

## Article

# Correlation of leg pain responses with ankle-brachial index and peripheral sensory responses in foot of type 2 diabetes mellitus

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## Abstract

**Introduction:** Type 2 Diabetes Mellitus (T2DM) is associated with changes that occur in the peripheral circulation that affect foot functions. Therefore, there is a need for a risk prediction test on foot abnormalities using the leg pain response parameters in T2DM patients with ankle-brachial index (ABI) and peripheral sensory changes as a preventive effort to manage foot care.

**Design and Methods:** This study employed a cross-sectional design in which 63 T2DM patients in a Public Health Center (PHC) in Malang were investigated. The instruments used include visual analog scale (VAS), monofilament, and foot doppler.

**Results:** The Pearson correlation test showed no relationship between the responses to leg pain and the ABI of the right and left feet (p-values = 0.217 and 0.692), but there was a significant relationship between the left foot ABI and sensory status (p-value 0.002; left foot  $r = 0.383$ ). Meanwhile, the Pearson's correlation and linear regression test also showed a relationship between the right foot ABI and sensory status (p-value = 0.007;  $r = 0.338$ ). Furthermore, a multiple linear regression test showed a relationship between the leg pain response and sensory perception of the right and left feet (p-value = 0.035;  $r = 0.325$ ).

**Conclusions:** The relationship between the sensory status of the right and left feet and the response to leg pain in T2DM patients were moderate with a negative direction. It, therefore, implies that a decrease in the sensory responses increased the leg pain. Meanwhile, the moderate relationship and positive direction between the ABI and sensory status of the feet of T2DM patients indicates that a higher ABI score led to an increase in the sensory status of the foot.

## Introduction

Chronic hyperglycemia in T2DM is associated with long-term damage, impaired function, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Patients with diabetes mellitus may probably experience complications of the foot by 30% with a prevalence of 6.3%; this condition is more

likely to occur in men with these characteristics, such as old age, low body mass index, longer duration of T2DM, hypertension, diabetic retinopathy, and those with a history of smoking.<sup>1-3</sup> Moreover, this condition is associated with changes in the macro and microcirculation which are present in the lower extremities. Macrocirculatory complications are associated with stroke, cardiovascular, and peripheral arterial disease; whereas microcirculation complications are associated with retinopathy, nephropathy, and neuropathy. T2DM patients are at risk of developing peripheral vascular disease twice or three times as high as people without diabetes mellitus. Subsequently, patients with peripheral vascular disorders will suffer from decreased pulses, intermittent claudication, and also sensory changes.<sup>4</sup> This condition is associated with changes in the peripheral circulation that affect the foot functions of T2DM.

Furthermore, functional changes in the diabetic foot can lead to complications that may result in foot amputation. Therefore, it is necessary to investigate the risk prediction for T2DM foot abnormalities with pain response parameters in patients with ankle-brachial index and sensory changes, as preventive measures to manage T2DM feet. This study is capable of providing an overview of the basic treatment methods used in detecting T2DM foot abnormalities that help prevent complications. Furthermore, the results obtained may be implemented to enable nurses and doctors in monitoring the functions of T2DM feet. This explained phenomenon prompted the researchers to carry out an analysis on the relationship between leg pain response in T2DM with ABI scores and peripheral sensory responses, as an effort to detect foot abnormalities.

## Design and Methods

The subject used in this study was made up of 63 T2DM patients in PHC, Malang. They were selected using a purposive sampling technique. Moreover, this study made use of a cross-sectional design. Furthermore, the patients' diabetic feet were examined by competent health staff with the aid of an equalization test of perceptions. The sample criteria include a patient that is more

### Significance for public health

*This study predicts the clinical conditions that affect foot comfort caused by T2DM in a community. Furthermore, it provides a rationale whereby community nurses are capable of determining the choice of modality intervention therapy that affects the macrovascular and microvascular complications. Comfort is an important aspect when providing care to T2DM patients experiencing complications of the feet when improving the quality of life of such patients.*

than 40 years of age, diagnosed with T2DM for more than 5 years, complains of tingling and pain in the legs, no paralysis and disability, and also no complications. The observations results were in the form of responses to leg pain, ABI scores, and peripheral sensory levels, and the data obtained were analyzed using the correlation and regression test with SPSS 16. The dependent variable for this study was leg pain responses, while the independent variables were ABI scores and sensory change levels. The instruments used in this study were visual analog scale (VAS), monofilament, and foot Doppler.<sup>5-7</sup> Permission was obtained to carry out this study from the Ethics Committee for Health and Medical Research, Faculty of Medicine, University of Brawijaya.

## Results and Discussion

### Characteristics of Respondents

The characteristics of the study subjects were age, duration of suffering from T2DM, systolic and diastolic pressures, blood sugar levels, uric acid, cholesterol, leg pain responses, ABI, sex, sensory responses, education, history of smoking, and exercise. These characteristics are presented in Table 1.

### Relationship of Leg Pain Response between ABI Scores and Sensory Status

The data normality test was first carried out before the bivari-

ate test, where the correlation coefficient value was shown to be less than 30%. This finding concludes that the data were normally distributed. The results of the analysis are summarized in Table 2.

Table 3 shows no relationship between the leg pain responses and ABI of the right and left feet ( $p$ -values = 0.21 and 0.69), but there was a significant relationship between the leg pain responses and the right and left foot sensory ( $p$ -values = 0.012 and 0.043). This study also showed that the right and left foot ABI was related to that of foot sensory ( $p$ -value = 0.010 and 0.003). Furthermore, it also shows a leg pain response and ABI modeling using the right and left foot sensory.

The results obtained signified that the independent variable in the regression modeling was the right and left foot sensory. According to Table 4, the coefficient of determination was 0.105, which means the regression model could explain 10.5% of the variation in the dependent variable. Moreover, the  $p$ -value of 0.035, implies that the regression model matched the existing data. Therefore, the relationship between the right and left foot sensory status and the leg pain responses in T2DM patients was moderate ( $R$ -value = 0.325).

The ABI and sensory status, in the foot of T2DM patients, had a moderate relationship ( $R$ -value of right foot = 0.338;  $R$ -value of left foot = 0.383) and a positive pattern. These findings denote that higher ABI scores escalate the foot sensory status of T2DM patients where the coefficient of determination of the right foot was 0.114, and it indicates that the line equation is capable of explaining 11.4% of the sensory variation in the right foot.

**Table 1. Characteristics of respondents.**

Characteristics (n=63)	Mean (SD)	Minimal-Maximal	95% CI
Age (years)	61.94 (7.62)	44-80	60.02-63.86
Duration of T2DM (years)	9.01 (3.22)	6-17	8.20-9.83
Systolic (mmHg)	137.46 (19.81)	100-175	132.47-142.45
Diastolic (mmHg)	83.49 (9.44)	65-100	81.11-85.87
BMI (kg/m <sup>2</sup> )	24.25 (4.68)	13.78-34.65	23.07-25.43
Blood Glucose (mg/dl)	283.89 (73.84)	166-460	265.29-302.49
Uric acid (mg/dl)	6.39 (1.58)	3.4-9.7	5.99-6.79
Cholesterol (mg/dl)	204.16 (46.70)	100-300	192.40-215.92
Leg Pain	5.62 (1.71)	3-8	5.19-6.05
Right Foot ABI	1.00 (0.15)	0.77-1.36	0.96-1.04
Left Foot ABI	0.97 (0.17)	0.64-1.33	0.93-1.01
Right Foot Sensory	5.84 (1.78)	2-9	5.39-6.29
Left Foot Sensory	5.90 (1.56)	2-9	5.51-6.30
	Total	%	
Sex			
Male	23	36	
Female	40	64	
Education			
Elementary School	38	60	
Primary High School	9	14	
Secondary High School	12	19	
College	4	7	
Smoking History			
Smoker	14	22	
Non-Smoker	49	78	
Exercises			
Always	21	33	
Often	10	16	
Seldom	28	44	
Never	4	7	

Meanwhile, the coefficient of determination of the left foot was 0.147 which implies that the line equation is capable of explaining 14.7% of the sensory variation in the left foot. The statistical tests revealed a significant relationship between the ABI scores and the sensory status of the right and left feet. The modeling results are illustrated in Table 5.

Chronic neuropathy is characterized by an exaggerated response to painful stimuli (hyperalgesia).<sup>8, 9</sup> While, the T2DM foot is characterized by spontaneous pain, hyperalgesia, and paresthesia that has a complex mechanism. This pain is caused mainly by blocked blood vessels in the legs and it affects the changes in the ABI scores. However, from this study, there was no relationship between leg pain responses and the ABI scores of the right and left feet. Changes in ABI may not reflect the occurrence of atherosclerosis, which causes pain in the legs.<sup>10</sup> Furthermore, the pain responses in the DM foot were influenced by complex conditions that changed the ABI score and this requires a longer process. The results, therefore, affirmed that the mean ABI scores of the right and left feet were within normal limits with an average duration of 9.01 years. Factors that influence ABI include age, gender, smoking history, hypertension, duration of DM, and BMI.<sup>11</sup> The sample characteristics used in this study include, the elderly, mainly women without a smoking history, mild hypertension, and excess BMI, and those affected by ABI condition while, the respondents' characteristics contributed to the occurrence of neuropathic pain.<sup>12, 13</sup> Furthermore, this study showed a negative direction and a moderate relationship between the sensory status of the right and left feet and the leg pain responses in patients with DMT2

and it also proposed a decrease in sensory responses with monofilament examination. The sensory status of diabetic feet was measured with a 10-g Semmes-Weinstein monofilament test.<sup>12, 14, 15</sup> Moreover, this condition verifies that microcirculation may improve the peripheral sensory status; thereby helping the patient to reduce their response to pain which impacted their comfort and also improve the quality of life.<sup>12</sup> This study was used to develop a model that aids in leg comfort for patients with DM. Therefore, further studies are needed to investigate the standard of treatment for diabetic neuropathic pain which may involve the combinations of therapy and drug that offers an opportunity to develop a nursing modality therapy to manage the pain of DM foot.<sup>16-18</sup> Modeling the sensory status of the right and left feet with pain response can guide practitioners to predict any emerging changes.

The ABI and sensory status in the feet of T2DM patients showed a moderate relationship and a positive pattern. These findings imply that a higher ABI score increases the foot's sensory status. The ABI is a macrocirculation indicator, while the sensory status of the foot skin is a microcirculation indicator.<sup>19, 20</sup> The process of complications in diabetic foot periphery may be influenced by macrocirculation conditions. Therefore, it is crucial to predict any emerging changes in macrocirculation conditions due to changes in microcirculation. From the results obtained in this study, an understanding of macro and microcirculation conditions in diabetic foot management must be considered as a means of improving treatment. This method may also be used as a future target for the management of macro and microcirculation foot conditions of DM patients.<sup>21</sup>

**Table 2. Normality test results.**

	Leg Pain		Foot ABI		Foot Sensory	
	Right	Left	Right	Left	Right	Left
SD	1.7	0.15	0.17	0.17	1.7	1.5
Mean	5.6	1	0.97	0.97	5.8	5.9
Covariance coefficient	30.35	15	17.52	17.52	29.31	25.42

**Table 3. Correlation, means, and SD of variable models.**

Variable	Mean (SD)	p				
		1	2	3	4	5
1. Leg pain	5.62 (1.71)	-	-	-	-	-
2. Right foot ABI	1.00 (0.15)	0.21	-	-	-	-
3. Left foot ABI	0.97 (0.17)	0.69	0.000*	-	-	-
4. Right foot sensory	5.84 (1.78)	0.012*	0.010*	0.003*	-	-
5. Left foot sensory	5.90 (1.56)	0.043*	0.000*	0.003*	0.000*	-

\* Significantly different p-value < 0.05.

**Table 4. Correlation and regression analysis of right and left foot sensory status with leg pain responses in T2DM patients.**

Variable	r	R <sup>2</sup>	Equation	p
Sensory status of right and left feet	0.325	0.105	Leg pain = 7.66 -0.244 right foot sensory - 0.105 Left foot sensory	0.035

**Table 5. Analysis of ABI correlation and regression with sensory status in the foot of T2DM patients.**

Variable	r	R <sup>2</sup>	Equation	p
Right Foot ABI	0.338	0.114	Right Foot Sensory = 1.76 + 4.16 Right Foot ABI	0.007
Left Foot ABI	0.383	0.147	Left Foot Sensory = 2.23 + 3.89 Left Foot ABI	0.002

This study showed that there was no relationship between leg pain responses and ABI scores of the right and left feet in T2DM. Therefore, it is known that the ABI score reflects the macrocirculation conditions and the pain response because of the defects in microcirculation which is measured using TcPO<sub>2</sub>.<sup>22,23</sup> This finding may be due to the presence of hyperglycemia that induces changes in the microvascular function, which increases the capillary pressure of the lower extremity and reduces the vasodilation response that occurs in diabetic neuropathy.<sup>24</sup> However, there was a moderate relationship and a negative direction between the sensory status of the right and left feet and the leg pain responses. This finding, therefore, confirms that monofilament examination increases pain responses. Moreover, there was a positive pattern and a moderate

relationship between the ABI and sensory status. According to the result, a higher ABI score improves the sensory status of the feet of T2DM patients. Therefore, it is important to understand the central pain mechanism and how it affects neuropathic diabetes. The central pain mechanism occurs due to cellular changes in response to the central and peripheral system in the form of excessive synaptic input, decreased neuronal activation threshold, increased response for the unlimited stimuli, and expansion of the receptor areas,<sup>9</sup> which leads to a simulation in the neuropathic pain. In addition, the aberration in the transmission of a signal between the neurons and glia also contributes to the factors that trigger neuropathic pain. Some hypotheses also suggest that microglia, loss of oligodendrocytes in the spinal cord and axons in the dorsal horn of the spine stimulate neuropathic pain.<sup>25,26</sup> The mechanism of alteration in neuropathic pain is unclear, hence, several studies have suggested that the coexistence of pain may lead to a series of maladaptive neuroplastic changes involving the thalamus and other parts of the central projection of the somatosensory system.<sup>27</sup> It is pivotal to conduct further studies with the use of large study subjects which will aid in achieving a clinical intervention for diabetic foot care.

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## Conclusions

The relationship between the sensory status of the right and left feet and the leg pain responses in T2DM patients was moderate with a negative direction. It implies that a decrease in sensory responses led to an increase in leg pain. Meanwhile, a moderate relationship and a positive direction between the ABI and sensory status indicates that a higher ABI score will lead to an increase in the sensory status of the T2DM foot.

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