HİPERTANSİF HASTALARDA NABIZ BASINCI ARALIĞI İLE SOL VENTRİKÜL DİASTOLİK FONKSİYON İLİŞKİSİ

Association of Pulse Pressure Index with Left Ventricular Diastolic Function in Hypertensive Patients

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ÖZET

Amaç: Bu çalışmanın amacı, hipertansiyonu olan hastalarda nabız basıncı indeksi ile doku doppler görüntüleme ile ölçülen sol ventrikül diyastolik fonksiyonlar arasındaki ilişkiyi ölçmektir.

Gereç ve Yöntemler: Hipertansiyon dışında hastalığı olmayan 18 ile 55 yaş arası 75 hasta çalışmaya dahil edildi. Yazılı kılavuzlara uygun olarak kan basıncı ölçümleri ve ekokardiyografik incelemeler yapıldı. E/A oranı>1, Em>8 cm/s, Em/Am >1 veya E/Em <8 olması normal diyastolik fonksiyon olarak tanımlandı.

Bulgular: Çalışmaya 26 erkek ve 49 kadın hasta dahil edildi. Ortalama yaş 47±6 yıldı. Ortalama sistolik ve diyastolik kan basınçları sırasıyla 133±15 ve 83±6 mmHg idi. Vakaların %52'si (n=39) normal diyastolik fonksiyona sahipken 32 hastada evre I, 4 hastada da evre II diyastolik disfonksiyon mevcuttu. Normal diyastolik fonksiyonu olan hastalarla karşılaştırıldığında, diyastolik disfonksiyonu olan hastalar istatistiksel olarak daha yüksek sistolik ve diyastolik kan basıncı, daha yüksek nabız basıncı ve nabız basıncı indeksine sahipti.

Sonuç: Bu çalışmada, artmış nabız basıncı indeksinin, anlamlı biçimde artmış E/Em ve sol ventrikül diyastolik disfonksiyonu ile ilişkili olduğu göstermiştir.

Anahtar kelimeler: *Diyastolik fonksiyon, Ekokardiyografi, Hipertansiyon, Nabız basıncı indeksi*

ABSTRACT

Introduction: The aim of this study was to investigate association between pulse pressure index (PPI) and left ventricular diastolic function measured via tissue Doppler imaging in hypertensive patients.

Material and Methods: Seventy five 18 to 55 years old otherwise normal patients with hypertension were included in the study. Blood pressure measurement, echocardiographic examination were carried out according to the published guidelines. Normal diastolic function was defined as E/A ratio >1, Em>8 cm/s, Em/Am >1 or E/Em <8.

Results: There were 26 men and 49 women in the study population with average age of 47±6 years. Average systolic and diastolic blood pressures were 133±15 mmhg and 83±6 mmhg respectively. 52% of the subjects (n=39) had normal diastolic function, 32 patients had grade I diastolic dysfunction and 4 patients had psuedonormal pattern. Patients with diastolic dysfunction had significantly higher systolic and diastolic blood pressure, pulse pressure, and PPI values compared to patients with normal diastolic function.

Conclusion: This study showed that elevated PPI significantly correlates with increased E/Em and left ventricular diastolic dysfunction in hypertensive patients.

Key words: *Diastolic Function, Echocardiography, Hypertension, Pulse pressure index*

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INTRODUCTION

Hypertension is still one of the most important preventable contributor to morbidity and mortality (1). It gives rise to myocardial infarction, stroke, renal failure, and death if not diagnosed and treated promptly. It is the most widespread risk factor for heart failure in the general population (2). In hypertensive patients, diastolic dysfunction precedes heart failure with preserved ejection fraction. So measuring and grading of diastolic functions are extremely vital for understanding of heart failure due to hypertension. Long lasting unproperly treated hypertension leads diastolic dysfunction of the different stage alongside ultrastructural rearrangement in the myocardium (3). Thus, early detection of diastolic dysfunction is crucial in the management of hypertension. Left ventricle diastolic functions can be easily defined echocardiographic ally either by standard pulse wave mitral flow pattern or tissue Doppler imaging of mitral annulus or left ventricle myocardium.

Pulse pressure (PP), the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP), has been shown to be related significantly to coronary heart disease, heart failure, and stroke, especially in elders (4-6). Elevated brachial PP is associated with increased risks of myocardial infarction, congestive heart failure, and both cardiovascular and total mortality It reflects vascular compliance and directly related to vascular structural changes in long-term (7). But there are some limiting points for PP to consider it as an index. Large fluctuations in blood pressure during a day is one of them. In this case, large variability in blood pressure leads unsteady PP. The other limiting point is “floating” aspect of PP. Two different sets of SBP and DBP values can result in same PP so decreasing assessibility of severity in vascular compliance and cardiovascular outcomes (8). To overcome these limitations, pulse pressure index (pulse pressure/ systolic blood pressure) is proposed for assessment of cardiovascular outcomes. In the study by Lee et al., it was shown that the pulse pressure index was well associated with left ventricular filling pressure and diastolic dysfunction in patients with chronic kidney disease. The Number of studies searching the relation between the pulse pressure index (PPI) and left ventricular diastolic in hypertensive patients is limited. This study investigated whether PPI correlated with left ventricular diastolic function measured via tissue Doppler imaging in hypertensive patients.

MATERIALS AND METHODS

Study subjects

This study was prospectively designed. The study population consisted of subjects with a diagnosis of hypertension aged between 18 to 55 years old who were indicated for echocardiography examination for any chest pain or dyspnea. All subjects were under treatment for hypertension with at least one drug and recruited at the outpatient setting consecutively. Subjects with cardiomyopathies, LV systolic dysfunction (LV ejection fraction <55%), significant valvular disease, arrhythmia, peripheral artery disease, coronary artery disease, pulmonary hypertension, chronic obstructive lung disease, diabetes mellitus or renal insufficiency (serum creatinine >1.4 mg/ml), patients with resting heart rate >90 bpm and <60 bpm were excluded. Each subject provided informed consent, and our study was approved by our institutional ethical committee.

Blood Pressure Measurement

The blood pressure (BP) levels were measured from the right and left arms of the subjects in a sitting position by one trained observer blind to the study in the echocardiography laboratory. BP was measured twice with five minutes interval. The systolic BP (SBP) and diastolic BP (DBP) were recorded at the first and fifth Korotkoff phases respectively using a mercury sphygmomanometer. The average of the four BP measurements was used for analysis. Pulse Pressure (PP) =SBP - DBP, and PP index = PP / SBP were derived from these average measurements.

Two-dimensional and Doppler echocardiography

Two-dimensional, M-mode, pulsed Doppler and tissue Doppler echocardiography were performed on an ultrasound machine (Presound alpha 7, IPF 1701 Model, 2009; Hitachi Aloka Medical, Ltd. Tokyo, Japan) with a 2.5-MHz transducer.

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Standard 2-dimensional measurements (LV diastolic and systolic dimension, the ventricular septum and posterior wall thickness, left atrial diameter) were obtained as recommended by the American Society of Echocardiography (10). LV ejection fraction (LVEF) calculated by using modified Simpson method accordingly. From the apical window, a 1- to 2-mm pulsed Doppler sample volume was placed at the tip of the mitral valve, and mitral flow velocities from 5 to 10 cardiac cycles were recorded. The mitral inflow velocities were traced and peak velocity of early diastolic mitral inflow (E) and late diastolic mitral inflow (A) were obtained. Mitral annular velocities were obtained by Doppler tissue imaging using the pulsed-wave mode. The filter was set to exclude high-frequency signals, and the Nyquist limit was adjusted to a range of 15 to 20 cm/s. Gain and sample volume were reduced as possible to allow a clear tissue signal with minimal background noise. Early diastolic mitral annular (Em), late diastolic (Am) and systolic velocities (Sm) of the mitral annulus were measured from the apical 4-chamber view with a 2- to 5-mm sample volume placed at the lateral edge of the mitral annulus. All measurements were carried out at expirium. Normal diastolic function (DD) was defined as E/A ratio >1, Em>8 cm/s, Em/Am >1 and E/Em <8. Grade I DD was defined E/A ratio <1, Em<8 cm/s, Em/Am <1, and E/Em <8. Grade II DD was defined E/A ratio >1 and <2, Em<8 cm/s, Em/Am <1 and E/Em between 8 and 15; Grade III DD was defined E/A ratio >2, Em <8 cm/s and E/Em >15.

Statistical analysis

Statistical analyzes were performed using the SPSS software version 15. Continuous variables are presented as mean ± SD and categorical variables are presented as frequencies (%). Except body mass index, all other continuous variables didn't have normal distribution according to Kolmogorov-Smirnov test. Categorical variables were compared using the chi-square test. Spearman simple correlation analysis was performed to determine the association between pulse pressure index and diastolic function parameters (E/A ratio, Em/Am ratio, E/Em ratio) accordingly while Mann-Whitney U test and Kruskal-Wallis were used to compare diastolic function categories in respect to pulse pressure index. A p value of less than 0.05 was considered to show the statistically significant result.

RESULTS

Of the 164 patients with hypertension enrolled in the study but 89 patients were excluded according to the exclusion criteria described elsewhere. Thus, the remaining 75 patients constituted the study group for the analysis. There were 26 men and 49 women in the study population with an average age of 47±6 years. Of 75 subjects, only 33% (n=25) were obese according to BMI >30 kg/m². 65% of the patients were using angiotensin-converting enzyme inhibitor or angiotensin receptor blockers for the treatment of hypertension. Average systolic and diastolic blood pressures were 133±15 and 83±6 respectively. PPI values of the subjects were 0.376±0.051 in average. The rest of clinical characteristics were expressed in Table 1.

Echocardiographic examination revealed that 52% of the subjects (n=39) had normal diastolic function defined as E/A ratio >1, Em>8 cm/s, Em/Am >1 and E/Em <8. Four patients had pseudonormal pattern (E/A ratio >1 and <2, Em<8 cm/s, Em/Am <1 and E/Em between 8 and 15). The rest (n=32) had grade I abnormal relaxation pattern. None of the subjects had grade III DD. All other findings were shown in Table 2.

There was no statistically significant gender difference in respect to age, BMI, SBP, DBP, PP, PPI, and diastolic parameters of the subjects. Similarly, diastolic function subgroups (normal, grade I diastolic dysfunction, and pseudonormal pattern) didn't differ statistically in respect to age and BMI values (p-values 0.667 and 0.308 accordingly). Pulse pressure and pulse pressure index didn't show correlation with age or BMI (p-values 0.251 and 0.799 respectively). We found that PPI showed strong negative correlation with Em velocity, E/A, and Em/Am ratios while the positive correlation with E/Em ratio (Table 3).

Table 1. Clinical characteristics of the subjects

	n=75
Age (years)	47±6
Male/Female (%)	26/49 (35/65)
Height (m)	1,63±0,08
Weight (kg)	76±11
Resting Heart rate (bpm)	74±7
Body Mass Index (kg/m²)	28.6±3.7
Medication history	
ACE inhibitor or ARBs (%)	49 (65)
Calcium Channel Blockers (%)	17 (23)
Beta-blockers (%)	19 (25)
Diuretics (%)	41 (55)
Duration of hypertension history	4±3
Level of Dyspnea	
NYHA class I (%)	59 (79)
NYHA class II (%)	16 (21)
SBP(mmHg)	133±15
DBP(mmHg)	83±6
Pulse Presure (mmHg)	51±12
Pulse Pressure Index	0.376±0.051

Values are mean ± SD or n (%).
ACE:angiotensin converting enzyme; ARB:angiotensin receptor blocker; DBP:diastolic blood pressure; SBP:systolic blood pressure; NYHA: New York Heart Association

Table 2. Baseline echocardiographic findings of the subjects

	n=75
LVEDD (mm)	47±4
LVESD (mm)	30±3
IVSd (mm)	12±1
LV mass index (g/m2)	91±18
LV ejection fraction (%)	66±3
LA diameter (mm)	39±3
E velocity (cm/s)	66±15
A velocity (cm/s)	61±14
E/A ratio	1.1±0.3
Em velocity (cm/s)	9±2
Am velocity (cm/s)	8±3
Sm velocity (cm/s)	7±1
Em/Am ratio	1.2±0.5
E/Em ratio	7±2
Presence of diastolic dysfunction	
Present (%)	36 (48)
Absent (%)	39 (52)

Values are mean ± SD or n (%).
A:late diastolic mitral inflow; Am:late diastolic mitral annular; E:early diastolic mitral inflow; Em:early diastolic mitral annular; IVS:interventricular septum; LA:left atrial; LV:left ventricular; LVEDD:left ventricular end-diastolic dimension; LVESD: left ventricular end-systolic dimension; Sm :systolic mitral annular;

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Table 3. Simple Correlations between age, body mass index, diastolic function and blood pressure parameters

	SBP		DBP		Pulse Pressure		PPI	
	r	p value	r	p value	r	p value	r	p value
Age	0.21	0.076	0.25	0.032	0.13	0.251	0.03	0.799
BMI	-0.06	0.619	-0.11	0.368	-0.03	0.811	-0.05	0.703
E/A ratio	-0.80	0.000	-0.60	0.000	-0.75	0.000	-0.64	0.000
Em/Am ratio	-0.82	0.000	-0.61	0.000	-0.76	0.000	-0.64	0.000
Em	-0.74	0.000	-0.49	0.000	-0.72	0.000	-0.60	0.000
E/Em	0.3	0.001	0.18	0.134	0.45	0.000	0.43	0.000

BMI: body Mass Index, A:late diastolic mitral inflow; Am:late diastolic mitral annular; E:early diastolic mitral inflow; Em:early diastolic mitral annular

Similarly; in subgroup analysis, it was found that the patients with pseudonormal pattern (n=4) had the highest PPI value (0.411±0.054), while patients with normal diastolic function (n=39) had the lowest PPI value (0.350±0.044) (Figure 1). Average PPI value of subgroup with grade I diastolic dysfunction (n=32) was 0.403±0.043. Both pseudonormal and grade I subgroups had significantly higher PPI value than subgroup with normal diastolic function ($p<0.05$ and $p<0.001$ respectively) while pseudonormal and grade I subgroups had statistically similar PPI values ($p=0.706$).

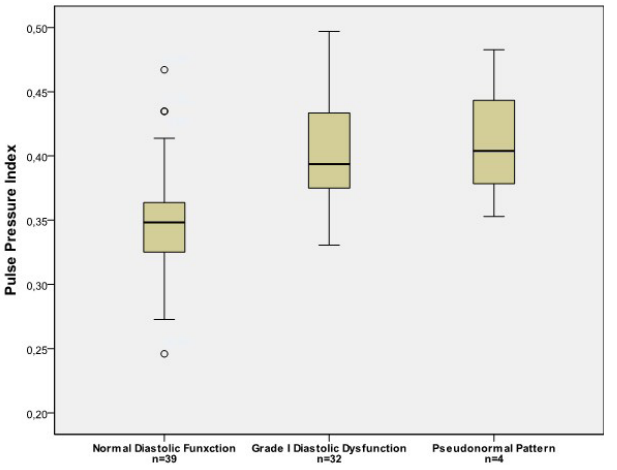

Figure 1. Pulse pressure index values of diastolic function categories

DISCUSSION

The present study demonstrated the association between pulse pressure index and diastolic functional parameters in subjects with hypertension. The study was first in the literature searching pulse pressure index relation with diastolic function status.

Hypertension is the most prevalent cardiovascular risk factor seen in primary care and causes to myocardial infarction, stroke, renal failure, and death if not diagnosed promptly and treated appropriately (1). In this respect, detection of target organ damage is crucial for intensification of the treatment accordingly. Microalbuminuria, retinopathy, arterial stiffness, left ventricular diastolic dysfunction (LVDD) are some parameters reflecting the presence of target organ damage (11, 12). Recently Wan et al. described preclinical diastolic dysfunction as left ventricular diastolic dysfunction without the diagnosis of congestive heart failure (HF) and with normal systolic function (13). Therefore, before the development of HF with preserved LVEF, detection and proper treatment of diastolic dysfunction is very important. In our study population, prevalence of diastolic dysfunction was 48%. Although LVDD is an important component of HF, the relation between level of symptom and severity of diastolic dysfunction is not clear (13, 14). We also found that level of dyspnea defined by New York Heart Association (NYHA) wasn't correlated with severity of LVDD.

The patients with NYHA class I dyspnea had a similar rate of diastolic dysfunction compared to the patients with NYHA class II (46% vs. 56% with p= 0.456). But pulse pressure index was found to be higher in patients with NYHA class II than patients with NYHA I (0.407±0.048 vs. 0.367±0.049 with p= 0.006). In this respect, PPI may be used in the evaluation of HF with preserved ejection fraction. The pulse pressure index, the ratio of pulse pressure over systolic blood pressure, reflects vascular compliance (9). Vascular compliance is reportedly correlated with left ventricular diastolic function (15). The clinical implications of PPI in different clinical setting hasn't been established yet. In a study conducted in patients with chronic renal failure, it was found that increased PPI significantly associated with elevated E/Em and LVDD (9). Similarly, we also found PPI was well correlated with increased diastolic dysfunction in patients with hypertension.

Patients with diastolic dysfunction had higher pulse pressure, higher PPI and SBP values. Also, PPI was associated with an increase in left ventricular filling pressure that can be estimated indirectly via E/Em ratio. It is known that E/Em ratio increases in parallel with the level of dyspnea. We also found that patients with NYHA I had lower E/Em value compared to ons with NYHA II (6.9±1,3 vs. 8.8±2.4 with p =0.001). In case of normal diastolic function, E/Em ratio is normally less than 8 and but in grade III-IV diastolic dysfunction, expected E/Em ratio is >15. Values within this range don't give any clue about the level of diastolic dysfunction (2). Also in this interval, E/A ratio isn't so definitive, <1 in grade I DD but reversed in grade II DD. So we need better parameters reflecting left ventricular filling pressure in hypertensive patients. Continuous relation of PPI with DD degree can help to fill this gap. We found that PPI is well correlated with the level of DD. As the level of DD increased, PPI value increased. Patients with normal diastolic function had significantly lower PPI value than patients with grade I DD (0.350±0.044 vs. 0.403±0.043, p<0.001 respectively) and grade II DD (0.411±0.054, p<0.05). Although there was the tendency of higher PPI in patients grade II DD than patients with grade I DD, it didn't reach the level of significance due to less number of patients with grade II DD in the analysis. With large-scale studies including patients with higher level of diastolic dysfunction, such significance may be obtained.

There are some limiting points in the use of PPI. Although its use allow us to get rid of "'alterability" and "floating" aspects of pulse pressure, there isn't any clear-cut threshold values to categorize patients accordingly. What we know from the literature is that the more PPI is near to 1, the less vascular compliance is and the more PPI is near to 0, the higher vascular compliance is (8, 9). So further studies should be conducted for classification of PPI.

A Small number of the study population and fewer number patients with diastolic dysfunction of grade II or more were some limitations to the study. And also the study included hypertensive patients with relatively controlled blood pressure values.

CONCLUSION

Elevated PPI significantly correlates with increased E/Em and left ventricular diastolic dysfunction in hypertensive patients. Also, PPI is well correlated with the level of dyspnea. Since PPI can be easily obtained during blood pressure measurement, it may be beneficial for detection of hypertensive patients with a high left ventricular filling pressure and left ventricular diastolic dysfunction.

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