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Changes In Aortic Flow Propagation Velocity Before and After Treatment In Patients With Hypertension

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ABSTRACT

Purpose of this study is to evaluate whether the aortic resistance measured by Aortic flow propagation velocity (APV) is improved or not by the treatment by comparing pre- and post-treatment APV values in patients with newly diagnosed essential hypertension.

117 patients with hypertension and 100 volunteers of similar age group without hypertension were included in this study. 24-hour Holter blood pressure and APV values before and after the treatment were compared.

There was a statistically significant difference in APV values before the treatment between the patient group (41.07±7.82 cm/sec) and the control group (58.75±5.19 cm/sec) ($p<0.001$). The statistical difference in APV values between the patient (54.35±8.28) and control groups disappeared after the treatment (p:0.822) and APV values showed a positive increase.

In this study, APV values were lower in patients with hypertension compared to healthy individuals during the early periods of diagnosis, and a certain level of improvement was achieved in APV values with the hypertension treatment.

Key Words: Aortic flow propagation velocity, hypertension, Blood pressure Holter, color M-mode propagation velocity, echocardiography

Introduction

Hypertension is a global health problem that constitutes a significant burden in both healthcare and economics due to its association with conditions such as cardiac diseases, stroke, renal disease and early death (1, 2). The worldwide prevalence of hypertension is around 30-45% while the prevalence in Turkey is found to be 31.8%(3).

Despite the exact pathophysiological mechanisms are unknown, irregular functioning of the neural, humoral and metabolic factors is held responsible for high blood pressure (4, 5). The type and quantity of these disorders are usually different from each other among patients. Blood pressure rises, i.e. hypertension occurs, in case of increased cardiac output and increased arterial resistance(6).

Various tests are recommended to find the predominant pathophysiological mechanism in each patient (such as urinary elimination of sodium, renin levels in the renal arteries, or hormone tests). These tests reveal the causes that underlie either increased cardiac output or increased arterial resistance. Methods and tools used to detect the changes in arterial resistance include pulse pressure, cardiac output, Doppler echocardiography (p valve velocity) and cardiac magnetic resonance imaging(7, 8). In addition, some publications associate increased aortic resistance with the decrease in flow distribution velocity inside the arterial lumen (9).

Aortic flow propagation velocity (APV) may be used to measure this flow distribution velocity in the aorta. APV in the descending aorta measured by color M-Mode is a novel hemodynamic measurement and recently has been used in the assessment of arterial stiffness besides other conventional organ damage parameters (9-12). In previous studies, APV was observed to be lower in individuals with hypertension than in the normal population (13). The Study investigating the effect of antihypertensive treatment on APV is not available in literature.

The objective of this study is to evaluate whether the aortic resistance measured by APV is improved or not by the treatment by comparing pre- and post-treatment APV values in patients diagnosed with essential hypertension.

Material and Method

This study complies with the World Medical Association Declaration of Helsinki and was

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approved by the Ethics Committee of Van Yuzuncu Yil University.

117 hypertension patients aged 18-80 years, who were treated in the clinic we studied between 2019-2020, were included in the study. The study group included patients with newly diagnosed essential hypertension without a previous diagnosis of hypertension according to ESC/ESH 2018 hypertension guidelines. The control group comprised 100 contributors without hypertensive disease.

Patients with pregnancy, coronary artery disease, peripheral artery disease, renal failure, chronic liver disease, familial hyperlipidemia aortic aneurysm, organ damage and malignancy were excluded. Additionally patients with any history of medications for DM and HT as well as those who show arrythmia in ECG were excluded Electrocardiograms (ECG) and medications used were interrogated for each individual enrolled in the study.

Patients with a low ejection fraction (EF <%50), severe valvular pathology, left ventricular hypertrophy in echocardiography, and those with a congenital heart disease were also excluded.

24-hour ambulatory blood pressure monitorization was performed for further investigation of individuals with a systolic blood pressure higher than 140 mmHg and a diastolic blood pressure higher that 90 mmHg based on the recommendation of ESC/ESH 2018 hypertension guidelines. The diagnosis of HT was established, and treatment was started in patients with an average day/night systolic blood pressure of ≥135/≥120 and a day/night diastolic blood pressure of ≥85/≥70 in 24-hour blood pressure Holter monitorization. Additionally, 24-hour ambulatory blood pressure monitorization was repeated after 6 months of treatment.

Blood pressure levels recommended by ESC/ESH 2018 hypertension guidelines were targeted by using single-agent/combined antihypertensive treatment for stage 1 and combined antihypertensive treatment for stage 2 and 3 based on the stages indicated in Table-1 for patients diagnosed with hypertension. The patients were given training for diet adaption and drug taking hours. Effort was made to maintain target blood pressures by advising patients to monitor home blood pressure. Drug control and blood pressure regulation were evaluated by monthly office visits and patients who fail to remain within target range were excluded from the study (10 patients).

Blood pressure lowering drugs used in patients included angiotensin receptor blockers (candesartan, telmisartan, valsartan), angiotensin converting enzyme inhibitors (ramipril, enalapril, lisinopril), calcium channel blockers (*lercanidipine,* amlodipine), beta blockers (nebivolol) and thiazide drugs (hydrochlorothiazide). The above-mentioned drugs were used interchangeably if they lead to side effects and target blood pressure values were taken into consideration during the switch.

Echocardiographic examination was performed with the patient in left lateral position following at least 20 minutes of resting using Vivid E9 device and X5-1 transthoracic probe of this device through parasternal and apical windows. Echocardiography was performed for each contributor in line with the standard images and techniques provided in the guidelines of European Association of Cardiovascular Imaging (EACVI) (14). In addition, APV was measured in supine position with the head tilted backwards. The measurements were performed using a 3.0 MHz transducer by two experienced operators unaware of the subject group.

Color M-mode records were taken in supine position with a cursor parallel to the main flow along descending aorta through a suprasternal window. Color Doppler Nyquis limit was adapted to 30–50 cm/sec. Flame-shaped M-mode spatiotemporal velocity was obtained by taking records at a scanning speed of 200 mm/sec. Then, aortic flow speed was calculated by dividing the distance between the starting and ending points of the slope by the time elapsed (Figure 1). The mean value of at least three measurements was established as the APV value. APV values were measured and recorded again after 6 months using the same methods for patients in whom blood pressure regulation was achieved.

Statistical Method: Data were analyzed using IBM SPSS. Suitability for normal distribution was analyzed using Kolmogorov Smirnov test. Independent samples were examined using Student t and paired t test when comparing data with normal distribution according to the groups. Chi-square test was used to investigate categorical data. The relation between APV and the variables was analyzed using pearson or spearman correlation. Results of the analyses were presented as mean and standard deviation for quantitative data and as frequency and percentage for categorical data. Significance was assumed at a 2-sided p value of <0.05.

Results

117 patients with hypertension were included in this study. 18 patients who failed to maintain targeted blood pressure levels were excluded and 100 subjects without hypertension was included as controls. Clinical and demographic characteristics are presented in Table-2.

There was no difference between the groups regarding gender in the patient group was 58(58.5%) male patients, males in the control group of 59(59%). Mean age was 47.90 ± 8.27 in patients with hypertension and 44.42 ± 9.47 in those without hypertension. A poor statistical difference was seen between the groups for age which was not clinically significant. The distribution of smoking status was also similar among the groups (p=0.718). No difference was observed between the groups for mean LDL (p=0.141).

Mean APVPre values were different between groups as seen in Table-3 and figure 2 (p<0.001) with a mean value of 41.07 ± 7.82 cm/sec and 58.75 ± 5.19cm/sec in the patient and control groups, respectively.

The mean pre-treatment systolic pressure was 153.14 ± 8.77mmhg and diastolic pressure was 89.84 ± 4.62mmhg in the patient group, post-treatment while the mean systolic 114.02 ± 5.24mmhg and diastolic pressure was 71.51 ± 5.12mmhg after treatment.

Post-treatment APV value was 54.35 ± 8.28 which was closer to the values measured in the control group, eliminating the statistical difference between the two groups (Table-4 and figure-3).

The association between LDL, creatinine, BMI and age and changes in APV was evaluated using Pearson and/or Spearman correlation analysis, and no statistically significant association was found (p>0.05).

The correlation between APV changes and the change in blood pressure during daytime and nighttime were not statistically significant (p>0.05). (Tablo-5).

The most frequently used treatment (45.5%) in the patient group was Ace + thiazide + ca block. The rates of other treatments were as follows: Ace + thiazide 14.1%, ARB + thiazide 7.1%,

Ace + thiazide + block 13.1% and Ace + thiazide + ca + block 12.1% (Tablo-6). No statistically significant relationship was found with the APV change of drugs used.

Discussion

In this study, pre- and post-treatment APV values were compared for patients diagnosed with essential hypertension and the effectiveness of the treatment was investigated.

1) Pre-treatment APV values showed a significant difference between the patient group and control group (p<0.001). The mean values in the patient and control groups were 41.07 ± 7.82 and 58.75 ± 5.19, respectively.

2) An improvement was found in APV value with antihypertensive treatment, but this was not statistically associated with the change in blood pressure.

3) There was no statistically significant difference in APV values between patient group at 6 months and controls (p=0.822); whereas, APV values did show a difference between controls and the patient group before starting treatment. This difference was no longer present after the treatment.

Hypertension is a risk factor that can lead to cerebral diseases and diseases of the vascular bed, particularly in the heart, and is a community health problem that can be controlled and prevented (15). Echocardiography is an important tool for early diagnosis in order to prevent target organ damage and adverse cardiovascular events in patients with hypertension (16). An echocardiographic finding frequently seen in patients with hypertension is the increase in left cardiac mass (17). In addition, the effect of hypertension on the heart may be evaluated with many echocardiographic assessments including left ventricular performance, diastolic function, dimensions and performance of the left atrium (18).

This study focused on the parameter APV. The first study conducted with APV measured the flow velocity in the descending aorta in patients with coronary artery disease and compared this with the syntax score, and APV was considered to be an indicator in coronary artery disease (CAD)(19). Endothelial dysfunction starts at the first step of atherosclerosis. This dysfunction is caused by predisposing risk factors such as hypertension, diabetes mellitus, hyperlipidemia, smoking, genetic predisposition, and heart failure (20, 21). The fact that hypertension is a predisposing factor for coronary artery disease and that APV value is considered as an indicator in CAD as well as the significant APV change in patients with hypertension gave rise to the idea that APV may

Table 1. Hypertension staging based on ESC/ESH 2018 hypertension guidelines

Category	Systolic (mmHg)	Diastolic (mmHG)
Optimal	<120	<80
Normal	120-129	80-84
High normal	130-139	85-89
Grade 1 hypertension	140-159	90-99
Grade 2 hypertension	160-179	100-109
Grade 3 hypertension	≥180	≥110

Table 2. Comparison of patient and control groups

	Patient (n=99)	Control (n=100)	p
LDL (mmol/L)	115.19 ± 38	107.05 ± 39.67	0.141
Creatinine (mg/dl)	0.90 ± 0.24	0.92 ± 0.27	0.503
HGB (g/dl)	13.61 ± 1.82	13.6 ± 1.95	0.981
Age	47.90 ± 8.27	44.42 ± 9.47	0.006
EF(%)	61,46 ± 5,27	62,25 ± 4,31	0,357
Non-smoker(%)	85(86)	83(83)	0.718
Male(%)	58(59)	60(60)	0.953
Female(%)	41(42)	40(40)	

#Student t test, Chi-square test, EF: ejection fraction, Hgb: Hemoglobulin, LDL: low density lipoprotein

Table 3. Comparison of APV and blood pressure between the patient and control groups

	Patient (n=99)	Control (n=100)	p
APVPre (cm/sec)	(41.07 ± 7.82)	(58.75 ± 5.19)	<0.001
APVPost (cm/sec)	(54.35 ± 8.28)	(58.75 ± 5.19)	0.822
Systolic blood pressure daytime	(153.14 ± 8.77)	(100 ± 6.7)	<0.001
Diastolic blood pressure daytime	89.84 ± 4.62	(70 ± 5.4)	<0.001

#Student t test, Chi-square test, APVpre: Aortic-flow propagation velocity pre-treatment, APVpost: Aortic-flow propagation velocity post-treatment, APVpost:

be used to evaluate if treating hypertension reduces the possibility to develop CAD or not. Our perspective of APV is not solely limited to arterial resistance since there are other studies in the literature regarding the association between APV and coronary artery disease, most of which suggest that APV is underestimated because of impaired vascular endothelium due to changes that occur during atherosclerotic process (13, 19, 22, 23). We investigated whether treating early diagnosed hypertension improves flow velocity which indicates vascular dysfunction. We hypothesized that an improvement in APV may directly proportionally reduce the risk of CAD.

In follow-ups, the relation between APV and carotid intimal thickness was investigated and was found to be present (22, 23). Güntekin et al. investigated the association between APV and hypertension and found a negative correlation between high blood pressure and APV value (13).

In the literature, the relationship between hypertension and the change in APV is attributed to the increase in arterial resistance caused by stiffness and thickening of the arterial wall due to atherosclerosis (24). Increased aortic resistance also leads to a reduction in flow dispersion velocity within the arterial lumen (24). Besides, hypertension itself has an impact on the heart that increase the mass and stiffness of the ventricle. Active relaxation cannot be achieved at desired levels as a response to diastolic filling periods in the stiffened ventricle (25-27). Thus, the flow dispersion velocity gradually decreases in the presence of stiffened ventricle (25).

In this study, we proposed an opinion on arterial resistance paying regard to the ratio of the start and end of this flow velocity in the descending aorta to time, and in line with this theory, we found that APV values of the subjects in this study was statistically lower than controls. Moreover, we evaluated the change in APV with

Table 4. The association between LDL, creatinine and age and changes in APV in the patient group

	r	p
LDL	0.146	0.150
Creatinine	0.081	0.424
Age	-0.038	0.712

r: Spearman correlation BMI: body mass index

Table 5. Results of correlation analysis between APV and blood pressure change in the patient group

		APV change
Systolic blood pressure daytime change	r	-0.143
	p	0.157
Diastolic blood pressure daytime change	r	-0.065
	p	0.524
Systolic blood pressure nighttime change	r	0.014
	p	0.887
Diastolic blood pressure nighttime change	r	0.004
	p	0.972

r: Spearman correlation

Table 6. Antihypertensive drugs used

	Patient
Medications	N (%)
ACE + thiazide	14 (14.1)
ARB + thiazide	7 (7.1)
Ca block	8 (8.1)
ACE + thiazide + Ca block	45 (45.5)
ACE + thiazide + block	13 (13.1)
ACE + thiazide + Ca + block	12 (12.1)

ACE: angiotensin converting enzyme inhibitors, ARB: angiotensin receptor blocker, thiazide: thiazide group diuretics, Ca block: calcium channel blocker, B block: beta blocker

treatment, unlike the articles mentioned above and many other studies in the literature. APV values were increased at 6 month after the treatment, and the statistical difference that was found in APV values of the patients and controls before the treatment was no longer seen. Our conclusion is that APV values in patients treated for hypertension show an improvement that is close to that seen in controls, but this improvement did not show any correlation with changing blood pressure levels before and after the treatment. To be more precise, it is not correct to propose that the more blood pressure decreases, the higher APV levels become; i.e. staying within target blood pressure levels is sufficient to achieve APV values close to that of healthy individuals. Briefly, this study may provide a guidance for early prevention of adverse effects caused by hypertension by demonstrating the improvement in APV with optimal treatment. In addition, Tosun et al. (21) claimed in their recent study that APV shows meaningful changes in patients with hypertension and in patients with proteinuria and left ventricular hypertrophy, and suggested APV as a new method for end organ damage. In our study, patients with newly diagnosed hypertension were included while patients with signs of end organ damage were excluded from the study. We also demonstrated that it is one of the first echocardiographic parameters that is impaired in patients with newly diagnosed hypertension that has the chance of improvement with treatment.

APV is an easy-to-measure, affordable and reliable echocardiographic parameter for diagnosis. In our study, we found that APV values were lower in patients with hypertension compared to healthy individuals even early after the diagnosis of hypertension. We achieved an improvement in APV values to a certain extent with treatment and presented a new data in this field. Additionally, we demonstrated that APV may provide information

in the long term for if blood pressure is within target levels or not.

Limitations of The Study: Relatively low number of subjects and focusing on a single group when selecting subjects restrict the application of our findings to general population. While the follow-up duration in this study was 6 months, longer follow-up periods are needed in this field. We intensely monitored study patients and achieved blood pressure regulation, and we are aware that it would be difficult to monitor patients such closely in daily life.

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