SECTION 1. CARDIOLOGY

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1.1 Detection of early markers of destabilization of stable angina and prevention of complications

According to the American College of Cardiology, ischemic heart disease leads to 17.3 million deaths worldwide each year and is projected to be the leading global cause of death for men and women by 2020. Current trends confirm this forecast [18,33]. In Ukraine, ischemic heart disease remains the most common pathology with a prevalence and incidence rate of 34.1% and 28.0% respectively among adults, and 27.3% and 24.3% respectively among the working-age population. The primary disability rate due to ischemic heart disease has consistently ranked first in the structure of primary disability causes among the adult population in recent years [7, 15]. The predominance of cardiovascular diseases in the overall mortality structure in Ukraine is an unfavorable indicator of population health. In 2012, the mortality rate from these diseases was about 65.8%, with the contribution of ischemic heart disease being 71.1% [14, 9]. Therefore, further research into the characteristics of stable ischemic heart disease remains relevant.

To investigate the clinical and functional characteristics of stable angina of various functional classes with post-infarction and diffuse cardiosclerosis, 120 patients were included in the study. These patients were admitted to the Chernivtsi Regional Cardiology Center, where they were examined and treated with an objectively confirmed diagnosis of stable angina of functional classes II and III. The obtained results were processed into distributions of patients into the following clinical groups. By the severity of angina, Group 1 included patients with verified stable angina of functional class II, and Group 2 included those with stable angina of functional class III (25.83% and 74.17% of cases, respectively). Based on the presence or absence of a history of myocardial infarction, Group A included patients with post-infarction cardiosclerosis after a Q-wave myocardial infarction (44.17% of cases), Group B included patients with post-infarction cardiosclerosis after a non-Q-wave myocardial

infarction (17.50% of cases), and Group C included patients with diffuse cardiosclerosis (38.33% of cases). At the beginning of inpatient treatment and after 6 months in the outpatient phase, all patients underwent clinical, laboratory, and instrumental examinations.

The groups were comparable in terms of age, sex, and the presence of arterial hypertension. The average age of patients in the group with post-infarction cardiosclerosis after a Q-wave myocardial infarction was 51.91±0.76 years, in the group with post-infarction cardiosclerosis after a non-Q-wave myocardial infarction – 50.76±1.42 years, and in the group of patients with diffuse cardiosclerosis – 51.57±0.78 years (in all cases, $p>0.5$). The ratio of women to men in these groups was as follows: (11.32±4.35 and 88.68±4.35), (14.29±7.64 and 85.71±7.64), and (30.43±6.78 and 69.57±6.78), % of cases, respectively. The proportion of patients with arterial hypertension in the group with post-infarction cardiosclerosis after a Q-wave myocardial infarction was 73.58±6.06% of cases, in the group with post-infarction cardiosclerosis after a non-Q-wave myocardial infarction – 85.71±7.64% of cases, and in the group of patients with diffuse cardiosclerosis – 78.26±6.08% of cases (in all cases, $p>0.5$).

As expected, in the group with a history of Q-wave myocardial infarction, the proportion of patients with stable angina of functional class III was significantly higher (51.69±5.30% and 22.58±7.51% of cases, respectively, $p<0.01$), with a significantly lower detection of severe angina among individuals without a history of myocardial infarction (32.58±4.97% and 54.84±8.94% of cases, respectively, $p<0.05$). The presence of a history of non-Q-wave myocardial infarction does not affect the severity of angina, with an equal proportion of these patients in both groups (22.58±7.51% and 15.73±3.86% of cases in Groups 1 and 2, respectively, $p>0.5$).

Analyzing the results of coronary angiography, severe angina is associated with more hemodynamically significant coronary artery lesions, as expected. In the stable angina group of functional class III, significantly more frequently, stenosis of the left anterior descending coronary artery >50% is found (16.85±3.97 vs. 3.23±0.17% of cases, respectively, $p<0.01$), and hemodynamically insignificant changes of coronary

arteries are less likely (11.24±3.35 vs. 29.03±8.15% of cases, respectively, $p<0.05$). Only in patients in this group is multivessel coronary artery disease determined (23.60±4.50% of cases, $p<0.001$) and stenosis of the right coronary artery >50% (8.99±3.03% of cases, $p<0.01$). In contrast, stable angina of functional class II is less likely to be associated with stenosis of the left anterior descending coronary artery <50% (6.45±3.41 vs. 1.12±0.12% of cases, respectively, $p>0.1$). Stenosis of the left main coronary artery >50% is detected with the same frequency in patients with stable angina of functional class II and III (10.11±3.20 vs. 6.45±4.41% of cases, respectively, $p>0.5$), as well as stenosis of the right coronary artery <50% (1.12±1.12 vs. 0% of cases, respectively, $p>0.5$).

It is notable that in patients with ventricular extrasystole, non-Q-wave myocardial infarction is more likely to be found compared to those with normal rhythm history (19.80±3.97 vs. 5.26±1.12% of cases, respectively, $p<0.05$), which is associated with higher total cholesterol levels (5.82±0.14 vs. 5.21±0.24 mmol/L, respectively, $p<0.05$), a trend towards increased amino-terminal propeptide of natriuretic peptide (313.86±39.82 vs. 214.74±67.74 pg/mL, respectively, $p>0.1$), and C-reactive protein (11.53±1.02 vs. 8.88±1.57 mg/L, respectively, $p>0.1$), and more hemodynamically significant coronary artery lesions. Only in patients in this group is stenosis of the left anterior descending coronary artery >50% (15.84±3.64% of cases, $p<0.001$) and stenosis of the left main coronary artery >50% (10.89±3.10% of cases, $p<0.01$) determined.

Analyzing the results of echocardiography, it was noted that the left ventricular dimensions are likely higher in stable angina of functional class III (by end-systolic size – (3.82±0.08) vs. (3.56±0.08) cm, respectively, $p<0.05$; by end-diastolic size – (5.30±0.08) vs. (5.05±0.09) cm, respectively, $p<0.05$). There was no difference in these left ventricular dimensions depending on the history of Q-wave and non-Q-wave myocardial infarction. Thus, the end-systolic size in patients without myocardial infarction, after Q-wave and non-Q-wave myocardial infarction, was (3.74±0.13), (3.81±0.01), (3.66±0.12) cm, respectively (in all cases $p>0.5$). The end-diastolic size in patients without myocardial infarction, after Q-wave and non-Q-wave myocardial

infarction, was (5.35±0.13), (5.25±0.10), (5.10±0.13) cm, respectively (in all cases $p>0.5$).

However, there was no significant dependence on the severity of stable angina either in the left ventricular ejection fraction – (53.48±0.90) vs. (55.62±0.92) %, respectively ($p>0.5$), or in the mass of the left ventricular myocardium – (283.78±10.26) vs. (263.12±20.55) g, respectively ($p>0.5$). According to our data, there was no dependence of these indicators on the history of Q-wave and non-Q-wave myocardial infarction (by left ventricular ejection fraction – (56.17±1.56), (52.79±0.99), (55.05±1.42) %, respectively (in all cases $p>0.5$); by mass of left ventricular myocardium – (307.47±21.49), (275.69±11.85), (263.23±19.44) g, respectively (in all cases $p>0.5$)).

Analyzing the results of bicycle ergometry, in group with stable angina functional class III, lower thresholds of workload – (48.67±2.02) vs. (79.73±4.39) W, respectively ($p<0.001$), and physical exercise tolerance – (44.07±2.22) vs. (62.86±2.92) %, respectively ($p<0.001$), were expectedly noted, as well as significantly greater total ST segment depression – (5.39±0.39) vs. (3.84±0.38) mm, respectively ($p<0.001$). There was no difference in these parameters of bicycle ergometry depending on the history of Q-wave and non-Q-wave myocardial infarction. Thus, the workload threshold in patients without myocardial infarction, after Q-wave and non-Q-wave myocardial infarction, was (62.36±3.99), (59.67±10.17), (64.40±5.45) W, respectively (in all cases $p>0.5$). Physical exercise tolerance in patients without myocardial infarction, after Q-wave and non-Q-wave myocardial infarction, was (52.08±2.67), (58.00±9.29), (52.40±4.83) %, respectively (in all cases $p>0.5$). The total ST segment depression during stress was significant in patients without myocardial infarction, after Q-wave and non-Q-wave myocardial infarction – (4.64±0.37), (4.00±1.2), (5.22±0.49) mm, respectively (in all cases $p>0.5$).

The level of total cholesterol in the blood is significantly higher in patients with stable angina of functional class III – (5.86±0.14) vs. (5.33±0.21) mmol/L, respectively ($p<0.05$), regardless of the history of Q-wave and non-Q-wave myocardial infarction – (5.81±0.20), (5.67±0.16), (5.81±0.20) mmol/L, respectively (in all cases $p>0.5$).

The level of uric acid is significantly higher in patients with stable angina of functional class III – (500.58±17.52) vs. (374.14±20.89) μmol/L, respectively ($p<0.001$). However, this indicator only increases in combination with stable angina and Q-wave myocardial infarction (compared to patients without myocardial infarction – (517.32±23.34) vs. (425.73±21.99) μmol/L, respectively, $p<0.01$), without significant difference in this parameter in combination with stable angina and non-Q-wave myocardial infarction (compared to patients without myocardial infarction – (435.63±32.336) vs. (425.73±21.99) μmol/L, respectively, $p>0.5$).

The values of blood creatinine were likely higher in patients with more severe stable angina - (111.19±3.88) vs (96.48±4.36) μmol/L, respectively ($p<0.05$), as well as in patients with stable angina combined with a history of Q-wave myocardial infarction - (115.60±5.28) vs (94.37±2.98) μmol/L, respectively ($p<0.001$), and non-Q-wave myocardial infarction - (115.19±8.78) vs (94.37±2.98) μmol/L, respectively ($p<0.05$).

A likely increase in the levels of amino-terminal pro-B-type natriuretic peptide - (365.28±52.03) vs (191.16±29.23) pg/mL, respectively ($p<0.01$), and C-reactive protein - (13.60±1.18) vs (6.77±0.40) mg/L, respectively ($p<0.001$), was noted in patients with stable angina III functional class. There was no difference in these biomarkers depending on the presence of a history of Q-wave or non-Q-wave myocardial infarction. Thus, the level of amino-terminal pro-B-type natriuretic peptide in patients without myocardial infarction, after Q-wave and non-Q-wave myocardial infarction, was (241.49±49.61), (334.63±55.39), (340.18±92.93) pg/mL, respectively (in all cases $p>0.5$). The concentration of C-reactive protein measured in patients without myocardial infarction, after Q-wave and non-Q-wave myocardial infarction was (10.34±1.19), (11.34±0.86), (12.76±5.50) mg/L, respectively (in all cases $p>0.5$).

Unlike triglyceride levels, which do not significantly depend on the severity of stable angina - (2.33±0.07) vs (2.16±0.12) mmol/L, respectively ($p>0.5$), or on the presence of Q-wave or non-Q-wave myocardial infarction, the levels of triglycerides in patients without myocardial infarction, after Q-wave and non-Q-wave myocardial infarction, are (2.28±0.13), (2.31±0.07), (2.09±0.08) mmol/L, respectively (in all cases $p>0.5$).

A similar trend is observed for total testosterone - depending on the severity of stable angina (1.45±0.14) vs (2.76±0.69) ng/mL, respectively ($p>0.5$), and in patients without myocardial infarction, after Q-wave and non-Q-wave myocardial infarction - (1.90±0.60), (1.92±0.31), (2.18±0.78) ng/mL, respectively (in all cases $p>0.5$).

Thus, a history of Q-wave myocardial infarction more often predicts the development of severe stable angina ($p<0.01$), unlike non-Q-wave myocardial infarction, where stable angina II and III functional classes are observed with equal frequency ($p>0.5$). The absence of a history of myocardial infarction predicts a lower functional class of stable angina ($p<0.05$).

Data from coronary angiography indicate more hemodynamically significant lesions of the coronary arteries among patients with stable angina of functional class III (with >50% stenosis of the left anterior descending coronary artery ($p<0.01$), >50% stenosis of the right coronary artery ($p<0.01$), and multivessel coronary artery disease ($p<0.001$)), and significantly less frequently the presence of hemodynamically insignificant changes in the coronary arteries ($p<0.05$).

According to the lipid profile study, a higher functional class of stable angina is accompanied by a significant increase in total cholesterol ($p<0.05$), but not by an increase in triglycerides ($p>0.5$), regardless of the history of Q-wave and non-Q-wave myocardial infarction (in all cases $p>0.5$).

Levels of amino-terminal pro-brain natriuretic peptide and C-reactive protein are significantly higher in patients diagnosed with stable angina of functional class III ($p<0.01$ and $p<0.001$, respectively), which does not depend on the history of Q-wave and non-Q-wave myocardial infarction (in all cases $p>0.5$). Elevated uric acid levels contribute to more severe stable angina ($p<0.001$), especially in patients with a history of Q-wave myocardial infarction ($p<0.01$). This trend is associated with impaired kidney function and higher levels of creatinine ($p<0.05$), both in patients with a history of Q-wave myocardial infarction ($p<0.001$) and non-Q-wave myocardial infarction ($p<0.05$).

The presence of a history of non-Q-wave myocardial infarction potentiates the development of high-grade ventricular extrasystoles (frequent, paired) ($p<0.05$), which is associated with higher levels of total cholesterol ($p<0.05$) and more hemodynamically

significant lesions of the coronary arteries, predominantly with >50% stenosis of the left anterior descending coronary artery ($p<0.001$) and >50% stenosis of the left circumflex coronary artery ($p<0.01$).

According to the results of echocardiography, patients with stable angina of functional class III have larger left ventricular dimensions (based on end-diastolic and end-systolic sizes) (in all cases $p<0.05$), regardless of the history of Q-wave and non-Q-wave myocardial infarction (in all cases $p>0.5$). There was no significant association found between the presence of left ventricular hypertrophy (based on left ventricular myocardial mass) or left ventricular ejection fraction and the functional class of stable angina (in both cases $p>0.5$) or the history of Q-wave and non-Q-wave myocardial infarction (in all cases $p>0.5$).

Results from exercise stress testing indicate that the presence of stable angina of functional class III is associated with lower threshold exercise capacity and physical tolerance (in both cases $p<0.001$) and significantly more pronounced exercise-induced ischemia ($p<0.001$), regardless of the history of Q-wave and non-Q-wave myocardial infarction (in all cases $p>0.5$).

Therefore, higher functional class angina is more often caused by more hemodynamically significant coronary artery lesions and is accompanied by increased levels of amino-terminal pro-B-type natriuretic peptide and C-reactive protein. A history of Q-wave myocardial infarction predicts higher uric acid levels.

Recently, there has been active discussion regarding the relationship between blood uric acid levels and the development of cardiovascular pathology in the absence of gout with asymptomatic hyperuricemia [34, 10, 11, 25, 9]. The results of previous epidemiological studies have demonstrated that hyperuricemia is closely associated with the risk of heart failure, arterial hypertension, subclinical atherosclerosis, ischemic heart disease, myocardial infarction, and ischemic stroke [33, 16, 19, 29, 10, 5], particularly in patients with high cardiovascular risk [17, 9, 22]. The combination of hyperuricemia and ischemic heart disease worsens the quality of life for patients and contributes to premature disability due to complications [6, 15, 36]. Experimental studies have shown that the mechanisms linking ischemic heart disease and hyperuricemia promote pro-

atherogenic processes, including inflammation, endothelial dysfunction, and oxidative stress [26, 19, 17].

According to the results of the MONICA/CORA study, the Rotterdam study, and others, cardiovascular risk associated with an increase in uric acid levels by 1 mg/dL is comparable to an increase in systolic blood pressure by 10 mmHg or an increase in total cholesterol level by 46 mg/dL [5]. Many researchers believe that further investigation into the pathogenetic and prognostic role of hyperuricemia in ischemic heart disease is justified [4,1,3].

To study the influence of changes in uric acid levels on the functional state of the myocardium, coronary reserve, biomarkers, and homeostasis parameters in patients with stable angina, 120 patients were included in the study. The study design in this chapter was based on the criterion of hyperuricemia distribution (uric acid level > 357.0 μmol/L), dividing patients into two groups: Group 1 - without signs of hyperuricemia (34 patients, 28.33% of cases) and Group 2 - with elevated uric acid levels (86 individuals, 71.67% of cases). The severity criteria of hyperuricemia were selected based on literature data [33, 14, 12, 32], with uric acid levels in the distribution being <386.66 μmol/L, ≥416.4 μmol/L, ≥467.9 μmol/L, and ≥500.0 μmol/L (34.17%, 44.17%, 32.50%, and 26.67% of cases, respectively). Additionally, distribution was conducted based on gender with uric acid levels ≥303.37 μmol/L for women and ≥386.66 μmol/L for men (95.95% and 65.98% of cases, respectively). At the beginning of inpatient treatment and at 6 months during the outpatient stage, all patients underwent clinical, laboratory, and instrumental examinations.

Age was identified as a predictor of hyperuricemia, as patients in Group 1 were likely older - (52.36±0.54) vs. (49.59±1.10) years, $p < 0.05$. However, this pattern became more pronounced when uric acid levels exceeded 467.9 μmol/L - (52.95±0.64) vs. (50.91±0.68) years, $p < 0.05$. In our study, the proportion of women was higher in the hyperuricemia group - (23.26±4.56)% vs. (8.82±4.86)%, $p < 0.05$.

In the hyperuricemia group, stable angina of III functional class was more frequently diagnosed - (87.21±3.60)% vs. (41.18±8.44)%, $p < 0.001$, regardless of the level of uric acid. The same pattern was observed for a history of Q-wave myocardial

infarction - (56.60±6.81)% vs. (32.84±8.05)%, $p < 0.05$, with nearly the same frequency of non-Q-wave myocardial infarction in history - (19.40±6.78)% vs. (10.26±4.86)%, $p > 0.5$.

The difference in the frequency of high-grade ventricular extrasystoles (frequent, paired) becomes likely when the uric acid level exceeds 416.4 μmol/L - (92.45±3.63)% vs. (22.39±7.15)% of cases, $p < 0.001$.

There was an unlikely trend towards higher systolic blood pressure in the hyperuricemia group ($p > 0.1$), which occurred with uric acid levels exceeding 500.0 μmol/L - (167.19±4.76) mmHg vs. (159.02±4.20) mmHg, $p > 0.1$.

Patients with hyperuricemia were likely to have higher levels of total cholesterol ($p < 0.01$), creatinine ($p < 0.01$), C-reactive protein ($p < 0.001$), and likely lower levels of total testosterone in the blood ($p < 0.05$), regardless of uric acid levels. The trend towards higher levels of amino-terminal pro-B-type natriuretic peptide became significant when uric acid levels exceeded 467.9 μmol/L - (413.44±63.14) pg/ml vs. (206.42±31.43) pg/ml, $p < 0.01$. As shown in Table 1.

Table 1.

Indicators of Functional State, Biomarkers, and Homeostasis Indicators in Patients with Different Levels of Uric Acid

Indicator	**Hyperuricemia**	**Normal Uric Acid Level**
Systolic Blood Pressure (mm Hg)	165.64±2.74	156.47±4.70
Heart Rate (beats/min)	73.52±1.19	73.85±1.88
Total Cholesterol (mmol/L)	5.93±0.13	5.19±0.25*
Triglycerides (mmol/L)	2.27±0.07	2.30±0.18
Creatinine (μmol/L)	112.20±4.06	95.24±3.37*
Uric Acid (μmol/L)	523.80±17.35	326.57±4.98*
NT-proBNP (pg/mL)	316.33±41.78	215.14±50.68
C-Reactive Protein (mg/L)	12.07±0.97	5.37±0.60*
Total Testosterone (ng/mL)	1.55±0.21	4.09±1.19*

Note: * - significant differences between groups with hyperuricemia and normal uric acid levels ($p<0.05$).

During the analysis of echocardiography (EchoCS) data, a dependence on changes in ejection fraction and the occurrence of left ventricular hypertrophy from uric acid levels was noted. When comparing the sizes of the left ventricle and the ejection fraction of the left ventricle in groups with and without hyperuricemia, no likely differences were found, and only a tendency towards an increase in left ventricular myocardial mass with hyperuricemia was noted ($p > 0.1$), as shown in Table 2. However, when uric acid levels exceeded 467.9 μmol/L, the ejection fraction of the left ventricle is likely reduced - (51.17±1.37)% vs. (55.77±0.73)%, $p < 0.01$, and eccentric left ventricular hypertrophy develops more frequently - (46.15±7.98)% vs. (20.99±4.52)%, $p < 0.01$. Moreover, when uric acid levels exceeded 500.0 μmol/L, left ventricular myocardial mass likely increased - (294.28±13.05) vs. (255.90±14.33)%, $p < 0.05$.

Table 2.

Echocardiography Indicators in Patients with Different Levels of Uric Acid

Indicator	**Hyperuricemia**	**Normal Uric Acid Level**
LVED (cm)	5.24±0.08	5.22±0.13
LVES (cm)	3.77±0.08	3.72±0.12
Left Ventricular Ejection Fraction (%)	53.74±0.87	54.80±1.26
Left Ventricular Myocardial Mass (g)	282.74±10.71	265.83±17.48
Normal Left Ventricular Geometry (% cases)	15.12±3.86	20.59±6.93
Eccentric Left Ventricular Hypertrophy (% cases)	33.72±5.10	17.65±6.54
Concentric Left Ventricular Hypertrophy (% cases)	17.44±4.09	11.76±5.53
Concentric Left Ventricular Remodeling (% cases)	17.44±4.09	8.82±4.86

During the comparison of data from bicycle ergometry in patients with hyperuricemia, significantly lower thresholds for exercise load ($p < 0.01$) and physical exercise tolerance ($p < 0.01$) were observed. However, the severity of hyperuricemia did not impact the main parameters of the exercise test, as the exercise load thresholds

and physical exercise tolerance were consistently lower in patients with any degree of elevated uric acid compared to individuals with normal uric acid levels.

Simultaneously, the presence of hyperuricemia, regardless of its level, did not affect the total test-induced ischemia index ∑ST ($p > 0.2$). Therefore, hyperuricemia significantly limits coronary reserve. As shown in Table 3.

Table 3.

Bicycle ergometry Indicators in Patients with Different Levels of Uric Acid

Indicator	Hyperuricemia	Normal Uric Acid Level
Threshold Load (W)	53.65±2.89	72.74±5.18*
Physical Exercise Tolerance (%)	46.88±2.42	58.87±3.47*
Total ST Segment Depression (mm)	4.91±0.39	4.56±0.48

Note: * - significant differences between groups with hyperuricemia and normal uric acid levels ($p<0.05$).

Upon analysis of the results obtained during coronary angiography, it was noted that hyperuricemia serves as a predictor of more hemodynamically significant coronary artery lesions. Specifically, only in the hyperuricemia group were there significant findings such as >50% stenosis of the left anterior descending artery, circumflex artery, right coronary artery, and multivessel coronary artery disease (18.60±4.20), (12.79±3.60), (9.30±3.13), and (24.42±4.63) % of cases, respectively ($p < 0.01$). Additionally, cases of hemodynamically insignificant coronary artery lesions were less likely to be observed in the hyperuricemia group (6.98±2.75), compared to (38.24±8.33) % of cases ($p < 0.001$).

This pattern was observed for uric acid levels exceeding 416.4 μmol/L for the circumflex artery (16.98±5.16) % vs. (2.99±0.91) % of cases ($p < 0.05$), for the right coronary artery (13.21±4.65) % vs. (1.49±0.08) % of cases ($p < 0.05$), for multivessel coronary artery disease (28.30±6.19) % vs. (7.46±2.51) % of cases ($p < 0.01$), and for hemodynamically insignificant coronary artery lesions (5.66±1.17) % vs. (23.88±7.31) % of cases ($p < 0.05$).

Considering gender criteria, the following was observed. Analysis of the results obtained during coronary angiography indicates that under conditions of hyperuricemia, male gender is associated with the development of more hemodynamically significant coronary artery lesions. The findings are as follows:

- Left coronary artery:
- 50% stenosis of the left anterior descending artery: (25.00±5.41) % of cases in men with hyperuricemia, compared to (0%) in women ($p < 0.01$).
- 50% stenosis of the left circumflex artery: (15.63±4.54) % of cases in men with hyperuricemia, compared to (4.55±2.44) % in women ($p < 0.05$).
- Multivessel coronary artery disease: (31.25±5.79) % of cases in men with hyperuricemia, compared to (4.55±2.44) % in women ($p < 0.001$).
- Less frequent cases of hemodynamically insignificant coronary artery lesions: (1.56±0.55) % in men with hyperuricemia, compared to (18.18±8.22) % in women ($p < 0.05$).

Unlike women, in men, hyperuricemia is associated with higher levels of various biomarkers, as follows:

- Higher levels of total cholesterol: $p < 0.001$
- Higher levels of triglycerides: $p < 0.05$
- Higher levels of creatinine: $p < 0.01$
- Higher levels of amino-terminal pro-B-type natriuretic peptide (NT-proBNP): $p < 0.05$
- Higher levels of C-reactive protein (CRP): $p < 0.001$
- Lower levels of total testosterone: $p < 0.001$

These quantitative data presented in Table 4.

Table 4.

Biomarkers and Homeostasis Indicators in Male Patients with Hyperuricemia

Indicator	Men with Hyperuricemia	Men without Hyperuricemia
Total Testosterone (mmol/L)	6.17±0.15	5.11±0.23*
Triglycerides (mmol/L)	2.28±0.08	2.05±0.08*
Creatinine (μmol/L)	115.88±4.93	98.52±3.53*

Indicator	Men with Hyperuricemia	Men without Hyperuricemia
Uric Acid (μmol/L)	539.76±19.81	332.47±4.42
NT-proBNP (pg/mL)	399.25±66.03	200.14±59.31*
C-Reactive Protein (mg/L)	14.28±1.55	5.91±0.67*
Total Testosterone (ng/mL)	2.10±0.28	5.52±0.92*

Note: * - significant differences between men with/without hyperuricemia ($p<0.05$).

The estimated regression equation based on the selected examination data for comparing uric acid levels (Y) and amino-terminal pro-B-type natriuretic peptide (X) will have the form Y = 0.6501 * X - 38.0834. According to the R.E. Chaddock scale, the correlation between Y and X is noticeable and direct ($r_{XY} = 0.552$). Since $|t_{observ}| > t_{crit}$, we reject the hypothesis of a zero correlation coefficient, and the correlation coefficient itself is statistically significant. The Fisher's F-test indicates that the actual F value is greater than the tabular value, making the coefficient of determination statistically significant, and the estimated regression equation reliable.

The correlation between uric acid levels (Y) and C-reactive protein levels (X) is described by the equation Y = 0.02142 * X - 0.26, which is high and direct ($r_{XY} = 0.701$), and statistically reliable according to the F-test.

In the equation relating uric acid (Y) and left ventricular ejection fraction (X) with the formula Y = 0.0134 * X + 45.0824, the correlation is weak ($r_{XY} = 0.224$) and statistically unreliable according to the F-test.

Similarly, the relationship between uric acid (Y) and exercise tolerance threshold (X) according to the equation Y = -0.03104 * X + 41.0479 is statistically unreliable based on the F-test.

In addition, multiple regression was conducted to create a model with a large number of factors, determining the impact of each individually as well as their combined effect on the modeled indicator. Multiple regression allows for the analysis of the relationship between several independent variables (regressors or predictors) and a dependent variable (Y), where the dependent variable is the uric acid level upon first

admission. The factors influencing the model, where X = X (X_1, X_2, ..., X_m), are proposed to evaluate the following indicators: X_1 - amino-terminal pro-B-type natriuretic peptide at first admission, and X_2 - its level at follow-up; X_3 - C-reactive protein at first admission, and X_4 - its level at follow-up; X_5 - left ventricular ejection fraction at first admission, and X_6 - its level at follow-up; X_7 - exercise tolerance threshold at first admission, and X_8 - its achievement at follow-up examination after 6 months. The multiple regression equation is presented as follows: Y = -12.0028 + 0.3893X_1 - *0.08975*X_2 + 13.4637X_3 - *3.9902*X_4 + 8.8012X_5 - *2.0567*X_6 - 6.233X_7 + *3.594*X_8

The observed t-statistic values for r_{YX1-8} were calculated using the formula:

$$t_{\text{спостер}} = r_{yx_{1-8}} \frac{\sqrt{n-m-1}}{\sqrt{1-r^2_{yx_{1-8}}}}$$

where m=1 - the number of factors in the regression equation, according to the Student's t-distribution table determined by t_{tab}, t_{crit}(n-m-1;α/2). Since $t_{observed} > t_{crit}$, the hypothesis of equality of the correlation coefficient to 0 is rejected, and the correlation coefficient is statistically significant, which is registered for factors X_1 (amino-terminal pro-B-type natriuretic peptide$_1$) $t_{observed}$=4.5; t_{crit}(n-m-1;α/2)=(46;0.025)=2.009; X_3 (C-reactive protein$_1$) statistically significant, $t_{observed}$=4.5; X_6 (left ventricular ejection fraction$_2$) statistically significant, $t_{observed}$=3.52.

No significant dependence of uric acid content on indicators X_5 (left ventricular ejection fraction1), X_7 (exercise tolerance threshold1), and X_8 (exercise tolerance threshold2) was found. At the same time, the initial uric acid level was not affected by the second admission factors X_2 (amino-terminal pro-B-type natriuretic peptide$_2$), X_4 (C-reactive protein$_2$). The overall quality of the multiple regression equation was tested using the F-statistic (Fisher's criterion) with an assessment of the predominance ratio of the actual F-value > F_{crit}, and therefore in this case, the coefficient of determination was statistically significant and the regression equation was statistically reliable. It was found that factor X_1 (amino-terminal pro-B-type natriuretic peptide$_1$) F_{X1}(50.094) > 2.25, therefore factor X_1 should be included in the model after introducing factors X_j, with a similar dependency for X_3 (C-reactive protein$_1$) F_{X3}(55.276) > 2.25; X_4 (C-

reactive protein$_2$) $F_{X4}(6.848) > 2.25$; X_5 (left ventricular ejection fraction$_1$) $F_{X5}(22.6) > 2.25$ and X_7 (exercise tolerance threshold$_1$) $F_{X7}(37.024) > 2.25$. Since the density of the joint influence of factors on the result allows for the determination of the multiple correlation index, the coefficient of multiple correlation was investigated through the matrix of pairwise correlation coefficients:

$$R = \sqrt{1 - \frac{s_\varepsilon^2}{\sum (y_i - \bar{y})^2}} = \sqrt{1 - \frac{427216.29}{2115530.21}} = 0.8933$$

It was determined that as R approaches 1 (in our own study R=0.8933), the regression equation better describes the actual data, and the factors have a stronger impact on the outcome.

Investigation of Pearson correlation coefficients, depending on changes in uric acid, amino-terminal pro-B-type natriuretic peptide, and C-reactive protein, showed the following. It was found that the level of uric acid in the first examination demonstrates a direct moderate relationship with the level of creatinine (r-Pearson 0.443, $p<0.01$), a direct moderate relationship with amino-terminal pro-B-type natriuretic peptide1 (r-Pearson 0.363, $p<0.01$), a direct moderate relationship with C-reactive protein1 (r-Pearson 0.454, $p<0.01$), a reverse moderate relationship with left ventricular ejection fraction1 (r-Pearson -0.351, $p<0.01$), which becomes a more pronounced direct high correlation with the level of creatinine at the second admission (r-Pearson 0.772, $p<0.01$), a direct moderate relationship with amino-terminal pro-B-type natriuretic peptide2 (r-Pearson 0.438, $p<0.01$), a direct high relationship with C-reactive protein2 (r-Pearson 0.765, $p<0.01$), and a reverse moderate relationship with left ventricular ejection fraction2 (r-Pearson -0.351, $p<0.01$).

In turn, amino-terminal pro-B-type natriuretic peptide1 demonstrates a significant direct relationship with C-reactive protein1 (r-Pearson 0.533, $p<0.01$), a significant reverse relationship with left ventricular ejection fraction1 (r-Pearson -0.561, $p<0.01$). Furthermore, amino-terminal pro-B-type natriuretic peptide2 at the second admission indicates an even more pronounced significant direct relationship with C-reactive protein2 (r-Pearson 0.619, $p<0.01$), and a significant reverse relationship with left ventricular ejection fraction2 (r-Pearson -0.611, $p<0.01$).

The relationship between C-reactive protein and left ventricular ejection fraction is a moderate reverse correlation in the first (r-Pearson -0.340, $p<0.01$) and a significant reverse correlation in the second (r-Pearson -0.504, $p<0.01$) examinations. It is noteworthy that there is no correlation, according to Pearson, in the assessment of achieved workload during bicycle ergometry, due to the exclusion of a weak reverse relationship in the second examination with amino-terminal pro-B-type natriuretic peptide2 (r-Pearson -0.319, $p<0.05$).

Thus, according to the results of our study, age has been identified as a predictor of hyperuricemia when uric acid levels exceed 467.9 μmol/L ($p<0.05$).

In the presence of hyperuricemia, stable angina of III functional class is diagnosed more frequently ($p<0.001$), including against the background of a history of Q-wave myocardial infarction ($p<0.05$), although this relationship is not confirmed regarding the presence of non-Q-wave myocardial infarction in the history ($p>0.5$).

When uric acid levels exceed 416.4 μmol/L, high-grade ventricular extrasystoles occur more frequently ($p<0.001$), and when uric acid levels exceed 500.0 μmol/L, systolic arterial pressure is unlikely to be higher ($p>0.1$).

Regarding echocardiography data, when uric acid levels exceed 467.9 μmol/L, the left ventricular ejection fraction is likely to be lower ($p<0.01$), with a greater proportion of patients having eccentric left ventricular hypertrophy ($p<0.01$), and when uric acid levels exceed 500.0 μmol/L, left ventricular myocardial mass is likely to be higher ($p<0.05$).

The impact of hyperuricemia on bicycle ergometry results manifests as significantly lower thresholds for exercise testing ($p<0.01$) and physical exercise tolerance ($p<0.01$), irrespective of uric acid levels.

Comparison of the correlation between two indicators, one of which is the outcome that changes under the influence of predictor variables and is uric acid itself (Y), shows a high and direct correlation among evaluation factors for C-reactive protein ($r_{XY}=0.701$), significant and direct for amino-terminal pro-B-type natriuretic peptide ($r_{XY}=0.552$), both statistically reliable according to the F-criterion, unlike the

weak and statistically unreliable correlation for left ventricular ejection fraction (r_{XY}=0.224) and threshold workload.

Investigation of changes in the Pearson correlation coefficient, depending on uric acid levels and amino-terminal pro-B-type natriuretic peptide and C-reactive protein, demonstrates mainly a direct moderate correlation upon arrival (for amino-terminal pro-B-type natriuretic peptide$_1$ (r-Pearson 0.363, p<0.01), C-reactive protein$_1$ (r-Pearson 0.454, p<0.01)), which reaches a significant and even high correlation in the second examination (for amino-terminal pro-B-type natriuretic peptide$_2$ (r-Pearson 0.438, p<0.01), for C-reactive protein$_2$ (r-Pearson 0.765, p<0.01)), with a reverse moderate correlation for left ventricular ejection fraction (for left ventricular ejection fraction$_1$ (r-Pearson -0.351, p<0.01), for left ventricular ejection fraction$_2$ (r-Pearson -0.351, p<0.01)). The Pearson correlation coefficient, depending on the levels of amino-terminal pro-B-type natriuretic peptide and C-reactive protein, indicates a direct moderate correlation upon arrival (for C-reactive protein$_1$ (r-Pearson 0.533, p<0.01)), which becomes more pronounced in the second examination (for C-reactive protein$_2$ (r-Pearson 0.619, p<0.01)), with a reverse moderate correlation for left ventricular ejection fraction (for left ventricular ejection fraction$_1$ (r-Pearson -0.561, p<0.01), for left ventricular ejection fraction$_2$ (r-Pearson -0.611, p<0.01)). The Pearson correlation coefficient, depending on the levels of C-reactive protein and left ventricular ejection fraction, demonstrates a reverse moderate correlation upon arrival (for left ventricular ejection fraction$_1$ (r-Pearson -0.340, p<0.01)) and a significant reverse correlation in the second examination (for left ventricular ejection fraction$_2$ (r-Pearson -0.504, p<0.01)).

The analysis of coronary angiography data indicates that hyperuricemia is associated with a more frequent occurrence of hemodynamically significant lesions of the coronary arteries when the level of uric acid exceeds 416.4 μmol/L. Specifically, this includes:

- 50% stenosis of the left anterior descending coronary artery (p<0.05),
- 50% stenosis of the left circumflex coronary artery (p<0.05),
- 50% stenosis of the right coronary artery (p<0.05),

- and multivessel coronary artery disease ($p<0.01$), with less frequent occurrence of hemodynamically insignificant lesions of the coronary arteries ($p<0.05$).

In addition, male gender is associated with the development of more hemodynamically significant lesions of the coronary arteries, predominantly manifested by >50% stenosis of the left anterior descending coronary artery and right coronary artery (in both cases, $p<0.01$), more frequent determination of >50% stenosis of the left circumflex coronary artery ($p<0.05$), and multivessel coronary artery disease ($p<0.001$), with less frequent occurrence of hemodynamically insignificant lesions of the coronary arteries ($p<0.05$).

Higher levels of total cholesterol ($p<0.01$), creatinine ($p<0.01$), C-reactive protein ($p<0.001$), and lower levels of total blood testosterone ($p<0.05$) are associated with hyperuricemia regardless of the level of uric acid. An increase in amino-terminal propeptide of brain natriuretic peptide occurs when uric acid exceeds 467.9 μmol/L ($p<0.01$). In the case of hyperuricemia, male gender is a predictor of increased levels of total cholesterol ($p<0.001$), triglycerides ($p<0.05$), creatinine ($p<0.01$), amino-terminal propeptide of brain natriuretic peptide ($p<0.05$), and C-reactive protein ($p<0.001$).

Therefore, advanced age is a predictor of hyperuricemia when uric acid levels exceed 467.9 μmol/L. Hyperuricemia leads to more frequent development of severe stable angina, independent of the uric acid level, against the backdrop of more hemodynamically significant coronary artery lesions. These coronary artery lesions are determined when uric acid levels exceed 416.4 μmol/L, and are observed in men regardless of uric acid levels.

Hyperuricemia, predominantly in men, causes a significant increase in total cholesterol, creatinine, indicating more frequent kidney involvement, and C-reactive protein, which is due to greater vascular inflammation activity. When uric acid levels exceed 467.9 μmol/L, there is a decrease in left ventricular ejection fraction and an increase in amino-terminal propeptide of brain natriuretic peptide, suggesting more frequent progression of heart failure with this comorbidity.

The development of left ventricular hypertrophy with an increase in left ventricular myocardial mass occurs with hyperuricemia when uric acid levels exceed 500.0 μmol/L. Hyperuricemia leads to a reduced coronary reserve with decreased thresholds for exercise tolerance and physical stress, regardless of the uric acid level.

Uric acid, as a routine biochemical marker, can be used in clinical practice to assess the severity and prognosis of ischemic heart disease.

Therefore, a predictive regression equation was constructed based on selective examination data at the first visit to compare uric acid levels with amino-terminal pro-B-type natriuretic peptide (NT-proBNP), indicating a significant and direct relationship. C-reactive protein (CRP) showed a high and direct relationship according to the F-criterion, unlike the weak and statistically unreliable relationship with left ventricular ejection fraction (LVEF) according to echocardiography and threshold load during bicycle ergometry.

The construction of a multiple regression equation with uric acid levels as the dependent variable and the influencing factors of CRP, NT-proBNP, LVEF, and threshold load was statistically reliable with a high coefficient of multiple correlation ($r = 0.89$). The Pearson correlation coefficient depending on the levels of uric acid, NT-proBNP, and CRP indicated mainly a direct moderate relationship on initial examination, with a significant and even high relationship on repeat examination, while a reverse moderate relationship was observed for LVEF, unlike the threshold load during bicycle ergometry.

The identified patterns are important for predicting the course of the disease and quality of life dynamics. Further research is warranted to optimize the management strategy for patients with comorbid stable angina and hyperuricemia in both inpatient and outpatient settings.

With the aim of studying the pathogenetic role of biomarker changes in stable angina, depending on uric acid levels, and assessing myocardial functional status and coronary reserve to improve disease prognosis, 120 patients diagnosed with stable angina were examined. The criterion for significant changes was chosen as an increase

(Δ%) in the studied parameters greater than 5%. Based on the dynamics of these parameters, patients were grouped as follows:

1. Left ventricular ejection fraction (LVEF) and contractile function of the left ventricle (LV):

- Increase in LVEF and decrease in LV contractile function (31 individuals (70.45% of cases) and 13 individuals (29.55% of cases), respectively).

2. Threshold load during exercise:

- Increase and decrease in threshold load (33 individuals (66.00% of cases) and 17 individuals (34.00% of cases), respectively).

3. Uric acid levels:

- Increase and decrease in uric acid levels (both groups with 60 individuals (50.00% of cases)).

4. Amino-terminal pro-B-type natriuretic peptide (NT-proBNP) concentration:

- Increase and decrease in NT-proBNP concentration (16 individuals (34.78% of cases) and 30 individuals (65.22% of cases), respectively).

5. C-reactive protein (CRP) levels:

- Increase and decrease in CRP levels (14 individuals (31.11% of cases) and 30 individuals (68.89% of cases), respectively).

6. Total testosterone levels:

- Increase and decrease in total testosterone levels (31 individuals (67.39% of cases) and 15 individuals (32.61% of cases), respectively).

At the start of inpatient treatment and after 6 months of outpatient care, all patients underwent clinical, laboratory, and instrumental examinations.

Positive dynamics in left ventricular contractile function were accompanied by a likely significant decrease in systolic blood pressure (Δ% -22.64±1.60, compared to -14.31±1.80%, $p<0.001$). At the same time, there was no significant difference in the degree of heart rate slowing depending on the dynamics of left ventricular ejection fraction (Δ% -7.50±2.45, compared to -6.94±3.64%, $p>0.5$).

Positive dynamics of left ventricular ejection fraction (LVEF) is associated with a likely decrease in total cholesterol (Δ% -17.76±3.89, compared to +12.51±6.01%, $p<0.001$), creatinine (Δ% -11.20±8.75, compared to +64.73±31.25%, $p<0.01$), uric acid (Δ% -30.89±8.60, compared to +53.35±12.20%, $p<0.001$), C-reactive protein (CRP) (Δ% -34.42±1.46, compared to +148.38±38.88%, $p<0.001$), and amino-terminal pro-B-type natriuretic peptide (NT-proBNP) (Δ% -65.81±9.06, compared to +175.31±10.58%, $p<0.001$). Additionally, there was a likely greater decrease in triglyceride levels (-46.91±2.45 vs -18.61±3.64%, $p<0.001$).

Analyzing the dynamics of echocardiographic parameters, it has been determined that the enhancement of left ventricular systolic function is accompanied by a likely decrease in left ventricular dimensions. Specifically, the end-systolic dimension shows a decrease (Δ% -11.77±2.21 vs +19.16±3.33%, $p<0.001$), as does the end-diastolic dimension (Δ% -6.42±2.04 vs +9.77±2.81%, $p<0.001$), and left ventricular mass (Δ% -15.13±3.73 vs +18.74±5.71%, $p<0.001$). During this observation period, no dependence of changes in left atrial size on left ventricular ejection fraction was detected.

Positive dynamics of left ventricular ejection fraction (LVEF) is associated with improved coronary reserve, evidenced by a likely increase in exercise tolerance as indicated by an increase in workload (Δ% +59.19±7.31 vs -14.46±2.96%, $p<0.001$), physical exercise tolerance (Δ% +57.82±10.70 vs -11.61±1.20%, $p<0.001$), and a likely more significant reduction in ischemia during physical exercise, shown by the total ST segment depression (Δ% -46.00±11.50 vs -19.34±1.20%, $p<0.05$).

Positive dynamics of workload are accompanied by a non-significant greater decrease in systolic blood pressure (Δ% -18.31±1.90 vs -13.61±1.75%, $p>0.1$), with no difference in the extent of heart rate slowing (Δ% -7.95±2.27 vs -9.27±2.40%, $p>0.5$).

The positive dynamics of workload predict a likely decrease in creatinine levels (Δ% -9.52±3.80 vs +11.81±6.35%, $p<0.01$), uric acid (Δ% -14.98±5.91 vs +10.99±4.57%, $p<0.01$), amino-terminal pro-B-type natriuretic peptide (Δ% -61.65±26.95 vs +88.99±34.95%, $p<0.001$), and C-reactive protein (Δ% -26.10±3.37 vs +101.37±45.85%, $p<0.01$).

Positive dynamics of workload are associated with a likely decrease in left ventricular size (for end-systolic dimension Δ% -9.36±3.30 vs +9.12±4.18%, respectively ($p<0.001$); for end-diastolic dimension Δ% -6.84±1.11 vs +4.59±0.89%, respectively ($p<0.001$)), and left ventricular myocardial mass (Δ% -18.86±3.30 vs +14.21±4.18%, $p<0.001$). There is also a likely increase in left ventricular ejection fraction (Δ% +7.51±2.42 vs -9.46±3.24%, $p<0.001$).

An increase in workload is associated with a likely increase in physical exercise tolerance (Δ% +46.26±6.91 vs +1.55±0.49%, $p<0.001$) and a likely decrease in ischemia during physical exercise (for total ST segment depression Δ% -30.36±7.47 vs +3.71±0.49%, $p<0.05$).

In comparing groups based on the increase/decrease in blood uric acid levels, it was determined that a positive decrease in uric acid content over 6 months is associated with a likely significant decrease in systolic blood pressure (Δ% was -20.33±1.30 vs -12.12±1.30%, $p<0.001$), as well as total cholesterol (Δ% was -19.66±1.50 vs -4.71±3.01%, $p<0.001$) and triglycerides (Δ% -45.78±10.50 vs -19.83±6.01%, $p<0.05$). Specifically in the group with a decrease in uric acid levels, a decrease in creatinine (Δ% -17.24±2.26 vs +21.57±6.88%, $p<0.001$), amino-terminal pro-brain natriuretic peptide (Δ% -64.43±15.89 vs +63.28±13.88%, $p<0.001$), and C-reactive protein (Δ% -50.21±5.46 vs +153.49±56.04%, $p<0.001$) was observed. There was no significant difference in the slowing of heart rate depending on the dynamics of blood uric acid content (Δ% -7.32±1.66 vs -8.17±1.39%, $p>0.5$).

Positive reduction in blood uric acid levels is associated with a likely significant decrease in left ventricular size, both in terms of end-systolic dimension (Δ% -7.25±2.09 vs Δ% +4.71±0.09, respectively, $p<0.001$) and end-diastolic dimension (Δ% -4.15±2.10 vs Δ% +2.34±0.10, respectively, $p<0.01$), as well as a likely increase in left ventricular ejection fraction (Δ% +8.11±2.75 vs Δ% -13.54±0.99, $p<0.001$).

In comparing patients with increased/decreased uric acid levels, it was found that decreasing uric acid levels are associated with increased coronary reserve, with a likely more significant increase in exercise tolerance (Δ% +47.14±5.14 vs +12.68±3.29, $p<0.01$), and a decrease in ischemia during physical exertion, as assessed by the

increase in the sum of ST segment depression (Δ% -37.58±9.81 vs -13.35±3.15, $p<0.05$).

Positive reduction in amino-terminal pro-brain natriuretic peptide (NT-proBNP) levels, compared to an increase in this marker, is associated with a likely significant decrease in systolic blood pressure (Δ% -22.81±1.49 vs -12.05±1.69%, $p<0.001$), a non-significantly greater slowing of heart rate (Δ% -8.30±2.35 vs -3.86±1.02%, $p>0.1$), as well as a decrease in triglyceride concentration (Δ% -45.68±5.14 vs -14.65±3.35%, $p<0.001$). Only this group is characterized by decreased levels of total cholesterol (Δ% -16.75±4.00 vs +6.12±8.44%, $p<0.05$), creatinine (Δ% -8.91±4.18 vs +60.33±19.53%, $p<0.001$), uric acid (Δ% -28.72±8.89 vs +45.49±11.13%, $p<0.001$), and C-reactive protein (Δ% -35.07±10.98 vs +145.02±55.59%, $p<0.01$).

As in the previous comparison, positive reduction in amino-terminal pro-brain natriuretic peptide (NT-proBNP) levels is associated with a likely significant decrease in the size of the left ventricle, as assessed by end-systolic dimension (Δ% -10.09±2.22 vs +13.15±3.61%, $p<0.001$), end-diastolic dimension (Δ% -5.81±2.03 vs +6.52±2.52%, $p<0.001$), and left ventricular mass (Δ% -15.59±3.58 vs +12.96±4.72%, $p<0.001$). Additionally, it is likely to improve left ventricular ejection fraction (Δ% +12.75±5.05 vs -11.34±4.78%, $p<0.001$).

Positive reduction in amino-terminal pro-brain natriuretic peptide (NT-proBNP) levels is associated with a likely significant decrease in systolic blood pressure (Δ% -22.81±1.49 vs -12.05±1.69%, $p<0.001$), a non-significant slowing of heart rate (Δ% -8.30±2.35 vs -3.86±1.02%, $p>0.1$), and a decrease in triglyceride concentration (Δ% -45.68±5.14 vs -14.65±3.35%, $p<0.001$). Only this group is characterized by reductions in total cholesterol levels (Δ% -16.75±4.00 vs +6.12±8.44%, $p<0.05$), creatinine (Δ% -8.91±4.18 vs +60.33±19.53%, $p<0.001$), uric acid (Δ% -28.72±8.89 vs +45.49±11.13%, $p<0.001$), and C-reactive protein (Δ% -35.07±10.98 vs +145.02±55.59%, $p<0.01$).

In comparing patients with an increase or decrease in C-reactive protein levels, it was found that a decrease in this biomarker is associated with a likely significant decrease in systolic blood pressure (Δ% -21.83±1.51 vs -12.72±2.20%, $p<0.001$), as

well as triglyceride levels (Δ% -42.76±3.56 vs -16.26±3.69%, $p<0.001$). Only in this group, there is a decrease in total cholesterol (Δ% -19.59±2.12 vs +17.17±10.05%, $p<0.001$), creatinine (Δ% -20.96±4.03 vs +96.26±19.20%, $p<0.001$), uric acid (Δ% -36.72±4.32 vs +72.49±11.36%, $p<0.001$), and amino-terminal pro-brain natriuretic peptide (Δ% -34.43±17.68 vs +132.46±49.26%, $p<0.01$). However, the group of patients with increased inflammatory activity is characterized by a likely significant increase in total testosterone levels (Δ% +28.57±4.16 vs +8.09±2.31%, $p<0.001$). There was no significant difference in the degree of slowing of heart rate depending on the dynamics of C-reactive protein content (Δ% -5.64±2.37 vs -8.26±3.09%, $p>0.5$).

In this comparison, positive reduction in C-reactive protein (CRP) levels is associated with a likely significant decrease in left ventricular size, as assessed by end-systolic dimension (Δ% -7.11±2.22 vs +11.05±5.08%, $p<0.01$), end-diastolic dimension (Δ% -4.59±1.91 vs +6.24±3.26%, $p<0.01$), and left ventricular mass (Δ% -13.08±3.56 vs +12.33±5.97%, $p<0.001$). Additionally, there is a likely increase in left ventricular ejection fraction (Δ% +9.79±2.27 vs -8.65±4.07%, $p<0.001$).

A decrease in CRP levels is associated with an increase in coronary reserve during likely significant increase in exercise tolerance (Δ% +56.64±6.47 vs -11.90±3.15%, $p<0.001$) and decrease in ischemia during physical exertion as evaluated by total ST segment depression (Δ% -43.38±13.96 vs -7.41±1.97%, $p<0.05$).

Analyzing the interaction between changes in total testosterone levels and the dynamics of myocardial functional indicators, coronary reserve, and other vasoactive and homeostasis markers, it's important to consider the gender composition of the groups, which influenced the dynamics of this marker and the course of the disease. In the group with an increase in total testosterone, men predominated over women (64.52±8.59% and 35.48±8.59% cases, respectively, $p<0.05$), with a reversed distribution in the group with decreased testosterone (33.01±12.17% and 66.99±12.17% cases, respectively, $p<0.05$).

A likely decrease in heart rate is noted only with an increase in total testosterone in men (73.39±1.99 vs 68.06±1.09 beats/min, $p<0.05$). Conversely, in women, an increase in total testosterone does not significantly slow down the heart rate

(73.60±2.90 vs 68.40±1.75 beats/min, $p>0.5$). Therefore, there is no significant difference in the slowing of heart rate depending on the dynamics of total testosterone levels (Δ% -5.92±2.09 vs -5.74±3.25%, $p>0.5$).

A decrease in systolic blood pressure is likely both with an increase in total testosterone in men and with a decrease in this marker in women; however, this trend is significantly more likely in women (Δ% -16.82±1.75 vs -22.65±2.00%, respectively, $p<0.05$). A similar trend is observed regarding triglyceride levels, with a likely more intensive decrease in women (Δ% -31.09±2.03 vs -41.36±4.31%, respectively, $p<0.05$). Specifically in women, a likely decrease in total cholesterol is observed with a decrease in total testosterone (Δ% -18.22±3.31 vs -4.02±1.88%, $p<0.01$).

No significant differences were found in the changes in creatinine, uric acid, and amino-terminal pro-brain natriuretic peptide levels. It's noteworthy that in the women's group, a decrease in total testosterone was associated with a decrease in C-reactive protein concentration (Δ% -18.64±3.54 vs +31.06±17.50%, respectively, $p<0.05$).

The decrease in total testosterone levels in women is associated with a likely reduction in left ventricular dimensions, whereas according to our own data, the dimensions and geometry of the left ventricle do not change significantly over the selected observation period (for end-systolic size Δ% (-9.54±3.60) vs. (+1.76±0.11) %, respectively, $p<0.01$; for end-diastolic size Δ% (-6.96±2.63) vs. (+1.1±0.21) %, respectively, $p<0.01$), as well as left ventricular myocardial mass Δ% (-14.88±5.56) vs. (-0.80±0.21) %, respectively, $p<0.05$).

Increased coronary reserve occurs both with an increase in total testosterone in men and with a decrease in this indicator in women, with a significantly greater increase in the threshold load in the group of women (Δ% +25.98±4.73 vs. +61.03±4.85%, respectively, $p<0.001$) and physical load tolerance (Δ% +20.96±4.20 vs. +60.85±4.95%, respectively, $p<0.05$), as well as reduced ischemia during physical exertion (by total ST segment depression Δ% -23.83±4.40 vs. -36.44±2.66%, respectively, $p<0.05$).

Therefore, it is noted that an increase in left ventricular ejection fraction is accompanied by a decrease in total cholesterol ($p<0.001$), creatinine ($p<0.01$), uric acid

($p<0.001$), C-reactive protein ($p<0.001$), and amino-terminal pro-B-type natriuretic peptide ($p<0.001$). Strengthening of the left ventricular ejection fraction is associated with a reduction in left ventricular dimensions (for end-systolic size ($p<0.001$) and end-diastolic size ($p<0.001$)), regression of left ventricular hypertrophy (for left ventricular myocardial mass ($p<0.001$)), and improvement in coronary reserve (for threshold load ($p<0.001$), physical exercise tolerance ($p<0.001$)), and reduction of exercise-induced ischemia (by total ST segment depression ($p<0.05$)).

Positive dynamics of threshold load, with an increase in physical exercise tolerance ($p<0.001$) and reduction of exercise-induced ischemia (by total ST segment depression ($p<0.05$)), occur with a decrease in creatinine ($p<0.01$), uric acid ($p<0.01$), amino-terminal pro-B-type natriuretic peptide ($p<0.001$), and C-reactive protein ($p<0.01$). Increased threshold load is associated with a decrease in left ventricular dimensions (for end-systolic size ($p<0.001$) and end-diastolic size ($p<0.001$)), regression of left ventricular hypertrophy (for left ventricular myocardial mass ($p<0.001$)), and an increase in left ventricular ejection fraction ($p<0.001$).

Therefore, positive dynamics in the form of a decrease in uric acid content is accompanied by primarily reduced creatinine ($p<0.001$), amino-terminal pro-B-type natriuretic peptide ($p<0.001$), and C-reactive protein ($p<0.001$), and a significant decrease in systolic blood pressure ($p<0.001$), total cholesterol ($p<0.001$), and triglycerides ($p<0.05$). A decrease in uric acid results in reduced left ventricular size (for end-systolic size ($p<0.001$) and end-diastolic size ($p<0.01$)), regression of left ventricular hypertrophy (for left ventricular myocardial mass ($p<0.01$)), and an increase in left ventricular ejection fraction ($p<0.001$), increased coronary reserve with a significant increase in threshold load ($p<0.001$) and physical exercise tolerance ($p<0.01$), and reduced exercise-induced ischemia (by total ST segment depression ($p<0.05$)).

Positive reduction in amino-terminal pro-B-type natriuretic peptide content occurs with a predominant decrease in total cholesterol ($p<0.05$), creatinine ($p<0.001$), uric acid ($p<0.001$), and C-reactive protein ($p<0.01$), significant reduction in systolic blood pressure ($p<0.001$), and triglyceride concentration ($p<0.001$). This positive trend

in amino-terminal pro-B-type natriuretic peptide content is associated with reduced left ventricular size (for end-systolic size ($p<0.001$) and end-diastolic size ($p<0.001$)) and left ventricular myocardial mass ($p<0.001$), improvement in left ventricular ejection fraction ($p<0.001$), increased coronary reserve with increased threshold load ($p<0.001$), physical exercise tolerance ($p<0.001$), and reduced exercise-induced ischemia (by total ST segment depression ($p<0.05$)).

Decreased C-reactive protein levels are associated with predominantly reduced total cholesterol ($p<0.001$), creatinine ($p<0.001$), uric acid ($p<0.001$), and amino-terminal pro-B-type natriuretic peptide ($p<0.01$), as well as significantly reduced systolic blood pressure ($p<0.001$) and triglyceride levels ($p<0.001$). This trend in C-reactive protein dynamics is accompanied by a reduction in left ventricular size (for end-systolic size ($p<0.01$) and end-diastolic size ($p<0.01$)), left ventricular myocardial mass ($p<0.001$), an increase in left ventricular ejection fraction ($p<0.001$), and increased coronary reserve with increased threshold load ($p<0.001$) and physical exercise tolerance ($p<0.05$), as well as reduced ischemia during physical exertion (by total ST segment depression ($p<0.05$)).

Increase in total testosterone in men and its decrease in women is associated with reduced systolic blood pressure (in both cases $p<0.05$, with greater intensity in women ($p<0.05$)), decreased triglyceride levels (in both cases $p<0.05$, with more pronounced reduction in women ($p<0.05$)), increased coronary reserve with greater intensity in women (by threshold load ($p<0.001$), physical exercise tolerance ($p<0.05$), and total exercise-induced ischemia (by total ST segment depression ($p<0.05$))). Decrease in total testosterone in women is accompanied by reduced total cholesterol levels ($p<0.01$) and decreased C-reactive protein ($p<0.05$).

Thus, uric acid can be used as a biomarker for functional and coronary reserve limitations, as its dynamics have prognostic value for reducing left ventricular size and regression of left ventricular hypertrophy, improving systolic function, and increasing coronary reserve. Even with preserved left ventricular systolic function and normal ejection fraction, amino-terminal pro-B-type natriuretic peptide has predictive value for reducing left ventricular size, regression of hypertrophy, and increasing coronary

reserve. C-reactive protein is identified as a biomarker for assessing prognosis in heart remodeling, enhancing left ventricular systolic function, and coronary reserve. Given the prognostic value for the progression of dyslipidemia, changes in coronary reserve, and functional status of stable angina patients, uric acid levels, amino-terminal pro-B-type natriuretic peptide, and C-reactive protein can be used as biomarkers for individual sensitivity to therapy and patient selection for intensified drug treatment to maintain functionality and for interventional procedures. Considering the interest in circulating cardiovascular biomarkers and the lack of consistent data on their clinical significance, further research in patients with stable ischemic heart disease is warranted.