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Assessment of association between ankle-brachial pressure index and pulse wave velocity in patients with isolated hypertension according to gender

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ABSTRACT

Aims: Endothelial dysfunction and atherosclerosis are well-known risk factors for cardiovascular diseases in hypertension (HT). This study investigated the relationship between ankle-brachial pressure index (ABPI) and pulse wave velocity (PWV) in patients with isolated HT (IHT) and the difference according to gender.

Methods: This single-center, cross-sectional, and observational study was carried out between November 2014 and May 2015 in the outpatient clinic of the Department of Internal Medicine of Gülhane Military Medical Academy.

Results: The study included 90 patients with IHT (mean±SD age: 57.25±14.5 years, 63.3% female). No statistically significant difference was detected in ABPI (1.1±0.1 vs. 1.1±0.2, p=0.342) and PWV (10.9±2 vs. 10.5±1.9, p=0.341) measurements between male and female patients. In both sexes, SBP and DBP values correlated with CAP (Female: r=0.935, p<0.001; r=0.637, p<0.001, respectively. Male: r=0.944, p<0.001; r=0.749, p<0.001, respectively). SBP values correlated with ABPI among female patients (r=-0.277, p=0.037) but not among male patients. DBP did not correlate with ABPI in both sexes. No correlation was found between CAP and PWV in both sexes.

Conclusions: ABPI and PWV values may not be alternative to each other in patients with IHT.

Introduction

Hypertension (HT) is a chronic disease that threatens public health due to its complications and has an increasing prevalence (1). The prevalence of HT in the adult population is 30.3%, while it is 28.4% in males and 32.3% in females in Turkey (2). High blood pressure (BP) is a potent risk factor for the development of cardiovascular diseases (CVDs) (3,4). HT is a primary factor for CVD, which is the leading cause of the death. The 50-75% of strokes and 45-55% of both myocardial infarction and also congestive heart failure detected in the population were caused by HT.

HT leads to the development of endothelial dysfunction (ED) and atherosclerosis that play a crucial role in the pathogenesis of the damage of target organs (5). It has shown that ED is a precursor of atherosclerosis, which may occur prior to atherosclerosis in the presence of increased risk factors (6,7). ED is the first step for the atherosclerotic process that leads to plaque formation. Also, ED induces the growth and rupture of the formed plaque and triggers thrombogenic events (8). A study conducted with young patients with coronary artery disease (CAD) showed that ED was seen not only in atherosclerotic vessels, but also in non-atherosclerotic vessels (9). It is thought that ED may indicate the tendency for the development of atherosclerosis. Also, the presence of ED may be a bad prognostic indicator in CVDs (10). To evaluate the presence of atherosclerosis and the potential stiffness of the vessel wall, Ankle-Brachial Pressure Index (ABPI) and pulse wave velocity (PWV) can be used as non-invasive methods.

Measurement of ABPI is an inexpensive and easy-to-implement method. It can be calculated by dividing the ankle systolic pressure value by the simultaneously measured brachial systolic pressure value. Regularly, the systolic pressure measured in the ankle is equal to or greater than the systolic pressure measured in the arm. Therefore, the normal ABPI value is equal to or greater than 1, but, due to technical differences in measurements and acceptable mild vascular stenosis, the values above 0.90 are considered as normal (11). Lower levels of ABPI (<0.90) can predict CVDs and atherosclerosis. Additionally, an ABPI value equal to or lower than 0.90 has 90% sensitivity and 98% specificity for peripheral artery disease (PAD) (12). Whereas, a low ABPI value can be used for confirmation of PAD, and also, it may indicate the presence of PAD in asymptomatic patients (13). Low levels of ABPI may be an indicator for poor prognosis in long-term risk assessment in patients with PAD. A 3- to 6-fold increased risk of death due to CVD is associated with low ABPI values. On the other hand, high ABPI (>1.4) has also been found to be associated with an increased mortality rate (14).

In the assessment of arterial stiffness, various parameters have been defined. Because of the difficulty in the application of catheter-based interventional measurements, noninvasive methods have been developed. Measurement of PWV by using an arterial tonometer is a frequently used noninvasive method for determining arterial stiffness. Left ventricle contracts provide the strength to push the blood through the ascending aorta, which creates a pressure wave on the arterial vessels of the whole body. The spreading speed of this wave is PWV, which is an indicator for arterial stiffness (15). As arterial stiffness increases, PWV spreading through the arterial system also increases (16,17). The higher the PWV, the weaker the arterial expansion ability (distensibility) (15). According to the 2013 criteria of the European Society of Cardiology and the European Society of HT (ESC/ESH), the threshold value of PWV is determined as 10 m/s (18). The increase in PWV leads to an early reflection and a faster access of the pulse wave to the periphery vessels. The attainment of the reflected wave to the heart removes from diastole to systole with time. Consequently, a rise in arterial stiffness causes an increased pressure at the aortic root, also named central aortic pressure (CAP), in late systole, decreased pressure in diastole, and an increase in mean arterial pressure (19). Measurement of ABPI and PWV can predict the presence of aggravated atherosclerosis and arterial stiffness, and may aware physicians of increased CVD risk in patients with HT.

This study aimed to evaluate the relationship between ABPI and PWV values in male and female patients with HT, the role of these parameters to get precautions for CVD and providing contributions to the follow-up and treatment of CVD.

Methods

Study Design and Patient Selection

This was a single-center, cross-sectional, and observational study that was carried out between November 2014 and May 2015 in the outpatient clinic of the Department of Internal Medicine of Gülhane Military Medical Academy, Ankara, Turkey. A total of 90 patients who were followed up with isolated HT (IHT) according to the recommendations of the 2013 ESC/ESH guidelines were included in the study (18). Written informed consents were obtained from all participants.

HT was defined as a systolic BP (SBP) equal to and greater than 140 mmHg and a diastolic BP (DBP) equal to and greater than 90 mmHg, or elevated BP that increases the risk of damage in the target organs such as the heart, brain, kidney, and retina. Participants' age, gender, smoking status, comorbid diseases, and medications were recorded. Biochemical parameters including renal function tests, transaminase levels, serum lipid profile, and blood glucose levels, and complete blood count levels which were evaluated within three months were recorded in the patients' follow-up forms. Body mass index (BMI) calculated by dividing weight by height squared (kg/m²) was recorded for each participant. Patients who had malignancies, diabetes mellitus (DM), hyperlipidemia, PAD, CAD, and thyroid disease, who were under 18 years old, and who did not approve to participate in the study were excluded from the study.

Measurement of ABPI

ABPI measurement was made by a trained physician with a hand-held Doppler probe (Hadeco, Japan) and calibrated standard sphygmomanometers with a 12 cm cuff width (ERKA, D-83646, Germany) in an isolated room. The patients rested for at least 5 minutes before the measurement. ABPI measurement was performed while the patient was lying in the supine position with a cuff wrapped around just above both arms and ankles, beginning from the right arm. Consequtive measurements were taken from the right leg, the left leg and the left arm. The hand-held Doppler device placed on the brachial artery, the anterior tibial artery, and the posterior tibial artery determined SBP. While deflating the cuff slowly, the first pulse detected from the Doppler was noted as BP. The highest value of right and left brachial pressure was noted as the value of the upper extremity. The procedure was repeated for both right and left anterior and posterior tibialis arteries and the highest value was accepted as the ankle pressure. ABPI was calculated for both right and left by dividing the lower extremity value by the upper extremity value. The lowest value from the right and left extremity was accepted as the ABPI value of the patient.

Measurement of PWV

PWV measurement was performed by The TensioMed (Budapest, Hungary) brand arteriography, in an isolated room after a rest for at least 5 minutes in the supine position. Smoking and caffeinated beverages were stopped within 30 minutes before measurement. The distance between the jugular notch and the symphysis pubis was measured and recorded in the device in centimeters. After the pressure was measured with the arteriography device, the cuff was inflated at least 35 mmHg above the systolic pressure value detected simultaneously. During the measurement (for 8-20 seconds), the blood flow cessation was provided by the complete brachial artery occlusion. The signals obtained were transferred to the computer and analyzed to receive SBP, DBP, central aortic (or aortic) pressure ‘CAP’, and PWV values automatically by the device.

Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences for Windows version 21.0 package program (Armonk, NY: IBM). Numerical variables were summarized with mean±standard deviation or median (minimum-maximum) values, and categorical variables with numbers and percentages. Whether numerical variables showed normal distribution or not was examined using the Kolmogorov-Smirnov test. Similarity of group variances was investigated by the Levene test. Difference between the two groups in terms of numerical variables (if any) was investigated using the t-test in independent groups if the parametric test assumptions were met, and with the Mann-Whitney U test if not. Whether there was a difference between the groups in terms of categorical variables was examined using the chi-square test. The relationship between numerical variables was evaluated with the Pearson correlation coefficient. Level of statistical significance was accepted as $p<0.05$.

Results

A total of 90 patients with IHT, including 33 (36.7%) male and 57 (63.3%) female, were included in the current study. The mean age of the patients was 57.3±14.5 years. According to the 2013 ESC/ESH guideline, 5 (5.6%) patients had optimal BP, 9 (10%) had normal BP, 12 (13.3%) had high-normal BP, 38 (42.2%) had stage 1 HT, 15 (16.7%) had stage 2 HT, and 11 (12.2%) had stage 3 HT. There was no significant difference between male and female patient groups in terms of HT stages ($p>0.05$). Female patients had higher BMI and waist circumference than male patients ($p<0.001$ and $p=0.002$, respectively), whereas male patients were taller than female patients ($p<0.001$). The smoking rate was higher among males than females ($p=0.002$). Forty-seven (82.5%) female patients and 27 (81.8%) male patients were receiving treatment for HT ($p>0.05$). There was no difference between male and female patients in terms of the number of antihypertensive drugs used ($p>0.05$) (Table 1).

The mean value of PWV was 10.9±2 m/s in male patients and 10.5±1.9 m/s in female patients ($p=0.341$). The mean ABPI value was 1.1±0.1 in male patients and 1.1±0.2 in female patients ($p=0.342$). Normal ABPI values were present in 60 (66.7%) patients, whereas 10 (11.1%) patients had low values, 19 (21.1%) patients had borderline ABPI values, one (1.1%) patient had high ABPI value (Table 2). In female patients, as BP increased, CAP increased and ABPI values decreased ($p=<0.001$ and $p=0.003$, respectively). In male patients, as arterial BP increased, CAP increased ($p=<0.001$). There was no relationship between arterial BP and PWV values in male or female patients (Table 3).

A positively significant correlation was present between CAP and values of SBP and DBP in female and male patients. On the other hand, a significant negative correlation was present between ABPI and SBP values in female patients. There was no relationship between ABPI and PWV values in male and female patients (Table 4).

Discussion

Determination of arterial stiffness and atherosclerosis with non-invasive methods in patients with increased risk for CVD is inexpensive and these methods are easily applicable methods that help physicians in follow-up and treatment course of CVDs. The current study evaluated arterial stiffness and atherosclerosis by non-invasive methods and showed that, because of the relationship between ABPI and SBP, these patients should be assessed for PAD cautiously. Additionally, according to the findings of the current study, PWV and ABPI cannot be used instead of each other.

ED may appear as an important risk factor for CVD in the early stages of atherosclerosis. Detection of ED at early stages may provide early diagnosis, effective treatment, and follow-up for CVD. Therefore, recent studies tried to reveal parameters that recognize CVD earlier by assessing arterial stiffness. To investigate the relationship between the risk of CVD and arterial stiffness parameters, 2,232 participants were assessed in the Framingham Heart Study, which showed higher PWV values were related to an increased risk for CVD (20). According to the study performed by Scuteri with 4,000 participants who were followed-up for 9.4 years, the increase of BP with age did not directly influence PWV, besides, gender and the other factors that lead to arterial stiffness might affect SBP, PWV and pulse pressure (21). In the current study, though it was not statistically

Table 1. Demographic and clinical characteristics of the study groups

		Female (n=57)	Male (n=33)	p
Age*		58.6±14.2	55.9±16.6	0.417[a]
Height (cm)*		159.1±6.7	171.8±7.5	<0.001[a]
Weight (kg)*		82±13.7	81.5±14.1	0.865[a]
BMI (kg/m²)*		32.4±5.6	27.5±4.3	<0.001[a]
Waist circumference (cm)*		109.1±11	101.2±11.5	0.002[a]
SBP (mmHg)*		148.5±22.5	151.6±24.9	0.543[a]
DBP (mmHg)*		87.7±10.4	88.4±12.9	0.813[a]
Mean AP (mmHg)*		108.5±13.7	109.5±16.1	0.769[a]
Smoking	Yes, n (%)	9 (15.8)	16 (48.5)	0.002[b]
	No, n (%)	48 (84.2)	17 (51.5)	
Receiving treatment	Yes, n (%)	47 (82.5)	27 (81.8)	1.000[b]
	No, n (%)	10 (17.5)	6 (18.2)	
Number of antihypertensive drugs**		1 (0-3)	2 (0-5)	0.275[b]
Leucocyte (/mm³)*		6904.7±1494.7	7452.1±1960.8	0.140[a]
Hemoglobin (g/dL)*		13.3±1.4	15.3±1.6	<0.001[a]
Thrombocyte (x1000/mm³)*		277.3±66.8	245.8±61.4	0.029[a]
Creatinine (mg/dL)*		0.9±0.2	1.1±0.3	<0.001[a]
Sedimentation (mm/h)*		22.3±13.2	13.9±12.2	0.005[a]

[a]t test in independent groups, [b]Mann-Whitney U test, *: Mean±SD **: Median (minimum-maximum).
BMI: Body mass index, AP: Arterial pressure, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation

Table 2. Comparison of arterial stiffness parameters according to gender

		Female (n=57)	Male (n=33)	p
PWV (m/s) *		10.9±2	10.5±1.9	0.341[a]
CAP (mmHg) *		145.3±21.2	148.1±29.1	0.642[a]
ABPI *	Total*	1.1±0.1	1.1±0.2	0.342[a]
	Low, ≤0.90, n (%)	7 (12.3)	3 (9.1)	0.477[b]
	Intermediate, 0.91-0.99, n (%)	13 (22.8)	6 (18.2)	
	Normal, 1.00-1.40, n (%)	37 (64.9)	23 (69.7)	
	High, ≥1.41, n (%)	-	1 (3)	

[a]t test in independent groups, [b]Chi-square test, *: Mean±SD.
PWV: Pulse wave velocity, CAP: Central aortic pressure, ABPI: Ankle-Brachial Pressure Index, SD: Standard deviation

significant, an increase in PWV was found with increasing SBP similar to the study performed by Scuteri et al. (21). However, increased systolic and DBP were strongly associated with increased CAP.

In CVD, increased CAP due to the early return of the reflected wave in late systole develops additional load on the ventricle, and consequently causes a decrease in ejection fraction, a rise in the requirement of myocardial oxygen, and increase in mortality (22). Totaro et al. (23) investigated 430 normotensive participants and showed that 16% of the participants had high CAP levels and increased risk for target organ damage. There was a relationship between high central BP and early cardiovascular dysfunction. Similarly, a meta-analysis of 11 studies with a total of 5,488 cases presented by Vlachopoulos et al. (24) found out that an increase of 10 mmHg in CAP was associated with mortality related to CVD. In this respect, as recommended by guidelines in new-onset HT, in addition to the measurement of PWV, measuring CAP associated with BP levels may be crucial in the treatment and follow-up of patients with HT.

HT, DM, hyperlipidemia, smoking and aging are risk factors associated with both atherosclerosis and PAD (25). Most of the patients with PAD have risk factors for CVD. Ness et al. (26) demonstrated that HT was an independent risk factor for PAD. Albuquerque et al. (27) found out that patients with HT, who had low ABPI levels but without clinical complaints associated with PAD, had increased risk for left ventricular hypertrophy and CVD. High also low ABPI levels in patients with HT were found to be related to death and CVD (28). When participants without HT were followed-up for 47 months, the development of HT was found to be related to normal or high ABPI levels at the beginning (29). Similar to the literature, the current study showed a relationship between BP and ABPI levels in female patients. CVD risk factors, such as HT, that pose a risk for atherosclerosis and PAD may play a role in long-term morbidity and mortality rates. Physicians should be aware of applying

Table 3. Comparison of hypertension stages and arterial stiffness parameters according to gender

Female	Optimal	Normal	High normal	Stage 1 HT	Stage 2 HT	Stage 3 HT	p
PWV* (m/s)	10.3 (9.0-11.9)	11.1 (8.8-12.7)	10.5 (6.9-14.6)	10.8 (8.3-14.5)	10.6 (8.5-14)	10.1 (8.3-16)	0.890
CAP* (mmHg)	115.3 (108.6-119.4)	119.2 (112.4-133.3)	127.4 (122-141.8)	147.0 (126.1-159)	156.5 (143.9-178.5)	194.4 (178.7-219.5)	<0.001
ABPI*	1.0 (1.0-1.08)	1.0 (0.87-1.12)	1.0 (0.85-1.29)	1.1 (0.86-1.25)	1.0 (0.91-1.26)	0.9 (0.81-0.95)	0.003
Male	**Optimal**	**Normal**	**High normal**	**Stage 1 HT**	**Stage 2 HT**	**Stage 3 HT**	**p**
PWV* (m/s)	9.4 (8.1-10.7)	9.5 (7.4-11.8)	8.8 (8.3-13.5)	10.4 (7-15.3)	10.1 (9.7-11.1)	11.8 (8.5-13.4)	0.695
CAP* (mmHg)	106.6 (102.7-110.5)	118.5 (108.5-122.0)	131 (123.8-138.0)	143.7 (119.7-156.4)	167.5 (154-185.8)	190 (155.3-212.1)	<0.001
ABPI*	1.1 (1-1.28)	1.1 (0.96-1.23)	1.1 (0.99-1.63)	1.1 (0.9-1.19)	1.1 (0.85-1.18)	1.0 (0.85-1.28)	0.889

Kruskal-Wallis test, *: Median (minimum-maximum).
PWV: Pulse wave velocity, CAP: Central aortic pressure, ABPI: Ankle-Brachial Pressure Index, HT: Hypertension

Table 4. The relationship between central aortic pressure and Ankle-Brachial Pressure Index values between systolic and diastolic blood pressures and arterial stiffness parameters according to gender

	CAP			
	Female		Male	
	r	p	r	p
SBP (mmHg)	0.935	<0.001	0.944	<0.001
DBP (mmHg)	0.637	<0.001	0.749	<0.001
	ABPI			
PWV (m/s)	-0.071	0.600	-0.229	0.199
CAP (mmHg)	-0.204	0.128	-0.116	0.522
SBP (mmHg)	-0.277	0.037	-0.154	0.393
DBP (mmHg)	-0.154	0.253	-0.061	0.734

Pearson correlation coefficient.
SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PWV: Pulse wave velocity, CAP: Central aortic pressure, ABPI: Ankle-Brachial Pressure Index

protective measures and should treat CVD risk factors. There are limited data in the literature regarding the comparison of arterial stiffness and ABPI measurements. A recent study presented that ABPI values were associated with PWV in nondiabetic patients with PAD (30). Patients without CVD at baseline were followed up for 8.5 years by Zi et al. (31). At the end of the follow-up time, significant increases in vascular stiffness and PWV were recognized in patients with low ABPI levels at baseline. In a study, which evaluated arterial stiffness and ABPI values in patients without PAD, no statistically significant relationship between PWV and ABPI was found (32). In our study, to exclude the effect of gender-related factors, such as hormonal status and muscle mass, levels of PWV and ABPI were evaluated in male and female patients. Similar to the study performed by Rabkin et al. (32), the current study found no relationship between ABPI values and PWV in female and male patients with HT and without PAD.

Our study had some limitations. To evaluate the differences between hypertensive and normotensive individuals, normotensive healthy individuals as a control group could be included in the study. To investigate the effect of treatment on arterial stiffness parameters, patients could be separated into groups according to the treatment. Further studies with larger samples in prospective design will address more accurate information about the clinical importance of ABPI and PWV.

Conclusion

In conclusion, PWV and ABI measurements, which are the noninvasive indicators of arterial stiffness and atherosclerosis related to vascular remodeling due to HT, could not be used instead of each other. Additionally, due to the relationship between BP levels and CAP and the relationship between SBP and ABPI especially in female patients, high CAP and low ABPI levels should be considered to provide the early diagnosis, effective treatment, and prevention from cardiovascular morbidity and mortality in patients with HT.

Ethics

Ethics Committee Approval: The study was approved by the Gülhane Military Medical Academy Ethics Committee (Code: 1491-585-14/1648.4-2006, date: 10.14.2014).

Informed Consent: Verbal and written informed consents were obtained from all participants.

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Authorship Contributions

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