RESEARCH ARTICLE

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Correlation between Ankle-Brachial Index Score and Diabetic Polyneuropathy Degree of Severity

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Abstract

Diabetic polyneuropathy (DPN) is the most prevalent chronic microvascular complication of type 2 diabetes mellitus (DM). The severity of DPN is categorized based on symptoms, signs, and nerve conduction study (NCS) abnormality into grades 0, 1a, 2a, and 2b. Pathogenesis of DPN consists of metabolic and vascular processes. In addition, macrovascular factor also plays a role in the pathogenesis of DPN. Macrovascular diseases, such as peripheral arterial disease (PAD), could be diagnosed using the ankle brachial index (ABI). Several studies have proven a strong correlation between ABI and DPN; hence, this study aimed to examine the correlation between ABI score and DPN severity. This was a cross sectional analytic study on. 73 type 2 DM patients who met the inclusion and exclusion criteria and visited the outpatient Endocrine Clinic and Neurophysiology laboratory of the Department of Neurology Dr. Hasan Sadikin General Hospital Bandung, during the priod of June to October 2018. ABI examination were performed after DPN indication was evident from results of physical examination, lab tests, and NCS. Rank Spearman statistical analyses were performed to assess the correlation between ABI score with DPN severity and the result was considered significant if p value <0.05. No correlation was found between ABI score DPN severity and between ABI score and DPN symptoms, signs, and NCS abnormality. Hence, ABI score does not correlate with DPN severity stage.

Key words: Ankle brachial index, diabetic polyneuropathy, nerve conduction study

Hubungan Skor *Ankle-Brachial Index* dengan Derajat Keparahan Polineuropati Diabetika

Abstrak

Komplikasi kronis mikrovaskular diabetes mellitus (DM) tipe 2 yang sering ditemukan adalah polineuropati diabetika (PND). Derajat keparahan PND berdasar gejala, tanda, dan abnormalitas pemeriksaan konduksi saraf tepi (KST) dibagi atas derajat 0, 1a, 2a, dan 2b. Patogenesis PND terdiri atas proses metabolik dan vaskular. Faktor makrovaskular diduga memiliki peranan terhadap terjadinya PND. Penyakit arteri perifer oklusif (PAPO) adalah penyakit makrovaskular yang dapat dideteksi dengan pemeriksaan *ankle brachial index* (ABI). Beberapa penelitian membuktikan hubungan antara skor ABI dan PND. Penelitian ini bertujuan menilai hubungan antara skor ABI dan derajat keparahan PND. Penelitian bersifat observasi analitik studi potong lintang yang dilakukan pada 73 penyandang DM tipe 2 yang memenuhi kriteria inklusi dan eksklusi di Instalasi Rawat Jalan Klinik Endokrin dan Laboratorium Neurofisiologi KSM/Departemen Neurologi RSUP Hasan Sadikin Bandung periode Juni sampai Oktober 2018. Pemeriksaan ABI dilakukan setelah pemeriksaan klinis PND, laboratorium darah, dan KST. Korelasi antara skor ABI dengan derajat keparahan PND dinilai menggunakan analisis statistik *Rank* Spearman, signifikan jika p<0,05. Tidak terdapat korelasi antara skor ABI dan derajat keparahan PND. Tidak terdapat korelasi gejala PND, tanda PND, maupun abnormalitas uji KST dengan skor ABI. Skor ABI tidak berkorelasi dengan derajat keparahan PND, baik gejala PND, tanda PND, maupun abnormalitas uji KST.

Kata kunci: *Ankle brachial index*, konduksi saraf tepi polineuropati diabetika

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Introduction

World Health Organization (WHO) predicts an increase in the number of people with diabetes mellitus (DM) and has considered the disease as one of the global health threats. The worldwide prevalence of DM is estimated at 8.3% in the adult population or 382 million people.[1-3] Indonesia has been estimated to have increased number of people with DM based on the prediction from WHO that predicts an increase from 8.4 million in 2000 to around 21.3 million in 2030.[4]

Complications of DM may take the form of acute as well as chronic complications, whic is further divided into macroangiopathy and microangiopathy. Among the most frequent complications of DM, distal sensorimotor polyneuropathy, or better known as diabetic polyneuropathy (DPN), is the most frequently seen with 75% of all diabetic neuropathy (DN) present this condition. DPN complications can aggravate the patient's condition and may lead to the amputation of the limbs due to infected ulcers. This makes early diagnosis of this complication very important.[3-11]

Ankle brachial index (ABI) is an examination commonly used for atherosclerosis screening, especially in occlusive peripheral arterial disease (PAD). A positive correlation between PAD and DPN has already proven by several studies on the relationship between ABI and DPN.[10,12-15] The purpose of this study was to assess the correlation between ABI scores and the severity of DPN.

Methods

This was a cross-sectional analytical observational study on people with type 2 diabetes aged >18 years. The target population was type 2 DM people who met the inclusion criteria and exclusion criteria criteria. Subjects were sampled using convenient sampling until a predetermined number of subjects was reached. Anamnesis, physical examination, and laboratory tests were performed to look for symptoms or signs of DPN while the peripheral nerve conduction were tested by electromyography machine. The ABI measurement was carried out twice using the Doppler method. Patients were ask to lay down in a supine position and the systolic blood pressure was measured by a Doppler probe (8 MHz) on the posterior and anterior tibial (or dorsal pedis) arteries of each foot and on the brachial artery of each arm after 5–10 minutes of resting.. The ABI of each leg was calculated by dividing the highest ankle systolic blood pressure (SBP) by the highest arm SBP.[16] The study was conducted during the period of June 2018 to October 2018 at the Endocrine Outpatient Clinic and the Laboratory of Neurophysiology, Department of Neurology Dr. Hasan Sadikin General Hospital Bandung. From a total of 92 patients visiting the clinic, 73 subjects met the criteria and agreed to participate in the study as depicted in Figure.

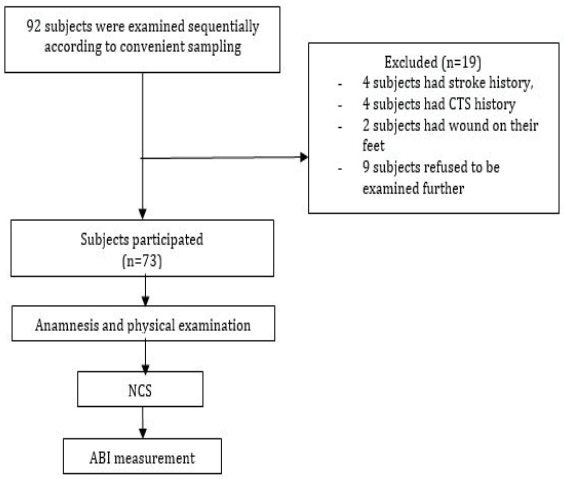

Figure Flow of Inclusion of Research Subjects

Results

There were more females than males participating in this study (53.4%vs.46.6%). Most subjects (60.3%) consumed oral hypoglycemic agent (OHA) to control their blood sugar levels. More than half of the subjects (68.5%) also claimed to had never smoked up to one hundred cigarettes in their lifetime. In addition, most subjects presented DPN symptoms and clinical signs, as well as NCS abnormalities, supporting the diagnosis of DPN. Most subjects suffered from degree 2a DPN (83.6%, n=61). The characteristics of subjects are described in Table 1.

No significant correlation was found between the ABI scores and DPN severity for 0,1b, and 2a degree DPN ($p > 0.05$). (Table 2).

Table 3 shows the relationship between each DPN sign and symptom,, NCS abnormalities, and ABI scores. No significant correlation was found between the symptoms of DPN, signs of DPN, or abnormal NCS with ABI scores.

Table 1 Subject Charateristics

Variable	n=73
Age (years), mean±SD	56±10
Gender, n (%)	
Male	34 (47)
Female	39 (53)
BMI (kg/m^2), mean±SD	26.48±4.31
Blood pressure (mmHg),	
Systole, median (min-max)	130 (90–190)
Diastole, median (min-max)	80 (60–100)
HbA1C level (%), median (min-max)	7.5 (5.0–13.4)
DM Therapy, n (%)	
Diet	6 (8)
Insulin	14 (1)
OHA	44 (60)
Insulin+OHA	9 (12)
Dyslipidemia, n (%)	
Yes	59 (81)
No	14 (19)
Smoking status, n (%)	
Yes	23 (31)
No	50 (69)
DM duration (years), median (min-max)	4 (1–40)
DPN symptoms, n (%)	
Present	61 (84)
Not present	12 (16)
DPN signs, n (%)	
Present	66 (90)
Not present	7 (10)
NCS (nerve conduction study), n (%)	
Abnormal	66 (90)
Normal	7 (910)
DPN degree, n (%)	
0	7 (10)
1a	-
1b	5 (7)
2a	61 (84)
2b	-
ABI score, median (min-max)	1.05 (0.61–1.63)
ABI category	
Low (≤0,9)	4 (5)
Borderline (0,91–1,00)	18 (25)
Normal (1,01–1,4)	50 (69)
High (>1,4)	1 (1)

Note: SD=Standard Deviation, n= number, %=percentage

Discussion

The result of this study is quite surprising despite the absence of other similar study because several previous studies have suggested a positive correlation between PAD and APN. In their study, Lee and Hsieh[17] discovered a significant relationship between DPN severity (based on NCS results) and PAD, which was characterized by an ABI score of <0.9. This is different from the result in this study where all patients with a low ABI score suffered from 2a degree DPN but no

Table 2 Bivariate Analysis of Relationship between Independent Variables and DPN Degree

Independent variables	DPN Degree			p-value	Correlation Coefficient (r_s)
	0 n=7	1b n=5	2a n=61		
ABI Category	1.04 (1.0–1.13)	1.04 (1.0–1.27)	1.06 (0.61–1.63)	0.483	-0.005[a]
Low (≤0.9)	0 (0)	0 (0)	4 (7)	0.950	0.148[b]
Borderline (0.91–1.00)	2 (29)	2 (40)	14 (23)		
Normal (1.01–1.4)	5 (71)	3 (60)	42 (69)		
High (>1.4)	0 (0)	0 (0)	1 (1)		

Note: analysis using [a]Spearman's rank, [b]contingency coefficient, * significant if p <0.05

Table 3 Bivariate analysis of the Relationship of Symptoms and Signs of DPN. and Abnormalities of NCS with ABI scores

Independent Variables	ABI	
	Coefficient Correlation (r_s)	p-value
Clinical symptoms DPN	-0.048	0.344
Clinical signs of DPN	-0.009	0.470
Nerve conduction study	-0.009	0.470

Note: analysis using point biserial. *significant p<0.05

significant correlation was found. This might be explained from the perspective of the difference in methods in the two studies.

The first difference is the categorization of DPN severity. In their study, Lee categorized DPN severity only by NCS result. This is different from this study that categorized the DPN severity based on symptoms, signs, and NCS abnormalities. The second probable difference is the method used to perform ABI examination by Lee et al.[17] since they do not state whether the AHA gold standard using the Doppler's method was used.[16] The mean age of the 160 patients in their study (67.45±11.35 years) is also older than the one in this study, i.e. 56±10 years.

However, the result of this study is supported by Hwang et al.[18] who only found associations between DPN severity and DM duration, HbA1C levels, DM nephropathy, pulse wave velocity (PWV) in the ankle arm, LDL, and microalbuminuria levels, but not with ABI scores. The number of abnormalities in ABI was noticeably small that the accurate relationship with the severity of DPN could not be established. This is similar to the abnormal ABI distribution found in this present study, which was ranged between 0.61 and 1.63 with a median of 1.05. There were a lot of subjects with DPN who had normal ABI score that it was statistically difficult to establish its significant correlation with DPN severity degree that was assessed based on DPN signs and symptoms or abnormal NCS.

Despite many complaints of DPN symptoms among the subjects, no significant correlation was found in terms of ABI score. In contrast to this result, Chevtchouk et al.[19] found a significant difference between normal and abnormal ABI groups (<0.9) with neuropathic pain in people with DM with a duration of >10 years. However, only few subjects in this study had had DM for >10 years.

On the other study, Chevtchouk et al.[19] had measured ABI and NDS scores on 126 people with DM and it was found that the sensitivity and specificity of the two scores for predicting DPN were 47% and 90.7%, respectively. NDS is a DPN clinical scoring consisting of vibration perception threshold, perceptions of temperature on the back of the foot, excitatory pain in the big toe, and Achilles reflex examinations. An NDS score of ≥6 supports the diagnosis of DPN. Therefore, there is clearly a fundamental difference between the methods used in the two studies because this study included subjects with an ABI score of ≥1.3 as one of the exclusion criteria.

In contrast to Chevtchouk et al.,[19] Ogbera et

al.[20] who examined 225 people with DM found no significant role of low ABI scores in predicting the presence of DPN although they had excluded subjects with high ABI scores (>1.4). DPN diagnosis in the study was based on clinical signs, namely the result of biothesiometer examination which is one of the methods for testing vibration sensibility.

The incidence of NCS abnormalities in this study was similar to the DPN sign found with no significant correlation with the ABI score. Lee and Hsieh[17] studied 60 people with DM and found a significant correlation between the severity of DPN and the appearance of PAD (ABI score <0.9). The correlation was mainly found in the NCS of lower limb, namely compound muscle action potentials (CMAP)/amplitude and motoric nerve conduction velocity (NCV) both for tibial and sensory nerve action potentials (SNAP)/amplitude and sensory NCV of both sural nerves ($p<0.05$). Hence, it is considered that this result has successfully proven the presence of a relationship between lower limb ischemia and nerve fiber function.

Hwang et al.[18] also categorized DPN severity based on NCS abnormalities, just as used in Lee and Hsieh[17]; however, the details were different, i.e. mild DPN if the sural nerve amplitude <5 μv was accompanied by one other criterion or amplitude >5 μv but accompanied by two other criteria; Moderate DPN if the amplitude of the sural nerve <5 μv was accompanied by two to four other criteria; Severe DPN if the sural nerve amplitude <5 μv is accompanied by five other criteria. Other criteria included sural nerve amplitude ≤5 μv, median nerve sensory amplitude ≤10 μv, motor amplitude of peroneus nerve <1 mv, distal peroneus nerve motor latency ≥6 ms or peroneus nerve motor NCV <40 m/sec, latency F wave in the peroneus nerve has no response or >55 ms, H-reflex is absent, and the presence of fibrillation in the lower limb muscles (tibialis anterior, gastrocnemius, etc.) on electromyography (EMG) examination.

No relationship was established between ABI score and DPN severity and existence. Low, borderline, and high ABI scores cannot reflect the severity of symptoms, signs, and abnormalities of NCS test in DPN sufferers.

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