https://doi.org/10.23934/2223-9022-2020-9-4-511-520

Predictive Value of N-Terminal Prohormone of Brain Natriuretic Peptide in Long-Term Remodeling of the Left Ventricle in Diabetic Patients of Young and Middle Age With Acute Coronary Syndrome After Percutaneous Coronary Intervention

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ABSTRACT Recently, quantitative analysis of the level of the N-terminal prohormone of the brain natriuretic peptide (NT-proBNP) has been widely used to diagnose heart failure (HF). A statistically significant correlation was found between the serum NT-proBNP concentration and HF stage. It was found that in patients with high cardiovascular risk, NT-proBNP has the highest predictive value in relation to mortality. In young and middle-aged patients with diabetes mellitus (DM) with myocardial infarction (MI) and stents of an infarct-associated artery, the frequency of unfavorable remodeling (UR) of the left ventricle (LV) in the long-term prognosis was studied. The frequency of atherosclerotic lesions of the coronary arteries (CA) in patients with diabetes in acute coronary syndrome (ACS) was determined, the results of echocardiographic parameters were presented in the follow-up dynamics, the value of serum NT-proBNP in predicting LV UR 12 months after myocardial infarction (MI) was determined.

AIM OF STUDY To assess the diagnostic capabilities of NT-proBNP in the long-term prediction of the development of LV infarction in patients with MI with diabetes in young and middle age after percutaneous coronary intervention (PCI).

DESIGN Prospective controlled non-randomized trial. The patients were examined twice: on the first day of ACS after PCI with stenting of infarct-associated coronary artery and 12 months after AMI. The study included 191 patients with ACS with/without ST-segment elevation, who were divided into two groups. The main group included 76 patients with ACS with diabetes mellitus, the comparison group included 115 patients with ACS without diabetes mellitus. Patients in both groups were comparable in age, gender, comorbidity, and complications of AMI. The duration of diabetes was, on average, 6 years (from one to 12 years).

MATERIAL AND METHODS All patients underwent electrocardiography, echocardiography, tests for the content of troponin I, NT-proBNP, glycosylated hemoglobin, lipids, determined the level of creatinine in the blood and the glomerular filtration rate according to the Modification of diet in renal disease (MDRD). All patients were examined twice: on the first day of ACS after PCI with stenting of infarct-associated coronary artery and 12 months later.

RESULTS In 69% of diabetic patients with anterior myocardial infarction and in 63% of patients with posterolateral MI 12 months after PCI, signs of LV inferiority were revealed in the form of an increase in the indices of end-diastolic and systolic volumes of the LV and low ejection fraction (≤45%). In patients without diabetes, these figures were 18% and 31%, respectively. High concentrations of NT-proBNP on the first day of myocardial infarction after PCI were of the greatest value in the diagnosis and prognosis of LV UR after 12 months.

CONCLUSION The NT-proBNP level of more than 776 pg/ml on the first day after PCI is an indicator of an unfavorable long-term prognosis in patients with young and middle-aged diabetes in terms of the development of LV systolic dysfunction.

Keywords: acute coronary syndrome, myocardial infarction, diabetes mellitus, coronary angiography, N-terminal prohormone of brain natriuretic peptide, index local motion, adverse remodeling

For citation Wang Z, Asafieva EA, Makeyeva TI. Predictive Value of N-Terminal Prohormone of Brain Natriuretic Peptide in Long-Term Remodeling of the Left Ventricle in Diabetic Patients of Young and Middle Age With Acute Coronary Syndrome After Percutaneous Coronary Intervention. *Russian Sklifosovsky Journal of Emergency Medical Care.* 2020;9(4):511–520. https://doi.org/10.23934/2223-9022-2020-9-4-511-520 (in Russ.)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments, sponsorship The study had no sponsorship

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ACS - acute coronary syndrome
AHF - acute heart failure
BMI - body mass index
CA - coronary artery

CI - confidence interval
DM - diabetes mellitus
EchoCG - echocardiography
EDVI - end-diastolic volume index
EF - ejection fraction
ESVI - end-systolic volume index
GFR - glomerular filtration rate
HF - heart failure
IQR - interquartile range
LV - left ventricle
MDRD - modification of diet in renal diseases
MI - myocardial infarction
NT-proBNP - N-terminal prohormone of brain natriuretic peptide
PCI - percutaneous coronary intervention
UR - unfavorable remodeling
VLCI - violation of local contractility index

INTRODUCTION

According to numerous studies, in patients with diabetes mellitus (DM) mortality from myocardial infarction (MI) reaches 39%, which is significantly higher than in patients without diabetes [1]. This is associated with the high frequency of atherosclerotic lesions of the coronary arteries (CA) on the one hand [2], and with specific changes in the microvasculature of the myocardium due to the accumulation of under-oxidized glucose metabolism products in the blood [3] on the other hand, while the frequency of diabetic microangiopathies is 14– 55% of cases [4, 5]. The development of these changes, according to different authors, is influenced by the duration of diabetes mellitus, the presence of arterial hypertension, the age of the patients, the degree of diabetes compensation and the tendency to accumulate ketone bodies [6–9]. In general, all this leads to a more unfavorable course of myocardial infarction in patients with diabetes [10]. Thus, in DM, the incidence of unfavorable remodeling (UR) of the left ventricle (LV) in the post-infarction period reaches 31% [11], systolic dysfunction with a reduced ejection fraction (EF) is observed in 28% of patients [12, 13] versus 7% in patients with MI without diabetes mellitus [14]. At the same time, the dynamics of echocardiographic (EchoCG) parameters after percutaneous coronary intervention (PCI) in patients with acute coronary syndrome (ACS) with diabetes has been little studied, there is no data on changes in the N-terminal prohormone of brain natriuretic peptide (NT-proBNP) on the first day after PCI and 12 months later, its prognostic value of NT-proBNP for patients with diabetes in the dynamics of myocardial infarction has not been determined.

Aim of study: to determine the prognostic value and diagnostic value of NT-proBNP in relation to the development of LV infarction in MI patients with diabetes of young and middle age after PCI.

MATERIAL AND METHODS

The study is prospective, controlled, non-randomized, and included 191 patients aged 36 to 59 years with ACS, who were divided into two groups. The main group included 76 patients with diabetes, the comparison group - 115 patients without diabetes. Patients in both groups were comparable in age, gender, comorbidity and complications of MI. The duration of diabetes was, 6 years, on average (1-12 years) (Table 1).

Table 1
Characteristics of the examined patients with acute myocardial infarction

Indicators	Median (*IQR*)	
	Patients with diabetes (*n* = 76)	Patients without diabetes (*n* = 115)
Age, years	52 (36-59)	53 (38-59)
Gender m/f, *n*	59/17	101/14
BMI, kg/m ^{2}	29 (23-44)	27 (22-33)
Duration of DM, *n* (%): - up to 12 months - from 1 to 5 years - more than 5 years (maximum 12 years)	 16 (21%) 24 (32%) 36 (47%)	
Arterial hypertension, *n* (%): 1st degree 2nd degree 3rd degree	 32 (42%) 10 (14%) 34 (44%)	 72 (63%) 25 (22%) 18 (15%)
History of myocardial infarction, *n*	24	20

AHF according to *Killip* classification , *n* (%): I degree II degree III degree	 48 (63%) 27 (35%) 12%)	 85 (74%) 28 (23%) 2 (3%)
Anterior myocardial infarction, *n* (%)	35 (46%)	56 (49%)
Posterior-lateral myocardial infarction, *n* (%)	41 (54%)	59 (51%)
Troponin I, pg/ml	11152.8 ± 10099.3 *	9650.6 ± 9181.3
Glycosylated hemoglobin,%	7.12 (6.45-10.21) *	5.31 (5.00-5.49)
GFR according to *MDRD* , ml/min/1.73 m2	67 (55-80) *	76 (67-88)
NT-proBNP, pg/ml	881 (618-1418) *	508 (319-739)

Notes: * - p <0.05; AHF - acute heart failure; BMI - body mass index; DM - diabetes mellitus; GFR - glomerular filtration rate; IQR - interquartile range; MDRD - diet modification in renal disease; NT-proBNP - N-terminal prohormone of brain natriuretic peptide

The first group of examined patients consisted of 76 patients with ACS with diabetes, age from 36 to 59 years, median 52 years. Group 2 included 115 ACS patients without diabetes, age from 38 to 59 years, median 53 years. Body mass index (BMI) in patients with diabetes - from 23 to 44 kg/m2, median BMI - 29 kg/m2 does not have a statistically significant difference compared to patients without diabetes (from 22 to 33 kg/m^2, median 27 kg/m^2). Glomerular filtration rate (GFR) according to MDRD (Modification of Diet in Renal Disease) in patients with diabetes was 55 to 80 ml/min/1.73 m^2, median 67 ml/min/1.73 m^2 statistically significantly lower than in patients without diabetes (from 67 to 88 ml/min/1.73 m^2, median 76 ml/min/1.73 m^2). The history of myocardial infarction was detected in 24 patients with diabetes, and in 20 patients without diabetes. Among 76 patients with diabetes, 35 (46%) had anterior MI and 41 (54%) patients had posterolateral MI. Among 115 patients without diabetes, 56 (49%) had anterior MI and 59 (51%) patients had posterolateral MI. Among patients with diabetes, the following degrees of AHF were observed according to the Killip classification: in 48 patients (63%) - I degree, in 27 patients (35%) - II degree, in 1 patient (2%) - III degree. Among patients without diabetes, the following degrees of AHF were observed according to the Killip classification: in 85 (74%) - I degree, in 28 (23%) - II degree, in 2 (3%) - III degree. Among diabetic patients with arterial hypertension, the following degrees were observed: in 32 people (42%) - I degree, in 10 people (14%) - II degree, in 34 (44%) people - III degree. Among patients without diabetes, the following degrees were observed: in 72 (63%) people - I degree, in 25 (22%) - II degree, in 18 (15%) - III degree. Troponin I in patients with diabetes (11152.8 ± 10099.3 pg/ml) was significantly higher than in patients without diabetes (9650.6 ± 9181.3 pg/ml). Glycosylated hemoglobin was 7.12% (from 6.45% to 10.21%), which is statistically significantly higher than in patients without diabetes (median 5.31% from 5.05 to 5.49%). NT-proBNP on the 1st day after PCI in patients with diabetes (from 618 to 1418 pg/ml, median 881 pg/ml) was statistically significantly higher than in patients without diabetes (from 319 to 739 pg/ml, median 508 pg/ml).

Echocardiography performed in M- and B-modes was used to determine the EF (Simpson), the indices of end-diastolic (EDVI) and end-systolic (ESVI) volumes of the LV, as well as the index of local contractility disorder (VLCI). EF was assessed according to the recommendations of the American Society of Echocardiography (ASE) and the European Association for Cardiovascular Imaging (EACI) (2015) [17]. EF of at least 46% was considered satisfactory; and EF not more than 45% was considered reduced. On repeated examination 12 months later, the criteria for LV UR were considered to be an increase in EDVI by more than 20% and ESVI by more than 15% compared to baseline, while the ESVI value was 35 ml/m^2 or more [18].

The definition of NT-proBNP is considered the gold standard in the diagnosis of heart failure. Serum NT-proBNP levels were measured twice - on day 1 after PCI and 12 months later. The measurements were carried out on a Cobas apparatus using the Elecsys platform (Roche Diagnostics, USA, 2017). The norm is less than 125 pg/ml.

According to coronary angiography, 76% of diabetic patients had two- and three-vessel lesions. Only 24% of patients had lesions of one CA. In patients without diabetes, this ratio was 44% and 56%, respectively (Fig. 1).

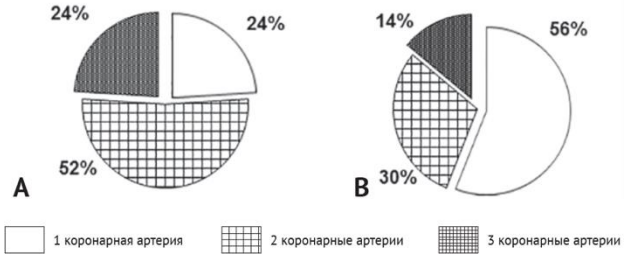

Fig. 1. The incidence of coronary artery disease according to angiography in patients with myocardial infarction of young and middle age with diabetes mellitus (A) and without diabetes mellitus (B)

In diabetic patients with anterior myocardial infarction, the incidence of two-three- and single-vessel lesions was 66% and 34%; while in patients without diabetes - 34% and 66%, respectively. In this regard, in diabetic patients with anterior myocardial infarction more often than in patients without diabetes, myocardial reperfusion was performed by implanting two or even three stents simultaneously or with an interval of several days (Table 2).

Table 2

Coronary artery stenting frequency in patients with myocardial infarction depending on the presence of diabetes mellitus

	Anterior MI		Posterior-lateral MI	
	Patients with diabetes (*n* = 35)	Patients without diabetes (*n* = 56)	Patients with diabetes (*n* = 41)	Patients without diabetes (*n* = 59)
1 stent	21	50	33	48
2 stents	9	4	8	9
3 stents	5	2	0	2

Notes: IM - myocardial infarction; DM - diabetes mellitus

Contrary to the popular belief that posterolateral MI is most often small in area and has a more favorable outcome, it turned out that in these cases, in young and middle-aged diabetic patients, the incidence of two- and three-vessel coronary artery disease was 85%, which was higher than in anterior MI. At the same time, two stents were placed in 8 patients.

In patients without diabetes with posterolateral MI, multivessel coronary artery disease was detected less frequently - in 54% of cases.

Statistical processing of the research results was carried out using the statistics programs Statasoft (2015) and Medcalc (2018) to analyze the operating characteristics of the receiver (ROC analysis). All indicators are presented as median and their interquartile range. The significance of differences in variables between the compared groups of patients was assessed using the Mann – Whitney U-test. Correlation analysis was performed according to Spearman's method; $p < 0.05$ was considered statistically significant.

RESULTS

According to echocardiography, in 11 patients with diabetes (31%) of 35 and in 46 patients (82%) of 56 without diabetes with anterior MI, LVEF was normal, and the data did not differ statistically significantly (Table 3). EDVI was normal in both groups, but in diabetic patients this indicator was statistically significantly higher ($p_1 = 0.0409$). ESVI was moderately statistically significantly increased in diabetes mellitus compared to patients without diabetes ($p_1 < 0.008$). The area of MI in both groups was approximately the same, as evidenced by VLCI ($p_1 = 0.3$).

After 12 months, 15 diabetic patients with anterior MI of 35 left ventricular ejection fraction reached 50–60%, on average 56% ($p_3 = 0.0026$, statistically significant). A similar positive dynamics of EF was also recorded in patients without diabetes ($p_4 = 0.0001$, statistically significant). EDVI in group 1 remained the same ($p_3 = 0.4949$), while its value was statistically significantly higher than in group 2 (63 ml/m^2 and 54 ml/m^2, $p^2 = 0.0059$).

After 12 months in patients without diabetes, ESVI significantly decreased (28 ml/m^2 and 21 ml/m^2, $p_4 = 0.0001$). At the same time, in patients with diabetes, there was only a tendency towards a decrease in this indicator (37 ml/m^2 and 30 ml/m^2, $p_3 = 0.0624$). VLCI significantly decreased in both groups, but in diabetic patients the number of affected LV segments was statistically significantly higher (1.25 and 1.13; $p_2 = 0.0270$).

In 24 patients with diabetes (69%) out of 35 and in 10 patients without diabetes with anterior MI (18%) out of 56, LVEF was significantly reduced (42% and 41%, $p_1 = 0.3107$). At the same time, patients of both groups with decreased LVEF had a larger lesion area than patients with normal EF, as evidenced by VLCI (Tables 3, 4).

Table 3

Dynamics of echocardiography in patients with anterior MI with LVEF ≥46%, depending on the presence of diabetes

	1st day after PCI, median *(IQR)*		*R*	12 months later, median *(IQR)*	
	Patients with diabetes 1st group (*n* = 11)	Patients without diabetes 2nd group (*n* = 46)		Patients with diabetes 1st group (*n* = 15)	Patients without diabetes 2nd group (*n* = 44)
EF,%	51 (49-53)	54 (50-57)	$p_1 = 0.0921$ $p_2 = 0.0001$ $p_3 = 0.0026$ $p_4 = 0.0001$	56 (50-60)	59 (55-65)
EDVI, ml/m ^{2}	69 (56-76)	61 (56-64)	$p_1 = 0.0409$ $p_2 = 0.0059$ $p_3 = 0.4949$ $p_4 = 0.0045$	63 (57-73)	54 (44-62)
ESVI, ml/m ^{2}	37 (28-40)	28 (24-32)	$p_1 = 0.0085$ $p_2 = 0.0001$ $p_3 = 0.0643$ $p_4 = 0.0001$	30 (27–38)	21 (17-26)
VLCI	1.38 (1.25-1.63)	1.31 (1.13-1.56)	$p_1 = 0.3153$ $p_2 = 0.0270$ $p_3 = 0.0380$ $p_4 = 0.0002$	1.25 (1.06-1.44)	1.13 (1.06-1.25)

Notes: p_1 - baseline values between groups with and without diabetes; p_2 - 12 months later between the DM and non-DM groups; p 3 - between the baseline and after 12 months in patients with diabetes; p 4 - between the baseline and after 12 months in patients without diabetes. DM - diabetes mellitus; EDVI - index of end-diastolic volume of the left ventricle; EF - ejection fraction; ESVI - index of end-systolic volume of the left ventricle; IM - myocardial infarction; IQR - interquartile range; LV - left ventricle; PCI - percutaneous coronary intervention; VLCI - index of violation of local contractility

Table 4

Dynamics of echocardiography in patients with anterior MI with LVEF ≤45% depending on the presence of diabetes mellitus

	First day after PCI, median *(IQR)*		*R*	12 months later, median *(IQ R)*	
	Patients with diabetes 1st group (*n* = 24)	Patients without diabetes 2nd group (*n* = 10)		Patients with diabetes 1st group (*n* = 20)	Patients without diabetes 2nd group (*n* = 12)
EF,%	42 (38-44)	41 (37-42)	$p_1 = 0.3107$ $p_2 = 0.0052$ $p_3 = 0.0005$ $p_4 = 0.0295$	35 (30-39)	39 (37–43)
EDVI, ml/m ^{2}	68 (63-72)	69 (65-76)	$p_1 = 0.6091$ $p_2 = 0.4245$ $p_3 = 0.6136$ $p_4 = 0.6374$	70 (65-76)	67 (62-75)
ESVI, ml/m ^{2}	40 (38–45)	43 (39–46)	$p_1 = 0.3235$ $p_2 = 0.0937$ $p_3 = 0.1251$ $p_4 = 0.9061$	47 (42-54)	42 (35-45)
VLCI	1.69 (1.49-2.00)	1.75 (1.63-1.88)	$p_1 = 0.2798$ $p_2 = 0.3178$ $p_3 = 0.7792$ $p_4 = 0.1823$	1.63 (1.47-1.88)	1.56 (1.28-1.81)

Notes: p_1 - baseline values between groups with and without diabetes; p_2 - after 12 months between the DM and non-DM groups; p 3 - between the baseline and after 12 months in patients with diabetes; p 4 - between the baseline and after 12 months in patients without diabetes. DM - diabetes mellitus; EDVI - index of end-diastolic volume of the left ventricle; EF - ejection fraction; ESVI - index of end-systolic volume of the left ventricle; IM - myocardial infarction; IQR - interquartile range; LV - left ventricle; PCI - percutaneous coronary intervention; VLCI - index of violation of local contractility

EDVI in patients with diabetes on the 1st day after PCI was 68 ml/m^2 and did not differ statistically significantly from the same indicator in patients without diabetes (69 ml/m^2, $p_1 = 0.6091$). After 12 months, the number of affected LV segments in all patients with reduced EF remained significantly increased, while there was no statistically significant difference in EDVI values between both groups (70 ml/m^2 and 67 ml/m^2, $p_2 = 0.4254$).

Severe LV systolic dysfunction in diabetic patients was evidenced by high ESVI values on day 1 after PCI and 12 months later (40 ml/m^2 and 47 ml/m^2, respectively) ($p_3 = 0.1251$). It should be noted that in patients with MI without DM, there was a similar trend (43 ml/m^2 and 42 ml/m^2, respectively) ($p_4 = 0.9061$). Comparative analysis of such indicators as age, gender, blood pressure and MI in history showed that the duration of diabetes in patients with low LVEF was statistically significantly greater than in patients with satisfactory LVEF (6 years and 3 years, $p < 0.01$).

In 15 patients with diabetes (37%) out of 41 and in 41 patients without diabetes with posterolateral MI (69%) out of 59, LVEF on day 1 after PCI was normal (51% and 53%, respectively), and the indicators were not statistically significantly different (Table 5). EDVI was normal in both groups. ESVI turned out to be moderately, but statistically significantly increased in patients with diabetes compared to patients without it (32 ml/m^2 and 26 ml/m^2, respectively) (p_1 <0.03). The number of affected LV segments in both groups was approximately the same, as evidenced by VLCI (p_1 = 0.1710).

Table 5

Dynamics of echocardiography in patients with posterolateral MI with LVEF ≥46% depending on the presence of diabetes

	First day after PCI, median (*IQR*)		*R*	12 months later, median (*IQR*)	
	Patients with diabetes 1st group (*n* = 15)	Patients without diabetes 2nd group (*n* = 41)		Patients with diabetes 1st group (*n* = 26)	Patients without diabetes 2nd group (*n* = 48)
EF,%	51 (48-54)	53 (49-56)	p_1 = 0.114 p_2 = 0.0028 p_3 = 0.0001 p_4 = 0.0001	57 (55-59)	61 (56-65)
EDVI, ml/m ^{2}	63 (59-67)	60 (55-63)	p_1 = 0.0849 p_2 = 0.3497 p_3 = 0.2272 p_4 = 0.6890	60 (56–67)	59 (52-68)
ESVI, ml/m ^{2}	32 (27-34)	26 (24-31)	p_1 = 0.0279 p_2 = 0.0087 p_3 = 0.0002 p_4 = 0.0001	26 (24-29)	23 (19-26)
VLCI	1.31 (1.19-1.50)	1.25 (1.13-1.31)	p_1 = 0.1710 p_2 = 0.0370 p_3 = 0.0686 p_4 = 0.0001	1.21 (1.12-1.31)	1.13 (1.06-1.25)

Notes: p_1 - baseline values between groups with and without diabetes; p_2 - after 12 months between the DM and non-DM groups; p_3 - between the baseline and after 12 months in patients with diabetes; p_4 - between the baseline and after 12 months in patients without diabetes. . DM - diabetes mellitus; EDVI - index of end-diastolic volume of the left ventricle; EF - ejection fraction; ESVI - index of end-systolic volume of the left ventricle; IM - myocardial infarction; IQR - interquartile range; LV - left ventricle; PCI - percutaneous coronary intervention; VLCI - index of violation of local contractility

After 12 months, in 26 diabetic patients with preserved EF out of 41, this indicator increased from 51 to 57% (p_3 = 0.0001, statistically significant). The similar positive dynamics of EF was observed in patients without diabetes (53% and 61%, respectively) (p_4 = 0.0001, statistically significant). EDVI indices in both groups remained normal and practically did not differ from each other (60 ml/m^2 and 59 ml/m^2, respectively) (p_2 = 0.3497).

After 12 months, in both groups of patients, there was a positive dynamics of ESVI in the form of a statistically significant decrease in this indicator (p_3 <0.001; p_4 <0.001). Nevertheless, in patients with diabetes, ESVI was statistically significantly higher than in patients without diabetes (26 ml/m^2 and 23 ml/m^2, respectively) (p_2 = 0.0087).

VLCI in both groups of patients remained low, but in patients with diabetes this indicator was statistically significantly higher (1.21 and 1.13, respectively) (p_2 = 0.0370).

In 26 patients with diabetes (63%) of 41 and in 18 patients without diabetes with posterolateral MI (31%) of 59 LV EF on day 1 after PCI, was significantly reduced (43% and 41%, respectively). VLCI in the 1st group was 1.63 (1.25–1.75), and in the 2nd group - 1.56 (1.38–1.75), which indicated a greater EF, the area of myocardial damage (Table 6). After 12 months, the number of affected LV segments with signs of hypo-, a- and dyskinesia in patients with diabetes was greater than in the group without diabetes (1.63 and 1.25, respectively) (p_2 = 0.1035)

Table 6

Dynamics of echocardiography in patients with posterolateral MI with LVEF ≤45% depending on the presence of diabetes

	First day after PCI, median *(IQR)*		*R*	12 months later, median *(IQR)*	
	Patients with diabetes 1st group (*n* = 26)	Patients without diabetes 2nd group (*n* = 18)		Patients with diabetes 1st group (*n* = 15)	Patients without diabetes 2nd group (*n* = 11)
EF,%	43 (39-44)	41 (38-44)	$p_1 = 0.9230$ $p_2 = 0.0346$ $p_3 = 0.0081$ $p_4 = 0.1170$	34 (28-40)	40 (35-42)
EDVI ml/m ^{2}	67 (64-70)	66 (63-72)	$p_1 = 0.8107$ $p_2 = 0.1067$ $p_3 = 0.0156$ $p_4 = 0.0452$	75 (73-83)	71 (70-76)
ESVI, ml/m ^{2}	38 (37–41)	40 (38–43)	$p_1 = 0.4430$ $p_2 = 0.0254$ $p_3 = 0.0105$ $p_4 = 0.0259$	52 (48-59)	48 (44-50)
VLCI	1.63 (1.25-1.75)	1.56 (1.38-1.75)	$p_1 = 0.9808$ $p_2 = 0.1035$ $p_3 = 0.0656$ $p_4 = 0.0098$	1.63 (1.25-1.63)	1.25 (1.25-1.50)

Notes: p_1 - baseline values between groups with and without diabetes; p_2 - after 12 months between the DM and non-DM groups; p_3 - between the baseline and after 12 months in patients with diabetes; p_4 - between the baseline and after 12 months in patients without diabetes. DM - diabetes mellitus; EDVI - index of end-diastolic volume of the left ventricle; EF - ejection fraction; ESVI - index of end-systolic volume of the left ventricle; IM - myocardial infarction; IQR - interquartile range; LV - left ventricle; PCI - percutaneous coronary intervention; VLCI - index of violation of local contractility

EDVI in the group of diabetic patients was 67 ml/m^2, statistically significantly different from the same indicator in patients with normal EF (63 ml/m^2, p = 0.0311). With regard to ICDI values 12 months after PCI, both in diabetic patients (67 ml/m^2 and 75 ml/m^2) ($p_3 = 0.0156$) and without it (66 ml/m^2 and 71 ml/m^2) ($p_4 = 0.0452$), there was a negative trend represented by statistically significant increase, thus indicating dilation of the LV cavity. The decrease in LV contractility in diabetic patients with posterolateral MI on the 1st day after PCI was evidenced by a high ESVI - 38 ml/m^2, in the group without diabetes - 40 ml/m^2. After 12 months, there was a clear negative statistically significant dynamics in the 1st group (52 ml/m^2, $p_3 = 0.0105$) and in the 2nd group of patients (48 ml/m^2, $p_4 = 0.0259$). It should be noted that at the same time, in patients with diabetes, the ESVI value was higher than in patients without diabetes ($p_2 = 0.0254$).

As in diabetic patients with anterior MI and EF no more than 45%, in patients with posterolateral MI with low EF, the duration of DM was longer than in normal EF (7 years and 4 years, p <0.04, statistically significant). This suggests that under such equal conditions, such as the age of patients, gender, the presence of hypertension and MI in anamnesis, the experience of diabetes for more than three years has an adverse effect on the development of LV systolic dysfunction and prognosis in MI.

Determination of NT-proBNP in patients with anterior myocardial infarction and satisfactory EF (at least 46%) showed that on the 1st day after PCI in patients with diabetes, the level of this indicator in blood serum exceeded the norm 4.5-fold and amounted to 564 pg/ml, which was statistically significantly higher than in patients without diabetes (389 pg/ml, $p_1 = 0.0180$) (Table 7). After 12 months, all patients with anterior MI and EF of at least 46% had a statistically significant decrease in NT-proBNP levels. So, in patients with diabetes, it was 243 pg/ml ($p_3 = 0.0007$); in patients without diabetes - 141 pg/ml ($p_4 = 0.0001$), which was close to normal. At the same time, in patients with diabetes, the serum NT-proBNP content remained higher than in patients without diabetes ($p_2 = 0.0359$, statistically significant).

Table 7

Dynamics of NT-proBNP in patients with anterior MI, depending on the value of LVEF

	Patients with anterior MI with LVEF no more than 45%			Patients with anterior myocardial infarction with LVEF of at least 46%		
	NT-proBNP, pg/ml median *(IQR)*		*R*	NT-proBNP, pg/ml median *(IQR)*		*R*
	Patients with diabetes 1st group (*n* = 24)	Patients without diabetes 2nd group (*n* = 10)		Patients with diabetes 1st group (*n* = 11)	Patients without diabetes 2nd group (*n* = 46)	
PCI 1st day	1592 (815-2474)	1234 (861-1576)	$p_1 = 0.3643$ $p_2 = 0.2758$ $p_3 = 0.0002$ $p_4 = 0.0037$	564 (416-724)	389 (272-619)	$p_1 = 0.0180$ $p_2 = 0.0359$ $p_3 = 0.0007$ $p_4 = 0.0001$
After 12 months	796 (619-970)	692 (444-851)		243 (122-288)	141 (103-238)	

Notes: p_1 - baseline values between groups with and without diabetes; p_2 - after 12 months between the DM and non-DM groups; p 3 - between the baseline and after 12 months in patients with diabetes; p 4 - between the baseline and after 12 months in patients without diabetes. DM - diabetes mellitus; EF - ejection fraction; IQR - interquartile range; LV - left ventricle; MI - myocardial infarction; PCI - percutaneous coronary intervention

In diabetic patients with anterior MI and EF of no more than 45% on the 1st day after PCI, the serum NT-proBNP level was increased 6.5–20-fold and reached 2474 pg/ml (on average, 1592 pg/ml). In patients without diabetes and low EF, the NT-proBNP concentration was increased 6.9–12.6-fold and averaged 1234 (861–1576) pg/ml.

After 12 months, the NT-proBNP level in patients of both groups decreased, but at the same time it was significantly higher than normal values. So, in the 1st group of patients, it was increased 5–7.8-fold (796 pg/ml); and in group 2 - 3.6–6.8-fold (692 pg/ml). There was no statistically significant difference between the values of these indicators.

In diabetic patients with anterior MI (r = -0.89; p = 0.0001; 95% CI - confidence interval) and in patients without diabetes (r = -0.73; p = 0.0001; 95% CI) a negative correlation was obtained between the NT-proBNP level taken on the 1st day after myocardial reperfusion and LVEF 12 months later (Table 8). The direct correlation was found with ESVI (r = 0.54; p = 0.0008; 95% CI) and VLCI (r = 0.63; p = 0.0001; 95% CI).

Table 8

Correlation of serum levels NT-proBNP on the 1st day after PCI with echocardiography after 12 months in patients with MI, depending on the presence of diabetes

Indicators	Patients with anterior MI				Patients with posterolateral MI			
	Patients with diabetes (*n* = 35)		Patients without diabetes (*n* = 56)		Patients with diabetes (*n* = 41)		Patients without diabetes (*n* = 59)	
	r	*R*	r	*R*	r	*R*	r	*R*
EF,%	-0.89	0.0001	-0.73	0.0001	-0.57	0.0001	-0.36	0.0058
ESVI, ml/m ^{2}	0.54	0.0008	0.79	0.0001	0.85	0.0001	0.86	0.0001
EDVI, ml/m ^{2}	0.23	0.0641	0.60	0.0001	0.47	0.0020	0.50	0.0001
VLCI	0.63	0.0001	0.69	0.0001	0.56	0.0001	0.42	0.0009

Notes: DM - diabetes mellitus; EDVI - index of end-diastolic volume of the left ventricle; EF - ejection fraction; ESVI - index of end-systolic volume of the left ventricle; IM - myocardial infarction; VLCI - index of violation of local contractility

In diabetic patients with anterior myocardial infarction, with an increase in NT-proBNP levels on the 1st day after PCI by more than 790 pg/ml, the sensitivity of this indicator in predicting LV infarction reached 95%, and the specificity was 80% (Table 9).

Table 9

Diagnostic value of NT-proBNP on day 1 after PCI as a predictor of unfavorable LV remodeling after 12 months in patients with different localization of myocardial infarction depending on the presence of diabetes

	Patients with anterior MI		Patients with posterolateral MI	
	Patients with DM	Patients without DM	Patients with DM	Patients without DM
NT-proBNP, pg/ml	> 790	> 841	> 776	> 896
Sensitivity,%	95%	67%	87%	73%
Specificity,%	80%	98%	58%	92%

Notes: MI - myocardial infarction; LV - left ventricle; DM - diabetes mellitus

Determination of NT-proBNP in patients with posterolateral MI and satisfactory EF (at least 46%) showed that on day 1 after PCI in patients with diabetes, the level of this indicator 4.3-fold exceeded the norm and amounted to 541 pg/ml, which was statistically significantly higher than in patients without diabetes (408 pg/ml, $p_1 = 0.0029$) (Table 10). After 12 months, all these patients had a statistically significant decrease in NT-proBNP levels. Thus, in patients with diabetes, it was 196 pg/ml ($p_3 = 0.0001$); and without diabetes - 148 pg/ml ($p_4 = 0.0001$), which was close to the norm. At the same time, in patients with diabetes, the serum NT-proBNP content remained higher than in patients without diabetes ($p_2 = 0.0170$, statistically significant).

Table 10

Dynamics of NT-proBNP in patients with posterolateral myocardial infarction depending on the value of LVEF and the presence of diabetes

	Patients with posterolateral MI with LVEF no more than 45%			Patients with posterolateral MI with LVEF of at least 46%		
	NT-proBNP, pg/ml median *(IQR)*		*R*	NT-proBNP, pg/ml median *(IQR)*		*R*
	Patients with diabetes 1st group (*n* = 26)	Patients without diabetes 2nd group (*n* = 18)		Patients with diabetes 1st group (*n* = 15)	Patients without diabetes 2nd group (*n* = 41)	
PCI 1st day	996 (815-1331)	1125 (819-1491)	*p* 1 = 0.8113 *p* 2 = 0.1535 *p* 3 = 0.0012 *p* 4 = 0.0033	541 (397-599)	408 (277-511)	*p* 1 = 0.0029 *p* 2 = 0.0170 *p* 3 = 0.0001 *p* 4 = 0.0001
After 12 months	942 (693-1156)	692 (709-902)		196 (143-273)	148 (99-204)	

Notes: p 1 - baseline values between groups with and without diabetes; p2 - after 12 months between the DM and non-DM groups; p3 - between the baseline and after 12 months in patients with diabetes; p 4 - between the baseline and after 12 months in patients without diabetes. DM - diabetes mellitus; EF - ejection fraction; IQR - interquartile range; LV - left ventricle; MI - myocardial infarction; PCI - percutaneous coronary intervention

In diabetic patients with posterolateral MI and low EF (no more than 45%) on the 1st day after PCI, the NT-proBNP level was increased 6.5-10.6-fold and reached 1331 pg/ml (on average, 996 pg/ml). In patients without diabetes and low EF, the NT-proBNP concentration was increased 6.6–11.9-fold and averaged 1125 (819–1491) pg/ml.

After 12 months, the NT-proBNP level in patients of both groups decreased, but at the same time it was significantly higher than normal values. So, in the 1st group of patients it was increased 5.5-9.-fold, averaging 942 pg/ml, and in the 2nd group - 5.6-7.2-fold (on average, 692 pg/ml). There was no statistically significant difference between these indicators.

In diabetic patients with posterolateral MI (r = -0.57; p = 0.0001; 95% CI) and in the same patients, but without diabetes (r = -0.36; p = 0.0058; 95% CI) there was negative correlation between the level of NT-proBNP taken on the 1st day after myocardial reperfusion and LVEF 12 months later (see Table 8). At the same time, the direct correlation was found between the NT-proBNP level and ESVI (r = 0.85; p = 0.0001; 95% CI); EDVI (r = 0.47; p = 0.0020; 95% CI) and VLCI (r = 0.56; p = 0.0001; 95% CI).

In diabetic patients with posterolateral MI, the diagnostic level of NT-proBNP was more than 776 pg/ml (Table 9). At the same time, the sensitivity of the method as a predictor of LV UR was 87%, and the specificity was 58%.

DISCUSSION

According to the results of our work, in young and middle-aged diabetic patients with MI, the frequency of two- and three-vascular CA lesions in anterior MI reaches 66%, and in posterolateral MI - 85%. In patients without diabetes, these changes were less common and amounted to 34% and 54%, respectively. Early reperfusion and stenting of infarction-associated coronary artery had a beneficial effect on the course of MI. There were no lethal outcomes neither in the acute period of the disease nor the next 12 months of outpatient follow-up.

At the same time, in 69% of patients with diabetes with anterior MI and in 63% of patients with other localization of MI on the first day after PCI, signs of unfavorable LV remodeling were determined represented by low EF (no more than 45%) and high indices of EDV and ESV, which tended to increase even more within 12 months. According to a number of authors, the frequency of systolic dysfunction in diabetic patients after MI reaches 28-31% [12, 13, 14].

The analysis of numerous factors that determine the long-term prognosis of the MI course showed that the duration of the disease had the strongest direct effect on the processes of myocardial remodeling in patients with diabetes. Under such equal conditions as age, gender, BPI and MI in history, patients with unfavorable LV remodeling had twice the experience of diabetes mellitus than with favorable ones, and exceeded 6 years.

The results of our work confirmed the prognostic significance of an increase in the blood level of the N-terminal prohormone brain natriuretic peptide in long-term myocardial remodeling after PCI. The level of N-terminal prohormone of brain natriuretic peptide of more than 776 pg/ml on the first day after PCI proved to be a reliable long-term predictor of unfavorable LV remodeling, with the diagnostic accuracy of the method reaching 95%.

CONCLUSION

Our study requires further continuation in order to clarify the tactics of managing patients with acute myocardial infarction with diabetes mellitus with two- and three-vascular lesions in order to reduce the risk of developing unfavorable left ventricular remodeling. Apparently, the advantage in treatment should be given to percutaneous coronary intervention with stent installation not only in the infarction-associated coronary artery, but also in other coronary arteries with significant stenoses.

FINDINGS

1. In patients with diabetes mellitus of young and middle age with acute myocardial infarction, the frequency of two- and three-vascular lesions reaches 66%,in anterior myocardial infarction and 85% in other location. In patients without diabetes mellitus, these figures are 34% and 54%, respectively.

2.In 69% of patients with diabetes mellitus with anterior myocardial infarction and in 63% of patients with other MI location, signs of unfavorable remodeling of the left ventricle were determined 12 months after percutaneous coronary intervention, represented by low ejection fraction and an increase in the indices of end-diastolic and end-systolic volumes.

3. The level of N-terminal prohormone of brain natriuretic peptide in the blood of more than 776 pg/ml on the 1st day after percutaneous coronary intervention in patients with diabetes mellitus and acute myocardial infarction is a predictor of unfavorable left ventricular remodeling, while the diagnostic accuracy of the method reaches 95%.

4. The long-term prognosis of the course of myocardial infarction in young and middle-aged patients is directly affected by the duration of diabetes mellitus. If diabetes lasts more than 6 years, the number of cases of unfavorable remodeling of the left ventricle of the heart more doubles.

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Received on 08.06.2020

Review completed on 21.09.2020

Accepted on 29.09.2020