Association of aortic flow propagation velocity with ankle-brachial blood pressure index in patients with hypertension: an observational study

Hipertansiyonlu hastalarda aortik akımın ilerleme hızı ile bilek-brakiyal indeksin ilişkisi: Gözlemsel bir çalışma

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ABSTRACT

Objective: Endothelial dysfunction is considered the first stage in the development of atherosclerosis and assessed by flow-mediated dilatation (FMD) and aortic flow velocity propagation (AVP). Ankle-brachial index (ABI) is used to assess peripheral arterial disease and is associated with FMD but the relationship between ABI and AVP is unknown. In this study, we aimed to search the association between AVP, and ABI in patients with newly diagnosed hypertension.

Methods: Sixty-eight patients with newly diagnosed hypertension and 34 healthy subjects were enrolled in the crosssectional observational study. The maximum ankle arterial pressures were divided by the maximum of the brachial arterial pressures to calculate the ABI. AVP was calculated from dividing the distance between points corresponding to the beginning and end of the propagation slope, to the duration between corresponding time points proximally descending aorta. Statistical analysis was performed using Student t-test, Chi-square test, Pearson correlation and linear regression analyses.

Results: Age and gender of both groups were similar. Compared to control group E deceleration time of early diastolic flow velocity (184.0±32.2 vs. 217.1±38.6, p<0.001), isovolumic relaxation time (95.5±19.4 vs. 105.7±18.1, p<0.001) and body mass index (25.6±5.1 vs. 27.5±3.8, p=0.044) values were significantly higher, while ABI (1.08±0.07 vs. 1.14±0.07, p=0.001) and AVP (54.97±9.3 vs. 69.17±10.8 cm/sec, p=0.001) values were significantly lower in hypertensive patients. There was a significant correlation between AVP and ABI (r=0.279, p=0.005). Both ABI and AVP were independent predictors of hypertension (OR - 0.353, 95%CI 0.151-0.826, p=0.02 and OR - 0.133, 95%CI 0.0502-0.35, p=0.001, respectively).

Conclusion: Our data indicate that in patients with isolated hypertension AVP and ABI decrease. We also conclude that AVP is directly associated with ABI. *(Anadolu Kardiyol Derg 2012; 12: 568-73)*

Key words: Hypertension, ankle-brachial index, propagation velocity, regression analysis

ÖZET

Amaç: Endotel disfonksiyonu ateroskleroz gelişiminin ilk basamağı olarak kabul edilir ve akım aracılı dilatasyon (FMD) ve aortik yayılım hızı (AVP) ile değerlendirilebilir. Ankle-brakiyal indeks (ABİ) periferik arter hastalığı varlığını değerlendirmek için kullanılır. ABİ'nin FMD ile ilişkili olduğu bilinmektedir, ancak AVP ile ilişkisi bilinmemektedir. Bu çalışmada, yeni tanı konmuş hipertansif hastalarda AVP ile ABİ arasındaki ilişkiyi araştırmayı hedefledik.

Yöntemler: Yeni tanı konmuş 68 hipertansiyonlu hasta ve 34 sağlıklı birey bu enine-kesitli gözlemsel çalışmaya alındı. ABİ maksimum ayak bileği kan basıncının brakiyal kan basıncına bölünmesi ile elde edildi. AVP inen aortanın başlangıcına konan renkli M-mod eğimi olarak kabul edildi.İstatistiksel analizde Student t-testi, Ki-kare testi, Pearson korelasyon ve lineer regresyon analizleri kullanıldı.

Bulgular: Yaş, cinsiyet ve vücut kitle indeksi (VKİ) her iki grupta benzer bulundu. Kontrol grubuyla karşılaştırıldığında erken diyastolik hızının deselerasyon zamanı (184.0±32.2 ve 217.1±38.6, p<0.001), izovolümetrik gevşeme zamanı değerleri (95.5±19.4 ve 105.7±18.1, p<0.001) ve vücut kitle indek-

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si (25.6±5.1 ve 27.5±3.8, p=0.044) anlamlı derecede yüksek bulundu. ABİ (sırasıyla 1.08±0.07 ve 1.14±0.07, p=0.001) ve AVP değerleri sırasıyla (54.97±9.3 ve 69.17±10.8 cm/sn, p=0.001) kontrol grubuyla karşılaştırıldığında hipertansif hastalarda anlamlı derecede düşük bulundu. AVP ve ABİ arasında anlamlı bir korelasyon bulundu (r=0.279, p=0.005). Hem ABI and AVP hipertansiyonun bağımsız öngördürücüleri idi (OR-0.353, %95GA 0.151-0.826, p=0.02 ve OR - 0.133, %95GA 0.0502-0.35, p=0.001).

Sonuç: Bizim veriler; izole hipertansiyonda AVP ve ABİ'nin azaldığını, AVP'nin da ABİ ile doğrudan ilişkili olduğu sonucuna varıldı.

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Anahtar kelimeler: Hipertansiyon, ayak bileği-kol indeksi, yayılma hızı, regresyon analizi

Introduction

Endothelial dysfunction develops in response to a number of risk factors or injuries, such as hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), smoking (1-3). The first stage in the development of atherosclerosis is considered endothelial dysfunction (1, 2, 4). Peripheral arterial disease (PAD) commonly results from progressive narrowing of arteries in the lower extremities and is a manifestation of systemic atherosclerosis (4-6). Defining PAD by measurement of ABI is most accurate (7) and determination of ankle-brachial index (ABI) is a simple non-invasive procedure that can easily be performed in the outpatient setting (8).

Atherosclerosis leads to increased arterial resistance through thickening and stiffening of the arterial wall. Increased aortic resistance may decrease the flow propagation velocity within the arterial lumen. Recently color M-mode propagation velocity measured along origin of descending thoracic aorta-aortic flow velocity propagation (AVP) has been reported to be associated with atherosclerosis (9). Hypertension is one of the risk factors that lead to arterial stiffness. Previous studies have shown that impaired ABI in hypertensive patients (10, 11) although the association ABI and AVP remains to be assessed.

In this study, we aimed to search the association between AVP which is a newly defined predictor of endothelial dysfunction and ABI in patients with new diagnosed hypertensive patients.

Methods

Study design, sample size and power of the study

This is an observational cross-sectional study. A priory power analysis based on AVP values of first 12 patients (effect size 0.7, α=0.05, β=0.80) required patient number as 68. So, we decided decided to enroll minimum 34 patients in each group.

Study population

Between 01.01.2011-01.09.2012, sixty-eight consequently patients with newly diagnosed hypertension who applied to our cardiology clinic of hospital and 34 healthy subjects were enrolled in the study. ABI and AVP levels of patients and healthy volunteers groups were measured and recorded by two experienced cardiologists. In addition, baseline characteristics, laboratory parameters, other echocardiographic characteristics were also recorded. Exclusion criteria included: acute myocardial infarction, diabetes mellitus, cigarette smoking, dyslipidemia, creatinine level >2 mg/dL or need for dialysis, severe hepatic failure, aneurysm of aorta, severe valvular heart disease, atrial fibrillation, frequent premature beats, left bundle branch block and inadequate echocardiographic image quality.

The study had been approved by the local Ethic Committee. All participants were informed about the study and their consent was obtained.

Baseline variables

The baseline variables of study were as following: age, sex, height, weight, use of smoking, values of heart rate, systolic (SBP) and diastolic (DBP) blood pressure, history of DM, HT and HL. In addition, fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), and high-density (HDL-C) and low-density (LDL-C) lipoprotein cholesterol, body mass index (BMI).

Definitions

Hypertension is defined as SBP of 140 mmHg and above, DBP of 90 mmHg and above or usage of use of antihypertensive medications (12). Newly diagnosed HT was defined as patients without high blood pressure previously and not using any antihypertensive agent.

BMI was obtained by body weight in kilograms divided by the square of height in meters.

Ankle/brachial blood pressure index measurement

Determination of ABI systolic blood pressures of the brachial, anterior and posterior tibial arteries were measured using mercury manometer with inflatable cuffs (13, 14). Doppler was used for to be heard better Korotkoff sounds on the anterior tibial artery. The maximum ankle arterial pressures were divided by the maximum of the brachial arterial pressures to calculate the ABI. Measurement of ABI was performed according to the Transatlantic Inter-Society Consensus (TASC II) guidelines for the management of PAD (15). The measurements were performed at least 5 min rest.

Transthoracic echocardiographic examination

The echocardiographic examination was performed at rest, with the patient in the left lateral decubitus position, using a commercially available echocardiographic device (Vivid S6, General Electric, Horton, Norway) with a 3.0 MHz transducer, by two experienced echocardiographers who were blinded to the clinical data. Left-ventricular diameters and left atrial systolic diameter were determined from M-mode traces recorded from parasternal

long axis view according to established standards (16). The pulsed Doppler sampling volume was placed between the tips of the mitral valve leaflets to obtain maximum filling velocities. Early diastolic flow (E), atrial contraction signal (A), E/A ratio and E deceleration time (DT) were measured. Isovolumic relaxation time (IVRT) was determined as the interval between the end of the aortic outflow and the start of the mitral inflow signal.

From suprasternal window, at supine position, color M-mode Doppler recordings were obtained with the cursor parallel to main flow of direction in descending aorta. Color Doppler Nyquist limit is adapted to 30-50 cm/s and switching to M-mode with recorder sweep rate of 200 mm/s, an M-mode spatio-temporal velocity map with the shape of a flame is displayed (Fig. 1). If the slope of flame was unclear baseline shifting was used to change the aliasing velocity until a clear delineation of isovelocity slope was seen. AVP was then calculated from dividing the distance between points corresponding to the beginning and end of the propagation slope, to the duration between corresponding time points. Thus, AVP corresponds to the velocity at which the flow is propagating down the artery. Mean of at least three measurements was recorded as AVP value.

Evaluation of AVP may be difficult in some cases include obese, restricted neck movements, undergoing thoracic surgery, patients with severe emphysema and taller. These patients were excluded due to lack of image.

The intra- and inter-observer variations for AVP were less than 10 % and less than 5% for ABI and all were non-significant.

Statistical analysis

All tests were performed in the SPSS for Windows (SPSS Inc., Chicago, Illinois, USA). Quantitative variables are expressed as mean±standard deviation (SD), and qualitative variables as numbers and percentages. Differences between independent groups were assessed by Student t-test for normally distributed quantitative variables and Mann-Whitney's U test for variables without normal distribution and Chi-square test for qualitative variables. Logistic regression analysis was performed to determine independent predictors of hypertension. Pearson correlation analysis was used to assess the bivariate correlations between variables and linear regression analysis was used to determine independent factors associated with AVP. All results were considered statistically significant at the level of $p<0.05$.

Results

Clinical and echocardiographic characteristics

Age and gender of both groups were similar. Compared to control group DT, IVRT and BMI values were significantly higher ($p<0.05$ for all) and , ABI and AVP values were significantly lower ($p<0.05$ for both) in hypertensive patients and both ABI and AVP were independent predictors of hypertension (OR-0.353, 95%CI 0.151-0.826, p=0.02 and OR-0.133, 95%CI 0.0502-0.35, p=0.001, respectively) (Table 1).

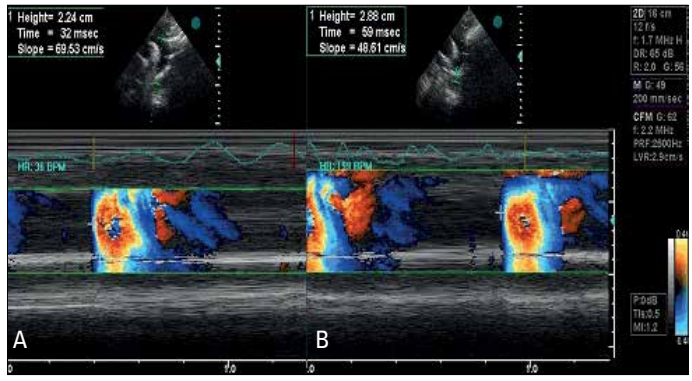

Figure 1. Measurement of descending aortic flow velocity propagation in a subject in the control group (A) and in a patient with hypertension (B)

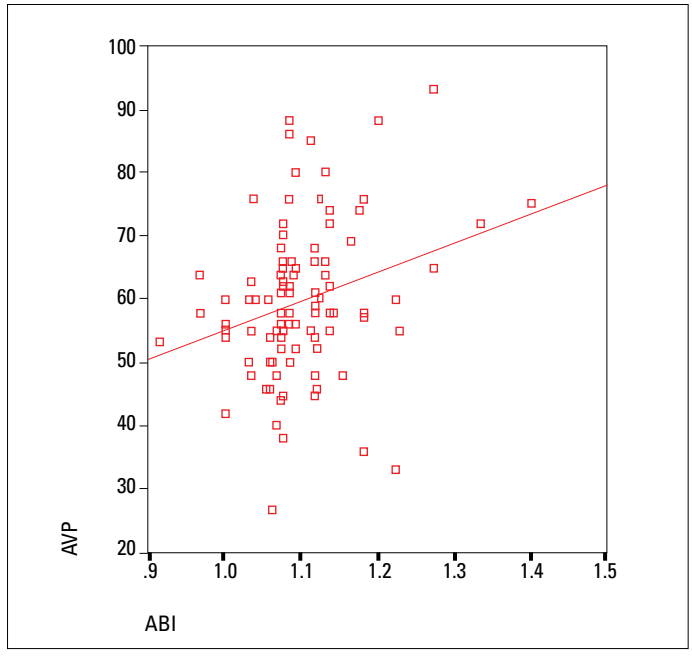

Figure 2. Correlation between AVP and ABI
ABI - ankle-brachial index, AVP - aortic flow velocity propagation

Association of AVP and clinical, echocardiographic and laboratory measurements

There were significant correlations between AVP and ABI (r=0.279, p=0.005) (Fig. 2), AVP was significantly correlated with brachial SBP (r=-0.504, p<0.001) and ankle SBP (r=-0.496, p<0.001). ABI was also significantly correlated with brachial systolic (r=-0.619, p<0.001) and ankle systolic (r=-0.318, p<0.001) blood pressures and DT was the only independent factor associated with AVP (beta -0.245, p=0.016) (Table 2).

Discussion

The present study suggests that ABI and AVP values are decreased in hypertension patients and have predictive value for HT. ABI is correlated with AVP.

Endothelial dysfunction is considered the first stage in the development of atherosclerosis. According to the response-to-

Table 1. Comparison of clinical and echocardiographic characteristics of hypertension patients with control group

Variables	Patients` Group (n=68)	Control Group (n=34)	*p	**OR [95%CI]	**p
Age, years	55.5±13.6	51±9.1	0.065		
Sex, male, n (%)	32 (47)	20 (58)	0.181		
Body mass index, kg/m^2	27.5±3.8	25.6±5.1	0.044	2.24 [0.96-5.22]	0.082
Brachial systolic BP, mmHg	142.2±20.6	114±12.4	0.001	30.59 [9.92-94.32]	
Ankle systolic BP, mmHg	153.2±20.0	129.4±10.6	0.0002	17.37 [2.04-145.0]	0.002
ABI	1.08±0.07	1.14±0.07	0.0001	0.353 [0.151-0.826]	0.02
LVDD, cm	4.8±0.4	4.8±0.3	0.620		
LVSD, cm	3.3±0.6	3.2±0.4	0.725		
LVEF, %	64.7±2.5	64.5±2.4	0.795		
DT, msec	217.1±38.6	184.02±32.2	0.0004	3.91 [1.43-10.66]	0.011
IVRT, msec	105.7±18.1	95.5±19.4	0.0098	2.48 [0.94-6.51]	0.076
AVP, cm/sec	54.97±9.3	69.17±10.8	0.0006	0.133 [0.0502-0.35]	0.001
E/A	0.96±0.3	1.3±0.4	0.001	0.206 [0.085-0.499]	0.001

Data are presented as mean±SD and number (percentage)
*Student's t-test and Chi-square test
**Logistic regression analysis
ABI - ankle/brachial indeks, AV - aortic velocity, AVP - aortic flow propagation velocity, BP - blood pressure, DT - deceleration time, EF - left ventricular ejection fraction, IVRT - isovolumic relaxation time, LVDD - left ventricular diastolic dimension, LVSD - left ventricular systolic dimension

Table 2. Relationship between AVP and clinical and echocardiographic variables

Variables	Pearson correlation coefficient	p	Beta regression coefficient	p
Age	-0.253	0.010	-0.032	0.756
IVS	-0.335	0.001	0.075	0.517
ABI	0.279	0.005	0.606	0.137
EF	0.198	0.046	0.135	0.154
DT	-0.378	0.0009	-0.245	0.016
TABs	-0.504	0.0007	1.295	0.243
TAAs	-0.496	0.0001	-1.449	0.115
Sex	-0.124	0.215		
LVDD	-0.086	0.391		
LVDS	-0.052	0.604		
BMI	-0.158	0.113		
IVRT	-0.180	0.070		
E/A	0.397	0.0004		

Pearson correlation analysis and linear regression analysis
ABI - ankle brachial index, BMI - body mass index, DT - deceleration time, E/A - mitral E and A velocity, EF - ejection fraction, IVRT - isovolumic relaxation time, IVS - interventricular septum diameter, LVDD - left ventricular diastolic dimension, LVSD - left ventricular systolic dimen-sion, TAAs - tension arterial of ankle, TABs - tension arterial of brachial

injury model of atherosclerosis various factors such as hypertension, heart failure, diabetes mellitus or insulin resistance syndrome, hyperlipidemia, smoking, postmenopausal period and genetic predisposition can cause dysfunctional alterations in the overlying endothelium. This injury may then predispose arteries to the development of atherosclerosis (1, 2, 17-19). PAD is a clinical manifestation of the atherosclerotic process (20, 21). Hypertension is a major chronic disease, which accelerates atherosclerosis. Numerous studies have identified hypertension as a key risk factor for PAD (22). The ABI, which is the ratio of systolic pressure at the ankle to that in the arm, is quick and easy to measure and has been used for many years in vascular practice to confirm the diagnosis and assess the severity of PAD in the legs. However, the ABI is also an indicator of generalized atherosclerosis because lower levels have been associated with higher rates of concomitant coronary and cerebrovascular disease, and with the presence of cardiovascular risk factors (10).

Color M-mode propagation velocity measured along origin of descending thoracic aorta may reflect atherosclerosis (9). Arterial stiffness has been shown to be associated with coronary artery disease (CAD) (23) and cardiovascular risk factors such as hypertension (24, 25), smoking (26), obesity, hypercholesterolemia (27), diabetes mellitus (23, 28, 29) and elderly (30). The noninvasive evaluation of diastolic dysfunction using ultrasound color M-mode Doppler interrogation of transmitral flow has been proposed (31). The flow propagation speed within the ventricle decreases in the presence of stiffer ventricle. Similarly, atherosclerosis leads to increased arterial resistance through thickening and stiffening of the arterial wall. Therefore, increased aortic resistance may decrease the flow propagation speed within the arterial lumen. Accordingly, color M-mode propagation velocity of descending aorta has been shown to be significantly lower in patients with CAD (9).

Systemic endothelial function reflects the propensity of arteries to develop atherosclerosis in response to exposure to

cardiovascular risk factors (32). Consistent with the idea that impaired systemic endothelial function is an early event in atherosclerosis (33, 34). We found significant associations between AVP and ABI. In the present study, compared to healthy control group AVP and ABI were lower in patients with hypertension. In the study of Güneş et al. (9) AVP was 28.3±10.4 cm/sec in patients with CAD and 57.3±9.1 cm/sec in patients having normal coronary arteries.

The ankle/brachial blood pressure index is a measure of asymptomatic PAD that is known to coexist with a variety of cardiovascular risk factors when it falls below 0.9 (10, 11). A large number of studies that report strong associations of ABI with diabetes, hypertension, elevated total cholesterol, cigarette smoking, and other cardiovascular risk factors (10,11). In the study Luo et al. (35), patients with low ABI were also associated with higher SBP.

In the present study we found that AVP were significantly correlated with systolic blood pressures and ABI. In our previous study (36) there was correlation between blood pressures and AVP. Further studies are required to answer the association between ABI and AVP.

Study limitations

Small size of the study population may have biased the statistical results. Reproducibility of the acquisition of the AVP is an important limitation. Limited echo image quality may put an obstacle to measurement of AVP. To confirm applicability of the method as a screening method, large population studies are needed. However, low AVP measurements may at least lead physician to a more careful evaluation for possible hypertension and underlying risk factors. Although we could investigate atherosclerosis with ultrasonographic imaging of carotid arteries in the whole population, coronary angiographic data for excluding coronary artery disease was unavailable. Meanwhile, absence of clinical symptoms and demonstrable wall motion abnormalities on echocardiography decreased the possibility of CAD. Additionally, because of ethical considerations, patients were studied under concurrent medications, and this might have had an influence on the precision of the measurements.

Conclusions

Our data indicate that in patients with isolated hypertension AVP and ABI decrease. We also conclude that AVP is directly associated with ABI. We showed that AVP may be used instead of the ABI measured in peripheral atherosclerosis.

Conflict of interest: None declared.

Authorship contributions: Concept - A.G., Ü.G.; Design - A.G., Ü.G.; Supervision - Ü.G., S.Y.; Resource - A.G., Y.S., Z.K., R.D.; Materials - E.D., B.C.K.; Data collection&/or Processing - A.G., Ü.G., S.Y., E.D., B.C.K., A.Y.B.; Analysis &/or interpretation - Ü.G., A.G., S.Y., R.D.; Literature search - A.G., Z.K., Y.S., A.Y.B.; Writing - A.G., Ü.G., S.Y.; Critical review - R.D., Y.S., Z.K.

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