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DAILY BLOOD PRESSURE PROFILE AND HEART RATE VARIABILITY IN PATIENTS WITH ESSENTIAL HYPERTENSION

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This article presents the results of a study investigating changes in the daily blood pressure profile and heart rate variability in patients with stage II hypertension. The daily blood pressure profile was studied utilizing data acquired from daily blood pressure monitoring. Furthermore, heart rate variability, as an indicator of autonomic nervous system status, was investigated through the analysis of 5-minute cardiogram recordings. The study revealed that, in most patients with stage II hypertension, a disturbance exists in the daily blood pressure profile, characterized by either insufficient or excessive nocturnal reduction in blood pressure or, conversely, an elevation in nocturnal blood pressure. There was a tendency toward more frequent detection of nocturnal elevation of systolic blood pressure and excessive reduction of diastolic blood pressure in the subgroup of patients with stage 3 hypertension. In the presence of concomitant ischemic heart disease, daytime and nighttime diastolic blood pressure levels exceeded the corresponding indicators in patients with isolated hypertension. When assessing autonomic nervous regulation in patients with stage II hypertension, significant changes in its indicators were found relative to the control group, without a significant difference depending on the degree of hypertension, with the exception of a decrease in the standard deviation of the R-R interval and an increase in the LF/HF ratio in patients with stage III hypertension, which indicated an increase in the influence of the sympathetic branch of autonomic regulation. Thus, patients with stage II hypertension show an increase in the tone of the sympathetic branch of the autonomic nervous system, as evidenced by an increase in the proportion of pathological blood pressure profiles and changes in heart rate variability indicators.

Key words: hypertension, blood pressure variability, daily blood pressure profile, heart rate variability, autonomic nervous system status, sympathovagal index, sympatho-parasympathetic ratio.

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ДОБОВИЙ ПРОФІЛЬ АРТЕРІАЛЬНОГО ТИСКУ ТА ВАРІАБЕЛЬНІСТЬ СЕРЦЕВОГО РИТМУ У ХВОРИХ НА ГІПЕРТОНІЧНУ ХВОРОБУ

В статті відображені результати дослідження особливостей змін добового профілю артеріального тиску та варіабельності серцевого ритму у хворих на гіпертонічну хворобу II стадії. Добовий профіль артеріального тиску вивчали за допомогою даних добового моніторингу артеріального тиску, а варіабельність серцевого ритму як показник стану автономної нервової системи – на підставі аналізу 5-хвилинних записів кардіоінтервалограми. Встановлено, що у більшості хворих на гіпертонічну хворобу II стадії спостерігається порушення добового профілю артеріального тиску, що характеризується недостатнім чи надмірним зниженням артеріального тиску вночі або навпаки його нічним підвищенням. Спостерігалась тенденція до більш частого виявлення нічного підвищення систолічного і надмірного зниження діастолічного артеріального тиску у підгрупі хворих з 3-м ступенем гіпертензії. При наявності супутньої ішемічної хвороби серця рівні денного і нічного діастолічного артеріального тиску перевищували відповідні показники хворих з ізольованою гіпертензією. При оцінці автономної нервової регуляції у пацієнтів з гіпертонічною хворобою II стадії виявлені істотні зміни її показників відносно контрольної групи без суттєвої їх різниці залежно від ступеня гіпертензії за виключенням зменшення величини стандартного відхилення інтервалу R-R і зростання коефіцієнта LF/HF у хворих з третім ступенем гіпертензії, що свідчило про підвищення впливу симпатичної ланки вегетативної регуляції. Отже, у пацієнтів з гіпертонічною хворобою II стадії спостерігається підвищення тону симпатичної ланки автономної нервової системи, свідченням чого є зростання частки патологічних профілів артеріального тиску і зміни показників варіабельності серцевого ритму.

Ключові слова: гіпертонічна хвороба, варіабельність артеріального тиску, добовий профіль артеріального тиску, варіабельність серцевого ритму, стан автономної нервової системи, симпатовагальний індекс, симпто-парасимпатичне співвідношення.

The study is a fragment of the research project "Cardiovascular remodeling, structural and functional state of the liver and kidneys and their relationship with cardiometabolic risk factors in patients with cardiac pathology and comorbidities. Possibilities for optimizing treatment", state registration No. 0124U002036.

Arterial hypertension (AH) is not only a pathological condition of the body manifested by a persistent increase in blood pressure but also the most common cause of complications such as myocardial infarction, stroke, and chronic heart failure, making this pathology one of the most pressing health problems worldwide [4, 12]. According to WHO data, one in four men and one in five women worldwide suffer from hypertension, totaling more than one billion people. The proportion of the Ukrainian population with high blood pressure increases sharply with age: from 12.7 % in the 18–29 age group to 71.1 % in the 60–69 age group [1].

The neurohumoral regulation system, together with hormonal and metabolic factors, determines the course of adaptive cardiac and hemodynamic reactions involved in maintaining blood circulation homeostasis and controlling blood pressure (BP) [14]. Despite numerous data on the pathogenetic mechanisms of arterial hypertension (AH) and theories of the onset of hypertensive disease (HD), the question of choosing methods for adequate assessment of the state of neurohumoral regulation of BP and heart rhythm in patients with HN and their impact on the course and severity of the disease in such patients remains unresolved.

The purpose of the study was to evaluate the characteristics of changes in the daily profile of blood pressure and heart rate variability in patients with stage II hypertensive disease.

Materials and methods. The patients included in the study sought consultative assistance and signed an informed consent form to participate. The study was conducted based on the Clinical Hospitals No. 1 and No. 2 in the period from 2016 to 2023

A total of 231 patients with stage II hypertension (105 men and 126 women, with an average age of 52.3 ± 1.2 years) and 30 practically healthy individuals from the control group, matched for age and gender, without a family history of hypertension, were examined. The average duration of hypertension in patients was 9.7 ± 0.45 years. In 121 of 231 patients, concomitant stable ischemic heart disease (IHD) was diagnosed – exertional angina pectoris of functional class (FC) II-III. The average duration of IHD was 4.21 ± 1.6 years.

The diagnosis of hypertension was established after a detailed clinical and instrumental examination in a hospital setting using additional examination methods, which allowed to exclude the secondary nature of hypertension, in accordance with guideline 00069 “Hypertension: examination and initial treatment” dated 07.03.2017, Order of the Ministry of Health of Ukraine No. 384 “On the Approval and Implementation of Medical and Technological Documents for the Standardization of Medical Care for Arterial Hypertension” dated May 24, 2012, and the clinical recommendations of the European Society of Hypertension (2023). IHD and exertional angina were verified using a bicycle ergometer test and daily ECG monitoring.

The study did not include patients with stage I and III hypertension, severe cardiac arrhythmias and conduction disorders, kidney or liver disease with impaired function, diabetes mellitus, grade III obesity, heart defects, or severe chronic heart failure (stage II-B–III according to the classification of M.D. Strazhesko and V.H. Vasilenko), chronic respiratory diseases, and respiratory failure. After examination, patients with established symptomatic hypertension were excluded.

Daily blood pressure monitoring (DBP) was performed using ABPM-04 (Meditech, Hungary). The intervals between measurements were 15 minutes from 7:00 a.m. to 10:00 p.m. and 30 minutes at night from 10:00 p.m. to 7:00 a.m. The indicators studied included: mean daily systolic blood pressure (SBP/day), mean daily diastolic blood pressure (DBP/day), systolic and diastolic blood pressure elevation time index (SBP TI, DBP TI) – pressure load, % of measurements from the total number at which BP values exceed “normal” values (during the day – 140/90 mm Hg, at night – 120/80 mm Hg, respectively), daily BP indices (DI SBP, DI DBP), variability of systolic and diastolic BP per day (VBP SBP, VBP DBP), respectively, morning rise rate (MRR SBP, MRR DBP) from 5 to 10 a.m., which was determined as the difference between the maximum and minimum values. Analysis of ABPM indicators was performed according to the recommendations of the European Society of Cardiology [11].

Heart rate variability (HRV) as an indicator of the state of the autonomic nervous system (ANS) was studied based on the analysis of 5-minute recordings of the cardiointervalogram in a relaxed state of wakefulness in a horizontal position and with free breathing after 15 minutes of adaptation. HRV was recorded using a “Cardiolab 2000” computer electrocardiograph. Neurohumoral regulation was assessed by temporal and spectral analysis of HRV, according to the recommendations of the Expert Committee of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [3]. The following indicators were studied: 1. temporal – standard deviations of the mean R-R intervals (SDNN), square root of the mean square of the differences between consecutive R-R intervals (RMSSD), frequency of consecutive R-R intervals with a difference exceeding 50 ms (pNN50%); 2. spectral – total power spectrum (TP) and its components in the very low frequency (0.003-0.05 Hz) VLF, ms^2 , low (0.05–0.15 Hz) – LF, and high frequencies (0.15–0.4 Hz) – HF, reflecting humoral, sympathetic, and parasympathetic regulation, respectively, as well as the ratio of sympathetic to parasympathetic influence – LF/HF, units. When evaluating the data, the norms of the specified HRV indicators were used in accordance with the recommendations of the working group of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [3], which were refined in a control group of healthy individuals.

The statistical processing of the results obtained was carried out using parametric and nonparametric statistical methods with the use of Microsoft Excel and Statistica for Windows 10.0 software packages. The results of the study are presented as the median and interquartile range Med (kvar_t_1;kvar_t_3), where Med is the median, and kvar_t_1 – kvar_t_3 are the 1st and 3rd quartiles and percentiles, respectively. Discrete values (%) between groups were compared using the χ^2 criterion. Sample values were compared using a nonparametric Mann-Whitney U test. Kendall's nonparametric correlation analysis was used to determine the relationship between individual parameters.

Results of the study and their discussion. It was determined that the levels of SBP and DBP in patients with stage II hypertension during the daytime significantly ($p < 0.001$) exceeded their levels during the nighttime period. Significant fluctuations in SBP and DBP levels during the day did not cause significant changes in pulse pressure (PP) during the day, the average level of which was 60.0 (54.0; 65.0) mmHg and did not differ significantly between day and night, but significantly exceeded the values in the control group ($p < 0.001$).

The variability of both SBP and DBP was slightly higher during the day. The average daily SBP variability values exceeded the DBP variability values and amounted to 16.0 (14.0; 19.0) and 13.0 (12.0; 16.0), respectively. The daily index (DI) of DBP exceeded the DI of SBP by 58.6 % ($p < 0.0001$).

Analysis of the circadian rhythm of SBP showed that a normal SBP profile (dipper) was observed in only one-third (32.9 %) of patients with stage II hypertension, while the majority of patients (41.1 %) did not have an adequate decrease in SBP at night (non-dipper), a rise in SBP at night (night-peaker) was recorded in 15.6% of patients, and an excessive decrease in SBP (over-dipper) was observed in 10.4 % of patients. Disturbances in the daily profile of diastolic BP were more pronounced. Thus, 24.2 % of patients had a normal DBP rhythm (dipper), in the vast majority of patients (45.9%) DBP remained stable throughout the day (non-dipper), 12.6 % of patients had an increase in DBP at night, and an excessive decrease in DBP at night was determined in 17.3 % of patients (Fig. 1). Thus, the detected disturbance of the daily BP profile in patients with stage II AH requires an individual approach to the prescription of antihypertensive therapy, taking into account the time of administration of antihypertensive drugs depending on their pharmacodynamics.

When comparing data from patients with stage II hypertension with varying degrees of AH, it was found that the indicators of BP variability, DI, and the daily profile of SBP and DBP did not differ significantly in these subgroups, however, there was a tendency toward more frequent detection of nocturnal SBP elevation (up to 19.4 %) and excessive DBP reduction (up to 22.6 %) in the subgroup of patients with grade 3 AH.

Analysis of ABPM indicators in patients with stage II hypertension, depending on the presence of IHD, showed that the addition of IHD to hypertension did not significantly affect the level of SBP during the day, while the levels of daytime and nighttime DBP in patients with IHD exceeded the indicators in the group with isolated hypertension. Thus, the level of daily DBP in the presence of IHD was 91.0 (85.0; 97.0) mmHg compared to 87.0 (82.0; 92.0) mmHg in patients with GH without IHD ($p = 0.032$). The identified features led to the fact that the level of daily SBP in patients with stage II GH without IHD was 3.4 % ($p = 0.038$) higher than in the group with IHD. The variability and SD of SBP and DBP during the day in patients with AH and IHD exceeded ($p > 0.05$) the similar indicators in the group without IHD. A direct correlation was found between daily SBP variability and the presence of IHD ($r = 0.31$, $p = 0.017$) in patients with AH. Analysis of the daily BP profile did not reveal significant differences between the frequency of detection of different types of BP in groups with stage II AH depending on the presence of concomitant IHD (Fig. 2).

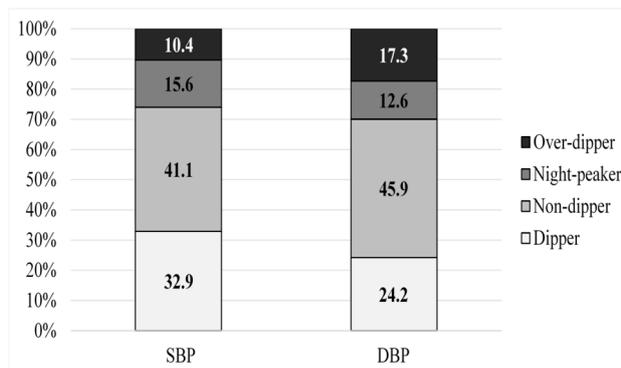


Fig. 1. Analysis of the daily BP profile in patients with AH depending on the stage of the disease.

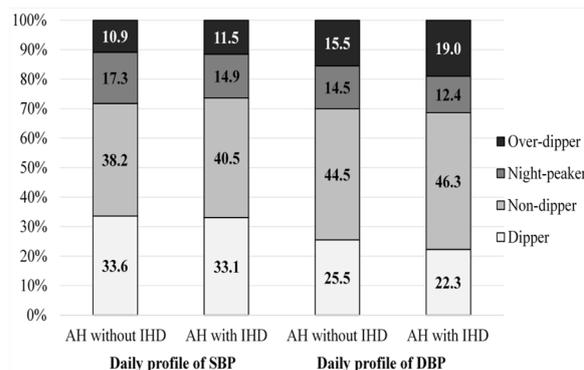


Fig. 2. Analysis of the daily BP profile in patients with stage II AH depending on the presence of IHD.

The increase in FC of stable angina pectoris did not have a significant effect on ABPM parameters in patients with combined hypertension and IHD, but a direct correlation was found between daily SBP variability and FC of angina pectoris ($r=0.31$, at $p=0.017$).

When assessing autonomic nervous regulation in patients with stage II hypertension, disturbances were found, as evidenced by a significant change in HRV indicators compared to the control group (Table 1).

Table 1

Heart rate variability indicators in the examined individuals

Indicator	Control group (n=30)	Patients with stage II IHD (n=231)
SDNN, ms	153 (110; 165)	97* (48; 120)
RMSSD, ms	37.4 (26.5; 40.0)	36 (22; 88)
pNN50, %	21.4 (19.4; 25.7)	13* (9; 29)
TP, ms ²	3197 (2900; 3760)	2961 (2370; 3560)
VLF, ms ²	1299 (975; 1390)	1386* (1014; 2006)
LF, ms ²	1123 (750; 1860)	1114 (669; 2036)
HF, ms ²	774 (658; 912)	461* (396; 971)
LF/HF, units	1.45 (0.9; 1.6)	2.11* (1.0; 2.51)

Note: * – significance of differences in indicators relative to the control group ($p<0.05$).

At the same time, HRV indicators in patients with CH did not differ significantly depending on the severity of AH ($p>0.05$), with the exception of a decrease in the standard deviation of the R-R interval and an increase in the LF/HF ratio in patients with grade 3 AH ($p<0.05$), which indicated an increase in the influence of the sympathetic link of vegetative regulation.

Since IHD may be accompanied by autonomic regulation disorders, we conducted a comparative analysis of HRV changes in patients with AH depending on the presence or absence of stable angina and its severity (Table 2).

Table 2

Heart rate variability indicators in patients with stage II hypertension depending on the presence of IHD and its severity

Indicator	Stage II AH without IHD (n=110)	Stage II AH with IHD (n=121)	P ₁₋₂	Stage II AH with IHD (n=121)		P ₃₋₄
				Stable angina pectoris FC II (n=41)	Stable angina pectoris FC III (n=80)	
				3	4	
SDNN, ms	103 (68; 132)	81 (42; 104)	<0.05	99 (57; 121)	67 (43; 98)	<0.05
RMSSD, ms	47 (33; 110)	32* (21; 74)	<0.05	88* (45; 175)	47* (28; 96)	<0.01
pNN50, %	12* (9; 27)	15 * (8; 32)	ns	16* (12; 47)	13* (8; 29)	<0.05
TP, ms ²	3109 (2175; 3680)	3166 (2100; 3800)	ns	3017 (2025; 3750)	3159 (2060; 3900)	ns
VLF, ms ²	1403 (1102; 2276)	1341 (790; 2387)	ns	1298 (490; 2306)	1504 (490; 2743)	ns
LF, ms ²	1018 (649; 1926)	1375 (995; 3217)	<0.01	1051 (513; 2158)	1100 (595; 2391)	ns
HF, ms ²	688 (494; 1276)	450 (226; 916)	<0.05	668 (403; 1286)	555 (321; 1088)	<0.05
LF/HF, units	1.49 (0.90; 2.17)	2.99 (1.56; 3.46)	<0.01	1.57 (0.96; 2.51)	1.98 (1.34; 2.87)	<0.05

Notes: * – significance of differences in indicators relative to the control group ($p<0.05$); P₁₋₂, P₃₋₄ – significance of differences between different groups of patients with AH; ns – no significant difference ($p>0.05$).

As can be seen from the table, the addition of IHD is accompanied by a greater degree of reduction in total HRV, a more significant reduction in parasympathetic activity, characterized by a decrease in RMSSD and HF with higher sympathetic activity (a significant increase in LF compared to the control group). The LF/HF index, which characterizes the sympatho-parasympathetic ratio, increased in patients with hypertension combined with IHD due to both a decrease in vagal activity and an increase in sympathetic nervous system activity.

The presence of unequal directionality of HRV changes depending on the FC of angina pectoris is of particular interest. It was noted that the increase in the severity of IHD, characterized by an increase in the FC of stable angina, was accompanied by more significant changes in the overall HRV, a decrease in all temporal and spectral indicators of vagal activity (RMSSD, pNN50%, HF). At the same time, the degree

of changes in LF and VLF was approximately the same. Thus, the onset of IHD and its progression are accompanied by prognostically unfavorable changes in autonomic regulation: a decrease in overall variability and a decrease in the activity of the parasympathetic nervous system.

Analysis of HRV indicators in patients with different daily BP profiles showed that more pronounced changes in overall variability occurred in patients with a non-dipper daily profile. In this group of patients, SDNN was 73 (45; 95) ms, which was significantly lower compared to the dipper type ($p=0.033$), night-peaker ($p=0.006$) and tended to be significant ($p=0.08$) when compared to the group of patients with the over-dipper type. The decrease in SDNN was also accompanied by a decrease in HF to 461 (380; 932) ms^2 , which was also significantly different when compared with patients with a dipper ($p<0.05$), night-peaker ($p<0.05$), and over-dipper ($p<0.05$) daily profile. The same pattern was found for the LF/HF ratio, which in the group of patients with the non-dipper type was increased to 2.11 (1.56; 2.57) units and differed significantly from patients with other types of daily BP profiles: dipper, night-peaker, and over-dipper ($p=0.003$; $p=0.021$ and $p=0.037$, respectively). The identified disorders indicate relative hypersympathicotonia in patients with a non-dipper daily profile. It should be noted that in the group with an over-dipper daily profile, a significant increase in RMSSD was observed compared to patients with non-dipper and night-peaker types ($p=0.044$ and $p=0.039$, respectively), as well as in relation to the RMSSD indicator in the dipper group ($p=0.09$). Perhaps the relative increase in parasympathetic activity compared to sympathetic activity leads to an excessive decrease in blood pressure during the night.

When comparing HRV indicators with ABPM parameters, a negative correlation was found between the degree of nighttime BP reduction and indicators characterizing hypersympathicotonia – the LF/HF ratio ($r=-0.57$ for the degree of nighttime SBP reduction and $r=-0.55$ for the degree of nighttime DBP reduction, $p<0.01$) and the LF index ($r=-0.37$ for the degree of nighttime SBP reduction and $r=-0.34$ for DBP, $p<0.05$), and a direct relationship between daily BP variability and the criterion for hypersympathicotonia – the LF/HF ratio ($r=0.59$ for SBP variability and $r=0.53$ for DBP variability, $p<0.01$). A positive but less close relationship was also found between decreased parasympathetic tone (RMSSD), on the one hand, and SBP variability ($r=0.34$, $p<0.05$) and the degree of nocturnal reduction in SBP ($r=0.39$, $p<0.05$) and DBP ($r=0.37$, $p<0.05$). These data confirm the role of neurohumoral system discoordination in the development and progression of AH. It is known that increased activity of the sympathetic nervous system is an important factor in the development of left ventricular myocardial hypertrophy and undesirable metabolic effects, such as insulin resistance, hyperinsulinemia, hyperglycemia, and hyperlipidemia, which can worsen the prognosis of the disease and contribute to the development of severe cardiovascular complications [8, 9].

Elevated SBP and DBP levels led to a significant increase in PBP, which characterizes the pressor effect on the left ventricular myocardium and reflects the increased rigidity of large arterial vessels, which, according to the literature, may contribute to more significant damage to target organs [13]. In addition, there is currently evidence of a negative prognostic association between increased peripheral PBP and the development of IHD, chronic heart and renal failure, and an increased risk of cardiovascular and overall mortality [7, 15].

The data we obtained indicate significant changes in all temporal and frequency parameters of HRV in patients with AH compared to the control group, which were determined by the degree of AH and the presence and severity of concomitant IHD. Thus, patients with AH showed a marked decrease in indicators characterizing the tone of the parasympathetic nervous system (RMSSD and HF) with a moderate decrease in the LF indicator, which to a certain extent characterizes the tone of the sympathetic component of the ANS, i.e., relative hypersympathicotonia taking place in most patients with AH, which was reflected in an increase in the indicator of vegetative imbalance – the LF/HF sympathovagal index. The increase in the degree of AH and the disturbance of the daily profile was accompanied by a significant decrease in the total variability index (SDNN) below critical values, which are considered by researchers to be harbingers of an unfavorable prognosis, the occurrence of fatal cardiac arrhythmias, and sudden death [2, 5, 6, 10].

Thus, our data indicate that patients with stage II hypertension experience changes in autonomic nervous regulation toward hypersympathicotonia, as evidenced by an increase in the proportion of pathological blood pressure profiles and changes in heart rate variability indicators. Analysis of heart rate variability and daily blood pressure profiles in patients with hypertension will not only allow for better stratification of cardiovascular risks in patients but also enable differentiated prescription of antihypertensive drugs, including taking into account the effect on individual links of the ANS.

Conclusion

Analysis of ABPM indicators showed that patients with stage II hypertension have elevated levels of not only SBP and DBP but also PBP, and increased variability of SBP and DBP, especially during the daytime, which may contribute to target organ damage. A normal daily SBP profile was found in only 32.9 % of patients, and a normal DBP profile in 24.2 % of patients with stage II hypertension. The presence of concomitant IHD is characterized by higher DBP values throughout the day and increased SBP and DBP variability.

Patients with hypertension are characterized by a decrease in heart rate variability, a decrease in all its temporal and frequency parameters compared to the control group, a pronounced decrease in the tone of the parasympathetic nervous system with a moderate decrease in the tone of the sympathetic link, which led to the development of relative hypersympathicotonia, which was reflected in an increase in the indicator of vegetative imbalance – the LF/HF sympathovagal index.

Analysis of heart rate variability in patients with AH is a highly informative non-invasive method that is of practical importance, as it allows for assessing the tone of the ANS divisions and identifying a group of individuals at increased risk of developing serious complications.

Further research in this area will improve the effectiveness of treatment for patients with uncomplicated hypertension through individualized therapy selection to improve the prognosis for such individuals.

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Стаття надійшла 26.12.2024 р.