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Features of the Clinical Course of Coronary Artery Disease in Patients with Covid-19 Depending on the Presence of Metabolic Syndrome

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Annotation

This analysis will not only allow for a more precise understanding of the development of metabolic syndrome and the progression of coronary artery disease, but it will also help identify the impact of 2019-nCoV infection on heart damage.

Objective: To study the pathogenetic significance of COVID-19 in the progression of metabolic syndrome and destabilization of coronary artery disease (CAD).

Object of the Study: 147 patients with CAD against the background of metabolic syndrome who received treatment in a COVID specialized center.

Subject of the Study: Blood and blood serum of patients with CAD for the quantitative determination of key biochemical parameters (lipid profile).

Conclusions: A notable feature of the clinical course of CAD with metabolic syndrome in patients with COVID-19 is the frequent occurrence of multiple anginal attacks, episodes of tachycardia, rhythm variability impairments such as ventricular extrasystoles, complete left bundle branch block, ST-segment elevation on the ECG, enhanced T-wave inversion, and progression of unstable angina. Patients with CAD and metabolic syndrome infected with COVID-19 demonstrated an increase in the atherogenic index, elevated mean triglyceride levels, and decreased mean serum HDL concentrations compared to optimal parameters and values in the group of patients without metabolic syndrome.

Keywords: COVID-19, metabolic syndrome, coronary artery disease, comorbidity, cardiovascular complications.

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At the end of 2019, with the emergence of a new coronavirus SARS-CoV-2, which causes COVID-19, humanity faced a global threat with severe consequences [6]. Despite worldwide efforts to find treatment methods and countermeasures, the disease continues to spread, with unfavorable course variations being observed against the backdrop of an overloaded healthcare system [7].

A larger and deeper study of the etiopathogenetic and clinical manifestations of COVID-19 in individuals with chronic conditions of various organs and systems confirms a pattern of adverse outcomes and poor prognosis [6; 7]. The complications emerging in patients infected with SARS-CoV-2, both with overt clinical manifestations and asymptomatic cases, are of significant interest to the scientific community.

The most common comorbidities leading to a severe course and complications of COVID-19 have been arterial hypertension (49.7%), obesity (48.3%), chronic lung disease (34.6%), diabetes mellitus (28.3%), and other cardiovascular diseases (27.8%) [9]. Arterial hypertension, obesity, and hyperglycemia, which are socially significant diseases with epidemic proportions, fit within the concept of metabolic syndrome [1-3; 13].

It is known that metabolic syndrome is strongly associated with adipose tissue dysfunction in obesity, and the presence of comorbid conditions such as chronic kidney disease, chronic respiratory, and cardiovascular diseases worsens the prognosis of COVID-19 [13]. The phenomenon of "metabolically healthy obesity" is discussed in the literature; however, most authors agree that the body's compensatory mechanism lasts for a relatively short period. The duration of high visceral fat in the human body plays a key role in the development of associated complications, primarily disorders in carbohydrate and lipid metabolism as well as cardiac dysfunctions.

Excess body weight in certain areas of the body leads to the formation of adipose tissue depots, mainly in subcutaneous adipose tissue, visceral fat, yellow bone marrow, mammary glands, and omentum. An increase in adipose tissue mass potentiates the systemic action of tissue angiotensin II, ultimately disrupting microcirculation, reducing vascular wall elasticity, and leading to various cardiovascular complications [10-12].

It has been well-established that the causative agent of the new coronavirus infection enters the human body through the epithelium of the upper respiratory tract and the epithelial cells of the stomach and intestines. Adipose tissue has a high concentration of ACE2 receptors, facilitating the entry of the SARS-CoV-2 virus into cells [4; 5; 8].

Given the number of complications for which patients with metabolic syndrome infected with SARS-CoV-2 required hospitalization and even intensive care, the problem of metabolic syndrome has become even more acute than in the "favorable" period before the spread of the new coronavirus infection.

Materials and Methods. In this study, 147 people over 18 years of age were examined for viral infection, and all patients were categorized as follows: the main group, which included 59 patients with COVID-19 and CAD on the background of metabolic syndrome; the comparison group, which included 58 patients with COVID-19 and CAD without metabolic syndrome; and the control group, which consisted of 30 healthy individuals without clinical signs of CAD or metabolic syndrome. CAD was diagnosed at the prehospital stage through anamnesis collection and clinical, instrumental, and laboratory data. The determination of interdependencies of the examined parameters was performed using the Student’s t-test and Pearson’s chi-square test ($\chi 2$).

Results. We examined 147 patients hospitalized at the COVID Specialized Center and Samarkand Regional Infectious Diseases Hospital with a confirmed diagnosis of COVID-19. Of these, 59 patients (30 men and 29 women) had CAD with metabolic syndrome, while 58 patients (26 men and 32 women)

had CAD without metabolic syndrome. Table 1 presents the complaints of hospitalized patients, anamnesis indicating the presence of bad habits (smoking), physical and ECG data.

The study results showed that in women with CAD and COVID-19 on the background of metabolic syndrome, painless forms of CAD were 26.4% more common than in women without metabolic syndrome. This is likely due to the pre-manifest period, specifically latent type 2 diabetes mellitus and the development of diabetic neuropathy in 54% of CAD patients with metabolic syndrome. Among men, more than 50% were smokers, and anamnesis indicated an earlier onset of CAD.

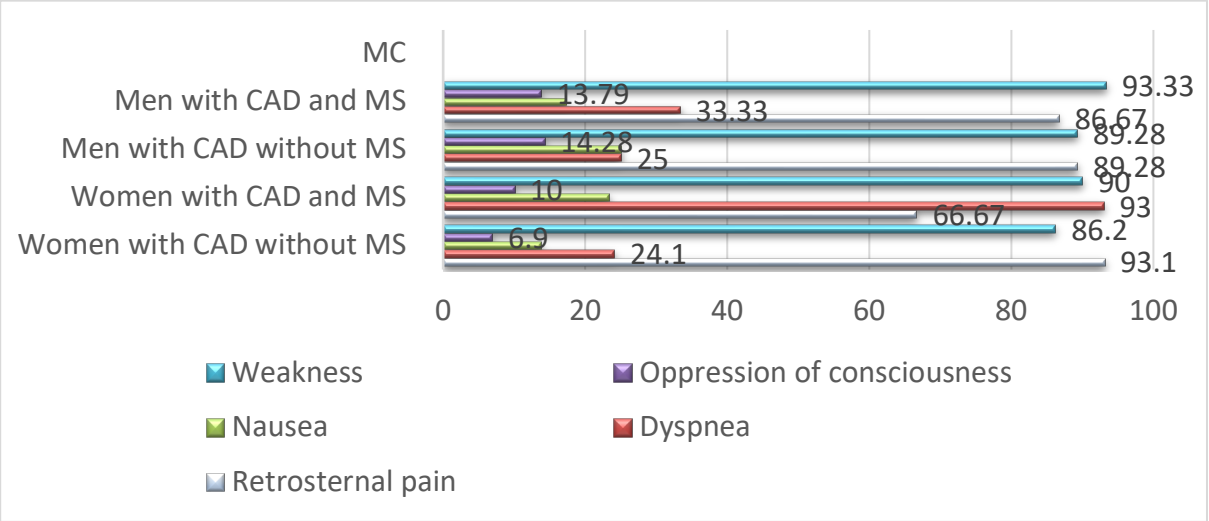

Fig. 1. Distribution of symptoms among patients.

In men without MS, systolic blood pressure was 137.6 ± 23.6 mm Hg. Art., diastolic - 82±13.4 mm Hg. Art.; in men with MS - 129.4±252.7 and 78.9±12.7 mm Hg. Art. respectively. There were no significant differences in blood pressure values among patients (Table 1).

Table 1. Physical examination data

	Women with CAD without MS (n=32)	Women with CAD and MS (n=29)	Men with CAD without MS (n=26)	Men with CAD and MS (n=30)
Wheezing in the lungs	7 (24,1%)	11 (36,67%)	7 (25%)	11 (39,28%)
Complaints about palpitations	6 (20,68%)	9 (30%)	6 (21,43%)	8 (28,57%)
High level BP	26 (87,5%)	28 (96,7%)	19 (67,8%)	26 (87,5%)
ECG changes:				
ST segment elevation	17 (58,62%)	22 (73,33%)	21 (75%)	21 (75%)
ST segment depression	12 (41,38%)	8 (26,67%)	6 (21,43%)	9 (32,14%)

* χ^2=7,276, p=0,003493 **χ^2=3,8, p=0,02496

In hospitalized patients, type 2 diabetes mellitus was newly diagnosed in 24% of cases among those with CAD and MS, emerging against the background of COVID-19.

During hospitalization, blood glucose levels were as follows: in women with CAD without MS, the average was 7.7±2.8 mmol/l; in women with MS, it was 9.8±5 mmol/l. Among men without MS, the level was 7.7±2.4 mmol/l, while in men with MS, it was 12 ± 4.9 mmol/l. These findings indicate elevated glucose levels, particularly among men with both CAD and MS in the context of COVID-19.

The study revealed that a quarter of the patients experienced persistent hyperglycemia, with newly diagnosed type 2 diabetes mellitus following in these cases (Table 2).

Table 2. The frequency of newly diagnosed type 2 diabetes mellitus among patients with coronary artery disease and COVID-19

	Women with CAD without MS (n=32)	Women with CAD and MS (n=29)	Men with CAD without MS (n=26)	Men with CAD and MS (n=30)
Absolute number of patients with DM	3*	18**	1*	11**
% ratio of patients	12,5	60	1,7	37,5
Type 2 DM compensation phase:				
Compensated	1 (25%)	4 (22,2%)	0 (0%)	4 (33,3%)
Subcompensated	2 (75%)	12 (66,7%)	1 (100%)	3 (25%)
Decompensated	0 (0%)	2 (11,1%) ***	0 (0%)	4 (33,3%) ***

* χ^2= 4,665, p=0,01539

** χ^2=3,139, p=0,03823

*** χ^2=3,578, p=0,02628

In patients without metabolic syndrome, diabetes mellitus was detected in 12.5% of women, whereas in women with metabolic syndrome, type 2 diabetes developed due to COVID-19 in 60% of cases. Additionally, severe hyperglycemia and decompensated diabetes mellitus were notably observed in patients with CAD and MS, likely because advanced forms of diabetes often coexist with other MS components.

Thus, COVID-19 acted as a pathogenetic trigger, accelerating the progression of metabolic syndrome and destabilizing coronary artery disease, leading to the onset of decompensated type 2 diabetes.

The analysis of lipid profile parameters in patients with COVID-19 and coronary artery disease on the background of metabolic syndrome showed a 2.66-fold increase in the atherogenic index compared to those without metabolic syndrome. Triglyceride levels were 1.37 mmol higher than in the comparison group, and VLDL levels were also relatively elevated in CAD patients with MS. Although serum levels of total cholesterol (TC) and low-density lipoprotein (LDL) exceeded optimal values in patients with CAD, the differences between groups were not statistically significant. Additionally, HDL levels were lower in patients with MS compared to those with CAD alone (Table 3).

The main study group showed a significant increase in hyperlipidemia and dyslipidemia prevalence. The most frequent pattern of lipid metabolism disturbance in metabolic syndrome was a combination of elevated triglycerides, reduced HDL levels, and increased LDL fraction (Table 4).

Table 3. Indicators of blood lipid spectrum in patients with CAD

Index (M ± m)	Study Group	
	CAD+MS (*n* = 59)	CAD (*n* = 58)
Total cholesterol, mmol/l	6,49 ± 1,93	6,38 ± 2,04
Triglycerides, mmol/l	3,89 ± 0.67*	1,52 ± 0,49
LDL, mmol/l	5,61 ± 1,72	4,50 ± 1,05
HDL, mmol/l	0,67 ± 0,09•	2,26 ± 0,54
Atherogenic index	5,34 ± 1,23*	2,68 ± 0,21

* - significance of differences in indicators when compared with the CHD group at $p < 0.05$, • - at $p < 0.01$

Table 4. Lipid metabolism disorders among patients with COVID-19 and coronary artery disease

Index (M ± m)	CAD+MS (*n* = 59)		CAD (*n* = 58)	
	Number of patients	%	Number of patients	%
Triglycerides, mmol/l	38	64*	25	43
LDL > 2,6 mmol/l	39	66	37	64
TC > 5,0 mmol/l	35	59	42	72
HDL < 1,0 mmol/l (male), < 1.3 mmol/l (female)	40	68•	21	36

* - significance of differences in indicators when compared with the group of coronary artery disease without MS at $p < 0.05$, • - at $p < 0.01$

In patients with CAD and metabolic syndrome, elevated triglyceride levels (>1.7 mmol/l) were found in 38 individuals in the main group, while low HDL levels (<1.0 mmol/l in men and <1.3 mmol/l in women) were observed in 40 patients, accounting for 68%.

Echocardiographic analysis showed that the average ejection fraction and stroke volume, calculated using the disk method, were 50.93 ± 3.63 and 26.56 ± 2.48 ml/m² in the main group, compared to 56.52 ± 2.29 and 30.18 ± 1.34 ml/m² in the comparison group.

Normal left ventricular geometry was significantly lower among patients with COVID-19 and CAD with metabolic syndrome compared to the comparison group (12% vs. 31%). In the pattern of left ventricular remodeling among patients with COVID-19 and CAD without metabolic syndrome, the concentric type was more common (55.5% vs. 25%, $p<0.005$). In patients with COVID-19 and CAD with metabolic syndrome, concentric left ventricular hypertrophy was observed more frequently than in those with CAD without metabolic syndrome (59% vs. 10%).

Overall, a marked increase in the prevalence of hyperlipidemia and dyslipidemia was observed in patients with CAD and metabolic syndrome. In these patients, there was an increase in the atherogenic index, a rise in average triglyceride levels, and a decrease in mean serum HDL concentration compared to the optimal parameters and values in the COVID-19 and CAD group.

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