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Early Prediction and Severity Assessment of Cardiovascular Complications in Comorbid Coronary Heart Disease Based on Acid-Base Balance and Hemostasis Biomarkers

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Abstract In the study, the indicators of the acid-base balance and hemostasis system in comorbid conditions with coronary heart disease were studied. With an increase in the level of comorbidity, a tendency towards metabolic acidosis and an increase in hypercoagulation changes were revealed. The highest imbalance was noted in the group of CHD+AH+DM2+obesity ($p<0.001$). In patients with complications, low pH and HCO3−, high levels of fibrinogen and D-dimer were noted ($p<0.01$). The obtained results indicate the expediency of using biomarkers of ABB and hemostasis in early prediction and risk stratification. The obtained results indicate the expediency of using biomarkers of blood pressure and hemostasis in the stratification of clinical risk and early prediction of complications.

Keywords Ischemic heart disease, Comorbid conditions, Arterial hypertension, Type 2 diabetes mellitus, Obesity, Acid-base balance, Metabolic acidosis, Hemostasis system

1. Introduction

Coronary heart disease (CHD) remains one of the leading causes of mortality and disability worldwide [1]. In the development of CHD, myocardial ischemia, endothelial dysfunction, inflammation, and thrombogenesis manifest themselves as interconnected pathogenetic mechanisms [2]. Especially in the presence of comorbid conditions (arterial hypertension, diabetes mellitus, obesity), metabolic disorders deepen, and changes in the acid-base balance (ABB) and hemostasis system are observed [3].

It has been noted in the literature that metabolic acidosis or subclinical ABB imbalance can exacerbate hypercoagulation, increase platelet activity, and affect the fibrinolysis system [4]. At the same time, biomarkers of hemostasis - D-dimer, fibrinogen, APTT and other indicators - have important prognostic significance in assessing the severity of CHD and the risk of complications [5].

Therefore, the study of the relationship between ABB indicators and biomarkers of the hemostasis system in comorbid conditions with CHD, the assessment of their clinical significance, and their use in risk stratification is a pressing issue.

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The purpose of the study was to determine the relationship between acid-base indicators (pH, pCO2, HCO3, BE) and blood hemostasis biomarkers (D-dimer, fibrinogen, APTT, PTI, platelets) in comorbid conditions with coronary heart disease, as well as to scientifically substantiate their significance in assessing the severity and clinical course of the disease.

2. Material and Methods

The study was conducted on 120 patients with coronary heart disease (CHD) who were treated in the cardiology department of the Bukhara Regional Multidisciplinary Medical Center. Patients were divided into 3 groups according to comorbid conditions: 1st group - CHD + arterial hypertension (AH); 2nd group - CHD + type 2 diabetes mellitus (DM2) + obesity; 3rd group - CHD+AH+DM2+obesity. 30 healthy individuals were examined as a control group.

All participants underwent a general clinical examination (history, arterial blood pressure, body mass index), standard cardiological examinations (ECG, echocardiography). Within the framework of laboratory studies, the acid-base status (pH, pCO2, HCO3, excess of bases in arterial blood) and hemostasis system parameters (platelet count, APTT, prothrombin time/IRR, fibrinogen, D-dimer) were assessed. Comparative analysis of the obtained data was carried out in the context of groups, correlation analysis between AAB and

hemostasis indicators, as well as a multifactorial regression method was used to assess the influence of the degree of comorbidity.

3. Results and Analyses

As comorbid conditions deepened, the clinical course of CHD, changes in the ABB and hemostasis system became more pronounced (Table 1).

Analysis of the distribution by functional classes of CHD clearly showed that the severity of the disease increases with an increase in the number of comorbid pathologies.

In group 1 (CHD+AH, n=37), the majority of patients were located in FC II (43.2%) and FC I-II stages, the proportion of classes III-IV was 32.4%. This indicates a relatively stable clinical course, despite the presence of arterial hypertension.

In group 2 (CHD+DM2+obesity, n=42), the proportion of more severe clinical conditions increased, and FC III-IV totaled 54.8%. In particular, the fact that the proportion of patients with FC III reached 40.5% indicates that metabolic disorders (hyperglycemia, insulin resistance, dyslipidemia) exacerbate the course of myocardial ischemia.

In group 3 (CHD+AH+DM2+obesity, n=41), the highest clinical severity was noted: the proportion of FC III-IV was 73.1%, including FC IV 26.8%. This indicates that the combination of comorbid factors significantly increases the degree of hemodynamic disorders and functional limitations.

In comorbid conditions with CHD, an acid-base imbalance can arise as a result of changes in the activity of metabolic and respiratory mechanisms. Tissue hypoxia, a tendency to lactic acidosis, and gas exchange disorders develop especially in coronary heart disease accompanied by diabetes mellitus and obesity. In this regard, the indicators of arterial blood gases and the buffer system were assessed in all groups (Table 2).

Table 1. Distribution of patients by functional classes of CHD (NYHA), n (%)

Functional class (FC)	Group 1 CHD+AH (n=37)	2nd group CHD+DM2+obesity (n=42)	Group 3 CHD+AH+DM2+obesity (n=41)
FC I	9 (24.3%)	4 (9.5%)	2 (4.9%)
FC II	16 (43.2%)	15 (35.7%)	9 (22.0%)
FC III	9 (24.3%)	17 (40.5%)	19 (46.3%)
FC IV	3 (8.1%)	6 (14.3%)	11 (26.8%)

Table 2. ABB indicators in comorbid conditions with CHD (M ±m)

Indicator	Control (n=30)	Group 1 (n=37)	p1	Group 2 (n=42)	p2	Group 3 (n=41)	p3
pH	7.40 ±0.02	7.38 ±0.03	0.041	7.34 ±0.04	0.008	7.31 ±0.05	<0.001
pCO2 (mm Hg)	39.8 ±2.0	41.9 ±2.5	0.038	44.2 ±2.8	0.006	46.1 ±3.2	<0.001
HCO3− (mmol/l)	24.5 ±1.1	23.0 ±1.5	0.029	21.7 ±1.7	0.004	20.1 ±1.9	<0.001
Base excess (mmol/l)	0.6 ±0.5	−1.5±0.8	0.033	−2.9±1.0	0.005	−4.2±1.2	<0.001

Note: p1 - difference of group 1 compared to the control group, p2 - difference of group 2 compared to the control group, p3 - difference of group 3 compared to the control group

Table 3. Biomarkers of hemostasis in comorbid conditions with CHD (M ±m)

Indicator	Control (n=30)	Group 1 (n=37)	p1	Group 2 (n=42)	p2	Group 3 (n=41)	p3
Platelets (×109/l)	248 ±20	271 ±23	0.036	289 ±26	0.004	318 ±31	<0.001
Fibrinogen (g/l)	3.0 ±0.3	3.7 ±0.6	0.021	4.3 ±0.7	0.002	5.1 ±0.8	<0.001
APTT (sec.)	32.1 ±2.0	29.4 ±1.8	0.028	27.6 ±1.6	0.003	25.3 ±1.4	<0.001
D-dimer (ng/ml)	205 ±30	355 ±50	0.018	428 ±60	0.001	590 ±80	<0.001

Note: p1 - difference of group 1 compared to the control group, p2 - difference of group 2 compared to the control group, p3 - difference of group 3 compared to the control group

Table 4. Frequency of adverse cardiovascular complications, n (%)

Indicator	Group 1 CHD+AH (n=37)	2nd group CHD+DM2+obesity (n=42)	Group 3 CHD+AH+DM2+obesity (n=41)	p
Acute coronary syndrome	4 (10.8%)	7 (16.7%)	12 (29.3%)	0.021
Decompensation of heart failure	6 (16.2%)	11 (26.2%)	18 (43.9%)	0.008
Thrombotic complications	3 (8.1%)	6 (14.3%)	10 (24.4%)	0.034
Total complications	9 (24.3%)	17 (40.5%)	25 (61.0%)	<0.001

The obtained results showed that with the deepening of comorbid conditions with CHD, step-by-step and statistically significant changes in the acid-base balance occur.

In group 1 (CHD+AH), the pH indicator significantly decreased compared to the control group (p=0.041), pCO2 increased (p=0.038), HCO3− and base excess decreased (p<0.05). This condition refers to a tendency toward mild mixed (metabolic-respiratory) acidosis. Disorders of microcirculation and decreased tissue perfusion associated with arterial hypertension are a possible cause of these changes.

In the 2nd group (CHD+DM2+obesity), the imbalance of ABB was further exacerbated: the pH decreased to 7.34±0.04 (p=0.008), HCO3− to 21.7±1.7 mmol/l (p=0.004). These indicators indicate the development of metabolic acidosis against the background of diabetic metabolic disorders, insulin resistance, and lipotonic effects. An increase in pCO2 (p=0.006) indicates insufficient compensation mechanisms.

In group 3 (CHD+AH+DM2+obesity), the most profound and highly significant (p<0.001) changes were noted. A decrease in pH to 7.31±0.05, a sharp decrease in HCO3− and base excess indicators indicate a significant decrease in buffer system reserves. An increase in pCO2 to 46.1±3.2 mm Hg indicates gas exchange disorders and the addition of a respiratory component.

Increased thrombogenic potential in comorbid conditions with CHD plays an important role in the course of the disease and the development of complications. Especially against the background of diabetes mellitus and obesity, endothelial dysfunction, inflammation, and activation of the blood coagulation system increase (Table 3).

The obtained results showed that the symptoms of hypercoagulation syndrome gradually worsened in all clinical groups.

In group 1 (CHD+AH), the number of platelets and the level of fibrinogen were significantly increased compared to the control (p<0.05), APTT decreased (p=0.028), the level of D-dimer increased to 355±50 ng/ml (p=0.018). This indicates a mild increase in thrombogenic activity.

In the 2nd group (CHD+DM2+obesity), the changes were even more pronounced: fibrinogen increased to 4.3±0.7 g/l (p=0.002), D-dimer to 428±60 ng/ml (p=0.001). A reliable decrease in APTT indicates activation of the blood coagulation system. Diabetic microangiopathy and metabolic inflammation form the pathogenetic basis of this condition.

In the 3rd group (CHD+AH+DM2+obesity), the highest thrombogenic potential was noted: platelets 318±31×109/l, fibrinogen 5.1±0.8 g/l, D-dimer 590±80 ng/ml (p<0.001 in all). APTT decreased to 25.3±1.4 sec. These indicators indicate a deepening of hypercoagulation and a significant increase in the risk of thrombosis.

The frequency of adverse cardiovascular complications (acute coronary syndrome, decompensation, thrombotic conditions) in comorbid conditions with CHD was analyzed by groups. The obtained results showed that the risk of complications increases with an increase in the level of comorbidity (Table 4).

As can be seen from the results, the frequency of complications gradually and statistically significantly increased with an increase in the level of comorbidity (i.e., with the addition of hypertension, type 2 diabetes mellitus, and obesity in addition to CHD).

Acute coronary syndrome (ACS) was 10.8% in group 1, increased to 16.7% in group 2, and to 29.3% in group 3 (p=0.021). This indicates that comorbid metabolic and hemodynamic factors (DM2, obesity, AH) contribute to the development of ACS, exacerbating the instability of coronary atherothrombosis and myocardial ischemia. In practice, the frequency of ACS in group 3 was approximately 2.7 times higher than in group 1.

Differences in heart failure decompensation were even more pronounced: 16.2% in group 1, 26.2% in group 2, and 43.9% in group 3 (p=0.008). This means that an increase in comorbidity leads to a decrease in the functional reserves of the myocardium, difficulty in blood pressure control, and faster decompensation of heart failure against the background of hemodynamic load characteristic of diabetic cardiomyopathy and obesity. In group 3, the frequency of decompensation was almost 2.7 times higher than in group 1.

Thrombotic complications (prone to thrombosis) also increased in parallel with comorbidity: 8.1% in group 1, 14.3% in group 2, and 24.4% in group 3 (p=0.034). This result indicates a predominance of hypercoagulation in the 3rd group, endothelial dysfunction, and a high thrombogenic potential against the background of metabolic inflammation. In the 3rd group, thrombotic complications occurred approximately 3 times more often than in the 1st group.

The most important generalizing indicator - the total number of complications - was 24.3% in the 1st group, 40.5% in the 2nd group, 61.0% in the 3rd group, and the difference between the groups was highly significant (p<0.001). That is, the probability of adverse cardiovascular events significantly increased in patients with hypertension, diabetes mellitus, and obesity simultaneously: in group 3, the total number of complications was approximately 2.5 times higher than in group 1.

The role of indicators of the acid-base state and hemostasis system in the development of adverse cardiovascular complications in comorbid conditions with CHD was assessed separately. For this purpose, the patients were divided into groups with complications (n=51) and without complications (n=69), and the biomarkers of ABB and hemostasis were compared between them (Table 5).

Table 5. Biomarker depending on the presence of complications (M±m)

Indicator	Complications (n=51)	No complications (n=69)	p
pH	7.32±0.04	7.37±0.03	0.002
HCO3− (mmol/l)	20.9±1.8	23.1±1.5	<0.001
Fibrinogen (g/l)	4.8±0.7	3.9±0.6	<0.001
D-dimer (ng/ml)	575±75	390±60	<0.001

According to the table data, the indicators of the acid -base state in patients with complications were significantly

impaired. The pH decreased to 7.32 ±0.04, and a statistically significant difference was noted compared to the group without complications (p=0.002). A decrease in HCO3− to 20.9 ±1.8 mmol/l (p<0.001) indicates a deepening of the tendency towards metabolic acidosis and a limited reserve of the buffer system.

The indicators of the hemostasis system also differed significantly: fibrinogen increased to 4.8 ±0.7 g/l and D-dimer to 575 ±75 ng/ml (p<0.001 in both). This indicates increased hypercoagulation and activation of the fibrinolytic system, i.e., a high thrombogenic potential.

In general, in patients with complications, signs of metabolic acidosis and hypercoagulation syndrome were pronounced. The identified statistically significant differences indicate that these biomarkers can be considered as independent prognostic factors of adverse cardiovascular events. Also, a comprehensive assessment of SCS and hemostasis indicators has important clinical significance in the early stratification of risk in comorbid conditions with CHD.

4. Discussion

This study demonstrates that the increasing comorbidity burden in patients with coronary heart disease is associated with progressive metabolic and hemostatic disorders that significantly influence clinical severity and the risk of adverse cardiovascular events. The stepwise deterioration of acid-base balance, particularly the decrease in pH, HCO3−, and base excess values, indicates the development of metabolic acidosis, which became most pronounced in patients with combined arterial hypertension, type 2 diabetes mellitus, and obesity.

Metabolic acidosis is not only a biochemical abnormality but also an important pathophysiological factor affecting vascular homeostasis. Even mild chronic acidosis can impair endothelial function, reduce nitric oxide bioavailability, and promote inflammatory activation [2,7,11]. In diabetic and obese patients, tissue hypoxia, insulin resistance, and mitochondrial dysfunction enhance anaerobic metabolism and lactate accumulation, further aggravating acidosis [3]. These mechanisms contribute to vascular instability and coronary microcirculatory disorders.

In parallel with ABB disorders, our study revealed a progressive increase in thrombogenic activity. Elevated platelet count, fibrinogen, and D-dimer levels, combined with shortened APTT, reflect the activation of coagulation pathways and hypercoagulable state. It is well established that the structure and density of fibrin clots significantly influence the thrombotic risk [4,6], while elevated D-dimer concentrations are strongly associated with adverse cardiovascular outcomes [5]. A pronounced increase in fibrinogen and D-dimer in the third comorbid group confirms the amplification of thrombin generation and fibrinolytic activity in advanced metabolic dysregulation.

Importantly, patients with documented cardiovascular complications demonstrated significantly lower pH and HCO3− values and higher fibrinogen and D-dimer concentrations. These findings suggest that metabolic acidosis and hypercoagulation are not independent phenomena but interconnected components of a unified pathophysiological cascade. Acidosis may enhance platelet aggregation and coagulation factor activation, while systemic inflammation and endothelial dysfunction further accelerate thrombogenesis [2,7,8].

The observed increase in acute coronary syndrome, decompensation of heart failure, and thrombotic events with an increasing comorbidity burden supports the concept of the cardio-metabolic continuum [9,10,12]. Combined hypertension, diabetes, and obesity create a hemodynamic and metabolic environment that promotes myocardial remodeling, endothelial damage, and atherothrombosis. Chronic neurohumoral activation and oxidative stress aggravate both myocardial ischemia and systemic prothrombotic state [2,9].

Thus, our findings substantiate the pathogenetic link between acid-base imbalance and activation of the hemostasis system in comorbid CHD. The combined assessment of blood pressure parameters and hemostasis biomarkers provides additional prognostic information beyond traditional clinical evaluation. The integration of these laboratory markers into routine cardiological practice may enhance early risk stratification and allow for timely preventive interventions, especially in patients with multiple metabolic comorbidities.

Overall, the results confirm that metabolic acidosis and hypercoagulability represent key mechanisms contributing to an unfavorable cardiovascular prognosis in comorbid ischemic heart disease.

5. Conclusions

The presence of comorbid conditions with coronary heart disease (AH, type 2 DM and obesity) significantly increases the clinical severity of the disease, manifested by an increase in the proportion of functional classes III-IV; at the same time, with an increase in the level of comorbidity, the tendency towards metabolic acidosis in the acid-base state intensifies (pH, HCO3− and base excess significantly decreased), hypercoagulation disorders in the hemostasis system (increased platelets, fibrinogen and D-dimer, decreased APTT) increase, especially in the group of CHD+AH+ DM2+obesity (p<0.001), which substantiates the presence of a pathogenetic link between the imbalance of ABB and thrombogenic activity, and the expediency of using these biomarkers in the stratification of clinical risk and early prediction of complications.

It was established that the development of adverse cardiovascular complications in comorbid conditions with coronary heart disease is reliably associated with a tendency towards metabolic acidosis and an increase in hypercoagulation: in patients with complications, the pH and HCO3− indicators decreased significantly, while the levels of fibrinogen and D-dimer increased significantly (p≤0.002). In groups with a combination of comorbid factors, the

frequency of complications was high, which indicates that the imbalance of the ABB and the activation of the hemostasis system play an important role in the clinical course and prognosis of CHD. Therefore, a comprehensive assessment of these biomarkers can be used as an effective clinical instrument for the early detection of adverse cardiovascular events and risk stratification.

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