UDC 612.172.2: 612.216: 616-07

ASSESSMENT OF CHANGES IN THE DISTRIBUTION RATIOS OF ULTRA-LOW-FREQUENCY, LOW-FREQUENCY AND HIGH-FREQUENCY COMPONENTS OF HEART RATE VARIABILITY DURING THE PACED BREATHING TEST IN PATIENTS WITH ARTERIAL HYPERTENSION

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Were studied the distribution ratios of ultra-low-frequency, low-frequency and high-frequency components of the heart rate variability (HRV) as an indicator of the state of humoral and autonomic sympathetic and parasympathetic elements in regulation of heart rate in 35 patients with arterial hypertension (AH) aged 59 ± 5 years in the paced breathing test. Evaluation of spectral parameters of HRV was performed with the help of hardware and software «Kardiolab» («HAI-Medica»). Patients were divided into 3 groups according to the degree of power reduction of low-frequency and high-frequency waves of HRV during the transition from spontaneous breathing to paced one: 1st group- less than 5 times; 2nd group – 5–20 times; 3rd group – more than 20 times. Statistical analysis was performed by means of parametric and nonparametric methods using Microsoft Excel 7.0. It was found that in patients with hypertension was observed prevalence of humoral effects in comparison with the sympathetic and parasympathetic parameters. The greater was the contribution of humoral component to the HRV spectrum, the lower was the response of HRV to the respiratory modulation.

KEY WORDS: arterial hypertension, heart rate variability, paced breathing

ОЦІНКА ЗМІНИ РОЗПОДІЛУ СПІВВІДНОШЕНЬ УЛЬТРАНИЗЬКОЧАСТОТНИХ, НИЗЬКОЧАСТОТНИХ І ВИСОКОЧАСТОТНИХ КОМПОНЕНТІВ ВАРІАБЕЛЬНОСТІ СЕРЦЕВОГО РИТМУ У ПАЦІЄНТІВ З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ В ПРОБІ З МЕТРОНОМІЗОВАННИМ ДИХАННЯМ

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Було вивчено розподіл співвідношень ультранизькочастотних, низькочастотних і високочастотних компонентів варіабельності (ВСР) як показників стану гуморальної і вегетативної симпатичних і парасимпатичних ланок регуляції серцевого ритму у 35 пацієнтів з артеріальною гіпертензією (АГ) у віці 59 ± 5 років у пробі з метрономізованним диханням. Оцінка спектральних параметрів ВСР проводилася за допомогою програмно-апаратного комплексу «Кардіолаб» («ХАІ-Медика»). Пацієнти були розділені на 3 групи за ступенями зниження відношень потужностей низькочастотних і високочастотних хвиль ВСР при переході зі спонтанного на метрономізованне дихання: 1 група – менш ніж в 5 разів; 2 група – в 5–20 разів; 3 група – більш ніж в 20 разів. Статистична обробка даних проводилася параметричними і непараметричних методами з використанням Microsoft Excel 7.0. Було встановлено, що у пацієнтів з АГ спостерігається переважання гуморальних впливів над симпатичними і парасимпатичними. Чим більше виражений внесок у ВСР гуморальної складової спектру, тим нижче реакція показників ВСР на модуляцію дихання.

КЛЮЧОВІ СЛОВА: артеріальна гіпертензія, варіабельність серцевого ритму, метрономізоване дихання

ОЦЕНКА ИЗМЕНЕНИЯ РАСПРЕДЕЛЕНИЯ СООТНОШЕНИЙ УЛЬТРАНИЗКОЧАСТОТНЫХ, НИЗКОЧАСТОТНЫХ И ВЫСОКОЧАСТОТНЫХ КОМПОНЕНТОВ ВАРИАБЕЛЬНОСТИ СЕРДЕЧНОГО РИТМА У ПАЦИЕНТОВ С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ В ПРОБЕ С МЕТРОНОМИЗИРОВАННЫМ ДЫХАНИЕМ

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Изучено распределение соотношений ультранизкочастотных, низкочастотных и высокочастотных компонентов вариабельности сердечного ритма (ВСР) как показателей состояния гуморального и вегетативных симпатического и парасимпатического звеньев регуляции сердечного ритма у 35 пациентов с артериальной гипертензией (АГ) в возрасте 59 ± 5 лет в пробе с метрономизированным дыханием. Оценка спектральных параметров ВСР проводилась с помощью программно-аппаратного комплекса «Кардиолаб» («ХАИ-Медика»). Пациенты были разделены на 3 группы по степеням снижения отношения мощностей низкочастотных и высокочастотных волн ВСР при переходе со спонтанного на метрономизированное дыхание: 1 группа – менее чем в 5 раз; 2 группа – в 5–20 раз; 3 группа – более чем в 20 раз. Статистическая обработка данных проводилась параметрическими и непараметрическими методами с использованием Microsoft Excel 7.0. Установлено, что у пациентов с АГ наблюдается преобладание гуморальных влияний над симпатическими и парасимпатическими. Чем больше выражен вклад в ВСР гуморальной составляющей спектра, тем ниже реакция показателей ВСР на модуляцию дыхания.

КЛЮЧЕВЫЕ СЛОВА: артериальная гипертензия, вариабельность сердечного ритма, метрономизированное дыхание

INTRODUCTION

One of the important pathogenetic links of hypertension is a violation of the autonomic balance with a predominance of sympathetic and humoral effects, reduced activity of parasympathetic components of autonomous nervous system [1–2]. These changes are making a tangible contribution to the severity of the disease and may complicate the selection of antihypertensive therapy that frequently is empirical. The use of heart rate variability techniques (HRV) is a valuable addition to the standard set of diagnostic procedures in modern medicine that makes possible not only to assess the severity of pathological changes in the autonomic regulation [3–5], and take them into account in the prescription of antihypertensive drugs, as well as dynamically control the functional state of the cardiovascular system during patient treatment [6–7].

Spectral analysis of HRV allows evaluate the frequency characteristics of the components of the spectrum and their distribution in influencing the modulation of heart rate, which is particularly important when examining patients with arterial hypertension.

Spectral indices of heart rate HF, LF, VLF are defined as high, low and ultra-low-frequency components of HRV spectrum, and reflect the sympathetic, parasympathetic and suprasegmentally influences in the regulation of heart rate. HF is characteristic for vagal control of autonomic modulation of heart rate, LF – to sympathetic and, to a certain extent, the parasympathetic components of HRV, VLF contributes to humoral component of HRV spectrum [8].

A paced breathing test allows determine the state of autonomous regulation and first of all the level of vagal response at controlled respiration [9], and the level of return to its initial state in the final stage of test [10]. Therefore, researches in this field are not only of theoretical but also of practical interest and allow determine the pathogenetic links of hypertension in each individual patient, and thus provide opportunities for more effective and targeted therapy in these patients.

OBJECTIVE

The purpose of this article is to determine the changes in the ratios of distribution of ultra-low-frequency, low-frequency and high-frequency components in patients with essential arterial hypertension in the paced breathing test.

MATERIALS AND METHODS

A total of 35 hypertensive patients aged 40 to 70 years (mean age – 59 ± 5 years).

Inclusion criteria were: hypertension I-III degree, stage I-III with stable angina of FC I–III, chronic heart failure FC I–III I–IIA stage.

Exclusion criteria were: acute myocardial infarction, unstable angina, chronic heart failure IV FC, valvular heart disease, implanted pacemakers, endocrinological diseases (diabetes, thyroid disease, etc.), exacerbation of systemic diseases.

Clinical diagnosis of essential arterial hypertension was determined in accordance with the recommendations of the Ukrainian Association of Cardiology [11].

Blood pressure measurement was carried out by the method of Korotkov using the tonometer Microlife BP AG1-20.

The study of HRV was performed using the «CardioLab» («HAI-Medica») computer software containing the algorithm for determining the HRV parameters.

The test with the modulated (paced) breathing with double (visual and sound) metronome was performed in the supine position of patients, at the same time and consisted of 3 stages. In the first initial resting stage the patients were maintained at rest breathing freely in familiar to them rhythm and depth of breathing for 5 minutes to ensure that a true resting HRV values were obtained; in the second stage of paced breathing patients were instructed to perform breathing in breathing rate of 6 times per minute with additional control of visual and sound metronome for 5 minutes; in the third final resting stage the patients were breathing in a free manner for 5 minutes.

As a result of the test next indices were evaluated: TP (total power of the spectrum), LF (low-frequency waves), VLF (very-low-frequency waves), HF (high-frequency waves), LF/HF (ratio of the low-frequency waves to high-frequency waves).

The test results were interpreted on the basis of international standards (protocols of the European Society of Cardiology) [8].

Depending on the changes of LF/HF ratio between paced breathing stage and the initial stage, reflecting the level of regulatory capacity of the autonomic nervous system, patients were divided into 3 groups: the first group – LF/HF decrease of less than 5 times, second group – reducing the LF/HF in 5–20 times, group 3 – LF/HF decrease of more than 20 times in paced breathing stage compared to the initial one.

In each group clinical and spectral parameters of HRV were compared and evaluated in all 3 stages of the paced breathing test.

The Microsoft Excel 7.0 software was used in statistical processing of obtained data. Parametric statistical data were used. Authenticities of differences between groups were evaluated with non-parametric Mann-Whitney U test. To establish the relationship between quantities parametric variables was used Spearman's correlation analysis. The level of significance was set at $p < 0.05$.

RESULTS AND DISCUSSION

The results of the comparison of the distribution ratio of ultra-low-frequency, low-frequency and high-frequency components in hypertensive patients are shown in fig. 1 and tab. 1.

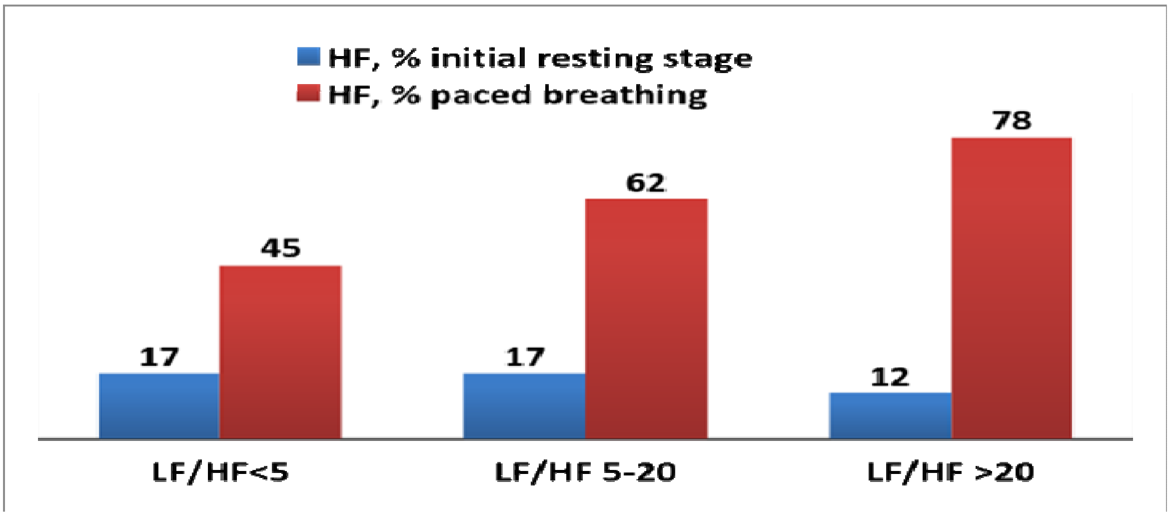

Fig. 1. The extent of HF index growth in the paced breathing stage

Table 1

Spectral HRV parameters depending on the reduction LF/HF in the paced breathing test

Spectral HRV parameters		The degree of reduction of LF/HF in the paced breathing test			Accuracy of differences between the samples, p
		less than 5 times (group 1)	In 5–20 times (group 2)	More than 20 times (group 3)	
TP, ms^2	Initial resting values	1357 ± 2143	787 ± 554	2157 ± 2373	$P_{1-2} > 0,05$ $P_{2-3} < 0.01$ $P_{1-3} > 0,05$
	Paced breathing values	1376 ± 1411	2421 ± 3156	4502 ± 3988	$P_{1-2} > 0,05$ $P_{2-3} < 0.05$ $P_{1-3} < 0.05$
	Final resting values	858 ± 612	825 ± 391	2201 ± 2291	$P_{1-2} > 0,05$ $P_{2-3} < 0.05$ $P_{1-3} > 0,05$
LF, %	Initial resting values	15 ± 3	30 ± 8	36 ± 16	$P_{1-2} < 0,01$ $P_{2-3} > 0,1$ $P_{1-3} < 0.05$
	Paced breathing values	13 ± 8	12 ± 4	7 ± 3	$P_{1-2} > 0,05$ $P_{2-3} < 0.01$ $P_{1-3} < 0.05$
	Final resting values	27 ± 7	30 ± 13	31 ± 17	$P_{1-2} > 0,05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
VLF,%	Initial resting values	67 ± 18	53 ± 15	52 ± 15	$P_{1-2} < 0.05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
	Paced breathing values	42 ± 16	27 ± 14	15 ± 12	$P_{1-2} < 0.05$ $P_{2-3} < 0.01$ $P_{1-3} < 0.01$
	Final resting values	59 ± 11	55 ± 17	59 ± 21	$P_{1-2} > 0,05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
HF, %	Initial resting values	17 ± 16	17 ± 11	12 ± 7	$P_{1-2} > 0,05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
	Paced breathing values	45 ± 20	62 ± 16	78 ± 14	$P_{1-2} > 0,05$ $P_{2-3} < 0.01$ $P_{1-3} < 0.01$
	Final resting values	14 ± 5	15 ± 11	10 ± 6	$P_{1-2} > 0,05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
LF/HF	Initial resting values	1,7 ± 1	2,6 ± 1,8	4,4 ± 4	$P_{1-2} > 0,05$ $P_{2-3} < 0.1$ $P_{1-3} < 0.05$
	Paced breathing values	0,4 ± 0,4	0,4 ± 0,8	0,1 ± 0,07	$P_{1-2} > 0,05$ $P_{2-3} < 0.01$ $P_{1-3} < 0.01$
	Final resting values	2,0 ± 0,5	2,8 ± 2	3,8 ± 1,5	$P_{1-2} > 0,05$ $P_{2-3} < 0.05$ $P_{1-3} < 0,05$

At the initial resting stage an autonomic imbalance with predominance of VLF waves was observed in all 3 groups, indicating the presence of enhanced humoral component of HRV spectrum. The most pronounced prevalence of waves of very low frequency was observed in the first group of patients (VLF = 67 ± 18; $P_{1-2} < 0.05$), whereas in the second and third groups, these values were 53 ± 15 and 52 ± 15, respectively. LF/HF ratio showed fluctuations with increased involvement of low-frequency parameters of

HRV, which was especially pronounced in the third group (LF/HF = 4.4 ± 4, $P_{2-3} < 0.1$, $P_{1-3} < 0.05$). In the 1st group, on the other hand, the share of the low-frequency component of the LF spectrum was less pronounced compared to the 2nd and 3rd groups ($P_{1-2} < 0,01$, $P_{1-3} < 0.05$) and was 15 ± 3. High-frequency indices were approximately at the same level in all groups with no meaningful significant differences between the groups – 16 ± 19, 17 ± 11 and 12 ± 7, respectively in the 1st, 2nd and 3rd groups.

At the stage of paced breathing in third group of patients was noted the most significant involvement of parasympathetic components of HRV spectrum in response to the controlled breathing, high-frequency parameter in this group was observed at the level of – 78 ± 14 ($P_{2-3} < 0.01$, $P_{1-3} < 0.01$). In the same group were observed minimal values of LF compared to the other groups – 7 ± 3 ($P_{2-3} < 0.01$, $P_{1-3} < 0.05$). LF/HF has demonstrated also the same distributions, reflecting vagotonia prevalence in the third group – 0,1 ± 0,07 ($P_{2-3} < 0.01$, $P_{1-3} < 0.01$). The extent of growth in the low-frequency waves of HRV spectrum was different in all 3 groups, and was as follows: in the first group – 28, in the second group – 45 % in the third group – 66 %, thus demonstrating the unequal levels of autonomous regulatory capacity in the examined groups.

Fluctuations of VLF waves also showed different degrees of decline in suprasegmentally influences at paced breathing: in the third group of patients such changes were less pronounced - very low frequency level value decreased by 37 % compared to the initial resting stage and was recorded at 15 ± 12; while in the 1st and 2nd groups, this value fell by only 23 % and 26 %, respectively, and appeared to be 42 ± 16 and 27 ± 14, with significant difference between the groups $P_{1-2} < 0.05$, $P_{2-3} < 0.01$, $P_{1-3} < 0.01$ (fig. 2).

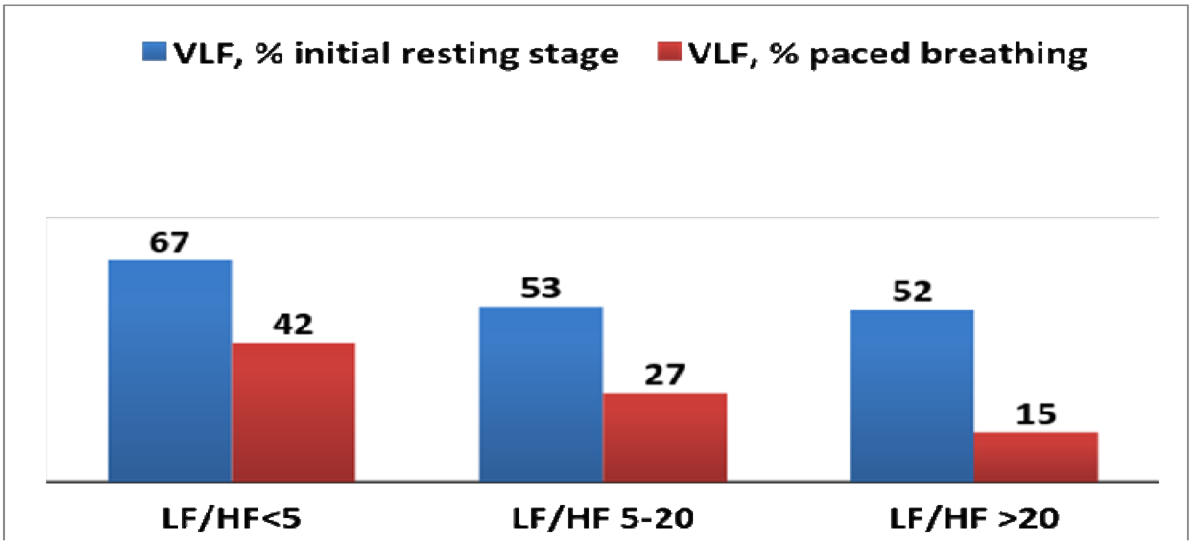

Figure 2. The degree of reduction VLF index in paced breathing stage

Correlations between changes of distribution of VLF and HF waves in paced breathing stage compared with the initial resting stage are shown in tab. 2.

Table 2

Correlations between changes of distribution of VLF and HF waves in paced breathing stage compared with the initial resting stage

	Initial stage-paced breathing Group 1	Initial stage-paced breathing Group 2	Initial stage-paced breathing Group 3
Correlations between increase of HF, ms^2 and decrease of VLF, ms^2	$r_s = -1$; $p < 0.001$;	$r_s = -0.074$; $p > 0.05$;	$r_s = 0.297$; $p > 0.05$;

where r_s – Spearman's rank correlation coefficient, p – p-value

In the final resting stage there were detected slight decrease in the proportion of high-frequency waves of HF in all groups of patients(13 ± 5 – in the 1st group, 15 ± 11 – in the 2nd, 10 ± 6 in the third group of patients); At the same time, the humoral involvement was enhanced, demonstrating increase in VLF waves from 2 % to 7 %, compared with the initial resting stage and was recorded at level of 60 ± 12, 55 ± 17, 59 ± 21 in the 1st, 2nd and 3rd groups respectively. Low-frequency parameter of HRV in the third group in the final resting stage of the breathing test has decreased in comparison with the initial resting stage by 5 % to 31 ± 17; in the 2nd group LF values showed no differences from the same values in initial resting stage (30 ± 13), while in the 1st group, the low-frequency component of HRV spectrum has increased by 11 % to 27 ± 8.

Changes in the total power of the spectrum are shown in fig. 3 demonstrating a lack of growth in TP in response to the paced breathing in the 1st group, while in the second and third groups of patients this parameter had a positive growth during the phase of controlled breathing. In the final resting stage, a decrease of the total power of the spectrum compared to initial values in the 1st group was established; in the 2nd and 3rd groups the value of TP returned back to the initial level.

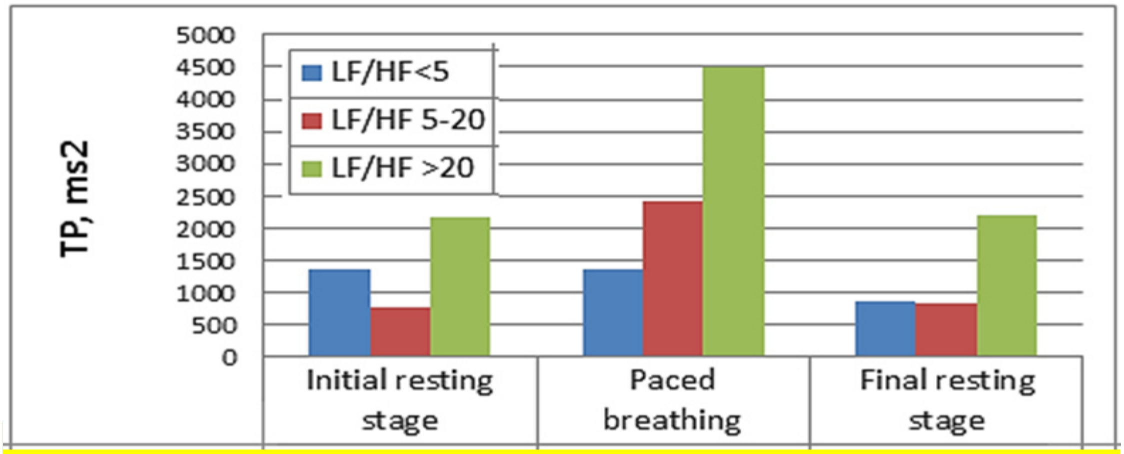

Fig. 3. Changes in the value of total power TP during all stages of the paced breathing test in three groups of patients

Data, according to which in the initial resting stage in all groups of patients a significant rise and even prevalence of humoral effects were shown, while the ratio of LF/HF demonstrated shift towards sympathicotonia, confirms [1, 3, 12–14].

Dysregulation of the autonomous nervous system has been less pronounced in patients with higher levels of vegetative regulation, in which the HRV response to paced breathing with a predominance of vagal component was more significant; also there was the significant increase in the total power TP and a marked reduction in humoral influences. In turn, in patients where the regulatory possibilities of the autonomous nervous system were reduced was observed sufficiently high level of HRV suprasegmentally spectral components not only in the resting (initial) state, but in the stage of paced breathing; the extent of HF wave growth in this group with controlled breathing was very small, also there was found a negative correlation between the degree of increase of HF waves and reduce the level of VLF waves at this stage of the test.

At the final resting stage in patients of all groups remained disturbed state of relations between the components of HRV spectrum, more pronounced in patients with a lower level of autonomous regulation. The degree of inhibition of vegetative response to the groups correlated with excessive activation of humoral mechanisms of heart rate regulation.

Increased humoral effects along with the weakening of autonomous control of heart rate may exacerbate hypertension, thereby adversely affecting the prognosis of the disease, as evidenced by the study [1, 7, 14].

In accordance with these data defined violations in the relations between the spectral parameters of HRV can be a useful tool for the detection of pathogenetic components of arterial hypertension, which can be used for more accurate and careful selection of antihypertensive drugs [6], and also to stratify the risk of complications in hypertensive patients.

CONCLUSIONS

In patients with arterial hypertension there is a decrease of the total power of the HRV spectrum with a predominance of humoral effects in comparison with sympathetic and parasympathetic influences. Intensity of these changes depends on the autonomous control of heart rate regulation: in patients with reduced regulatory capacity of the autonomous nervous system there is a significant prevalence of suprasegmentally regulatory mechanisms that is characterized not only by disrupted static, but also dynamic balance of HRV.

Reduced possibility of regulation of heart rate can also negatively affect the change in the total power of HRV spectrum in all stages of the paced breathing test; in patients with a decreased level of autonomous regulation there is a lack of TP growth in response to controlled breathing, as well as paradoxical decrease in total power parameter during the final resting stage of the test. These changes contribute negatively in a course of arterial hypertension and are the poor prognostic factor for its outcome.

PROSPECTS FOR FUTURE STUDIES

Considering the fact that the vagal imbalance especially along with the excessive humoral involvement has a significant share in the pathogenesis and clinical picture of arterial hypertension thus influencing on the outcomes of the disease the further investigation of this topic has not only theoretical but also practical value.

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