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Prehypertension is associated with peripheral arterial disease and low ankle-brachial index

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ABSTRACT

Patients with prehypertension suffer endothelial dysfunction and are at increased cardiovascular risk. Ankle-brachial index (ABI) constitutes an efficient tool for diagnosing peripheral arterial disease; but also an ABI < 0.9 is an independent and positive predictor of endothelial dysfunction and is associated with increased cardiovascular risk and mortality.

The aim: of this study was testing whether ABI was decreased in prehypertensive patients when compared with normotensive subjects.

Methods: We included 70 prehypertensive patients older than 19 years, in whom the ABI was registered with a 5 megahertz Doppler (Summit Doppler L250, Life Dop., USA). The highest ankle systolic pressure was divided by the highest brachial systolic pressure. We also included 70 normotensive subjects in whom the ABI was registered in the same way. The measurements were performed by the same physician who was blinded about the study.

Statistical analysis was performed with odds ratio and student *t*-test.

Results: The ABI values in normotensive subjects were 1.023 ± 0.21, whereas prehypertensive patients significantly had lower ABI (0.90 ± 0.14p = 0.00012).

We found ABI <0.9 in 30 prehypertensive patients (42.85%) and 13 normotensive patients (18.5%). The odds ratio of ABI <0.90 in prehypertensive patients was 3.288 (IC_{95} 1.5–7.0, p = 0.0023).

A regression analysis failed to show any independent association between ABI values and any other clinical parameter.

Conclusions: Prehypertensive patients had lower ABI and higher prevalence of peripheral artery disease when compared with normotensive subjects; this fact increases their cardiovascular risk. ABI must be included in global evaluation of prehypertensive subjects.

1. Introduction

Prehypertension, which was defined as the presence of systolic blood pressure (BP) between 120 mmHg to 139 mmHg and/or a diastolic BP between 80 mmHg and 89 mmHg by "the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)"; has a prevalence of 26.5% in Mexico.[1,2]

Usually being asymptomatic, peripheral arterial disease (PAD) is an underdiagnosed disease that affects 23.8% of Mexicans over 55 years old.[3] Moreover, PAD is rarely an isolated condition; it is also an indicator of generalized atherosclerosis. Indeed patients with PAD have an increased risk of coronary artery disease and/or cerebrovascular disease.[4]

Ankle-brachial index (ABI) is the ratio of the ankle and brachial systolic pressure; it is a non-invasive, low-cost, quick, office measurement method for diagnosing PAD. In fact, an ABI < 0.9 has high sensibility (91%–95%) and specificity (85%–100%) to diagnose lower extremity atherosclerosis.[3,4]

Furthermore, a low ABI could be considered as a marker of end organ damage and a predictor of cardiovascular and cerebrovascular disease. Patients with an ABI < 0.9 significantly have a reduced survival compared with those with normal ABI. According to the evidence, there is an increase of 10.2% in the relative risk of cardiovascular events and mortality by every 0.1 of reduction in the ABI.[5] A very high ABI (>1.40) is related to stiffness of arteries, and also is associated with increases in mortality.[6]

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The aim of this study was to test whether ABI was decreased in prehypertensive patients when compared with normotensive subjects.

2. Methods

We evaluated 70 prehypertensive patients older than 19 years, statin-naive and without previous antihypertensive drug therapy. Blood pressure was recorded in triplicate with a mercurial sphygmomanometer (Tycos, Rochester, New York, USA), in the sitting position after a 5-min rest and at 5-min intervals; an average of the three measurements was recorded, the personnel measuring each patient's BP was blinded to the study.

In all of them the ABI was registered with a 5 megahertz doppler (Summit doppler L250, Life Dop., USA). We also included 70 normotensive subjects in whom the ABI was registered in the same way. The measurements were performed by the same physician who was blinded about the study.

Measurement of ABI was performed by placing the patient in the supine position, with the arms and legs at the same level as the heart, for a minimum of 10 min before register. The systolic blood pressures was registered in right and left posterior tibial arteries and right and left brachial arteries respectively. The register was done by using a standard mercury sphygmomanometer and a hand-held validated Doppler instrument (5 MHz, Summit Doppler L250, Life Dop., EUA). The higher ankle systolic pressure was divided by the higher brachial systolic pressure.[4,7] All registers were performed in the morning, between 8:00 and 10:00 h, on fast, by personnel blinded to the study. Readings were taken only one day per patient.

Additionally, there were measured serum glucose (glucose oxidase, Beckman Coulter, Brea. CA, USA), creatinine (JAFFE, Beckman Coulter, Brea. CA, USA), lipid profile (CHOD-PAP, Beckman Coulter, Brea. CA, USA) and triglycerides (triglyceride-pap, Beckman Coulter, Brea. CA, USA) using a UniCel Dace 600 Synchron Clinical Systems (Beckman Coulter, Brea. CA, USA) automatic equipment, in all subjects. All venous samples were collected in the morning, after 12 h overnight fast.

Patients with any of the following diagnoses were excluded from the study: decompensated Diabetes mellitus (glucose $\geq$ 250 mg/ml), heart, hepatic, or renal failure, evidence of valvular heart disease, heart block or cardiac arrhythmia, acute coronary syndrome or cerebrovascular disease six months before the baseline of the study. There also were excluded subjects with autoimmune disease, pregnancy and alcohol or psychotropic drugs abuse.

The study was conducted with the approval of the Research and Ethics Committee of our hospital, in accordance with the Helsinki declaration. The register number is 208/010/017/16. Participants gave written informed consent before their inclusion in the study protocol.

Statistical analysis was performed with odds ratio and student-t test. A $p < 0.05$ was considered as statistically significant.

A regression analysis was performed to asses if the difference in ABI values is independent of variables that have a significantly difference between groups.

3. Results

The basal characteristics of the patients and controls are shown in Table 1; briefly, prehypertensive patients were older than normotensive subjects.

The blood pressure range (minimum and maximum) observed for prehypertensive group was 122/82–138/88 mm Hg, and for subjects with normal blood pressure was 92/56 to 112/80 mm Hg.

Table 1
Basal characteristics of the patients.

	Prehypertensive	Normotensive	P
Gender (M/F)	21/49	20/50	NS
Age (years)	35.9 ± 6.3	32.1 ± 5.3	0.01
Body Mass Index	30.2 ± 6	29.5 ± 4	0.12
Blood Pressure (mm Hg)	128 ± 5.3 /80 ± 4.8	102 ± 5.3 /66 ± 4	0.0001
Glucose (mmol/L)	5 ± 0.51	5.16 ± 0.39	0.33
Creatinine (μmol/L)	90.17 ± 8.3	83.3 ± 9.72	0.20
Low density lipoprotein (mmol/L)	2.80 ± 0.19	2.72 ± 0.10	0.92
High density lipoprotein (mmol/L)	0.88 ± 0.20	0.91 ± 0.20	0.45
Triglycerides (mmol/L)	2.8 ± 0.72	2.83 ± 1.1	0.19

The difference between groups was calculated with student *t*-test

The ABI values in normotensive subjects was 1.024 ± 0.21, whereas in prehypertensive patients was 0.90 ± 0.14. When both groups were compared with student-t test, the prehypertension group had a significantly lower ABI than normotensive subjects (p = 0.00012, Fig. 1).

We found PAD (defined as an ABI < 0.9), in 30 prehypertensive patients (42.85%), and 13 normotensive subjects (18.5%). However, no patient complains of associated symptoms.

The odds ratio for an ABI < 0.90 in prehypertensive patients was 3.28 (IC_{95} 1.5–7.0, p = 0.0023).

A regression analysis failed to show any independent association between ABI values and any other clinical parameter.

4. Discusion

A higher prevalence of peripheral arterial disease in prehypertensive subjects was found in this study. At the same time it was observed a lower ABI when compared with normotensive subjects. It is important to underline the fact that the ABI was measured by the same physician who was unaware of the study. Observer variation was taken into account when statistical analysis was performed. Unexpectedly, the prevalence of peripheral artery disease was higher in prehypertensive patients in our study than previous reports of Mexican people >55 years.[3] Al this time we do not have an explanation for that, this item requires further research.

None of our patients complains of associated symptoms; This is an expected finding since patients with PAD are usually asymptomatic.[3,8]

Previously, Korhonen et al. demonstrated that hypertensive patients had lower ankle-brachial index than normotensive patients[9]; and that those patients with resistant or uncontrolled

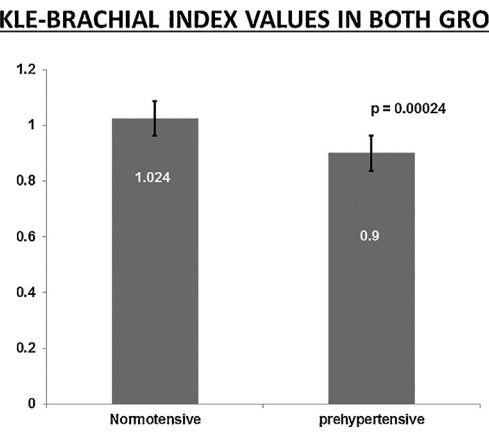

Fig. 1. Ankle-brachial index values in both groups.

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