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## Interrelation of indicators of ambulatory blood pressure monitoring with structural and functional parameters of the left ventricle in hypertensive patients

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### Abstract

**Objective.** To find the parameters of the ambulatory blood pressure monitoring (ABPM), which play a significant role for the development of the structural and functional changes of left ventricle (LV) in hypertensive patients. **Design and methods.** We included 94 hypertensive patients (55 males, 39 females), mean age —  $51 \pm 6$  years. ABPM and echocardiography were performed in all patients. **Results.** There was a significant relation between mean hemodynamic blood pressure (BP) and a relative wall thickness and LV myocardial mass index. Pulse BP significantly correlated with the early LV diastolic dysfunction. **Conclusions.** As an indicator of LV postload, mean hemodynamic BP might be used to determine the target organ (heart) damage.

**Key words:** arterial hypertension, structural and functional changes of left ventricle, blood pressure

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## Взаимосвязь показателей суточного мониторинга артериального давления со структурно-функциональными параметрами левого желудочка у больных гипертонической болезнью

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### Резюме

**Цель исследования** — выявить наиболее значимые показатели суточного мониторинга артериального давления (СМАД) в формировании структурно-функциональных изменений левого желудочка (ЛЖ) у больных гипертонической болезнью (ГБ). **Материалы и методы.** Обследованы 94 амбулаторных пациента, из них 55 мужчин, 39 женщин. Обследуемые были сопоставимы по возрасту, стажу и стадии ГБ, тяжести артериальной гипертензии, индексу массы тела. Средний возраст составил  $51 \pm 6$  лет. Обследуемым проведены СМАД, эхокардиография. **Результаты.** Наиболее значимая связь среднего артериального давления (АД) выявлена с индексом относительной толщины стенок и индексом массы миокарда ЛЖ. Пульсовое АД наиболее значимо коррелировало с показателем ранней диастолической дисфункции ЛЖ E/em. **Выводы.** При оценке поражения органов-мишеней (сердца) целесообразно использовать интегральный показатель — среднее АД — как показатель постнагрузки на миокард ЛЖ.

**Ключевые слова:** артериальная гипертензия, структурно-функциональные изменения левого желудочка, показатели артериального давления

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### Introduction

The recommendations of the European Society of Arterial Hypertension (2013) and All-Russian Scientific Society of Cardiology highlight the importance of diagnosing subclinical target organ damage (TOD), including structural and functional parameters of the left ventricle (LV) for

cardiovascular risk stratification and the choice of treatment strategy [1].

National recommendations on arterial hypertension also include pulse pressure (PP) as a cardiovascular risk factors in elderly patients [2, 3]. The increase of systolic BP (SBP) and PP accelerates arterial damage and associated TOD [4].

Currently, the role of average hemodynamic BP associated with essential hypertension (HTN) has not been recognized yet. Instead, the derivatives from the average blood pressure, i.e. SBP and diastolic BP (DBP), are considered to be the criteria of disease and treatment, as well as the target pressure [5]. At the same time, the average BP is the most important hemodynamic characteristic [6].

**Objective of our study** is to find the most important indicators of ambulatory monitoring of BP (ABPM) for structural and functional changes of the LV in patients with HTN.

### Design and methods

We included 45 outpatients with HTN stage 1 (24 males and 21 females), 49 outpatients with HTN stage 2 (31 males and 18 females). All of them signed informed written consent in accordance with international ethical requirements for biomedical research involving human subjects, and paragraph 4.6.1. of order No. 163 (Industrial Standard OST 91500.140001–2002) of the Ministry of Healthcare of Russian Federation. All patients took antihypertensive medications, including angiotensin-converting enzyme inhibitors, calcium antagonists, thiazide diuretics, and  $\beta$ -blockers.

All patients (without drug discontinuation) underwent ABPM and echocardiography (Echo-CG). ABPM was conducted using a system of BP long-term registration (Schiller, 2006), outpatient BP BR-102 PLUS recorders, and MT-300 program. The measurements were carried out every 15 minutes in the daytime and every 30 minutes at night; the time from 11 p. m. till 7 a. m. was taken as a night period. During the study, average daily and mean day and night values of SBP, DBP, PP, and average BP values were determined. Average BP was calculated based on the auscultatory measurements as follows:  $BP_{av} = DBP + 1/3 (SBP - DBP)$ . In oscillometric measurements, the average BP is a value measured by the device.

Echo-CG study was performed with the use of Artida 4D device (Toshiba Medical Systems, 2008) in accordance with the recommendations of the European Society of Cardiology (2006). Standard measurements of the LV size and volume, wall thickness, and ejection fraction according to Simpson's method were made. Calculation of LV mass (LVM) was performed in 2D mode according to the area-length algorithm [7]. Index of LVM (LVMI) was calculated as a ratio of ideal body height to the corresponding body surface area [8, 9]. Relative thickness of LV posterior wall was calculated by the following formula (in

Table 1

### GROUP CHARACTERISTICS

Parameter	HTN stage I (n = 45)	HTN stage II (n = 49)	p
Male, n (%)	44.7	38.3	0.53
Female, n (%)	55.3	61.7	
Age, yr	51 ± 7	50 ± 4	0.31
Grade 1 HTN, n (%)	6.4	0	0.001
Grade 2 HTN, n (%)	87.2	66.0	
Grade 3 HTN, n (%)	6.4	34.0	
Duration of HTN, n (%)			0.002
< 1 year	6.4	0	
1–5 years	44.7	17.0	
> 5 years	48.9	83.0	
BMI, kg/m <sup>2</sup>	31.0 (28.4–35.1)	30.0 (27.7–33.5)	0.49
Smoking, n (%)	36.4	37.8	0.89
Total cholesterol, mmol/L	5.86 (5.50–7.14)	6.03 (5.51–6.89)	0.86
AI, Units	3.2 ± 0.60	4.8 ± 0.60	0.001

**Note:** HTN — essential (arterial) hypertension; BMI — body mass index; AI — atherogenic index; p — significant differences between groups.

conventional units):  $LV\ RWT = (LV\ PWT\ (D) + IVST)/(EDD)$ , where LV RWT is LV relative wall thickness, LV PWT (D) is LV posterior wall thickness, IVST (D) is interventricular septum thickness, and EDD is end-diastolic diameter. The standard criterion in 2D mode (LVMI above 94 g/m<sup>2</sup> for males and above 89 g/m<sup>2</sup> for females) was considered as a sign of LV hypertrophy. Diastolic dysfunction of the LV was evaluated in accordance with the recommendations of the American Society of Echocardiography [11].

Statistical data processing was performed using Statistica application program package (version 6.0) and Excel (2007 version). Normality of data distribution was checked with the Shapiro–Wilk criterion. The study results are presented by mean values (M), mean-square deviation values ( $\delta$ ) or a median and interquartile (percentile) interval (Q25–Q75). The evaluation of differences between the samplings upon standard distribution of variables was made using Student t-criterion. Upon distribution differing from the standard, Mann–Whitney criterion was used.

The correlations were assessed using Spearman's rank correlation coefficient ( $r$ ). The differences among three groups were evaluated by Kruskal–Wallis test with Bonferroni adjustment. In case of discrete variables (qualitative signs),  $\chi^2$  Pearson criterion with Yates's correction was used. Differences were considered significant at  $p$ -level  $< 0.05$ .

## Results

Clinical characteristics are provided in Table 1.

The examined subjects were compared by gender, age, BMI, bad habits (smoking). The groups differed significantly by the duration of HTN ( $p = 0.002$ ), HTN degree ( $p = 0.001$ ), and atherogenic index (AI) ( $p = 0.001$ ). Higher BP level and significantly longer history of HTN were registered in patients with HTN II. AI was higher in patients with HTN II.

Based on Echo-CG (Table 2), patients with HTN II had higher indices of LV myocardium as compared to group I. LV myocardial contractility in the studied groups was within normal limits, but it was higher in group with HTN II. The parameters of LV diastolic dysfunction differed significantly in both groups.

In the studied groups, ABPM parameters (Table 3) were calculated separately in daytime, at night, and within 24 hours.

The values of SBP, DBP, average BP, PP in daytime, at night, and within 24 hours differed significantly between the groups ( $p < 0.001$ ); moreover, average values were higher in the group with HTN II.

The correlations between ABPM values and LV structural and functional parameters are provided in Table 4.

We found a moderate but significant correlation of the LV RWT index with SBP, DBP and average

Table 2

### ECHOCARDIOGRAPHY DATA IN PATIENTS WITH ESSENTIAL HYPERTENSION

Parameter	HTN stage I (n = 45)	HTN stage II (n = 49)	p
PWT LV, cm	0.97 (0.90–1.06)	1.28 (1.22–1.35)	$< 0.001$
IVST LV, cm	$1.06 \pm 0.15$	$1.40 \pm 0.13$	$< 0.001$
EDD LV, cm	4.7 (4.6–4.8)	4.7 (4.5–4.9)	0.65
LAD, cm	3.4 (3.2–3.5)	3.8 (3.4–4.1)	$< 0.001$
LVMI, g/m <sup>2</sup>	68.0 (57.6–82.0)	127.9 (102.8–140.3)	$< 0.001$
RWT	0.42 (0.40–0.45)	0.57 (0.53–0.61)	$< 0.001$
EF LV, %	$60 \pm 4$	$59 \pm 5$	0.003
E/Em	6.31 (5.21–7.71)	7.85 (6.56–9.61)	$< 0.001$
IVRT, ms	$98 \pm 23$	$112 \pm 17$	0.001
DT, ms	200 (160–229)	233 (159–279)	0.043

**Note:** HTN — essential (arterial) hypertension; LV — left ventricle; PWT LV — posterior LV wall end-diastolic thickness; IVST — interventricular septum thickness; EDD LV — LV end-diastolic diameter; LAD — left atrium diameter; LVMI — LV mass index; RWT — relative wall thickness; EF — ejection fraction; E/Em — the ratio of the diastolic peak early transmitral flow velocity and peak early diastolic mitral annular velocity; IVRT — isovolumic relaxation time; DT — deceleration time; p — significant differences between groups.

Table 3

**THE RESULTS OF AMBULATORY BLOOD PRESSURE MONITORING  
IN PATIENTS WITH ESSENTIAL HYPERTENSION STAGE I AND STAGE II (M ± Δ)**

Parameter	HTN stage I (n = 45)	HTN stage II (n = 49)	p
Day			
SBP, mm Hg	132.1 ± 13.1	146.2 ± 16.4	< 0.001
DBP, mm Hg	83.6 ± 9.2	93.1 ± 11.3	< 0.001
Mean arterial BP, mmHg	103.2 ± 11.1	111.3 ± 11.7	< 0.001
PP, mm Hg	48.6 ± 7.0	52.4 ± 10.3	< 0.001
Night			
SBP, mm Hg	122.2 ± 3.5	134.6 ± 3.2	0.001
DBP, mm Hg	74.1 ± 11.2	82.4 ± 10.6	0.001
Mean arterial BP, mmHg	93.1 ± 11.2	101.7 ± 12.5	< 0.001
PP, mm Hg	46.2 ± 7.04	50.2 ± 11.9	< 0.001
24h			
SBP, mm Hg	129.6 ± 13.1	141 ± 15.9	< 0.001
DBP, mm Hg	82.1 ± 9.1	89.5 ± 9.8	< 0.001
Mean arterial BP, mmHg	99.0 ± 13.3	110.2 ± 12.3	< 0.001
PP, mm Hg	48.5 ± 5.1	51.4 ± 4.1	0.09
HR, beats/min	74.9 ± 7.5	72.9 ± 10.3	< 0.001

**Note:** HTN — essential hypertension; SBP — systolic blood pressure; DBP — diastolic blood pressure; PP — pulse pressure; BP — blood pressure; HR — heart rate; p — significant differences between groups.

Table 4

**SPEARMAN'S RANK CORRELATION COEFFICIENT(R)  
BETWEEN LEFT VENTRICULAR STRUCTURAL AND FUNCTIONAL  
PARAMETERS AND VALUES OF AMBULATORY BLOOD PRESSURE MONITORING**

Parameter	SBP (24h)	DBP (24h)	Mean arterial BP, mmHg (24h)	PP	
				Day	Night
RWT	0.32*	0.31*	0.40*	0.21	0.09
LVMI	0.24*	0.23*	0.29*	0.16	0.04
E/Em	0.34*	0.25*	0.28*	0.31*	0.34*
IVRT	0.16	0.05	0.07	0.10	0.25*
DT	-0.07	-0.05	-0.06	-0.05	-0.01
EF LV	-0.13	-0.13	-0.19	-0.06	-0.14

**Note:** BP — blood pressure; SBP — systolic blood pressure; DBP — diastolic blood pressure; PP — pulse pressure; RWT — relative wall thickness; LV — left ventricle; LVMI — LV mass index; E/Em — the ratio of the diastolic peak early transmitral flow velocity and peak early diastolic mitral annular velocity; IVRT — isovolumic relaxation time; DT — deceleration time; EF LV — ejection fraction of LV; \* — p < 0.05 statistically significant differences.

BP, with a slightly higher correlation with the latter one. A weak but significant correlation was found between the LVMI and ABPM parameters. As for the indicator of LV early diastolic dysfunction, E/Em, a moderate relationship with SBP and PP, as well as a weak but relevant correlation with DBP and average BP was detected.

### Discussion

The performed study showed that ABPM values were significantly higher in patients with HTN II as compared to patients with HTN I (p < 0,001). LV concentric hypertrophy was diagnosed in all patients with HTN II. In 84 % patients, LV diastolic dysfunction type I (non-restrictive) was also diagnosed in patients with HTN II. LV



structural indices (LV posterior wall thickness, LVMI) were most associated with average BP, while E/Em index was strongly correlated with PP.

BP has two components, i. e. permanent, characterized with the value of average BP, and pulse, characterized by pulse pressure. Average BP is determined by the LV contractile function and total peripheral vascular resistance, and pulse pressure (the difference between SBP and DBP) is determined by the interaction between the LV contractile function and distensibility of main arteries (direct component) and the magnitude of the reflected wave (indirect component). Increase of PP and SBP is associated with increased stiffness of main arteries and accompanied by increase in the amplitude of the reflected wave [12].

To date, the correlation of PP with the LV diastolic dysfunction is well investigated. The closest correlation is found between arterial stiffness, diastolic dysfunction and diastolic heart failure as a result of direct exposure to abnormally high load on cardiomyocytes during contraction and relaxation and indirectly as a result of LV hypertrophy [13, 14]. Our results are consistent with these data.

According to pathophysiology, average BP is one of significant hemodynamic parameters of BP, that affect LV afterload [15]. If SBP and DBP in peripheral arteries are not always equal to the same indicators in the aorta, average BP on the way from the aorta to peripheral arteries remains basically unchanged [16]. Invasive assessment of average BP is equal to the area under the BP curve, divided by the duration of the cardiac cycle and averaged over several consecutive cycles [17]. Therefore, it identifies the heart as a pump of cardiac activity more accurately. One of the most fundamental equations of cardiovascular physiology is the one that indicates how average BP is correlated with the cardiac output and total peripheral resistance: average BP = COxTPR, where CO is cardiac output, TPR is total peripheral resistance. All changes in average BP are determined by changes in CO or TPR [6]. A more pronounced correlation of average BP with structural indices of LV shown in our study, may reflect LV afterload more accurately and may be a predictor of HTN-associated cardiac dysfunction.

## Conclusions

1. For TOD evaluation (regarding myocardial damage), average BP being an integral index is useful.
2. Average BP is most correlated to structural LV changes in patients with HTN.
3. PP is most correlated to the LV diastolic dysfunction.

## Conflict of interest

The authors declare no conflict of interest.

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