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Changes in the Power of the Low- and High-Frequency Bands of the Heart Rate Variability Spectrum in Coronary Heart Disease Patients with Different Severities of Coronary Atherosclerosis in the Course of Load Tests

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Abstract—The specific features of the changes in the low-frequency (*LF*) and high-frequency (*HF*) bands of the heart rate variability (HRV) spectrum were studied in coronary heart disease (CHD) patients with different numbers of coronary arteries affected by hemodynamically significant stenosis in the course of a bicycle exercise test. Male patients (143) with CHD aged 49 ± 8 years participated in the study. Subgroups with hemodynamically significant stenosis in one, two, or three coronary arteries; with no stenosis; and with a varying degree of total coronary bed lesion were distinguished. Tachograms were recorded in the course of bicycle exercise tests with loads of 25 and 50 W with spontaneous respiration for 3 min at each stage of a test. The frequency estimates of HRV in the *LF* and *HF* bands of the spectrum were obtained using the parametric method for constructing the spectrum based on the autoregressive model. It was shown that hemodynamically significant coronary stenoses significantly influenced the state of the mechanisms of autonomic regulation of the heart, which, in CHD patients with a three-vessel coronary lesion, is characterized by an extremely low adaptability.

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INTRODUCTION

An intricate multilevel system of different regulatory structures with a large number of internal relations, which may be regarded as an integrated functional system of autonomic control of the heart, is involved in the formation of the heart rate (HR) variability (HRV) structure. The mechanisms of regulation of the cardiac function mediated by influences of the autonomic nervous system are modulated by various external factors (respiration, physical loads, changes in the body position, psychoemotional state, etc.) [1]. This system of control ensures adequate adaptation of the cardiac function to different states [2]; the study of data on the adaptation processes in different functional states is possible using the HRV parameters [3–5].

At present, there is an opinion that the power of the high-frequency (*HF*) band of the HRV spectrum primarily reflects the level of respiratory arrhythmia and parasympathetic influences on the heart rhythm [6, 7]. There exist several points of view on the nature of the low-frequency (*LF*) band of the HRV spectrum. According to one hypothesis, slow HRV oscillations are determined by the properties of the baroreflex feedback loop of the cardiovascular system control [8–10]. According to another hypothesis, low-frequency HR oscillations are centrogenic: they are generated by the brainstem neuronal network, which determines the oscillations of the flow rate of impulses of both sympathetic and parasympathetic cardiomotor neurons with a period of about 10 s, i.e., at a frequency of about 0.1 Hz [11]. In an earlier study [12], we showed a decrease in the HRV level and, in particular, in the activity of 0.1-Hz oscillations in coronary heart disease (CHD).

The goal of this work was to study the specific features of the changes in the *LF* and *HF* bands of the HRV spectrum in CHD patients with different numbers of stenosed coronary arteries in the course of bicycle exercise (BE) tests.

EXPERIMENTAL

One hundred and forty-three male CHD patients aged 49 ± 8 who were treated and examined at the clinic of the Saratov Research Institute of Cardiology participated in the study. All the subjects gave their informed written consent to participate in the study. Patients over 70 years of age; patients afflicted with valvular heart defects or HR and conduction disorders interfering with HRV analysis; and patients with contraindications for BE tests; endocrine pathology; symptomatic arterial hypertension; peripheral circulatory disorders (obliterating endarteritis); or chronic diseases of the gastrointestinal tract (hepatitis, gastric or duodenal ulcer,

cholecystitis), kidneys, or other organs and systems at the stage of exacerbation were excluded.

To study the specific features of the functional relationship between the HRV spectrum *HF* and *LF* bands in CHD patients with and without hemodynamically significant atherosclerotic coronary artery stenoses, two groups were formed: group 1, including 88 CHD patients aged 49 ± 8 years with at least one coronary artery stenosis of more than 50%, and group 2, including 55 CHD patients aged 46 ± 9 years with no coronary artery stenoses of more than 50%.

To study the specific features of the relationship between the *HF* and *LF* bands of the HRV spectrum in CHD patients with different numbers of coronary arteries affected with atherosclerotic stenosis greater than 50%, the following groups were formed: group A, including 49 CHD patients aged 49 ± 7 years with a coronary stenosis greater than 50% in one artery; group B, including 29 CHD patients aged 50 ± 7 years with a coronary stenosis greater than 50% in two arteries; and group C, including 14 CHD patients aged 45 ± 5 years with a coronary stenosis greater than 50% in three arteries.

The study of the specific features of autonomic regulation of the heart in CHD patients depending on the total coronary bed lesion (TCBL) value was also conducted.

All patients underwent the following instrumental examinations: 12-channel electrocardiography (a VSD-804 digital electrocardiograph (Volzhskie peredovye tekhnologii, Russia), Doppler echocardiography (Sonoline Si-450, Siemens), a BE test (ES 1200, Hellige, Germany), and selective coronarography (Polydiagnost-C, Philips, Netherlands) according to the method described in [13]. The TCBL was calculated according to Petrosyan and Ioseliani [14].

Tachogram (RR interval series) recording was performed in the course of BE tests with loads of 25 and 50 W under conditions of spontaneous breathing. The choice of load levels of 25 and 50 W is determined by the fact that a number of studies have shown a low information content of HRV spectral analysis at high-intensity physical loads [15, 16]. In the BE test, we determined the HRV spectral characteristics. For this purpose, the RR interval values were recorded at rest and 1.5 min after the beginning of each loading step; thus, the processes of adaptation of cardiac activity were excluded from the recording. The duration of the RR recording was 3 min at each stage both at rest and during load.

In tests with spontaneous breathing, the operation of one or another mechanism of autonomic regulation in the HRV spectrum can be assessed under the conditions of natural interaction between the cardiovascular and respiratory systems.

All the functional tests were performed in the morning (9:00–10:00 a.m.), which allowed the influence of diurnal HRV fluctuations on the results of the investigation to be precluded [17–19].

In order to obtain HRV frequency estimates, the parametric method for constructing the spectrum of the temporal RR series based on the autoregressive model up to the 14th order was used. The spectral analysis software (Certificate of Official Registration of a Computer Program no. 980656 of November 12, 1998) ensured a calculation step of the spectral power density by frequency of the order of 0.01 Hz in the range 0.01–0.5 Hz; the period of quantization of the RR intervals was 0.5 s. For further analysis, two bands were used, high-frequency (*HF*, 0.15–0.4 Hz) and low-frequency (*LF*, 0.04–0.15 Hz) [20, 21], in which the HRV spectrum frequency power was calculated (in ms^2). Three-minute tachograms free of noise, extrasystoles, a noticeable linear trend, and transitional processes were selected for spectral analysis.

The statistical analysis of the results included the following. With a view to selecting a method for further analysis of the parameters obtained, we tested the null hypothesis of their accordance with the normal distribution law based on calculation of the Shapiro–Wilk *W* statistic. It was found that the data structure in terms of the HRV spectral parameters studied cannot be described by the normal distribution law; therefore, further studies of relationships were conducted using nonparametric statistical methods. Comparisons between the variables were made with the Mann–Whitney *U* test. Correlations were assessed using Spearman's rank-order correlation coefficient. The data are represented as the median (Me) and the quartile range values (25 and 75%). The significance of the statistical estimates used was taken to be no less than 95%. For statistical calculations, the MS Office Excel 2003 and Statistica 6.1 software packages were used.

RESULTS

Regarding the clinical picture and case histories of the CHD patients, it can be noted that the severity of the clinical manifestations of the underlying disease (CHD, angina pectoris) normally increases with the degree of atherosclerotic coronary bed lesion. The subgroups of CHD patients studied were comparable with respect to the global myocardial contractile function values, the number of myocardial infarctions in the case histories, and the group composition with respect to angina pectoris functional classes.

Figure 1 shows a graph of the simultaneous changes in the power of the *HF* and *LF* bands of the HRV spectrum in the total group of CHD patients in the course of the BE tests under spontaneous breathing conditions. As can be seen in Fig. 1, when a load increased to 25 or 50 W, a synchronous decrease in the power of both the *LF* and *HF* bands of the HRV spectrum occurred, with the decrease being relatively proportional, which is indicative of a more or less comparable decrease in the

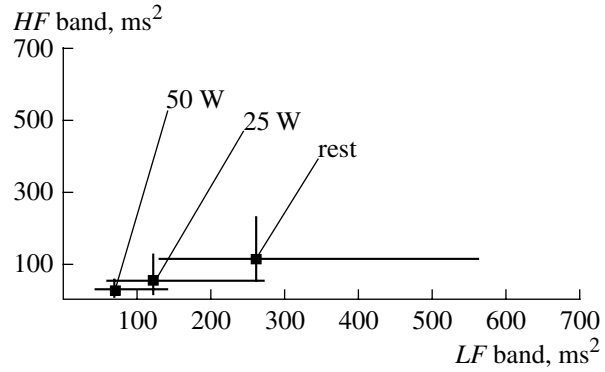

Fig. 1. Simultaneous changes in the power of the *LF* and *HF* bands of the HRV spectrum in the total group of CHD patients in the course of bicycle exercise tests under the conditions of spontaneous breathing.

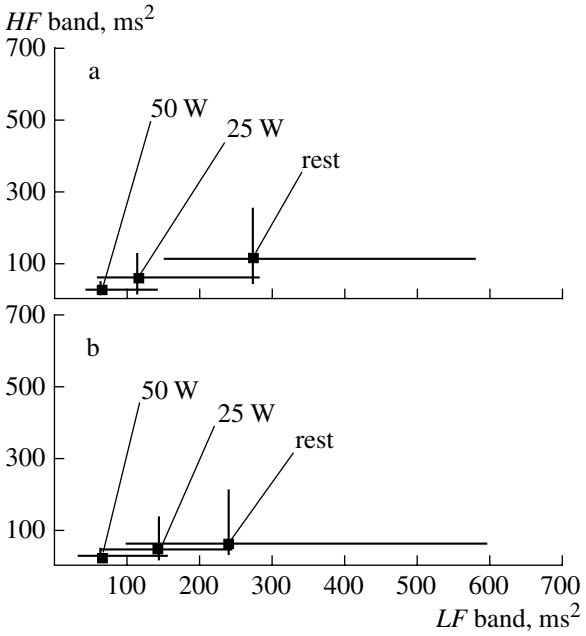

Fig. 2. Simultaneous changes in the power of the *LF* and *HF* bands of the HRV spectrum in CHD patients (a) with hemodynamically significant coronary artery stenoses and (b) without them in the course of bicycle exercise tests under the conditions of spontaneous breathing.

involvement of the mechanisms of autonomic regulation determining the power of these spectral bands in the formation of the HRV structure.

Comparative analysis of the simultaneous changes in the power of the *HF* and *LF* bands of the HRV spectrum in the course of the BE tests under conditions of spontaneous breathing in the groups of CHD patients with and without at least one hemodynamically significant coronary artery stenosis (Fig. 2) showed a comparable profile of the changes in the *LF* band of the spectrum, whereas the *HF* band power had lower initial values and was characterized by a significantly ($p < 0.05$) lower amplitude of the dynamic profile in the group of CHD patients without hemodynamically significant stenoses.

In CHD patients with atherosclerotic lesions of one or two coronary vessels, the power of the *HF* and *LF* bands of the HRV spectrum was approximately identical and had a significantly higher value (Fig. 3) compared to the group with lesions of three vessels.

It should be noted that the profile of simultaneous changes in the power of the *LF* and *HF* bands of the HRV spectrum in CHD patients with hemodynamically significant stenosis of three coronary arteries differed significantly ($p < 0.05$) from that in the other two groups.

The TCBL value does not influence significantly the specific features of the profile of the simultaneous changes of the *LF* and *HF* bands of the HRV spectrum in CHD patients (Fig. 3).

When the load increased, a significant ($p < 0.001$) increase in the HR and blood pressure comparable in all the groups studied (Tables 1, 2) was detected, which testifies to the absence of differences between the groups in terms of conventional sympathetic–parasympathetic balance.

Table 1. The mean HRs in CHD patients with hemodynamically significant coronary artery stenoses and without them at the stages of the bicycle exercise test

Stages	Absence of stenoses >50%	Stenoses >50%	*p*
Rest	82 (70; 90)	78 (70; 90)	>0.05
25-W load	94 (74; 103)	95 (85; 105)	>0.05
50-W load	102 (92; 109)	103 (92; 113)	>0.05

DISCUSSION

Based on the data obtained (Fig. 2), it may be concluded that CHD patients with hemodynamically significant coronary stenosis show an increase in respiratory and parasympathetic influences in the autonomic regulation of the heart reflected in the *HF* band power of the HRV spectrum. This observation is probably determined by a compensatory increase in the activity of additional regulatory mechanisms under the conditions of a relative functional insufficiency of the 0.1-Hz mechanism of the autonomic regulation of the heart. The insufficiency of the 0.1-Hz regulatory mechanism is mainly determined by its dysfunction in CHD compared to healthy individuals, which was shown by us earlier [12]. In addition, hemodynamically significant coronary artery stenosis necessitates the adaptation of the heart to functioning under pathological conditions, which contributes to an increase in the functional requirements for the mechanisms of autonomic regulation of the heart.

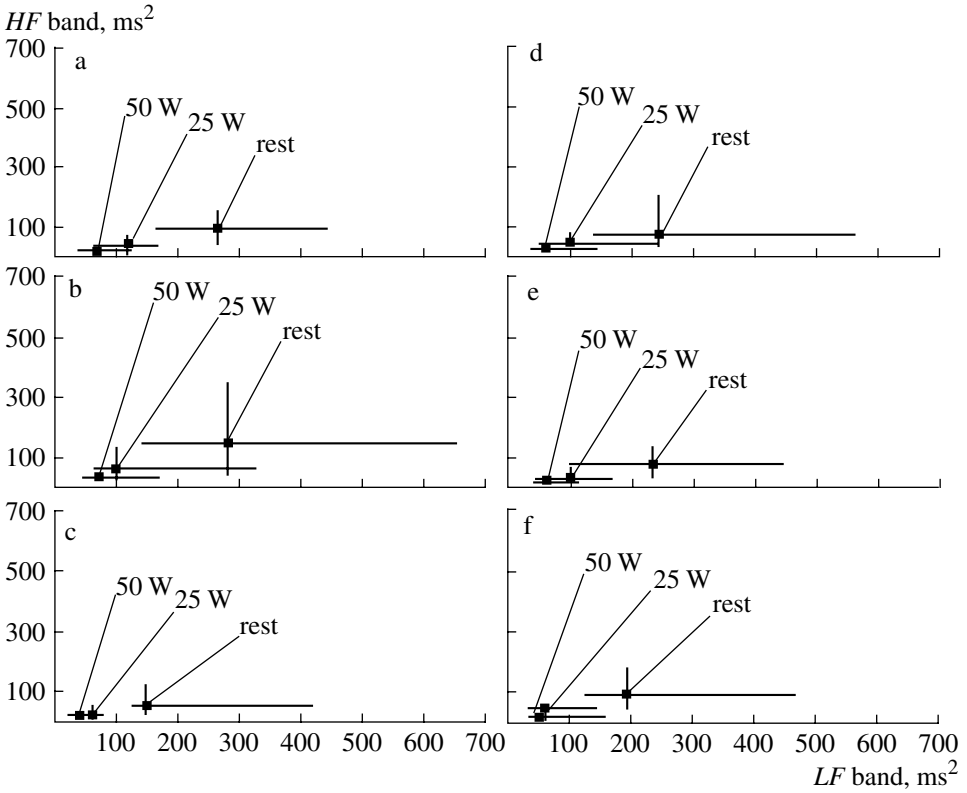

Fig. 3. Simultaneous changes in the power of the *LF* and *HF* bands of the HRV spectrum in CHD patients with hemodynamically significant stenosis of (a) one, (b) two, or (c) three coronary arteries and with a total coronary bed damage of (d) less than 5%, (e) 5–30%, or (f) more than 30% in the course of bicycle exercise tests under the conditions of spontaneous breathing.

With an increase in the number of coronary arteries with hemodynamically significant stenosis, increased autonomic dysfunction both in the central (0.1 Hz) regulation link and in more autonomous respiratory and parasympathetic influences on the autonomic regulation of the heart is observed, which is expressed by a decreased power of both the *LF* and *HF* bands of the HRV spectrum (Fig. 3). In CHD patients with one or two coronary arteries affected with atherosclerotic stenosis, the severity of dysfunction of the mechanisms of autonomic regulation of the heart is approximately identical and is less marked (Fig. 3) than in the group of patients with a three-vessel lesion. If three coronary vessels are involved, dysfunction of all mechanisms of autonomic regulation is observed, which determines an extremely low adaptive potential of the heart in these CHD patients.

Considering the data that the TCBL value, characterizing the degree of the total atherosclerotic coronary bed lesion, is not significantly connected with the specific features of the changes in the *LF* and *HF* bands of the HRV spectrum in the course of load tests in CHD patients with a different number of hemodynamically significant coronary stenoses (Fig. 3), we can assert that the presence of hemodynamically significant stenoses of the coronary arteries and their number, but not the degree of the total atherosclerotic involvement of the coronary bed, exert a significant influence on the state of the autonomic regulation of the heart.

The results obtained in this study show that, with an increase in the number of coronary arteries with hemodynamically significant stenosis (three-vessel involvement), simultaneous functional disorders of the central (0.1 Hz) mechanism of autonomic regulation and autonomic respiratory and parasympathetic influences on the heart is observed, which may evidence the presence of common functional and structural elements disrupted when the number of coronary stenoses

Table 2. The mean HRs in CHD patients with different numbers of coronary arteries with hemodynamically significant stenosis at the stages of the bicycle exercise test

Stage	Stenosis of one artery	Stenosis of two arteries	Stenosis of three arteries
Rest	79 (70; 92)	75 (68; 86)	83 (77; 94)
25-W load	97 (88; 107)	95 (86; 105)	100 (91; 102)
50-W load	103 (92; 115)	102 (91; 113)	109 (97; 115)

* Significant ($p < 0.05$) differences from the groups of CHD patients with a one- or two-vessel coronary bed lesion;

significant ($p < 0.05$) differences from the group of CHD patients with a two-vessel coronary bed lesion.

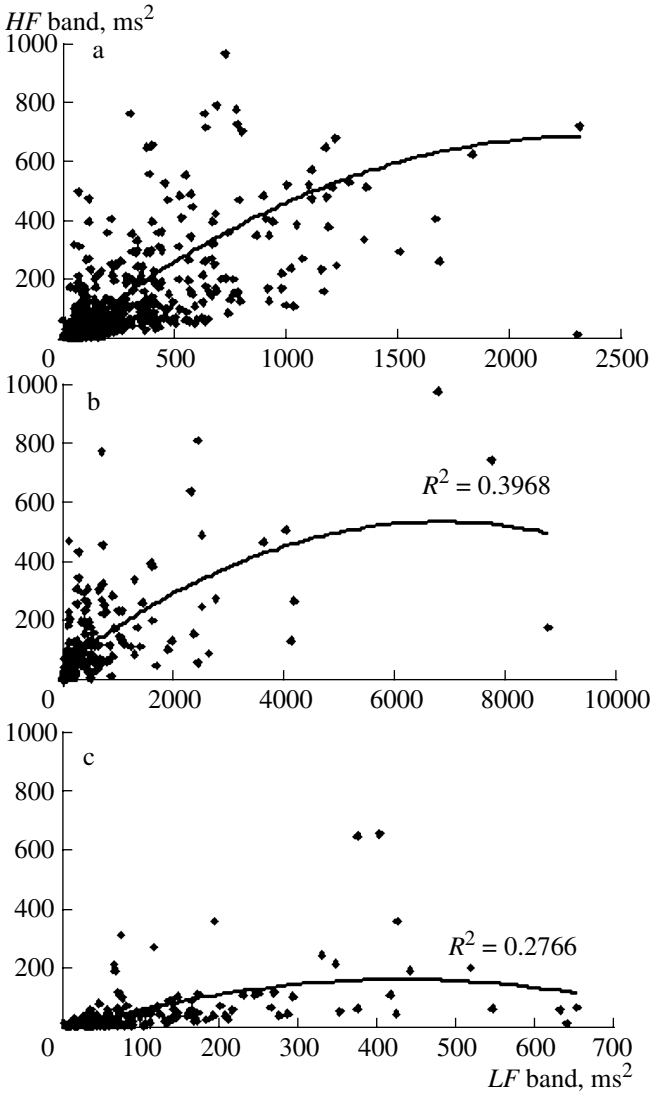

Fig. 4. Relationship between the power of the *LF* and *HF* bands of the HRV spectrum in CHD patients (a) at rest and (b, c) during exercise with an intensity of (b) 25 or (c) 50 W under the conditions of spontaneous breathing.

increases. Considering the significant increase in the dysfunction of the regulatory mechanisms in question only in the case of a three-vessel involvement of the coronary bed, it is possible to assert that the functional organization of the system of autonomic regulation ensures sufficient adaptive possibilities and allows the autonomic regulation of the cardiac function to be sustained at a stable level in one- and two-vessel coronary bed lesions; however, in stenotic lesions of three coronary arteries, a failure of adaptation of the autonomic regulation of the heart is observed.

Analyzing the interrelationship between the spectral power in the *LF* and *HF* bands, we found that, with an increase in the power of one of them, the spectral power of the other increased accordingly. Note that, under the conditions of spontaneous breathing at rest, the strength of this relationship is moderate, which testifies to the sufficient autonomy of the physiological mechanisms determining the spectral power formation in the *LF* and *HF* bands of the HRV spectrum (Fig. 4). With an increase in the physical load to 25 W, the general pattern of the relationships between these bands of the HRV spectrum in CHD patients does not change on the whole; only the range of variability of the power values of both HRV spectral regions decreases (Fig. 4). With a further increase in the load level to 50 W, a decrease in the strength of the relationship between the power of the *LF* and *LF* bands of the HRV spectrum is noted (Fig. 4). The range of variability of the *HF* component of the HRV spectrum begins to decrease considerably, which is indicative of a lesser influence of respiratory disturbances on the mechanisms of autonomic regulation of the heart. This may be determined by both a change in the state of autonomic balance towards the predominance of the sympathetic division of the autonomic nervous system and a change in the state of the humoral mechanisms of regulation.

It should be noted that the strength of the correlation between the power of the *LF* and *HF* bands of the HRV spectrum in CHD patients increases with the severity of the atherosclerotic coronary bed lesion. In particular, comparison between the groups of CHD patients with at least one hemodynamically significant coronary artery stenosis and without hemodynamically significant stenoses shows that a stenosis exceeding 50% of the arterial diameter considerably increases the correlation between the *LF* and *HF* bands at rest, which is indicative of the formation of a more rigidly organized and less dynamic functional system of autonomic regulation of the heart (Table 3). This observation testifies to a potentially lower adaptability of the autonomic regulation of the heart in CHD patients whose coronary arteries are stenosed by more than 50%. This assertion is based on the fact that, from the point of view of the functioning of complex systems, a biological system with the largest number of degrees of freedom has the greatest adaptation potential.

At present, it is customary to consider that the *LF* band of the HRV spectrum mainly characterizes the properties of the 0.1-Hz oscillations in HRV, which are a consequence of the functional activity of the central mechanisms of autonomic regulation of the heart function, and the *HF* band of the HRV spectrum characterizes the processes of interaction between the cardiovascular system and the respiratory center of regulation under the conditions of spontaneous breathing and may partly reflect the parasympathetic activity. Free interaction of these mechanisms of autonomic regulation ensures a sufficiently high lability of the functional adjustments of the system of autonomic regulation of the heart, thus increasing its adaptation potential. A greater degree of relationship between the spectral power values of these bands is determined by a lesser freedom of interaction between the components of the

Table 3. Relationship between the power of the *LF* and *HF* bands of the HRV spectrum in CHD patients with hemodynamically significant coronary artery stenoses and without them at the stages of the bicycle exercise test

Stages	Absence of stenosis >50%	Stenosis >50%
	Correlation coefficient (r)	
Rest	0.45**	0.7***
25-W load	0.48**	0.73***
0-W load	0.43**	0.61***

Note: Here and in Table 4, the significance of correlation is as follows: ** $p < 0.01$; ** $p < 0.001$.

system of autonomic regulation of the heart and, as a consequence, by a decrease in its adaptation potential.

When the load was increased to 25 W, no significant changes in the type of relationship between the powers of the *LF* and *HF* bands of the HRV spectrum were observed in CHD patients with hemodynamically significant coronary artery stenoses and without them compared to the resting state (Table 3); the initial functional peculiarities of autonomic regulation of the heart were retained. A further increase in the load to 50 W was not accompanied by significant changes in the interrelationships between the HRV spectral bands studied (Table 3).

When studying the influence of the number of hemodynamically significant atherosclerotic stenoses in the coronary bed on the relationship between the power of the *LF* and *HF* bands of the HRV spectrum, we found that the strongest correlation between the powers of these bands was observed in the group of CHD patients with a three-vessel coronary bed lesion; as the number of stenotic coronary arteries decreased, the strength of the relationship between these parameters weakened (Table 4).

With a load increase to 25 W, a significant decrease in the strength of the correlation between the HRV spectrum power is observed in the group of CHD patients with a three-vessel coronary bed lesion (Table 4), which indicates, considering the values of this parameter at rest in this group, a breakdown of the system of autonomic regulation of the heart as an integrated functional system and a mismatch of the mechanisms of autonomic regulation of the heart. This observation further supports the earlier suggestion that, with an increase in the number of stenosed coronary arteries, the adaptation potential of the autonomic regulation of the heart decreases. To confirm this suggestion, we may only add that, in patients with a three-vessel atherosclerotic coronary bed lesion, the system of autonomic regulation of the heart is characterized by a low resistance to low-intensity loads, exposure to which results in the disruption of functional interrelationships between the components of this system.

In CHD patients with one- or two-vessel coronary bed lesions, as well as in those without hemodynamically significant coronary bed stenosis, the correlation between the *LF* and *HF* bands of the HRV spectrum did not change significantly upon the transition to a load of 25 W compared to the resting state, which is indirect evidence for the relative resistance of the system of autonomic regulation to a load of 25 W.

With a further increase in the load, a lesser degree of interrelationship is observed between the HRV spectrum power in the *LF* and *HF* bands in the group of CHD patients with a three-vessel involvement of the coronary bed (Table 4). In all the other groups of CHD patients, the tendencies characteristic of the resting state and the 25-W load are retained.

The data obtained allow us to draw the conclusion that hemodynamically significant stenoses in the coronary bed substantially and significantly influence the functional state of the autonomic regulation of the heart, the main factor being the number of stenosed arteries, which determines a decrease in the adaptive potential of the system of regulation via formation of a more dynamically rigid functional system of regulation.

A limitation for interpreting the results of the study is the comparatively small number of CHD patients with three stenosed coronary arteries, which may, to a certain degree, influence the quality of the results obtained. However, the use of the nonparametric statistical methods listed in Experimental may, to a certain extent, lessen the distortion of the results when small groups of subjects are compared.

Table 4. Relationship between the power of the *LF* and *HF* bands of the HRV spectrum in CHD patients with hemodynamically significant coronary artery stenosis in one, two, or three vessels at the stages of the bicycle exercise test

Stages	Absence of stenosis >50%	Stenosis of one artery	Stenosis of two arterie	Stenosis of three arteries
	Correlation coefficient (r)			
Rest	0.45**	0.79***	0.63***	0.92***
25-W load	0.48**	0.73***	0.81***	0.44 ($p > 0.05$)
50-W load	0.43**	0.62***	0.91***	0.15 ($p > 0.05$)

CONCLUSIONS

1. The presence of hemodynamically significant stenoses and the number of stenosed coronary arteries, rather than the degree of the total atherosclerotic damage of the coronary bed, influences significantly the parameters of the autonomic regulation of the heart.

2. In CHD patients with hemodynamically significant coronary bed stenosis, an increase in the respiratory and parasympathetic influences on the heart is observed against the background of a relative functional insufficiency of the 0.1-Hz mechanism of autonomic regulation of the heart compared to CHD patients without hemodynamically significant stenosis.

3. The autonomic regulation of the heart in CHD patients with three-vessel atherosclerotic damage of the coronary bed is characterized by an extremely low adaptation potential.

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