Am J Cardiovasc Dis 2014;4(4):177-187
www.AJCD.us /ISSN:2160-200X/AJCD0003547

*Original Article*

# 24-hour central blood pressure and intermediate cardiovascular phenotypes in untreated subjects

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Received November 2, 2014; Accepted December 15, 2014; Epub December 29, 2014; Published December 31, 2014

**Abstract:** Background: Recently, 24-hour monitoring of central systolic blood pressure (SBP) has become available. However, the relation between end-organ damage and the 24-hour central SBP profile and variability has not so far been analyzed. Therefore, the aim of this cross-sectional study was to evaluate the relation between 24-hour central SBP, 24-hour central SBP profile as well as central SBP short-term variability and parameters of cardiac and vascular intermediate phenotypes. Methods: The study group consisted of 50 patients with newly diagnosed, untreated hypertension (age 40.4 ± 11.5 years, 35 men) and 50 normotensive subjects (age 38.3 ± 12.0 years, 35 men). Applanation tonometry of the radial artery and the "n-point forward moving average" method were used to determine 24-hour central SBP. Each study participant underwent echocardiography and carotid ultrasonography. Results: 24-hour, daytime, and nighttime central SBP was related to left ventricle end-diastole diameter ($p < 0.05$), left ventricular mass index ($p < 0.001$), relative wall thickness ($p < 0.05$), E/E' ratio ($p < 0.01$), and left atrium volume ($p < 0.01$). The nocturnal central SBP fall was not related to any of the mentioned parameters, whereas parameters of short-term variability were related to IMT in hypertensives only ($p < 0.05$). Conclusions: The present study showed that 24-hour central SBP is related to intermediate cardiac phenotypes as assessed by echocardiography whereas short-term central SBP variability is mainly related to vascular phenotype as determined by IMT.

**Keywords:** Blood pressure, central blood pressure, pressure amplification, blood pressure profile, ambulatory blood pressure monitoring

## Introduction

Although brachial blood pressure (BP) measurements have been used for over a century more and more data suggest that measuring of brachial BP has important limitations. First, a few office BP readings may not be representative of BP during a patient's daily life. Second, brachial BP may differ from systolic BP measured at the level of the ascending aorta, i.e. central BP, which is responsible for left ventricle afterload and determines blood flow through coronary and brain arteries [1].

The development of the technique made it possible to perform 24-h ambulatory BP monitoring (ABPM). The general consensus is that ABPM is a better method for hypertension diagnosis and predicting cardiovascular risk than conventional office brachial BP measurements [2]. ABPM is also more closely correlated with markers of end-organ damage, and is significantly better predictor of cardiovascular events when compared with office BP [3, 4].

Several methods of non-invasive central BP determination have been described recently [5-8]. Subsequently, the correlation between end-organ damage and central as well as peripheral BP has been assessed showing a closer relation of left ventricular mass (LVM) [9], carotid intima-media thickness (IMT) [10] and glomerular filtration rate (GFR) [11] with central BP. Recently, the monitoring of central systolic pressure over 24-hours has become available [12, 13]. However, the relation between end-organ damage and 24-h central SBP profile and variability has not been analyzed so far.

Therefore, the aim of the present cross-sectional study was to evaluate the relation between 24-h central SBP, 24-h central SBP profile as well as central SBP short-term variability and parameters of the heart and arteries structure.

## Methods

### *Study group*

The study group consisted of 50 subjects (referred from a primary care center) with newly diagnosed, never treated hypertension and 50 normotensive healthy volunteers matched for age and sex. The subjects were deemed suitable for the study if they were aged ≥ 18 and < 65 years. We excluded all subjects who had been prescribed any BP-lowering drug, patients with diabetes, subjects with atrial fibrillation or atrial flutter, and patients with a glomerular filtration rate of < 30 ml/minute/1.73 $m^2$. We also excluded subjects with any clinically overt vascular disease. The study procedures were in accordance with institutional guidelines. The study protocol was approved by the Bioethics Committee of the Jagiellonian University and all participants gave the informed and written consent.

### *Data collection*

Brachial BP was measured using an Omron M6 Comfort BP monitor (Omron Healthcare, Milton Keynes, UK). The measurements were made by a trained researcher in standardized conditions, between 8:00 am and 11:00 am. The patients remained seated for the measurements, refrained from eating and smoking for at least 30 minutes, and had rested for 10 minutes prior to measurement. We took at least two measurements spaced by 2 minutes intervals during each of the two outpatient visits. BP for an individual participant was calculated as the average of the 4 readings. Hypertension was defined as a high office brachial BP (systolic pressure ≥ 140 mm Hg and/or diastolic pressure ≥ 90 mm Hg) on at least 2 occasions.

BP monitoring was performed using a radial pulse wave acquisition device (BPro, HealthSTATS, Singapore). The BPro device uses a tonometer embedded within a wrist strap, which is calibrated to oscillometric brachial BP. When used for 24-h central SBP, the BPro device (which is calibrated once at the beginning) captures BP waveforms every 15 minutes (for 8-10 seconds for each measurements) over a 24-hour period, allowing for peripheral BP monitoring. The study participants were instructed to hold the hand at heart level during the measurements (the device beeps before each measurements). The participants' central blood pressure was assessed by applying the n-point moving average method, a mathematical low pass filter, to the radial pulse waves [7]. This method was validated against invasive measurements as well as against validated noninvasive methods of central pressure determination [7].

We repeated the 24-h central SBP monitoring if less than 70% of the measurements were valid because of artefacts. The physician who performed all the measurements had previously been trained in how to use this technique. Daytime and nighttime was assessed on the basis of patients' diary. Nocturnal BP fall was defined as the difference between daytime and nighttime pressure values divided by the daytime pressure. We used the standard deviation (SD) of all BP measurements over the 24-hour period, the coefficient of variation (within-subject SD divided by BP level), and average real variability (the arithmetic average of the differences in consecutive pressure readings) as the measures of short-term, within-subject BP variability.

Two-dimensional M mode echocardiography was performed with the patient in the lateral decubitus position. The measurements were obtained in accordance with the recommendation of the European Association of Echocardiography [14]. All the echocardiographic exams were performed and recorded by the same highly qualified physician using the Vivid 7 Pro (GE Healthcare, Horten Norway) device. The exams were analyzed off-line using the EchoPack system (GE Healthcare, Horten Norway) separately by two investigators and the mean values were used in the analysis. LVM was calculated according to the method devised by Deveraux et al. [15]. Left ventricular mass index (LVMI) was obtained by dividing left ventricular mass by the body surface area. Relative wall thickness (RWT) was calculated using the following formula: the sum of the interventricular septum (IVS) and posterior wall (PW) thickness

**Table 1.** Characteristics of the analyzed population

| Variable | Hypertensives N = 50 | Normotensives N = 50 | P | All N = 100 |
|---|---|---|---|---|
| Men | 35 (70%) | 35 (70%) | 1.00 | 70 (70%) |
| Women | 15 (30%) | 15 (30%) | | 35 (30%) |
| Age, y | 39.6 ± 11.8 | 39.0 ± 11.8 | 0.80 | 39.3 ± 11.7 |
| Smoking | 8 (16%) | 9 (18%) | 0.79 | 17 (17%) |
| Body mass index, kg/m$^2$ | 28.1 ± 3.5 | 25.9 ± 3.9 | < 0.01 | 27.0 ± 3.9 |
| Total cholesterol, mg/dl | 219 ± 39 | 221 ± 43 | 0.90 | 220 ± 41 |
| Glucose, mg/dl | 97.2 ± 9.1 | 93.7 ± 8.9 | 0.22 | 95.4 ± 9.0 |
| Creatinine, mg/dl | 0.80 ± 0.15 | 0.86 ± 0.14 | 0.10 | 0.83 ± 0.15 |
| Glomerular filtration rate, ml/min/1.73m$^2$ | 105.1 ± 18.5 | 98.4 ± 22.6 | 0.07 | 101.8 ± 20.8 |
| Ejection fraction, % | 64.5 ± 6.1 | 65.5 ± 6.0 | 0.42 | 65.0 ± 6.0 |
| Office systolic BP, mm Hg | 148.2 ± 11.6 | 126.3 ± 10.5 | < 0.001 | 137.3 ± 15.5 |
| Office diastolic BP, mm Hg | 95.4 ± 9.3 | 81.7 ± 7.7 | < 0.001 | 88.6 ± 10.9 |
| Central SBP, mm Hg | | | | |
| 24 h | 129.3 ± 11.4 | 111.1 ± 12.3 | < 0.001 | 120.2 ± 14.9 |
| Day | 133.5 ± 12.0 | 114.8 ± 13.1 | < 0.001 | 124.1 ± 15.7 |
| Night | 123.1 ± 11.1 | 105.6 ± 11.9 | < 0.001 | 114.4 ± 14.5 |
| Nocturnal central SBP fall, % | 7.8 ± 3.8 | 7.8 ± 3.7 | 0.94 | 7.8 ± 3.7 |
| SD central SBP, mm Hg | | | | |
| 24 h | 10.9 ± 2.6 | 10.1 ± 2.6 | 0.07 | 10.5 ± 2.6 |
| Day | 10.2 ± 2.5 | 9.2 ± 2.6 | 0.06 | 9.7 ± 2.6 |
| Night | 8.5 ± 2.3 | 8.2 ± 2.2 | 0.45 | 8.3 ± 2.3 |
| Average real variability, mm Hg | 8.6 ± 2.4 | 8.4 ± 2.2 | 0.56 | 8.5 ± 2.3 |
| Coefficient of variation | 0.084 ± 0.018 | 0.091 ± 0.020 | 0.07 | 0.088 ± 0.020 |
| 24 h heart rate, beats per minute | 70.3 ± 7.9 | 67.6 ± 5.5 | < 0.05 | 69.0 ± 6.9 |

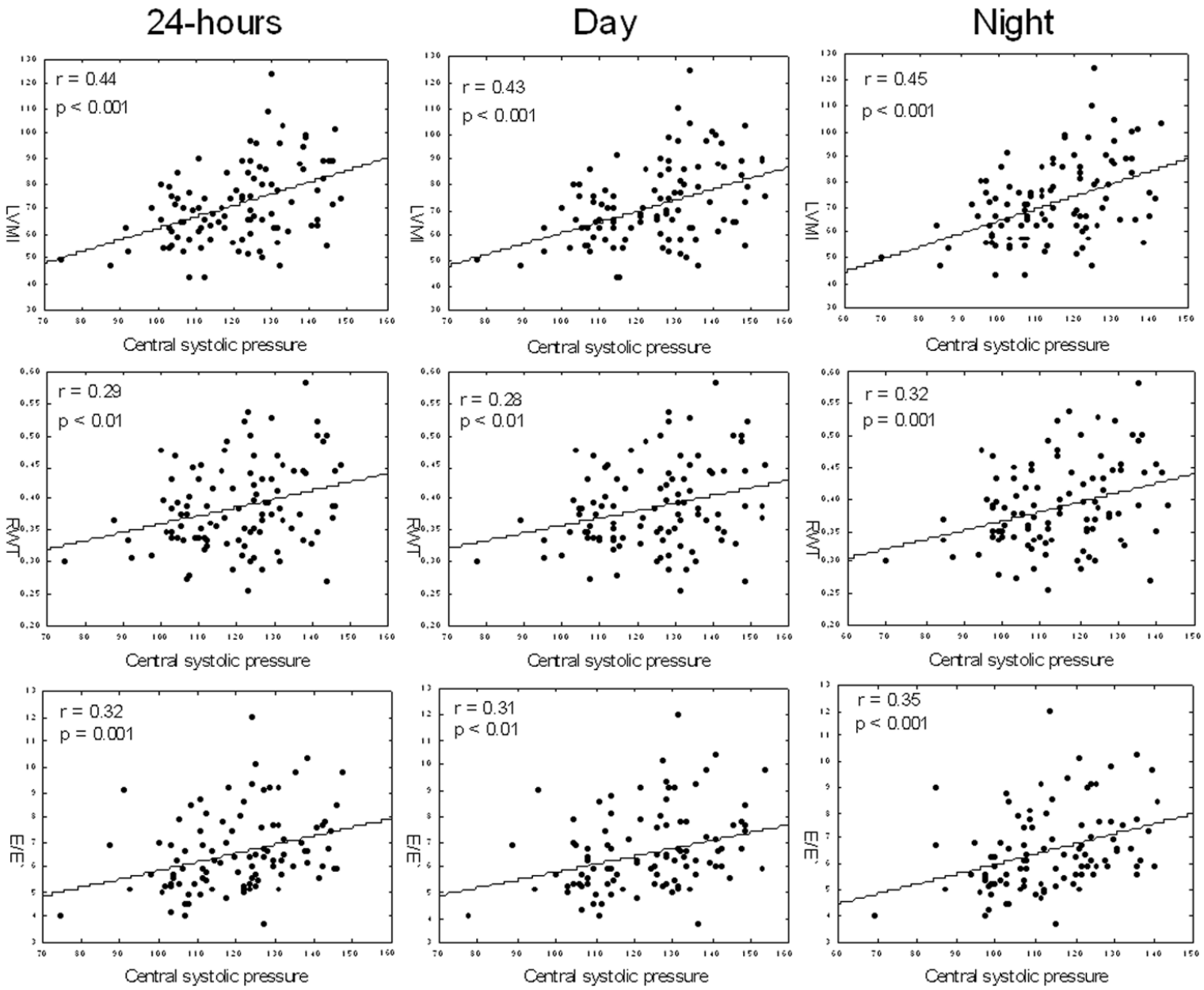
BP, blood pressure; SBP, systolic blood pressure; SD, standard deviation. Data are expressed as mean ± standard deviation or numbers (percentage of the group).

**Table 2.** Intermediate cardiovascular phenotypes in the study groups

| Variable | Hypertensives N = 50 | Normotensives N = 50 | P |
|---|---|---|---|
| Interventricular septum, diastole, mm | 10.10 ± 1.78 | 9.24 ± 1.29 | < 0.01 |
| Left ventricle end-diastole diameter, mm | 48.98 ± 4.54 | 48.60 ± 4.34 | 0.67 |
| Posterior wall, diastole, mm | 9.48 ± 1.62 | 8.60 ± 1.44 | < 0.01 |
| Left ventricle mass, g | 153.10 ± 42.22 | 131.64 ± 34.44 | < 0.01 |
| Left ventricle mass index, g/m$^2$ | 76.50 ± 16.93 | 66.52 ± 12.64 | 0.001 |
| Left atrium volume, ml | 54.81 ± 17.12 | 50.56 ± 17.54 | 0.22 |
| Relative wall thickness | 0.40 ± 0.08 | 0.37 ± 0.05 | 0.01 |
| E/E' | 7.1 ± 2.2 | 6.2 ± 1.6 | 0.03 |
| Intima-media thickness, mm | 0.60 ± 0.12 | 0.57 ± 0.10 | 0.25 |

Data are expressed as mean ± standard deviation.

in diastole divided by the left ventricular end-diastolic diameter (LVEDd) in diastole. The pulsed-wave (PW) Doppler was performed in an apical 4-chamber view to obtain mitral inflow velocities to assess left ventricular filling. PW Doppler tissue imaging (DTI) was also performed in apical views to acquire mitral annulus velocities. Then, the mitral inflow E velocity to tissue Doppler E' average (E/E') ratio was calculated. Left atrium (LA) volume was estimated using the apical 4- and 2-chamber views with biplane method.


24-hours
Day
Night
r = 0.44
p < 0.001
r = 0.43
p < 0.001
r = 0.45
p < 0.001
LVMI
Central systolic pressure
r = 0.29
p < 0.01
r = 0.28
p < 0.01
r = 0.32
p = 0.001
RWT
Central systolic pressure
r = 0.32
p = 0.001
r = 0.31
p < 0.01
r = 0.35
p < 0.001
E/E'
Central systolic pressure

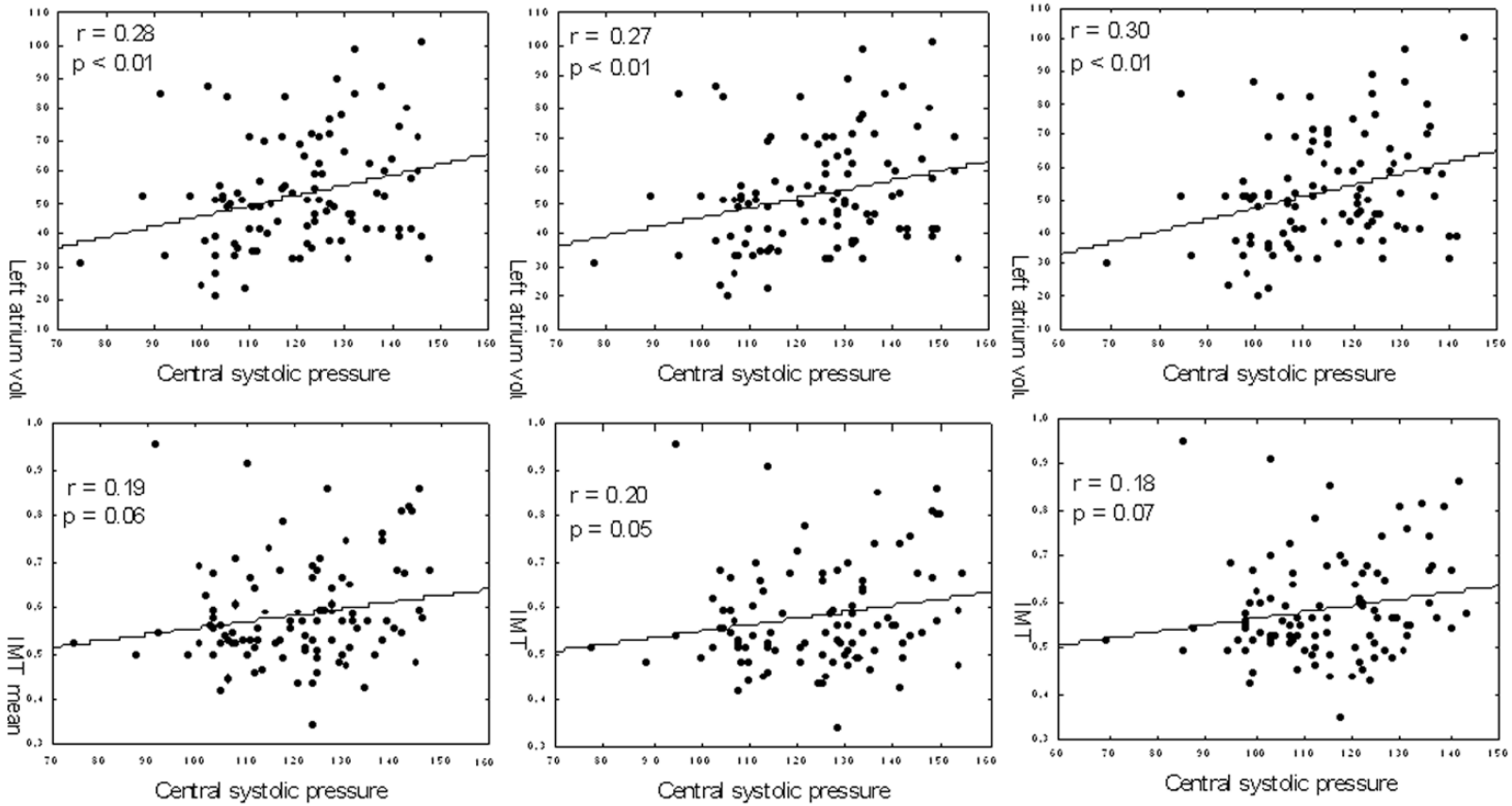



**Figure 1.** Scatterplots of the relation between 24-hour central systolic pressure and cardiac and vascular phenotypes (N = 100).

All participants underwent carotid ultrasonography using a VIVID 7 Pro (GE Healthcare, Horten Norway) device equipped with a 10 MHz vascular probe in accordance with the Mannheim Carotid Intima-Media Thickness (IMT) Consensus [16]. All the exams were recorded and analyzed off-line using the Echo-Pack system (GE Healthcare, Horten Norway) separately by two investigators and the mean values were used in the analysis.

Fasting blood samples were taken for total cholesterol, glucose, and creatinine levels. The estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease formula. Height and weight were measured in standing position without shoes and heavy outer garments using standard scales with a vertical ruler. Body Mass Index (BMI) was calculated according to the following formula: BMI = weight [kg]/(height [m])$^2$. Current smokers were defined as those who had smoked any tobacco in the previous month.

*Statistical analysis*

All the data were analyzed using STATISTICA 8.0 software (StatSoft Inc, Tulsa, OK). The categorical variables were reported as percentages, and the continuous variables as means ± SDs. Normally distributed continuous variables were compared using the Student's *t* test for independent samples. The Mann-Whitney *U* test was applied in case of variables without normal distribution. The Pearson's $\chi^2$ test was adopted for the categorical variables. The relations between central BP and cardiac and vascular phenotypes were presented as correlation coefficients. The correlation coefficients were compared using the r-to-Fisher-z transformation. Multivariate regression analysis was used in order to show the independent of age and sex relations between central SBP and cardiac and vascular phenotypes. A 2-tailed *P* value of < 0.05 was established as the level of statistical significance.

## Results

The characteristics of the analyzed groups are presented in **Table 1**. In the hypertensive group 33 (66%) subjects had stage 1 hypertension and 17 (34%) had stage 2 hypertension. Hypertension was diagnosed 5.3 ± 10.9 months before the participants entered the study. Hypertensives had higher central SBP and HR values over the 24-hour period, as well as during day and night hours compared to normotensives. Nocturnal central SBP fall as well as the parameters of short-term central SBP variability did not differ significantly between the groups.

The echocardiographic findings are presented in **Table 2**. Hypertensives had thicker IVS and PW in diastole, as well as higher LVM and LVMI values. The mean value of IMT did not differ significantly between the groups.

The correlations between cardiac and vascular phenotypes and 24-hour central SBP as well as daytime and nighttime central SBP are presented in **Figure 1**. The correlation coefficients between cardiac and vascular phenotypes and daytime central BP did not differ from the correlation coefficients between cardiac and vascular phenotypes and nighttime central BP (all p = NS). The age- and sex-independent relations between echocardiographic parameters as well as IMT and central systolic BP and parameters of its short-term variability are presented in **Tables 3** and **4**. In general, the absolute values of SBP were related to left ventricle diastolic diameter, LVMI, RWT, E/E' and LA volume. Nocturnal central SBP fall was not related to any of the analyzed parameters whereas parameters of short-term variability were related to IMT in hypertensives only.

## Discussion

Central BP was shown to predict cardiovascular risk [17]. It was also shown that central BP is more closely correlated with preclinical cardiac and vascular disease [18]. The likely underlying mechanism for this observation is more accurate representation of loading conditions on the heart and coronary and cerebral vessels. More and more evidence is available on the usefulness of ABPM in research and clinical practice [4]. In a previous paper we described the pattern of 24-hour central SBP in healthy subjects and hypertensives who had never been treated 12. Similar results were obtained by Williams et al. in a group of 171 patients with hypertension treated with a renin-angiotensin system blocker [19]. In this report we have sought to identify a relationship between 24-hour central BP parameters and intermediate cardiovascular phenotypes.

**Table 3.** Regression coefficients of the association between echocardiographic parameters and central systolic blood pressure and parameters of its short-term variability. Age and sex are included in the statistical models

| | Hypertensives | | Normotensives | | All patients | |
|---|---|---|---|---|---|---|
| | ß | p | ß | p | ß | p |
| Left ventricular mass index | | | | | | |
| Central SBP - 24 h | 0.36 | 0.02 | 0.26 | 0.07 | 0.41 | < 0.001 |
| Central SBP - day | 0.31 | 0.04 | 0.27 | 0.06 | 0.40 | < 0.001 |
| Central SBP - night | 0.42 | < 0.01 | 0.24 | 0.09 | 0.43 | < 0.001 |
| SD 24 h central SBP | -0.03 | 0.83 | 0.20 | 0.20 | 0.13 | 0.24 |
| SD day central SBP | 0.15 | 0.33 | 0.16 | 0.29 | 0.21 | 0.05 |
| SD night central SBP | -0.23 | 0.15 | 0.26 | 0.12 | 0.01 | 0.93 |
| Average real variability | -0.08 | 0.60 | 0.28 | 0.09 | 0.08 | 0.47 |
| Coefficient of variation | -0.18 | 0.30 | 0.08 | 0.60 | -0.11 | 0.31 |
| Nocturnal central SBP fall | -0.17 | 0.27 | 0.07 | 0.67 | -0.06 | 0.55 |
| Relative wall thickness | | | | | | |
| Central SBP - 24 h | 0.14 | 0.33 | 0.08 | 0.57 | 0.21 | 0.03 |
| Central SBP - day | 0.12 | 0.42 | 0.07 | 0.63 | 0.19 | 0.04 |
| Central SBP - night | 0.19 | 0.21 | 0.08 | 0.57 | 0.22 | 0.02 |
| SD 24 h central SBP | -0.09 | 0.53 | 0.12 | 0.42 | 0.04 | 0.70 |
| SD day central SBP | 0.04 | 0.79 | 0.06 | 0.69 | 0.09 | 0.34 |
| SD night central SBP | -0.20 | 0.18 | 0.41 | < 0.01 | 0.04 | 0.72 |
| Average real variability | -0.13 | 0.34 | 0.27 | 0.07 | 0.01 | 0.89 |
| Coefficient of variation | 0.11 | 0.45 | -0.16 | 0.30 | -0.08 | 0.46 |
| Nocturnal central SBP fall | -0.11 | 0.44 | -0.02 | 0.85 | -0.06 | 0.51 |
| E/E' | | | | | | |
| Central SBP - 24 h | 0.19 | 0.22 | 0.38 | < 0.01 | 0.31 | < 0.01 |
| Central SBP - day | 0.13 | 0.37 | 0.36 | < 0.01 | 0.29 | < 0.01 |
| Central SBP - night | 0.29 | 0.07 | 0.36 | < 0.01 | 0.34 | < 0.001 |
| SD 24 h central SBP | -0.05 | 0.73 | 0.22 | 0.14 | 0.09 | 0.36 |
| SD day central SBP | 0.14 | 0.44 | 0.11 | 0.43 | 0.16 | 0.10 |
| SD night central SBP | -0.07 | 0.65 | 0.20 | 0.22 | 0.05 | 0.64 |
| Average real variability | -0.04 | 0.77 | 0.13 | 0.43 | 0.03 | 0.76 |
| Coefficient of variation | -0.13 | 0.41 | 0.03 | 0.84 | -0.10 | 0.38 |
| Nocturnal central SBP fall | -0.23 | 0.11 | 0.02 | 0.90 | -0.12 | 0.22 |
| Left ventricle end-diastole diameter | | | | | | |
| Central SBP - 24 h | 0.20 | 0.18 | 0.20 | 0.13 | 0.20 | 0.03 |
| Central SBP - day | 0.19 | 0.19 | 0.21 | 0.11 | 0.20 | 0.03 |
| Central SBP - night | 0.21 | 0.17 | 0.18 | 0.17 | 0.20 | 0.04 |
| SD 24 h central SBP | 0.10 | 0.50 | 0.06 | 0.66 | 0.10 | 0.32 |
| SD day central SBP | 0.13 | 0.38 | 0.05 | 0.72 | 0.10 | 0.30 |
| SD night central SBP | 0.02 | 0.91 | -0.10 | 0.49 | -0.00 | 0.97 |
| Average real variability | 0.14 | 0.32 | -0.03 | 0.84 | 0.09 | 0.37 |
| Coefficient of variation | 0.19 | 0.19 | -0.01 | 0.94 | 0.05 | 0.62 |
| Nocturnal central SBP fall | -0.01 | 0.94 | 0.08 | 0.54 | 0.03 | 0.78 |
| Left atrium volume | | | | | | |
| Central SBP - 24 h | 0.28 | 0.08 | 0.32 | 0.04 | 0.30 | < 0.01 |
| Central SBP - day | 0.22 | 0.17 | 0.30 | 0.04 | 0.28 | < 0.01 |
| Central SBP - night | 0.36 | 0.03 | 0.33 | 0.03 | 0.33 | 0.001 |

Due to short-term BP variability 24-hour brachial BP is more closely related to end-organ damage when compared with office BP. To our best knowledge this is the first report to show a significant relation between 24-hour central SBP and left ventricular mass, left ventricular diastolic function, and LA volume. In addition, we showed a significant relation between IMT and parameters of short-term central SBP variability. It should be underlined that a unique feature of our study was that it focused solely on untreated subjects. Moreover, we included both subjects with and without hypertension; therefore, it was therefore possible to compare the relation between intermediate cardiovascular phenotypes and 24-hour systolic BP in hypertensives and normotensives.

Left atrial size has been shown to be an independent predictor of death, heart failure, atrial fibrillation and ischemic stroke [20]. Central BP indices obtained from single measurements were reported to be associated with LA diameter and volume [21, 22]. In the present study, we found that LA volume was significantly associated with 24-hour, daytime, and nighttime central BP. Of note, LA volume was related neither to central BP variability nor to nocturnal central SBP fall, both in the univariate analysis and after adjustment for age and sex.

| | | | | | | |
|---|---|---|---|---|---|---|
| SD 24 h central SBP | -0.16 | 0.32 | 0.14 | 0.41 | 0.01 | 0.91 |
| SD day central SBP | -0.00 | 1.00 | 0.22 | 0.19 | 0.12 | 0.25 |
| SD night central SBP | -0.23 | 0.15 | -0.07 | 0.69 | -0.13 | 0.25 |
| Average real variability | 0.07 | 0.63 | 0.16 | 0.35 | 0.13 | 0.26 |
| Coefficient of variation | -0.30 | 0.08 | -0.04 | 0.82 | -0.19 | 0.11 |
| Nocturnal central SBP fall | -0.22 | 0.14 | -0.04 | 0.76 | -0.13 | 0.20 |

SBP, systolic blood pressure, SD, standard deviation, ß, standardized regression coefficient.

**Table 4.** Regression coefficients of the association between intima-media thickness and central systolic blood pressure and parameters of its short-term variability. Age and sex are included in the statistical models

| | Hypertensives | | Normotensives | | All patients | |
|---|---|---|---|---|---|---|
| | ß | p | ß | p | ß | p |
| Central SBP - 24 h | 0.10 | 0.46 | -0.00 | 0.99 | 0.11 | 0.24 |
| Central SBP - day | 0.15 | 0.29 | 0.01 | 0.93 | 0.12 | 0.17 |
| Central SBP - night | 0.06 | 0.68 | -0.02 | 0.85 | 0.08 | 0.36 |
| SD 24 h central SBP | 0.31 | 0.02 | 0.07 | 0.60 | 0.23 | 0.02 |
| SD day central SBP | 0.29 | 0.03 | 0.03 | 0.84 | 0.19 | < 0.05 |
| SD night central SBP | 0.21 | 0.15 | 0.04 | 0.81 | 0.16 | 0.12 |
| Average real variability | 0.34 | 0.01 | 0.03 | 0.87 | 0.24 | 0.01 |
| Coeffcient of variation | 0.34 | 0.02 | 0.09 | 0.54 | 0.20 | 0.04 |
| Nocturnal central SBP fall | 017 | 0.19 | 0.11 | 0.40 | 0.13 | 0.14 |

SBP, systolic blood pressure, SD, standard deviation, ß, standardized regression coefficient.

Left ventricular hypertrophy, even in the absence of any other risk factors, is associated with increased cardiovascular morbidity and mortality [20]. The relation between LVMI and the shape of the central pressure waveform was presented by other investigators [22-25]. The Czech Post-Monica Study showed that central SBP was more closely related to left ventricular hypertrophy, as detected by electrocardiography, than brachial SBP and pulse pressure [23]. In the Strong Heart Study central SBP was also more strongly associated with left ventricular hypertrophy, as determined by echocardiography, than brachial SBP and central PP [9]. It is noteworthy that none of these studies analyzed the circadian profile of central SBP. The association between left ventricular hypertrophy and 24-hour central SBP in patients with type 1 diabetes was investigated by Theilade et al. [26]. The authors found that 24-hour central SBP was higher in patients with left ventricular hypertrophy in univariate analysis, but the difference was not significant after multivariate adjustments. It should be underlined that there are several methodological differences between our study and the Theilade's analysis. Firstly, in Theilade's study population consisted of patients with type 1 diabetes and 21% of the subjects suffered from cardiovascular diseases, whereas we included healthy subjects or patients with hypertension without diabetes. Secondly, Theilade et al. assessed left ventricular hypertrophy on the basis of electrocardiography, which is less sensitive than echocardiography. Lastly, 71% of the patients studied by Theilade et al. were taking antihypertensive treatment. It is well known that antihypertensive drugs may influence central BP in different ways. It is also logical to suspect that antihypertensive treatment may weaken the relation between BP and left ventricular hypertrophy. Using a single measurement DeLoch et al showed an independent relationship between RWT and central SBP in a group of 120 adolescents [25]. Similarly, in the Strong Heart Study a relationship was proven to exist between RWT and central systolic BP [9]. Our present study has extended these observations to the relationship between 24-hour central SBP and RWT.

In a recent paper the relation between 24-hour central SBP and left-ventricular mass was shown in a group of subjects containing a substantial proportion of patients taking blood-pressure lowering drugs [27]. Our present study has extended these observations to the relationship between 24-hour central SBP and parameters of LV diastolic function, indexes of the heart structure IMT in subjects not taking any blood pressure lowering agent. Importantly, we also assessed the relation between the short-term variability of central SBP and cardiovascular phenotypes.

E/E' ratio is a sensitive index of diastolic function, and its correlation with peripheral BP was

proved in several studies [28, 29]. However, there is lack of evidence with respect to central SBP. In our study, the E/E' ratio was significantly associated with 24-h, daytime, and nighttime central BP in normotensives, but this relationship did not achieved significance in subjects with hypertension. This issue should be addressed in future studies.

One of the major advantages of 24-hour BP monitoring is the possibility it offers to assess short-term BP variability, which is usually presented as an SD of all measurements from a specific time period [4]. It has been shown that higher SD is correlated with target organ damage in patients with hypertension. Tatasciore et al. demonstrated that daytime peripheral SBP variability positively correlates with LVMI and IMT in patients with newly diagnosed, untreated hypertension [30]. The relation between short-term variability of central SBP and end-organ damage has not been analyzed so far. The only previous data regarding the correlation between central SBP and IMT were related to a single measurement of central SBP. Roman et al. proved that central SBP was more strongly correlated with IMT and the number of atherosclerotic plaques in carotid arteries than peripheral SBP10. The potential limitation of this study was the fact that 70% of the subjects with hypertension had taken antihypertensives and it might have had an impact on the results. Similarly, in patients with chronic kidney disease central PP was highly correlated with IMT [31]. We showed a significant relation between the variability of central SBP and IMT in hypertensives.

We used a BPro device to assess 24-hour central SBP. The BPro device uses the applanation tonometry of the radial artery and is calibrated with brachial BP. The accuracy of central BP measurements was validated against previously validated non-invasive methods in a large number of subjects as well as against invasively acquired BP with considerable agreement between the two [7]. Recently, another study was published that demonstrated the adequate validity of the BPro device vs. the reference device [32]. In addition, validation studies of other devices were published that suggests that 24-hour central pressure measurements will be also possible in the future using devices other than BPro [33, 34].

Our study does have some limitations. First, we studied a relatively low number of subjects. Indeed, it should be stressed that our results need to be confirmed by much larger studies. It is possible that we would be able to detect other significant relations between intermediate cardiovascular phenotypes and central SBP or its variability if we studied a larger group of subjects. Second, most hypertensive participants suffered from mild hypertension. Moreover, we excluded subjects with diabetes or any clinically overt vascular disease. Therefore, our results should be directly applied only to relatively young and relatively healthy subjects. Third, we excluded all patients that had been prescribed BP-lowering medications. As antihypertensive agents may differ in their influence on both 24-BP profile and BP variability our results should not be directly applied to pharmacologically treated patients.

In conclusion, the present study showed that 24-hour central SBP is related to intermediate cardiac phenotypes as assessed by echocardiography whereas short term central SBP variability is related mainly to vascular phenotypes as determined by IMT. However, these results require confirmation in larger studies.

## Acknowledgements

Funding source: supported by unrestricted educational grant from Ministry of Science and Higher Education in Poland (nr N N402 523839).

## Disclosure of conflict of interest

The authors declare no conflict of interest.

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