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Features of the hospital course of myocardial infarction in patients with impaired carbohydrate metabolism

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Resume

Objective

To study the influence of concomitant diabetes mellitus (DM) on the course of myocardial infarction with the ST segment elevation (STEMI) and hospital prognosis for patients.

Material and methods

The study included 83 patients with STEMI, admitted in 2014. Patients were analyzed in 2 groups: group I — patients with type 2 diabetes (n = 38; average age 58,4 ± 8,1 years; male / female — 28/10); and group II — patients with normal carbohydrate metabolism (n = 45; average age 59,9 ± 7,2 years; male / female — 32/13). We studied the baseline clinical and hemodynamic laboratory parameters of patients, as well as hospital prognosis of MI.

Results

Comparative analysis showed that among patients with diabetes, hypertension occurred significantly more often as the background of the disease, and the middle class of acute heart failure according to the Killip classification was significantly higher at the admission time in patients of the first group. Ventricular arrhythmias of the heart: couplets, group PVCs, unstable paroxysms of ventricular tachycardia were detected in 2.5 times more frequently in patients with STEMI and DM. In addition, patients with diabetes were characterized by relatively severe dilation of the cavity of the left ventricle (LV) and the left atrium, at relatively low values of LV ejection fraction. During the period of hospital treatment in patients with STEMI and the type 2 diabetes, more cases of early post-infarction stenocardia (11 %) and of acute left ventricular aneurysm were recorded (9 %), (both p> 0.05), while the prevalence of the hospital mortality cases.

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Conclusion

The presence of concomitant diabetes burdens the course of STEMI, manifesting by a pronounced left ventricular dysfunction, a high risk of ventricular arrhythmias and cardiac complications of acute myocardial, associated with a trend to an increase in index of hospital mortality.

Key words

Myocardial infarction, diabetes mellitus, hospital prognosis.

Diabetes mellitus (DM), being common «social» disease, is simultaneously a risk factor for cardiovascular diseases; at the same time, it is a factor burdening their course [1, 2]. Numerous studies prove the effect of diabetes on the prognosis of chronic heart failure, arterial hypertension (AH) and various forms of coronary heart disease (CHD) [3–5]. Thus, according to the assertions of the American Heart Association, patients with diabetes had the risk of myocardial infarction (MI) 2 times higher than patients with normal glycemic status; at the same time, the first group characterized as a lower survival [6]. Sub analysis of the study VALIANT (Valsartan in Acute Myocardial Infarction Trial) showed that in patients with MI and newly diagnosed diabetes, the disease outcomes were significantly worse than in patients without diabetes [7]. By analyzing the results of a retrospective cohort study (n> 118 thousand), a 30-day and 1-year mortality in patients with acute MI on a background of diabetes was studied. It shows a significant predominance of incidence of both endpoints in patients, suffering from diabetes, compared to patients without diabetes [8].

However, a number of studies emphasizes the clinical and prognostic significance of the reverse state — namely a hypoglycemia in patients with diabetes and acute myocardial damage. The results of other studies also show the negative impact of severe hypoglycemia on a MI course in patients with diabetes, according to which fatal arrhythmic complications can develop in such patients [9]. Ambiguity in the question of the possible mechanisms of the effect of hyper and hypoglycemia on the course, prognosis of MI, including a short-term one, in diabetic patients supports the interest of researchers to further study this issue.

The purpose of research is to study the influence of concomitant diabetes mellitus (DM) on the course of myocardial infarction with the ST segment elevation (STEMI) and hospital prognosis for patients.

Material and Methods

In the register study, 83 patients with STEMI were included, hospitalized in 2014 to the intensive care and the cardiology departments of Domodedovo central hospital. Inclusion criteria were a presence of STEMI within a period of 48 hours in patients with diabetes and without it. Exclusion criteria were the duration of STEMI > 48 hours, patients > 75 years old, known cancer pathology.

In addition to the evaluation of clinical status, registration 12-lead ECG, all patients were underwent a transthoracic echocardiography using ultrasonic apparatus IE-33 («Phillips», The Netherlands). On admission to the hospital, blood sampling was carried out for general clinical and biochemical blood tests. Levels of glycated hemoglobin (HbA1c) were measured, using the method of immunoturbidimetric endpoint test with a help of analyzer «Sapfire 400» (Japan). In addition, the concentration of cardio-specific enzymes were determined: Troponin I, MB fraction of creatine phosphokinase (CP-MB).

Patients were analyzed in 2 groups: group I — patients with type 2 diabetes (n = 38; average age 58,4 ± 8,1 years; male / female — 28/10); and group II — patients with normal carbohydrate metabolism (n = 45; average age 59,9 ± 7,2 years; male / female — 32/13). Age-gender and clinical-anamnestic characteristics of patients are shown in Table 1.

The diagnosis of type 2 diabetes was established by medical history, as well as on the basis of medical documentation. Newly diagnosed diabetes were diagnosed during the hospital period, based on the repeated determinations of glucose on an empty stomach, HbA1c, as well as the test results on glucose tolerance. Treatment of patients in the hospital was carried out according to the recommendations of the Russian Society of Cardiology (2014).

Statistical processing of data was performed by the application package Statistica, designed for Microsoft Windows. Data are presented as arithmetic means (M) and standard deviation (SD). The significance of differences was determined in accordance with the use of non-parametric Student's *t* test for normal distribution of feature, non-compliance with the last — the Mann-Whitney. Differences are considered

Table 1. **Clinical-anamnestic characteristics of patients with STEMI, included in the study**

Sign	I group (with DM, n=38)	II group (without DM, n=45)	*p*; χ^2
Average age, years	58.4±8.1	59.9±7.2	0.37
Gender Female, n (%)	10 (26.3)	13 (28.8)	0.9
ИМТ>30, n (%)	14 (36.8)	13 (28.8)	0.59
Burdened by MI heredity, n (%)	8 (21)	6 (13.3)	0.47
AH, n (%)	28 (73.7)	22 (49)	0.03; 4.3
Smoking, n (%)	24 (63.1)	28 (62.2)	0.8
PICS, n (%)	8 (21)	8 (17.8)	0.9
Prior therapy of CHD, n (%)	8 (21)	9 (20)	0.87
Localization of MI: — front, n (%) — back, n (%) — other localizations, n (%)	 17 (45) 12 (31) 9 (24)	 21 (47) 16 (35) 8 (18)	 0.96 0.88 0.17
Class of AHF according to Killip, average.	1.46±0.6	1.23±0.57	0.047; 3.94
Terms of admission / appeal since the development of the first symptoms, hours	24.4±38.4	21.2±34.5	0.69

Note: p — accuracy of intergroup differences; BMI — body mass index, PICS — post-infarction cardio-sclerosis.

reliable at values of $p < 0.05$. The accuracy of differences of quality indicators was determined using the criterion χ^2.

Results of the study

Analysis of initial clinical-anamnestic parameters of patients, admitted to hospital, showed that groups, compared by middle age and gender distribution, were similar (Table 1). In addition, female patients were 26.3 % and 28.8 % respectively. It was noted that the number of patients with obesity (body mass index — BMI ⩾ 30) was 36.8 % in I group vs 28.8 % in II group; although the differences did not reach statistical significance. Comparative analysis showed, that AH was recorded significantly more often as the background of the disease among patients with diabetes — 74 % and 49 % respectively; and at the moment of admission, the middle class of acute heart failure (AHF) according to the Killip classification was significantly higher in patients of I group. Hereditary factor traced in medical history a bit more often in patients with type 2 diabetes: 21 % of them said that there were cases of MI among the relatives of the first line.

Approximately 1/5 of the patients in each group followed an adequate ambulatory therapy of coronary heart disease (CHD), but among patients with known medical history of CHD, this index did not reach 40 %. There is the noteworthy rate of hospitalization and / or treatment of patients since the development of the first symptoms, which was average almost one day — 24.4 ± 38.4 21.2 ± hours and 34.5 hours respectively ($p > 0.05$), in patients of both groups. However, it is need to be noted, that these averages are caused due to individual cases, when patients consulted a doctor on 2nd-7th day after development of a long intensive anginal attack; while the time of the ambulance call and hospitalization held < 60 minutes. Distribution of patients according to localization of myocardial injury has shown, that in most cases front and front-spread MI was recorded, and in approximately 1/3 of the cases — the bottom / back localization.

When analyzing the clinical and hemodynamic parameters according to their glycemic status, the following results were revealed. Baseline systolic blood pressure (SBP), as an indicator of central hemodynamics in patients with diabetes, were higher by 4.5 % than in the comparison group of patients (Table 2). In patients of groups I and II, a permanent form of atrial fibrillation was recorded. At the same time in group II in 2 (4.5 %) patients, the STEMI was complicated by the development of paroxysmal tachycardia with narrow QRS complexes. However, ventricular cardiac arrhythmias: couplets, group ventricular premature beats (PVCs), unstable paroxysms of ventricular tachycardia were detected 2.5 times more frequently in patients with STEMI and DM.

Echocardiography was performed by a transthoracic access on 2nd-5th day of hospital treatment. At comparison of terms and localization of MI, the number of patients with post-infarction cardio-sclerosis, diabetic patients were characterized by relatively severe dilation of the cavity both in the left ventricle (LV) and the left atrium (LA), at relatively low values of the ejection fraction (EF) of the LV.

Comparative analysis of laboratory parameters revealed the expected hyperglycemia in patients of group I. In addition, the maximum values of fasting glucose were > 20 mmol / l in some patients. Nevertheless, only 20 (52.6 %) patients with type 2 diabetes followed

Table 2. **Clinical-hemodynamic and laboratory parameters in patients with MI, depending on the impaired carbohydrate metabolism**

Sign	I group (with type 2 DM, n=38)	II group (without DM, n=45)	p
SBP, mmHg	138±30.6	132±32.7	0.39
DBP, mmHg	78.8±12.8	80.7±13.2	0.51
HR, beats / min	80.7±14.6	78.9±16.3	0.60
Basic rate — AF, n (%)	1 (2.6%)	2 (4.5%)	0.88
Ventricular arrhythmias of the heart, n (%)	8 (21)	3 (6.7)	0.1
EDS LV, mm	58.6±15.4	55.4±14.3	0.3
EF LV, %	49.6±9.1	52±8.6	0.2
LA, mm	41.2±7.8	40.8±6.3	0.83
Thickness of IVS, mm	11.8±3.2	11±2.4	0.19
Thickness of RWLV, mm	10.1±2.8	10.4±2.4	0.89
Glucose fasting, mmol / l	11.7±3.1	5.6±0.87	0.000
HbA1c, %	8.1±1.23	—	
Urea, mmol / l	8.87±2.5	7.01±2.6	0.03
Creatinine, micmol / l	106.3±23.9	92.6±29.4	0.07
Total cholesterol, mmol / l	6.4±1.3	6.2±1.42	0.94
LDL, mmol / l	3.7±0.91	3.47±1.03	0.98
Triglycerides, mmol / l	2.34±1.29	1.96±1.04	0.14
Troponin I, ng / ml	8.4±10.9	11.7±20.1	0.36
CP-MB, u / l	40.3±42.8	38.8±50.2	0.88

Note: p — the accuracy of intergroup differences; SBP — systolic blood pressure, DBP — diastolic blood pressure, HR — heart rate, EDS LV — end-diastolic size of left ventricular, IVS — interventricular septum, RWLV — the rear wall of the left ventricle, LDL — low-density lipoprotein.

an adequate and regular hypoglycemic therapy before MI. The mean values of HbA1c were higher than the norm by 24.6% in patients of group I. At comparable mean values of total cholesterol in patients with MI, a significant prevalence of cholesterol low-density lipoprotein and triglycerides was revealed in patients with diabetes. Also in patients with type 2 diabetes, plasma concentrations of urea and plasma creatinine are significantly higher than in the comparison group by 25.7% and 11.2% respectively (both $p < 0.05$). In the comparative aspect, levels of cardiac enzymes did not reveal any significant differences.

The next stage of the study was the studying of hospital prognosis of patients with STEMI in connection with the state of carbohydrate metabolism. During the period of hospital treatment, patients with STEMI and type 2 diabetes had an increased incidence of early post-infarction stenocardia (EPS) by 11% ($p > 0.05$) and acute aneurysm of LV by 12% ($p < 0.05$) (Table 3). Moreover, among patients in both groups, by one case of acute cerebrovascular accident was detected in the hospital. In addition, the prevalence of the hospital mortality cases was noted in patients with STEMI and DM, which was almost 2 times higher than in group II. To stabilize the condition and following the next stages of rehabilitation, patients in group I needed 11% more hospital days ($p < 0.05$).

Table 3. **The study of hospital prognosis for patients with STEMI depending on the impaired carbohydrate metabolism**

Sign	I group (with DM, n=38)	II group (without DM, n=45)
Cardiogenic shock, n (%)	3 (7.9)	2 (4.4)
Acute aneurysm LV, n (%)	6 (16)	2 (4.4)*
Early post-infarction stenocardia, n (%)	5 (13.1)	1 (2.2)
Relapse of MI in hospital, n (%)	2 (5.2)	3 (6.6)
AIS, n (%)	1 (2.6)	1 (2.2)
Hospital death, n (%)	6 (16)	4 (8.9)
Gap of LV (anatomic-pathological), n (%)	1 (2.6)	1 (2.2)
The duration of hospitalization, days	18.1±4.1	16.3±3.6*

Note: * — $p < 0.05$, AIS — acute ischemic stroke.

Discussion

The results of studies, on the problem of studying the clinical features of acute coronary conditions when combined with diabetes, show existence of a sufficiently close relationship between the course and the outcome in particular of MI and the level of hyperglycemia, both at the stationary phase and during long-term hospital period [10].

In this study, the initial clinical-anamnestic parameters in patients with and without diabetes did not show significant intergroup differences. However, among patients in group I, concomitant AH prevailed, as well as at the time of admission, they were characterized

by a higher class of AHF according to Killip. According to a meta-analysis of the well-known British 30-year study UKPDS (UK Prospective Diabetes Study), patients with diabetes and asymptomatic MI were characterized by older age and the prevalence of the female gender. It was also specific, that the average BP in a group of patients with MI and diabetes were higher despite the more aggressive antihypertensive therapy, with the prevalence of microvascular complications [11].

In the analysis of the electrocardiogram (ECG) in the vast majority of patients in both groups, a sinus rhythm was recorded as a base. But attention is drawn to the fact that in patients with STEMI and diabetes, episodes of ventricular cardiac arrhythmias of high grade were more common, the frequency of which was > 2.5 times higher than in the comparison group. In previous studies, the effect of hyperglycemia on the electrophysiological processes was proven in patients with heart diseases.

The study [12] showed that increased levels of HbA1c > 8.5% in patients with CHD and type 2 diabetes was accompanied by an increased ventricular arrhythmias, which was reflected in statistically significant differences, in relative indexes and a positive correlation of HbA1c level with the amount of PVCs. The research results of other Russian authors also show, that prolonged hyperglycemia is capable of causing cardiac arrhythmia, particularly recurrent tachyarrhythmia, the development of which is caused by abnormal automaticity [13]. Finnish researchers studied the particular parameters of Holter monitoring in patients with diabetes. Within 3–12 months after the coronary angiography, 1001 patients were examined, of whom 526 patients had diabetes. The heart rate turbulence and the T wave alternation were analyzed as powerful predictors, including fatal arrhythmias in patients with CHD. Significant prevalence of interruptions of these parameters was noted in the group of patients with CHD and diabetes — 58% vs 24% ($p < 0.001$) and LV EF < 50% [14]. On models of transgenic mice using an implantable ECG telemetry, we tried to explain the cause of arrhythmias in the presence of hyperglycemia. The authors argue that the increase in the intracellular concentration of lipids in cardiomyocytes and the overexpression of receptors-activators of the peroxisome proliferation, observed in patients with diabetes and obesity, lead to QT prolongation and associated with it spontaneous ventricular arrhythmias, including a polymorphic ventricular tachycardia and ventricular fibrillation [15].

The parameters analysis of intracardiac hemodynamics in patients with STEMI showed that in the case of type 2 diabetes, the concomitant LV dysfunction was more pronounced. End-diastolic size of LV in patients of group I, exceeding the analogous index by 5.7%, was accompanied by a corresponding decrease in LV EF by 4.6% relatively to the comparison group.

The results of the published study, which included 210 patients with MI, showed that hyperglycemia, occurs in the first 24 hours of the disease, is associated with the development of the LV dysfunction; which is a powerful predictor of the worst long-term prognosis due to the development of AHF. Multivariate analysis showed, that hyperglycemia in the first 24 hours of the disease is an independent risk factor for the LV dysfunction and consequently the development of heart failure and adverse outcome in patients with MI [14]. Global contractility of LV was assessed using magnetic resonance tomography in 4998 patients of 45–84 years old, including those without clinical signs of CHD. 13% of patients had impaired glucose tolerance, 12% had diabetes. A significant correlation between the presence of diabetes and a decreased shortening fraction of LV, subsequently a chronic heart failure developed in 96 cases [16].

Finally, certain differences are revealed in the study of the short-term prognosis of patients with STEMI with and without diabetes. According to the observations, diabetic patients were received with a higher class of AHF. In addition, an acute phase of MI in these patients was often complicated by the development of an acute LV aneurysm, including established post-mortem and the EPIS. Kemerovo researchers describe features of hospital prognosis of patients with MI and carbohydrate metabolism disorders. By the study results with a number of observations > 600, the authors showed the presence of significant differences in the prognosis already at a stationary stage. In patients with diabetes, having STEMI, more cases of EPIS, a stent retrombosis and recurrence of MI were recorded. In addition, negative effect of hyperglycemia on the prognosis of patients was also evident in individuals with impaired glucose tolerance [17]. The study Cooperative Cardiovascular Project (USA) analyzed the prognosis of MI patients with diabetes and without it, depending on the level of blood glucose on admission. In the analysis involving 141 680 patients in the period 1994–1996, the proportion of patients with severe hyperglycemia > 240 mg / dl was 26%.

It was revealed that the mortality rate within 30 days among patients with diabetes and blood glucose

> 240 mg / dl was 24 %, while patients with severe hyperglycemia on admission but without the previously diagnosed diabetes, this index was 39 % ($p < 0.001$) [8]. The relationship between impaired glucose tolerance, diabetes and the development of sudden cardiac death was studied in the study Honolulu Heart Program. They studied the sudden death within 1–24 hours after the onset of acute symptoms. The hazard ratio of death within 24 hours in patients with high normal blood glucose values (151–224 mg / dl) and diabetes, compared with persons without diabetes, was 1.59 and 2.76 respectively ($p < 0.05$). A similar association was revealed in the analysis of sudden death within 1 hour, which the authors associated with a high risk of life-threatening ventricular arrhythmias in these patients, rather than coronary [18]. The values of glycemia at admission was identified as an independent predictor of death in patients with acute coronary syndrome according to the results of the Dutch scientists study. It has been shown that increasing the concentration of blood glucose at 1 mmol / l (with initial values > 9 mmol / l) increases the risk of death by 10 %. At the same time, indicators of 30-days mortality among patients with diabetes and without it amounted 16.8 % and 5.2 % respectively [19].

Regarding the mechanisms of negative influence of diabetes on the MI course, we can state the following. The experimental studies have shown the damaging effect of hyperglycemia on endothelial function, the development of collateral circulation and increasing microvascular dysfunction [20]. Acute hyperglycemia can also degrade the coagulation properties of the blood, increasing the tendency to thrombosis [21]. Researchers at the Health Science Center (Oklahoma, USA) showed in a cell culture of umbilical vein, that high concentrations of glucose may be a trigger of apoptosis. Subsequently, they proved their hypothesis at the models of mice with streptozotocinum-induced diabetes [22].

Conclusion

Thus, the presence of concomitant diabetes burden the course of STEMI, manifesting as a pronounced LV dysfunction, as a high risk of ventricular arrhythmias and complications of an acute MI period. Also negative effect of hyperglycemia associated with a trend to an increased index of hospital mortality in patients with STEMI.

Conflict of interest: None declared.

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