Original Article

Plantar Pressure Changes and Correlating Risk Factors in Chinese Patients with Type 2 Diabetes: Preliminary 2-year Results of a Prospective Study

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Abstract

Background: Plantar pressure serves as a key factor for predicting ulceration in the feet of diabetes patients. We designed this study to analyze plantar pressure changes and correlating risk factors in Chinese patients with type 2 diabetes.
Methods: We recruited 65 patients with type 2 diabetes. They were invited to participate in the second wave 2 years later. The patients completed identical examinations at the baseline point and 2 years later. We obtained maximum force, maximum pressure, impulse, pressure-time integral, and loading rate values from 10 foot regions. We collected data on six history-based variables, six anthropometric variables, and four metabolic variables of the patients.
Results: Over the course of the study, significant plantar pressure increases in some forefoot portions were identified ($P < 0.05$), especially in the second to forth metatarsal heads. Decreases in heel impulse and pressure-time integral levels were also found ($P < 0.05$). Plantar pressure parameters increased with body mass index (BMI) levels. Hemoglobin A1c (HbA1c) changes were positively correlated with maximum force ($\beta = 0.364$, $P = 0.001$) and maximum pressure ($\beta = 0.366$, $P = 0.002$) changes in the first metatarsal head. Cholesterol changes were positively correlated with impulse changes in the lateral portion of the heel ($\beta = 0.179$, $P = 0.072$) and pressure-time integral changes in the second metatarsal head ($\beta = 0.236$, $P = 0.020$). Ankle-brachial index (ABI) changes were positively correlated with maximum force changes in the first metatarsal head ($\beta = 0.137$, $P = 0.048$). Neuropathy symptom score (NSS) and common peroneal nerve sensory nerve conduction velocity (SCV) changes were positively correlated with some plantar pressure changes. In addition, plantar pressure changes had a correlation with the appearance of infections, blisters ($\beta = 0.244$, $P = 0.014$), and calluses over the course of the study.
Conclusions: We should pay attention to the BMI, HbA1c, cholesterol, ABI, SCV, and NSS changes in the process of preventing high plantar pressure and ulceration. Some associated precautions may be taken with the appearance of infections, blisters, and calluses.

Key words: Plantar Pressure Changes; Risk Factors; Type 2 Diabetes

Introduction

In 2013, 382 million patients were suffering from diabetes worldwide, and it has been estimated that this number may surpass 592 million by 2035.[1] Previous studies have shown that lower leg amputations in diabetes patients account for more than 50% of all amputations and that two-thirds of these amputations may result from foot ulcerations.[2] As diabetic foot ulcerations constitute a major cause of lower leg amputations, ulcerations must be treated at early stages. Various factors may lead to ulceration development.[3,4] Several studies have shown that plantar pressure plays a major role in predicting foot ulcerations in diabetes patients.[3,5-7] The higher the peak plantar pressure level, the higher the commensurate risk of foot ulceration.[8] Diabetes patients have a different plantar pressure distribution than individuals without diabetes. We previously studied risk factors correlated with plantar pressure levels in Chinese

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patients with type 2 diabetes in a cross-sectional study which demonstrated that high plantar pressure levels in diabetes patients were correlated with weight, height, neuropathy symptom score (NSS), ankle-brachial index (ABI), sex, history of ulcer and callus, intima-media membrane of the lower limb blood vessels, and fasting blood glucose (FBG).[9] However, few prospective studies have examined plantar pressure changes in diabetes patients. In addition, there is little information available on correlating risk factors in Chinese patients with type 2 diabetes. This study aims to examine plantar pressure changes in Chinese patients with type 2 diabetes and to identify prospective factors related to plantar pressure changes in this patient population.

Methods

Participant selection

This study was conducted based on *Declaration of Helsinki* principles and was approved by ethical committees of the local hospital. Written informed consent was obtained from all of the participants. According to preexperimental requirements, we should require at least 48 patients to participate in this study. Sixty-five diabetes patients were enrolled in the study from March of 2012 to August of 2012. These individuals were invited to participate in the second wave of the study 2 years later. The diabetes patients completed identical examinations at the baseline point and 2 years later. The inclusion criteria included: (1) Adults (aged $\geq$18 years); (2) diagnosis of type 2 diabetes; (3) no obvious gait abnormalities by visual inspection. Diagnosis of type 2 diabetes was confirmed through a review of laboratory data and medical records or via communication with the participants' primary care physicians. The exclusion criteria included: (1) An active foot ulcer, foot deformity, foot surgical history, or individuals who were unable to walk unaided; (2) serious circulatory system disease (New York Heart Association functional Class III or IV), nephropathy (chronic kidney disease Class IV or V), hepatopathy (alanine transaminase or aspartate transaminase of higher than five times of the normal level), or hematopathy (leucocythemia, lymphadenoma, multiple myeloma and other diseases that impair quality of life and movement); (3) neuropathy, with the exception of diabetic neuropathy; and (4) severe mental illness (patients who could not complete the study examinations). Prior the study, the participants were questioned about their medical history and were subjected to a physical examination to exclude the presence of neurological disorders, with the exception of diabetic neuropathy. When a diagnosis could not be confirmed, we conducted electromyography, computed tomography, or magnetic resonance imaging tests. In addition to imaging studies, we invited doctors in a related clinical department to make diagnoses.

Data collection

We interviewed the participants to collect data on their demographic, height, and weight characteristics. We surveyed the participants regarding the presence or absence of several selected symptoms related to neuropathy to determine their NSS.[10] We recorded the height of shoe heels they always worn over the course of the study and noted the appearance of infections, ulcers, calluses, or blisters in the 2 years.

Dynamic plantar pressure levels were measured using the footscan gait system (RSscan International, Olen, Belgium). The participants walked barefoot across the sensor platform at 90–110% speed of the established speed before conducting our measurements. The plantar pressure data included the maximum force, maximum pressure, impulse, pressure-time integral and loading rate values under each region. These data were obtained from 10 parts of the foot (toe 1, the hallux; toe 2–5, the second to fifth toes; meta 1, the first metatarsal head; meta 2, the second metatarsal head; meta 3, the third metatarsal head; meta 4, the fourth metatarsal head; meta 5, the fifth metatarsal head; midfoot; medial heel, the medial portion of the heel; and lateral heel, the lateral portion of the heel).[9] No parameter difference between the left and right foot was found via the Wilcoxon signed ranks test ($P > 0.05$). Therefore, only the left foot plantar pressure data were used for the following data analysis.

A portable continuous-wave Doppler device (ACC113; Huntleigh, Cardiff, Wales, United Kingdom) was used to measure systolic blood pressure levels for ABI.[11] A diagnostic iU22 ultrasound system (Philips Medical Systems, Bothell, WA, USA) was used to detect the intima-media membrane of lower limb blood vessels. Each sonography was performed by three operators who had more than 10 years of professional experience. Foot sensations were evaluated using a Semmes–Weinstein monofilament (10 g) test kit (SENSELab Aesthesiometer, Hörby, Sweden).[12] Sensory and motor nerve conduction velocities of the common peroneal nerve (SCV/MCV) measurements were carried out on a Nicolet Viking II electromyography (Nicolet Company, Madison, Wisconsin, USA) by two operators with more than 15 years of professional experience.

Hemoglobin A1c (HbA1c) levels were measured using a DCA Vantage analyzer (Siemens Medical Solutions Diagnostics, NY, USA). FBG, plasma cholesterol, and triglyceride concentrations were measured using an AU-2700 automated analyzer (Olympus, Mishima, Japan).

Statistical analysis

The data analysis was performed using SAS version 9.1.3 software (SAS Institute Inc., Cary, NC, USA). After testing for normality levels via Kolmogorov–Smirnov testing, all normally distributed data were expressed as the mean ± standard deviation, and other continuous data were expressed as median (interquartile range). Rank data and categorical data are expressed with numbers. A paired-samples t-test was used to evaluate any potential data differences between the normally distributed results at the baseline point and 2 years later, and a related-samples Wilcoxon Signed Rank test was used for abnormally distributed data and ranked data. A McNemar test was selected to evaluate any potential differences between categorical variables at the baseline point and 2 years later. Spearman's bivariate correlation was used to analyze the correlation between the significant plantar pressure variable changes and the significant clinical characteristics changes (including continuous data and ranked data). To evaluate the association between the plantar pressure changes and the categorical variables of clinical characteristics, a Mann–Whitney *U*-test for independent samples was used to compare the means of significant plantar pressure changes in different groups divided by the categorical variables. A value of $P < 0.05$ was considered as statistically significant.

Multiple linear regression analyses were conducted to analyze the correlation between clinical characteristic changes and plantar pressure variable changes. Low, weak, strong, and very strong correlations were denoted by β coefficient values of 0.00–0.25, 0.26–0.5, 0.51–0.75, and 0.76–1.00, respectively.[13]

Results

Sixty-five participants with type 2 diabetes were recruited to participate in this study. The clinical characteristics of the participants are summarized in Table 1. The sample consisted of 36 women and 29 men, with a mean age of 59 years (range, 40–78 years) and a mean disease course of 8.20 years (range, 0.04–27.00 years).

Table 2 summarizes the plantar pressure parameters at the baseline point and 2 years later. Maximum force and pressure levels of the first to the fourth metatarsal head increased over the course of the 2 year study. The impulse of the third metatarsal head and the pressure-time integral value of the second to the fourth metatarsal head also increased. Impulse levels in the medial and lateral portions of the heel declined. The pressure-time integral of the lateral portion of the heel decreased as well. The participants showed no progression in the loading rate of each plantar region by the end of the 2 year study.

Correlations between the significant plantar pressure variable changes and the significant clinical characteristic changes (including continuous data and ranked data) are summarized in Table 3, and the data without significant changes have been excluded. The plantar pressure variable changes showed a correlation with body mass index (BMI), HbA1c, FBG, cholesterol, triglyceride, the intima-media membrane of lower limb blood vessels, NSS, ABI, and SCV changes.

The results of Mann–Whitney *U*-tests for evaluating the association between the significant plantar pressure changes and the categorical variables of clinical characteristics are summarized in Table 4. The plantar pressure changes showed association with the appearance of blisters, calluses, infections, and ulcers over the course of the study.

Multiple linear regressions that could explain the changes of the plantar pressure parameters are summarized in Table 5. Plantar pressure parameters increased with BMI levels. HbA1c changes were positively correlated with maximum force and maximum pressure changes in the first metatarsal head. Cholesterol changes were positively

Table 1: Clinical characteristics of the patients with type 2 diabetes ($n = 65$)

Items	Baseline	2 years later	t	P
History-based				
Height of shoe heels (0/<5 cm/>5 cm) (*n*)	NA	59/6/0	NA	NA
Blisters (without/with) (*n*)	NA	62/3	NA	NA
Calluses (without/with) (*n*)	NA	52/13	NA	NA
Infections (without/with) (*n*)	NA	46/19	NA	NA
Ulcers (without/with) (*n*)	NA	63/2	NA	NA
NSS	4.00 (3.00)	4.00 (3.00)	1.974	0.048
Anthropometric				
BMI (kg/m^2)	25.91 ± 3.02	26.35 ± 3.28	−2.165	0.034
Left foot sensation (normal/weaken/disappear) (*n*)	54/10/1	51/13/1	2.000	0.046
Left ABI	1.21 (0.20)	1.18 (0.19)	−4.033	0.000
Left intima-media membrane (not thick/thick) (*n*)	48/17	39/26	5.818	0.012
MCV (m/s)	47.78 ± 11.45	46.75 ± 12.18	1.292	0.201
SCV (m/s)	39.00 (15.00)	37.00 (16.00)	−2.980	0.003
Metabolic				
FBG (mmol/L)	8.10 (3.02)	8.17 (4.15)	−2.065	0.039
HbA1c (%)	8.7 ± 1.6	8.2 ± 1.6	2.506	0.015
Cholesterol (mmol/L)	4.68 (1.33)	5.61 (1.90)	4.369	0.000
Triglyceride (mmol/L)	1.83 (1.19)	2.18 (1.67)	4.287	0.000

Normally distributed data are expressed as mean ± SD. Abnormally distributed data are expressed as the median (interquartile range). Rank data and categorical data are expressed with numbers. The *P* values are derived from the comparison between the clinical characteristics data at the baseline point and 2 years later. NSS: Neuropathy symptom score; BMI: Body mass index; ABI: Ankle-brachial index; Intima-media membrane: Intima-media membrane of the lower limb blood vessels; MCV: Motor nerve conduction velocity of the left common peroneal nerve; SCV: Sensory nerve conduction velocity of the left common peroneal nerve; FBG: Fasting blood glucose; HbA1c: Hemoglobin A1c; SD: Standard deviation; NA: Not available.

Table 2: Plantar pressure parameters at the baseline point and 2 years later of the patients with type 2 diabetes ($n = 65$)

Plantar pressure parameters	Baseline point		2 years later		t	P
	Median	IQR	Median	IQR		
Maximum force (N)						
Toe 1	67.200	76.530	64.320	78.540	−0.078	0.937
Toe 2–5	4.500	11.200	5.610	13.950	−0.971	0.332
Meta 1	69.500	68.265	79.860	75.510	−2.094	0.036
Meta 2	137.430	81.365	164.060	87.080	−3.134	0.002
Meta 3	138.900	66.850	171.440	105.590	−3.364	0.001
Meta 4	107.500	63.330	112.620	79.820	−2.356	0.018
Meta 5	65.730	57.850	67.200	66.260	−1.474	0.141
Midfoot	103.100	117.250	98.540	61.940	−0.180	0.857
Medial heel	179.200	98.185	152.740	76.480	−1.513	0.130
Lateral heel	136.700	94.835	133.680	51.040	−1.389	0.165
Maximum pressure (N/cm^2)						
Toe 1	4.500	3.635	4.460	4.150	−0.111	0.912
Toe 2–5	0.500	0.930	0.640	1.040	−1.187	0.235
Meta 1	6.200	4.950	7.440	6.320	−2.323	0.020
Meta 2	14.400	6.400	20.430	9.525	−4.231	0.000
Meta 3	16.070	6.430	20.720	10.080	−3.477	0.001
Meta 4	11.800	6.530	14.480	10.700	−2.581	0.010
Meta 5	6.100	5.400	6.220	5.720	−1.271	0.204
Midfoot	3.400	2.265	3.190	1.830	−0.049	0.961
Medial heel	9.800	4.065	9.580	3.460	−0.964	0.335
Lateral heel	9.800	4.755	9.160	2.860	−0.951	0.342
Impulse (N·s)						
Toe 1	10.670	14.995	9.700	11.510	−0.281	0.779
Toe 2–5	0.400	1.150	0.400	1.280	−0.237	0.813
Meta 1	15.930	18.995	14.720	14.840	−0.758	0.448
Meta 2	33.270	20.265	36.640	21.370	−1.807	0.071
Meta 3	31.400	19.635	36.640	24.820	−2.441	0.015
Meta 4	27.730	19.185	26.720	26.280	−1.513	0.130
Meta 5	18.700	18.500	17.040	24.360	−0.637	0.524
Midfoot	29.750	36.985	24.500	19.145	−0.291	0.771
Medial heel	42.730	37.615	37.860	19.860	−2.676	0.007
Lateral heel	34.970	30.465	31.860	14.270	−2.166	0.030
Pressure-time integral ($N·s·cm^{-2}$)						
Toe 1	0.630	0.715	0.660	0.690	–0.056	0.956
Toe 2–5	0.050	0.100	0.080	0.110	–0.946	0.344
Meta 1	1.430	1.285	1.340	1.550	–1.244	0.214
Meta 2	3.300	1.465	3.920	2.100	–2.402	0.016
Meta 3	3.700	1.855	4.720	2.800	–3.359	0.001
Meta 4	3.100	1.720	3.300	2.990	–2.202	0.028
Meta 5	1.600	1.535	1.460	1.780	–1.751	0.080
Midfoot	0.900	0.700	0.840	0.570	–0.271	0.787
Medial heel	2.470	1.365	2.300	1.060	–1.565	0.118
Lateral heel	2.600	1.550	2.280	0.875	–2.189	0.029
Loading rate ($N·cm^{-2}·s^{-1}$)						
Toe 1	0.030	0.020	0.020	0.010	–1.705	0.088
Toe 2–5	0.010	0.025	0.000	0.035	–0.904	0.366
Meta 1	0.040	0.020	0.040	0.020	–0.370	0.712
Meta 2	0.050	0.030	0.050	0.020	–1.561	0.118
Meta 3	0.050	0.020	0.050	0.020	–0.535	0.593
Meta 4	0.040	0.015	0.040	0.020	–1.721	0.085
Meta 5	0.020	0.015	0.020	0.010	–0.289	0.773
Midfoot	0.030	0.030	0.040	0.030	–1.365	0.172
Lateral heel	0.210	0.275	0.210	0.250	–0.993	0.321

The P values are derived from the comparison between the plantar pressure parameters at the baseline point and 2 years later. IQR: Interquartile range; Toe 1: The hallux; Toe 2–5: The second to the fifth toes; Meta 1–Meta 5: Each of the first to the fifth metatarsal heads; Medial heel: The medial portion of the heel; Lateral heel: The lateral portion of the heel.

Table 3: Correlation coefficients between the significant plantar pressure changes and the significant clinical characteristics changes (continuous data and ranked data) of the patients with type 2 diabetes (n = 65)

Plantar pressure parameters	Change of BMI	Height of shoe heels	Change of HbA1c	Change of FBG	Change of cholesterol	Change of triglyceride	Change of intima-media membrane	Change of NSS	Change of ABI	Change of SCV
Maximum force										
Meta 1	0.298 (0.016)	−0.003 (0.982)	0.936 (0.000)	0.429 (0.000)	0.252 (0.043)	−0.105 (0.407)	0.304 (0.014)	0.562 (0.000)	0.247 (0.047)	0.941 (0.000)
Meta 2	0.496 (0.000)	−0.006 (0.964)	0.408 (0.001)	0.171 (0.173)	0.372 (0.002)	0.036 (0.773)	0.265 (0.033)	0.357 (0.003)	0.201 (0.109)	0.447 (0.000)
Meta 3	0.530 (0.000)	0.144 (0.251)	0.159 (0.207)	−0.055 (0.666)	0.197 (0.115)	0.071 (0.572)	0.195 (0.120)	0.450 (0.000)	0.008 (0.950)	0.215 (0.085)
Meta 4	0.495 (0.000)	0.154 (0.219)	0.150 (0.233)	−0.130 (0.303)	0.169 (0.178)	−0.036 (0.774)	0.109 (0.386)	0.378 (0.002)	0.069 (0.586)	0.165 (0.189)
Maximum pressure										
Meta 1	0.267 (0.032)	0.031 (0.805)	0.880 (0.000)	0.411 (0.001)	0.261 (0.036)	−0.069 (0.584)	0.300 (0.015)	0.547 (0.000)	0.190 (0.129)	0.887 (0.000)
Meta 2	0.502 (0.000)	0.062 (0.622)	0.484 (0.000)	0.219 (0.079)	0.361 (0.003)	0.058 (0.647)	0.311 (0.012)	0.364 (0.003)	0.203 (0.105)	0.524 (0.000)
Meta 3	0.540 (0.000)	0.143 (0.256)	0.229 (0.066)	0.011 (0.928)	0.231 (0.064)	0.063 (0.616)	0.239 (0.055)	0.395 (0.001)	0.067 (0.599)	0.302 (0.014)
Meta 4	0.488 (0.000)	0.187 (0.136)	0.228 (0.067)	−0.077 (0.541)	0.210 (0.092)	−0.062 (0.625)	0.162 (0.198)	0.375 (0.002)	0.095 (0.449)	0.250 (0.044)
Impulse										
Meta 3	0.506 (0.000)	0.102 (0.419)	0.191 (0.127)	−0.029 (0.816)	0.191 (0.128)	0.054 (0.670)	0.175 (0.163)	0.415 (0.001)	0.060 (0.633)	0.254 (0.041)
Medial heel	0.467 (0.000)	0.082 (0.515)	0.371 (0.002)	0.194 (0.121)	0.366 (0.003)	−0.004 (0.974)	0.258 (0.038)	0.270 (0.030)	0.012 (0.924)	0.353 (0.004)
Lateral heel	0.478 (0.000)	0.085 (0.501)	0.359 (0.003)	0.129 (0.304)	0.406 (0.001)	−0.018 (0.886)	0.223 (0.074)	0.341 (0.006)	−0.067 (0.597)	0.377 (0.002)
Pressure-time integral										
Meta 2	0.402 (0.001)	−0.054 (0.670)	0.468 (0.000)	0.239 (0.056)	0.359 (0.003)	0.040 (0.754)	0.262 (0.035)	0.387 (0.001)	0.159 (0.207)	0.517 (0.000)
Meta 3	0.444 (0.000)	0.095 (0.452)	0.232 (0.063)	0.003 (0.978)	0.175 (0.163)	0.063 (0.618)	0.195 (0.120)	0.368 (0.003)	0.083 (0.510)	0.303 (0.014)
Meta 4	0.437 (0.000)	0.108 (0.393)	0.167 (0.184)	−0.086 (0.494)	0.188 (0.134)	−0.046 (0.716)	0.116 (0.358)	0.290 (0.019)	0.141 (0.264)	0.174 (0.166)
Lateral heel	0.334 (0.006)	0.086 (0.494)	0.221 (0.076)	0.077 (0.540)	0.268 (0.031)	0.009 (0.945)	0.144 (0.251)	0.370 (0.002)	−0.090 (0.474)	0.266 (0.032)

The data was shown as correlation coefficients (*P*). Toe 1: The hallux; Toe 2–5: The second to the fifth toes; Meta 1–Meta 5: Each of the first to the fifth metatarsal heads; Medial heel: The medial portion of the heel; Lateral heel: The lateral portion of the heel; BMI: Body mass index; HbA1c: Hemoglobin A1c; FBG: Fasting blood glucose; Intima-media membrane: Intima-media membrane of the lower limb blood vessels; NSS: Neuropathy symptom score; ABI: Ankle-brachial index; SCV: Sensory nerve conduction velocity of the left common peroneal nerve.

Table 4: Results of Mann–Whitney *U*-tests for evaluating the association between the significant plantar pressure changes and clinical characteristics (the categorical variables) of the patients with type 2 diabetes (n = 65)

Plantar pressure parameters	Blisters	Calluses	Infections	Ulcers
Maximum force				
Meta 1	0.969 (0.332)	−0.049 (0.961)	0.793 (0.428)	1.633 (0.102)
Meta 2	2.470 (0.014)	2.542 (0.011)	2.611 (0.009)	1.368 (0.171)
Meta 3	1.657 (0.098)	2.985 (0.003)	0.938 (0.348)	1.368 (0.171)
Meta 4	1.032 (0.302)	2.452 (0.014)	1.075 (0.283)	1.519 (0.129)
Maximum pressure				
Meta 1	1.094 (0.274)	−0.303 (0.762)	1.298 (0.194)	1.709 (0.087)
Meta 2	2.470 (0.014)	2.034 (0.042)	2.957 (0.003)	1.519 (0.129)
Meta 3	2.064 (0.039)	2.452 (0.014)	1.976 (0.048)	1.235 (0.217)
Meta 4	1.532 (0.126)	1.870 (0.062)	1.716 (0.086)	1.709 (0.087)
Impulse				
Meta 3	1.626 (0.104)	3.395 (0.001)	1.370 (0.171)	0.798 (0.425)
Medial heel	2.282 (0.022)	0.476 (0.634)	2.019 (0.043)	2.127 (0.033)
Lateral heel	2.189 (0.029)	0.738 (0.461)	2.214 (0.027)	2.051 (0.040)
Pressure-time integral				
Meta 2	2.455 (0.014)	1.968 (0.049)	2.394 (0.017)	1.045 (0.296)
Meta 3	1.829 (0.067)	3.067 (0.002)	1.731 (0.083)	0.665 (0.506)
Meta 4	1.438 (0.150)	2.698 (0.007)	1.500 (0.134)	0.950 (0.342)
Lateral heel	1.970 (0.049)	0.090 (0.928)	1.212 (0.226)	2.279 (0.023)

The data was shown as standardized test statistics (P). The P values were derived from the comparison between the means of significant plantar pressure changes in different groups divided by the categorical variables. Toe 1: The hallux; Toe 2–5: The second to the fifth toes; Meta 1–Meta 5: Each of the first to the fifth metatarsal heads; Medial heel: The medial portion of the heel; Lateral heel: The lateral portion of the heel.

correlated with impulse changes in the lateral portion of the heel and pressure-time integral changes in the second metatarsal head. ABI changes were positively correlated with maximum force changes in the first metatarsal head. NSS and SCV changes were positively correlated with some plantar pressure changes. Plantar pressure changes also had a correlation with the appearance of infections, blisters, and calluses over the course of the study.

Discussion

Our previous study showed that the sampled patients with type 2 diabetes exhibited higher maximum force, maximum pressure, impulse, and pressure-time integral levels in certain forefoot regions and lower maximum pressure levels under the lateral portion of the heel than the sample of participants without diabetes.[9] This complemented the conclusions of Pataky *et al*.[14] which showed an anterior displacement of weight-bearing during walking in the patients with diabetes. In the present study, we explored plantar pressure changes in patients with type 2 diabetes in 2 years, and found significant increases in plantar pressure levels in some forefoot portions, especially in the second to forth metatarsal heads. A decrease in heel impulse and pressure-time integral levels was also found. In addition, the diabetes patients exhibited an increase in plantar pressure levels and were at a risk of foot ulceration.[3,7] Ledoux *et al*.[15] previously reported that higher peak plantar pressure levels in metatarsals was significantly associated with greater ulcer risk. Our current study revealed high plantar pressure levels in the metatarsal heads. Based on these results, more attention should be paid to high plantar pressure levels and to increased plantar pressure level. Moreover, some associated precautions (e.g., the provision of suitable footwear, appropriate insoles, and hosiery) should be taken immediately.[16,17]

In our previous cross-sectional association study, weight was identified as a determining factor of high plantar pressure levels.[9] Flynn *et al*.[18] supported 20% of a participant's body weight using a Zuni exercise system and reported that plantar pressure levels can be reduced with weight loss. Arnold *et al*.[19] achieved an increase in weight through the application of a weighted vest and found that peak and mean plantar pressure levels increase depending on the plantar region involved. These two studies described immediately obtained weight changes through the use of instruments and found that planter pressure increased with weight increase. In the present study, we studied spontaneous changes in weight with no statistical significance and chose the variable of BMI to reflect the heaviness and lightness. We found that plantar pressure parameters increase with BMI levels. All of the above findings illustrate plantar pressure responses to an increase in weight or BMI. These results suggest that body weight management plays a critical role in preventing the development of high plantar pressure levels in diabetes patients. Accordingly, weight loss may play a role in reducing risks of developing foot ulcerations.

Ahroni *et al*.[20] demonstrated that HbA1c was not an independent factor of plantar pressure. In this study, FBG changes showed no correlation with plantar pressure variable changes. HbA1c changes were only positively correlated with maximum force and maximum pressure changes in the first metatarsal head, and the β was lower than 0.5. Therefore, the elevation of blood glucose concentrations above normal levels for patients with type 2 diabetes may not significantly

Table 5: Results of multiple linear regression analyzing the correlation between plantar pressure changes and clinical characteristic changes (n = 65)

Plantar pressure parameters	Independent variables	β	P	R	R^2
Meta 1					
Maximum force	Change of ABI	0.137	0.048	0.876	0.767
	Change of BMI	0.147	0.040		
	Change of HbA1c	0.364	0.001		
	Change of NSS	0.343	0.000		
	Change of SCV	0.244	0.018		
Maximum pressure	Change of BMI	0.162	0.055	0.814	0.663
	Change of HbA1c	0.366	0.002		
	Change of NSS	0.252	0.004		
	Change of SCV	0.285	0.016		
Meta 2					
Maximum force	Calluses	0.224	0.010	0.775	0.601
	Change of BMI	0.281	0.004		
	Change of NSS	0.160	0.090		
	Change of SCV	0.416	0.000		
	Infections	0.251	0.004		
Maximum pressure	Change of BMI	0.329	0.000	0.803	0.645
	Change of SCV	0.559	0.000		
	Infections	0.255	0.002		
Pressure-time integral	Blisters	0.244	0.014	0.695	0.483
	Change of cholesterol	0.236	0.020		
	Change of NSS	0.269	0.011		
	Change of SCV	0.323	0.003		
	Infections	0.210	0.035		
Meta 3					
Impulse	Calluses	0.314	0.001	0.755	0.570
	Change of BMI	0.319	0.001		
	Change of NSS	0.251	0.010		
	Change of SCV	0.303	0.002		
Maximum force	Calluses	0.251	0.008	0.716	0.512
	Change of BMI	0.400	0.000		
	Change of NSS	0.372	0.000		
Maximum pressure	Calluses	0.165	0.064	0.756	0.572
	Change of BMI	0.323	0.001		
	Change of NSS	0.257	0.009		
	Change of SCV	0.333	0.001		
	Infections	0.176	0.047		
Pressure-time integral	Calluses	0.254	0.012	0.668	0.447
	Change of BMI	0.271	0.014		
	Change of NSS	0.279	0.012		
	Change of SCV	0.238	0.029		
Meta 4					
Maximum force	Calluses	0.177	0.076	0.656	0.431
	Change of BMI	0.404	0.000		
	Change of NSS	0.332	0.002		
Maximum pressure	Change of BMI	0.403	0.000	0.677	0.458
	Change of NSS	0.184	0.085		
	Change of SCV	0.302	0.005		
Pressure-time integral	Calluses	0.224	0.040	0.578	0.334
	Change of BMI	0.359	0.002		
	Change of NSS	0.242	0.034		
Medial heel					
Impulse	Change of BMI	0.400	0.000	0.706	0.499
	Change of SCV	0.418	0.000		
	Infections	0.169	0.071		
Lateral heel					
Impulse	Change of BMI	0.295	0.006	0.726	0.526
	Change of cholesterol	0.179	0.072		
	Change of NSS	0.178	0.087		
	Change of SCV	0.321	0.002		
	Infections	0.199	0.035		
Pressure-time integral	Change of BMI	0.297	0.011	0.550	0.302
	Change of NSS	0.370	0.002		

The P values were derived from the significant associations between clinical characteristic changes and plantar pressure changes. $P<0.1$ was considered significant. Meta 1–Meta 4: Each of the first to the forth metatarsal heads; Medial heel: The medial portion of the heel; Lateral heel: The lateral portion of the heel; ABI: Ankle-brachial index; BMI: Body mass index; HbA1c: Hemoglobin A1c; NSS: Neuropathy symptom score; SCV: Sensory nerve conduction velocity of the left common peroneal nerve.

and directly contribute to plantar pressure changes. However, the indirect impact of blood glucose levels remains unclear. Changes in cholesterol levels were related to impulse changes in the lateral portion of the heel and pressure-time integral changes in the second metatarsal head. However, triglyceride level changes were not correlated with plantar pressure changes. Few studies have been conducted on the association between the lipid and plantar pressure parameters. The correlation between blood glucose or lipid and plantar pressure warrants additional exploration.

Existing evidence suggests that diabetic neuropathy and high plantar pressure levels are closely related.[21] Patients with mild diabetic neuropathy show an increase in pressure-time integral levels in the forefoot, and plantar pressure changes are aggravated during later stages.[17] Payne *et al*.[22] reported that neuropathy-related variables played a key role in plantar pressure levels in a diabetic foot, and especially in the hallux, in the first metatarsal head, and in the heel region. The present study showed that NSS and SCV level changes were positively correlated with plantar pressure changes in diabetes patients. NSS and SCV measures are used to assess diabetic neuropathy from neuropathic symptoms and conduction velocities of large-diameter neurons, respectively.[23,24] However, no remarkable correlation was found between plantar pressure changes and foot sensation changes identified via our Semmes–Weinstein monofilament test, which serves as another method of diabetic neuropathy diagnosis.[25] The results of this study were consistent with those of our previous study, which demonstrated that NSS was associated with plantar pressure levels, but that foot sensations were not related to plantar pressure levels.[9] Based on the above findings, NSS and SCV may play more pivotal role in predicting plantar pressure changes than foot sensations.

Doppler arterial pressure and ABI levels are used to evaluate peripheral arterial diseases.[9,26] Pataky *et al.*[26] reported a relationship between plantar pressure and Doppler arterial pressure levels of both the tibial posterior and dorsalis pedis artery. In the present study, ABI changes were found to be related to maximum force changes in the first metatarsal head. Peripheral vascular diseases may also contribute to high plantar pressure levels. In this study, changes in the intima-media membrane of lower limb blood vessels showed no correlation with plantar pressure changes. The inconformity was attributed to several causes. First, the data were not primed to address the correlation, as the intima-media membrane examined in this study was the thickest intima-media membrane of lower limb blood vessels. Hence, an inevitable personal error resulted without a fixed position for measuring thickness levels, though all of participants were examined by the same expert operator. Second, the intima-media membrane of the lower limb blood vessels may play a less important role than the above peripheral vascular disease variables in predicting high plantar pressure levels.

Our preceding study proved that a history of foot ulcers was unrelated to plantar pressure levels.[20] We monitored the appearance of ulcers over the course of the study and showed that ulcers had no correlation with plantar pressure changes. These results indicated that the appearance of ulcers may not play a key role in the formation of high plantar pressure levels. One of Potter's studies noted that participants without calluses showed 25% lower pressure levels than those with calluses.[27] In this study, the appearance of calluses over the course of the study showed a relationship with plantar pressure changes in the second to the fourth metatarsal head. We must pay more attention to plantar pressure levels in diabetes patients with calluses. Moreover, we also studied the relationship between planter pressure changes and the appearance of blisters and infections over the course of the study. The appearance of blisters was related to the pressure-time integral in the second metatarsal head. The appearance of infections was correlated with maximum force and pressure-time integral changes in the second metatarsal head, maximum pressure changes in the second and third metatarsal head, and impulse changes in the medial and lateral portions of the heel. The appearance of blisters or infections may serve as an indicator of plantar pressure changes.

It is unfortunate that we did not examine walking behavior variables. There was inevitable personal error in the sonography detecting intima-media membrane of the lower limb blood vessels. In addition, none of the participants wore shoes with ≥5 cm heels daily. Furthermore, two participants had ulcers and three participants developed blisters over the course of the study, and this may have contributed to the development of bias in the data analysis, affecting our conclusions. It is a pity that MCV changes had no statistical significance. All of the blood samples were collected from the participants at 7 AM on a regular weekday morning after 12 h of fasting and limited activity to make the data relatively stable, and blood glucose, cholesterol, and triglyceride concentrations after the fasting period may reflect a rough change trend. However, the data are unstable and susceptible, and cannot reflect exact changes in concentrations over the 2 years and may include a degree of bias.

Overall, plantar pressure changes showed a remarkable correlation with BMI, HbA1c, cholesterol, ABI, SCV, NSS changes and with the appearance of infections, blisters, and calluses over the course of the study. While the ultimate result of diabetic foot ulceration is devastating, foot ulcerations can be prevented. We must pay more attention to factors that are correlated with plantar pressure changes.

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Conflicts of interest

There are no conflicts of interest.

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