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Daily monitoring of arterial blood pressure with measurement of stiffness of arterial vessels in hypertensive patients

Суточное мониторирование артериального давления с измерением показателей жесткости сосудов у пациентов с гипертонической болезнью

──────── **Abstract** ────────

The purpose of the study is to identify the features of indices of daily monitoring of blood pressure and to evaluate the indicators of stiffness of arterial vessels using a modern daily monitor of blood pressure in male patients with stage I and II hypertension.

Materials and methods. The results of the study are based on complex examination of 105 male patients with stage I and II hypertension at the age from 35 to 55 years. Assessment of the total risk of cardiovascular complications was carried out according to the SCORE scale. The median point values of the SCORE scale showed no significant differences between the groups of patients. In the main group it was 1.68 [1,25; 3,52] vs 1,38 [0,86; 2,66] in the control group (p>0.05). Patients of both groups were comparable in cardiovascular risk.

Results. The median time index of the SBP in the group of patients with the stage II HT was 73 [65; 81], and it was 73 [72; 76] in the control group. It had a significant difference in comparison with the group of healthy individuals, 31 [30; 33] (p<0.05). A significant increase of the time index of the DBP in the groups of patients in comparison with practically healthy persons was 2.3 times.

In the group of patients with the stage II hypertension PWV 9.8 [9.2; 9.9] m/s was significantly higher than in the group of healthy individuals 7.6 [7.2; 7.9] m/s (p<0.05). On the base of that PWV, no significant difference between the control group and the group of healthy individuals was revealed (p>0.05).

In statistical processing of the obtained data, we revealed a significant (2.8 times) increase of Aix on the shoulder in the control group in comparison with practically healthy individuals. Increase of this indicator in the main group of patients was by 3.7 times if compared with the group of healthy individuals. High values of Aix in the aorta were registered in the main group (25.8% [12.5; 29.8]). It showed a significant difference with the control group – 9.5% [–10.5; 28.7] (p<0.05).

Using the correlation analysis, we revealed interrelations between the indicators of remodeling of arterial blood vessels of elastic and muscular type and the indices of daily monitoring of BP in patients with essential hypertension. We found a positive correlation between the time index of DBP and IMT (R=+0.29, p=0.001), and negative correlation between daily index of DBP and PWV (R=–0.25, p=0.01).

Keywords: hypertension, vascular stiffness, daily monitoring of blood pressure, thickness of the intima-media complex.

─────────────────── **Резюме** ───────────────────

Цель исследования: выявить особенности индексов суточного мониторирования АД и оценить показатели жесткости сосудов с помощью современного суточного монитора АД у мужчин с гипертонической болезнью I и II стадии.

Материалы и методы. Результаты исследования основываются на комплексном обследовании 105 мужчин с гипертонической болезнью (ГБ) I и II стадии заболевания в возрасте от 35 до 55 лет. Оценку суммарного риска сердечно-сосудистых осложнений проводили по шкале SCORE. Медианы значений баллов по шкале SCORE не имели достоверных отличий между группами пациентов и составили в основной группе 1,68 [1,25; 3,52] против 1,38 [0,86; 2,66] в контрольной группе (p>0,05). Таким образом, пациенты обеих групп были сопоставимы по кардиоваскулярному риску.

Результаты. Медиана индекса времени САД в группе пациентов с ГБ II стадии составила 73 [65; 81] и 73 [72; 76] в контрольной группе и имела достоверную разницу по сравнению с группой здоровых лиц 31 [30; 33] (p<0,05). Достоверное увеличение индекса времени САД в группах пациентов по сравнению с практически здоровыми лицами было 2,3 раза.

В группе пациентов с ГБ II стадии СРПВ 9,8 м/с [9,2; 9,9] была достоверно выше, чем в группе здоровых лиц, – 7,6 м/с [7,2; 7,9] (p<0,05). При этом в СРПВ между контрольной группой и группой практически здоровых лиц не было обнаружено достоверной разницы (p>0,05).

При статистической обработке полученных данных было выявлено достоверное увеличение Aix на плече в контрольной группе пациентов по сравнению с практически здоровыми лицами в 2,8 раза. Тогда как увеличение значения данного показателя в основной группе пациентов было в 3,7 раза по сравнению с группой практически здоровых лиц. Сравнивая Aix на аорте между основной группой 25,8% [12,5; 29,8] и практически здоровыми мужчинами 0,4% [0,2; 24,4], была установлена достоверная разница (p<0,05).

С помощью корреляционного анализа выявляли взаимосвязь между показателями ремоделирования артериальных сосудов эластического и мышечного типа и индексами суточного мониторирования АД у пациентов с гипертонической болезнью. Была обнаружена положительная взаимосвязь между индексом времени ДАД и ТКИМ (R=+0,29, p=0,001) и отрицательная взаимосвязь между суточным индексом ДАД и СРПВ (R=−0,25, p=0,01).

Ключевые слова: артериальная гипертензия, жесткость сосудов, суточное мониторирование артериального давления, толщина комплекса интима-медиа.

■ INTRODUCTION

To date, the cardiovascular diseases remain the key health and social problem, since they lead to the invalidity and mortality of active working age population worldwide. Hypertension (HT) is one of the most urgent problems that cause major cardiovascular complications. Hypertension morbidity range in general population is very high and is increasing with patients age [1, 2].

Currently, the management of patients with HT is regulated by the recommendations developed on the basis of leading European and American consensus. However, in spite of well-developed recommendations, the problem of study of impact of various factors on the development of unfavorable course of cardiovascular diseases, especially in patients under the supervision of general practitioners – family medicine still remains an actual one [3].

Therefore, the task of seeking new ways to solve this problem in the presence of available approaches tends to be more urgent. In recent years, several studies have shown that the arterial bed stiffness can be deemed an independent predictor of such cardiovascular events as stroke, dementia and acute myocardial infarction. The basis of the morphological substrate of increasing the stiffness of the aorta-arterial link in hypertension is a remodeling of the arteries. The most studied among the indicators reflecting the stiffness of the vascular wall is the propagation pulse wave velocity (PWV) [4].

The importance of the early recognition of cardiovascular risk encourages researchers to seek new opportunities to obtain information on the formation of cardiovascular pathology as early as at the preclinical stage. Modern devices for the daily monitoring of blood pressure constitute non-invasive highly informative systems that allow to assess the condition of the cardiovascular system as well as to determine central aortic pressures and arterial vessels stiffness. According to the recommendations of the European Society of Cardiology, the oscillometric method is the Gold Standard for noninvasive measurement of central blood pressure [5].

The introduction of modern non-invasive equipment into clinical practice is one of directions of scientific search. This study is intended to assess possibilities of the modern system of daily monitoring of blood pressure with registration of arterial vessels stiffness indicators.

■ OBJECTIVES

Is to identify particularities of indices of blood pressure daily monitoring and to evaluate indicators of the arterial vessels stiffness using a modern daily monitor of blood pressure in male patients with stage I and II hypertension.

■ MATERIALS AND METHODS

The results of the study are based on comprehensive examination of 105 male patients with stage I and II hypertension at the age from 35 to 55 years old. Prior to the study, all trial subjects had to sign a form of voluntary informed consent for participation in the study. Verification of the diagnosis of HT was performed according to the recommendations of the European Society of Cardiology (2013) after preclusion/exclusion of symptomatic hypertension.

The criteria for inclusion in the study: patients with HT. These patients were asked to complete a written informed consent to participate in the study, age from 35 to 55 years old, male.

The criteria for exclusion from the study: HT stage III, grade 3 hypertension, secondary hypertension, ischemic heart disease, hemodynamically significant congenital and acquired heart disease, cardiomyopathy, chronic obstructive pulmonary disease and bronchial asthma, atrial fibrillation and atrial flutter, ventricular fibrillation, ejection fraction of left ventricle less than 45%, oncologic disease 6 months before the study entry, atrioventricular block of II–III degree, the blockade of the left bundle branch block, diabetes mellitus, body mass index above 30 kg/m^2.

After ascertainment of patients' correspondence to the criteria for inclusion in/exclusion from the studies were divided them into groups

depending on the HT stage. All examined individuals were matched for age and social status as follows:

- the first group included 70 patients with stage II hypertension (median age was 44 [40; 47] years old);
- the second group included 55 patients with stage I HT (median age was 45 [42; 46] years old);
- the third group consisted of practically healthy persons – 31 people (median age was 41 [38; 45] years old).

The estimation of the total risk of cardiovascular complications was carried out according to the SCORE scale. The median point values of the SCORE scale showed no significant differences between the groups of patients and made up in the main group of 1.68 [1,25; 3,52] vs 1,38 [0,86; 2,66] in the control group (p>0.05), thus, patients of both groups were matched for cardiovascular risk.

Research methods

All patients were examined for eligibility for inclusion/exclusion. All patients underwent laboratory and instrumental investigations according to the Order No. 384 of the Ministry of Health of Ukraine of 24.05.2012.

Daily blood pressure monitoring (DBPM) was performed using the "BAT41-2" modern complex (Ukraine). We recorded the data on the recorder for subsequent processing and printing of results in tabular and graphical reports. Monitoring was carried out for 24 hours according to the Standard Protocol with 15-minute intervals in the daytime and 30-minute intervals at night [6].

The study the intima-media thickness (IMT) of carotid arteries was performed using Siemens X-700 (Germany) ultrasonic device. Measurement of IMT was performed according to the requirements of the consensus [1].

The determination of the propagation pulse wave velocity was also performed using "BAT41-2" apparatus (Ukraine). To conduct the contour and velocity analysis of the pulse wave the software "ARIADA+" was used, with which we calculated basic indicators of central aortic pressures and arterial vessels stiffness [7].

Statistical processing of the obtained results

The data obtained are represented as the median and range quartile Me [Q25; Q75]. The results of the research were processed using methods of parametric or nonparametric statistics depending on the nature of the sample distribution with the help of special computer applications ApacheOpenOffice (version 4.1) and PSPP (version 0.10.2, GNU Project, 1998–2016). When comparing more than two independent variables we used analysis of variance (One-way ANOVA), followed by the use of a posteriori tests. Equality of variances was checked using Levene's test. At the equality of variances in the studied groups, the Scheff criterion was applied, and in the absence of equality of variances, the Tukey's test was applied. In the case when data distribution was different from the normal one we used the analogy of analysis of variance using Kruskal – Wallis method followed by post-hoc analysis using the Dana criterion [8].

The results obtained

Demographic characteristics of the examined individuals is shown in Table 1.

The median age in the main group of patients was 44 [40; 47] years old, in the control group – 45 [42; 46] years old and in the group healthy individuals – 41 [38; 45] years old (p>0.05), there were no significant differences between the age groups. When analyzing the body mass index (BMI), we identified significant differences between groups of healthy individuals and groups of patients, at that this value in the group of healthy individuals made 23.2 kg/m^2 [23,0; 24,1] vs 25.9 kg/m^2 per [24,1; 27,2] in the control group (p<0.05). Based on BMI, the groups of patients were comparable to those in patients of the main group, where this value made up 26.0 kg/m^2 [24,1; 27,2] vs 25.9 kg/m^2 per [24,1; 27,2] in the control group (p>0.05).

Duration of hypertension in both groups was comparable and amounted to 4 [2; 5] years (p>0.05). It is established that in the groups of HT patients, both with stage II and stage I, there was a significant increase in systolic blood pressure (SBP) as compared to healthy individuals, whereas between the groups of patients there was no significant difference based on this indicator. Indicators of diastolic blood pressure (DBP) had no significant differences between the groups of patients and made up in the main group 100.0 [94.0; 104.0] mm Hg against 98,0 [91,0; 104,0] mm Hg in the control group (p>0.05). Values of heart rate (HR) in all groups of the examined persons had no significant differences (p>0.05).

We further determined indices of daily BP monitoring in the examined persons. The data obtained are shown in Table 2.

The median time index of the SBP in the group of patients with stage II HT was 73 [65; 81] and 73 [72; 76] in the control group and had a significant difference as compared with group of healthy individuals 31 [30; 33] (p<0.05). A significant increase in the time index of the DBP in the groups

Table 1
Demographic characteristics of the groups at screening (Me [Q$_{25}$; Q$_{75}$], n=156)

Variable	HT stage II Main group (n=70)	HT stage I Control group (n=55)	Healthy individuals (n=31)
	1	2	3
Median age, years	44 [40; 47]	45 [42; 46]	41 [38; 45]
P-value	p=0,39		
BMI, kg/m^2	26,0 [24,1; 27,2]	25,9 [24,1; 27,2]	23,2 [23,0; 24,1]
P-value	p$_{1-2}$=1,0	p$_{2-3}$=0,01	p$_{1-3}$=0,01
Duration of hypertension, years	4 [2; 5]	4 [2; 5]	–
P-value	p$_{1-2}$=0,93		
SBP, mm Hg	160 [145; 163]	151 [145; 165]	125 [120; 130]
P-value	p$_{1-2}$=0,92	p$_{2-3}$=0,01	p$_{1-3}$=0,01
DBP, mm Hg	100 [94; 104]	98 [91; 104]	80 [80; 85]
P-value	p$_{1-2}$=1,0	p$_{2-3}$=0,01	p$_{1-3}$=0,01
HR, beats per minute	66 [65; 71]	66 [65; 71]	68 [65; 71]
P-value	p=0,74		

Table 2
Indices of daily BP monitoring of patients with hypertension (Me [Q_{25}; Q_{75}], n=156)

Variable	HT stage II Main group (n=70)	HT stage I Control group (n=55)	Healthy individuals (n=31)
Time index of the SBP	73 [65; 81]	73 [72; 76]	31 [30; 33]
P-value	p_{1-2}=1,0	p_{2-3}=0,001	p_{1-3}=0,001
Time index of the DBP	74 [64; 87]	71 [65; 76]	28 [22; 30]
P-value	p_{1-2}=1,0	p_{2-3}=0,001	p_{1-3}=0,001
Daily index of SBP, %	13 [10; 15]	12 [10; 14]	8 [7; 9]
P-value	p_{1-2}=1,0	p_{2-3}=0,001	p_{1-3}=0,001
Daily index of DBP, %	18 [16; 20]	20 [18; 21]	7 [6; 8]
P-value	p_{1-2}=0,07	p_{2-3}=0,001	p_{1-3}=0,001

of patients as compared with practically healthy persons making 2.3 times was revealed.

The highest time index of DBP was revealed in the main group making 74 [64; 87] having no significant difference with the value 71 [65; 76] in the control group (p>0.05). When comparing the values of the group of patients of the main group with the group of healthy individuals we revealed a significant increase of this index by 2.6 times (p<0.05).

High values of the daily index of SBP were recorded in the main group – 13% [10; 15] and control groups – 12% [10; 14] and had a significant difference as compared with the group of healthy individuals – 8% [7; 9] (p<0.05). The main group of patients showed the reliable increase in the value of the daily index of DBP by 62.5% as compared to healthy persons, and the increase in that value by 50% (p<0.05) in the control group as compared to practically healthy individuals.

When analyzing daily index of DBP we recorded the highest rates in the control group making 20% [18; 21] and the main group making 18% [16; 20] and revealed a significant difference with the group of healthy individuals (p<0.05). When comparing the daily index of DBP between the control group making 20% [18; 21] and the group of healthy individuals making 7% [6; 8] we identified a statistically significant difference (p<0.05). Increasing in the value of the daily index of DBP was reliable both in the main group of patients as compared to the group of healthy individuals that made 2.6 times, and of to the control group as compared to healthy individuals that made 2.5 times (p<0.05).

We determined indicators for the remodeling of arterial vessels of elastic and muscular type in the examined patients. The data obtained are shown in Table 3.

The highest IMT value was significantly revealed in the main group 1.0 [0.9; 1.1] mm, both against the value of 0.9 [08; 0.9] mm in the control group (p<0.05) and the values 0.7 [0.6; 0.7] mm in the group healthy individuals (p<0.05).

In the group of patients with stage II hypertension PWV 9.8 [9.2; 9.9] m/s was significantly higher than in the group of healthy individuals 7.6 [7.2; 7,9] m/s (p<0.05). Based on that PWV, no significant difference between the control group and the group of healthy individuals was revealed (p > 0.05).

Table 3
Indicators of remodeling of arterial blood vessels of elastic and muscular type in patients with hypertensive disease (Me [Q25; Q75], n=156)

Variable	HT stage II Main group (n=70)	HT stage I Control group (n=55)	Healthy individuals (n=31)
IMT, mm	1,0 [0,9; 1,1]	0,9 [0,8; 0,9]	0,7 [0,6; 0,7]
P-value	p_{1-2}=0,002	p_{2-3}=0,001	p_{1-3}=0,001
PWV, m/s	9,8 [9,2; 9,9]	7,7 [6,6; 8,6]	7,6 [7,2; 7,9]
P-value	p_{1-2}=0,001	p_{2-3}=1,0	p_{1-3}=0,001
SAI, %	49,4 [45,5; 52,8]	52,7 [37,2; 54,7]	51,4 [44,6; 52,5]
P-value	p=0,55		
Aix shoulder, %	−23,3 [−49,4; −14,8]	−66,7 [−86,7; −15,8]	−86,6 [−95,8; −55,9]
P-value	p_{1-2}=0,001	p_{2-3}=1,0	p_{1-3}=0,002
Aix aorta, %	25,8 [12,5; 29,8]	−9,5 [−10,5; 28,7]	0,4 [0,2; 24,4]
P-value	p_{1-2}=0,001	p_{2-3}=0,20	p_{1-3}=0,01

While assessing the value of SAI, we revealed no significant difference in all three groups.

When calculating Aix on the shoulder, we have identified a significant difference in the patients of the main group −23.3% [−49.4; −14.8] against the value of −66.7% [−86.7; −15.8] of the control group (p<0.05), and values −66.7% [−86.7; −15.8] in the patients of the control group against the value of −86.6% [−95.8; −55.9] of the group of healthy individuals (p<0.05). At the statistical processing of the obtained data we revealed a significant 2.8 times − increase in Aix on the shoulder of the control group in comparison with practically healthy individuals. Whereas, increase in the value of this indicator in the main group of patients made 3.7 times as compared with the group of healthy individuals.

High values of Aix in the aorta were recorded in the main group made 25.8% [12.5; 29.8] and showed a significant difference with the control group −9.5% [−10.5; 28.7] (p<0.05). Comparing these indicators between the control group −9.5% [−10.5; 28.7] and the group of healthy individuals 0.4% [0.2; 24.4], we revealed no significant difference between the indicators (p>0.05). Comparing Aix on the aorta between the main group making 25.8% [12.5; 29.8] and practically healthy men making 0.4% [0.2; 24.4] we revealed a statistically significant difference (p<0.05).

Using the correlation analysis we revealed interrelations between indicators of remodeling of arterial blood vessels of elastic and muscular type and indices of daily monitoring of BP in patients with essential hypertension. We found a positive correlation between the time index of DBP, and IMT (R=+0.29, p=0.001) and negative correlation between daily index of DBP and PWV (R=−0.25, p=0.01).

■ RESULTS AND DISCUSSION

In accordance with the consensus of experts of the European Society for the study of hypertension (ESH, 2013) "At present, DBPM is a mandatory technique in the detection and treatment of hypertension." Daily monitoring

enables us to track changes in blood pressure during a specified period of time, and can be a valuable tool to predict the development of cardiovascular complications [1, 9].

The scientists are working upon further development of improved equipment for monitoring blood pressure, as well as methods of data analysis that opens up new diagnostic and prognostic capabilities in the treatment of patients with hypertension. With more extensive data obtained through ABPM, the doctor will be able to administer a more informed therapy tailored to the individual hemodynamic characteristics of the patient and to assess the adequacy of the treatment provided [10].

Fluctuations of DBP have a direct damaging effect on the target organs and has a higher predictive value than a single measurement of blood pressure. The possibility of simultaneous monitoring of blood pressure rate and measurement of the arterial vessels stiffness opens new opportunities to study these fluctuations while making prognosis of hypertension progress [11].

Thus, the use of a non-invasive highly informative system will enable a general practitioner on an outpatient basis to easily and conveniently monitor the changes in central hemodynamics in conditions of patient's everyday life. This will allow to select the required dose and time of hypotensive medication intake using a patient-tailored approach. Furthermore, the application of the device that we used in our study enables to calculate all the studied parameters based on standardized algorithms and protocols.

■ CONCLUSIONS
1. Indices of daily monitoring of BP between patients with essential stage I and stage II hypertension showed no significant difference.
2. The highest IMT value was significantly found in the group of patients with stage II essential hypertension.
3. In the group of patients with stage II essential hypertension, PWV was significantly higher than in patients with I stage hypertension.

■ PROSPECTS FOR FURTHER RESEARCH
Hemodynamic heterogeneity of patients with HT can be used to select drug therapy. In addition, the issue of the predictor value of indicators of arterial vessels stiffness for forecasting the development of cardiovascular complications in this category of patients requires additional focusing.

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