International Journal of Medical Toxicology & Legal Medicine **Volume 27, No. 5, 2024**
e-ISSN: 0974-4614
p-ISSN: 0972-0448
https://doi.org/10.47059/ijmtlm/V27I5/007

Study of the Influence of Humoral Factors on the Development of Remodeling Of the Cardiovascular System in Patients with Chronic Heart Failure

Zulfiya M. Shoalimova[1], Nigora B. Nuritdinova[2], Munira S. Makhmudova[3], Dilfuza Z. Yarmuxamedoova[4], Surayyo M. Shukurdjanova[5], Maksuda T. Zubaydullaeva[6], Rano Sh. Rajabova[7]

[1,2,3,4,5,6,7]Researcher Tashkent Medical Academy Tashkent, Uzbekistan

Received: 15.09.2024 Revised: 16.10.2024 Accepted: 26.11.2024

ABSTRACT
The purpose of the study. To study functional-humoral markers of endothelial dysfunction and their relationship with the progression of CHF(chronic heart failure) in patients with postinfarction cardiosclerosis.
Materials and methods of research: The study involved 100 patients with postinfarction cardiosclerosis (PIC) complicated by CHF: men aged 38-60 years (average age - 51.8±1.03 years).The patients were in the cardiology department of the 1st clinic of the Tashkent Medical Academy. All patients underwent ECG, EchoCG, Doppler ultrasonography of the brachial artery with reactive hyperemia(RH) and a nitroglycerin test(NTG), a study of platelet aggregation activity and the level of Willebrand factor in blood plasma.
Results: In patients with I FC CHF, the systolic and diastolic blood flow rate in the BA(brachial artery) was lower compared to the control group. In patients with I FC CHF, the diameter of the BA was less by 2.4%. In patients with CHF, in response to an increase in blood flow rate by 125.4±5.1, the diameter of the BA increased by 8.7±1.0 versus 11.4±1.76% in healthy individuals. In patients with I FC, there was a decrease in endothelium-dependent vasodilation, the indications EIV(endothelium-independent vasodilation) of were 14.8±2.4% versus 17.8±2.4% in healthy individuals.The pulsatile index (Pi) in patients with FC I CHF exceeded by 14.4, and the resistive index (Ri) by 8.8. A decrease in EDV(endothelium-dependent vasodilation) was noted in 68% of patients, pathological vasoconstriction - in 30%, in 2% of patients with EDV of BA persisted. There was a decrease in systolic blood flow rate by 28.2%, diastolic by 62% ($P<0.01$).In patients with b, the platelet aggregation activity index (PAAI) was significantly lower by 2.6 times.The level of Willebrand factor in patients with CHF I FC was 11.7% higher than the control.
Conclusions: Endothelial dysfunction in patients with CHF is characterized by a decrease in EDV, pronounced paradoxical vasoconstriction, increased platelet aggregation activity and von Willebrand factor, which are more pronounced in patients with CHF III FC.

Keywords: chronic heart failure, endothelial dysfunction, platelet aggregation activity, Willebrand factor

Relevance
Chronic heart failure (CHF) is one of the most common, progressive and prognostically unfavorable diseases of the cardiovascular system, as well as one of the most frequent causes of hospitalizations [2, 12, 48, 56, 68, 245].The most common cause of CHF is coronary heart disease (CHD), which is 54-68.6%. The suffered myocardial infarction, being one of the main causes of the development of CHF, is characterized by postinfarction remodeling of the left ventricle (LV): structural and functional restructuring of the LV and violation of its systolic and diastolic functions [3, 11, 14, 15, 107, 110]. The sympathoadrenal system is activated, which, in turn, stimulates the renin-angiotensin system and other neurohormones and mediators, including tumor necrosis factor, cytokines, Willebrand factor, endothelins [16, 62, 88, 131 ,170, 205, 207]. By the beginning of the century, the attention of clinicians was clearly focused on the role of endothelial dysfunction (ED) in the formation of chronic heart failure [2, 17, 19, 20, 45, 46, 180, 237]. It is proved that the markers of endothelial dysfunction are a decrease in endothelium-dependent vasodilation of vessels, a change in the content of regulatory peptides in the blood: endothelin-1, Willebrand factor [122, 151, 202, 216]. Most studies in this area are related to the assessment of vascular reactions in the method of endothelium-dependent vasodilation. At the same time, a marker of developing ED can serve as a change in the content of von Willebrand factor in the blood, the main source of which is endothelium [18, 99, 138, 151, 215, 246].

Few studies have revealed positive correlations between LV remodeling and platelet functional activity [7, 97, 243, 245]. Modern principles of CHF therapy, taking into account the complex and multicomponent genesis of the disease, require an impact on the remodeling processes of the cardiovascular system: the concept of the so-called "reverse remodeling", in which a fundamental impact on the course and outcome of heart failure (HF) is possible [57, 64, 123, 159, 187].

The purpose of the study

To study functional-humoral markers of endothelial dysfunction and their relationship with the progression of CHF in patients with postinfarction cardiosclerosis(PIC).

Materials and methods of research

The study involved 100 patients with PIC complicated by CHF: men aged 38-60 years (average age - 51.8±1.03 years). The prescription of what MI suffered was 2 months to 3 years. The patients were randomized according to FC CHF according to the New York Classification of Cardiologists, according to the six-minute walk test (SWT) and according to the clinical condition assessment scale (CCAS) of patients.All patients were hospitalized in the cardiology department of the 1st clinic of the Tashkent Medical Academy and were registered in the consultative polyclinic. The diagnosis was established according to the data of clinical and laboratory-instrumental studies. The examination did not include patients with acute cerebral circulatory disorders, severe diabetes mellitus, cardiac arrhythmias, chronic obstructive pulmonary disease.

All patients underwent an ECG, the whole complex of clinical and biochemical examinations, TSH, EchoCG. Dopplerography of the brachial artery with reactive hyperemia (RH) and nitroglycerin (NTG) test was performed, the aggregation activity of platelets and the level of Willebrand factor in blood plasma was studied.Determination of the Willebrand factor in blood plasma was determined using a quantitative enzyme immunoassay method using "RENAM" reagents on a Vidas analyzer (France).

Study of the vasomotor function of the endothelium.The state of endothelial function was assessed by Doppler ultrasonography of the brachial artery according to the method of D. S. Celemajer (1992) using a test with reactive hyperemia and nitroglycerin [223]. Changes in the diameter of the right brachial artery were evaluated using a 7 MHz linear sensor with a phase array of the Acuson 128 ultrasound system (USA). The BA was located in the longitudinal section 4-5 cm above the elbow bend, the image was synchronized with the ECG wave (Fig.1). The study was carried out in triplex mode (B-mode, color Doppler flow mapping, spectral analysis up to of the pleurian frequency shift). Before the start of the study, the patient lay on his back for at least 10 minutes. In the initial state, the diameter of the artery and the velocity of arterial blood flow were measured using spectral analysis. Then, to obtain increased blood flow around the shoulder, a sphygmomanometer cuff was applied (above the location of the brachial artery), it was pumped up to a pressure of 50 mm m. exceeding systolic blood pressure, and it was kept for 5 minutes. The absence of BA blood flow was controlled using color Doppler flow mapping. The diameter and velocity of the BA blood flow were measured immediately after the release of air from the cuff for the first 15 seconds. and after 60 seconds. After 15 min. after rest, after restoring the original diameter of the BA, an image of the artery was recorded at rest, the patient received sublingual 500 mcg of nitroglycerin. The image of the artery was recorded at 1 and 3 minutes. The change in vascular diameter after reactive hyperemia and after taking nitroglycerin was estimated as a percentage of the initial value. The normal reaction of BA was considered to be its expansion against the background of reactive hyperemia by 10% or more of the initial diameter. A lesser degree of vasodilation and vasoconstriction was considered a pathological reaction. The shear stress on the endothelium was calculated according to the formula of O. V. Ivanova, [39]:

□ □4□ □ □V/D

where: τ - shear stress, n - blood viscosity (on average equal to 0.05), V- maximum blood flow velocity in BA (cm/sec), D - diameter of BA.

A unified indicator K was used − "sensitivity of the PA to a change in the stimulus − shear stress on the endothelium":

$K= (\Delta D/D_0)/(\Delta\tau/\tau_0)$,

where: ΔD is the change in the diameter of the BA, D_0 is the initial diameter of the PA, Δτ is the change in the shear stress, τ_0 is the initial shear stress.

The following parameters were evaluated:

- D is the diameter of the right brachial artery (BA), cm
- D1 is the diameter of the BA after the RH test, cm
- D2 is the diameter of the BA after the nitroglycerin test, cm
- Vs - systolic blood flow rate in BA, m/s
- Vd - diastolic blood flow rate in BA, m/s
- Vsr - average blood flow rate in BA, m/s
- Pi - pulsation index: PI=(Vs - Vd)/ Vsr , rel. units.

- Ri - resistive index: Ri=(Vs - Vd)/ Vs , rel. units
- EDV= (D- D)/ Dx100%
- EDV= (D2- D)/ Dx100%
- K, sensitivity BA, rel. units.

Statistical processing of the study results was carried out using the ECXEL 6.0 Windows-95 spreadsheet package. The parameters were described as: arithmetic mean ± standard deviation (M±SD). If the normal distribution law was not observed, the data were described as median ± standard deviation. With a normal distribution of values, intergroup comparisons of quantitative variables were carried out using the Student's criterion (t): for cases of equal and unequal variances. The Wilcoxon rank criterion was used to estimate the difference in the averages for the two groups when the numbers did not correspond to the normal distribution law. The data in dynamics were analyzed by the corresponding paired criteria. To analyze the dependencies of the features, the Pearson pair correlation coefficient (r) was calculated.

The study was approved by the Ethics Committee of our Medical Academy. Patients were carefully informed of the scope and procedures of the study and gave informed written consent to participate in the study.

The results of the study. Indicators of endothelial dysfunction assessed by the results of the vasomotor reaction of BA revealed that, as CHF progresses, the blood flow rate significantly decreases (Table 1). In patients with I FC CHF, the systolic blood flow rate (Vs) in BA was initially lower by 19.5, and the diastolic velocity (Vd) by 35% compared with the control group. The baseline level of the average blood flow velocity was 46.7±1.85cm/s. In patients with I FC CHF at rest, the BA diameter is 0.43±0.023 cm versus 0.41±0.02 cm in healthy individuals. In patients with I FC CHF, the diameter of the BA was smaller compared to the control group by 2.4%. Changes in the diameter of the BA on the RH in the control group occur with an increase in the diameter of the vessel, unlike in patients with CHF, in whom, after the compression test, the diameter of the vessel decreases.

Table 1: Initial state of blood flow in the brachial artery in patients with I – III FC CHF, (M ±SD)

Indicators	CG	FC I	FC II	FC III
D_0 ,cm	0,41±0,02	0,43±0,023	0,38±0,047**	0,33±0,010**
D_1 ,cm	0,45±0,02	0,47±0,027	0,41±0,049**	0,34±0,017**
D_2 ,cm	0,47±0,02	0,49±0,022	0,43±0,022**	0,37±0,012**
Vs ,cm/s	92,14±3,77	74,40±2,1	67,1±1,91	66,3±3,05
Vd, cm/s	29,43±3,85	19,0±1,82	14,8±1,47	11,2±1,22
Vm, cm/s	60,79±3,59	46,7±1,85	40,95±1,55**	38,75±1,86*
Ri, rel.units	0,68±0,03	0,74±0,02	0,78±0,019	0,83±0,017
Pi, rel.units	1,04±0,07	1,19±0,05	1,28±0,05	1,42±0,049
EDV, %	11,4±1,76	8,7±1,0	7,2±1,1**	5±3,9**
EIV,%	14,8±2,4	14,0±2,29	12±3,14**	12,8±4,71**
τ_0, dyn/cm²	29,8±1,91	28,1±1,6	31,1±4,5**	34,8±4,9**
τ_1, dyn/ cm²	54,18±4,04	53,9±3,3	54,7±6,3**	59,9±4,2**
K, rel. units.	0,14±0,03	0,10±0,013	0,07±0,012**	0,05±0,043**

Note: significant difference from the control: * P<0.05; ** P<0.01

*CG-control group

*EIV-Endothelin-independent vasodilation

In patients with CHF, in response to an increase in blood flow rate by 125.4±5.1, the diameter of the BA increased by 8.7±1.0 versus 11.4±1.76% in healthy individuals. Endothelium-dependent vasodilation was 11.4±1.7% in the control group, and in patients with I FC there was a decrease in this indicator by 23.6 and 25.4% compared with the control group. The indicators of EIDV(Endothelium-independent vasodilation) were 14.8±2.4% versus 17.8±2.4% in healthy individuals.The pulsative index (Pi) initially exceeded the control by 14.4 in patients with CHF I FC, and the resistive index (Ri) by 8.8.

The shear stress was measured before and after the RH sample (τ_0 and τ_1), the level of which (t0) slightly differed from the control, and t1 was significantly lower by 7% of the CG index. As for the sensitivity of the BA to shear stress, i.e. the ability of the BA to vasodilation, in patients with I FC CHF, it was significantly lower than the control by 28.6%.

At II FC CHF, the diameter of the BA decreased by 7.3 from the control. There was a decrease in systolic blood flow rate in the BA by 27.4%, as well as diastolic blood flow rate by 49.7 (P<0.01) compared with the control group. The average blood flow rate in patients with FC II CHF was reduced by 32.6 compared to the data of healthy individuals.Analysis of the initial indicators of the resistive index revealed that in patients with CHF II

FC, this indicator was significantly higher compared to the control by 14.7. Initially, the pulsative index in these patients exceeded the indicators of the control group by 23.3% (P <0.01).

The diameter of the BA after the RH test increased in the control group by 11.4 ± 1.76%. In patients with CHF, in response to an increase in blood flow rate by 117.8 ±6.4, the diameter of the BA increased by 7.2± 1. In the phase of reactive hyperemia(RH), patients had an increase in the diameter of the BA to 0.41±0.049 cm, versus 0.45±0.02 in healthy individuals. The indicators of EDV in patients with FC II CHF were significantly lower by 36.8% (P<0.001), and EIV exceeded it by 9.9% compared to the values of the control group. The baseline level of τ0 and τ1 was 31.1±4.5 din/cm2 and 54.7±6.3 din/cm2 versus 29.8±1.91 and 54.2±4.04 din/cm2 in healthy individuals. Initially, the BA sensitivity index to shear stress in patients with CHF II FC was reduced by 28.5% from the control group.

In patients with FC III CHF, a serious violation of EDV was found, indicating a sharp deterioration in the functional state of the endothelium.Its decrease was noted in 68% of patients, pathological vasoconstriction - in 30%, only 2% of patients with EDV of BA persisted. There was a significant decrease in systolic blood flow rate by 28.2%, diastolic by 62% (P<0.01) from the control group. There was a decrease in the average blood flow rate in patients with III FC CHF by 36.2% compared with the data of healthy individuals, amounting to 38.7± 1.84 cm/s. The diameter of the BA was lower by 19.5%. At the III FC of CHF, the EDV was 5±3.9%, versus 11.4±1.7%, i.e. there was a decrease in this indicator by 56.52% (P<0.001). The pulsative index initially in patients with FC III CHF exceeded the indicators of the control group by 36.5% (P<0.01). Analysis of the resistive index data showed that this indicator was 29.6% higher (P<0.05) compared to the control group. In patients with FC III CHF, there was a marked decrease in the BA sensitivity to shear stress - by 64.3% (P<0.001) from the control group (Table 1).

The change in the diameter of the BA after the test with nitroglycerin is a functional and morphological substrate of endothelin-dependent vasodilation (EDV). In patients, the indicators of EIV were 14± 2.29; 14.2± 4.5 and 15.8± 5.2%, respectively, FC. In patients with FC III CHF, the shear stress at rest and after RH significantly increased by 1.2 times from the norm. Assessing the relationship between the severity of CHF and the severity of endothelial dysfunction, we found that all patients with CHF had endothelial dysfunction, and its severity increased with the progression of CHF.

A study of the functional activity of platelets in the first FC of CHF showed that in patients with b, the platelet aggregation activity index (PAAI) was significantly lower by 2.6 (Table 2) than in healthy individuals, amounting to 1.85±0.94 mmol of ADP versus 4.72±0.22 mmol of ADP. The platelet aggregation rate (Vagr) in was 1.79±0.52cm/min versus 0.34±0.5cm/min in healthy individuals, i.e. there was a significant increase in the aggregation rate by 5.2 times compared with the control. The maximum aggregation amplitude (Amax) was also significantly high, 4.8 times higher than in healthy individuals and was 2.43±0.46cm versus 0.5±0.21 cm.

In patients with FC II CHF, the decrease in PAAI was more pronounced - 2.7 times from the control. There was an increase in Vagr by 5.5 times (P<0.01) than the indicators of the control group, amounting to 1.89±0.13 cm/min, versus 0.34±0.5 cm/min. There was also an increase in Amax by 5.6 times (P<0.01) amounting to 2.84±0.46 cm, versus 0.5±0.07 cm in healthy individuals.

Table 2: Baseline indicators of ADP-induced platelet aggregation in patients of the first and second groups I – III FC CHF, (M±SD)

Groups of patients	V agr,cm/min	Amax, cm	PAAI, mkmol ADP
Control	0,34±0,5	0,5±0,07	4,78±0,22
FC I	1,79±0,52	2,43±0,46	1,85±0,94
FC II	1,89±0,13	2,84±0,46	1,78±1,28
FC III	2,9±0,47	3,5±0,53	1,5±1,60

The progression of CHF further disrupted the studied indicators. At III FC CHF, the decrease in PAAI from control was 3.2 times (P<0.001), amounting to 1.5 ± 1.60 mmol of ADP. The increase in the indicators of Vagr and Amax is 8.5 times (P<0.001) and 7 times (P<0.001). An integral marker in the formation of ED(endothelial dysfunction) is the activity of the von Willebrand factor. Its initial level in patients with CHF I FC was 11.7% higher than the control, amounting to 125.6 ± 5.30%, versus 112±13.9% in healthy individuals. In patients with FC II CHF, there was a significant increase in the level of von Willebrand factor(VWF), compared with the indicators of the control group by 40.5%. The baseline level of VWF in patients with CHF II FC was 158± 3.46%.In patients with CHF III FC, this indicator was significantly higher by 51.4% (P<0.001) than in the control group, amounting to 170.2±6.37%. Consequently, the level of VWF determined in blood plasma in patients with CHF depends on the degree of functional class, its greatest values are observed in patients with III FC (Fig. 1).

Thus, we found that endothelial function is impaired in patients with I-III FC CHF. This is expressed by a decrease in EDV, blood flow velocity indicators, paradoxical vasoconstriction, a decrease in endothelial sensitivity to shear stress, as well as an increase in vascular tone, platelet aggregation ability and the level of

FFV in blood plasma. In addition, an increase in vascular tone and vascular resistance, deterioration of vasorelaxation properties of the endothelium and, as a consequence, a decrease in the ability of the artery to vasodilation, is directly related to LV remodeling processes, which are especially pronounced in patients with III FC CHF.

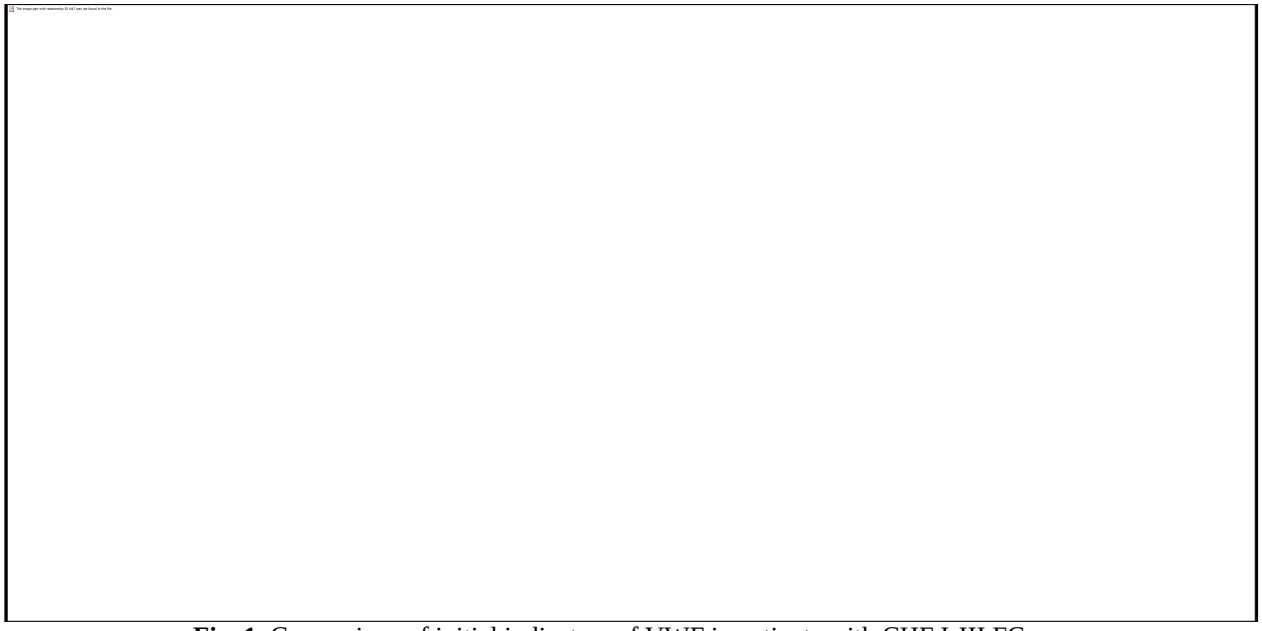

Fig. 1. Comparison of initial indicators of VWF in patients with CHF I-III FC

DISCUSSION

The problem of chronic heart failure is caused by the steady increase in its frequency, the continuing high morbidity and mortality, and the significant cost of treatment of decompensated patients [1, 12, 68].The complex of changes occurring in the heart after myocardial infarction, Preffer M. and Braunwald E. characterized as "postinfarction LV remodeling". Neurohumoral factors play an important role in the pathogenesis of LV: supporting cardiac output, they thereby cause energy imbalance and dysfunction of cardiomyocytes, which eventually leads to pronounced systolic dysfunction [200, 225, 229].

A long-term study of the cardiovascular system in normal and pathological conditions has shown that vascular homeostasis is largely supported by the normal operation of the vascular endothelium - a thin semi-permeable membrane separating the systemic blood flow from the internal structure of the vascular wall. Disruption of the vascular endothelium leads to impaired vasomotor tone, local and systemic spastic reactions, thrombosis, vascular remodeling and progression of CHF. With CHF, the endothelium cannot produce nitric oxide to meet metabolic needs, EDV is affected, the stimulated release of nitric oxide to acetylcholine, and bradykinin decreases. The state of the endothelium is characterized as a dysfunction, manifested by a decrease in vascular dilation and an increase in vasoconstriction, activation of the cytokine system and a violation of thrombosis resistance of the vascular wall. [2, 9, 17, 133, 145].

We examined 100 men with PIC, complicated by CHF, aged 40-60 years. The patients were randomized into groups of FC CHF according to the New York Classification of Cardiologists according to SWT, CCAS.Progression of clinical signs of HF in patients with PIC was accompanied by a violation of endothelial function. In CHF, it is very important to assess the functional and humoral markers of endothelial dysfunction - a decrease in EDV, an increase in platelet aggregation activity, tumor necrosis factor, cytokines, von Willebrand factor, endothelins [2, 4, 80].

The vasodilating function of the endothelium was evaluated by the parameters of blood flow BA, with a breakdown of RH and NTG. This method is based on the Ostroumov-Bayliss reflex: large vessels react to shear stress by vasodilation, reflex spasm and pressure restriction on the capillary wall are observed in resistive vessels.

To assess the vasodilating function of the endothelium, we studied the parameters of blood flow in the brachial artery with an assessment of endothelium-dependent and endothelium-independent vasodilation. In patients with I FC CHF, the diameter of the BA was 2.4% smaller compared to the control group. Systolic blood flow rate (Vs) in BA was significantly lower by 19.5% ($P<0.01$), and diastolic velocity (Vd) by 35% compared to the control group ($P<0.01$). Analysis of the initial data of the resistive index Ri – reflecting the state of resistance to blood flow distal to the measurement site, showed that in patients with I FC, CHF was significantly higher compared to the control group by 8.8% ($P<0.01$). The pulsatile index, indirectly reflecting the tone of the vessel,

exceeded the indicators of the control group by 14.4% (P<0.01). Endothelium-dependent vasodilation was 11.4±1.7% in the control group, and in patients with I FC, this indicator decreased by 23.6% compared with the control group. In patients with FC II CHF, there was a decrease in the diameter of the BA by 7.3%, compared with the indicators of the control group. There was a decrease in systolic blood flow rate in BA by 27.4%, and diastolic blood flow rate by 49.7% (P<0.01) compared to the control group. The average blood flow rate in patients with FC II CHF was reduced by 32.6 % compared to the data of healthy individuals.Analysis of the initial indicators of the resistive index revealed that in patients with CHF II FC, this indicator was significantly higher compared to the control by 14.7%. And the pulsative index initially in these patients exceeded the indicators of the control group by 23.3% (P < 0.01). There was a decrease in EDV by 36.8% compared to the control group. Initially, the BA sensitivity index to shear stress in patients with CHF II FC was reduced by 28.5% from the control group.

At the III FC of CHF, serious EDV disorders were noted, indicating a sharp deterioration in the functional state of the endothelium: in the III FC of CHF, EDV decreased in 68% of patients, pathological vasoconstriction was detected in 30%, and only 2% of EDV BA persisted. There was a significant decrease in systolic blood flow rate by 28.2%, diastolic by 62% (P<0.01) from the control group. There was a decrease in the average blood flow rate in patients with III FC CHF by 36.2% compared with the data of healthy individuals, amounting to 38.7± 1.84 cm/s. The diameter of the BA was lower by 19.5%. At the III FC of CHF, the EDV was 5±3.9% versus 11.4±1.7%, i.e. there was a decrease in this indicator by 56.5% (P<0.001). The pulsative index initially in patients with FC III CHF exceeded the indicators of the control group by 36.5% (P<0.01). Analysis of the resistive index data showed that this indicator was 29.6% higher (P<0.05) compared to the control group. In patients with FC III CHF, there was a marked decrease in the BA sensitivity to shear stress - by 64.3% (P<0.001) from the control group.

The change in the diameter of the BA after the test with NTG is a functional and morphological substrate of endothelin-dependent vasodilation (EDV). At the same time, almost the same reaction to vasodilation was observed in all patients. The indicators of EIV were 14± 2.29; 14.2± 4.5 and 15.8±5.2%, respectively, FC. Perhaps this is due to the processes of vascular remodeling in CHF: the predominance of the vasoconstrictor reaction during the RH test and the resulting decrease in NO production. And the exogenous introduction of NO made up for its deficiency, increasing vasodilation during the test with NTG (SchoemeN., 2001; Buvaltsev V.I., 2004; Sitnikova M.Yu., 2005).

One of the humoral markers characterizing the function of the endothelium is the determination of the functional activity of platelets. According to many studies in patients with CHF, there is an increase in platelet aggregation activity [33, 96].

The results of the study of platelet functional activity in patients with CHF I FC showed that in patients, platelet aggregation activity (PAA) was significantly 2.6 times higher than in healthy individuals, amounting to 1.85±0.94 mmol of ADP, respectively, versus 4.72±0.22 mmol of ADP. The initial platelet aggregation rate (Vagr) was 1.79±0.52 cm/min, versus 0.34±0.5 cm/min, and the maximum amplitude (Amax) was 2.43±0.46 cm, versus 0.5±0.07 cm. There was a significant increase in the aggregation rate by 5.2 times and the maximum aggregation amplitude by 4.8 times, compared with the CG data. At FC II, CHF PAA was 2.7 times lower, and the platelet aggregation rate and maximum amplitude were 5.5 times and 5.6 times higher than in healthy individuals. Similarly, but more pronounced, the indicators changed at III FC CHF: PAA was 3.2 times (P<0.001) less than in healthy individuals, the platelet aggregation rate and maximum amplitude were 8.5 and 5.5 times higher (P<0.02).

Thus, the analysis of platelet functional activity showed a more pronounced increase in platelet aggregation activity in patients with CHF III FC.

CONCLUSIONS

Endothelial dysfunction in patients with CHF is associated with the progression of the disease and is characterized by a decrease in EDV, pronounced paradoxical vasoconstriction, increased platelet aggregation activity and von Willebrand factor secretion, which are more pronounced in patients with CHF III FC.

Funding

This research received no external funding

Conflicts of Interest

The authors declare no conflict of interest.

REFERENCES

1. Abdullaev T.A. Quadropril in the treatment of circulatory insufficiency // Eastern news. - Tashkent, 2001. No. 9, - p. 32.

2. Ageev F.E., Skvortsov A.A., Mareev V.Yu., Belenkov Yu.N. Heart failure against the background of coronary heart disease: some issues of epidemiology, pathogenesis and treatment // Rus.med. zhurn.– 2000. – Vol.8, No. 15/16. – Pp.622–626.
3. Ageev F.T., Ovchinnikov A.G., Mareev V.Yu., Belenkov Yu.N. Endothelial dysfunction and heart failure: pathogenetic relationship and possibilities of therapy with angiotensin converting enzyme inhibitors. // Consilium–medicum. – M., 2001 – vol. 3, No.2, – pp. 61-65.
4. Baluda V.P., Barkagan Z.S., Goldberg E.D. Laboratory methods of hemostasis system research. Tomsk, 1990.pp. 112-116.
5. Belenkov Yu.N., Mareev V.Yu. On the classification of chronic heart failure at the turn of the century // Heart failure – 2000. – No. 3. – pp. 24-30.
6. Belenkov Yu.N., Mareev V.Yu., Ageev F.T. – Chronic heart failure. Selected lectures on cardiology. – M.: GEOTAR–Media, 2006 -p. 432.
7. Belenkov Yu.N., Mareev V.Yu., Ageev F.T. Classification of chronic heart failure // Heart failure. - 2001. – Vol. 2, No. 6. – pp. 249-250.
8. Belenkov Yu.N., Mareev V.Yu., Arutyunov G.P., Ageev F.T. National recommendations for the diagnosis and treatment of CHF. // Journal of Heart Failure. – M., 2003 – vol.4, No. 6 (22) -pp. 276 – 297.
9. Bespalko I.A., Vasilyeva E.Yu., Varlamova N.A. The relationship between the levels of tissue plasminogen activator and Willebrand factor in normal and in patients with coronary heart disease. Cardiology No. 5 1996, pp.27-29.
10. Berezin. A.E. The state of endothelial function in patients with coronary heart disease and heart failure of elderly and senile age// Problems of aging and longevity.-2000.-No. 1.-pp.47-52.
11. Bokarev I.N., Privalova E.V., Privalova N.V. Features of the Willebrand factor change in patients with coronary heart disease. Cardiology 1988, volume 28, No. 5: -pp.101-103.
12. Vizir V. A., Berezin A. E. Prospects of reversion of endothelial dysfunction in patients with congestive heart failure // Clinical medicine: Monthly scientific and practical journal. - 2000. - Volume 78, N 7. - pp. 36-39.
13. Volkova E.V. Functional state of the endothelium and hypolipidemic therapy in patients with ischemic heart disease who suffered a myocardial infarction at a young age //Abstract of the diss. for the degree of Candidate of Medical Sciences, St. Petersburg, 2000; – pp. 10-13.
14. Kovalev I.A., Martsinkevich G.I., Suslova T.E., Sokolov A.A. Endothelial dysfunction in individuals with heredity burdened by atherosclerosis.// Cardiology.- 2004.- No. 1.- pp. 39-42.
15. Kovalenko V.N., Gulaya N.M., Semikopnaya T.V., etc. Endothelial dysfunction in patients with ischemic heart disease in combination with arterial hypertension // Ukr. cardiol. Journal. – 2003. – No. 3. – pp. 34-37.
16. Kurbanov R. D., Mamutov R.S. Analysis of the activities of the specialized cardiological service of the Republic of Uzbekistan for 2003.-Tashkent, 2004.- p.16.
17. Leluk V.G., Leluk S.E. Basic principles of hemodynamics and ultrasound examination of blood vessels. Clinical guidelines for ultrasound diagnostics // Edited by V.V. Mitkov. – M., 1997. – pp. 185-220.
18. Malaya L.T., Korzh A.N., Balkova L.B. Endothelial dysfunction in pathology of the cardiovascular system. Kharkov. TORSING. 2000, - P. 10-20.
19. Mareev V.Yu., Danielyan M.O., Belenkov Yu.N. On behalf of the EPOCH–O–HSN research working group. Comparative characteristics of patients with CHF depending on the value of the PV according to the results of the Russian multicenter study EPOCH–O–CHF. // J. Heart failure, 2006. No. 2: 18-21.
20. Mareev V.Yu.. The results of the most interesting studies on the problem of heart failure in 1999 // J. Heart failure. 2000; Vol. 1, No. 1: -pp. 8-17.
21. Nasonov E.L. Markers of endothelial activation (thrombomodulin, Willebrand factor and angiotensin converting enzyme): clinical significance // Clinical Medicine. - 1998. - No.11.–p– 4-6
22. National Recommendations on the diagnosis and treatment of CHF (second revision) //Journal of Heart Failure 2007 Volume 8 No. 2 pp.1-34.
23. Olbinskaya L.I., Sizova Zh.M. Chronic heart failure // Monograph. – M.: "Reafarm", 2001. – 344 p.
24. Tereshchenko S.N., Demidova I.V., Borisov N.E., Moiseev V.S. Clinical and hemodynamic efficacy of carvedilol in patients with congestive heart failure // Cardiology. - 1998. – No. 2. – pp. 43-46.
25. Shlyakhto E.V., Moiseeva O.M., Lyasnikova E.A., etc. Rheological properties of blood and endothelial function in patients with hypertension //Cardiology, 2004. No. 4. - p. 20 -23.
26. Al Khadra AS, Salem DN, Rand WM et al. Antiplatelet agents and survival: a cohort analysis from the Studies of Left Ventricular Dysfunction (SOLVD) trial. //J Am CollCardiol. 1998;31: – P. 419–425.
27. Andreotti F., Hackett D.R., Haider A.W. et al.VonWillebrand factor, plasminogen activator inhibitor-1 and C-reactive protein are markers of thrombolytic efficacy in acute myocardial infarction.//Thromb.Haemost.2002., 68 – P. 678-682.

28. Bolger A.P.,Al-Nasser F. Beta-blockers for chronic heart failure surviving longer but feeling better // Int J Cardiol.-2003.- Vol.10.-P.24-28.
29. Brehm B., Wolf S. C., Gorner S. et al. Effect of carvedilol on left ventricular function in patients with chronic heart failure: a pilot study// Europ.J.HeartFailure.–2002.-V.4.–P.757-763.
30. Cice G, Ferrara L, D'Andrea, et al. Carvedilol increases two-year survival in dialysis patients with dilated cardiomyopathy: a prospective, placebo-controlled trial // J Am CollCardiol 2003;41: - P.1438-1444.
31. Cleophas TJ, Zwinderman AH. Beta-blockers and heart failure: meta-analysis of mortality trials // Int J ClinPharmacolTher 2001;39: - P.383-388.
32. Cowburn P.J., Cleland J.G.F. Endothelin antagonists for chronic heart failure: do they have a role? // Eur Heart J 2001;22:19: - P.1772-1784
33. Galbusera M, Zoja C, Donadelli R, et al. Fluid shear stress modulates von Willebrand factor release from human vascular endothelium // Blood 1997, V.90 №4, P.1558-1564
34. Guidelines for the diagnosis and treatment of Chronic Heart Failure: full text (update 2005) The Task Force for the diagnosis and treatment of CHF of the European Society of Cardiology // (European Heart Journal doi:10.1093/eurheartj/eh i 2005).
35. Guidelines for the diagnosis and treatment of chronic heart failure. //European Heart Journal 2001; 22: - P. 1527-1560
36. Kalra D., Bozkurt B., Deswal A. et al. Experimental options in the treatment of heart failure: the role of cytokine antagonism? // Heart Failure Monitor. – 2001. – Vol. 1. – P. 114-121.
37. Laucevicius, Petrulioniene Z., Ryliskyte L et al. Vascular Dysfunction and wall structural changes in the assessment of cardiovascular risk: are we ready for «more soft» arterial damage criteria? // Seminars in Cardiology 2004, Vol 10, No2A.- P.12-15.
38. McMurey J., Cohen-Solal A, Dietz R et al. Practical recommendation for the use of ACE inhibitors, beta-blockers and spironolactone in heart failure: putting guidelines into practice // Eur J Heart Fail. 2001; - P. 495-502
39. Olsen SL, Gilbert EM, Renlund DG, et al. Carvedilol improves left ventricular -1231.
40. Pacher R., Stanek B., Hulsmann M. et al. Prognostic impact of big endothelin-1 plasma concentrations compared with invasive hemodynamic evaluation in severe heart failure // J. Amer. Coll. Cardiology. – 1996. – Vol. 27. – P. 633-641.
41. Paulus W.J. How are cytokines activated in heart failure? // Eur. J. Heart Failure. – 1999. – Vol. 1. – P. 309-312.
42. Poelz G., Frick M., Huegel H. et al. Chronic heart failure is associated with vascular remodeling of the brachial artery // Eur. J. Heart Failure. – 2005. – Vol. 7. – P. 43-48.
43. Ruggeri Z.M. Structure and function of von Willebrand factor // Thrombus. Haemost.-1999.-Vol. 82.- P. 576-584.
44. Ruddock V and Meade TW Factor VIII activity and ischaemic heart disease: Fatal and non-fatal events // Q. J. Med. 1994, 87: - P. 403-406.
45. Stewart S., Mac Intyre K., Whole D.J. More malignant than cancer? Five-year survival following a first admission for heart failure // Eur. J. Heart Failure. – 2001. – Vol. 3. – P. 315-322.
46. Swedberg K., Cleland J., Dargie H. et al. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005) // Eur. Heart. J. – Vol. 26. – P. 1115-1140.
47. Thuillez C., Richard V. Targeting endothelial dysfunction in hypertensive subjects // J Human Hypertens 2005;19:S21-S25
48. Warnhoitz A., Wendt M., Munzel T. When sleeping beauty turns ugly //Thrombosis and vascular biology. 2002;22: - P. 525-527.
49. Watkins L.O. Epidemiology and burden of cardiovascular disease // Clin. Cardiology. - 2004. – Vol. 27 (Suppl. 3). – P. 2-6.
50. Webb D., Vallance P. (Eds) Endothelial function in congestive heart failure // Am Heart J 1998- P.89-91