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FUNCTIONAL STATE OF THE MYOCARDIA IN DEVELOPMENTAL PATHOGENESIS CHRONIC HEART FAILURE IN PATIENTS WITH HYPERTENSION

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SAMARKAND STATE MEDICAL UNIVERSITY

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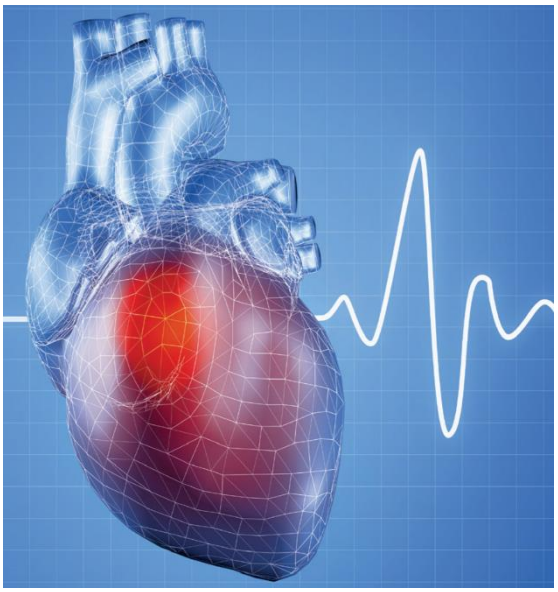
ANNOTATION



On the monograph of the staff of the department of propaedeutics of internal diseases, Samarkand State Medical University, S.Kh. Yarmukhamedova, F.Yu. Nazarov, D.Zh. Kamalova and Kh.D. Makhmudova on the topic: ***"FUNCTIONAL STATE OF THE MYOCARDIA IN THE PATHOGENESIS OF THE DEVELOPMENT OF CHRONIC HEART FAILURE IN PATIENTS WITH HYPERTENSION".***

The leading mechanism for the development of CHF in arterial hypertension is most often isolated diastolic dysfunction of the left ventricle (LV). The main mechanism of impaired diastolic function of the heart is LV hypertrophy, which determines the prognosis of the disease, and is also an independent risk factor for the development of cardiovascular complications and mortality. The monograph is devoted to the study of the functional state of the myocardium and its influence on the development of chronic heart failure.

Currently, much attention is paid to other pathogenetic mechanisms for the development of hypertension and chronic heart failure. These include vascular remodeling, which is accompanied by an increase in pre- and afterload, hyperactivation of neurohormonal systems, etc. Scientific works devoted to the study of the etiology and pathogenesis of hypertension do not sufficiently explain the issues of its development, stabilization, and prognosis.

The main task of researchers in the last decade is to determine accurate, universal, and affordable laboratory and instrumental markers of CHF in patients with hypertension without clinical signs of heart failure.

The importance in the pathophysiology and pathogenesis of changes in the structure and geometry of the left ventricle of the heart in a number of studies has suggested that concentric LV remodeling, in contrast to concentric hypertrophy, is underloaded by volume. In response to volume underloading, obvious LV hypertrophy does not develop. These factors are described as "myocardial stress markers" or "offload factors". The study of the mechanisms of "LV underload" and "unload factors" will provide new strategies for optimizing treatment, and

preventing the development of myocardial remodeling and chronic heart failure in patients with hypertension.

The data of echocardiographic studies of patients with AH prove that the progression of CHF is accompanied by worsening of the longitudinal deformity and impaired systolic function of the left ventricle.

Assessment of the functional state of the myocardium is an important point in the early diagnosis and prevention of systolic and diastolic dysfunction of the heart in hypertension. In connection with the above, the purpose and objectives of our study were the following.

Currently, the pathogenetic role of cardiac remodeling in the development of CHF progression in patients with arterial hypertension is still being actively discussed.

Heart remodeling is understood as "structural and geometric changes in the left ventricle, including the processes of myocardial hypertrophy and dilatation of the heart, which lead to a change in its geometry and a violation of systolic and diastolic function." This term was introduced into clinical practice in the 70s.

In addition, in practice, such concepts as "mechanical remodeling" and "structural remodeling" are distinguished. Mechanical remodeling is also called functional. Functional remodeling is called local LV contractile dysfunction, which occurs independently and does not depend on structural and geometric rearrangement.

Currently, problem of arterial hypertension is one of the most significant medical and social problems. According to the literature, by 2025, an increase in the number of cases of AH by more than 1.5 times is predicted. This monograph reflects one of the most urgent problems of modern cardiology.

The great importance of early and timely detection of arterial hypertension, as well as effective control of blood pressure in reducing the risk of cardiovascular complications, is reflected in numerous clinical and epidemiological studies. In no less than 80% of cases, arterial hypertension leads to the development of chronic heart failure (CHF). According to the authors, the prevalence of CHF is growing by 1.2 people per 1000 per year. The frequency of chronic heart failure among the male population is significantly higher in the age group from 40 to 59 years compared with other age groups. By 2020, according to available data, about 80% of patients with CHF will have preserved LV systolic function. These studies

make it possible to call CHF with preserved left ventricular ejection fraction a non-infectious epidemic of the 21st century.

At present, questions about the pathogenetic mechanisms of the development of heart remodeling in hypertension are still debatable. An urgent problem of diagnosis is the early detection of structural and functional disorders of cardiac hemodynamics.

There are modern data on the development of cardiac remodeling as a result of functional and structural changes in patients with AH. So, Konradi A. O. and Grachev O. V. indicate that in arterial hypertension for the heart character no development of left ventricular hypertrophy (LVH). Belenkov Yu.N. and Mareev V.Yu. described the development of diastolic dysfunction (DD) and a decrease in global cardiac contractility in CHF. But in the absence of a decrease in EF, LVH, and PD of the left ventricle in patients with hypertension, early diagnosis of heart remodeling is very important. Therefore, diagnostic issues in these cases are very relevant.

The bibliography for the monograph is extremely extensive and uses materials published over the past 5-6 years. The monograph is intended for general practitioners, primary care physicians, clinical residents, and residents.
The monograph is devoted to an actual problem and contains data from modern research. There are no serious comments on the monograph, and I strongly recommend that it be given permission for the next stages of consideration.

Reviewers

Tashkenbayeva E.N. – DSc, Professor Samarkand State Medical University

Karimova G.N.- PhD, docent SEI “TSMU named after A. Sino”,

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LIST OF CONDITIONAL ABBREVIATIONS

AG - arterial hypertension
BP - blood pressure
HRV - heart rate variability
GB - hypertension
LVH - left ventricular hypertrophy
DBP - diastolic blood pressure
DD - diastolic dysfunction
iKDR - indexed end diastolic size of the left ventricle iKSR - indexed end systolic size of the left ventricle LVMI - indexed mass of the myocardium of the left ventricle IO - volume index
IOT - index of relative thickness of the left ventricle
KDD - end-diastolic pressure
EDV - end diastolic volume of the left ventricle
ESV - end systolic volume of the left ventricle
KDD - end-diastolic pressure
KDR - end diastolic size of the left ventricle
CSR - final systolic size of the left ventricle
LV - left ventricle
LP - left atrium
IVS - interventricular septum
MS - myocardial stress
TVR - total peripheral vascular resistance
CCA - common carotid artery
PAP - pulse blood pressure
SBP - systolic blood pressure
SI - daily index
GFR - glomerular filtration rate
ABPM - ambulatory blood pressure monitoring
CVD - cardiovascular diseases
PVSLV - thickness of the posterior wall of the left ventricle TIMT - thickness of the intima-media complex TMZhP - thickness of the interventricular septum SV - stroke volume EF - ejection fraction
HM - Holter monitoring
CHF - chronic heart failure
SEF - saved ejection fraction
ECG – electrocardiography
EchoCG - echocardiograph

Introduction

Currently, problem of arterial hypertension is one of the most significant medical and social problems. According to the literature, by 2025, an increase in the number of cases of AH by more than 1.5 times is predicted. [2, 44, 47, 48, 59, 66].

The great importance of early and timely detection of arterial hypertension, as well as effective control of blood pressure in reducing the risk of cardiovascular complications, is reflected in numerous clinical and epidemiological studies [18, 34, 54, 76, 82, 86]. In no less than 80% of cases, arterial hypertension leads to the development of chronic heart failure (CHF) [35, 36]. According to the authors [2, 45, 59], the prevalence of CHF is growing by 1.2 people per 1000 per year. The frequency of chronic heart failure among the male population is significantly higher in the age group from 40 to 59 years compared with other age groups. By 2020, according to available data, about 80% of patients with CHF will have preserved LV systolic function. These studies make it possible to call CHF with preserved left ventricular ejection fraction a non-infectious epidemic of the 21st century [1, 5, 45].

The leading mechanism for the development of CHF in arterial hypertension is most often isolated diastolic dysfunction of the left ventricle (LV). The main mechanism of impaired diastolic function of the heart is LV hypertrophy, which

determines the prognosis of the disease, and is also an independent risk factor for the development of cardiovascular complications and mortality [46].

Currently, much attention is paid to other pathogenetic mechanisms for the development of hypertension and chronic heart failure. These include vascular remodeling, which is accompanied by an increase in pre- and afterload, hyperactivation of neurohormonal systems, etc. Scientific works devoted to the study of the etiology and pathogenesis of hypertension do not sufficiently explain the issues of its development, stabilization, and prognosis [4, 6].

The main task of researchers in the last decade is to determine accurate, universal, and accessible laboratory and instrumental markers of CHF in patients with hypertension without clinical signs of heart failure [17, 25-26, 54, 56, 65, 70, 87, 88].

The importance in the pathophysiology and pathogenesis of changes in the structure and geometry of the left ventricle of the heart in several studies has suggested that concentric LV remodeling, in contrast to concentric hypertrophy, is underloaded by volume. In response to volume underloading, obvious LV hypertrophy does not develop. These factors are described as "myocardial stress markers" or "unloading factors" [11]. The study of the mechanisms of "LV underload" and "unload factors" will provide new strategies for optimizing treatment, and preventing the development of myocardial remodeling and chronic heart failure in patients with hypertension.

The data from echocardiographic studies of patients with AH prove that the progression of CHF is accompanied by worsening of the longitudinal deformity and impaired systolic function of the left ventricle [15, 38-39, 69].

Assessment of the functional state of the myocardium is an important point in the early diagnosis and prevention of systolic and diastolic dysfunction of the

heart in hypertension. In connection with the above, the purpose and objectives of our study were the following.

The prevalence of chronic heart failure in the world population.

Modern sources indicate that the development of heart failure proceeds according to common pathogenetic mechanisms, regardless of the etiological factor. Myocardial hypertrophy and cardiac remodeling are the two main stages of the cardiovascular continuum.

At present, questions about the pathogenetic mechanisms of the development of heart remodeling in hypertension are still debatable. An urgent problem of diagnosis is the early detection of structural and functional disorders of cardiac hemodynamics. [63, 74, 78, 80-81, 90].

There are modern data on the development of cardiac remodeling as a result of functional and structural changes in patients with AH. So, Konradi A. O. and Grachev O. V. indicate that in arterial hypertension, the heart is characterized by the development of left ventricular hypertrophy (LVH). Belenkov Yu.N. and Mareev V.Yu. described the development of diastolic dysfunction (DD) and a decrease in global cardiac contractility in CHF. But in the absence of a decrease in EF, LVH, and PD of the left ventricle in patients with hypertension, early diagnosis of heart remodeling is very important. Therefore, diagnostic issues in these cases are very relevant.

The place of cardiac remodeling in the development and progression of chronic heart failure in arterial hypertension

Currently, the pathogenetic role of cardiac remodeling in the development of CHF progression in patients with arterial hypertension is still being actively discussed.

Heart remodeling is understood as "structural and geometric changes in the left ventricle, including the processes of myocardial hypertrophy and dilatation of

the heart, which lead to a change in its geometry and a violation of systolic and diastolic function." This term was introduced into clinical practice in the 70s.

In addition, in practice, such concepts as "mechanical remodeling" and "structural remodeling" are distinguished. Mechanical remodeling is also called functional. Functional remodeling is called local LV contractile dysfunction, which occurs independently and does not depend on structural and geometric rearrangement.

Structural remodeling of the heart is understood as changes in the shape, volume, and thickness of the LV walls. [twenty].

If at first the concept of "remodeling" was considered only in the example of myocardial infarction, then at present it has undergone an expansion and applies to all patients with cardiovascular diseases (CVD), regardless of the etiological factor. Remodeling is a common pathogenetic mechanism at all levels of the structural organization of the heart, the result of which is a change in its shape, size, and functionality.

Cardiac remodeling precedes and accompanies the clinical manifestations of heart failure, and in turn, impairs diastolic and systolic cardiac function. Thus, remodeling is considered a risk factor for arrhythmias, sudden death, and poor prognosis.

Based on structural changes in the myocardium, detected by echocardiography (EchoCG), such as the relative LV wall thickness index (RTI), and indexed myocardial mass (IMM), four geometric models are distinguished. These include:

- ✓ concentric remodeling;
- ✓ normal geometry of the heart;
- ✓ left ventricular hypertrophy;eccentric hypertrophy of the left ventricle.

The prognostic value of cardiac geometry in patients with hypertension continues to be actively discussed.

The nature of myocardial adaptation to AH obviously depends on the hemodynamic load and the state of myocardial contractility. According to Laplace's law, to maintain normal myocardial stress (MS), an increase in LV wall thickness counteracts increased BP, and LV wall thickness should increase in proportion to the degree of AH. MS (“cardiac wall stress”) is understood as a quantitative reflection of post- and preload. MS characterizes the tension force of myocardial fibers per unit cross-section of the LV wall. At the same time, at the end of systole, it reflects afterload, at the end of diastole, it reflects preload.

Preload is the degree of stretching of the muscle fiber of the heart due to the filling of the ventricles with blood at the end of the diastole (ventricular filling pressure). It is numerically reflected in the value of end-diastolic pressure in the ventricle (EDP LV), which is normally about 8 mm Hg.

Afterload (afterload) is called instantaneous, total systemic vascular resistance (impedance value), which is overcome by the heart during contraction. Preload depends on blood pressure, blood viscosity, and total peripheral vascular resistance (OPVR).

Previously, it was assumed that systolic MS leads to the growth of cardiomyocytes in thickness and the development of concentric hypertrophy. Despite this, the results of A. Garneau's study contradicts generally accepted ideas. A.Ganau examined 165 patients with hypertension, who studied hemodynamic and contractile parameters of the left ventricle, depending on its geometric model. Normal heart geometry and a slight increase in peripheral vascular resistance were observed in the majority of patients with hypertension (52%). Concentric hypertrophy was noted in 8% of the examined patients. Eccentric LVH was found in 27% of cases, and 13% had concentric remodeling. Changes in the structural-geometric model of the left ventricle of patients with AH depend on the pathophysiological features of the heart and the circulatory system. Patients with concentric hypertrophy had an almost normal systolic MS, no left ventricular structural remodeling, an increase in peripheral vascular resistance, and a slight increase in cardiac index (CI). Concentric left ventricular

remodeling is characterized by almost normal systolic MS, and increased peripheral vascular resistance, such patients have a reduced stroke (SI) and systolic (SI) index. Eccentric LV hypertrophy is characterized by a high daily index (SI), an increase in the LV cavity, and end-systolic MS, as well as a normal TPVR.

The results of research by A.O. Conradi and O.S. Pavlova are comparable with the data of A. Garneau. A.O. Conradi studied the geometric models of the left ventricle in 734 patients with hypertension. At the same time, 30% were patients with normal heart geometry, concentric remodeling ovation was detected in 7% of cases, concentric hypertrophy was in 32% of all patients, and eccentric hypertrophy was detected in 31% of patients. In the studies of O.S. Pavlova, normal geometry was observed in 38% of the examined patients with AH, concentric remodeling was detected in 2% of cases, concentric LVH was observed in 27% of patients, and eccentric LVH was in 33% of the total number of patients with AH.

According to the results of the Framingham study, the highest cardiovascular risk is observed in patients with a concentric type of LV hypertrophy. Therefore, the most important point in the development of concentric hypertrophy to maintain LV function is the normalization of MS, since concentric hypertrophy can be maintained at a normal level even in the presence of elevated MS.

As a result of pressure overload during neurohormonal activation, structural disorganization of myocardiofibrils and hypertrophy of cardiomyocytes develop. This, in turn, causes a violation of the contractility and extensibility of cardiomyocytes and is also partially compensated by the thickening of the LV wall, which preserves its function at the level of the heart chambers. Concentric hypertrophy leads to a decrease in MS. In addition, it is characterized by an increase in the mass of the myocardium of the left ventricle, and this is a prognostically unfavorable factor. LV hypertrophy caused by pressure overload causes more pronounced changes at the structural level (at the level of sarcomeres

and extracellular matrix) than hypertrophy caused by LV overload with increased blood volume. Structural disturbance at the level of sarcomeres and the extracellular matrix is myocardial fibrosis, which can only be determined by myocardial biopsy. This significantly limits the application of this method and requires the use of a multimarker approach to stratification and prediction of patients with AH. It was determined that the LV concentric geometry prevails in hypertension and coronary disease, and eccentric LV hypertrophy prevails in the presence of coronary artery disease and LV systolic dysfunction.

There is an opinion that, unlike concentric hypertrophy, concentric remodeling is accompanied by "volume underload" as a result of "pressure natriuresis". As a result of "volume underloading", obvious LV hypertrophy does not develop.

Such factors are described in the current literature as "myocardial stress markers" or "unloading factors". A detailed study of these factors will make it possible to identify new approaches to optimize treatment and prevent the development of heart remodeling and CHF.

It is believed that hypertension causes LV hypertrophy. The frequency of LV hypertrophy depends on the degree of hypertension and is about 29% of all patients with hypertension. The frequency of detection of hypertrophy is also dependent on the research method. If in patients with I and II degree of hypertension, signs of cardiac hypertrophy are detected in 2-7% of cases according to the ECG results, then according to the echocardiographic method, hypertrophy is detected - in 13-31% of cases in the same group of patients, as well as in 59% of cases in patients with severe and complicated arterial hypertension. It should be noted that the severity of LV hypertrophy is not always correlated with blood pressure figures.

Studies show a weak correlation between the degree of reduction in LV hypertrophy and the degree of BP reduction.

The development of left ventricular hypertrophy is a complex pathogenetic mechanism because its development depends not only on the hemodynamic

volume load but also on the age of the patient, his gender, the presence of obesity, and the duration of hypertension. [4, 64].

The microvascular mechanism of CHF development in comorbid conditions leads to a decrease in the bioavailability of endogenous vasodilators, stimulation of an increase in the activity of oxidative stress, and the formation of dysfunction of the arterial endothelium and endocardium, which in turn is considered as the main condition for the occurrence of microvascular dysfunction of cardiomyocytes. [67, 68].

Dysmetabolic disorders of cardiomyocytes lead to a decrease in the efficiency of the functioning of membrane-dependent ion pumps. This causes a violation of the processes of phosphorylation of the main intracellular enzymes and structural proteins (phospholamban, cyclic guanosine monophosphate (cGMP), protein kinase G, and titin). Intracellular signaling systems are activated and myocardial hypertrophy is formed, associated with an increase in its "stiffness", and a violation of titin phosphorylation leads to a deterioration in the relaxation ability of the myocardium, the occurrence of mechanical dyssynergia and interventricular dissociation. Clinically, this process is manifested by chronic heart failure with preserved left ventricular ejection fraction (LVEF). However, with preserved EF during CHF, global contractile disorders are also observed. Studies show a close relationship between the magnitude of global heart contractility in the form of LV EF and the degree of reduction in the rate of longitudinal and/or circular deformity of the left ventricle, even after correction of diastolic function data (Doppler index, E' and E/Em), LV filling pressure, and circulating level of NT-proBNP [89].

It should be noted that the degree of reduction in longitudinal, radial, and circular deformation of the LV wall does not depend on LV EF and has a predictive value in patients with CHF in matters of cardiovascular death and readmissions. And the dyssynchrony of the global walls of the myocardium in patients with CHF did not depend, according to research data, on the cause of myocardial dysfunction. Early disruption of cardiac dysfunction depends on

“myocardial stiffness”, which results in impaired ventricular diastolic function. As a result, with intact LV EF, mechanical dyssynergia of the walls of the ventricles of the heart develops.

If signs of isolated diastolic disorders appear in the clinical picture, they speak of the formation of diastolic CHF. With further progression of myocardial dysfunction, the mechanical properties of the walls of the ventricles worsen, which leads to a spherical transformation of the heart chambers, disruption of the interventricular relationship, and a decrease in the global LV EF. It is generally accepted that a progressive decrease in LVEF is an indicator of the severity of CHF.

The value of the daily profile of blood pressure in patients with hypertension without and with CHF

Analysis of 24-hour blood pressure monitoring (ABPM) indicators is of great clinical importance. This is due to the prognostic role of the lack of an adequate decrease in blood pressure at night as an independent factor in the death of patients with hypertension.

Both exogenous (smoking, stress, excessive salt intake, physical inactivity, etc.) and endogenous (central, vegetative mechanisms, baroreflex system) factors influence the formation and maintenance of a normal level of the daily blood pressure profile. The relationship between the level of blood pressure and the values of adrenaline, natriuretic peptides, renin, angiotensin II, and noradrenaline was revealed [75]. In patients who have suffered a violation of cerebral circulation, the circadian rhythm of blood pressure is lost, which proves the role of central mechanisms in its formation.

Data from studies of indicators of the daily profile of blood pressure in patients with arterial hypertension and chronic heart failure are few and very contradictory. They suggest that the circadian BP profile in patients with hypertension and CHF can be both changed and preserved.

In patients with CHF, according to M.R. Caruana, there was a decrease in the degree of nighttime decrease in blood pressure. It depended on the severity of CHF, the contractility of the left ventricle, and pressure in the pulmonary artery. In more severe patients with III and IV functional class according to NYHA (n=29), according to the Borne study, there was a violation of the circadian rhythm of blood pressure according to the “non-dipper” type [13].

The same relationship between the violation of the circadian rhythm of blood pressure and the severity of chronic heart failure was revealed by a group of researchers led by T. Giles. According to the results of ABPM, patients were divided into two groups. The first group consisted of patients with CHF II and III functional class according to NYHA, their ABPM profile was "dipper"; the second group included patients with more severe CHF. In patients of the second group, there was no significant decrease in blood pressure and heart rate at night, and no relationship was established between EF and the circadian rhythm of blood pressure [31].

The dependence of the degree of nocturnal decrease in systolic blood pressure in patients with CHF was revealed in another clinical study (n=25; EF - 17%). In 36% of patients, the circadian rhythm of blood pressure was preserved, the remaining 64% of patients were "non-dipper". The control group consisted of patients without CHF (n=25). Of these, 5 subjects were assigned to the non-dipper group. In the group of patients, the decrease in SBP at night was 9±6 mm Hg; in the control group - 18±8 mm Hg. ($p<0.001$). At the same time, no relationship was found between changes in the circadian rhythm of blood pressure and the severity of CHF [80].

The results of the research Institute of Cardiology. A.L. Myasnikov showed that in patients with CHF, sinus rhythm, and no clinical signs of arterial hypertension, the daily ABPM profile was “non-dipper” [42].

According to the Fukuda hypothesis, the diurnal non-dipper profile can be explained by an increase in tubular sodium reabsorption or a decrease in glomerular filtration rate (GFR) during the daytime, therefore, at night, to maintain a diurnal balance of sodium, promoting its excretion, blood pressure rises at night [20].

The above data contradict the results of the study by C. Moroni. In this study, in patients with severe CHF (NYHA class III-IV), the circadian rhythm and BP variability were preserved.The results of the study by S.N. Tereshchenko are similar to the above. S.N. Tereshchenko studied the daily profile of blood pressure in 100 patients with III-IV FC CHF of ischemic origin. In 45% of the subjects with CHF and AH, a decrease in the daily index of SBP (5.5±0.9%) and DBP (7.6±0.8%) was observed, the monotony of the daily curve was recorded, no statistically significant correlations were found between the severity of CHF and circadian rhythm of blood pressure. In normotensive patients with CHF, there were no disturbances in the circadian rhythm of blood pressure.

E. Banker et al. monitored blood pressure and measured urinary electrolyte excretion during the day and night in 325 people of African descent from 73 families. E. Banker's study aimed to study the relationship between the level of nocturnal BP, the degree of nocturnal SBP reduction, and urinary sodium excretion. Multivariate analysis of the data proved the relationship between the concentration of sodium and potassium in the urine during the day and the degree of reduction in SBP at night.

Kimura G. in his studies studied the ratio of sodium excretion during the day and at night in patients with different daily blood pressure profiles [12-13, 20]. In individuals with a normal circadian BP profile, despite increased salt intake, the night/day BP/sodium excretion ratio was <0.9. In patients with insufficient BP reduction at night, the ratio was >1.0, indicating increased sodium excretion at night. Reducing salt intake in these patients resulted in a significant reduction in the night/day BP difference. Thus, it was once again proved that the glomerular filtration rate and tubular reabsorption of sodium are I am the main renal mechanisms that determine the daily profile of blood pressure. Therefore, the degree of nocturnal BP reduction and diurnal profile may be indicative of an impaired glomerular filtration rate. Kimura G suggested that this mechanism is the main one in the development of cardiovascular events in patients with hypertension.

There are no similar data in the literature on the possible mechanisms of the formation of the circadian rhythm of blood pressure in patients with chronic heart failure or scientific studies on the relationship between various types of circadian blood pressure profiles and remodeling of the cardiovascular system. Also, the prognostic possibilities of studying the daily profile of blood pressure in patients with CHF have not been sufficiently studied. There is an opinion that the rigid daily blood pressure curve in patients with CHF is a compensatory-adaptive reaction for the organ protection of the brain, kidneys, and heart from hypoperfusion.

In addition, the non-dipper diurnal profile can also be considered as a violation of kidney function in patients with CHF and one of the main causes of cardiovascular events in this category of patients.

Features of heart rate variability in patients with hypertension without and with chronic heart failure.

The literature provides evidence that sympathicotonia is the main efferent pathway for regulating vascular tone. At the same time, it leads to hemodynamic disturbances, and metabolic and rheological disorders, which lead to a complex mechanism for the development of hypertension, as well as to structural remodeling of target organs [42].

Mortality, including sudden death from cardiovascular causes in patients with hypertension and CHF, is associated with the state of autonomic regulation. Heart rate variability (HRV), being a new method for assessing the state of autonomic regulation, helps to determine the relationship between the incidence of life-threatening arrhythmias and an increase in sympathetic tone and inhibition of the parasympathetic parts of the autonomic nervous system. This method has fairly high reliability and is informative with the relative simplicity of the study.

The balance between sympathetic and parasympathetic influences on the heart is reflected in the changes in the cardiac cycle from contraction to contraction. In carrying out daily Holter monitoring (HM) ECG, an analysis of the variability of R-R intervals is used, which is called heart rate variability. The main methods for assessing HRV in HM ECG are temporal (time-domain) and spectral (frequency domain) methods.

Periodic changes in the frequency of sinus rhythm and their quantitative characteristics are revealed by spectral analysis using special mathematical methods. This makes it possible to assess the degree of vagosympathetic balance. HRV in most studies is analyzed in the following frequency ranges:

1. Power in the high-frequency range (HF) - 0.15-0.40 Hz, which is determined by changes in the parasympathetic division of the autonomic nervous system when breathing at a certain frequency. It increases with rotation and with the influence of cold. This power is considered the main marker of the activity of the parasympathetic division of the autonomic nervous system. But with an increase in sympathetic influences on heart rate variability, it decreases. And this affects the interpretation of the HF results, which makes them not so unambiguous;
2. Power in the low-frequency range (LF) - 0.04-0.15 Hz. It is affected by changes in both the sympathetic and parasympathetic divisions of the autonomic nervous system. They, in turn, are caused by the influence of the mechanisms of baroreflex regulation of vascular tone. It should be noted that in chronic heart failure, the change in LF activity more reflects the state of the sympathetic than the parasympathetic autonomic nervous system;

3. Power in the range of very low frequencies (VLF) - 0.003-0.04 Hz and ultra-low frequencies (ULF) less than 0.003 Hz depends on changes in the activity of the thermoregulation system, the state of the RAAS, the level of adrenaline, norepinephrine, etc. However, the diagnostic significance and impact on the power of this frequency range are not currently determined. It should be noted that in patients with CHF, the power in the VLF range increases.
4. Power ratio of low and high frequencies (LF/HF). According to this ratio, hypersympathicotonia can be judged. However, scientific research and disputes about the diagnostic capabilities of this method still do not stop. Thus, unidirectional changes in the LF range and the LF/HF ratio were not caused by stimulation of P-adrenergic receptors in healthy individuals.

The temporal analysis of HRV is estimated by statistical analysis of changes in the duration of the R-R intervals between sinus beats and the calculation of coefficients. The most commonly estimated standard deviation from the average duration of all sinus R-R intervals. This is the SDNN score. SDNN characterizes heart rate variability, being an integral indicator. It depends on the influence of parasympathetic sympathetic divisions of the autonomic nervous system and is most often used in scientific clinical studies [40].The relationship of HRV with the daily BP profile has been studied in numerous studies. However, the results are inconsistent. Thus, the studies of Kario K. were devoted to the study of HRV in elderly people with hypertension. At the same time, Kario K. et al. noted that at night, the "over-dipper" showed a decrease in the activity of sympathetic trends (LF, VLF), and a decrease in the activity of parasympathetic modulations was detected in the "non-dipper". The studies of Turna E.Yu. and co-authors [42], and Vasilets L.M. and co-authors [31] showed an insufficient decrease in blood pressure at night by an increase in the activity of sympathetic influences. And studies by Kohara K. and co-authors did not reveal the relationship between HRV indicators and daily fluctuations in blood pressure.

Currently, according to the literature, there are not enough data proving the relationship between HRV modulations and other parameters of the 24-hour BP profile (time index, BP variability, and its morning dynamics). The defeat of target organs and increased variability of blood pressure leads to an increase in vascular tone and the development of structural changes in them. Until now, there are disputes about the primacy of target organ damage and the development of structural changes in the vascular wall. So, organic changes in the vascular wall and dysregulation of vascular tone cause more pronounced variability in blood pressure. But the increased variability of blood pressure leads to an increase in tone and the development of organic changes in the vascular wall.

The results of modern studies in patients with CHF prove the importance of HRV. These studies have shown that low values of HRV spectral and temporal parameters are independent predictors of death in patients with CHF [42, 50, 51].

In the works of R. Bilge et al., the severity of CHF was assessed by the level of HRV. These studies suggest that spectral analysis of HRV is capable of characterizing the severity of CHF. Other studies [9, 10, 14] compared HRV in patients with CHF with reduced and preserved left ventricular EF. It was shown that HRV parameters in patients with systolic CHF were lower than in CHF patients with preserved LV EF.

Research data Kryukov N.N. showed that patients with restrictive LV filling differed from patients with other types of diastolic dysfunction. At the same time, more pronounced disorders of autonomic regulation were revealed in them. According to the obtained results, a certain relationship was revealed between heart rate variability and parameters of left ventricular diastolic dysfunction [9,10].

Strengthening the influence of the autonomic part of the sympathetic nervous system, according to the opinion of several authors, reduces early diastolic filling, while vagotonia increases it. However, disturbances in LV diastolic function may inversely cause hypersympathicotonia.

Thus, it can be assumed that the study of the mechanisms of the relationship between LV diastolic dysfunction and HRV parameters will help in further understanding the pathophysiology of hypertension, as well as determining the prognostic role of these parameters in patients with hypertension and CHF.

The study was conducted based on the cardiology department of the 1st clinic of the Samara State Medical Institute. We examined patients with hypertension who were hospitalized. An analysis of our own clinical and laboratory studies was carried out.

The design of the study included two stages: Stage 1: 86 patients with hypertension admitted to the cardiology department of the 1st Sammi clinic were examined. Clinical examination of patients was carried out following the National and European guidelines for the diagnosis and treatment of hypertension and CHF [27, 37, 59, 61]. All examined patients were divided into the following groups:

group 1 - patients with hypertension without CHF (n=36);

group 2 - patients with hypertension with CHF (n=17);

group 3 - patients with CHF without AH (n = 14).

The control group consisted of healthy people comparable in age (n = 80). In addition to the traditional clinical study, including the collection of complaints, anamnesis, examination, and objective studies, all patients underwent biochemical blood tests, ECG, ECG Holter monitoring, Doppler EchoCG, ABPM

Clinical characteristics of patients

Indicators of age, anthropometry, blood pressure, cholesterol, GFR and others are presented in Table 1

Clinical characteristics of the examined groups

Table 1.

Indicators	Control	Group 1	Group 2	Group 3
1	2	3	4	5
Number of patients, n	10	36	17	14

Age, years	54,23 ±1,85	60,93±1,08	58,02±0,50	59,10±2,11
Height, cm	175,37±1,33	173,71±0,78	174,07±0,53	176,67±2,08
Weight, kg	75,67±2,65	84,37±1,39	83,83±1,54	77,94±3,46
BMI, kg/m	24,72±2,03	27,96±2,28	27,41±3,02	25,22±4,05
SBP mm Hg	116,93±1,88	156,15±1,61	160,08±1,88	115,55±1,94
DBP, mm Hg	73,89±1,40	97,99±0,99	97,55±0,97	74,70±1,62
PAD, mm Hg	43,04±1,26	56,94±1,65	62,99±1,39	41.95±1,92
Heart rate, min	66,20±9,68	67,01±8,75	66,85±8,11	69,32±9,79
Cholesterol, mmol/l	3,31±1,13	4,73±1,35	4,67±1,25	4,56±1,16
GFR, ml/min/1.73m2	129,33±12,88	103,8±23,47	87,62±17,31	93,17±16,15
AG experience, years	-	3,04±0,46	6,33±0,41	-
Test-6-MX, m	675±80,8	613,14±63,3	468,17±61,5	422,13±91,5
CHF experience, years	-	-	4,79±0,34	3,27±0,82
FC HSN % -	- -	- -	69% 31%	53% 47%

The study included patients with AH, stage I chronic heart failure, c I and II FC. In the control group, BMI and weight were less than in 3 groups of examined patients. In the group of AH patients with CHF, the duration of AH was longer than in patients of the 1st group.

In group 2, the main cause of CHF development was AH - 17 people. (twenty%). In patients of the 3rd group, which consisted of patients with CHF without AH, the causes of heart failure were coronary artery disease - 14 people. (17%), such as: previous non-Q wave myocardial infarction (NQIM), coronary angiography-proven stable angina pectoris.

Of the patients with hypertension, 77% were taking ACE inhibitors (perindopril); 10% were taking sartans (losartan, valsartan); and beta-blockers (nebivolol) were taken by 65% of patients.

For the treatment of CHF, ACE inhibitors (perindopril) were used in 87% of cases; sartans (losartan, valsartan) - in 10% of patients; adrenoblockers (nebivolol) - 68% of patients were prescribed.

A total of 86 patients with CHF and GB were examined. The diagnosis of the underlying disease was made based on a comprehensive clinical and instrumental study, which included questioning of complaints and anamnesis, objective examination, ECG, echocardiography, ABPM, and Holter ECG study. Laboratory and instrumental research methods were carried out in the laboratory of the SamMI clinic No. 1. Such indicators as a general blood test, and a biochemical analysis with the determination of the level of total cholesterol, and creatinine were determined. An electrocardiographic study was performed on 12 standard leads. ECG was used to determine the signs of coronary artery disease, and the presence of ventricular hypertrophy. An echocardiographic study was performed according to the

generally accepted technique on the AQQUVIX QX apparatus in standard accesses using M- and B-modes, continuous-wave, pulsed, and color Dopplers.

Instrumental research methods. Blood pressure measurement

Arterial pressure was determined by the method of N.S. Korotkov, according to the recommendations of ESH and RKO [210]. The level of SBP and DBP (mm Hg) was determined; the level of blood pressure was >140/90 mm Hg. Art. considered arterial hypertension.

The degree of AH was determined based on the national clinical guidelines of the GNOC (2010) and the recommendations of the ESH/ESC (2013):

I degree of hypertension: SBP - 140-159 and/or DBP 90-99 mm Hg;

II degree of hypertension: SBP - 160-179 and/or 100-109 mm Hg;

III degree of AH: SBP -> 180 and/or DBP> 110 mm Hg.

Pulse arterial pressure (PAD, mm Hg) was calculated by the formula: PBP = SBP - DBP.

Echocardiographic study

An echocardiographic study (EchoCG) was performed after a 10-minute rest at rest following the Guidelines of the American Echocardiographic Society, in the supine position [37–39, 57, 79]. and B-modes, continuous wave, pulsed, and color Doppler.

The following standard quantitative indicators of the left ventricle were calculated: the thickness of the interventricular septum in systole and diastole (TMZhPs/d, cm); thickness of the posterior wall of the left ventricle in systole and diastole (TZSs/d, cm); the final systolic size of the left ventricle (KSR, cm); the final diastolic size of the left ventricle (EDC, cm); end-systolic (ESO, ml) and end-diastolic volume (EDV, ml) of the left ventricle. Volumetric indicators, KSR, and KDR were indexed to the body surface area (iBDO, UK, KR, DR).

The mass of the left ventricular myocardium (MMV, g) was calculated according to the ASE formula: LVMM=0.8+[1.04x(EDR+TMZhPd+T3SLVd)3-KDR3]+0.6 g, where TMZhPd is the thickness of the interventricular septum in

diastole, cm; TZSLZhd - thickness of the posterior wall of the left ventricle in diastole, cm; CDR - the end-diastolic size of the left ventricle, cm[34].

The mass index of the LV myocardium (MVVM, g/m2) was calculated as the ratio of the LVML to the body surface area. The body surface area was calculated according to the D DuBois formula (body surface area in square meters, weight in kg, height in cm. First, the relative wall thickness (RWT) of the left ventricle was determined using the formula AGanau 1992: RW=(TMZhPd+TZSLWd)/RDR.

Patients with normal values of LVMI and with a value of IoT < 0.42 made up the group with normal LV geometry. With a normal value of LVMI and a value of I0T>0.42, patients were assigned to the group with concentric LV remodeling. Patients with LVH and ITI<0.42 were included in the eccentric LVH group, while patients with LVH and ITI>0.42 left the concentric LVH group.

Normative indicators and threshold values of LVMM and geometry of the left ventricle are presented in Table 2.

Normative indicators and threshold values of LVML and geometry of the left ventricle

***Table** 2*

Indicators	Norm	Minor violation	Moderate	Expressed
MMLV, g/m2	88-224	225-258	259-292	≥293
IMMLJ	49-115	116-131	132-148	≥149
TMZhPd, cm	0,6-1,0	1,1-1,3	1,4-1,6	≥1,7
ZSLZhd, cm0	0,6-1,0	1,1-1,3	1,4-1,6	≥1,7
AND FROM	0,24-0,42	0,43-0,46	0,46-0,51	≥0,52

Table 3 shows the normative indicators of the volume of the left ventricle.

Normative indicators of LV volumes

Table 3.

Indicators	Norm	Minor violation	Moderate	Expressed

KDO, ml	67-115	158-178	179-201	≥202
202iKDO, ml/m2	35-75	76-86	87-96	≥97
CSR, ml	22-58	59-70	71-82	≥83
UCSO, ml/m2	12-30	31-36	37-42	≥43

In addition, we calculated the following indicators:

- volume load index (IO, ml/g) IO= EDV/MLV

-minute preload (MP, ml/min) MP=EDV×HR

- LV myocardial stress (MS, g/cm2) MS=0.334×D(CR)/T3SLV(1+T3SLV/CR), where MS is myocardial stress in systole or diastole;

D - systolic or diastolic pressure;

CR is the internal size of the left ventricle in systole or at the end of diastole;

TZSLV is the thickness of the myocardium of the posterior wall of the left ventricle.

Systolic myocardial stress was calculated using the formula:

MSsyst = 0.334 × SBP × TFR/TZSLZhsyst × (1 + (TZLZhsyst/KSR))

Diastolic myocardial stress was determined by the formula:

MSdiast \u003d 0.334 × DBP × EDD / TZSLZhdiast × (1 + (TZLZhdiast / EDD))

the stroke volume of the heart (SV, ml)

UO=KDO-KSO

minute volume (MO, l/min)

MO=SV × HR;

Ejection fraction (EF,%) and anterior-posterior shortening fraction (FU,%) of the LV were calculated according to the formula of L. Teichgoltz1976 [38].

The shortening fraction of medium fibers (FUSV%) was determined using a mathematical model that included CFR, CFR, and left ventricular wall thickness [38]

Inner shell = [(KDR + TMZhPd / 2 + TZSd / 2) 3 - KDR3 + KSR3] 1/3 - KSR FUCF = ([KDR + TMZhPd / 2 + TZSd / 2] - [KSR + inner "shell"])/(KDR+TMZhPd/2+TZSd/2)×100%.

With the help of Doppler echocardiography in pulsed wave mode from the apical access in the four-chamber section of the heart, the diastolic function of the left ventricle was assessed.

According to Doppler sonography, the following was determined:

- ✓ the maximum rate of early filling of the left ventricle (E, cm/s);
- ✓ the maximum rate of late filling of the left ventricle (A, cm / s);
- ✓ the ratio of peak speeds E/A;
- ✓ the deceleration time of the flow of early diastolic filling (DT, ms);
- ✓ isovolumic relaxation time of the left ventricle (IVRT, ms) - the time from the closure of the aortic valve to the opening of the mitral valve (non-invasive index of relaxation of the left ventricle).

Characteristics of the stages of LV diastolic dysfunction according to echodopplerography

Table 4.

Parameter	Relaxation disorder	Pseudonormalization	Restriction
E/A	<1	1-2	>1
DT. Mc	>220	150-200	<150
IVRT,мс	>100	70-100	<70

Note: IVRT - time of LV isovolumetric relaxation, DT - time of deceleration of blood flow of early diastolic filling of the left ventricle, E/A - ratio of the rates of early diastolic filling and filling in atrial systole.

Doppler study was performed against the background of shallow breathing, for at least three cardio cycles, followed by averaging the results. For the diagnosis of diastolic dysfunction, the statement of dilatation of the left atrium is important [23].

The linear dimensions of the left atrium (LA, cm) were determined according to the recommendations of the American Echocardiographic Society. The results obtained were indexed to the body surface area. The following were taken as normative indicators of LP (Table 5):

Normative parameters of LP in men [38]

Table 5.

Indicators	Norm	Minor violation	Moderate	Expressed
LP size, cm	3-4	4,1-4,6	4,7-5,2	≥5,2

From the parasternal approach along the long axis of the left ventricle, the dimensions of the right ventricle (RV, cm) were measured and the condition of the root and proximal aorta (A0, cm) was studied. The LV outflow tract was assessed in B-mode.

We studied total arterial compliance (OAP), which is an indicator of the stiffness of the vascular wall. PDA was calculated using the formula: PDA (ml/mm Hg) = SV /PAD.

Total peripheral vascular resistance (TPVR, Dyn-s-cm-5) was calculated using the following formula:

$$OPSS = ADsr\text{-}80/MO.$$

TPVR indices were indexed in relation to the body surface area.

Ambulatory blood pressure monitoring (ABPM)

24-hour blood pressure monitoring (ABPM) was performed on a 24-hour monitor for automatic measurement of blood pressure and pulse rate of the BAT41 brand, which allows for the oscillometric method of measuring blood pressure.

Monitoring was carried out during the day. The study began from 9:00 am to 11:00 am. The interval from 6:00 to 22:00 was taken as the day period, and the interval from 22:00 to 06:00 was taken as the night period. The interval between measurements in the daytime was 30 minutes, and at night - 60 minutes.

We analyzed the following ABPM parameters:

- 1. The daily index (SI) is the degree of nighttime reduction in blood pressure as a percentage of the corresponding daily indicator.

SI was calculated using the formula:

SI \u003d (ADd - ADn) x 100% / Add

where BPD is the average pressure during wakefulness, and ABP is the average blood pressure during sleep.

According to the degree of nocturnal BP reduction, patients differed in the following groups:

- "dipper", in which the normal physiological decrease in blood pressure is 10-20%
- "non-dipper", in which the decrease in blood pressure is 0-10%
- "night-peaker" with a nocturnal increase in blood pressure
- "over-dipper", in which the decrease in blood pressure is more than 20%.

- 2. Pulse pressure is the difference between SBP and DBP values. The mean BP was considered normal when the mean value was <46; borderline, or presumably elevated - with a value > 46; and at a value of > 53, it was assessed as undoubtedly increased.

We also studied the indicators of "pressure load" - the time index (TI), the measurement index (II), and the area index (AI) of hypertension. The time index (TI) is the percentage of time during which the BP threshold is exceeded. The measurement index (MI) is the percentage of measurements from the total number at which blood pressure values are beyond the threshold level. The area index (AI) is the area of the figure bounded above by the BP curve, and below by the line of BP threshold values. The normalized area index (IP) is taken equal to the ratio of the traditional area index to the time of analysis: IPn=IP/T. In this case, T is the pressure load analysis time. According to the Recommendations of the American Hypertensive Society in healthy individuals, the upper values of IV are the same for daytime and nighttime and do not exceed 15%. With IV values up to 30%, they are regarded as possibly increased, and undoubtedly increased with a VI value of more

than 30%. If the IV value (day and/or night) is more than 50%, then they speak of stable arterial hypertension.

According to studies by E. O'Brien and J. Staessen 1995, in healthy people, the values of IV SBP < 20% during the day and <10% at night, IV DBP < 15% during the day and < 10% at night, per day time index for systolic and diastolic blood pressure is less than 25%.

- 3. The value of the morning rise (PM) - is the difference between the maximum and minimum values of blood pressure in the period + 2 hours from the time of awakening and rise. The most informative indicator is the rate of morning rise in blood pressure. The rate of morning rise in blood pressure is the ratio of the value of BP to the time of the rise in blood pressure. There are normative values for indicators of the morning rise in blood pressure, but they are advisory in nature. So, the value of the morning rises in SBP < 56 mm Hg. Art., DBP < 30-36 mm Hg. The rate of morning rise in SBP < 10 mm Hg/hour, DBP < 6 mm Hg. st / hour.

Holter ECG monitoring

24-hour ECG monitoring allows for continuous recording of ECG changes during the day under the conditions of the patient's normal activity. Heart rate variability (HRV) was assessed using time and frequency domain analysis methods. Holter monitoring of the ECG was performed using the KR-01 monitor system manufactured by CARDIAN (Republic of Belarus) [24, 27, 40, 49].

When studying the time analysis of HRV, we studied the following indicators:

-SDNN is the standard deviation from the average durations of all sinus R-R intervals;

-SDANN is the standard deviation from the average durations of all sinus R-R intervals calculated for all 5-minute sections of the ECG recording;

-RMSSD - represents the mean square difference between the duration of adjacent sinus R-R intervals;

-pNN50 is the percentage of consecutive NN intervals that differ by 50ms or more.

In the study of spectral analysis of heart rate variability (HRV), or indicators such as:

1. LF, ms2 is the power of the frequency components in the low-frequency range (0.04-0.15 Hz);
2. HF, ms2 is the power of the frequency components in the high-frequency range (0.15-0.4 Hz);
3. VLF, ms2 is the power of the frequency components in the very low-frequency range (0.003-0.04 Hz);
4. nHF, % is the normalized power in the high-frequency range (HF (Total –VLF)) x 100%;
5. LF/HF is the ratio of power in the low-frequency range to the power in the high-frequency range

Determination of the stage of chronic heart failure

Determination of the stage of chronic heart failure was carried out on the basis of the National recommendations of the RSC and societies of specialists in heart failure (CHF) for the diagnosis and treatment of CHF (IV revision, 2013), comments on the classification of CHF [27].

1. Asymptomatic LV dysfunction (corresponds to stage I).

At the same time, there are no clinical manifestations of CHF at rest and during normal exercise. At this stage, systolic dysfunction of the left ventricle is observed, with the value of LV EF <45% and/or the value of the final

diastolic size (EDD) LV>5.5 cm (iEDD LV>3.3 cm/m). Diastolic dysfunction of the left ventricle can manifest itself in the hypertrophic type of the spectrum of the transmitral flow (E / A <1.0), as well as VTRV + TZSLV ÷2> 1.3 cm and/or TZSV> 1.2 cm. In this case, the index of relative thickness left ventricular wall IoT is more than 0.42 and the value of the sphericity index is less than 0.70.

2. Adaptive remodeling (corresponds to stage II A)

At the same time, there is a clinical manifestation of symptoms corresponding to the definition of stage II A of CHF and signs of systolic dysfunction (see the stage

I). Diastolic dysfunction is expressed in the pseudo-normal spectrum type of the transmitral Doppler flow (E/A >1.1 and <2.0). At the same time, the value of the index of the relative wall thickness of the left ventricle is IOT >0.30 and <0.42, and the sphericity index exceeds 0.70.

3. Maladaptive remodeling (corresponds to stage II B)

The clinical manifestation of symptoms corresponds to stage II B of CHF and echocardiographic signs of LV systolic dysfunction are detected in the form of a decrease in LV EF. Diastolic dysfunction of the heart is detected in the form of a restrictive type of the spectrum of the transmitral Doppler flow when the E/A ratio >2.0. In this case, the IoT value is less than 0.30 and the value of the sphericity index is more than 0.80.

Features of the geometry of the heart and central hemodynamics in patients with arterial hypertension in stage I chronic heart failure.

Indicators of geometric measurements of the heart are important in the study of the function of the left ventricle in the norm and in the process of its remodeling in arterial hypertension. An early sign of the onset of remodeling is the loss of the physiological original shape of the heart. This may serve as a trigger for the development of CHF. [16].

We have analyzed the structural parameters of the heart in the studied groups of patients. The 1st group of patients with hypertension were without signs of CHF compared with the control. LVMI (p=0.004) with thickening of the walls in the absence of a pronounced expansion of its cavity. At the same time, the revealed structural changes in the heart in patients of this group did not exceed the normal values recommended for EchoCG studies [38, 39].

In patients of the 2nd group (with hypertension and CHF (group 2), compared with control and patients with hypertension, an increase in the size of the left atrium and right ventricle, a significant increase in LV MM with thickening of its walls was detected. At the same time, there was no pronounced expansion of the LV cavity, but there was a statistically significant trend toward its dilatation (p<0.001).

Values of volume indicators of the left ventricle increased from the control group to the group of AH with CHF. Thus, CSR and CSR in patients 1-st group increased by 17%, in patients of the 2nd group by 74% compared with the control; EDV and EDV of patients of the 1st group increased by 6%, in patients

group 2 by 27% compared with the control ($p<0.001$).

Thus, in the examined groups 1 and 2 (patients with AH), in the dynamics of the development of CHF, a significant increase in preload was observed.

Echocardiographic parameters of patients with AH (groups 1 and 2)

Table 6.

Indicators	Control n=10	Group 1 n=36	Group 2 n=17
1	2	3	4
LP, cm	3,28±0,06	3,46±0,03	4,17±0,04
DAC, cm	3,23±0,06	3,44±0,04	4,01±0,06
uKSR, cm	1,71±0,04	1,75±0,02	1,94±0,03
KDR, cm	5,13±0,06	5,26±0,04	5,66±0,05
uKDR, cm/m2	2,70±0,04	2,67±0,03	2,73±0,03
CSR, ml	42,37±1,88	49,65±1,31	73,86±2,70
UCSO, ml/m2	22,73±1,09	25,19±0,73	35,36±1,29
KDO, ml	126,13±3,63	134,01±2,56	160,18±3,25
ECDO, ml/m2	65,59±1,78	66,81±1,44	76,76±1,51
ZSS, cm	1,30±0,02	1,36±0,01	1,40±0,02
ZSD, cm	0,83±0,01	0,90±0,01	1,03±0,02
MZhPd, cm	0,84±0,01	0,90±0,01	1,05±0,02
MZHPS, cm	1,29±0,02	1,36±0,01	1,40±0,02
LVMI,	93,38±2,42	106,59±2,64	143,58±3,65

g/m2	180,03±6,56	212,68±5,61	293,54±8,05
MMLV, g	0,33±0,00	0,34±0,01	0,38±0,01
AND FROM	2,47±0,03	2,60±0,02	2,78±0,02

We carried out a comparative analysis of the echocardiographic parameters of the examined patients of the 1st and 3rd groups in order to study the influence of etiological factors on the structural remodeling of the heart. (table 7). Echocardiographic parameters of patients in patients of the 1st and 3rd groups.

Table 7.

Indicators	Group 1 n=180	Group 3 n=74
LP, cm	3,46±0,03	3,95±0,16
DAC, cm	3,44±0,04	3,78±0,17
ICSR	1,75±0,02	1,92±0,09
KDR, cm	5,26±0,04	5,32±0,13
uKDR, cm/m2	2,67±0,03	2,76±0,09
CSR, ml	49,65±1,31	63,11±6,62
UCSO, ml/m2	25,19±0,73	30,07±3,31
BWW, ml	66,81±1,44	71,32±4,22
ZSS, cm	1,36±0,01	1,26±0,03
ZSD, cm	0,90±0,01	0,88±0,01
MZhPd, cm	0,90±0,01	0,93±0,04
MZHPS, cm	1,36±0,01	1,26±0,03
LVMI, g/m2	106,59±2,64	111,71±4,49
MMLV, g	212,68±5,61	212,97±10,35
AND FROM	0,34±0,01	0,34±0,01
PZh, cm	2,60±0,02	2,81±0,08

Comparative analysis of echocardiographic parameters in patients with AH (Group 1) compared with AH patients without CHF (Group 3) revealed thickening of the LV wall: VCs (p=0.002), IVS (p=0.008). At the same time, there was no statistically significant difference in the parameters of LV myocardial mass (p=0.948): LVMI (p=0.290), IOT (p=0.550). In patients of the 3rd group, compared with patients of the 1st group, there was an increase in the size of the left atrium (p=0.003) and the right ventricle (p=0.004).

In patients of the 3rd group (CHF without AH), when analyzing the volume parameters of the left ventricle, a statistically insignificant increase in ESV, uESO, EDV, uODV was observed (p>0.05).

In order to study the effect of hypertension on the structural remodeling of the myocardium, we carried out a comparative analysis of EchoCG parameters in patients of the 2nd and 3rd groups. (table 8)

Results of echocardiography of patients in groups 2 and 3

Table 8.

Icdicators	Control n=10	Group 2 n=17	Group 3 n=14
LP, cm	3,28±0,06	4,17±0,04	3,95±0,16
DAC, cm	3,23±0,06	4,01±0,06	3,78±0,17
uKSR, cm/m2	1,71±0,04	1,94±0,03	1,92±0,09
KDR, cm	5,13±0,06	5,66±0,05	5,32±0,13
uKDR, cm/m2	2,70±0,04	2,73±0,03	2,76±0,09
CSR, ml	42,37±1,88	73,86±2,70	63,11±6,62
uXO ml	22,73±1,09	35,36±1,29	30,07±3,31
BWW, ml	126,13±3,63	160,18±3,25	140,58±7,81
ECDO, ml/m	65,59±1,78	76,76±1,51	71,32±4,22
ZSS, cm	1,30±0,02	1,40±0,02	1,26±0,03
ZSD, cm	0,83±0,01	1,03±0,02	0,88±0,01
MZhPd, cm	0,84±0,01	1,05±0,02	0,93±0,04

MZHPS, cm	1,29±0,02	1,40±0,02	1,26±0,03
LVMI, g/m2	93,38±2,42	143,58±3,65	111,71±4,49
MMLV, g	180,03±6,56	293,54±8,05	212,97±10,35
AND FROM	0,33±0,00	0,38±0,01	0,34±0,01
PZh, cm	2,47±0,03	2,78±0,02	2,81±0,08

It was found that the presence of arterial hypertension had a significant impact on the development of cardiac remodeling in patients with CHF. So, in patients of the 2nd group (AH + CHF), there was a statistically significant increase in the value of EDR ($p=0.028$), IOT ($p=0.045$), LVMM ($p<0.001$), iMMLV ($p<0.001$), and tendency to increase in the size of the LA ($p=0.059$) in comparison with patients of the 3rd group (CHF without AH).

It was found that the volumetric parameters of the left ventricle (ESV and uESV) ($p=0.037$) in patients of the 2nd group were statistically significantly higher than in patients of the 3rd group: by 17% EDV and uVDV ($p>0.05$) by 7% respectively. One of the indicators reflecting the structural remodeling of the heart is ECDO. EDV (ml/m) is a parameter that reflects the amount of blood (ml) that is contained at the end of the diastole of the left ventricle at the end of diastole per unit of body surface area. This indicator also reflects the diastolic filling of the left ventricle. The value of KSO is affected by the value of BWW and the degree of shortening of myocardiofibrils.

In our study, the values of EDV were increased in all examined patients compared with the control group ($p<0.05$). At the same time, in patients of the 2nd group (AH + CHF), EDV was the highest and statistically significantly higher than in the 1st group ($p<0.001$). There were no differences in the values of EDV between the 1st and 3rd, as well as the 2nd and 3rd groups ($p=0.30$).

The main reason for the expansion of the cavity of the left atrium is volume overload. An increase in the size and volume of the LP leads, in turn, to various adverse outcomes. In addition, dilatation of the LA cavity is a kind of indicator of the severity and duration of diastolic dysfunction, as well as the degree of pressure increase in the

left atrium [23]. In our study, the greatest expansion of the LA cavity in comparison with other groups was detected in patients of the 2nd group (AH+CHF).

To clarify the predominance of pre- or afterload in the development of structural changes in the myocardium, in all examined groups, we calculated systolic and diastolic myocardial stress. Myocardial stress (MS) is an indicator of pre- and afterload on the LV myocardium [38, 79]. So, at the end of systole, MS reflects afterload, and at the end of diastole, it reflects preload.

Our studies showed that in patients of the 1st group, preload prevailed compared with the control ($p<0.0001$), group 2 ($p<0.015$), and group 3 ($p<0.001$). In the examined patients of the 2nd group (AH+CHF), an increase in both post- and preload was observed in comparison with the control ($p<0.0001$) and patients of the other groups ($p<0.001$). According to literature sources, it is known that afterload is caused by both pulse and vascular BP components [39]. The values of MSsyst, LVMM, IoT, RV depend on the duration of AH. At the same time, the duration of AH increases MSsyst, LVMM, IOT, RV and is inversely related to AI and MS diasts (Table 9). There was also a relationship between the degree of AH and MSsyst ($r=0.541$; $p<0.001$).

The relationship between the duration of hypertension and echocardiography parameters

Table 9.

Indicators	Duration AΓ
MSsist, g/m2	r=0,484; p=0,015
MSdiast, g/m	r=-0,170; p<0,001
MMLV, g	r=0,434; p<0,001
AND FROM	r=0,261; p=0,001
LVMI, g/m2	r=0,478; p=0,001
LP, cm	r=0,476; p=0,001
AND ABOUT	r=-0,354; p=0,001
PZh, cm	r=0,434; p=0,001

When conducting a correlation analysis of EchoCG parameters in patients of the 1st group, a relationship was revealed between the degree of AH and MSsyst (r=0.429; p=0.001), MSdiast (r=0.434; p=0.001); duration of AH and LVMM (r=0.329; p=0.04), AI (r=-0.322; p=0.04).

When conducting a correlation analysis of EchoCG parameters in patients of the 2nd group, a relationship was found between the functional class of CHF and LP (r=0.462; p=0.001), LVM (r=0.353; p=0.004), and LVM (r=0.386; p=0.001).

Important in the development of structural changes is the indicator of the predominance of LV hypertrophy over its dilatation. This is defined as the ratio of EDV / LVML or the volume load index (IV, ml / g). Statistical analysis of the data obtained by us showed that the AI value was reduced in all studied groups compared to the control group. Thus, in patients of the 1st group, there was a decrease in AI by 8.37% (p=0.002), in the examined patients of the 2nd group by 17.3% (p<0.001), in the 3rd group by 7.09% (p=0.029) in comparison with the control group, i.e. in these patients, LV hypertrophy predominated. A statistically significant maximum decrease in AI was found in patients of the 2nd group in comparison with patients of the 1st group (p=0.002).

The development of structural-geometric myocardial remodeling in patients with AH is associated with both the duration of AH and hemodynamic parameters (OPS, MP, PDA) [33].

In our study, we also analyzed the following hemodynamic parameters: minute preload (MP), total arterial compliance (OAP), and total peripheral resistance (OPS).

The indicator of minute preload (MP) differed in all studied groups. Thus, MP was increased in the examined patients of the 2nd and 3rd groups in comparison with the control (p<0.001 and p<0.044, respectively) and in comparison with the 1st group (p<0.001; p=0.268). At the same time, there were no differences in MP in patients of the 2nd group in comparison with the 3rd group (p = 0.186).

We found an increase in total peripheral resistance (TPR) in patients of the 1st and 2nd groups (with AH) in comparison with the control group (p=0.036 and p<0.001) and patients of the 3rd group (p=0.049 and p <0.001).

Total arterial compliance (OAP) was low in patients with AH (groups 1 and 2), but no statistically significant differences were found in comparison with the control group (p>0.05).

We have calculated and studied the indicator MSS/uKSO. This indicator reflects the degree of participation of the LV cavity dilatation in compensation, the increasing load on the myocardium as a result of the development of CHF and connects the contractile function and LV geometry.

Myocardial hypertrophy often compensates for the development of CHF. In our study, the ratio of MSS/uCSO was the highest in patients of the 1st group. In view of the fact that the type of LV remodeling is associated with an increased risk of developing cardiovascular complications, we studied the features of the geometry of the LV myocardium in patients in groups with AH.

Thus, the distribution of types of left ventricular remodeling in the examined patients is presented in Table 10. It follows from the table that in patients of the 1st group, normal geometry of the heart prevailed, in patients of the 2nd group, both normal geometry and hypertrophy were detected equally. LV (concentric and eccentric LVH).

Types of LV remodeling in groups 1 and 2.

Table 10.

Geometry of the left ventricle	Group 1 n=36	Group 2 n=17
Geometry not changed	71%	33%
Concentric remodeling	14%	2%
Concentric LVH	8%	31%

Eccentric LVH 7% 34%

It is known that with concentric remodeling, almost normal MS, an increase in total peripheral vascular resistance (OPS) and a decrease in stroke (SI) and cardiac (CI) indices are observed. Concentric LV hypertrophy is characterized by an almost normal systolic MS, an unchanged shape and normal size of the left ventricle, an increased OPS, and a slight increase in CI. Eccentric LVH in patients is characterized by a high SI value, a normal OPS value, an expansion of the LV cavity, and an increase in end-systolic MS.

We have studied the features of hemodynamics in patients with hypertension, depending on the types of remodeling (table 11).

Peculiarities of Hemodynamic Parameters in Different Types of Structural Myocardial Remodeling in Patients with Hypertension

Table 11.

Show	Norm n=11	Concentric remodeling n=27	Concentric LVH n=41	Eccentric LVH n=42
ECDO, ml/m2	64,36±9,37	63,63±7,01	58,89±11,78	77,37±11,66
MP,	82,49±1472,57	91,63±1898,71	82,90±1592,88	66,26±1848,26
ml/min	2,24±0,52	1,03±0,53	1,06±0,28	1,68±0,56
OAP	17,82±182,99	1925,88±365,71	2295,35±856,40	1474,62±327,54
ml/mmHg)	170,70±29,92	211,44±24,99#	184,11±32,87	196,37±34,05
OPS, dyn-s-cm-5	212,12±37,32	211,77±44,33	180,18±30,89	219,98±31,82
MSsist, g/cm2	7,51±1,74	6,97±0,55	8,18±2,12	6,42±1,26

In our study, in patients with AH with concentric remodeling, in comparison with normal heart geometry, an increase in MCsyst ($p<0.001$) and OPS ($p<0.001$) was observed; compared with concentric LVH, MSsist and MSdiast were increased. ($p<0.001$);

In patients with concentric LVH, in comparison with the control group, an increase in MSsyst was detected. ($p<0.001$). In comparison with patients of other groups, there was a decrease in MSdiast ($p<0.05$). Differences in the values of EDV, MP, PDA, OPS, and MSsyst/iKSO in patients with concentric remodeling and concentric LV hypertrophy were not revealed in the intergroup comparison. ($p>0.05$);

In patients with an eccentric type of heart geometry, an increase in EDV was observed, it was statistically significantly different from the control group ($p<0.001$), patients with concentric remodeling ($p<0.009$), and concentric hypertrophy ($p<0.001$) of the LV. Minute preload was increased, and OPS was reduced in comparison with patients of other groups ($p<0.05$).

Relative arterial compliance was increased compared to concentric LV hypertrophy. There were no changes in the values of MSdiast., MSsist/uKSO, MSsist. was increased in comparison with the control group ($p<0.05$). There was a decrease in MSsyst/uCSO in comparison with concentric LV hypertrophy ($p<0.009$).

When calculating the values of total arterial compliance, OPS, and AI, the EDV indicator is used, which shows the volume of blood (ml) contained in the cavity of the left ventricle at the end of the diastole. In patients with a concentric type of LV remodeling, in contrast to concentric hypertrophy, there is a “volume underload” of blood, possibly due to “pressure natriuresis”. At the same time, in response to volume underloading, obvious LV hypertrophy does not develop.

In the course of the study, we assessed the functional characteristics of the myocardium of patients based on the results of echocardiography. In accordance with the inclusion criteria in the examined patients, LV systolic function was preserved in all patients. When analyzing the values of EF and FU, it was

revealed that in patients of the 1st group, in comparison with the control, the EF and FU indicators were lower by 5% (p=0.001) and 6% (p<0.0001), respectively; in patients of the 2nd group it was reduced by 16% (p=0.003) and 21% (p<0.0001); and in patients of the 3rd group, the decrease was 15% (p=0.001) and 17% (p=0.001), respectively. The greatest decrease in the values of EF and FU was noted in patients of the 2nd group and, at the same time, it differed statistically significantly in an intergroup comparison with patients of the 1st group (p<0.0001).

Stroke (SV) and minute (MO) LV volumes did not differ from the control group and in intergroup comparison (p>0.05). This fact confirms the preservation of LV systolic function in the examined patients.

We studied the parameters of LV systolic function in patients with various types of cardiac remodeling.

At the same time, the LV ejection fraction in patients with concentric myocardial remodeling was reduced in comparison with patients with normal heart geometry (p<0.05) and was comparable in patients with concentric and eccentric LV hypertrophy in an intergroup comparison and in comparison with patients with normal heart geometry. (p>0.05).

When comparing patients with concentric remodeling and LV hypertrophy, it was noted that the FU of medium fibers (MFSF) of the myocardium was statistically significantly less in comparison with patients with normal geometry and eccentric type of LVH (p<0.001). The greatest decrease in the FUSF value was observed in patients with the concentric remodeling in the AH groups (groups 1 and 2) and LVH in the 3rd group.

Analysis of the results of the study of LV diastolic function (Table 10) in the examined groups showed that all patients showed a decrease in the ratio of peak velocities in the early and late filling of the LV (E/A) compared with the control group. Thus, in patients of the 1st group, this decrease was 13.71% (p=0.007), in patients of the 2nd group - 43.86% (p<0.0001), and in patients of the 3rd group - 35, 72% (p<0.0001).

A decrease in the E peak, an increase in the amplitude of the Ai peak, respectively, and a decrease in the E/A ratio indicated a violation of diastolic function in the form of delayed LV relaxation, which led to a redistribution of diastolic filling in favor of the atrial component. (table 10).

Results of EchoCG study of LV diastolic function

Table 10.

Show	Control n=10	Group n=36	Group 2 n=17	Group 3 n=14
max E, m/s	75,20±3,19	65,11±1,77	46,66±0,98	57,55±3,71
max A, m/s	44,67±1,51	45,33±0,71	55,25±1,34	54,45±3,26
E/A	1,68±0,08	1,45±0,04	0,96±0,05	1,08±0,08
DT, ms	205,12±3,08	210,11±2,12	235,19±4,15	228,32±3,08
IVRT, ms	72,23±2,03	71,11±1,65	115,75±3,35	102,26±4,14

During the study, certain differences in the contribution of risk factors to LV remodeling were identified. Thus, the age of patients increased TFR (r=0.254; p<0.001), myocardial mass (r=0.374; p<0.001), LVMI (r=0.416; p<0.001), and decreased EF (r=-0.458; p <0.001) and FUSF (r=-0.524; p<0.001), E/A ratio (r=-0.402; p<0.001), GFR (r=-0.414; p<0.001). BMI was correlated with LA size (r=0.514; p<0.001), LVMI (r=0.610; p<0.001), and LVMI (r=0.403; p<0.001).

There was a relationship between the functional state of the kidneys and GFR and the left atrium (r=-0.256; p=0.034), IO (r=0.252; p=0.035), EF (r=0.245; p=0.043), FUSF (r=-0.296; p=0.014), E (r=0.390; p=0.009), A (r=-0.344; p=0.024).

Multivariate cluster analysis was performed to identify the correlation of the contribution of changes in the structural state of the heart in patients with AH (LA, LVMI, LVMI, IoT) to the development of stage I chronic heart failure.

Cluster analysis was carried out in several stages: preparatory, hierarchical analysis with the construction of a dendrogram, and the stage of dividing patients into clusters using the McKean k-means method.

At the first, preparatory stage, variables were preliminarily standardized, according to which further division into clusters was carried out. The LVML value is expressed in hundreds (100-300), the LA dimensions in units (3-5), and the IoT value in tenths (0.3-0.4). In this case, the main contribution to the distance between objects will be given by indicators with the highest values.

Standardized variables have zero mean (mean) unit variance.

Stage 2 of clustering included a hierarchical analysis with the construction of a dendrogram. In this case, the Euclidean distance was used as a metric and the Ward method was used to combine cluster objects into larger clusters. At stage 3, all patients with AH (groups 1 and 2) were divided into 4 clusters using the McKean k-means method.

Increased LVH and cardiac remodeling in hypertensive patients were associated with diastolic disturbances. Based on the analysis of the graph of the location of the centroids, it can be assumed that not only an increase in LVML but also a pronounced increase in LV IOTS (concentric remodeling and LVH) was associated with the progression of CHF.

The division into clusters is characterized by a different percentage of cases of isolated AH and combined AH with stage I CHF:

- 1 cluster - CHF in 95% of cases
- 2 cluster - CHF in 85% of cases
- 3 cluster - CHF in 35% of cases
- 4 cluster - CHF in 65% of cases

With the help of the analysis of variance, we compared the results of echocardiography in selected clusters.

In patients of cluster 1, a pronounced increase in the mass of the left ventricular myocardium (412.61±16.19 g), iMLV (198.09±6.52 g/m2), a moderate increase in the linear dimensions of the left ventricle (4.47±0.10 cm), IOT (0.42±0.01), the slight increase in LV volumes: EDV (180.53±6.54 ml), iEDV (83.21±2.56 ml/m2), ESV (82.26± 4.39 ml), uKSO (38.12±2.02 ml/m2). The value of the MCs/uKSR ratio was the lowest in this cluster. This indicator links contractile function and LV geometry and reflects the degree of participation of LV cavity dilatation in compensation, which increases as a result of CHF development, the load on the myocardium (5.62±0.23) ($p<0.001$).

In patients of cluster 2, a moderate increase in the mass of the left ventricular myocardium (LVML 279.75±4.53 g), a slight increase in the size of the LA (4.17±0.04 cm), EDV (164.72±3.40 ml), ECDO (78.33±1.99 ml/m2), ESV (76.20±2.80 ml), uESV (36.53±1.48 ml/m2), normal IOI (0.36±0, 01);

Cluster 3 was characterized by a normal mass of the left ventricular myocardium (201.84±3.31 g), LVMI (102.05±1.51 g/m2), LA (3.46±0.03 cm), IOT (0.34 ±0.01), LV volumes: EDV (132.12±2.05 ml), iEDV (66.85±1.13 ml/m2), ESV (48.24±0.98 ml), iESV (24 .63±0.52 ml/m2), MCs/uKSO - 7.76±0.15.

Cluster 4 patients were characterized by a moderate increase in LVMM (247.60±23.20 g), and LVMM (135.00±13.74 g/m2), a significant increase in the IOT value (0.61±0.05), normal LA sizes (3.72±0.03 cm), normal BWW volumes (104.12±11.58 ml), uCDV (46.07±5.63 ml/m2), CVD (37.78±4.82 ml), uCVD L (16.19±3.17 ml/m), as well as the highest ratio of MCs/uKSO - 10.68±1.29.

Analysis of the data obtained, taking into account the classification of types of LV remodeling, showed that a very high risk of developing stage 1 CHF (95%, 85%, and 65%) in clusters 1, 2, and 4, respectively, is due to different types of myocardial remodeling. So, in the 1st cluster - patients with the concentric type of LVH prevailed, in the 2nd cluster - the predominance of patients with eekscentric type of LVH, and in the 4th cluster, it was characterized by concentric LV remodeling. A decrease in the ratio of MSS / uKSO and dilatation of the LA in patients of the 1st cluster shows the degree of participation of the dilatation of the cavity of the LV and LA in compensating for the load on the myocardium and increasing intraventricular pressure. The load on the myocardium and the increase in intraventricular pressure, in turn, accompanied the development of CHF.

Characteristics of indicators of daily monitoring of blood pressure in patients with hypertension and CHF

In our study, we studied such indicators of ABPM as: daily index of SBP and DBP, pulse pressure, indicators of "pressure load": time index, measurement index, area index of hypertension. These indicators were studied in the group of patients with isolated course of arterial hypertension and in combination with chronic heart failure.

In the majority of patients of the 1st group (AH without CHF), according to ABPM data, a two-phase rhythm of SBP and DBP (“dipper”) was observed

(Table 11). At the same time, an insufficient decrease in SBP and DBP (“non-dipper”) was noted in 20% of cases.

Circadian profile of patients of the 1st (AH) and 2nd (AH+CHF) groups

Table 11.

SI DA	Group	Dipper %	Non-dipper%	Night-Peaker %	Over-dipper%
SAD	Group 1 (n=36)	80% (n=29)	20% (n=7)	-	-
	Group 2 (n=17)	33% (n=6)	44% (n=7)	2% (n=1)	21% (n=3)
DAD	Group 1 (n=36)	80% (n=29)	20% (n=7)	-	-
	Group 2 (n=17)	21% (n=4)	51 (n=9)	14 (n=2)	14 (n=2)

In the 2nd group of patients, the daily BP profile was not homogeneous in terms of SBP and DBP values. In the daily profile of SBP, both "dipper" - 33% and "non-dipper" - 44% were equally encountered. An excessive decrease in blood pressure at night ("over-dipper") was observed in 21% of cases, and "night-peaker". - in 2% of cases. The daily profile of DBP was dominated by patients with "non-dipper" (51%), and "dipper" accounted for 21%. Excessive decrease and increase in DBP at night were equally noted - "over-dipper" and "night-peaker" - 14%.

According to studies, the natural circadian rhythm of blood pressure is influenced by external and internal factors. External factors include smoking, alcohol abuse, and eating salty foods. Internal factors include mental and physical activity, age, and sleep-wake periods. In persons older than 70 years, the nocturnal decrease in blood pressure becomes less pronounced or disappears [8, 19].

The day-night pressure drop decreases as arterial hypertension progresses. At the same time, evening-night and evening variants of the circadian rhythm, which are characteristic only of AH, arise. Until now, the mechanism of insufficient decrease in blood pressure at night has not been finally established. At the same time, there is an assumption that two groups of factors play a leading role - hyperactivation of the sympathetic nervous system and an increase in the volume of circulating blood as a result of its redistribution in the vascular bed.

There is a linear relationship between mortality from CVD complications and the degree of BP reduction at night. Thus, a 5% increase in the night/day ratio is associated with a 20% increase in the risk of death. Moreover, this ratio exists even in cases where the average values of blood pressure for 24 hours do not exceed the norm.

It should be noted that the absence of an adequate decrease in blood pressure at night in patients with AH is accompanied by an increase in LVMI, the development of myocardial hypertrophy, the severity of microalbuminuria, and a higher incidence of cerebrovascular events [3, 19, 30, 83].

We carried out a correlation analysis between the values of SI ABPM and echocardiographic parameters. At the same time, a statistically significant relationship was found between SI SBP and LA sizes.

In the formation of the circadian rhythm of blood pressure, a special role is assigned to neurohumoral systems. The correlation between the level of blood pressure, the level of noradrenaline and angiotensin II, and the activity of plasma renin was studied. It is known that the level of vasoactive hormones is of some importance for increasing the level of blood pressure in the early morning hours.

The loss of the circadian rhythm of blood pressure in stroke patients and the strong relationship between diurnal fluctuations in blood pressure and the biorhythms of the sleep-wake cycle confirms the role of central mechanisms. According to K. Stolarz et al. [42, 55], The pathogenesis of nocturnal BP reduction includes a decrease in the activity of the sympathetic nervous system and an increase in the excretion of sodium ions.

The sympathetic nervous system has a direct effect on the direct mechanisms of increasing blood pressure, such as vasoconstriction of resistive vessels with an increase in OPS and an increase in cardiac output. In addition, the sympathetic nervous system has an indirect effect through the spasm of the kidney vessels, and activation of the renin-angiotensin II-aldosterone system [91].

When analyzing the level of pulsed arterial pressure, a borderline increase in the indicator was revealed in patients with hypertension in comparison with the norm and with the control group (p=0.049). An intergroup comparison of the level of PAD did not reveal significant differences (p=0.77).

An increase in PBP due to a decrease in the elasticity of the walls of blood vessels is associated with damage to target organs and is a serious risk factor, especially in patients of the older age group [7, 29, 41]. In our study, age over 85 years was the exclusion criterion. According to the results of the PIUMA study, with a decrease in PBP of less than 53 mm Hg. reduces the risk of cardiovascular mortality by more than 6 times [28].

Correlation analysis revealed a relationship between the values of PAP and iKDR (r=-0.570; p=0.005), TSd (r=0.381; p=0.003), VSd (r=0.343; p=0.02), IVSd (r= 0.363; p=0.01), EDV (r=-0.310; p=0.04), MOT (r=0.407; p=0.008), E/A (r=-0.422; p=0.02), MSdiast (r=-0.329; p=0.031), MO (r=-0.602; p=0.001), NT-proBNP (r=-0.477; p=0.025), triglycerides (r=0.429; p=0.035).

In order to quantify the time during which increased blood pressure is recorded, indicators of “pressure load” were developed: hypertensive time index, measurement index, and area index of hypertension. The hypertensive time index (MT) and the normalized area index (MPT) are used to quantify the magnitude of the pressure load on the target organs. They have a high degree of correlation with target organ damage. With an increase in average blood pressure, MV approaches 100% and ceases to reflect the load on target organs. This is the so-called “saturation effect”.

Thus, MV with an increase in blood pressure loses its information content, and therefore it is impossible to assess the effect activity of antihypertensive

therapy, as well as to conduct a comparative assessment of pressure load. At the same time, MT retains its information content, therefore, in patients with high MV, approaching 100%, it acquires special significance and provides additional information about the hyperbaric load on all target organs.

It is believed that in normotonic patients, the load with systolic blood pressure increases with age, and the load with diastolic pressure does not change. According to some studies, a closer correlation has been shown between the size of the left atrium, LVMI, diastolic dysfunction of the left ventricle, and pressure load than with clinical and average daily blood pressure values. This indicator is more often used by domestic authors in assessing the effectiveness of the treatment of hypertension.

In all the study groups in our study, the value of the morning rise in blood pressure (MBP) did not exceed the recommended values. Statistically significant intergroup differences in MBP BP (SBP and DBP) were not identified.

In patients of the 1st group (AH without CHF), the highest rate of morning rise in blood pressure (SBP and DBP) was observed, while it exceeded the normative values and differed statistically significantly in comparison with the control group.

In patients of the 2nd group, the rate of morning DBP rise was the lowest and tended to increase in the 1st group. At the same time, there were no intergroup differences in DBP SAF (Table 9).

Indicators of the morning dynamics of blood pressure

Show	Control n=10	Group 1 n=36	Group 2 n=17
VUP SAD, mm Hg	13,00±3,05	35,40±4,86	37,33±2,88
VUP DBP, mm Hg	15,50±4,95	29,00±5,02	29,81±1,81

SOUP SAD mmHg/hour	6,00±1,04	14,36±8,20	8,79±4,86
SOUP DBP mmHg/hour	7,00±2,13	8,20±0,04	3,48±1,05

Note: SBP - systolic blood pressure; DBP - diastolic blood pressure; VUP - the value of the morning rise; SUP - the speed of the morning rise

Holter ECG heart rate variability

Recently, a lot of evidence has been obtained on the relationship between the autonomic regulation of the activity of the heart and mortality from cardiovascular complications. It should be noted that there is still no consensus on the role of HRV research in the diagnosis and prognosis of cardiovascular diseases. It is known that individual indicators of heart rate variability are closely interconnected. There are three groups within which the indicators are significantly correlated with each other. The first group includes SDNN, SDANN, and ULF, the second group consists of SDNNindex, VLF, and LF. The third group combines RMSSD and pNN50. It should be noted that in the presence of pathology, these ratios of indicators do not change.

In the study groups, we analyzed the results of the study of HRV in patients. In patients of the 1st and 2nd groups, in comparison with the control group. During the day, a statistically significant ($p<0.05$) decrease in frequency analysis indicators (VLF, LF, HF) was revealed. In patients of the 1st group, a decrease in RMSSD was observed in comparison with patients of the 2nd group ($p=0.036$). Daily averages of SDNN ($p=0.011$) and SDNNidx ($p=0.032$), SDNN day ($p=0.005$), SDANN day ($p=0.003$), SDNN night ($p=0.047$) were reduced in the 2nd group compared to the group control, NN50 day in comparison with the control and patients of the 1st group ($p<0.05$).

In patients of the 1st group, the average daily indicators of time analysis pNN50 ($p=0.040$), RMSSD ($p=0.022$), and frequency analysis parameters VLF ($p=0.037$), LF($p=0.043$), HP($p=0.047$) were reduced in compared with patients of the 3rd group. The average NN was increased in patients of the 1st group

during the day, and LF was reduced both during the day (p=0.046) and at night (p=0.048). To study the effect of hypertension on changes in HRV in patients with CHF, we compared the HRV parameters in patients of the 2nd and 3rd groups.

In patients of the 3rd group (CHF without AH), in comparison with patients of the 2nd group, there was a significant decrease in the average daily indicators of frequency analysis LF (p=0.039), HP (p=0.025) and increased VLF at night (p=0.023). The RMSSD indicator in comparison with patients of the control group was increased (p=0.034), and the NN50 indicator during the day and night was reduced (p=0.018).

In patients of the 3rd group, the indicators of SDNN and SDANN temporal analysis did not differ from the control group, and in patients of the 2nd group they were reduced ($p<0.05$).

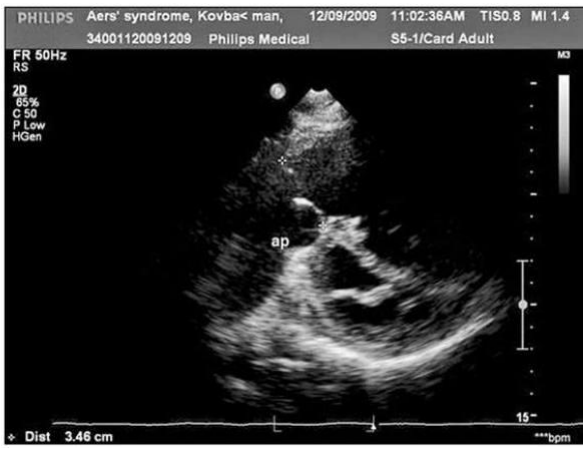
Currently, special attention is paid to the estimation of the standard deviation from the average duration of all sinus intervals (SDNN). SDNN is an integral indicator that characterizes HRV as a whole over the recording period and depends on the impact of both the sympathetic and parasympathetic divisions of the ANS. [28].

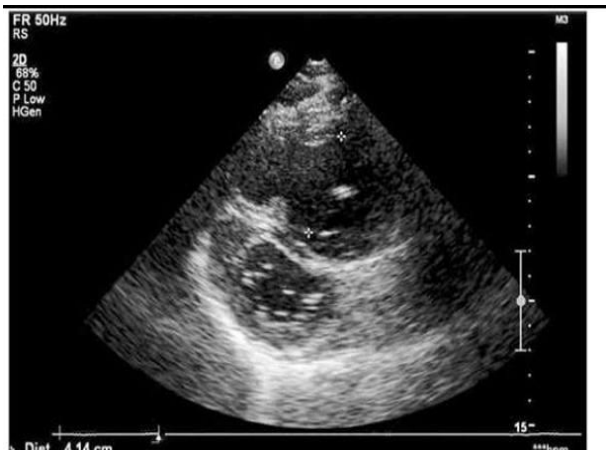
We correlated the results of the study of HRV and echocardiographic parameters.

According to P.M. Rothwell et al., an increase in the influence of the autonomic part of the sympathetic nervous system leads to a decrease in the early diastolic filling, and vagotonia increases it [77].

According to our correlation analysis, the maximum rate of early filling of the left ventricle (E, cm/s) of patients was statistically significantly correlated with SDNN (r=0.622; p=0.031), VLFnight (r=0.602; p=0.038); HF (r=0.652; p=0.028). SDNN, being an integral indicator, characterizes HRV as a whole for the recording period. It depends on the influence of both the sympathetic and parasympathetic divisions of the ANS. A decrease in SDNN will reduce the early diastolic filling of the left ventricle, which confirms the assumption that

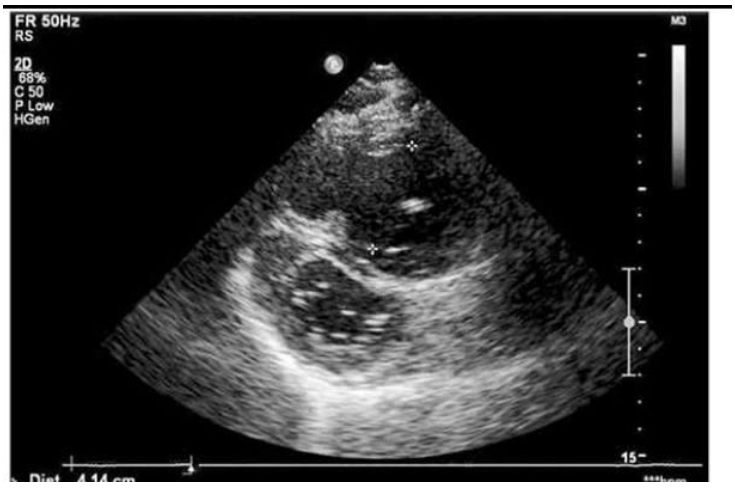
increased influences of the autonomic division of the sympathetic nervous system reduce early diastolic filling, and vagotonia increases it. Such indicators as the components of the spectral power VLF and HF are presumably due to the activity of the autonomic nervous system and RAAS. This also substantiates the involvement of the neurohumoral system in the formation of diastolic disorders and CHF.





The relationship between SDNN and duration of AH (r=-0.576; p=0.007), VUP DBP (r=0.828; p=0.042), VLF day, and IV SBP (r=0.667; p=0.02), HF day and IP SBP (r=0.512; p=0.039) IV SBP (r=0.385; p=0.014).

To confirm the contribution of HRV to the development of myocardial remodeling and CHF with preserved LV ejection fraction in patients with hypertension, we conducted a comparative analysis of HRV parameters (SDNN, RMSSD, VLF, LF, HF)



Thus, heterogeneity of HRV was revealed in patients with arterial hypertension with a predominance of different types of LV geometry and the

risk of developing CHF. Thus, in patients of the 1st cluster with HLH and the risk of developing CHF in 95% of cases, the level of sympathetic activity (SDNN) and the influence of the vasomotor regulation center were low (LF). In patients of the 4th cluster with CLV and the risk of developing CHF, hypersympathicotonia, and high activity of the vasomotor center prevailed in 65% of cases.

In patients of the 2nd cluster with LVH and the risk of CHF, in 85% of cases, there was a decrease in sympathetic activity, and an increase in power in the very low-frequency range (VLF). In this cluster, HRV may depend on changes in RAAS activity.

Chronic heart failure, being the result of any disease of the cardiovascular system, including hypertension, has been characterized by a steady increase in the general population in recent years. In addition, CHF leads to significant economic costs for healthcare to improve the quality of life of patients and reduce the risk of adverse clinical outcomes [49, 55, 76, 149, 208, 214, 256, 268, 340].

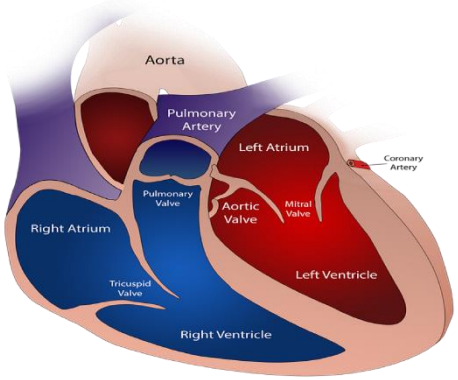
CHF is a syndrome that develops as a result of various cardiovascular diseases, which lead to the inability of the myocardium to provide systemic blood flow according to the metabolic needs of the body. This is accompanied by intracardiac and peripheral hemodynamic disorders, cardiac remodeling, and various disorders of neurohumoral regulation of blood circulation [49].

It should be noted that about half of all patients with CHF have preserved LV EF. This type of CHF is more common in patients with hypertension, as well as in obesity, anemia, chronic kidney disease, type 2 diabetes mellitus, chronic obstructive pulmonary disease, the elderly, in women [43, 228, 290, 348].

The number of patients with CHF with preserved ejection fraction annually increases by 1% per year. Research results of O.A. Smiseth, M.Tendera indicate that over 15 years the prevalence of CHF-PEF has increased from 38% to 54%. According to current forecasts, about 80% of patients with CHF should have preserved LV systolic function in 2020 [36, 208, 228].

The results of recent studies have shown that the survival curves of patients with CHF-PEF and those with reduced EF do not differ significantly. Although in patients with CHF-NFF there is a trend towards an improvement in the prognosis against the background of ongoing treatment, in patients with CHF-PFV the prognosis has hardly

changed over the past two decades [27-28, 40, 64, 83, 131, 151, 160, 202 -203, 208, 216, 335, 359].



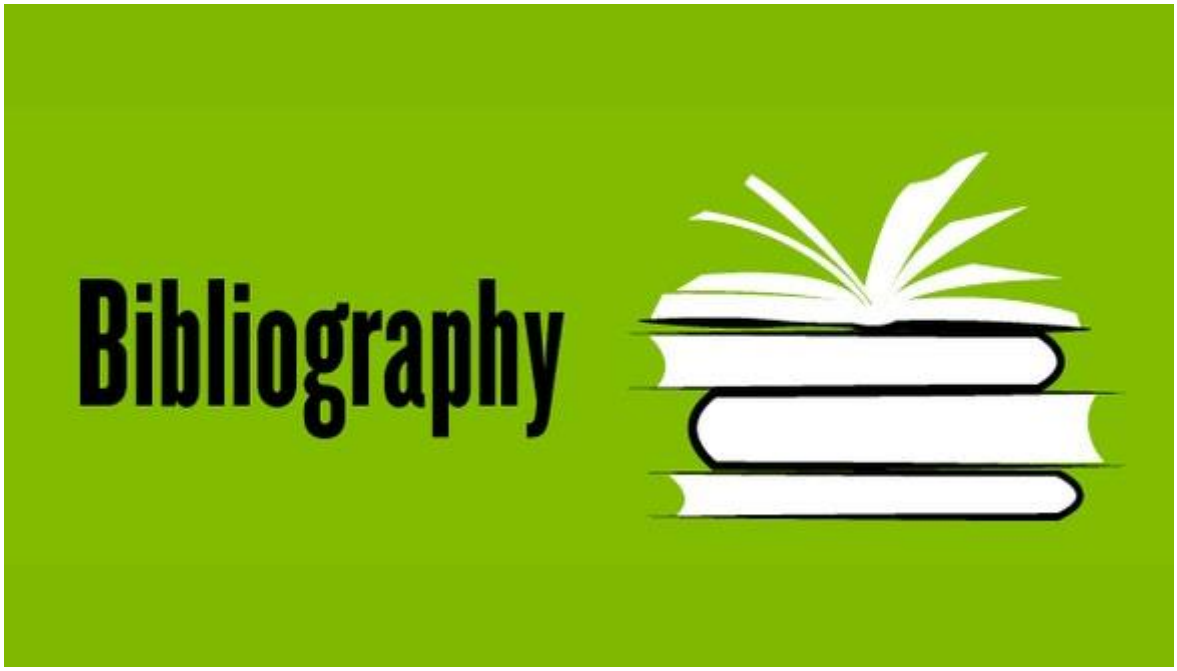
For a long time, there was an opinion that the formation of CHF with preserved LV EF is proved by a close relationship between the "pressure overload" of the LV and its structural and functional disorders [235, 263-264, 343, 369].

Further studies by scientists have established the predominance of concentric hypertrophy or concentric LV remodeling over eccentric forms of remodeling against the background of pronounced extracellular fibrosis in patients with AH with CHF, which leads to impaired relaxation function [296-297]. M.R. Zile et al suggested that quantitative assessment of LV diastolic function is not necessary for diagnosing CHF-PFV. In the writings of M.R. Zile et al. the results are presented showing that in patients with CHF-SFV with concentric hypertrophy or LV remodeling, one can confidently speak of the presence of diastolic dysfunction of the left ventricle.

According to W.J. Paulus et al., 2007 an increase and LVML >122 g/m2 in women and >149 g/m2 in men are also evidence of LV DD [297].

The fundamental difference between the modern pathogenetic model of the formation of CHF with preserved LV EF from the previous one is the change in ideas about the leading role of extracardiac mechanisms, for example, "overload" of the LV by volume or pressure, concerning cardiovascular, microvascular coronary dysfunction and asymptomatic ischemia. At the same time, the development of CHF-SFV is formed as a result of pro-inflammatory activation induced by comorbid conditions, which, in turn, are regarded as the direct cause of CHF. Hemodynamic disorders, according to the myocardial model of CHF, result from hemodynamic disorders in the neurohumoral activation of the sympathetic and RAAS systems, as well as impaired functional activity of cardiomyocyte ß-receptors and

inhibition of counterregulatory anti-inflammatory, antifibrotic factors. Thus, in patients with hypertension, depending on the progression of the degree of hypertension, there are corresponding clinical and hemodynamic changes. The occurrence of CHF is compensated by myocardial hypertrophy, the type of LV remodeling is associated with a violation of the geometry and diastolic function of the heart. LV EF in patients with concentric myocardial remodeling is reduced in comparison with patients with normal heart geometry and is comparable in patients with concentric hypertrophy and eccentric LV hypertrophy. In AH patients with CHF, concentric hypertrophy or concentric remodeling of the left ventricle prevails over eccentric forms of remodeling against the background of pronounced extracellular fibrosis, leading to impaired myocardial relaxation function. In patients with CHF-SFV with concentric hypertrophy or LV remodeling, one can confidently speak of the presence of left ventricular diastolic dysfunction.



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