping the probe perfectly perpendicular to the PF to reduce any bias related to anisotropy, and was adjusted according to the real-time visual marker for compression shown on the screen (a grey spring indicating insufficient or excessive tissue deformation, whereas a green spring indicates appropriate tissue deformation). The examiner tapped the tendon in the same place four times with a small and regular pressure: this external pressure generates a change in the structural shape of the PF that the probe detects as elastographic information. Depending on tissue deformability, one of four colors appears on the screen superimposed on the B-mode image: red for high stiffness, blue for intermediate stiffness and green for low stiffness. Following acquisition of all the images, each elastogram was subsequently processed with

the ElaXTo software, in order to quantitatively measure the percentage elasticity of hard tissue (Elx-Hrd). Windows with the same area (0.11 cm^2) were identified as region of interest (ROI) at the insertional region, that corresponds to the maximal PF thickness (Elx-Hrd insertion), in subcutaneous plantar tissue above the insertional area, and along the course of PF, at a distance of 4 cm from the calcaneal insertion (Elx-Hrd course). Another parameter detected was the Elx 2/1, *i.e.*, the strain ratio of subcutaneous ROI (zone 1) and the insertional PF ROI (zone 2). The system in fact provides a measure of the relationship between the deformations of the tissues enclosed in the two ROIs. The resulting value is directly proportional to the greater deformability of the tissue enclosed in zone 2 compared to zone 1.

Risk factors for cardiovascular disease (CVD)

All patients underwent a structured interview in order to collect information about demographics, lifestyle habits, known diabetes duration, and current treatments. Regarding lifestyle habits, patients were classified as never, former or current smokers; and sedentary or non-sedentary (if spending > or < 8 hours/day, respectively, in a sitting, reclining or lying posture while awake) and/or physically inactive or active (if spending < or > 150 min/week, respectively, in moderate-to-vigorous physical activity) (19).

Body mass index (BMI) was calculated from body weight and height; waist circumference was measured at the umbilicus; and fat mass and fat-free mass were assessed by body impedance (Tanita BF664, Vernon Hills, IL, USA). Blood pressure (BP) was measured with a with a mercury sphygmomanometer with the patients seated with the arm at the heart level.

Hemoglobin (Hb) A_{1c} was assessed by a DCCT-aligned high-performance liquid chromatography method (Adams TMA1C HA-8160, Menarini Diagnostics, Florence, Italy). Fasting glucose, triglycerides, total and HDL cholesterol were measured by using the VITROS 5,1 FS Chemistry System (Ortho-Clinical Diagnostics, Inc, Raritan, NJ, USA) and LDL cholesterol was calculated by the Friedewald formula.

Complications

Prevalent CVD was assessed from medical history by recording previous documented major acute CVD events, including myocardial infarction, stroke, foot ulcer, gangrene and amputation, and revascularization procedures (20). In addition, carotid intima-media thickness (IMT) and ankle-brachial index (ABI) were assessed as surrogate measures of diabetic macroangiopathy by color-coded duplex sonography (Agilent HP ImagePoint HX, Hewlett Packard, Rome, Italy) and a mercury sphygmomanometer plus a handheld continuous wave Doppler device (Super Doppler 2, Huntleight Healthcare, Lewis Center, OH), respectively.

Diabetic kidney disease (DKD) was evaluated by assessing serum creatinine and albuminuria. Serum creatinine was measured by the modified Jaffe method, traceable to IDMS, and estimated glomerular filtration rate (eGFR) was calculated by the Chronic Kidney Disease Epidemiology Collaboration equation (http://www.qxmd.com/calculate-online/nephrology/ckd-epi-egfr). Albuminuria was assessed as urinary albumin:creatinine ratio (ACR) by measuring albumin and creatinine concentration by immunonephelometry and the modified Jaffe method, respectively, in first-morning, urine samples. Patients were then classified as having DKD based on an eGFR < 60 ml/min/1.73 m^2 and/or an ACR > 30 mg/g (20).

Diabetic retinopathy (DR) was evaluated by fundus examination in mydriasis. Patients were classified as having DR based on the presence of either non-proliferative DR, proliferative DR, or maculopathy (20).

Diabetic peripheral neuropathy (DPN) was assessed based on anamnestic, clinical and instrumental evaluation (17). Symptoms and signs of DPN were assessed using the Michigan Neuropathy Screening Instrument comprising a 15-item self-administered questionnaire and a lower extremity examination that includes foot inspection, assessment of vibration perception threshold (VPT) at hallux and ankle reflexes, and monofilament testing. The VPT in the left and right malleolus and hallux was assessed by the use of a biothesiometer (Horwell, Nottingham, UK). The distal latencies, amplitudes, and conduction velocities of the peroneal motor nerve (PMN) and sural sensory nerve (SSN) were measured bilaterally by electromyography (EMG), using a Medelec MS 928 Neurostar (Oxford Instruments Medical, Old Woking, UK), and results were compared with age-related reference values (21). Small fiber nerves were evaluated non-invasively by using Sudoscan™ (Impeto Medical, Paris, France), which assesses the function of sweat glands innervated by the peripheral nerve system by measuring electrochemical skin conductance (ESC) at feet and hands, with values < 60 µS considered abnormal (22). Patients were then classified has having DPN based on the presence of signs and symptoms of DPN, confirmed by neuro-electrophysiological and/or small fiber nerve abnormalities, according to the Toronto Diabetic Neuropathy Expert Group (23).

Cardiac autonomic neuropathy (CAN) was evaluated by Sudoscan™ (Impeto Medical), which also provides a CAN score, which reflects the degree of sympathetic and baroreceptor dysfunction and predicts subclinical CAN with a sensitivity of 83% and specificity of 63% (24).

Statistical analysis

Data are expressed as mean ± SD, for continuous variables, and number of cases and percentages for categorical

variables. Patients were stratified by age (below and above median), sex, PA level, and complications and PF parameters were compared using the Student t-test or one-way ANOVA for continuous variables and the c^2 test for categorical variables.

Univariate analysis of correlations between PF parameters and the variables tested was performed using Spearman's rho. Then, linear regression analyses with stepwise variable selection were applied to assess independent correlates of PF parameters. Covariates were age and sex plus smoking, PA level, diabetes duration, BMI (or waist circumference or fat mass plus fat-free mass), triglycerides, HDL and LDL cholesterol, and systolic and diastolic BP (model 1) or plus presence/absence of CVD, DKD; DR, DPN and CAN (model 2). All the above analyses were conducted using either the mean value of the right and left measure of each PF parameter or the lowest and highest value between the two.

All P-values were two-sided, and a $p < 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The clinical features of study participants are shown in **table I**. There was no significant difference between female and male patients, except for smoking habits, adiposity and body composition, lipid profile and selected neuro-electrophysiological measures.

Ultrasonographic and elastosonographic parameters of the PF tended to be higher in males than in females, though a significant difference was observed only for the lowest Elx 1/2 value (**table II**). Moreover, no difference was detected by age category, physical activity and presence of complications (not shown), except CAN; thickness (non-significantly), Elx-Hrd insertion, and Elx 1/ were in fact higher in participants with than in those without CAN (**figure 1**).

Upon univariate analysis (**table III**), the mean value of PF parameters correlated significantly between each other as well as with BMI and, except for Elx-Hrd course, waist circumference and fat-free mass, but not fat mass. In addition, the mean value of PF thickness correlated inversely with PMN and SSN amplitude, whereas the mean value of Elx-Hrd insertion correlated directly with VPT at malleolus and mean values of all parameters except thickness with CAN score.

Upon multivariable analysis (**table IV**), BMI (model 1) and CAN score (model 2) were independently associated with the mean value of PF thickness, Elx-Hrd insertion, and Elx ½. When substituted for BMI, waist circumference or fat mass and fat-free mass were also independently associated with the mean value of PF thickness, Elx-Hrd insertion, and Elx 1/2 (model 1) (not shown). In addition, male sex was an independent correlate of the mean value of PF thickness, Elx-Hrd insertion, and Elx 1/2 in model 1 and of the mean value of Elx-Hrd insertion and Elx 1/2 in model 2. Finally, an independent and inverse correlation was detected for triglycerides (model 1) and age (model 2) with the mean value of PF thickness and for DR (model 2) with the mean value of Elx-Hrd insertion.

Correlations did not change when using the lowest or the highest value of each PF parameter instead of the mean value (not shown).

Table I. Clinical features of study participants.

Variables	All (n = 98)	Females (n = 39)	Males (n = 59)	P-value
Age, years	69.3 ± 9.7	69.2 ± 11.3	69.3 ± 8.5	0.984
Smoking				0.016
Never	54 (55.1)	28 (71.8)	26 (44.1)	
Former	30 (30.6)	9 (23.1)	21 (35.6)	
Current	14 (14.3)	2 (5.1)	12 (20.3)	
Physical activity				0.136
Sedentary/physically inactive	18 (18.4)	9 (23.1)	9 (15.3)	
Non-sedentary/physically inactive	34 (34.7)	17 (43.6)	17 (28.8)	
Sedentary/physically active	10 (10.2)	4 (10.3)	6 (10.2)	
Non-sedentary/physically active	36 (36.7)	9 (23.1)	27 (45.8)	
Diabetes duration, years	16.7 ± 9.3	17.2 ± 9.0	16.4 ± 9.6	0.693
HbA_{1c}, %	6.84 ± 1.76	6.95 ± 1.82	6.80 ± 1.73	0.778
Fasting plasma glucose, mmol/l	8.05 ± 2.32	8.07 ± 2.40	8.04 ± 2.29	0.677
Post-prandial plasma glucose, mmol/l	145.1 ± 41.8	145.4 ± 43.3	144.9 ± 41.2	0.954

Variables	All (n = 98)	Females (n = 39)	Males (n = 59)	P-value
BMI, kg/m²	29.2 ± 5.6	30.6 ± 6.4	28.3 ± 4.8	0.046
Fat mass, %	30.4 ± 9.9	36.6 ± 9.3	26.3 ± 8.0	< 0.0001
Fat-free mas, Kg	55.4 ± 11.6	47.5 ± 9.0	60.6 ± 10.1	< 0.0001
Waist circumference, cm	102.8 ± 14.2	103.4 ± 14.7	102.4 ± 13.9	0.731
Triglycerides, mmol/l	1.68 ± 0.81	1.66 ± 0.80	1.70 ± 0.83	0.825
Total cholesterol, mmol/l	4.28 ± 1.03	4.64 ± 0.86	4.04 ± 1.06	0.004
HDL cholesterol, mmol/l	1.19 ± 0.26	1.28 ± 0.24	1.13 ± 0.25	0.004
LDL cholesterol, mg/dl	2.35 ± 0.89	2.57 ± 0.82	2.20 ± 0.91	0.044
Systolic BP, mmHg	136.8 ± 18.5	135.9 ± 19.4	137.4 ± 18.0	0.702
Diastolic BP, mmHg	75.9 ± 10.3	75.5 ± 10.7	76.2 ± 10.2	0.754
Carotid IMT, mm	1.17 ± 0.12	1.14 ± 0.12	1.19 ± 0.12	0.047
ABI	0.93 ± 0.13	0.94 ± 0.13	0.93 ± 0.13	0.592
CVD, n (%)				0.504
No	88 (89.8)	36 (92.3)	52 (88.1)	
Yes	10 (10.2)	3 (7.7)	7 (11.9)	
Serum creatinine, µmol/l	96.4 ± 26.5	91.1 ± 24.8	99.9 ± 27.4	0.093
eGFR, ml/min/1.73 m²	67.5 ± 17.9	66.5 ± 19.7	68.1 ± 16.8	0.679
ACR, mg/g	33.5 ± 71.7	20.8 ± 47.4	41.9 ± 83.4	0.156
DKD, n (%)				0.766
No	56 (57.1)	23 (59.0)	33 (55.9)	
Yes	42 (42.9)	16 (41.0)	26 (44.1)	
DR, n (%)				0.125
No	75 (76.5)	33 (84.6)	42 (71.2)	
Yes	23 (23.5)	6 (15.4)	17 (28.8)	
VPT malleolus, mV	22.4 ± 10.7	21.9 ± 11.0	22.8 ± 10.6	0.691
VPT hallux, mV	21.6 ± 10.9	22.1 ± 11.6	21.2 ± 10.6	0.698
PMN distal latency, m/sec	5.00 ± 0.69	4.74 ± 0.56	5.18 ± 0.71	0.002
PMN amplitude, mV	3.30 ± 1.40	3.52 ± 1.27	3.16 ± 1.48	0.214
PMN nerve conduction velocity, m/s	46.0 ± 4.0	47.0 ± 3.0	45.3 ± 4.5	0.039
SSN distal latency, m/sec	3.23 ± 0.64	3.20 ± 0.47	3.25 ± 0.74	0.706
SSN amplitude, mV	11.7 ± 5.4	13.6 ± 4.5	10.5 ± 5.6	0.005
SSN nerve conduction velocity, m/s	40.5 ± 11.0	44.2 ± 7.4	38.1 ± 12.3	0.006
ESC feet, micro/s	70.8 ± 14.9	71.6 ± 14.3	70.2 ± 15.4	0.665
ESC hands, micro/s	60.4 ± 15.6	61.1 ± 15.8	59.9 ± 15.6	0.717
Peripheral neuropathy, n (%)				0.087
No	55 (56.1)	26 (66.7)	29 (49.2)	
Yes	43 (43.9)	13 (33.3)	30 (50.8)	
CAN score, %	46.4 ± 13.0	48.1 ± 13.9	45.2 ± 12.4	0.297
CAN, n (%)				0.104
No	67 (68.4)	23 (59.0)	44 (74.6)	
Yes	31 (31.6)	16 (41.0)	15 (25.4)	

HbA_{1c}: hemoglobin A_{1c}; BMI: body mass index; BP: blood pressure; IMT: intima-media thickness; ABI: ankle-brachial index; CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; ACR: albumin:creatinine ratio; DKD: diabetic kidney disease; DR: diabetic retinopathy; VPT: vibration perception threshold; PMN: peroneal motor nerve; SSN: sural sensory nerve; ESC: electrochemical skin conductance; DPN: diabetic peripheral neuropathy; CAN: cardiac autonomic neuropathy.

Table II. Ultrasonographic and elastosonographic parameters of PF.

Variables	All	Females	Males	P-value
	(n = 98)	(n = 39)	(n = 59)	
Mean thickness, mm	3.97 ± 0.77	3.83 ± 0.81	4.06 ± 0.74	0.155
Lowest thickness, mm	3.74 ± 0.76	3.58 ± 0.76	3.85 ± 0.75	0.087
Highest thickness, mm	4.20 ± 0.85	4.09 ± 0.95	4.27 ± 0.78	0.291
Mean Elx-Hrd insertion, %	81.2 ± 12.5	78.8 ± 13.3	82.7 ± 11.8	0.130
Lowest Elx-% insertion, %	81.2 ± 12.5	78.8 ± 13.3	82.7 ± 11.8	0.130
Highest Elx-% insertion, %	75.9 ± 15.3	78.8 ± 13.3	82.7 ± 11.8	0.130
Mean Elx-% course, %	80.4 ± 11.8	80.3 ± 10.2	80.4 ± 11.4	0.947
Lowest Elx-% course, %	75.7 ± 12.8	75.6 ± 12.6	75.9 ± 13.1	0.909
Highest Elx-% course, %	85.4 ± 11.2	85.4 ± 10.1	85.4 ± 11.9	0.979
Mean Elx 1/2	4.27 ± 2.26	3.78 ± 1.86	4.60 ± 2.45	0.077
Lowest Elx 1/2	3.24 ± 1.74	2.74 ± 1.17	3.57 ± 1.97	0.020
Highest Elx 1/2	5.32 ± 3.26	4.84 ± 3.17	5.64 ± 3.30	0.241

PF: plantar fascia; Elx: elasticity; Hrd: hard tissue.

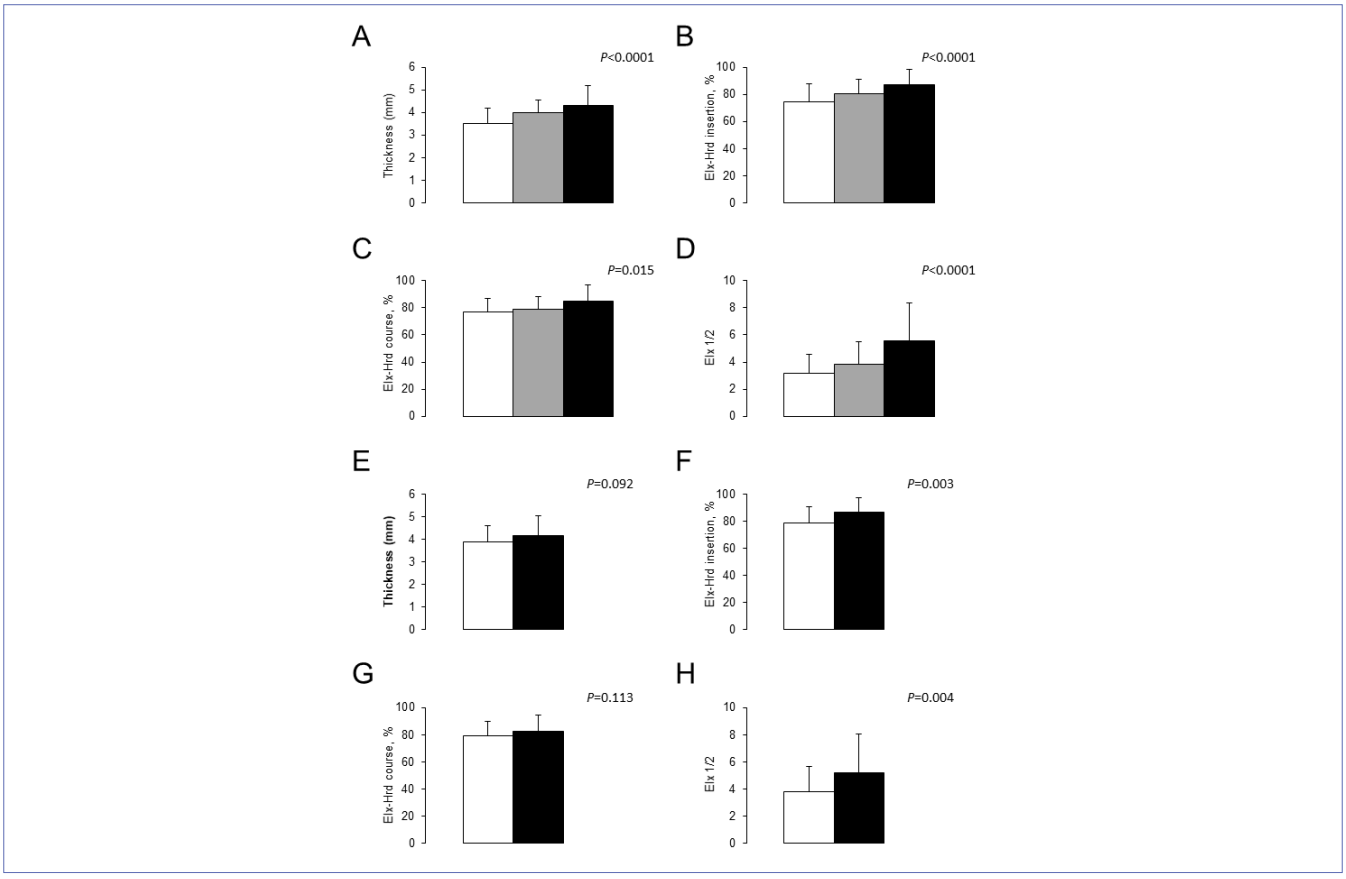

Figure 1. Ultrasonographic and elastosonographic parameters of PF by BMI category and presence of CAN. Mean thickness **(A, E)**, mean Elx-Hrd insertion **(B, F)**, mean Elx-Hrd course **(C, G)**, and mean Elx 1/2 **(D, H)** in normal-weight (white bar), overweight (grey bar) and obese (black bar) patients **(A-D)** and in those without (white bar) and with (black bar) CAN **(E-H)**.

PF: plantar fascia; BMI: body mass index; CAN: cardiac autonomic neuropathy; Elx: elasticity; Hrd: hard tissue.

Table III. Univariate correlations of ultrasonographic and elastosonographic parameters of PF between each other and with CVD risk factors and surrogate measures of complications.

Variables	Mean thickness		Mean Elx-Hrd insertion		Mean Elx-Hrd course		Mean Elx 1/2	
	r	p	r	p	r	p	r	p
Mean thickness	1.000	-	0.619	< 0.0001	0.175	0.084	0.618	< 0.0001
Maen Elx-Hrd insertion	0.619	< 0.0001	1.000	-	0.334	0.001	0.836	< 0.0001
Mean Elx-Hrd course	0.175	0.084	0.334	0.001	1.000	-	0.326	0.001
Mean ELX 1/2	0.618	< 0.0001	0.836	< 0.0001	0.326	0.001	1.000	-
Age	-0.143	0.160	0.014	0.894	0.149	0.143	-0.052	0.610
Diabetes duration	0.069	0.497	0.076	0.456	0.052	0.609	0.094	0.355
HbA_{1c}	-0.098	0.339	-0.071	0.485	0.101	0.320	-0.052	0.612
Fasting plasma glucose	-0.012	0.908	-0.079	0.438	0.088	0.388	-0.128	0.210
Post-prandial plasma glucose	-0.134	0.187	-0.075	0.465	0.183	0.071	-0.150	0.139
BMI	0.369	< 0.0001	0.384	< 0.0001	0.205	0.042	0.372	< 0.0001
Fat mass	0.105	0.303	0.089	0.383	0.082	0.420	0.074	0.469
Fat-free mass	0.373	< 0.0001	0.397	< 0.0001	0.126	0.217	0.382	< 0.0001
Waist circumference	0.447	< 0.0001	0.437	< 0.0001	0.159	0.117	0.422	< 0.0001
Triglycerides	-0.105	0.302	-0.095	0.350	0.023	0.821	-0.170	0.094
Total cholesterol	-0.035	0.729	-0.057	0.579	-0.137	0.179	-0.123	0.226
HDL cholesterol	-0.102	0.319	-0.130	0.202	-0.119	0.244	-0.125	0.221
LDL cholesterol	0.035	0.729	0.034	0.739	-0.101	0.320	0.020	0.842
SBP	0.032	0.758	0.046	0.652	0.113	0.268	-0.036	0.728
DBP	0.029	0.776	-0.091	0.373	-0.025	0.810	-0.165	0.105
eGFR	0.121	0.237	-0.016	0.873	-0.178	0.079	-0.017	0.866
ACR	0.041	0.687	0.025	0.803	-0.015	0.880	0.103	0.314
Carotid IMT	0.126	0.217	0.108	0.290	0.129	0.206	0.097	0.340
ABI	0.067	0.515	-0.017	0.869	-0.077	0.452	0.014	0.889
PMN distal latency	0.192	0.059	0.115	0.258	0.041	0.691	0.143	0.161
PMN amplitude	-0.231	0.022	-0.112	0.272	-0.102	0.316	-0.110	0.281
PMN nerve conduction velocity	-0.173	0.088	-0.129	0.206	-0.149	0.144	-0.170	0.095
SSN distal latency	0.068	0.508	0.003	0.979	-0.025	0.810	0.066	0.519
SSN amplitude	-0.222	0.028	-0.119	0.244	-0.074	0.466	-0.107	0.294
SSN nerve conduction velocity	-0.131	0.199	-0.143	0.159	-0.048	0.637	-0.149	0.144
VPT malleolus	0.083	0.416	0.229	0.023	0.150	0.141	0.191	0.060
VPT hallux	-0.066	0.520	0.132	0.194	0.200	0.048	0.101	0.323
ESC feet	0.041	0.688	-0.045	0.660	0.013	0.901	-0.017	0.865
ESC hands	0.149	0.142	-0.013	0.903	0.072	0.481	-0.005	0.960
CAN score	0.119	0.243	0.288	0.004	0.223	0.027	0.235	0.020

PF: plantar fascia; CVD: cardiovascular disease; Elx: elasticity; Hrd: hard tissue; HbA_{1c}: hemoglobin A_{1c}; BMI: body mass index; BP: blood pressure; IMT: intima-media thickness; ABI: ankle-brachial index; eGFR: estimated glomerular filtration rate; ACR: albumin:creatinine ratio; VPT: vibration perception threshold; PMN: peroneal motor nerve; SSN: sural sensory nerve; ESC: electrochemical skin conductance; CAN: cardiac autonomic neuropathy.

Table IV. Multivariable correlates of ultrasonographic and elastosonographic parameters of PF.

Independent variables	Mean thickness		Mean Elx-Hrd insertion		Mean Elx-Hrd course		Elx 1/2	
	Beta	p	Beta	p	Beta	p	Beta	p
Model 1								
Age, years	-	-	-	-	-	-	-	-
Male sex	0.383	0.009	6.034	0.014	-	-	1.414	0.002
Smoking	-	-	-	-	-	-	-	-
Physical activity	-	-	-	-	-	-	-	-
Diabetes duration	-	-	-	-	-	-	-	-
HbA_{1c}	-	-	-	-	-	-	-	-
BMI	0.065	< 0.0001	0.933	< 0.0001	-	-	0.172	< 0.0001
Triglycerides	-0.002	0.022	-	-	-	-	-	-
HDL cholesterol	-	-	-	-	-	-	-	-
LDL cholesterol	-	-	-	-	-	-	0.012	0.065
Systolic BP	-	-	-	-	-	-		
Diastolic BP	-	-	-	-	-	-	-0.040	0.058
Model 2			-	-	-	-		
Age	-0.017	0.050	-	-	-	-	-0.044	0.067
Male sex	0.298	0.059	6.281	0.013	-	-	1.123	0.012
CVD	-	-	-	-	-	-	-	-
DKD	-	-	-	-	-	-	-	-
DR	-	-	-5.885	0.043	-	-	-	-
DPN	-	-	-	-	-	-	-	-
CAN	0.453	0.011	10.136	< 0.0001	-	-	1.911	< 0.0001

PF: plantar fascia; Elx: elasticity; Hrd: hard tissue; HbA_{1c}: hemoglobin A_{1c}; BMI: body mass index; BP: blood pressure; CVD: cardiovascular disease; DKD: diabetic kidney disease; DR: diabetic retinopathy; DPN: diabetic peripheral neuropathy; CAN: cardiac autonomic neuropathy.

DISCUSSION

Plantar fasciitis is one of the most common causes of heel pain affecting people in their fourth and fifth decades (25) and, as other musculoskeletal disorders (2), is particularly frequent patients with type 2 diabetes (3). Though pain is usually self-limiting and resolves within a year with conservative treatment, including extracorporeal shockwave therapy (26), a few patients need surgery (27). This preliminary study assessed the correlates of PF ultrasonographic and elastosonographic parameters in these individuals by analyzing a wide range of CVD risk factors and long-term complications.

Regarding CVD risk factors, results showed that PF values correlated with parameters of adiposity, including BMI, waist circumference, and fat mass, in keeping with previous observations in non-diabetic (28) and diabetic (19, 21) individuals. However, they were also related to fat-free mass, suggesting a relationship with skeletal muscle mass, despite the fact that no association was found with the level of physical activity. Therefore, these findings seem to indicate a central role for the extent of pressure exerted on the PF due to gravitational loads from either increased body weight or ground reaction forces associated with movement. Noteworthy, no relationship was found with other CVD risk factors, including diabetes duration and HbA_{1c}, which were previously reported to be closely related with several musculoskeletal complications (29). This finding seems to argue against the involvement of AGE accumulation in worsening PF parameters to favor the development of plantar fasciitis, though the preliminary nature of this study does not allow drawing definitive conclusions. Moreover, no effect of age was observed, consistent with a previous report on diabetic individuals (5) and at odds with the findings that older individuals have increased incidence of plantar fasciitis (28) and worse outcomes after extracorporeal shockwave therapy (26). Finally, males were found to have higher PF values than female, though differences were generally non-significant. This finding seems to be at variance with the reported

higher incidence of plantar fasciitis in diabetic females (3), though contrasting data were reported in the general population for sex distribution (28).

Regarding long-term complications, results showed a strong independent association between CAN score and PF thickness and hardness, suggesting a major role of autonomic dysfunction in plantar fasciitis occurring in diabetic individuals. This finding is consistent with previous results from the SAMBA, showing that CAN is an independent correlate also of muscle (17) and bone (30) parameters, though the mechanism is unclear. Conversely, only sporadic relationships were detected between PF values and parameters of peripheral neuropathy in the univariate, but not in the multivariable analysis. This finding is also in keeping with a study indicating that somatic DPN was not a predictor of the development of plantar fasciitis in people with diabetes (5). Again, no conclusive evidence can be derived from our survey in this respect and further studies are needed to clarify this issue.

A clear strength of our study is the in-depth characterization of patients by assessing a wide range of CVD risk factors and complications together with ultrasonographic and elastosonographic parameters of PF. However, there are several limitations. First, the relatively small number of study participants, which may have resulted in an insufficient power to detect significant associations between PF parameters and the variables tested. Second, the lack of a control group, though comparison with healthy individuals was beyond the scope of our investigation, which was aimed at identifying correlates of PF parameters in diabetic patients with various degree of complications. Third, the cross-sectional design makes causal interpretation impossible.

CONCLUSIONS

In conclusion, this preliminary analysis in patients with type 2 diabetes showed that the main correlates of ultrasonographic and elastosonographic parameters of the PF are adiposity and body composition together with presence of CAN, suggesting that body weight reduction, maintenance of muscle mass, and prevention of neuropathic complications may result in a decreased incidence of plantar fasciitis in these individuals.

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DATA AVAILABILITY

Data are available under reasonable request to the corresponding author.

CONTRIBUTIONS

FS, MCV, GP, SB: conceptualization and design. FS, SM, MV, SMN, EL, JH: data acquisition. FS, MCV, GP, SB: data analysis and interpretation. GP: statistical analysis. GP: draft. FS, SM, MV, SMN, EL, MCV, JH, SB: critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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