UDC 612.172.2:615.22:616.12

# CHARACTERISTIC OF PARAMETERS OF HEART RATE VARIABILITY IN PATIENTS WITH DIFFICULT-TO-CONTROL AND CONTROLLED ARTERIAL HYPERTENSION

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Parameters of heart rate variability (HRV) were studied in 112 patients with arterial hypertension (AH) aged  $58.5 \pm 9$  years (60 patients with difficult-to-control arterial hypertension (DTCAH) and 52 patients with controlled arterial hypertension (CAH)). The control group was consisted of 20 conditionally healthy persons of the same sex and age. It has been established that patients with AH were characterized by decrease in the level of total power of the HRV spectrum, the power of the high-frequency (HF) and low-frequency (LF) domains of the spectrum, and increase in the level of the very low-frequency spectrum (VLF) and value LF/HF that reflect sympathovagal balance. It has been established that there were more significant disorders in neurohumoral regulation in patients with DTCAH in comparison with patients with CAH, which consist of the predominant adrenergic activation, primarily due to the sympathetic link of the autonomic nervous system. HRV can be used as an effective non-invasive method for the diagnosis and control of DTCAH.

KEY WORDS: difficult-to-control arterial hypertension, heart rate variability

## ХАРАКТЕРИСТИКА ПАРАМЕТРІВ ВАРІАБЕЛЬНОСТІ СЕРЦЕВОГО РИТМУ У ХВОРИХ НА ВАЖКОКОНТРОЛЬОВАНУ ТА КОНТРОЛЬОВАНУ АРТЕРІАЛЬНУ ГІПЕРТЕНЗІЮ

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Вивчено показники варіабельності серцевого ритму (ВСР) у 112 пацієнтів з артеріальною гіпертензією (АГ) у віці  $58,5\pm9$  років (60 пацієнтів з важкоконтрольованою артеріальною гіпертензією (ВАГ) і 52 пацієнта з контрольованою артеріальною гіпертензією (КАГ)). Групу контролю склали 20 умовно здорових осіб такої ж статі і віку. Встановлено, що для пацієнтів з АГ характерно зниження рівнів загальної потужності спектра ВСР (ТР), потужності високочастотного (НГ) і низькочастотного (LF) доменів спектра при більш високих рівні потужності дуже низькочастотного спектра (VLF) і значенні LF/HF, яке відображає симпатовагальний баланс. Встановлено, що у пацієнтів з ТАГ в порівнянні з пацієнтами з КАГ спостерігаються більш суттєві порушення в нейрогуморальної регуляції, які складаються в переважній адренергічній активації, перш за все, за рахунок симпатичної ланки вегетативної нервової системи. Робиться висновок, що ВСР може використовуватися як ефективний неінвазійний метод з метою діагностики та контролю ТАГ.

*КЛЮЧОВІ СЛОВА*: важкоконтрольована артеріальна гіпертензія, варіабельність серцевого ритму

# ХАРАКТЕРИСТИКА ПАРАМЕТРОВ ВАРИАБЕЛЬНОСТИ СЕРДЕЧНОГО РИТМА У ПАЦИЕНТОВ С ТРУДНОКОНТРОЛИРУЕМОЙ И КОНТРОЛИРУЕМОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

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Изучены показатели вариабельности сердечного ритма (ВСР) у 112 пациентов с артериальной гипертензией (АГ) в возрасте  $58,5\pm9$  лет (60 пациентов с трудноконтролируемой артериальной гипертензией (ТАГ) и 52 пациента с контролируемой артериальной гипертензией (КАГ)). Группу контроля составили 20 условно здоровых лиц такого же пола и возраста. Установлено, что для пациентов с АГ характерно снижение уровней общей мощности спектра ВСР (ТР), мощности высокочастотного (НF) и низкочастотного (LF) доменов спектра при более высоких уровне мощности очень низкочастотного спектра (VLF) и значении LF/HF, которое отображает симпатовагальный

© Tymoshenko O. S., Yabluchansky M. I., Martynenko O. V., 2017 баланс. При этом установлено, что у пациентов с ТАГ в сравнении с пациентами с КАГ наблюдаются более существенные нарушения в нейрогуморальной регуляции, которые состоят в преобладающей адренергической активации, прежде всего, за счет симпатического звена вегетативной нервной системы. Делается вывод, что ВСР может использоваться как эффективный неинвазивный метод с целью диагностики и контроля ТАГ.

*КЛЮЧЕВЫЕ СЛОВА*: трудноконтролируемая артериальная гипертензия, вариабельность сердечного ритма

#### INTRODUCTION

Difficult-to-control arterial hypertension (DTCAH) is arterial hypertension in which the level of blood pressure (BP) remains above the target value despite the use of a combination of three or more antihypertensive drugs, including a diuretic, in conjunction with the lifestyle modification [1]. The prevalence of DTCAH in the population of people with arterial hypertension (AH) is from 15 to 30 % [2].

Inadequate effectiveness of pharmacotherapy of DTCAH causes the search for additional non-pharmacological inter-ventions. In particular, one of such methods is heart rate variability (HRV) [3].

HRV is a noninvasive method for the study of regulatory systems in physiological and in pathological conditions, which allows to estimate a neuro-humoral regulation and its constituent elements, its stress resistance and physiological responses to stress [4]. It is known that observed in case of AH imbalance of the autonomic and humoral regulation, may be assessed using analysis of HRV. Studies have demonstrated the decrease in values of parameters of HRV in individuals with AH compared with those with normal blood pressure [5]. However, publications devoted to the study of HRV parameters in patients with DTCAH have not been revealed.

### **OBJECTIVE**

Identify the features of the HRV parameters in patients with DTCAH in comparison with patients with controlled hypertension (CAH).

#### MATERIALS AND METHODS

On the clinical base of the Kharkov city outpatient clinic  $N_2$  24 and the State Institution «Kharkov Clinical Hospital for Railway Transport No. 1» 112 patients with AH were examined (63 men and 49 women). Average age is  $58,5 \pm 9$  years. There were 56 patients with DTCAH and 56 patients with CAH. The control group was consisted of 20 healthy persons of the same sex and age.

The inclusion criteria in the study were any stage and degree of AH. The criterion of DTCAH was the presence of a persistent increase in BP above the target level, despite the simultaneous use of three or more antihypertensive drugs of various classes in adequate therapeutic doses, including a diuretic.

Exclusion criteria were heart failure functional class IV, acute coronary syndrome, rhythm and conduction disorders, diabetes mellitus, chronic respiratory insufficiency, bronchial asthma, chronic obstructive pulmonary diseases, peptic ulcer and duodenal ulcer at the stage of exacerbation, systemic diseases of connective tissue, tumors.

Analysis of HRV was carried out on the computer diagnostic complex CardioLab 2009 («HAI-Medica», Ukraine). The study was conducted in the sitting position after 15 min rest. The computation of HRV indices was performed in real time within the 7-minute session on the background of the ECG in the first standard lead with a sampling rate of the signal at 1000 Hz. There were allocated 3 types of waves using the fast Fourier transform: slow (VLF, 0,0033–0,05 Hz), medium (LF, 0,05–0,15 Hz), fast (HF, 0,15–0,40 Hz).

The following parameters of HRV were determined in all subjects in 5-minute intervals to assess the state of regulatory systems [6]: TP - total power of the spectrum, a measure of the power of the effects of neurohumoral reactions (ms2); VLF – the absolute power of the very low-frequency spectrum is associated with thermoregulation, renin-angiotensin system and sympathetic nervous system (ms2); VLF – the relative power of very low frequency spectrum (%); LF - the absolute power of the lowfrequency spectrum is associated mainly with the sympathetic and partially parasympathetic links of regulation (ms2); LF - the relative power of low frequency spectrum (%); HF – the absolute power of the high-frequency domain of the spectrum is associated mainly with the parasympathetic regulating unit (ms2); HF - the relative power of high frequency spectrum (%);

LF/HF – measure display sympathovagal balance.

Statistical analysis was performed in the program Statistica 10. An analysis was conducted of the data for outliers (Grabs test) and compliance data the hypothesis about the normal distribution (Kolmogorov-Smirnov test): after exclusion of cases with emissions data for further calculations used the sample of 50 patients with DTCAH and 50 patients with CAH. For statistical evaluation of the results

were used parametric tests: M – mean value, sd – standard deviation. The significance of differences between groups was determined using nonparametric T-Wilcoxon test.

#### RESULTS AND DISCUSSION

Mean values of HRV parameters in patients with DTCAH and CAH are presented in Table 1.

Table 1 The parameters of HRV in patients with DTCAH and CAH ( $M \pm sd$ )

The parameters of HRV	Control group	Groups of patients	
		DTCAH	САН
TP, ms2	1635 ± 145*	$1150 \pm 493$	$1052 \pm 388$
VLF, ms2	$446 \pm 67$	414 ± 161**	537 ± 188#
VLF', %	27	36	51
LF, ms2	$710 \pm 63$	335 ± 155**	244 ± 121#
LF', %	43	29	23
HF, ms2	$386 \pm 26*$	$200 \pm 121$	150 ± 77#
HF', %	24	17	14
LF/HF	$1.8 \pm 0.2$	$2,21 \pm 0,93$	$1,95 \pm 0,89$

Notes: \*-P < 0.05 – between the control group and the group DTCAH, \*\*-P < 0.05 – between the groups of patients with DTCAH and CAH, #-P < 0.05 – between the control group and the CAH.

In patients with AH compared with healthy individuals of the control group there were changes of the regulation systems, which were manifested with low levels of TP, HF, LF, and high level of VLF and value LF/HF. Whereas there were differences within the group of persons with AH between patients with DTCAH and CAH.

At lower TP in both groups of patients with AH, in patients with DTCAH it was higher by 1.09 times than in patients with CAH. The contribution of TP in patients with DTCAH was (36 %) less than in patients with CAH (51 %). In contrast, the proportion of LF and HF in TP in patients with DTCAH (29 % and 17 %) was more than its share of patients with CAH (23 % and 14 %). The ratio VLF:LF:HF in patients with DTCAH was 2.1:1,7:1, and in patients with CAH – 3,6:1,6:1.

The value LF/HF in patients with DTCAH was higher by 1.13 times than in patients with

CAH. It indicated a more expressed imbalance of sympatho-vagal regulation in the first group.

The obtained results confirm existing ideas about the changes of HRV indexes in case of AH [7–9]. We had found that patients with DTCAH had less significant reducing in the total power spectrum of HRV than in patients with CAH, accompanied by more significant decrease in VLF and increase in LF and HF. Greater deviation of the value LF/HF was the evidence of a greater imbalance of regulatory systems and of more severe disease.

These results show a more significant violations of neurohumoral regulation in patients with DTCAH in comparison with patients with CAH, which are the predominant adrenergic activation, especially due to the sympathetic link of vegetative nervous system and explain the difficulties in achieving the target BP in this group of patients [10–11].

The data obtained should be taken into account in the conduct of the patient and the choice of therapeutic tactics.

#### **CONCLUSIONS**

- 1. Patients with AH was characterized by decrease in levels of TP, HF and LF, higher levels of VLF and the value of LF/HF.
- 2. Patients with DTCAH in comparison with patients with CAH were observed more significant abnormalities in neurohormonal regulation, which were the predominant

adrenergic activation, especially due to the sympathetic link of vegetative nervous system.

3. HRV can be used as an effective non-invasive method of diagnostics and control of DTCAH.

#### PROSPECTS FOR FUTURE STUDIES

In the future, it seems appropriate to study the dynamics of parameters of HRV in patients with the DTCAH at various stages of treatment.

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