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Hepatic Hemodynamics in Chronic Heart Failure of Ischemic Genesis

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Abstract

Heart remodeling processes in the development of chronic heart failure (CHF) play a key role in systemic damage to organs and systems. With worsening of CHF, the linear velocities of the liver blood flow (bf) decrease, the diameters of both the common hepatic artery and the portal vein increase. Changes in arterial bf in patients with CHF had a multidirectional character from group to group, narrowing of the lumen of the vessel at the initial stages of the disease and its progressive expansion to functional class IV, fully reflect changes in central hemodynamics, and are explained by the structure of the vessel and its lability in relation to neurohumoral influences characteristic of the development of CHF.

Introduction

The processes of heart remodeling in the development of chronic heart failure (CHF) play a key role in systemic damage to organs and systems; at the same time, the state of other organs and systems is vital [1], [2]. The liver is one of the main links of regulation, and the changes that develop in it are considered as extremely significant during CHF. Hepatic hemodynamic disturbances begin at an early stage and progress as the severity of CHF increases. The resulting functional and morphological changes in the liver exacerbate central hemodynamic disorders [3], [4], [5]. The role of hepatic hemodynamics and its relationship with the central one is one of the little-studied aspects of the pathology of the cardiovascular system.

Purpose of the study

The purpose of the study was to study the state of hepatic hemodynamics at different stages of CHF of ischemic genesis and to evaluate its relationship with central hemodynamics.

Material and Methods

At the first stage – for the period from 2020 to 2022, in the cardiology office of the polyclinic of the Almaty branch of the railway hospital Joint Stock Company “Medical Services of Transport“ after the initial examination, for further detailed examination, a selection of patients with stable forms of coronary heart disease was carried out. The study design was approved by the Local Ethics Committee of our university.

Randomly selected were 140 patients (95 men and 45 women), mean age - 65.4 ± 0.5 years, 120 of them with CHF of ischemic origin and 20 with no history of cardio-respiratory system and liver diseases.

The second stage (clinical) of our research program included clinical, laboratory, and instrumental

examination of patients, the establishment of violations of the hepatic and central hemodynamics, and the identification of their relationship.

To be included in the study, male and female patients must meet the following criteria: have clinical signs of CHF of ischemic origin, of varying duration; the patient has a desire and written informed consent for the study.

The exclusion criteria were as follows: Detection of diseases of the liver and biliary tract during examination and/or in the anamnesis; the presence at the time of examination of unstable forms of coronary heart disease; and legal incapacity or limited legal capacity.

The diagnosis of CHF was made on the basis of clinical symptoms, anamnesis data, general examination, objective examination of the cardiovascular system and other organs, laboratory, and instrumental methods of examination.

Clinical symptoms of CHF were determined based on the diagnostic criteria of the European Society of Cardiology (2020).

From the anamnestic data, it was taken into account – the duration of the disease, the past, and associated diseases.

General clinical research methods included: complete blood count; general urine analysis; in the biochemical blood test – total bilirubin, ALT, AST, thymol test, alkaline phosphatase, and total cholesterol.

Instrumental methods of examination: ECG, X-ray of the chest, EchoCG, ultrasound of the liver and biliary tract, and dopplerography of the liver vessels.

We examined 140 patients with CHF of ischemic origin, the average age of which was 67.4 ± 1.0.

All the patients were divided into two groups:

- Group 1 (control) – 20 healthy volunteers with no history of cardiorespiratory system and liver diseases.
- Group 2 (main) – 120 patients with CHF of ischemic origin, which is divided into four subgroups depending on the functional class (FC) of CHF. Functional classes of CHF were assessed using the 6-min walk test (European Society of Cardiology and Society of Heart Failure Specialists).

Among those examined – 67.9% (95) were male and 32.1% (45) female. From the anamnesis, the "experience" of CHF was clarified, so in the group of patients with FC I, the duration of CHF averaged 2.2 ± 1.8 years, in the group of patients with FC II – 5.3 ± 1.8 years, and FC III and IV – 8.5 ± 01.7 and 10.2 ± 1.7 years.

Hepatic hemodynamics was determined by duplex dopplerography in pulsed mode using a transducer with a frequency of 2.5 MHz.

The studies were conducted for all patients under the same conditions (in the morning, on an empty stomach after a 3-day slag-free diet), on the same apparatus, by the same specialist.

Pulsed Doppler and color Doppler imaging of the abdominal vessels examined the vessels of the liver – the portal vein, the common hepatic artery.

In the study in the spectral Doppler mode, the blood flow (bf) in the proper hepatic artery in all cases had a two-phase (arterial) character.

The bf indices of both vessels (I_{bf}) were also calculated using the formula:

$$I_{bf}PV = V_{vv}PV\backslash S_{body},$$

which: VvvPV – Portal vein volumetric velocity of bf (mL\min), Sbody – Body surface area.

The pulsation index (PI) was calculated using the formula:

$$PI = V_{max}CHA – V_{min}CHA \backslash V_{lv}CHA,$$

which: VmaxCHA – Maximum systolic bf velocity of the common hepatic artery (CHA), VminCHA – End-diastolic bf velocity of the CHA, and VlvCHA – Linear velocity (lv) of bf of the CHA.

The use of a system of indices of central and hepatic hemodynamics made it possible to conduct a reliable mathematical analysis of the results.

The ratio between the volumetric velocities (vv) of bf of both vessels ($V_{vv}PV\backslash V_{vv}CHA$) was calculated, which is necessary to determine the significance of one or another fraction in the progression of CHF during the study.

Statistical research methods – calculated the average values (M) and the error of their representativeness (m). The significance of differences in arithmetic mean values was assessed by Student's t-test. The difference was considered statistically significant at $p < 0.05$. The relationship between quantitative indicators was determined by the linear correlation coefficient (r). The use of a system of indices of central and hepatic hemodynamics made it possible to conduct a reliable mathematical analysis of the results of linear correlation. With a correlation coefficient value of <0.3, there was a lack of connection between the compared series, with a value of more than 0.3 – a weak degree of correlation, from 0.31 to 0.5 – a moderate degree, at 0.51–0.7 – pronounced and more 0.7 a high degree of correlation [6].

Results

Analyzing the indicators of central hemodynamics, the following pattern was revealed (Table 1): heart rate in the control group was 72.10 ± 1.2 beats/min, and in the group of patients with FC I

Table 1: Indicators of the hemodynamic status of patients with chronic heart failure depending on the functional class (M ± m)

Indicator	Control group	Function class			
		I	II	III	IV
		n = 30	n = 30	n = 30	n = 30
Heart rate in minutes	72.10 ± 1.2	**	**	**	**
		81.35 ± 0.8	92.81 ± 0.5	95.70 ± 0.4	98.00 ± 0.3
			**	**	**
Blood pressure avg, mmHg	104.61 ± 6.7		*	*	*
		104.99 ± 5.5	96.86 ± 0.3	95.14 ± 0.4	94.4 ± 0.4
				*	**
Specific peripheral vascular resistance dyne-second\cm^{-5}m^{-2}	649.3 ± 4.2	**	**	**	**
		692.17 ± 3.2	852.85 ± 2.2	1127.2 ± 17.2	1213.15 ± 17.1
			**	**	*

*p < 0.05; **p < 0.01; in the upper corner – reliability with the control group; in the lower corner – reliability with the previous group.

81.35 ± 0.8, subsequently, there was a significant (p < 0.01) increase in heart rate, both with the control group and between subgroups, amounting to 92.81 ± 0.5 in the group with FC II, 95.70 ± 0.4 with FC III, and 98.00 ± 0.3 with FC IV. A progressive increase in heart rate during the transition from one stage to another indicates the "launch" of compensatory factors, on the one hand, maintaining cardiac output, and the degree of left ventricular (LV) dysfunction, on the other.

As shown in Table 1, the average blood pressure (BP) tended to decrease, moreover, due to systolic and pulse BP, which makes it possible to indirectly judge the value of the cardiac index (CI), which is an important indicator of central hemodynamics. Thus, in the control group, BP averaged 104.61 ± 6.7 mmHg, and in the group with FC I – 104.99 ± 5.5, subsequently, there was a significant (p < 0.05) decrease in average BP, both relative to the control group and between subgroups, amounting in the group with FC II – 96.86 ± 0.3, with FC III – 95.14 ± 0.4, and with FC IV 94.4 ± 0.4 mmHg.

We also revealed, as shown in Table 1, an increase in specific peripheral vascular resistance (SPVR) as the disease progresses. In the control group, the SPVR was 649.3 ± 4.2 dyne-second\cm^{-5}m^{-2}, and in the group of patients with FC I – 692.17 ± 2.9 dyne-second\cm^{-5}m^{-2}; correspondingly significant (p < 0.01) increase in SPVR in the groups with FC II and III – 852.85 ± 2.2 and 1127.2 ± 17.2 dyne-second\cm^{-5}m^{-2}. In the group of patients with FC IV, SPVR significantly increased to 1213.15 ± 17.1 dyne-second\cm^{-5}m^{-2}, (p < 0.01). An increase in SPVR in patients with CHF led to an increase in afterload on the left ventricle, which was reflected in a decrease in stroke volume (SV) (from 62.89 to 48.00 mL – Table 2), which led to a relative increase in circulating blood volume. All this together contributes to fluid retention in the body and ultimately leads to the development of edematous syndrome.

The results of the main parameters of the LV systolic function obtained during the examination are presented in Table 2.

In CHF of ischemic origin, dying myocardial cells (post-infarction or diffuse cardiosclerosis) are replaced by areas of fibrosis, leading to a decrease in cardiac output (minute volume [MV]). As shown in Table 2 – MV in the CG was 4.93 ± 0.5 L/min, in the group with FC I, there is a slight increase in MV – 4.96 ± 0.4 L/min, in our opinion, this is due to activation

Table 2: Indicators of echocardiography of patients with chronic heart failure depending on the functional class (M ± m)

Indicator	Control group	Function class			
		I	II	III	IV
	n = 20	n = 30	n = 30	n = 30	n = 30
EDV_{LV}, cm^3			*	**	**
	118.95 ± 6.8	123.76 ± 5.4	140.86 ± 5.4	149.70 ± 5.3	154.67 ± 5.3
			*		
ESV_{LV}, cm^3		**	**	**	**
	50.00 ± 1.6	60.87 ± 1.1	83.57 ± 0.7	99.33 ± 0.2	106.67 ± 5.5
			**	**	
EDS_{LV}, cm			*	*	**
	5.12 ± 0.5	5.11 ± 0.4	6.73 ± 0.3	6.80 ± 0.3	7.13 ± 0.3
			**		
ESS_{LV}, cm				*	*
	3.48 ± 0.6	3.48 ± 0.5	4.58 ± 0.4	4.96 ± 0.4	4.97 ± 0.4
				*	
SV, mL		**	**	**	**
	68.95 ± 1.3	62.89 ± 1.1	57.29 ± 1.2	50.37 ± 1.3	48.00 ± 1.3
			**	**	
SI, mL\min^2	37.17 ± 1.8	36.34 ± 1.5	35.95 ± 1.5	33.98 ± 1.5	*
					32.54 ± 1.5
EF, %			**	**	**
	57.38 ± 1.5	56.27 ± 1.1	45.99 ± 1.3	43.75 ± 1.3	38.67 ± 1.4
			**	*	
MV, L\min					*
	4.93 ± 0.5	4.96 ± 0.4	4.75 ± 0.4	3.97 ± 0.5	3.30 ± 0.5
CI, L\min\m^2	2.64 ± 0.6	2.58 ± 0.5	2.47 ± 0.5	2.15 ± 0.5	1.87 ± 0.5
				*	**
%ΔS, %	30.35 ± 1.9	30.14 ± 1.5	27.86 ± 1.6	25.90 ± 1.6	20.2 ± 1.6
$V_{CF}^{(c-1)}$	0.95 ± 0.1	0.92 ± 0.05	0.81 ± 0.08	0.77 ± 0.09	0.73 ± 0.09

*p < 0.05; **p < 0.01; in the upper corner – reliability with the control group; in the lower corner – reliability with the previous group. EDV_{LV}: End-diastolic volume of the left ventricle, ESV_{LV}: End-systolic volume of the left ventricle, EDS_{LV}: End-diastolic size of the left ventricle, ESS_{LV}: End-systolic size of the left ventricle, SV: Stroke volume, SI: Stroke index, EF: Ejection fraction, MV: Minute volume, CI: Cardiac index.

neurohumoral mechanisms, leading to compensatory tachycardia and due to this increase in MV. In the future, the continued redistribution of work to the remaining myocytes leads to secondary overload, this is indicated by the MV indicators of subsequent FCs: FC II – 4.75 ± 0.4 L/min, FC III – 3.97 ± 0.5 L/min, and FC IV 3.30 ± 0.5 L/min (p < 0.01), reflecting the increasing nature of LV myocardial dysfunction.

The above reasons, in turn, led to an increase in the end-diastolic volume of the left ventricle (EDV_{LV}) from group to group: in the CG, it was 118.95 ± 6.8 cm^3, in the group with FC I, there was a slight increase to 123.76 ± 5.4 cm^3. A slight increase between the CG and the group with CHF stage I is associated with an increase in preload, which plays a compensatory role at the beginning of the disease and maintains the indicators in the FC I group at the same level, but in subsequent groups, there was a significant (p < 0.05) in relation to the CG expansion of the LV cavity (FC II – 140.86 ± 5.4 cm^3 (p < 0.01); FC III – 149.70 ± 5.43 cm^3 (p < 0.01); and FC IV – 154.67 ± 5.3 cm^3 (p < 0.01), which indicates the termination of the work of adaptive mechanisms and their transition to maladaptive.

A similar trend persisted with indicators of LV end-systolic volume (ESV), LV end-diastolic size (EDS), and LV end-systolic size (ESS).

The ESV_{LV} values in the CG were 50.00 ± 1.6 cm^3, in the group with FC I – 60.87 ± 1.1 cm^3 ($p < 0.01$), in the group with FC II, there was a significant increase in ESV_{LV} compared to the CG and the group with FC I up to 83.57 ± 0.7 cm^3 ($p < 0.01$), an increase in ESV_{LV} in the FC III group up to 99.33 ± 0.2 cm^3 also had a significant value ($p < 0.01$) between the CG and the FC II group; and in the group with FC IV – ESV_{LV} significantly increased up to 106.67 ± 5.5 cm^3, $p < 0.01$ (Table 2).

A progressive increase in EDS_{LV} with an increase in the severity of CHF reflects general changes in the myocardium in CHF: thus, in the CG, EDS_{LV} was 5.12 ± 0.5 cm, in the groups with FC I – 5.11 ± 0.4 cm, FC II - –6.73 ± 0.3 cm, FC III – 6.80 ± 0.3 cm, and FC IV stage – 7.13 ± 0.3 cm. In the groups with FC II-III, the indicators had a significant value ($p < 0.05$) and highly significant in the group with FC IV ($p < 0.01$) relative to CG. A significant increase in EDS_{LV} was also noted between groups with FC I and II.

Similar changes were observed in the analysis of ESS_{LV} parameters, amounting to 3.48 ± 0.6 cm in the CG and 3.48 ± 0.5 cm in the group with FC I; in the future, there is a regular progressive increase in ESS_{LV} to 4.58 ± 0.4 cm in the group of patients with FC II, up to 4.96 ± 0.4 cm ($p < 0.05$) in the group with FC III and in the group with FC IV up to 4.97 ± 0.4 cm ($p < 0.05$) relative to the control group.

Based on the above data, an increase in the progression of the disease indicators of EDV_{LV}, EDS_{LV} leads to an increase in preload, which is determined by the stretching of myocardial fibers in diastole, depends on the venous return to the heart.

The earliest marker of LV myocardial dysfunction, depending on pre- and afterload indicators, is the ejection fraction (EF), which, based on the indicators of Table 2, tends to a significant decrease compared to the CG: where it was 57.38 ± 1.5%, in the group of patients with FC I – 56.27 ± 1.1%, with FC II – 45.99 ± 1.3%, ($p < 0.01$), with FC III – 43.75 ± 1.3%, ($p < 0.01$), and with FC IV – 38.67 ± 1.4%, ($p < 0.01$).

Another (except for EF) the most important hemodynamic indicator of LV systolic function is CI, we revealed the following changes: in the CG and the group with FC I, CI was approximately at the same level and amounted to 2.64 ± 0.6 and 2.58 ± 0.5 L\min\$m^2$, confirming the reasons described above (adaptive reaction). In subsequent groups with FC II, III, and IV, there is a gradual decrease in CI to 2.47 ± 0.5 L\min\$m^2$ in the second group, 2.15 ± 0.5 L\min\$m^2$ in the third, and to 1.87 ± 0.5 L\min\$m^2$ in the fourth group. CI indicators have a pattern characteristic of the course of CHF.

Although the indices of LV myocardial contractility (%ΔS and $V_{CF}^{(c-1)}$) are approximate and do not give a complete figure of myocardial contractility, but in our studies, the degree of shortening of the anteroposterior size of the left ventricle in systole (%ΔS), as shown in Table 2, has a natural tendency for CHF to decrease: in the CG was 30.35 ± 1.9%, in the group with FC I – 30.14 ± 1.5%, FC II – 27.86 ± 1.6%, FC III – 25.90 ± 1.6% ($p < 0.05$), and FC IV – 20.2 ± 1.6% ($p < 0,01$). For indicators of the rate of circular, shortening of myocardial fibers ($V_{CF}^{(c-1)}$) is also characterized by a gradual decrease, so in the CG, its value was 0.95 ± 0.1, in the group with FC I – 0.92 ± 0.05, in the group with FC II – 0.81 ± 0.08, and in the groups with FC III and IV, they were 0.77 ± 0.09 and 0.73 ± 0.09.

The decrease in SV in the process of CHF progression also led to a drop in the stroke index (SI). In turn, the parameters of SI are also affected by the body area (S), which, with the progression of CHF, tends to grow due to increased edematous syndrome, leading to an increase in body weight. Therefore, SI in the groups did not have a fatal significant decrease in indicators and was equal to 37.17 ± 1.8 mL/min^2 in the CG, in the group of patients with FC I – 36.34 ± 1.3 mL/min^2, with FC II – 35.95 ± 1.2 mL/min^2, with FC III – 33.98 ± 1.6 mL/min^2, and with FC IV – 32.54 ± 2.4 mL/min^2.

Summarizing the data obtained on the assessment of LV systolic dysfunction, we can conclude that at the initial stages of systolic dysfunction, SV is maintained at the proper level due to an increase in preload and the influence of the Frank-Starling mechanism, amounting to 62.89 mL, corresponding to normal parameters. Gradual overextension of myocardial fibers, a sharp dilatation of the left ventricle leads to the termination of the adaptive mechanism and a further increase in EDV_{LV} (from 123.76 to 154.67 cm^3), causes a decrease in SV (up to 48.0 ml in the group with CHF stage III), and a decrease in SV and an increase in the indicators of EDV_{LV}, ESV_{LV} (from 60.87 to 106.67 cm^3), ESS_{LV} (from 3.48 to 4.97 cm^3), and EDS_{LV} (from 5.11 to 7.13 cm) – turn into factors contributing to a decrease in EF (from 56.27% to 38.67%) and the progression of CHF.

From the above, it follows that those hemodynamic disturbances in CHF were progressive in nature and consisted in a sharp decrease in the systolic function of the left ventricle.

For a qualitative assessment of hepatic hemodynamics, knowledge of the ratios of arterial and venous bf is necessary. For this purpose, we analyzed the velocity and volume indicators for the portal vein and the common hepatic artery, which are presented in Table 3.

To exclude the influence of respiration on hemodynamics in the PV, the study was carried out with a breath hold.

As shown in Table 3, the diameter of the portal vein (DPV) in the control group was 8.9 ± 0.2 mm, while the linear velocity (VlvPV) in the portal vein was 19.2 ±

Table 3: Indicators of hepatic hemodynamics in patients with chronic heart failure, depending on the functional class (M ± m)

Indicator	Control group n = 20	Function class I n = 30	II n = 30	III n = 30	IV n = 30
DPV, mm	8.90 ± 0.2	* 12.90 ± 1.5	* 13.40 ± 1.7	* 13.60 ± 1.7	** 14.20 ± 1.7
VlvPV, cm\s	19.20 ± 2.1	16.40 ± 1.7 *	15.44 ± 1.7 **	14.31 ± 1.7 **	13.70 ± 1.7 **
VvvPV, mL\min	811.85 ± 3.1	803.76 ± 2.6	794.04 ± 2.6 *	789.50 ± 2.7 **	785.20 ± 2.7
IbfPV, mL\min\m^2	442.36 ± 5.4	434.46 ± 4.3	429.21 ± 4.4	426.76 ± 4.4	424.43 ± 4.4 *
DCHA, mm	5.41 ± 0.5	4.75 ± 0.4	5.90 ± 0.4 *	6.13 ± 0.4 **	7.10 ± 0.3 *
VmaxCHA, cm\s	99.35 ± 0.2	* 98.64 ± 0.2	** 85.67 ± 0.7 *	** 80.32 ± 0.8 **	** 73.30 ± 0.9 **
VminCHA, cm\s	25.45 ± 2.0	24.96 ± 1.6	21.11 ± 1.6 *	* 20.83 ± 1.6 **	* 19.92 ± 1.6 **
VlvCHA, cm\s	62.40 ± 1.4	60.08 ± 1.1	57.67 ± 1.2	55.67 ± 1.2	52.33 ± 1.3 *
RI	0.7 ± 0.1	0.73 ± 0.09	0.77 ± 0.09	0.82 ± 0.08	0.9 ± 0.06
PI	1.2 ± 0.7	1.2 ± 0.5	1.1 ± 0.5	1.1 ± 0.5 *	1.0 ± 0.6 *
VvvCHA, mL\min	218.10 ± 6.4	215.90 ± 5.1	208.19 ± 5.1	203.19 ± 5.2	199.10 ± 5.2
IbfCHA, mL\min\m^2	117.89 ± 6.8	116.70 ± 5.4	112.54 ± 5.4	109.83 ± 5.4	107.62 ± 5.4
VvvPV\VvvCHA relative units	3.72 ± 0.6	3.72 ± 0.5	3.81 ± 0.5	3.89 ± 0.5	3.94 ± 0.5

*p < 0.05; **p < 0.01; in the upper corner – reliability with the control group; in the lower corner – reliability with the previous group.

2.1 cm/s, volumetric bf velocity (VvvPV) in the control group reached 811.85 ± 3.1 mL/min, and bf index (IbfPV) was 442.36 ± 5.4 mL/min/m^2.

The diameter of the common hepatic artery (DCHA) averaged 5.41 ± 0.5 mm; the maximum systolic bf velocity of the common hepatic artery (VmaxCHA) was 99.35 ± 0.2 cm/s; the end-diastolic bf velocity (VminCHA) – 25.45 ± 2.0 cm/s; the average bf velocity (VlvCHA) – 62.40 ± 1.4 cm/s; the volumetric bf velocity (VvvCHA) reached 218.1 ± 6.4 mL/min; and bf index (IbfCHA) – 117.89 ± 6.8 mL/min/m^2.

The ratio of volumetric velocities for PV and CHA (VvvPV\VvvCHA), reflecting the distribution of blood entering the liver, was 3.72 ± 0.6 relative units, indicating that the hepatic hemodynamics of healthy people in the system of afferent vessels is characterized by the predominance of the portal fraction over the arterial, which corresponds to the literature data [7].

The analysis of hepatic hemodynamic parameters in the group of patients with FC I revealed the following changes, so the average group DPV in this group had a significant increase compared to CG and amounted to 12.90 ± 1.5 mm, p < 0.05; in response to DPV expansion, there was a decrease in PV bf: thus, VlvPV in the group increased to 16.40 ± 1.7 cm/s, and VvvPV had a significant increase to 803.76 ± 2.6 mL/min, p < 0.01; accordingly, there was an increase in IbfPV, which amounted to 434.46 ± 4.3 mL/min/m^2. The decrease in VvvPV and IbfPV is not pronounced and is not significant, since the decrease in bf velocity was compensated by an increase in the PV lumen, which maintained venous bf to the liver at a satisfactory level.

A decrease in SV, leading to activation of the sympathoadrenal system (SAS), primarily affects arterial bf – general hepatic bf, leading initially (FC I) to vessel vasoconstriction, while DCHA averaged 4.75 ± 0.4 mm. Vasoconstriction of the CHA (associated with the structure of the vessel, a more pronounced muscle layer, compared to the veins, gives a more "bright" response to neurohumoral influences), in turn, compensatory maintains the bf in the CHA at the same level: VmaxCHA was 98.64 ± 0.2 cm/s (p < 0.05), VminCHA was 24.96 ± 1.6 cm/s, VlvCHA was 60.08 ± 1.1 cm/s, VvvCHA was 215.90 ± 5.1 cm/s, and IbfCHA in the group was 116.7 ± 5.4.

Narrowing with preservation of bf according to CHA, on the one hand, and expansion with a decrease in bf according to PV, on the other hand, maintain the ratio of volumetric velocities VvvPV\VvvCHA at the same level in comparison with CG (3.72 ± 0.5 relative units in FC I and 3.72 ± 0.6 relative units in CG), stabilizing the ratio of blood entering the liver (Table 3).

The above changes in the hemodynamics of the liver indicate that the hepatic bf in CHF is disturbed already at an early stage and is characterized by hypertonicity of the common hepatic artery. From our point of view, a decrease in the lumen of the vessel is aimed at maintaining adequate arterial bf to the liver, maintaining normal linear and volumetric CHA bf rates, and being a compensatory reaction of the body in the initial stages of CHF.

Analysis of the parameters of hepatic circulation in the group of patients with FC II revealed the following changes.

Thus, there was an increasing, compared with the 1st group, a significant increase in DPV to 13.40 ± 1.7 mm, p < 0.05 compared with CG, leading to an even greater decrease in VlvPV to 15.44 ± 1.7 cm\s and VvvPV to 794.04 ± 2.6 mL/min, p < 0.01, compared with the CG group and with the group of patients with FC I (p < 0.05), which was reflected in a significant (p < 0.05) decrease in IbfPV to 429.21 ± 4.4 mL/min/m^2.

In contrast to the group with FC I, arterial bf in the group with FC II had the following figure: a progressive increase in SPVR and a weakening of compensatory-adaptive mechanisms led to a significant expansion of the CHA diameter and, on average, it was 5.90 ± 0.4 mm, $p < 0.05$; accordingly, this led to a decrease in linear and volumetric velocities according to CHA: thus, VmaxCHA decreased to 85.67 ± 0.7 cm/s with a high reliability of $p < 0.01$, both with the CG and with the group of patients with CHF stage I, VminCHA to 21.11 ± 1.6 cm/s, VlvCHA to 57.67 ± 1.2 cm/s, $p < 0.05$, VvvCHA to 208.19 ± 5.1 mL/min, and IbfCHA to 112.54 ± 5.4 mL\min\m^2.

The ratio of volumetric velocities VvvPV\VvvCHA in this group tended to increase to 3.81 ± 0.4 relative units, due to a decrease in bf in both vessels, but changes in PV prevailed, leading to the development of congestive phenomena in the liver, as evidenced by clinical manifestations.

Changes in bf in the liver in patients with FC II reflect the ratio of volumetric velocities, which tended to increase as the disease worsened, indicating a redistribution of blood flowing to the liver due to the portal fraction, leading to the deposition of blood in the liver, thereby exerting a regulatory effect on central hemodynamics.

The aggravation of central hemodynamics in group 3 with FC III also led to an aggravation in the hepatic bf system: thus, as shown in Table 3, there was an even more pronounced significant expansion of DPV, which amounted to 13.60 ± 1.7 mm, $p < 0.05$, which, accordingly, led to an even greater decrease in VlvPV to 14.31 ± 1.7 cm/s, VvvPV also decreased with high reliability to 789.50 ± 2.8 mL/min, $p < 0.01$, respectively, and had a significant decrease in IbfPV to 426.76 ± 4.4 mL\min\m^2, $p < 0.01$ compared to CG.

In the arterial bed, the dynamics are similar to changes in PV. Thus, an increase in DCHA to 6.13 ± 0.4 mm was noted, respectively, a decrease in all speed indicators was observed: VmaxCHA had a significant decrease to 80.32 ± 0.8 cm/s, $p < 0.01$, both with CG and between subgroups, VminCHA to 20.83 ± 1.6 cm/s, VlvCHA to 55.67 ± 1.2 cm/s, $p < 0.01$, and VvvCHA to 203.19 ± 5.5 mL/min, which led to a decrease in IbfCHA to 109.83 ± 5.4 mL/min/m^2.

A decrease in volumetric speed indicators revealed a progressive increase in the ratio VvvPV\VvvCHA from group to group and amounted to 3.89 ± 0.5 relative units, reflecting the general state of bf. This indicates a more pronounced, compared with the early stages, the predominance of the portal fraction over the arterial one, and the "compensatory deposition" of blood in the liver, as the severity of CHF increases, leads to hepatomegaly, thereby aggravating central hemodynamics. If at the initial stages, pathophysiological mechanisms had an adaptive effect on the vessels of the liver, then starting from FC III, they exacerbate hemodynamic disorders in the liver. These changes reflect general changes in the body in CHF.

Changes in liver hemodynamics in the group of patients with FC IV, developing with increasing decompensation of cardiac activity, looked as follows: progressive from stage to stage increase in DPV to 14.20 ± 1.7 mm ($p < 0.01$) led to a deeper decrease in linear and volumetric velocity indicators: VlvPV decreased to 13.70 ± 1.7 cm/sec and VvvPV had a significant decrease compared to CG to 785.20 ± 2.7 mL/min, $p < 0.05$. All this led to a steady decrease in IbfPV to 424.43 ± 4.4 mL/min/m^2.

Similar changes are typical for arterial bf. A progressive increase in DCHA to 7.10 ± 0.3 mm was noted, which was reflected in a significant decrease in VmaxCHA to 73.30 ± 0.9 cm/s, $p < 0.01$, VminCHA to 19.92 ± 1.6 cm/s, $p < 0.05$, VlvCHA to 52.33 ± 1.3 cm/s, and VvvCHA to 199.10 ± 5.2 mL/min.

Fluctuations in the pulsatile index in all groups were not significant and practically did not change (FC I – 1.2 ± 0.5; II and III – 1.1 ± 0.5; and FC IV – 1.0 ± 0.6), indicating about its lack of information in CHF. There was an increase from group to group with worsening CHF resistance index: FC I – 0.73 ± 0.09; FC II – 0.77 ± 0.09; FC III – 0.82 ± 0.09; and FC IV – 0.9 ± 0.06 ($p < 0.05$).

The decrease in VvvCHA led to a decrease in IbfCHA to 107.62 ± 5.4 mL/min/m^2. A further increase in CHA diameter against the background of high SPVR (1213.2 dyne-second\$cm^{-5}m^{-2}$) at this stage, it would seem, should, if not increase, then at least maintain adequate arterial bf, but these factors are not able to maintain a steady decline Vvv, further aggravating the current situation. An increase in the VvvPV\VvvCHA indicator to 3.94 ± 0.7 relative units confirms the above opinion, as evidenced by the clinical manifestations – the edematous syndrome is growing "avalanche-like."

Analyzing the blood circulation of the liver as a whole, we noted that with an increase in the FC of CHF, the values of linear and volumetric bf velocities decrease, the diameters of both the portal vein, and the common hepatic artery increase. Moreover, for the venous bed, the increase in diameter was more pronounced from 12.9 to 14.2 mm (most likely due to a violation of the outflow of blood through the hepatic veins). Changes in arterial bf in patients with CHF had a multidirectional character from group to group. The narrowing of the vessel lumen in stage I (4.75 mm) of the disease and its progressive expansion to stage III (7.10 mm) fully reflect changes in central hemodynamics and are explained by the structure of the vessel and its lability in relation to neurohumoral influences characteristic of the development of CHF. The bf in the liver is under the control of the SAS, the activation of the SAS is accompanied by a decrease in the total hepatic bf.

A decrease in bf in PV and preservation in CHA in stage I of CHF should be considered a manifestation

of neurohumoral hyperdynamic syndrome, and not a phenomenon of "arterialization."

Fluctuations in the pulsatile index in all groups were not significant and practically did not change, indicating that it was not informative in CHF. There was an increase from group to group with worsening CHF resistance index.

Changes in the hepatic circulation in patients with CHF allow us to conclude that in patients with FC I, they are compensatory in nature, depositing blood, exerting a regulatory effect on blood circulation, but as the severity of CHF increases and compensatory mechanisms weaken, they aggravate central hemodynamics.

The dynamics of hepatic circulation reflects general changes in the body that develops with progressive decompensation of cardiac activity.

In the conditions of CHF development, the main factor damaging the liver is hemodynamic disturbances of hepatic bf, leading to the development of cardiac cirrhosis of the liver and the associated changes in its functions.

For this purpose, we analyzed the biochemical parameters of the liver in patients with CHF. The functional state of the liver was assessed by the results of blood levels of bilirubin, aminotransferases (AST and ALT), alkaline phosphatase, thymol test, as well as the content of total cholesterol. The results were compared with the average values determined for each indicator among the entire population of the examined patients. Analysis of biochemical parameters reflecting the functional state of the liver in elderly patients did not reveal any significant differences and deviations from the average values.

The results of the study showed that as the stages of CHF increase, some features are observed in the violation of liver function, in comparison with the control group.

The worsening of the disease is accompanied by an increase in the level of total cholesterol at the beginning of the disease, which amounted to 5.72 ± 0.4 mmol/L in the group with CHF FC I, 6.55 ± 0.3 mmol/L with FC II, then there is a decrease in its indicators with FC III to 5.68 ± 0.4 mmol/L, at the same time, they did not reach the indicators of the CG; in the future, as CHF progresses, the level of total cholesterol continues to decrease and by FC IV, it reaches 4.1 ± 0.4 mmol/L, $p < 0.05$ (Table 4).

The progression of CHF, which is reflected in the violation of the central and hepatic hemodynamics, led to an increase in total bilirubin in the blood serum. Hence, in the CG, it was 10.2 ± 2.2, in the group of patients with FC I – 11.1 ± 1.7 mmol/L, in the 2nd group 11.4 ± 1.7, with FC III – 21.9 ± 1.7 mmol/L ($p < 0.01$), and with FC IV – 23.6 ± 1.6 mmol/L ($p < 0.01$).

There is also a slight increase in the activity of ALT and AST transaminases; however, the increase in the dynamics of the ALT level in the blood serum in patients with CHF as it progressed was higher than the increase in AST levels. Thus, the level of AST in the blood serum, as it progressed, increased from 0.34 ± 0.1 to 0.98 ± 0.02 mmol/L by the fourth group, and in FC III and IV, high reliability was observed ($p < 0.01$), and ALT from 0.41 ± 0.1 to 1.1 ± 0.5 mmol/L. The increase in indicators AST was 34.7% and ALT was 37.3%.

The content of alkaline phosphatase in the blood serum does not change significantly and is equal to: 3.96 ± 0.4 units in the group with FC I, 4.25 ± 0.4 units ($p < 0.05$) in the group with FC II, 4.78 ± 0.4 units ($p < 0.05$) with FC III, and 5.3 ± 0.4 units ($p < 0.01$) with FC IV.

Along with this, there is a decrease in the level of thymol test: 5.2 ± 0.4 units in the group with FC I, 3.3 ± 0.4 units with FC II, 2.3 ± 0.5 units with FC III, and 1.8 ± 0.5 units with FC IV (Table 4).

The study of some biochemical parameters of blood serum characterizing individual liver functions in patients suffering from CHF of ischemic genesis allows us to presumably speak about their dependence on the FC of CHF, namely, on hepatic hemodynamic disorders. Hemodynamic disorders are observed earlier, being the primary pathogenetic factor, and the resulting functional disorders of the liver are secondary, which makes it possible to consider hepatic bf disorders as one of the early markers of the initial manifestations of CHF.

To identify the existing relationships between the indicators obtained as a result of our study, a correlation analysis was carried out.

As shown in Figure 1, the relationship between cardiac and hepatic hemodynamics is manifested in

Table 4: Biochemical blood parameters of patients with chronic heart failure depending on the functional class (M ± m)

Indicator	Control group	Function class			
	n = 20	I	II	III	IV
		n = 30	n = 30	n = 30	n = 30
Total bilirubin, mmol\L				**	**
	10.2 ± 2.2	11.1 ± 1.7	11.4 ± 1.7	21.9 ± 1.7	23.6 ± 1.6
AST, mmol\L				**	**
	0.28 ± 0.1	0.34 ± 0.1	0.42 ± 0.1	0.69 ± 0.1	0.98 ± 0.02
ALT, mmol\L				**	
	0.32 ± 0.1	0.41 ± 0.1	0.56 ± 0.1	0.72 ± 0.1	1.1 ± 0.5
Alkaline phosphatase, units			*	*	**
	2.9 ± 0.6	3.96 ± 0.4	4.25 ± 0.4	4.78 ± 0.4	5.3 ± 0.4
Thymol test, units	2.8 ± 0.6	5.2 ± 0.4	3.3 ± 0.4	2.3 ± 0.5	1.8 ± 0.5
Total cholesterol, mmol\L					*
	5.41 ± 0.5	5,72 ± 0,4	6.55 ± 0,3	5.68 ± 0.4	4.1 ± 0.4

**p < 0.05; **p < 0.01; ***p < 0.001; in the upper corner – reliability with the control group; in the lower corner – reliability with the previous group.

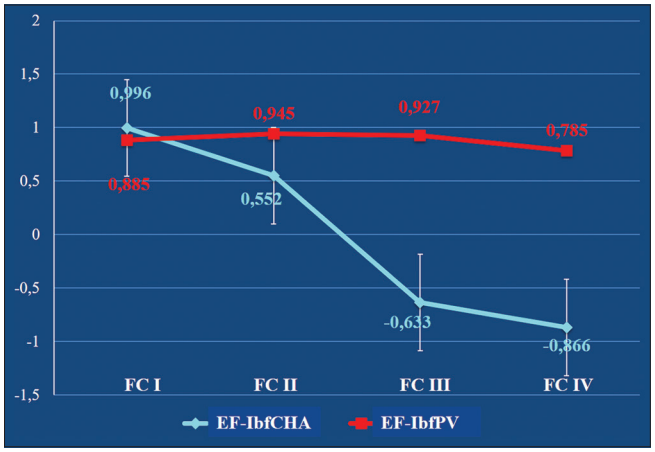

Figure 1: Relationship between CI, VIvPV, and IbfPV

a high correlation between CI and VIvPV. Moreover, this relationship was preserved, from stage to stage: FC I – r = 0.885 at p < 0.05; FC II – r = 0.945 at p < 0.05; FC III – r = 0.927 at p < 0.01; and FC IV – r = 0.785 at p < 0.01.

The values of the correlation coefficients remain within the same limits, which indicate that the progression of central hemodynamic disorders affects hepatic hemodynamics.

When analyzing the relationship between CI and IbfPV, a direct correlation was revealed (FC I – r = 0.996, p < 0.05 and FC II – r = 0.552, p < 0.05) characteristic of the initial stages of CHF. With an increase in the severity of CHF, there is a redistribution of venous bf to the liver and a moderate correlation of CI and IbfPV changes toward the emergence of feedback (FC III – r = −0.633, p < 0.05 and FC VI – r = −0.866, p < 0.05).

Interesting results were obtained in the analysis of arterial bf (Figure 2). At the earliest stages of CHF in patients with FC I, there was a positive relationship between CI and VIvCHA, as well as between CI and IbfCHA (r = 0.758, p < 0.05; r = 0.813, p < 0.01). This result most likely indicates that compensatory mechanisms are activated in patients of this group,

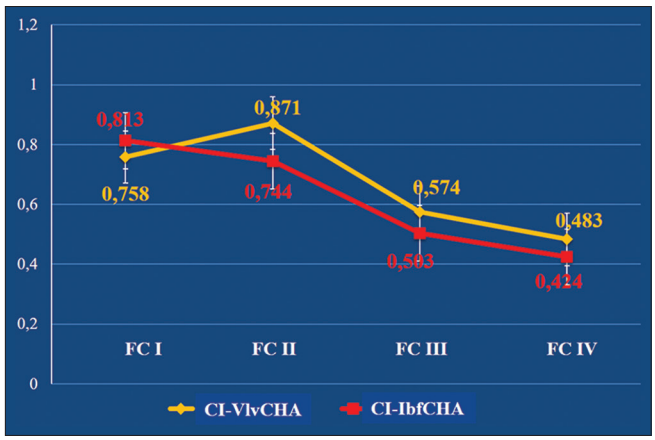

Figure 2: Relationship between CI, VIvCHA, and IbfCHA

maintaining arterial bf at an optimal level. As CHF progresses, the relationships appear in the presence of moderate direct correlations between CI and VIvCHA and CI and IbfCHA (FC II – r = 0.871 and 0.744 at p < 0.01; FC III – r = 0.574 and 0.503 at p < 0.01; and FC IV – r = 0.483 and 0.424 at p < 0.05).

As shown in Figure 3, a direct moderate relationship was revealed between the indicators of EF, IbfCHA, and IbfPV (FC I – r = 0.359 and 0.488 at p < 0.05; FC II – r = 0.403 and 0.549 at p < 0.01; FC III – r = 0.594 and 0.588 at p < 0.01; and FC IV – r = 0.533 and 0.632 at p < 0.05).

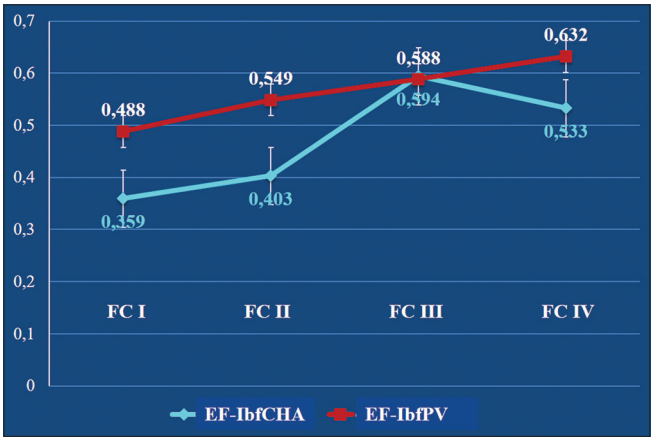

Figure 3: Relationship between EF, IbfCHA, and IbfPV

As a result of the correlation analysis, the fact of the influence of peripheral vascular resistance on the blood circulation of the liver was confirmed once again. Thus, an inverse correlation was observed from group to group (FC I – r = −0.569 and −0.681 at p < 0.01; FC II – r = −0.548 and −0.479 at p < 0.05; FC III – r = −0.468 and −0.756 at p < 0.05; and FC IV – r = −0.657 and −0.794 at p < 0.05), which is shown in Figure 4, the value of linear velocities is the lower, the higher the SPVR.

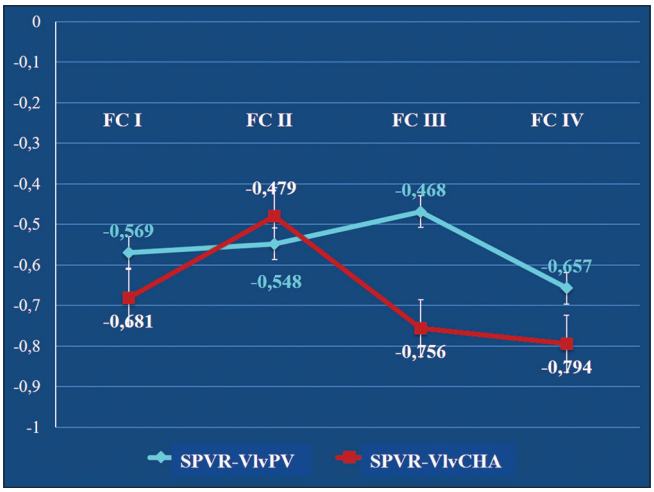

Figure 4: Relationship between SPVR, VIvPV, and VIvCHA

The dynamics of bf depends not only on the linear velocities but also on the diameter of the vessels and has a multidirectional character.

For bf in PV, in response to an increase in SPVR, an expansion of the PV diameter is inherent and the interdependence is most pronounced in patients with a severe course of the disease (FC III – r = 0.683 at $p < 0.05$ and FC IV – r = 0.423 at $p < 0.05$).

The values of the correlation coefficients between SPVR and DCHA with an increase in the severity of CHF are inverse (FC II – r = 2212-0.492; FC III – r = −0.894, $p < 0.01$; and FC IV – r = −0.428, $p < 0.05$).

An inverse close correlation was also established between the linear and volumetric velocities of the arterial and portal bf of the liver, which was most pronounced in patients with FC III (FC II – r = −0.458 and −0.662 at $p < 0.01$; FC III – r = −0.894 and −0.783 at $p < 0.01$; and FC IV – r = −0.428 and −0.556 at $p < 0.05$).

In the initial stage of CHF, there is a compensatory significant narrowing of the lumen of the common hepatic artery (up to 4.75 mm, $p < 0.05$), maintaining bf in it, but as the disease worsens, progressive dilatation of the vessel is observed (from 6.09 to 7.10 mm), leading to a decrease in inflow.

A close direct relationship between the indicators of the CI and the linear velocity of bf was revealed (FC I – r = 0.885, $p < 0.01$; FC II – r = 0.945, $p < 0.05$; FC III – r = 0.927, $p < 0.01$; and FC IV – r = 0.785, $p < 0.01$); inverse correlation between indicators of linear bf velocity in the portal vein, common hepatic artery and SPVR (FC I – r = −0.569 and −0.681, $p < 0.01$; FC II – r = −0.548 and −0.479, $p < 0, 05$; FC III – r = −0.468 and −0.756, $p < 0.05$; and FC IV – r = −0.657 and −0.794, $p < 0.05$), which will allow evaluating the effectiveness of drug therapy.

Conclusion

Thus, analyzing the blood circulation of the liver as a whole, we noted that with an increase in the FC of CHF, the values of linear bf velocities decrease, and the diameters of both the common hepatic artery and the portal vein increase. Moreover, for the venous bed, the increase in diameter was more pronounced (most likely due to a violation of the outflow of blood through the hepatic veins). Changes in arterial bf in patients with CHF had a multidirectional character from group to group, narrowing of the lumen of the vessel at the initial stages of the disease and its progressive expansion to FC IV, fully reflect the changes in central hemodynamics, and are explained by the structure of the vessel and its lability in relation to the neurohumoral influences characteristic of the development of CHF. The study of some biochemical parameters of blood serum characterizing individual liver functions in patients suffering from CHF of ischemic origin allows us to presumably speak about their dependence on FC of CHF, namely, from disorders of hepatic hemodynamics. Hemodynamic disorders are observed earlier, being the primary pathogenetic factor, and the resulting functional disorders of the liver are secondary, which makes it possible to consider hepatic bf disorders as one of the early markers of the initial manifestations of CHF.

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