

# Clinical Features and Prognosis Of Coronary Heart Disease In Patients With Metabolic Syndrome

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**Abstract:** Cardiovascular diseases (CVDs) are the leading cause of disability and death worldwide. In 2020, the WHO reported in Geneva that 17.3 million people died from CVDs, accounting for 30% of all deaths worldwide (WHO report, 2020). Of this number, 7.3 million people died from complications of coronary artery disease (CHD) (World Health Organization, 2021).

The study of coronary artery disease, its complications and the effectiveness of treatment dictates the need to study risk factors. It is known that metabolic disorders such as excess body weight, dyslipidemia and impaired glucose metabolism accelerate atherogenesis. All these disorders are components of metabolic syndrome (MS). The issue of the effect of MS on the cardiovascular system has been studied in sufficient detail in the literature, however, the effect of the syndrome on the results of angioplasty procedures and long-term prognosis of coronary artery disease requires further study.

**Keywords:** Cardiovascular diseases

**Aim:** studying the peculiarities of the course of coronary heart disease in patients with metabolic syndrome.

**Materials and Methods:** The study was conducted at the multidisciplinary clinic of the Tashkent Medical Academy. It is based on a retrospective analysis of the medical histories of 153 patients who were hospitalized on an emergency basis with a diagnosis of acute coronary syndrome (ACS) with and without ST-segment elevation. The outcomes of ACS included myocardial infarction with and without ST-segment elevation or unstable angina (new onset, progressive, Prinzmetal's angina). Among the patients, there were 91 men (59.5%) and 62 women (40.5%). The average age of hospitalized men was  $58.1 \pm 9.4$  years, and the average age of women was  $69.5 \pm 10.6$  years.

Upon hospitalization, complaints were collected, medical histories were taken, and physical examinations were conducted, including assessments of height and weight. Before performing coronary ventriculography, all patients underwent a complete blood count, urinalysis, biochemical blood analysis, and an ECG. The biochemical blood analysis determined cardi-specific markers (troponin, CK-MB), lipid profile, CRP, liver and kidney enzymes, serum glucose levels, HbA1C, total protein, and a coagulation profile.

Patients with ACS were divided into two groups: with and without metabolic syndrome. The diagnosis of metabolic syndrome (MS) was made according to the recommendations of the International Diabetes Federation from 2019. Patients with MS were identified by the presence of 3 out of 5 criteria: central obesity (waist circumference in men  $\geq 94$  cm, in women  $\geq 80$  cm), elevated TG levels:  $\geq 1.7$  mmol/L (150 mg/dL) or ongoing lipid-lowering therapy; reduced HDL-C levels:  $< 1.03$  mmol/L (40 mg/dL) in men and  $< 1.29$  mmol/L (50 mg/dL) in women, or ongoing specific therapy for dyslipidemia; hypertension (SBP  $\geq 130$  mm Hg or DBP  $\geq 85$  mm Hg) or antihypertensive therapy for previously diagnosed hypertension; elevated fasting plasma glucose levels  $\geq 5.6$  mmol/L (100 mg/dL) or previously diagnosed type 2 diabetes.

As part of the hospitalization, all patients underwent coronary ventriculography (CVG) and, if necessary, stenting of atherosclerotically affected arteries. For determining further patient management strategies, scoring was performed using the SYNTAX scale. Within 1-2 days of hospitalization, echocardiography was performed on the patients.

A total of 93 patients hospitalized with the diagnosis of "acute coronary syndrome" were examined. Table 1 presents the complaints of the hospitalized patients, the presence of harmful habits (smoking) in their medical history, physical data, and ECG changes.

Table 1  
 Clinical Characteristics of Patients with ACS

	Women without MS	Women with MS	Men without MS	Men with MS
Chest pain	30 (93,75%)*	20 (66,67%)* **	53 (89,83%)	28 (87,5%)**
Dyspnea	8 (25%)	9 (30%)	15 (25,42%)	10 (31,25%)
Interruptions in heart function	6 (18,75%)	7 (23,3%)	10 (16,95%)	7 (21,88%)
Nausea	5 (15,63%)	7 (23,33%)	14 (23,73%)	6 (16,75%)
Oppression of consciousness	2 (6,25%)	3 (10%)	6 (10,17%)	4 (12,5%)
Weakness	28 (87,5%)	28 (93,33%)	52 (88,14%)	29 (90,63%)
Smoking	2 (6,25%)	2 (6,67%)	29 (49,15%)	5 (15,63%)
Wheezing in the lungs	8 (25%)	11 (36,67%)	15 (25,42%)	12 (37,5%)
Interruptions in the heart during auscultation	7 (21,86%)	9 (30%)	12 (20,34%)	9 (28,13%)
ECG shows ST segment elevation	19 (59,38%)	22 (73,33%)	45 (76,27%)	22 (68,75%)
ECG shows ST segment depression	13 (40,62%)	8 (26,67%)	14 (23,73%)	10 (31,25%)

\*  $\chi^2=7,276$ ,  $p=0,003493$

\*\* $\chi^2=3,8$ ,  $p=0,02496$

The diagnosis of arterial hypertension was made based on medical history data: an increase in systolic BP to 140 mm Hg or higher and/or diastolic BP to 90 mm Hg or higher. Blood pressure levels were determined for all patients upon hospitalization. In women without MS, systolic pressure was  $138.3 \pm 18.3$  mm Hg, diastolic pressure was  $81.7 \pm 11.2$  mm Hg; in women with MS, it was  $140 \pm 40.7$  and  $83.1 \pm 22.4$  mm Hg, respectively. In men without MS, systolic pressure was  $130.4 \pm 21.9$  mm Hg, diastolic pressure was  $79 \pm 11.7$  mm Hg; in men with MS, it was  $131.1 \pm 22.9$  and  $81.1 \pm 10.9$  mm Hg, respectively.

No significant differences were found in the prevalence of arterial hypertension and blood pressure levels at the time of hospitalization between the groups.

The diagnosis of type 2 diabetes mellitus was based on medical history, with 2 men being diagnosed with diabetes for the first time. Upon hospitalization, the following glycemia levels were observed: in women without MS -  $7.7 \pm 2.8$  mmol/L; in women with MS -  $9.8 \pm 5$  mmol/L; in men without MS -  $7.7 \pm 2.4$  mmol/L; in men with MS -  $12 \pm 4.9$  mmol/L. For a long time, it was considered that hyperglycemia in an acute situation was stress-induced and did not require correction, but this is debatable.

Table 2 shows the distribution of type 2 diabetes mellitus in the groups.

Table 2  
 The Frequency of Diabetes Mellitus and the Degree of Its Compensation

	Women without MS	Women with MS	Men without MS	Men with MS
Number of people with diabetes (total)	4*	18**	1*	12**
% of the total in the group	12,5	60	1,7	37,5
Compensated Diabetes Mellitus	1 (25%)	4 (22,2%)	0 (0%)	4 (33,3%)
Subcompensated Diabetes Mellitus	3 (75%)	12 (66,7%)	1 (100%)	3 (25%)
Decompensated Diabetes Mellitus	0 (0%)	2 (11,1%) ***	0 (0%)	(41,7%) ***

\*  $\chi^2= 4,665$ ,  $p=0,01539$  \*\*  $\chi^2=3,139$ ,  $p=0,03823$  \*\*\*  $\chi^2=3,578$ ,  $p=0,02628$

Among patients without MS, diabetes mellitus was significantly more common in women. There were no cases of decompensated diabetes among patients without MS, which is likely due to the fact that severe forms of diabetes are associated with other components of MS.

In patients with MS, diabetes mellitus was significantly more common in women, but decompensated diabetes was more frequently observed in men. This can probably be explained by lower adherence to treatment and insufficient medical examination (in 2 out of 5 men with decompensated diabetes, hyperglycemia was detected for the first time).

The height and weight of all patients were measured, and BMI was calculated based on these measurements. The distribution of patients in the groups by the degree of obesity is shown in Figures 1 and 2.

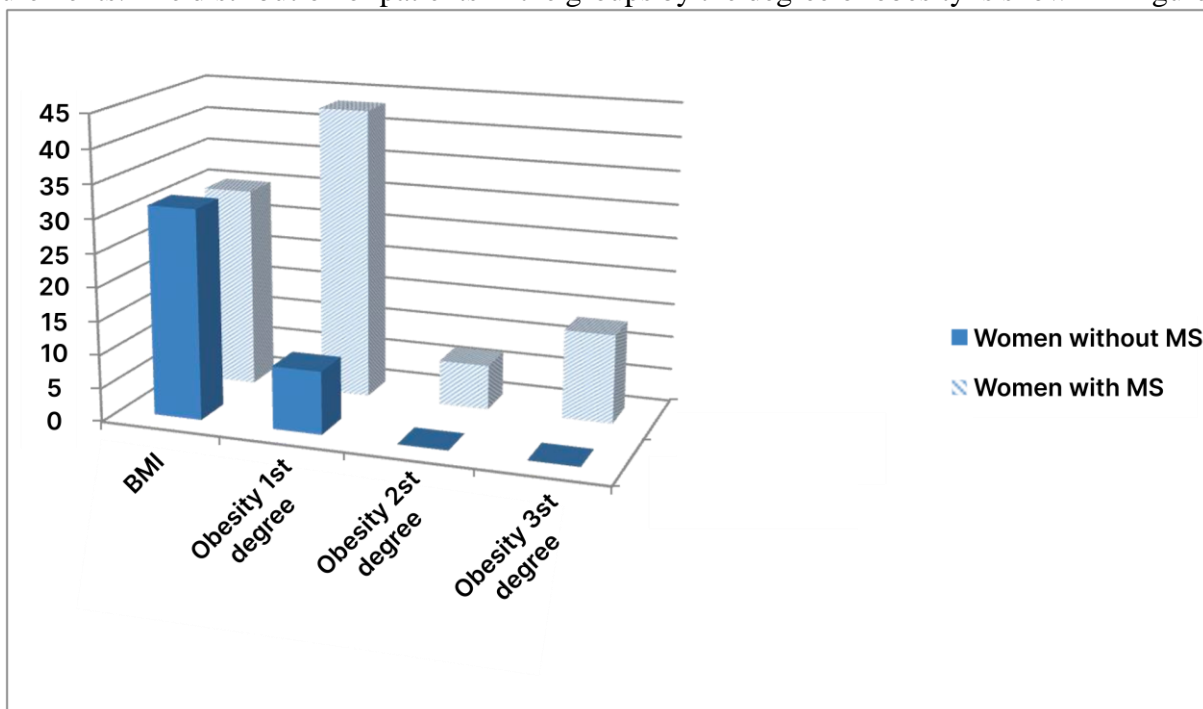


Figure 1. Frequency of Obesity in Women with and without Metabolic Syndrome

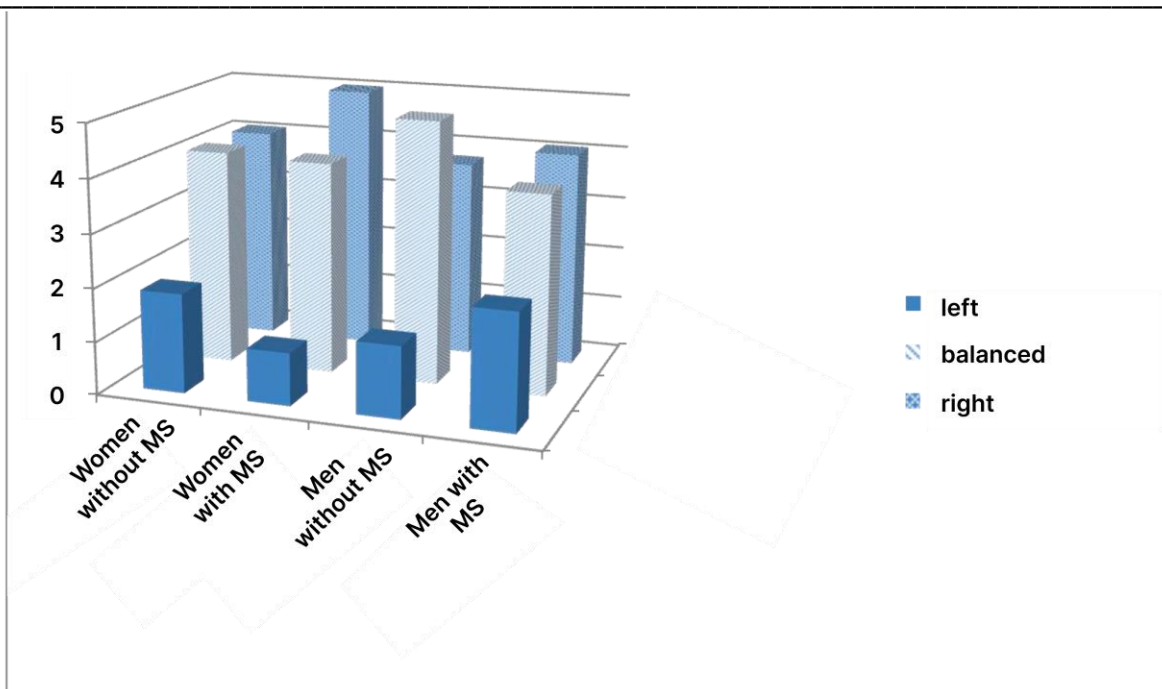


Figure 2. Frequency of Obesity in Men with and without Metabolic Syndrome

In men and women without MS, overweight and obesity occurred with the same frequency (39% and 40.7%, respectively), while in women with MS, the body mass index was more often above 25 than in men (93.3% and 84.4%, respectively). Additionally, women with MS more frequently had high-grade obesity. However, these differences are not statistically significant.

In men and women without MS, there was no occurrence of second and third-degree obesity. Apparently, this is due to the fact that in the presence of high-grade obesity, other components of MS are also present.

All patients had their lipid profiles examined upon admission.

Table 3 presents the data on total cholesterol levels and the number of patients with hypercholesterolemia.

Table 3  
 The Frequency of Hypercholesterolemia and Total Cholesterol Levels

	Women without MS	Women with MS	Men without MS	Men with MS
Number of People with Hypercholesterolemia	17	18	29	22
% of the Total Number in the Group	58,6	62,1	50	68,8
Total Cholesterol Levels	5,6±1,9	5,6±1,3	5,3±1,2	5,7±1,1

There were no gender differences in total cholesterol levels and the frequency of hypercholesterolemia.

Table 4 shows the changes in HDL-C levels in patients admitted to the hospital. A significant decrease was considered to be below 1.03 mmol/L for men and 1.29 mmol/L for women.

Table 4  
 High-Density Lipoprotein (HDL) Levels and Frequency of Their Decrease

	Women without MS	Women with MS	Men without MS	Men with MS
Number of People with Decreased HDL Levels	4	12	11	16
% of the Total Number in the Group	21,1	75	27,5	80
HDL Levels (mmol/L)	1,5±0,4	1,2±0,2	1,2±0,3	0,9±0,2

Thus, metabolic syndrome in women and men has different structures. In women, besides arterial hypertension, diabetes mellitus and excess weight contribute more significantly, whereas in men, elevated triglyceride levels and decreased HDL levels are more prominent.

All patients underwent coronary ventriculography during hospitalization. If a patient was admitted with ACS with ST-segment elevation within 24 hours of the onset of the anginal attack, CVG was performed on an emergency basis. If a patient showed ST-segment depression on the ECG, CVG was performed on an emergency basis only in life-threatening conditions (cardiogenic shock, ventricular arrhythmias, recurrent pain syndrome).

Figure 3 shows the distribution by blood flow type in different groups.

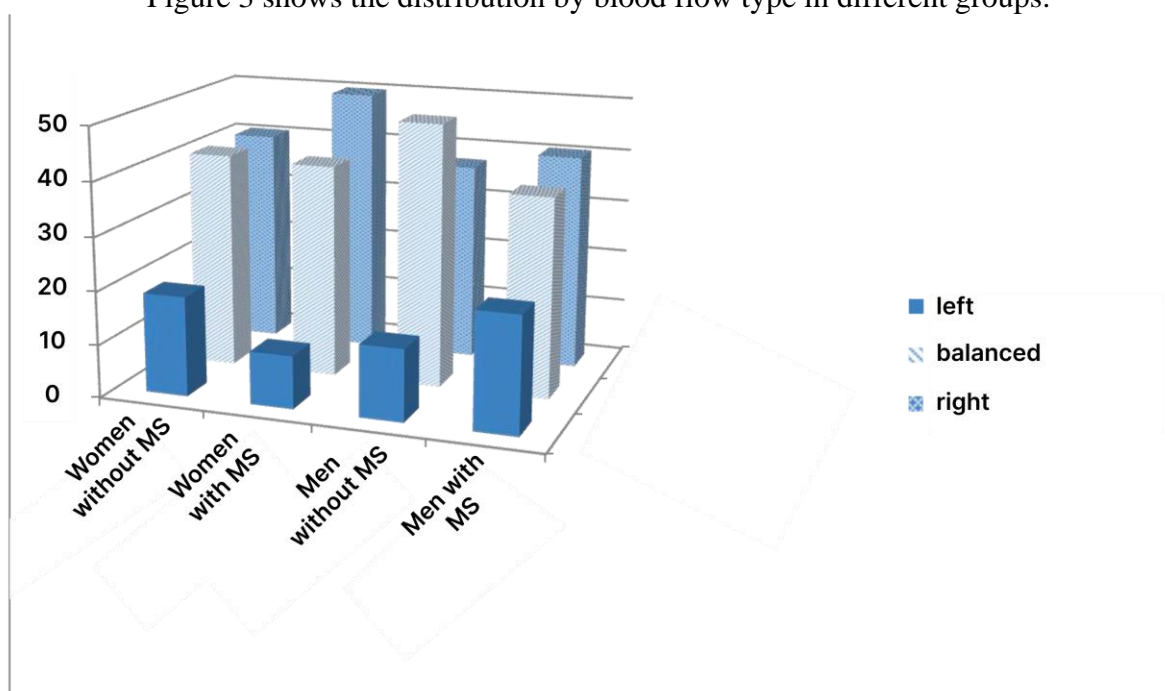


Figure 3. Types of Blood Flow in Patients with Acute Coronary Syndrome

It is evident that right and balanced types of blood flow were present in all groups, which is consistent with literature data.

In all patients, the most commonly affected arteries were the left anterior descending artery (LAD), right coronary artery (RCA), and the circumflex artery (Cx). Both women and men with metabolic syndrome more frequently exhibited multiple coronary artery lesions, affecting both major vessels and second-order branches.

To assess the impact of metabolic syndrome on the extent and nature of coronary artery lesions, correlations were examined between individual components of the syndrome and the number of hemodynamically significant stenoses, as well as the total SYNTAX score. These data are presented in Table 5.

Table 5  
 Correlation Between Components of Metabolic Syndrome and the Extent of Coronary Artery Lesions

	Number of Hemodynamically Significant Stenoses	SYNTAX
Age	<b>0,37</b>	<b>0,36</b>
Gender	N/A	N/A
Obesity	<b>0,16</b>	<b>0,19</b>
Diabetes Mellitus (DM)	<b>0,21</b>	<b>0,34</b>
Arterial Hypertension (AH)	<b>0,27</b>	<b>0,26</b>
Metabolic Syndrome (MS)	<b>0,24</b>	<b>0,37</b>
Cholesterol	N/A	N/A
Triglycerides (TG)	<b>0,22</b>	<b>0,22</b>
Low-Density Lipoprotein (LDL)	N/A	N/A
Very Low-Density Lipoprotein (VLDL)	N/A	N/A
High-Density Lipoprotein (HDL)	N/A	N/A

The table shows that all components of the metabolic syndrome (MS) are associated with hemodynamically significant stenoses and the extent of coronary artery lesions. Significant correlations were observed between age and the number of hemodynamically significant stenoses, the SYNTAX score (and consequently, the need for coronary artery bypass grafting - CABG). Type 2 diabetes mellitus significantly influenced the extent of arterial lesions and had a lesser impact on the formation of significant stenoses. The same pattern was observed for MS.

In Chapter 3, Table 10 showed the absence of a correlation between age and the components of MS (except for a weak correlation with arterial hypertension), indicating that age is an independent variable affecting atherogenesis. It should be noted that neither the total cholesterol level, nor the levels of the most atherogenic very low-density lipoproteins (VLDL) and low-density lipoproteins (LDL), nor the level of anti-atherogenic high-density lipoproteins (HDL) influenced the extent and nature of coronary artery lesions.

A total of 153 patients hospitalized with a diagnosis of ACS were monitored. The outcomes of ACS were either the development of myocardial infarction or unstable angina (new onset, progressive, Prinzmetal's angina). Six patients died within the first 24 hours after admission. The causes of death were cardiogenic shock and myocardial rupture. Thirty-two patients developed complications requiring additional resuscitative interventions. These included acute left ventricular failure, cardiogenic shock, complete AV block, and ventricular arrhythmias (fibrillation and flutter). Table 6 presents the outcome characteristics in different groups.

Table 6  
 Outcomes Characteristics of ACS

	Myocardial Infarction (MI)	% MI	Complications	% Complications	Lethal Outcome	% Deaths	Total Number of People

Women without MS	19	59,37	4	12,5	1	3,125	32
Women with MS	23	76,67	4	13,33	1	3,33	30
Men without MS	44*	74,58	14	23,73	0**	0	59
Men with MS	30*	93,75	10	31,25	4**	12,5	32

\*  $\chi^2=5,021$ ,  $p=0,01252$  \*\* $\chi^2=7,714$ ,  $p=0,002740$

The table shows that in women with and without MS, the frequency of ACS outcomes such as myocardial infarction (MI), the frequency of life-threatening complications, and lethal outcomes did not significantly differ. However, in men with MS, MI and lethal outcomes occurred significantly more frequently during hospitalization compared to men without MS.

Figures 4 and 5 display the predominant localization of MI based on the presence of hypo akinetic areas according to echocardiography (ECHO-CG) data.

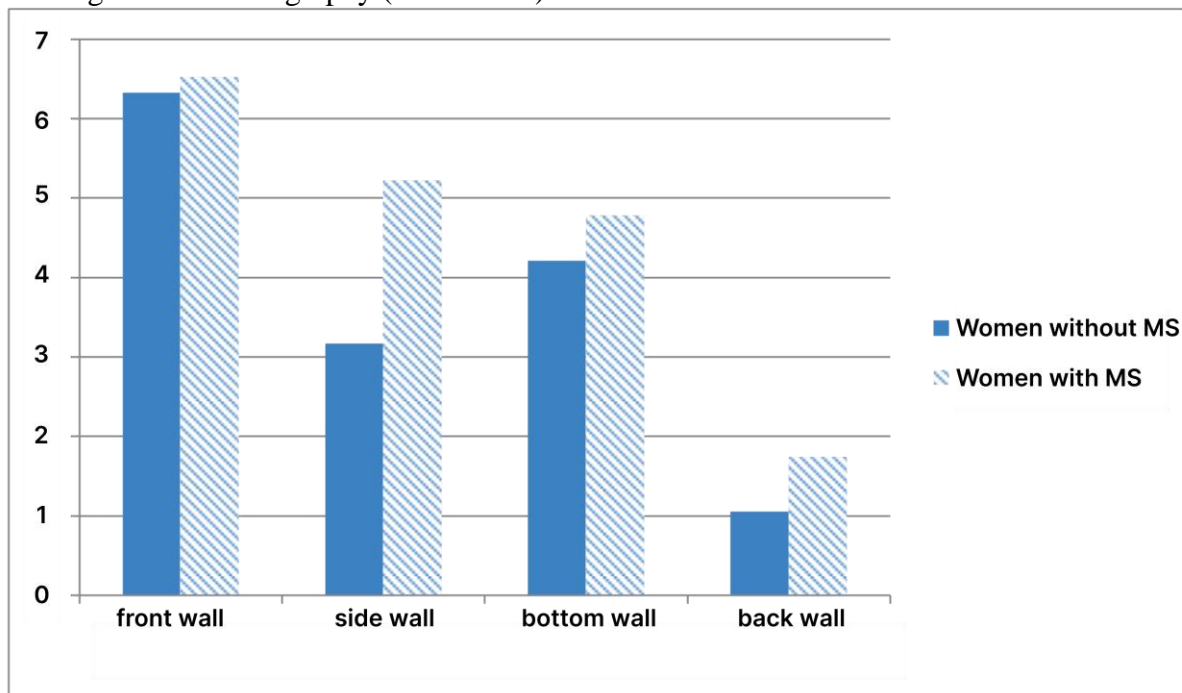


Figure 4. Localization of Myocardial Infarction in Women

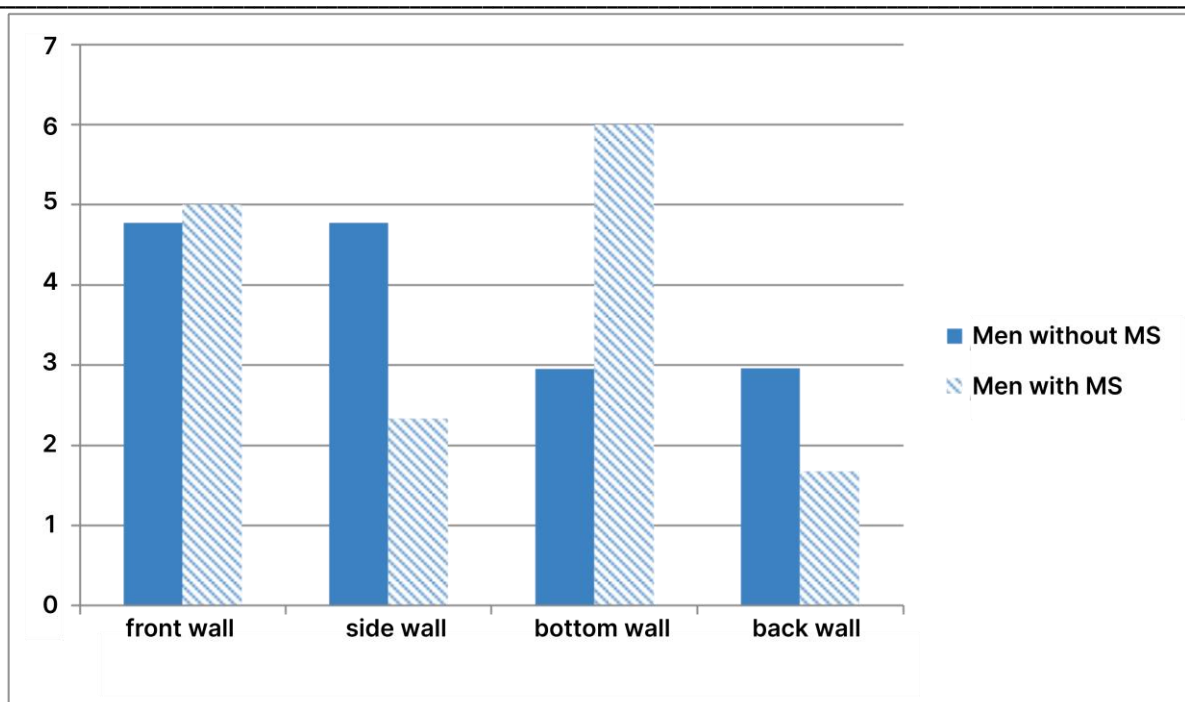


Figure 5. Localization of Myocardial Infarction in Men

The presented diagrams show that anterior MI localization is more common in women. In women with MS, compared to women without MS, myocardial damage is more extensive. In men without MS, the anterior and lateral walls of the left ventricle were predominantly affected, whereas in men with MS, the inferior wall was more commonly affected. The inferior wall of the left ventricle is supplied by the right coronary artery (RCA), as is the AV node via the atrioventricular artery, which in 90% of cases branches off from the RCA. This likely explains the higher frequency of life-threatening complications, such as ventricular arrhythmias and complete AV blocks, as well as lethal outcomes in men with MS.

Despite the more extensive myocardial damage associated with metabolic syndrome, neither myocardial damage markers nor changes in the lipid profile differed significantly.

Table 7 presents data on parameters affecting the short-term prognosis of ACS.

Table 7

Predictors of Myocardial Infarction, Complications of Acute Coronary Syndrome, and Lethal Outcome

	Myocardial Infarction (MI)	Complications	Lethal Outcome
Smoking	N/A	N/A	N/A
Age	N/A	N/A	N/A
Arterial Hypertension (AH)	N/A	-0,329073	N/A
Diabetes Mellitus (DM)	N/A	-0,501805	0,56463
Admission Glucose	0,61226	0,56234	0,854406
Obesity	N/A	-0,342727	N/A
Total Protein	-0,490969	N/A	-0,96667
Total Cholesterol	N/A	N/A	N/A
Triglycerides (TG)	0,229204	N/A	N/A
Low-Density Lipoprotein (LDL)	N/A	N/A	N/A
High-Density Lipoprotein (HDL)	-0,427978	-0,297634	N/A



Troponin	0,924537	0,232271	N/A
Fibrinogen	N/A	N/A	N/A
C-Reactive Protein (CRP)	0,333333	0,458678	N/A
Metabolic Syndrome (MS)	0,447099	N/A	0,77515
Left Ventricular Myocardial Mass Index (LVMI)	N/A	N/A	N/A
Concentric Hypertrophy	N/A	N/A	N/A

The table shows that age, the presence of harmful habits, and concentric left ventricular hypertrophy did not affect the risk of myocardial infarction (MI), life-threatening complications, or lethal outcomes. There is a negative correlation between diabetes mellitus (DM), arterial hypertension (AH), obesity, and the likelihood of complications. Most likely, despite the influence of these diseases on the development of hemodynamically significant stenoses and a greater extent of coronary artery lesions, the myocardium is more "trained" to ischemia over the long course of these diseases.

It is noteworthy that a history of DM and AH did not affect the risk of MI, although DM was a negative prognostic indicator for the short-term prognosis. Moreover, it was shown that admission glucose levels are an independent predictor of a negative prognosis: the higher the glucose level, the greater the risks of MI, complications, and death, with a strong correlation. The table shows that components of MS such as elevated triglyceride levels (TG) and reduced HDL levels significantly increase the frequency of MI, but only reduced HDL levels influenced the presence of complications. Elevated C-reactive protein (CRP) was also a poor prognostic indicator: patients with elevated CRP more frequently developed MI and its complications. Overall, the presence of MS significantly increased the outcomes of ACS in the form of MI and death during hospitalization.

Our study showed that the most significant contributors to the structure of MS in women are arterial hypertension, type 2 diabetes mellitus, and excess weight, while in men, AH, hypertriglyceridemia, and reduced HDL levels are more prominent. This difference in MS structure in men may be related to the higher frequency of abdominal obesity, which in turn leads to the development of insulin resistance. Lipolysis in visceral adipocytes results in the release of large amounts of free fatty acids (FFA), primarily into the portal circulation and liver.

Our study showed that women with metabolic syndrome more frequently had painless forms of acute coronary syndrome compared to women without MS and men. This is likely due to the presence of type 2 diabetes as a component of MS and the development of diabetic neuropathy.

Patients with metabolic syndrome more frequently had multiple coronary artery lesions, with significantly more hemodynamically significant stenoses compared to patients without metabolic disorders, which corresponds with literature data. In women with metabolic syndrome, coronary artery lesions were significantly more often polysegmental, affecting both major arteries and second-order vessels. In men, polysegmental lesions were found only in the left anterior descending artery (LAD) and the right coronary artery (RCA). Despite women having both large coronary arteries and second-order vessels affected, the frequency of ACS outcomes in the form of MI was the same in the group with and without MS. This could be explained by the revealed characteristics of the MS structure in women: diabetes mellitus and obesity were more common, and the gradual development of atherosclerosis led to a myocardium more trained for ischemia. Unlike women, men had a significantly higher frequency of MI as an outcome of ACS.

Correlation analysis showed that the presence of obesity and DM (more characteristic of women) did not influence the outcome of ACS, while hypertriglyceridemia and reduced HDL levels (leading components in the structure of MS in men) significantly increased the risk of MI. Besides the more frequent outcome of ACS in the form of MI, men more frequently developed ventricular arrhythmias compared to women. This can likely be explained by the revealed characteristics in MI localization. In men, MI more often developed in the inferior and posterior walls, which are supplied by the RCA. The atrioventricular node is supplied by the atrioventricular artery, which in 80-90% of cases branches off from the RCA (Lukyanova I.Yu., Shishkin A.N., 2009). Due to impaired blood supply in the node, life-threatening arrhythmias developed.

**Conclusions:** Men with metabolic syndrome, hospitalized with ACS, were significantly younger than women. The age of women with metabolic syndrome was over 50 years. Diabetes mellitus and obesity, as components of MS, were more common among women, while men showed a tendency towards higher triglyceride levels and lower HDL levels. Decompensated forms of diabetes mellitus were significantly more frequent in men with MS. Women with metabolic syndrome significantly more often had painless forms of ACS. For women in the postmenopausal period, active screening for components of metabolic syndrome and silent myocardial ischemia is necessary.

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