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Clinical Medicine Insights: Endocrinology and Diabetes

Plantar Pressure as a Risk Assessment Tool for Diabetic Foot Ulceration in Egyptian Patients with Diabetes

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ABSTRACT

BACKGROUND: Diabetic foot ulceration is a preventable long-term complication of diabetes. In the present study, peak plantar pressures (PPP) and other characteristics were assessed in a group of 100 Egyptian patients with diabetes with or without neuropathy and foot ulcers. The aim was to study the relationship between plantar pressure (PP) and neuropathy with or without ulceration and trying to clarify the utility of pedobarography as an ulceration risk assessment tool in patients with diabetes.

SUBJECTS AND METHODS: A total of 100 patients having diabetes were selected. All patients had a comprehensive foot evaluation, including assessment for neuropathy using modified neuropathy disability score (MNDS), for peripheral vascular disease using ankle brachial index, and for dynamic foot pressures using the MAT system (Tekscan). The studied patients were grouped into: (1) diabetic control group (DC), which included 37 patients who had diabetes without neuropathy or ulceration and MNDS ≤ 2; (2) diabetic neuropathy group (DN), which included 33 patients who had diabetes with neuropathy and MNDS >2, without current or a history of ulceration; and (3) diabetic ulcer group (DU), which included 30 patients who had diabetes and current ulceration, seven of those patients also gave a history of ulceration.

RESULTS: PP parameters were significantly different between the studied groups, namely, forefoot peak plantar pressure (FFPPP), rearfoot peak plantar pressure (RFPPP), forefoot/rearfoot ratio (F/R), forefoot peak pressure gradient (FFPPG) rearfoot peak pressure gradient (RFPPG), and forefoot peak pressure gradient/rearfoot peak pressure gradient (FFPPG/RFPPG) ($P < 0.05$). FFPPP and F/R were significantly higher in the DU group compared to the DN and DC groups ($P < 0.05$), with no significant difference between DN and DC. FFPPG was significantly higher in the DU and DN groups compared to the DC group ($P < 0.05$). RFPPP and FFPPG/RFPPG were significantly higher in the DU and DN groups compared to the DC group ($P < 0.05$) with no significant difference between the DN and DU groups ($P > 0.05$). FFPPP, F/R ratio, FFPPG, and FFPPG/RFPPG correlated significantly with the severity of neuropathy according to MNDS ($P < 0.05$). These same variables as well as MNDS were also significantly higher in patients with foot deformity compared to those without deformity ($P < 0.05$). Using the receiver operating characteristic analysis, the optimal cut-point of PPP for ulceration risk, as determined by a balance of sensitivity, specificity, and accuracy was 335 kPa and was found at the forefoot. Multivariate logistical regression analysis for ulceration risk was statistically significant for duration of diabetes (odds ratio [OR] = 0.8), smoking (OR = 9.7), foot deformity (OR = 8.7), MNDS (OR = 1.5), 2-h postprandial plasma glucose (2 h-PPG) (OR = 0.9), glycated hemoglobin (HbA1c) (OR = 2.1), FFPPP (OR = 1.0), and FFPPG (OR = 1.0).

CONCLUSION: In conclusion, persons with diabetes having neuropathy and/or ulcers have elevated PPP. Risk of ulceration was highly associated with duration of diabetes, smoking, severity of neuropathy, glycemic control, and high PP variables especially the FFPPP, F/R, and FFPPG. We suggest a cut-point of 355 kPa for FFPPP to denote high risk for ulceration that would be more valid when used in conjunction with other contributory risk factors, namely, duration of diabetes, smoking, glycemic load, foot deformity, and severity of neuropathy.

KEYWORDS: pedobarography, plantar pressure, diabetic neuropathy, diabetic foot ulceration

CITATION: Fawzy et al. Plantar Pressure as a Risk Assessment Tool for Diabetic Foot Ulceration in Egyptian Patients with Diabetes. *Clinical Medicine Insights: Endocrinology and Diabetes* 2014:7 31–39 doi:10.4137/CMED.S17088.

RECEIVED: May 21, 2014. **RESUBMITTED:** October 15, 2014. **ACCEPTED FOR PUBLICATION:** October 17, 2014.

ACADEMIC EDITOR: Nigel Irwin, Editor in Chief

TYPE: Original Research

FUNDING: Authors disclose no funding sources.

COMPETING INTERESTS: Authors disclose no potential conflicts of interest.

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Paper subject to independent expert blind peer review by minimum of two reviewers. All editorial decisions made by independent academic editor. Upon submission manuscript was subject to anti-plagiarism scanning. Prior to publication all authors have given signed confirmation of agreement to article publication and compliance with all applicable ethical and legal requirements, including the accuracy of author and contributor information, disclosure of competing interests and funding sources, compliance with ethical requirements relating to human and animal study participants, and compliance with any copyright requirements of third parties. This journal is a member of the Committee on Publication Ethics (COPE).

Introduction

Diabetic peripheral neuropathy (DPN) is one of the common complications of diabetes that predisposes the patient with diabetes to foot ulcers and amputations.[1] The prevalence of diabetic foot ulceration is approximately 4%–10%, and the annual population-based incidence is approximately 1%–4%. The ulcers frequently become infected and can cause great morbidity.[2]

Understanding foot biomechanics is an important component in the evaluation of diabetic foot. Pedobarography is the study of pressure fields acting between the surface of the foot and a supporting surface. One of the first studies on plantar pressure (PP) in diabetic patients using pedobarography was conducted in 1975 by Stokes et al.[3] They noted that the highest maximum load was present at the site of ulceration. High PP had been found to be useful in predicting foot ulceration in diabetic patients.[4]

Ethnic differences in PPs have been reported in diabetic patients with DPN. Solano et al[5] found that dynamic PP is lower in Hispanic diabetic patients with DPN compared to their Caucasian counterparts.

Pedobarographic studies have not previously been conducted on Egyptian patients having diabetes. MAT scan system has been recently introduced to diabetic foot services presented at Al Zahraa University Hospital.

The aim of the present work was to study the relationship between PP and neuropathy with or without ulceration trying to clarify the utility of pedobarography as an ulceration risk assessment tool in patients with diabetes.

Subjects and Methods

Subjects. A selective purposive sample of 100 patients with diabetes was recruited from the outpatient diabetes clinic at AL Zahraa University Hospital. Both sexes were involved, and no age limit was determined. Patients with type 1 and type 2 diabetes were included. The diagnosis of diabetes had been made pre-enrollment and was confirmed by reviewing their history and medical records. Exclusion criteria included critically ill patients, patients with history of amputation along lower limbs, and patients with gait and/or mobility disorders.

The case recruitment started in January 2011 and ended in January 2012. After explaining the study design, an informed consent was obtained from each patient prior to participation in the study. The study was approved by the Ethical Committee of the Faculty of Medicine for Girls, AL Azhar University. This committee is compliant with the principles of the Declaration of Helsinki.

Methods. All subjects were subjected to the following:

(1) Full medical history including age at onset of diabetes, duration of diabetes, smoking status, type of antihyperglycemic therapy, and history of foot ulceration.
(2) Complete clinical examination including anthropometric measurements (weight and height) and body mass index was calculated (BMI).
(3) Comprehensive foot examination including proper inspection for skin integrity, foot deformities, palpation of peripheral pulsations, and measurement of ankle brachial index (ABI).
(4) Neurological assessment according to the modified neuropathy disability score (MNDS) designed by Young et al (Table 1).[6] This was derived from examination of vibration perception (by means of a 128-Hz tuning fork), pin-prick, and temperature perceptions in the great toe and the presence or absence of ankle reflexes. The sensory modalities were scored as either present (0) or reduced or absent (1) for each leg. Ankle reflexes were scored as normal (0), present with reinforcement (1) or absent (2) for each leg. The total maximal abnormal score was 10; score >2 was defined as clinical DPN.
(5) PP measurement: This was recorded during walking barefoot using plantar software of the MAT system version 3.711 (Tekscan, Boston). Both static and dynamic PPs were measured. In dynamic recording, patients were allowed to walk at their chosen walking speed. The mean reading of three midgait steps was entered for final data analysis. Biomechanically, the midtarsal joints divides the foot into forefoot anteriorly and rearfoot posteriorly. The maximum PP under the forefoot (FFPPP) and the rearfoot (RFPPP) was separately measured for each foot, and the ratio between them was calculated (F/R).

Peak pressure gradient (PPG) was determined in a defined area around the peak plantar pressure (PPP) by calculating the highest change in pressure from one node to the next. The pressure gradient values were calculated by subtracting the pressure in each node around the PPP from that in the adjacent node and dividing it by the distance between the centers of the nodes. That was done at both forefoot (forefoot peak pressure gradient [FFPPG]) and rearfoot (rearfoot peak pressure gradient [RFPPG]) and the ratio between them (FFPPG/RFPPG) was calculated.

Table 1. Modified neuropathy score parameters.[6]

PARAMETERS	RIGHT	LEFT
1. Vibration perception Threshold normal = can distinguish vibrating/not vibrating	1	1
2. Temperature perception normal = can distinguish hot from cold	1	1
3. Pinprick normal = can distinguish sharp/not sharp	1	1
4. Achilles reflex	2	2
• **Score for each sensory modalities** Normal = 0 Abnormal = 1 • **Score for Achilles reflex** Present = 0 Present with reinforcement = 1 Absent = 2	**Total score = 10**	

(6) Biochemical studies included fasting and 2-hour postprandial plasma glucose (FPG and 2-h PPG), glycated hemoglobin (HbA1c), total cholesterol, serum triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and 24-h microalbuminuria (MAU).
(7) Statistical methods: The sample size was calculated using Epi Info Program version 7, by adjusting power of the test to 80%, confidence interval was set to 95%, and the margin of error was accepted to 5%. Data were collected, revised, and analyzed by Statistical Package for Social Science (SPSS) program version 16. Comparison between the three groups was done using one-way analysis of variance followed by post hoc least significant difference test when the results were found significant. Comparison between any two groups with quantitative data was done using independent *t*-test.

Measuring the mutual correspondence between two variants was done using Spearman rank correlation coefficients (*r*). Stepwise multivariate logistic regression analysis was performed to determine the most significant factor(s) associated with ulceration. Receiver operating characteristics (ROC) curves were employed using medical calculator program for complete analysis of cutoff value. Data are presented as mean ± standard deviation, and *P* value <0.05 was considered significant.

Results

According to the result of MNDS and the presence or absence of foot ulceration, the 100 studied patients having diabetes were grouped into the following groups:

(1) Diabetic control group (DC): This group included 37 patients who had diabetes without neuropathy or ulceration and MNDS ≤2.
(2) Diabetic neuropathy group (DN): This group included 33 patients who had diabetes with neuropathy and MNDS >2, without current ulceration or a history of ulceration.
(3) Diabetic ulcer group (DU): This group included 30 patients who had diabetes and current ulceration. Seven of those patients also gave a history of foot ulceration. They all had MNDS >2.

Table 2 shows descriptive characteristics of the entire studied population.

Demographic, clinical, and laboratory data were compared between the studied groups, and a significant difference was found as regards age, duration of diabetes, body weight, BMI, MNDS, FPG, and 2-h PPG, HbA1c, MAU, total cholesterol, and serum TG ($P < 0.05$). However, ABI, HDL and LDL were not significantly different among the studied groups. Age, duration of diabetes, HbA1c, MAU, and serum TG were significantly higher in both DN and DU compared to DC ($P < 0.05$). However, those variables were not significantly different in DN compared to DU. Body weight and BMI were significantly higher in DN compared to DC and DU ($P < 0.05$, Table 3).

Table 2. Descriptive characteristics of the Entire Study Population.

Age (years) (mean ± SD, range)	(43.8 ± 15.1) (14–67)
Sex (M/F)	43/57
Duration of diabetes (range/years)	(1–30)
Type of diabetes	
Type 1 diabetes	37%
Type 2 of diabetes	63%
Smoking state	
Non smoker	58%
Smoker	42%
Treatment modality	
Oral hypoglycemic	15%
Insulin therapy	46%
Combined therapy	39%
Severity of neuropathy (MNDS)	
No neuropathy (0–≤2)	37%
Mild neuropathy (3–4)	20%
Severe neuropathy (5–10)	43%

PP parameters were significantly different between the studied groups, namely, FFPPP, RFPPP, F/R, FFPPG, RFPPG, and FFPPG/RFPPG ($P < 0.05$). However, no significant difference was found as regards static pressure and RFPPG. FFPPP and F/R were significantly higher in DU group compared to DN and DC groups ($P < 0.05$) with no significant difference between DN and DC. FFPPG was significantly higher in DU and DN groups compared to DC group ($P < 0.05$). RFPPP and FFPPG/RFPPG were significantly higher in DU and DN groups compared to DC group ($P < 0.05$) with no significant difference between DN and DU groups ($P > 0.05$, Table 4).

Significant positive correlation was found between MNDS and FFPPP, F/R, FFPPG, and FFPPG/RFPPG ($P < 0.05$). No correlation was found between MNDS and both static pressure and RFPPG ($P > 0.05$, Table 5).

Patients with foot deformities had significantly higher MNDS, FFPPP, F/R, FFPPG, and FFPPG/RFPPG compared to those who did not have deformities ($P < 0.05$, Table 6).

The cut-point of FFPPP for risk of ulceration was found to be 335 kPa, using the ROC analysis (60% sensitivity, 74% specificity, and 71.8% accuracy) (Table 7). The optimal cut-point of RFPPP that is accepted for screening risk of ulceration was found to be 245 kPa (80% sensitivity, 47% specificity, and 58.0% accuracy) (Table 7, Fig. 1).

Multivariate logistical regression analysis for ulceration risk was statistically significant for duration of diabetes (odds ratio [OR] = 0.8), smoking (OR = 9.72), foot deformity

Table 3. Demographic, clinical and laboratory data of the studied groups.

	DC GROUP (n = 37)	DN GROUP (n = 33)	DU GROUP (n = 30)	ANOVA	
	MEAN ± SD	MEAN ± SD	MEAN ± SD	F	*P*-VALUE
Age (years)	29.162 ± 12.883	50.879 ± 9.943	54.167 ± 4.800	63.330	<0.05
Duration (years)	4.081 ± 2.586	12.133 ± 8.228	14.194 ± 6.377	27.136	<0.05
Weight (kg)	70.367 ± 16.635	86.667 ± 27.044	75.900 ± 13.732	5.316	<0.05
BMI (kg/m^2)	26.556 ± 7.108	41.670 ± 6.158	29.154 ± 5.845	4.231	<0.05
MNDS	0.324 ± 0.747	7.182 ± 2.592	8.533 ± 1.995	185.466	<0.05
ABI	1.065 ± 0.059	1.045 ± 0.179	1.030 ± 0.092	0.714	NS
FPG (mg/dl)	202.879 ± 43.862	213.333 ± 62.448	244.216 ± 84.662	3.865	<0.05
2 h-PPG (mg/dl)	281.233 ± 59.673	310.818 ± 73.071	328.486 ± 106.895	2.867	<0.05
HbA1c%	8.64 ± 1.1	10.88 ± 1.617	11.15 ± 2.263	17.328	<0.05
24 h-MAU (mg/dl)	37.19 ± 17.6	65.594 ± 70.037	60.003 ± 50.828	3.598	<0.05
Cholesterol (mg/dl)	234.606 ± 71.394	243.833 ± 80.466	284.378 ± 74.813	4.327	<0.05
TG (mg/dl)	164.061 ± 73.048	203.667 ± 65.368	230.622 ± 75.924	7.597	<0.05
HDL (mg/dl)	47.730 ± 16.013	46.818 ± 15.373	50.433 ± 12.204	0.507	NS
LDL (mg/dl)	180.189 ± 67.346	156.182 ± 126.201	197.827 ± 230.364	0.606	NS

PARAMETERS	POST HOC TESTS: LSD		
	DC vs DN	DC vs DU	DN vs DU
Age (years)	<0.05	<0.05	NS
Duration (years)	<0.05	<0.05	NS
Weight (kg)	<0.05	NS	<0.05
BMI (kg/m^2)	<0.05	NS	<0.05
MNDS	<0.05	<0.05	<0.05
FPG (mg/dl)	NS	<0.05	NS
2 h-PPG (mg/dl)	NS	<0.05	NS
HbA1c	<0.05	<0.05	NS
24 h-MAU (mg/dl)	<0.05	<0.05	NS
Cholesterol (mg/dl)	NS	<0.05	<0.05
TG (mg/dl)	<0.05	<0.05	NS

(OR = 8.72), MNDS (OR = 1.5), 2 h-PPG (OR = 0.9), HbA1c (OR = 2.1), FFPPP (OR = 1.0), and FFPPG (OR = 1.0). However, other variables including age, BMI, other biochemical parameters, RFPPP, and FFPPG/RFPPG, were not found to be statistically significant (Table 8).

Discussion

Foot ulceration is a major complication of diabetes and consumes a major portion of the resources allocated for the treatment of diabetes.[4] Diabetic foot ulceration is a significant cause of morbidity and can lead to prolonged hospital stays. The mortality rate in patients with diabetic foot ulceration is approximately twice that of patients without ulceration.[7]

Neuropathy has been identified as one of the major risk factors for diabetic foot ulceration and amputation. The lack of protective sensation from sensory neuropathy leads to repetitive trauma to an area of high pressure.[4] Motor neuropathy leads to atrophic changes in the foot musculature that may cause foot deformity and decreased joint mobility. Autonomic neuropathy can also cause increased blood pooling and swelling in the foot. These problems subsequently lead to an area of increased plantar foot pressure that may result in ulceration.[8]

In the present study, PP and other characteristics were assessed in a group of 100 Egyptian patients with diabetes with or without neuropathy and foot ulcers. The aim was to study the association between neuropathy and PP and to clarify the utility of PP measurement as a risk assessment tool for diabetic foot ulceration.

Patients having diabetes were purposively selected regardless of their age, type, or duration of diabetes. According to the presence or absence of neuropathy and foot ulceration, patients were divided into three groups, namely, DC, DN, and DU.

Table 4. Plantar pressure variables in the DC, DN and DU groups.

	DC GROUP (n = 37)	DN GROUP (n = 33)	DU GROUP (n = 30)	ONE WAY ANOVA	
	MEAN ± SD	MEAN ± SD	MEAN ± SD	F	*P*-VALUE
Static presure (kPa)	114.000 ± 27.635	119.788 ± 29.043	128.750 ± 46.325	1.504	NS
FFPPP (kPa)	292.757 ± 83.888	318.242 ± 58.815	348.567 ± 42.986	5.994	<0.05
RFPPP (kPa)	238.568 ± 46.238	278.030 ± 60.913	270.707 ± 52.538	5.454	<0.05
F/R (kPa)	1.271 ± 0.390	1.266 ± 0.339	1.782 ± 0.297	1.185	<0.05
FF PPG (kPa)	165.146 ± 61.885	248.712 ± 71.253	298.867 ± 68.518	34.296	<0.05
RF PPG (kPa)	176.565 ± 82.785	173.088 ± 72.901	193.500 ± 74.900	0.624	NS
FFPPG/RFPPG (kPa)	1.148 ± 0.638	1.545 ± 0.385	1.678 ± 0.432	10.215	<0.05
PARAMETERS	POST HOC TESTS: LSD				
	DC vs DN	DC vs DU	DN vs DU		
FFPPP (kPa)	NS	<0.05	<0.05		
RFPPP (kPa)	<0.05	<0.05	NS		
F/R (kPa)	NS	<0.05	<0.05		
FF PPG (kPa)	<0.05	<0.05	<0.05		
FFPPG/RFPPG (kPa)	<0.05	<0.05	NS		

Patients in DN and DU were significantly older and had longer duration of diabetes compared to DC. DN had higher BMI compared to DC and DU ($P < 0.05$, Table 3). Mayfield et al[9] demonstrated that the risk of ulcers and amputations increases two- to fourfold with both age and duration of diabetes.

In the current study, ABI was not found to be significantly different among the studied groups (Table 3). This may illustrate that the ulcer etiology in the studied diabetic subjects was mostly due to neuropathy rather than vascular insufficiency. Armstrong et al[10] also demonstrated that the reasons for foot ulceration in diabetes places PN and its sequel, which include loss of protective sensation, on top of the list with peripheral arterial disease (PAD) ranking a distant second. Kroger et al[11] proposed that different modes of ABI calculation may lead to different information. Their results support the hypothesis that these differences are determined by anatomic variations of the plantar arch. Additional angiographic-controlled studies are necessary to prove this hypothesis.

Table 5. Correlation between the MNDS and plantar pressure variables.

PRESSURE VARIABLES	MNDS	
	r	*P*-VALUE
Static presure (kPa)	0.177	NS
FFPPP (kPa)	0.292	<0.05
RFPPP (kPa)	0.200	NS
F/R	0.121	<0.05
FF PPG (kPa)	0.603	<0.05
RF PPG (kPa)	0.008	NS
FF PPG/RF PPG	0.430	<0.05

PPP is the highest pressure value experienced, and this could be measured at both forefoot and rearfoot and the ratio between them could be calculated. Caselli et al[12] studied PPP in 248 individuals with diabetes in a large multicenter 30-month prospective study. They found that PPP is considered to be a good measure of trauma to the plantar foot, and hence, is considered an important contributing factor to skin breakdown and ulceration in people with DPN.

In the present study, most parameters of PP were significantly different between the studied groups, namely, FFPPP, RFPPP, F/R, FFPPG, and FFPPG/RFPPG. However, no significant difference had been found as regards RFPPG (Table 4).

Contrary to dynamic PPP, no significant difference had been found as regards static pressures (Table 4). Periyasamy et al[13] investigated standing PP distribution variations in north Asian Indian diabetic subjects. PP distributions parameter–Power ratio (PR) was measured using portable PedoPowerGraph. They concluded that increased forefoot PR value is prevalent in the diabetic neuropathic subjects and may be responsible for the occurrence of foot sole ulceration.

Increased PP under the forefoot has been identified as a major risk factor for ulceration. Kernozek et al[14] studied American Indians with diabetes and reported greater asymmetry in plantar loading variables across the forefoot. They concluded that loading asymmetry may play a role in the development of diabetic foot ulcers in the forefoot region.

In the present study, both FFPPP and RFPPP were higher in DU compared to DC ($P < 0.05$). FFPPP was also higher in DU group compared to DN group, while RFPPP

Table 6. MNDS and plantar pressure variables in relation to foot deformities.

	NEGATIVE DEFORMITY		POSITIVE DEFORMITY		INDEPENDENT *t*-TEST	
	MEAN	SD	MEAN	SD	*t*	*P*-VALUE
MNDS	1.34	2.23	7.96	2.68	–13.180	<0.05
Static pressure	113.70	24.44	125.54	40.72	–1.702	NS
FFPPP	301.14	35.13	333.23	42.92	4.013	<0.05
RFPPP	249.09	49.11	270.77	59.00	–1.961	NS
F/R	1.21	0.18	1.29	0.21	–2.012	<0.05
FF PPG	189.13	75.70	267.18	79.61	–4.972	<0.05
RF PPG	178.11	80.60	182.37	74.73	–0.273	NS
FF PPG/RF PPG	1.26	0.62	1.58	0.45	–2.928	<0.05

was not significantly different between DN and DU groups. Mean FFPPP and RFPPP values were 348 and 270 kPa, respectively, in the DU group (Table 4).

Pitei et al[15] reported values of mean FFPPP and RFPPP of 242 and 240 kPa, respectively, which are slightly lower than our values. It is noteworthy that they used therapeutic shoes during their assessment, but the subjects in the present study were assessed barefooted.

Higher elevation of forefoot pressure compared to rearfoot pressure in diabetic patients could be explained by glycosylation of body proteins, which may result in functional shortening of the Achilles tendon at the back of the heels leading to a deformity called equines, limited joint mobility, and tiptoeing. Subsequently, there is an accumulative pressure on the forefoot.[16] Moreover, changes in gait characteristics induced by DPN-related muscle weakness may be the origin of the elevated PP. Savelberg et al[17] studied isometric strength of plantar and dorsal flexors as well as joint moments at ankle, knee, and hip joints in diabetes with and without DPN. Simultaneously, PP patterns were measured while walking barefoot. Patients with DPN walked with a significantly increased internal plantar flexor moment at the first half of the stance phase. The maximal braking and propelling force applied to the floor was also decreased. Moreover, the ratio of forefoot-to-rearfoot plantar pressures was increased, and the strength of dorsal flexors was reduced.

In the current study, F/R was found to be significantly different between all the studied groups ($P < 0.05$, Table 4) showing higher mean value in DU group (1.782) than in DN and DC groups (1.26 and 1.2, respectively). F/R significantly correlated with the severity of neuropathy ($P < 0.05$, Table 5). Patients with DPN are often confronted with ulceration of foot soles. Caselli et al[12] found that an F/R ratio >2 was able to predict ulcer development.

PPG is defined as the longitudinal change in PP around the PPP location. This could be measured at both forefoot, FFPPG and rearfoot, RFPPG, and the ratio between them was calculated (FFPPG/RFPPG).

In the present study, we found a statistically significant difference between the studied groups as regards FFPPG ($P < 0.05$). Mean FFPPG was higher than mean RFPPG in both DU and DN groups (348.5 and 270.7, respectively, Table 4). These results are in agreement with Mueller et al,[18] who evaluated the distribution of PPG in both the forefoot and the rearfoot and found that the FFPPG was much higher than the RFPPG in both the ulcer group and in the severe neuropathy group. The primary difference between PPG and PPP is that PPG represents the change in the pressure in the region of PPP. From a mechanical standpoint, a sharp change in pressure, ie, a high PPG may lead to internal stress and shearing of soft tissues causing tissue injury. Possible reasons for higher values for PPG in the forefoot than the rearfoot include greater soft tissue thickness under the heel than that under the metatarsal heads, which might help to distribute PPs and to attenuate PPP and PPG in the rearfoot.[19]

Significant positive correlation was found between MNDS and FFPPP, F/R, FFPPG, and FFPPG/RFPPG ($P < 0.05$). No correlation was found between MNDS and both static pressure and RFPPG ($P > 0.05$, Table 5).

Caselli et al[12] concluded that the FFPPP increased collinearly with the severity of neuropathy. Rich and Veves[20] also found that PPP measurements of the forefoot correlated with neuropathy measurements and was able to predict foot ulceration. In contrast, PPP of the rearfoot failed to show the

Table 7. Receiver Operating Characteristic analysis (ROC) as regards FFPPP and RFPPP.

	CUTOFF	SENSITIVITY	SPECIFICITY	PPV	NPV	ACCURACY
FFPPP	>335	60.0	74.3	50.0	81.2	71.8%
RFPPP	>245	80.0	47.1	39.3	84.6	58.0%

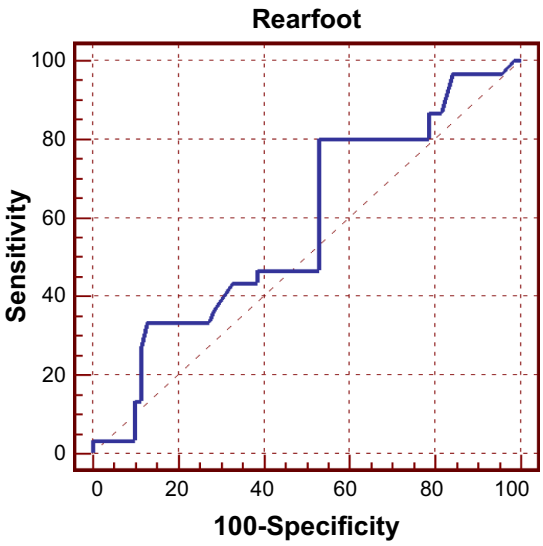

Figure 1. Receiver operating characteristic analysis (ROC) as regards RFPPP.

same correlation and thence could not predict foot ulceration. Veves et al[21] observed a 28% incidence of ulceration in neuropathic feet with high PP during a 2.5-year follow-up period. In contrast, no ulcers developed in patients with normal pressure.

MNDS as well as FFPPP, F/R, FFPPG, and FFPPG/RFPPG were significantly higher in patients with foot deformities compared to those who did not show deformities ($P < 0.05$, Table 6). Yu et al[22] evaluated PP distribution and its clinical significance in patients with diabetic foot toe deformities (claw or hammer toe deformities). PP in different regions of the foot was measured using the F-scan in-shoe PP dynamic analysis system. PP in the hallux and first to fifth metatarsal heads were significantly higher in the patient group compared with the control group. In the midfoot, there was no significant difference between the two groups. Hindfoot PPP was significantly lower in the patient group compared with the control group. The results indicated that toe deformities in patients with diabetes increased forefoot PP to abnormally high levels. However, Orendurff et al[23] found that equines deformity of the ankle was found to account for only a small amount of the increased forefoot PP in patients with diabetes.

Attempts to determine a PPP threshold for ulceration have failed, and the absolute magnitude of pressure values among different studies is not consistent.[24] In the current study, the optimal cut-point of PPP that is accepted for screening for risk of diabetic foot ulceration, as determined by a balance of sensitivity, specificity, and accuracy is 335 kPa and is present at the forefoot. Using the ROC analysis, this value was specific and sensitive (60% sensitivity, 74% specificity, and 71.8% accuracy) (Table 7). For the rearfoot, a cut-point of 245 kPa was found in the present study. This value was sensitive for detecting risk of neuropathic ulceration, but relatively nonspecific (80% sensitivity, 47% specificity, and 58.0% accuracy) (Table 7, Fig. 1).

Veves et al[21] found that a value of over 1000 kPa during barefoot walking is required for ulceration. In a case–control study of 219 patients with diabetes, Armstrong et al[25] measured peak pressure and suggested that 700 kPa is the threshold of ulceration. Lavery et al[26] conducted a large 2-year cohort study of 1666 patients with diabetes; 16% of patients subsequently developed a foot ulcer. The sensitivity and specificity for PPP (using an optimal cutoff value of 800 kPa) were 64% and 46%, respectively. Pitei et al[15] reported PPP of 242 kPa.

The wide variation of threshold described by earlier researchers could be attributed to the diversity of commercially available system to measure the PP, units of measurement, calibration methods, and computation algorithms analyses used. Hence, no proven pressure threshold for tissue damage exists, which could be true for all systems. In an attempt to resolve those discrepancies, Waldecker[27] designed a pedographic classification to identify patients at risk for a foot ulcer. He reported a combination of four variables (pressure time integral forefoot, peak pressure midfoot, pressure time integral heel, and peak pressure heel) identifying the foot ulcer with a sensitivity of 73% and a specificity of 87%.

The contribution of various demographic, clinical, and biochemical risk factors contributing to ulceration risk were evaluated using multivariate logistical regression analyses. Statistically significant OR was found for duration of diabetes (OR = 0.8), smoking (OR = 9.72), presence of foot deformity (OR = 8.7), MNDS (OR = 1.5), 2 h-PPG (OR = 0.9), HbA1c (OR = 2.1), FFPPP (OR = 1, $P < 0.01$), and FFPPG (OR = 1, $P < 0.05$) (Table 8).

A systematic review was performed by Crawford et al[28] to quantify the predictive value of diagnostic tests, physical signs, and elements from the patient's history in relation to diabetic foot ulcers. Diagnostic tests and physical signs that detect DPN, PPP, and joint deformity were all significantly associated with future diabetic foot ulceration.

Bennett et al[29] evaluated the importance of different risk factors for the development of diabetic foot ulceration. The role of nonenzymatic glycosylation and pressure beneath the sole of the foot in the pathogenesis of neuropathic foot ulcers was investigated. There was no significant difference in age, sex, BMI, and duration or type of diabetes between the ulcer and control groups. PPP was significantly elevated in cases with neuropathic foot ulceration compared with the control group. There was a trend toward elevation of HbA1c in the ulcer group. The results suggested that nonenzymatic glycosylation occurs at a more significant level in patients with diabetes with a history of neuropathic foot ulceration.

Qiu Xuan et al[30] assessed PP in 100 Chinese patients with type 2 diabetes using a Footscan gait system. They concluded that high PP in diabetes patients could be predicted based on weight, height, neuropathy symptom score, ABI, sex, history

Table 8. Multivariate logistic regression analysis for ulceration risk.

	P-VALUE	ODD RATIO (OR)	95.0% C.I. FOR ODD	
			LOWER	UPPER
Age (years)	NS	1.129	0.983	1.297
Duration (years)	<0.05	0.831	0.718	0.961
Smoking	<0.05	9.72	2.8593	33.0705
BMI (kg/m^2)	NS	0.952	0.860	1.054
Foot deformities	<0.05	8.7234	2.5483	29.8619
MNDS	<0.05	1.500	1.058	2.128
2 h-PPPG (mg/dl)	<0.05	0.991	0.983	1.000
HbA1c	<0.05	2.123	1.53	2.996
24 h-MAU	NS	1.01	0.997	1.02
S. cholesterol (mg/dl)	NS	1.003	0.989	1.016
TG (mg/dl)	NS	1.009	0.995	1.023
FFPPP (kPa)	<0.05	1.014	1.005	1.028
RFPPP (kPa)	NS	0.986	0.972	1.001
F/R	NS	2.2477	0.6420	7.8698
FF PPG (kPa)	<0.05	1.021	1.005	1.036
FFPPG/RF PPG	NS	0.727	0.122	4.325

of ulcer and callus, intima-media membrane of the lower limb blood vessels, and FPG.

In conclusion, persons with diabetes having neuropathy and/or ulcers have elevated PP. However, PP is only one factor in a multifaceted pathway to diabetic foot ulcer formation. Risk of ulceration was highly associated with duration of diabetes, smoking, severity of neuropathy, glycemic control, and high PP variables, especially FFPPP, F/R, and FFPPG. We suggest a cut-point of 355 kPa for FFPPP to denote high risk for ulceration. That would be more valid when used in conjunction with other contributory risk factors, namely, duration of diabetes, smoking, glycemic load, foot deformity, and degree of neuropathy. This may ultimately help in prediction and assessment of diabetic foot ulceration risk.

Study limitations include that the study was not prospective. Prospective studies are needed to evaluate causality between other variables of mechanical stress and diabetic foot ulceration. Studies of in-shoe PPs to evaluate and guide footwear modifications that may significantly reduce pressure in the neuropathic diabetic foot are also recommended.

Abbreviations

ABI, Ankle brachial index; ANOVA, One Way Analysis of Variance; BMI, body mass index; CI, confidence interval; DC, Diabetic Control Group; DN, Diabetic Neuropathy Group; DU, Diabetic Ulcer Group; DPN, Diabetic peripheral neuropathy; FPG, Fasting Plasma Glucose; FFPPP, Forefoot peak plantar pressure; FFPPG, Forefoot peak pressure gradient; FFPPG/RFPPG, Forefoot peak pressure gradient/Rearfoot peak pressure gradient; F/R, Forefoot/Rearfoot ratio; kPa, kilo Pascal; HDL, high density lipoprotein; LDL, low density lipoprotein; LSD, least significant difference; 24 h-MAU, 24 hour microalbuminuria; MNDS, Modified neuropathy disability score; NPV, negative predictive value; OR, Odds Ratio; PPV, Positive predictive value; PP, Plantar pressure; PPP, Peak plantar Pressure; PPG, Peak Pressure Gradient; 2 h-PPG, 2 h-Post prandial plasma glucose; RFPPP, Rearfoot peak plantar pressure; RFPPG, Rearfoot peak pressure gradient; ROC, Receiver operating characteristics; SPSS, Statistical Package for Social Science; TG, triglyceride.

Author Contributions

Conceived and designed the experiments: OAF, MAEW. Analyzed the data: AIA, SHAK. Wrote the first draft of the manuscript: OAF, AIA, MAEW, SHAK. Contributed to the writing of the manuscript: OAF, AIA, MAEW, SHAK. Agree with manuscript results and conclusions: AIA, MAEW. Jointly developed the structure and arguments for the paper: OAF, AIA. Made critical revisions and approved final version: OAF, AIA. All authors reviewed and approved of the final manuscript.

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