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ARAŞTIRMA / RESEARCH

Relationship between presystolic A wave and aortic distensibility in hypertensive patients

Hipertansif hastalarda presistolik A dalgası ile aort distensibilitesi arasındaki ilişki

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Abstract

Purpose: Arterial stiffness has been shown as an independent predictor of cardiovascular and all-cause mortality in hypertensive patients. commonly seen in pulse wave Doppler echocardiographic examination of the left ventricle outflow tract, is related to diastolic dysfunction and arterial stiffness parameters. Our study aims to investigate the relation between aortic distensibility (AD) and presystolic A wave (PSW),.

Materials and Methods: Hypertensive patients were included in the study. Aortic stiffness was calculated by measuring aortic diameters with m-mode in echocardiography, and the presence of PSW was noted from the left ventricle outflow tract just proximal to the aortic valve in apical five-chamber view.

Results: A total of 149 hypertensive patients were included. Diastolic blood pressure, septum diameter, posterior wall diameter, aortic diastolic, and systolic diameter were significantly higher in the presence of PSW. Aortic distensibility (AD) was higher in patients with PSW. Multivariable logistic regression analysis showed that AD (OR: 0.812, 95% CI: 0.712 – 0.927, p = 0.002) was an independent predictor of PSW presence.

Conclusion: PSW presence is associated with aortic stiffness evaluated by decreased aortic distensibility and highlights that PSW presence could be an independent predictor of aortic stiffness in patients with HT.

Keywords:. Hipertansiyon, aort sertliği, aortik distansibilite, presistolik A dalgası

Öz

Amaç: Arteriyel sertlik, hipertansif hastalarda kardiyovasküler ve tüm nedenlere bağlı mortalitenin bağımsız bir öngörücüsü olarak gösterilmiştir. Sol ventrikül çıkış yolunun nabız Doppler ekokardiyografik incelemesinde sıklıkla görülen presistolik A dalgası (PSW), diyastolik disfonksiyon ve arteriyel sertlik parametreleri ile ilişkilidir. Çalışmamız aort distensibilitesi (AD) ile PSW arasındaki ilişkiyi incelemeyi amaçlamaktadır.

Gereç ve Yöntem: Polikliniğimize ayaktan başvuran hipertansif hastalar çalışmaya dahil edildi. Aort sertliği, ekokardiyografide aort çapları m-modu ile ölçülerek hesaplandı ve apikal beş boşluk görünümde sol ventrikül çıkış yolunda, aort kapağının hemen proksimalinden PSW olup olmadığı kaydedildi.

Bulgular: Toplam 149 hipertansif hasta çalışmaya dahil edildi. PSW varlığında diyastolik kan basıncı, septum çapı, arka duvar çapı, aortik diyastolik ve sistolik çap anlamlı olarak yüksekti. Aort distensibilitesi (AD) PSW'li hastalarda daha. Çok değişkenli lojistik regresyon analizi, AD'nin (OR: 0,812, %95 GA: 0,712 – 0,927, p = 0,002) PSW varlığının bağımsız bir prediktörü olduğunu gösterdi.

Sonuç: PSW varlığı, azalmış aort distensibilitesi ile değerlendirilen aort sertliği ile ilişkilidir ve hipertansiyon hastalarında aort sertliğinin bağımsız bir prediktörü olarak kullanılabilir.

Anahtar kelimeler: Hypertension, aortic stiffness, aortic distensibility, presystolic A wave.

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INTRODUCTION

Arterial stiffness is an important predictor of mortality in hypertensive patients[1-4]. Aortic distensibility (AD) corresponds to the artery's ability to increase its volume to a given increase in blood pressure and is defined as the opposite of arterial stiffness. Aortic stiffness, depending on age and various pathologies, causes blood to be drawn during systole to cause more aortic pressure elevation due to decreased aortic distensibility[5]. It is also well-known that increased blood pressure has depressed effects on either left ventricle and left atrium functions[6]. As a result, elevated central blood pressure because of increased stiffness causes the development of left ventricular hypertrophy and diastolic dysfunction[7]. The carotid-femoral pulse wave velocity is considered the gold standard method for assessing arterial stiffness. However, it needs additional equipment and time for the assessment.

Echocardiography is a simple and routinely used imaging technique in hypertensive patients. Presystolic A wave (PSW), commonly seen in pulsed-wave Doppler echocardiographic examination of the left ventricular outflow tract (LVOT), is a late diastolic event whose pathophysiologic mechanism is thought to be a whirlpool flow pattern because of the stiffened ventricle[8,9]. The relationship between PSW and arterial stiffness was previously shown in Korkmaz et al[10]. However, a special device is required to measure the cardio ankle vascular index in this study, which is used to show arterial stiffness. Moreover, although carotid-femoral pulse wave velocity is recommended as the gold standard in arterial stiffness measurement in the literature, there is no tonometry device in many centers, and its use in daily practice is limited[11].

We aim to detect arterial stiffness more practically and simply without needing an additional device in daily use, using echocardiography, which is already a routine examination in hypertension patients. PSW can be easily obtained during the routine echocardiographic exam.

Our study aims to investigate the relation between aortic distensibility, which shows arterial stiffness, and PSW.

MATERIALS AND METHODS

This study is a single-center, prospective study held between February 2021 – March 2021. We evaluated 266 consecutive hypertensive patients admitted to our cardiology outpatient clinic. Among them, 117 patients were excluded for the following reasons: coronary artery disease, stroke, moderate to severe valvular heart disease, congestive heart failure, atrial fibrillation, infective endocarditis, hypertrophic cardiomyopathy, active malignancy, active infection/inflammatory disease, congenital heart disease, and less than optimal echocardiographic recordings. A total of 149 hypertensive patients enrolled after exclusion (Figure 1). We obtained all cardiovascular risk factors of the patients. Patients with a systolic blood pressure (BP) greater than 140 mmHg or diastolic BP higher than 90 mmHg or using antihypertensive drugs were considered hypertensive. Patients with fasting glucose 126 mg/dl or using the pharmacological treatment were considered as diabetes mellitus. We defined smoking habit as 'current smokers' or 'non-smokers.' Patients with total cholesterol of more than 200 mg/dl or taking medications were defined as hypercholesterolemia. We conducted the study following the Helsinki Declaration. We took a local ethics committee approval for the study (2021/15). All patients gave informed consent for the study.

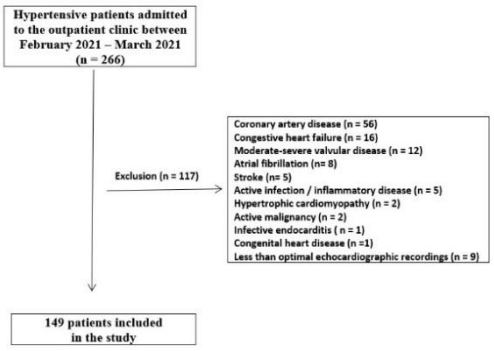

Figure 1. Study flowchart

Echocardiography

Transthoracic echocardiography was performed using a Philips Epiq 7 echocardiography device (Philips Medical Systems, Andover, MA, USA) with an S5-1 transducer. An experienced Cardiologist, who did not know the patient's clinical data, performed echocardiography. Standard echocardiographic parameters were measured according to the expert consensus document of the European Association of Cardiovascular Imaging [12]. Presence of PSW was noted from just proximal to the

aortic valve in apical five-chamber view in LVOT (Figure 2).

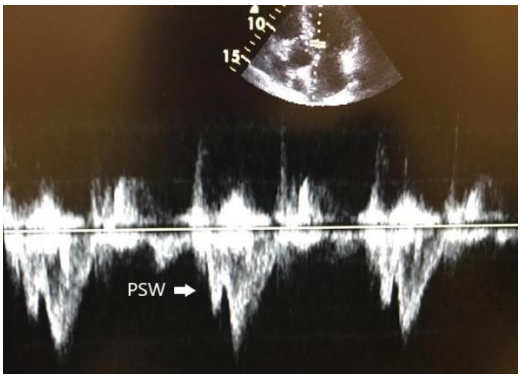

Figure 2. Presystolic A wave (arrow) on pulsed-wave Doppler of the left ventricle outflow tract, obtained from the apical five-chamber view.

Aortic distensibility

AD was obtained with an M-mode trace at a level 3 cm above the aortic valve in parasternal long-axis view (Figure 3)[13]. We measured aortic diameters from the lower edge of the upper wall to the upper edge of the lower wall. We measured the systolic aortic diameter at the maximal diameter of the aorta and diastolic diameter at the QRS complex's peak[14]. We calculated the average of three consecutive cardiac beats. Blood pressure was measured from the brachial artery with an external sphygmomanometer simultaneously with echocardiography during echocardiographic evaluation. Afterward, aortic stiffness parameters were calculated with the formulas below[15]

Aortic strain = (Systolic diameter – diastolic diameter) / diastolic diameter
Aortic distensibility (AoD) = 2 X (systolic diameter – diastolic diameter) / [(systolic blood pressure – diastolic blood pressure) X diastolic diameter] X 10^{-6} cm^2/dyn.

Statistical analysis

We did statistical analyses with SPSS (version 21.0 IBM, USA). We considered p-value < 0.05 as statistically significant. We detected the distribution of the variables with the Kolmogorov-Smirnov test. We presented quantitative variables as mean ± standard deviation and median (25^{th} to 75^{th} percentile) according to the variables' distribution. We expressed categorical variables as numbers (%). Student t-test or Mann-Whitney U test was used to compare quantitative variables according to the variables' distribution. Pearson chi-square and Fisher exact tests were performed for categorical variables. We used multivariable logistic regression analysis to detect independent predictors of the presence of PSW.

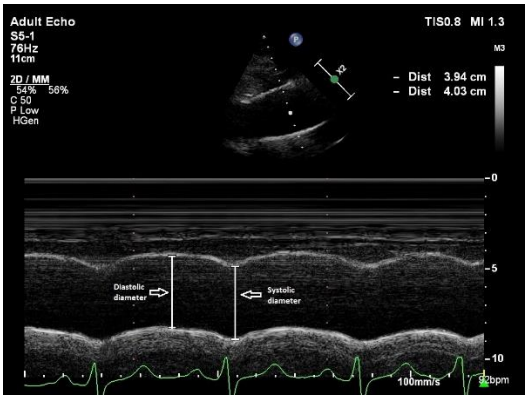

Figure 3. Measurement of aortic diameters using m-mode echocardiography in parasternal long-axis view.

RESULTS

All patients had hypertension (HT) (n=149). Of these, PSW was observed in 72 patients (48.3%). Baseline characteristics are summarized in Table 1 according to the PSW presence. PSW was seen at a significantly higher rate in male patients (p=0.029). Apart from this, there was no significant difference between the categories of other baseline characteristics in terms of PSW presence. Clinical and echocardiographic features of the patients with and without PSW are given in Table 2. Diastolic BP, septum diameter, posterior wall diameter, aortic diastolic, and systolic diameter were significantly higher in the presence of PSW ($p = 0.019$, $p = 0.047$, $p = 0.013$, $p < 0.001$, $p < 0.001$, respectively). Aortic distensibility (8.36 ± 3.52 vs. 6.35 ± 2.27, $p < 0.001$) was higher in patients with PSW.

We established a multivariable model with the parameters whose p-value below 0.20 according to the comparison results in Tables 1 and 2. We assessed the effects of these features on PSW presence. Septum diameter, posterior wall diameter, male sex, and AD were taken to the established model. The results of the analysis were shown in table 3. We revealed that AD (OR: 0.812, 95% CI: 0.712 – 0.927, $p = 0.002$) was an independent predictor of PSW presence.

Table 1. Baseline characteristics of study patients with or without PSW

Variables	Total cohort (n = 149)	No PSW (n = 77)	PSW (n = 72)	P value
Age, years	57.8 ± 8.9	57 ± 9.4	58.7 ± 8.3	0.235
BMI, kg/cm²	30.8 ± 4.6	31 ± 4.8	30.6 ± 4.4	0.576
Male Gender, n (%)	53 (35.6)	21 (27.3)	32 (44.4)	0.029
Diabetes Mellitus, n (%)	37 (24.8)	20 (26)	17 (23.6)	0.739
Hyperlipidemia, n (%)	69 (46.3)	34 (44.2)	35 (48.6)	0.586
Smoking, n (%)	31 (20.8)	18 (23.4)	13 (18.1)	0.424
Medication, n (%)				
-ACE-inh/ARB	118 (79.2)	63 (81.3)	55 (76.4)	0.415
-CCB	47 (31.5)	23 (29.9)	24 (33.3)	0.649
-Diuretic	21 (14.1)	12 (15.6)	9 (12.5)	0.589
-β-Blocker	36 (24.2)	17 (22.1)	19 (26.4)	0.539
-Statin	18(12.1)	10 (13)	8 (11.1)	0.726
-Oral antidiabetic	29 (19.5)	16 (20.8)	13 (18.1)	0.675
Fasting plasma glucose, mg/dl	96 (89 – 109)	96 (89 – 109)	97 (88 – 108)	0.704
Serum creatinine, mg/dl	0.8 (0.6 – 0.9)	0.7 (0.6 – 0.8)	0.8 (0.7 – 0.9)	0.128
Total cholesterol, mg/dl	207 ± 41	202 ± 37	211 ± 46	0.201
HDL cholesterol, mg/dl	50 ± 14	51 ± 14	48 ± 13	0.250
LDL cholesterol, mg/dl	124 ± 38	118 ± 36	130 ± 40	0.091
Triglyceride, mg/dl	156 ± 71	149 ± 63	165 ±79	0.191

BMI: body mass index, BSA: body surface area, ACE-inh:angiotensin-converting enzyme, ARB: angiotensin receptor blocker, CCB: calcium channel blocker, OAD: oral anti-diabetic

Table 2. Clinical and echocardiographic parameters of study patients with or without PSW

Variables	Total cohort (n = 149)	No PSW (n = 77)	PSW (n = 72)	P value
Systolic Blood Pressure, mm Hg	134 ± 16.7	131.4 ± 14.2	136.7 ± 18.4	0.065
Diastolic Blood Pressure, mm Hg	80 (70 -90)	80 (70 – 90)	82 (70 - 90)	0.019
LVEF, %	60 (60 - 62)	60 (60 - 63)	60.5 (60 - 62)	0.941
LVDD, mm	46 ± 4.2	46.3 ± 4.4	45.8 ± 3.9	0.518
LVSD, mm	29.5 ± 3.8	29.7 ± 3.9	29.3 ± 3.7	0.607
LAD, mm	33.2 ± 5.4	32.4 ± 5.2	34 ± 5.6	0.081
Septum diameter, mm	10.8 ± 1.4	10.6 ± 1.4	11.1 ± 1.5	0.047
Posterior wall diameter, mm	9.8 ± 1.2	9.5 ± 1.2	10.1 ± 1.3	0.013
LVMI, g/m2	93.5 ± 25.7	91.7 ± 25.4	95.6 ± 26	0.355
E/A, %	0.83 (0.71 – 1.11)	0.86 (0.72 – 1.04)	0.80 (0.69 – 1.11)	0.285
Septal E/e', %	9 ± 3.2	8.7 ± 3.5	9.3 ± 2.8	0.245
Diastolic aortic diameter, mm	33.9 ± 3.6	30.4 ± 3.5	33.2 ± 3.6	< 0.001
Systolic aortic diameter, mm	34.1 ± 3.9	32.8 ± 3.2	35.2 ± 3.6	< 0.001
Aortic distensibility, cm2. dyn-1	7.39 ± 3.14	8.36 ± 3.52	6.35 ± 2.27	< 0.001

LVEF: left ventricle ejection fraction, LVDD: Left ventricle diastolic diameter, LVSD: Left ventricle systolic diameter, LAD: Left atrium diameter, LVMI: Left ventricle mass index

Table 3. Multivariable logistic regression analyses to assess independent predictors of the presence of presystolic A wave.

	Odds Ratio	95% CI	P-value
Male sex	1.955	0.929 – 4.116	0.077
Septum diameter	0.932	0.645 – 1.345	0.705
Posterior wall diameter	1.371	0.882 – 2.129	0.161
Aortic distensibility	0.812	0.712 – 0.927	0.002

DISCUSSION

As a result of our study, a significant correlation was found between PSW presence and AD in hypertensive patients. According to the regression analysis, PSW presence was an independent predictor of AD.

HT is a common disease that causes end-organ damages and causes severe morbidity and mortality. LV hypertrophy (LVH), which occurs in hypertensive patients, causes LV remodeling and LV diastolic dysfunction in the long term[16]. The most common method to show LV diastolic dysfunction is Doppler measurements while performing the echocardiography[17]. PSW determined by Doppler evaluation during echocardiography has recently been associated with LV diastolic dysfunction and LV subclinical dysfunction[18]. It has been reported that PSW is seen higher in patients with LVH than those without LVH. This finding suggests that it may be effective in demonstrating end-organ damage in hypertensive patients. Indeed, in a study conducted by Akyuz et al., it was shown that the presence of PSW is associated with subclinical left ventricular dysfunction calculated by myocardial performance index (MPI)[19]. Korkmaz et al. have revealed the relationship of PSW with arterial stiffness[10]. There are reports that the presence of PSW is related to low ejection fraction, high rates of cardiovascular events, and complex cardiovascular anatomy in acute coronary syndrome patients[18,20,21]. PSW is a parameter that reflects the late diastolic period during Doppler evaluation of the left ventricular outflow tract. Although its mechanism is not fully understood, with the decrease of LV compliance, it fills the center of the ventricle with the vortex-like flow that creates early diastolic filling from the left atrium, and the late diastolic flow turns to the posterior part and creates PSW[18]. Confirming this, in a study by Joshi et al., PSW was found to be associated with atrial contraction. Therefore, PSW is frequently detected in hypertensive patients with impaired LV compliance. PSW was detected in 48% of the patients evaluated in our study. Moreover, patients with PSW had higher systolic and diastolic blood pressures and septum and posterior wall thicknesses.

One of the most critical factors determining cardiovascular outcomes in hypertensive patients is arterial stiffness. With increasing blood pressure, the impairment in the elastic tissue structure prepares the ground for collagen formation. Increased arterial stiffness causes systolic hypertension, left ventricular hypertrophy, and coronary perfusion impairment, leading to increased cardiovascular risk[22]. AD is one of the indicators of arterial stiffness[23]. Global arterial stiffness measured as carotid-femoral pulse wave velocity correlates with AD, which also can be easily measured by echocardiography[24]. At the same time, AD measurement provides more valuable information in terms of central hemodynamics[25]. The relationship between AD and cardiovascular disease outcomes has been shown in previous publications[23,25,26]. AD is impaired with the effect of aortic hardening in hypertensive patients. It has also been demonstrated that impaired aortic distensibility in hypertensive patients was associated with poor outcomes[27,28]. It is known that BP control has a positive effect on aortic stiffness in hypertensive patients. Therefore, it has become essential to prevent aortic distensibility in these patients and create early predictive parameters for this finding.

Even in asymptomatic individuals, the relationship of the presystolic wave with aortic stiffness has been previously shown[10]. It has been found that PSW was also associated with carotid intima-media thickness, which is another indicator of arterial stiffness[29]. In our study, the low AD values in patients with PSW in the hypertensive population reveal the relationship between these two parameters. Therefore, evaluation of PSW during echocardiography can provide information about AD and related arterial stiffness. Thus, assessment of the presence of PSW may be positioned as part of routine clinical practice in terms of predicting cardiovascular events in hypertensive patients.

There are several limitations to our study. First, we conducted the study in a single center, and the study population comprised only hypertensive patients. The results may not be extrapolated to the general population. Second, the sample size was small. Therefore, further prospective studies with larger cohorts may confirm the results.

In conclusion, our study suggests that PSW presence is associated with aortic stiffness evaluated by decreased AD and highlights that PSW presence could be used as an independent predictor of aortic stiffness in patients with HT. Echocardiography is a routinely used imaging modality to detect end-organ damage in hypertensive patients. As carotid-femoral pulse wave velocity, the gold standard for arterial stiffness, needs additional equipment, PSW

assessment in echocardiography could be a simple marker to predict aortic stiffness and guide the treatment of hypertensive patients. We need more extensive prospective studies to understand better the relations found in this study.

Yazar Katkıları: Çalışma konsepti/Tasarımı: CP, İG; Veri toplama: CP, İG, AG; Veri analizi ve yorumlama: CP; Yazı taslağı: CP, İG, AG; İçeriğin eleştirel incelenmesi: İG; Son onay ve sorumluluk: CP, İG, AG; Teknik ve malzeme desteği: -; Süpervizyon: İG; Fon sağlama (mevcut ise): yok.
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