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Short term blood pressure variability and diastolic function in middle-aged normotensive individuals

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ABSTRACT

Objective: Blood pressure variability (BPV), a non-conventional blood pressure parameter, has been shown to contribute to hypertensive target organ damage but its association with diastolic dysfunction is unknown. The present study investigates the association of BPV and left ventricular diastolic dysfunction (LVDD) in middle-aged normotensive individuals.

Materials and Methods: 264 normotensive patients aged between 45 and 65 were enrolled. 24-hour ambulatory blood pressure monitoring was performed, and BPV was defined as the standard deviation of systolic blood pressure measurements. Patients were divided into three groups according to BPV tertiles. Echocardiographic and tissue doppler diastolic function parameters were compared among the groups.

Results: Mean ages of the patients were 50.41 and similar among groups. Mitral inflow E/A (Tertile 1 vs 2 vs 3: 1.10[0.33] vs 1.05 [0.22] vs 1.02 [0.30], p=0.02) and average tissue doppler mitral annular E' velocity (12 [2] vs 10.5 [1.85] vs 10 [1.55], p=0.02) were highest in the tertile 1 and lowest in the tertile 3. Average E/E' (Tertile 1 vs 2 vs 3: 7.2 [2.2] vs 8.1 [3.2] vs 9.3 [2.9], p<0.001) was lowest in the tertile 1 and highest in the tertile 3. In addition, there was a positive correlation between BPV and Average E/E' (Rs =0.401, p<0.001). In contrary, E/A (Rs =- 0.286, p<0.001) and average E' (Rs =- 0.451, p<0.001) were negatively correlated with BPV.

Conclusion: BPV is positively correlated with average E/E' and negatively correlated with E/A and average E'. Further studies are required to elucidate the relationship between BPV and LVDD.

Keywords: blood pressure variability, left ventricular diastolic dysfunction

INTRODUCTION

Blood pressure is a dynamic parameter that continuously fluctuates over time due to the interaction of cardiovascular regulatory mechanisms and environmental, physical, and emotional factors (1). Blood pressure variability (BPV), a measure of blood pressure fluctuation, has emerged as a non-conventional blood pressure parameter and has been shown to contribute to hypertensive target organ damage independent of the absolute blood pressure levels, but it is rarely assessed in daily clinical practice(2).

Blood pressure variability can be classified as very short term (beat to beat), short term (24-hour ambulatory monitoring), mid-term (day by day in-home blood pressure monitoring), and long term (e.g., variability among clinical visits). Short-term BPV is associated with increased cardiac, vascular, and renal events (2).

Left ventricular diastolic dysfunction (LVDD) is characterized by increased viscoelastic chamber stiffness and impaired relaxation, which may lead to elevated filling pressures and diastolic heart failure (3). The Association of diastolic dysfunction and hypertension is well established, but the role of BPV in LVDD is unknown (4).

The present study investigates the association between short-term BPV in 24-hour ambulatory blood pressure monitoring and LVDD in middle-aged normotensive individuals.

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MATERIAL and METHODS

264 normotensive patients aged between 45 and 65 who were admitted to cardiology outpatient clinics and had 24-hour ambulatory blood pressure monitoring between January 2017 and September 2021 were enrolled in the study. Patients with hypertension or on antihypertensive drugs, atrial fibrillation, more than mild valvular heart disease, left ventricular hypertrophy, left ventricular ejection fraction < 55%, clinical heart failure, coronary artery disease, obesity, and diabetes mellitus were excluded from the study. Patients were divided into three groups according to BPV tertiles. Echocardiographic and tissue doppler diastolic function parameters were compared among the groups. All participants have given informed consent, and the study protocol was approved by the Institutional Ethics Committee.

24-hour ambulatory blood pressure monitoring was performed, and BPV was defined as the standard deviation of systolic blood pressure measurements. Normotension was defined as office blood pressure <140/90 mmHg, mean daytime blood pressure < 135/85, night-time blood pressure <120/70 and mean 24-hour blood pressure < 130/80 mmHg. Obesity was defined as body mass index > 30 kg/m2. Diabetes mellitus was defined as antidiabetic medication use, fasting blood glucose > 126 mg/dl or HbA1c > 6.5%.

Hospital records were used to obtain the patients' medical history and demographic information. Venous blood samples were drawn for basic hematologic and biochemical analysis. Two-dimensional, m-mode, doppler, and tissue doppler echocardiography (Toshiba Artida, Toshiba Medical Systems Co., Japan) were performed in the left lateral position according to the European Association of Cardiovascular Imaging recommendations (BB). Pulse wave doppler imaging was performed in the apical four chamber view with a sweep speed of 50 mm/s, sample volume of 1-3 mm, and averaged over three cardiac cycles. Mitral inflow velocities including peak early filling (E) velocity, late diastolic filling (A) velocity, E/A ratio, deceleration time (DT-time between peak and end of the E wave), and isovolumic relaxation time (IVRT-time between aortic valve closure and mitral valve opening) were recorded. In tissue doppler imaging, early (E') and late (A') diastolic velocities of the mitral annulus were recorded by placing sample volume at the insertion of mitral leaflets to septal and lateral walls.

SPSS Statistics version 18.0 for Windows (SPSS Inc., Chicago, IL) was used for statistical analysis. The distribution pattern of the continuous variables was determined by using The Kolmogorov-Smirnov method. According to the distribution pattern, continuous data were presented as mean and standard deviation or median and interquartile range. The one-way ANOVA was used to compare data with normal distribution, and the Kruskal-Wallis test was applied to compare the data without normal distribution. Bonferroni correction was used for multiple comparisons. Categorical variables were compared with the chi-square test. Spearman's correlation analysis was used to assess the correlation between BPV and diastolic function parameters. A two-tailed p value < 0.05 was considered to be statistically significant.

RESULTS

The mean age of the patients was 50.41 and similar among groups along with gender, hyperlipidemia, and body mass index. Serum levels of fasting glucose, creatinine, lipoproteins, and thyroid-stimulating hormone were also similar (**Table 1**).

Two dimensional and doppler echocardiographic examination revealed that left ventricular ejection fraction, wall thicknesses, left ventricular diameters, left ventricular mass index, deceleration time, tricuspid regurgitation velocity, right ventricular diameters, and tricuspid annular plane systolic excursion were similar among groups in. Mitral inflow E/A (Tertile 1 vs 2 vs 3: 1.10[0.33] vs 1.05 [0.22} vs 1.02 [0.30], p=0.02) and average tissue doppler mitral annular E' velocity (12 [2] vs 10.5 [1.85] vs 10 [1.55], p=0.02) were highest in the tertile 1 and lowest in the tertile 3. Average E/E' (Tertile 1 vs 2 vs 3: 7.2 [2.2] vs 8.1 [3.2] vs 9.3 [2.9], p<0.001) was lowest in the tertile 1 and highest in the tertile 3 (**Table 2**).

In post hoc analysis, the difference between tertile 1 and 3 for mitral inflow E/A (p=0.01) and average E' (p=0.008) was significant. For average E/E', difference between tertile 1 and 2 (p=0.003), tertile 1 and 3 (p<0.001) and tertile 2 and 3 (p=0.001) were significant. In addition, there was a positive correlation between BPV and Average E/E' (Rs =0.401, p<0.001).

In contrary, E/A (Rs =- 0.286, p<0.001) and average E' (Rs =- 0.451, p<0.001) were negatively correlated with BPV (**Figure 1**).

Table 1. Baseline characteristics of the groups

Variables	Blood Pressure Variability Tertile1 (n=88)	Tertile2 (n=88)	Tertile3 (n=88)	*P Value*
Age(years)	50.86 ± 9.18	50.23 ± 11.98	50.14 ± 9.42	0.787
Gender (Male)	49 (55.7)	51 (58.0)	49 (55.7)	0.645
Hyperlipidemia (n, %)	14 (15.9)	12 (13.6)	13 (14.8)	0.488
BMI (kg/m^2)	22.99 (3.43)	22.49 (7.62)	22.61 (5.34)	0.766
Glucose (mg/dl)	88.05 ± 28.42	87.50 ± 30.21	88.14 ± 31.75	0.688
Creatinine (mg/dl)	0.79 ± 0.18	0.78 ± 0.22	0.76 ± 0.21	0.877
Cholesterol (mg/dl)	186 (88)	181 (92)	184 (100)	0.729
LDL (mg/dl)	121 (54)	116(71)	118 (64)	0.516
HDL (mg/dl)	48 (21)	47 (18)	48 (20)	0.853
Triglycerides(mg/dl)	125 (72)	122 (64)	124 (71)	0.738
Hemoglobin (g/L)	14.52 ± 1.30	14.32 ± 2.52	14.10 ± 1.25	0.626
WBC (x 10^3/ml)	6.25 ± 1.57	6.63 ± 1.39	6.41 ± 1.65	0.344
TSH	1.80 (1.91)	1.70 (1.90)	1.70 (0.90)	0.566

BMI, body mass index; LDL, low density lipoprotein cholesterol; HDL, high density lipoprotein cholesterol; WBC, white blood cell; TSH, thyroid stimulating hormone.

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Table 2. Echocardiographic parameters of the groups

Variables	Blood Pressure Variability Tertile1 (n=88)	Tertile2 (n=88)	Tertile3 (n=88)	*P Value*
Left atrium (mm)	30 (5)	31 (2)	32 (6)	0.422
IV Septum (mm)	9 (2)	9 (2)	9 (2)	0.998
Posterior Wall (mm)	9 (2)	9 (2)	9 (2)	0.986
LVEDD (mm)	42 (4)	43 (3)	43 (5)	0.842
LVESD (mm)	26 (5)	27 (4)	27 (4)	0.874
LVEF (%)	64 (4)	65 (5)	65 (6)	0.752
LVMI	72 (20)	74 (13)	75 (18)	0.685
E/A	1.10 (0.33)	1.05 (0.22)	1.02 (0.30)	**0.02**
IVRT	94 (12)	97 (10)	99 (10)	0.054
DT	175 (32)	181 (36)	178 (36)	0.453
Average E’	12 (2)	10.5 (1.85)	10 (1.55)	**0.02**
Average E/E’	7.2 (2.2)	8.1 (3.2)	9.3 (2.9)	**<0.001**
TRV (m/s)	2.1 (0.6)	2.2 (0.5)	2.2 (0.5)	0.683
RV diameter (mm)	29 (5)	29 (4)	29 (7)	0.838
TAPSE	22 (6)	23 (5)	22 (5)	0.888

IV, interventricular; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; TRV, tricuspid regurgitation velocity; RV, right ventricle; TAPSE, Tricuspid Annular Plane Systolic Excursion.

Table 3. 24-hour ambulatory blood pressure monitoring parameters.

Variables	Blood Pressure Variability Tertile1 (n=88)	Tertile2 (n=88)	Tertile3 (n=88)	*P Value*
Office SBP	126.55 ± 18.69	127.73 ± 16.80	126.36 ± 14.08	0.866
Office DBP	78.22 ± 11.26	77.87 ± 10.45	77.98 ± 12.18	0.912
Mean 24h SBP	122.89 ± 16.30	121.98 ± 18.25	122.24 ± 14.74	0.886
Mean 24h DBP	74.15 ± 7.84	73.88 ± 7.24	74.32 ± 8.54	0.834
Mean daytime SBP	124.45 ± 16.32	124.18 ± 14.48	124.88 ± 18.54	0.788
Mean daytime DBP	76.20 ± 8.12	75.94 ± 6.24	76.10 ± 7.48	0.847
Mean night-time SBP	119.70 ± 16.49	119.27 ± 28.04	119.32 ± 16.84	0.911
Mean night-time DBP	72.69 ± 9.42	72.87 ± 11.12	72.90 ± 8.98	0.892
Blood pressure variability	7.89 ± 0.88	9.22 ± 1.51	13.14 ± 2.34	**<0.001**
Non-dipper pattern	24 (27.3)	25 (28.4)	26 (29.5)	0.127

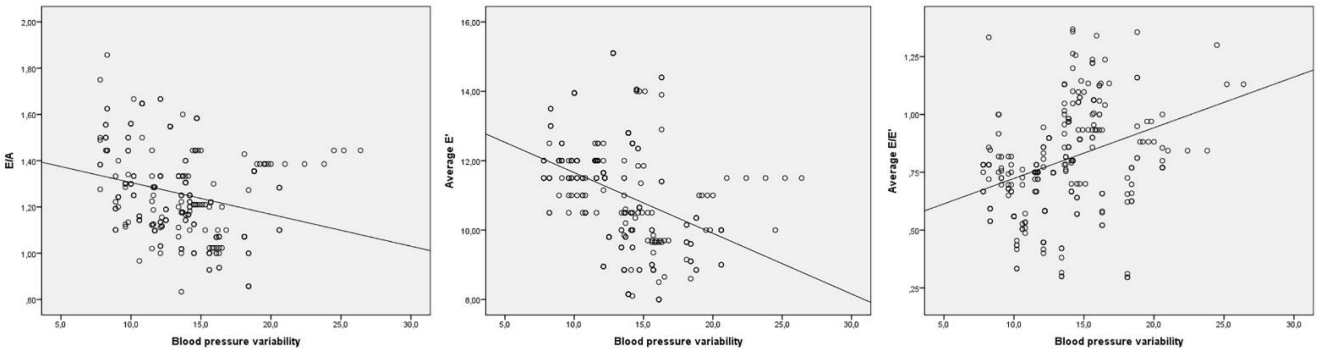

Figure 1. Correlation analysis between blood pressure variability and diastolic parameters.

DISCUSSION

In the present study, we demonstrated for the first time that higher BPV is positively correlated with E/E’ and negatively correlated with E/A and E’ in normotensive individuals. To the best of our knowledge, no study in the literature suggests a relation between BPV and LV diastolic parameters.

Diastolic dysfunction is characterized by impaired relaxation, reduced left ventricular diastolic distensibility, and filling of the myocardium, resulting incomplete cardiac chamber filling in the absence of an increase in the left atrial pressure. Consequently, higher atrial pressures may lead to diastolic heart failure symptoms (5).

Although several other risk factors such as coronary artery disease, obesity, and diabetes mellitus are implicated, hypertension is the most important risk factor for the development of LVDD in the community (4). Hypertension-induced inflammatory activation and endothelial dysfunction were shown to be associated with LVDD (6). Particularly, decreased nitric oxide-cyclic guanosine monophosphate-protein kinase G signaling predisposes cardiomyocytes to develop hypertrophy and high diastolic resting tension (7).

Blood pressure oscillates over the short and long-term periods. Oscillation of the blood pressure within 24 hours is called short-term BPV (8).

Early studies demonstrated that short-term BPV is increased in hypertensive patients and is related to cardiovascular risk (9,10). Subsequently, accumulated evidence showed that BPV is linked to end organ damage in the general population as well as hypertensive individuals (11). Short-term BPV was also found to be associated with cardiovascular morbidity and mortality (12-15).

Moreover, the PAMELA study showed that cardiovascular mortality was higher in patients with greater erratic blood pressure variations during 24 hours (13). In a study using microneurographic nerve traffic recording in peripheral nerves, Narkiewicz et al. demonstrated that sympathetic activity is directly linked with 24-hour BPV in normotensive individuals (16). It is also known that increased sympathetic activity may play a role in the development and progression of structural cardiovascular alterations such as endothelial dysfunction and left ventricular hypertrophy (17). Therefore, increased sympathetic activity and endothelial dysfunction are probably the cause of diastolic dysfunction in normotensive individuals with higher BPV.

The present study has several limitations. First, this is a single-center study. Second, cardiac magnetic resonance and novel echocardiographic techniques such as myocardial strain imaging were not available and not used.

CONCLUSION

In conclusion, in normotensive individuals, BPV is positively correlated with average E/E' and negatively correlated with E/A and average E'. Further studies are required to elucidate the relationship between BPV and diastolic functions.

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Ethical approval: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Local Ethical Committee. All procedures performed in studies with human participants met the ethical standards of the Institutional Research Commission and the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards.

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