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Research article

Significance of the N-terminal Fragment of Brain Natriuretic Peptides in Predicting Ventricular Arrhythmias in Young and Middle-Aged Patients with Diabetes and Myocardial Infarction

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ABSTRACT. Fatal ventricular arrhythmias in patients with diabetes mellitus (DM) in the acute stage of myocardial infarction (MI) and postinfarction period often cause adverse outcomes. Therefore, the search for new reliable biomarkers in predicting ventricular arrhythmias in the long term is necessary.

AIM: This study aimed to evaluate the value of N-terminal-pro hormone BNP (NT-proBNP) in predicting ventricular arrhythmias in young and middle-aged patients with MI and DM-associated ST-segment elevation.

MATERIALS AND METHODS: Seventy-six patients (59 men and 17 women) with DM and MI with ST-segment elevation (aged 36–59 years; mean 53 ± 5 years) were examined. Anterior MI was diagnosed in 35 patients, and non-anterior MI was detected in 41 patients. The DM duration was up to 1 year in 16 patients, 1–5 years in 24, and 5–12 years in 36. Patients were examined on day 1 after percutaneous coronary intervention (PCI) with implantation of 1–3 stents in the coronary arteries (CA) and again after 12 months. Holter monitoring, echocardiography, and blood tests for NT-proBNP were performed.

RESULTS: After PCI, ventricular extrasystole (VES) of grades III–V according to Lown and Wolf was detected in 21 of 37 (56.7%) patients with DM. The left ventricular ejection fraction (LVEF) was 42% (27%–45%), and the NT-proBNP level was 1127 (790–2530) at a rate of up to 125 pg/mL. After 12 months, VES was noted in 9 of 37 (24.3%) patients. The LVEF was 33% (28%–35%), and the NT-proBNP level was 938 (497–1294) pg/mL. A positive correlation was found between the blood serum level of NT-proBNP on day 1 after PCI and the number of grade III–V VES 12 months later. At an NT-proBNP level of > 898 pg/mL on day 1 after PCI, the sensitivity of this biomarker in predicting high-grade VES 12 months after MI in patients with DM was 100%.

CONCLUSIONS: The NT-proBNP level after PCI in patients with DM and MI is a reliable predictor of ventricular arrhythmias over the next 12 months.

Keywords: myocardial infarction; diabetes mellitus; percutaneous coronary intervention; N-terminal fragment of brain natriuretic peptide; ventricular extrasystole.

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Научная статья

Значение N-терминального фрагмента мозгового натрийуретического пептида в прогнозировании желудочковых нарушений ритма у больных сахарным диабетом молодого и среднего возраста с инфарктами миокарда

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Актуальность. Фатальные желудочковые нарушения ритма у больных сахарным диабетом (СД) в острой стадии инфаркта миокарда (ИМ) и в постинфарктном периоде часто являются причиной неблагоприятных исходов. Этим обусловлен поиск новых надежных биомаркеров в прогнозирования желудочковых аритмий в долгосрочной перспективе.

Цель — оценить значение NT-proBNP в прогнозировании желудочковых аритмий у больных молодого и среднего возраста с ИМ с подъемом сегмента *ST* на фоне СД.

Материалы и методы. Обследовано 76 больных СД (59 мужчин и 17 женщин) с ИМ с подъемом сегмента *ST* в возрасте 36–59 лет (средний 53 ± 5 года). У 35 больных диагностированы передние ИМ, у 41 — непередние ИМ. Длительность СД до 1-го года — у 16; от 1-го до 5 лет — у 24; от 5 до 12 лет — у 36. Больные обследовались в 1-е сутки после чрескожного коронарного вмешательства (ЧКВ) с имплантацией 1–3 стентов в коронарные артерии (КА) и повторно через 12 месяцев. Выполнялись холтеровское мониторирование (ХМ), ЭхоКГ, анализы крови на NT-proBNP.

Результаты. После ЧКВ желудочковая экстрасистолия (ЖЭС) III–V градаций по Лауну — Вольфу выявлялась у 21 из 37 (56,7 %) больных СД. Фракция выброса левого желудочка (ФВ ЛЖ) составила 42 % (27–45 %); уровень NT-proBNP — 1127 (790–2530) при норме до 125 пг/мл. Через 12 месяцев ЖЭС отмечалась у 9 из 37 (24,3 %) пациентов. ФВ ЛЖ составила 33 % (28–35 %); уровень NT-proBNP — 938 пг/мл (497–1294). Была выявлена положительная корреляционная зависимость между содержанием в сыворотке крови NT-proBNP в 1-е сутки после ЧКВ и количеством ЖЭС III–V градаций через 12 месяцев. При уровне NT-proBNP > 898 пг/мл в 1-е сутки после ЧКВ чувствительность данного биомаркера в прогнозировании ЖЭС высоких градаций через 12 месяцев после ИМ у больных СД составляет 100 %.

Заключение. Уровень NT-proBNP после ЧКВ у больных СД с ИМ является надежным предиктором желудочковых аритмий в течение ближайших 12 месяцев.

Ключевые слова: инфаркт миокарда; сахарный диабет; чрескожное коронарной вмешательство; N-терминальный фрагмент мозгового натрийуретического пептида; желудочковая экстрасистола.

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LIST OF ABBREVIATIONS

ESC — European Society of Cardiology
ACS — acute coronary syndrome
CA — coronary artery
CCF — chronic cardiac failure
DM — diabetes mellitus
EchoCG — echocardiography
EF — left ventricle ejection fraction
HF — heart failure
HM — Holter monitoring
LV — left ventricle
MI — myocardial infarction
NT-proBNP — N-terminal fragment of brain natriuretic peptide
PCI — percutaneous coronary intervention
ROC — receiver operating characteristic
VES — ventricular extrasystole
VT — ventricular tachycardia

INTRODUCTION

As knowledge is obtained, the level of understanding of factors that can predict the risk of fatal ventricular arrhythmias, sudden death, and progression of heart failure (HF) changes. This concept refers to young and middle-aged patients with diabetes mellitus (DM) because atherosclerotic lesions of large- and medium-sized CAs occur in this group 8–10 years earlier than that in the DM group [1], and the incidence of myocardial infarction (MI) is 3–5 times higher [2, 3]. Moreover, the 30-day mortality rate reaches 11.3% and 5.9% and the 1-year mortality rate is 14.5% and 8.9% in the non-DM group with MI [4].

Natriuretic peptides were discovered in the 1950s–1970s, among which type B natriuretic peptide (BNP) and its N-terminal fragment (NT-proBNP) proved to be the most discussed in cardiology [5]. They are secreted in the heart ventricles in response to increased myocardial tension and increased blood volume or pressure and are the most sensitive markers in diagnosing chronic cardiac failure (CCF) [6]. The BNP level measured on day 1 after acute coronary syndrome can be used as a marker of long-term mortality prognosis [7]. Moreover, only single reports have revealed that NT-proBNP concentrations are significantly higher in patients with ventricular arrhythmias than in those without ventricular arrhythmias [8]. In young and middle-aged patients with DM and MI, these issues are not covered enough.

AIM

This study aimed to estimate the NT-proBNP level that can predict ventricular arrhythmias in young and middle-aged patients with MI and DM-associated ST-segment elevation.

MATERIALS AND METHODS

A prospective, controlled, non-randomized cohort study was performed. We examined 76 patients with DM (59 men and 17 women) aged 36–59 (mean 53 ± 5) years (Table 1).

DM duration of up to 1 year was determined in 16 patients, 1–5 years in 24, and 5–12 years in 36. Moreover, 31.6% of the patients had a history of MI, and all patients had grade 1–3 AH. Anterior MI was diagnosed in 35 patients with DM admitted with a diagnosis of acute coronary syndrome (ACS) with ST elevation on echocardiography (ECG), and non-anterior MI in 41 patients. Patients were examined on day 1 after percutaneous coronary intervention (PCI) with implantation of 1–3 stents in the CA and again after 12 months. As the control group, 115 young, and middle-aged patients with MI and ST elevation without DM were examined. The DM and non-DM groups were completely comparable in terms of age, sex, and comorbid diseases.

Echocardiography was performed using Philips EnVisor (Philips Electronics N.V.), Toshiba Artida (Toshiba Medical Systems), and Vivid 7 Pro series (General Electric Company) devices on day 1 after PCI and 12 months later. The study was conducted according to the standard method using (B) and (M) scanning modes, pulsed wave and continuous wave modes, and color Doppler mapping. The left ventricular ejection fraction (LVEF) was calculated according to the Simpson method. To quantify local contractility disorders, the wall motion score index (WMSI) of the left ventricle was calculated [9, 10].

In the dynamics of the examination, LVEF was assessed according to the recommendations of the European Society of Cardiology for the diagnostics and treatment of chronic HF (2021), namely, (1) CCF with preserved EF (⩾ 50%) (HFpEF), (2) CCF with moderately reduced EF (40%–49%) (HFmrEF), and (3) CCF with low EF (⩽ 40%) (HFlEF) [11].

For Holter monitoring (HM), we used a portable HM "Kardiotekhnika 4000" (Inkart, St. Petersburg) with a multi-channel recorder, digital recording of information, and subsequent automatic data processing according to the attached software package KT-4000. HM analysis was performed using the Incardio Result v2.0 program (St. Guidelines for HM in clinical practice [12]. The daily dynamics of the heart rate was assessed, and ventricular ectopic activity was evaluated using the VES classification according to Lown and Wolf (1971) [13] and changes in repolarization according to the ECG with the calculated ischemia index and ischemia duration during the day. The eligibility of patients for HM was determined by the severity of their condition (classes II–III according to Killip and Kimballe) [14].

The blood serum NT-proBNP level was measured on the Cobas device using the Elecsys platform (Roche Diagnostics, USA). The normal value is < 125 pg/mL.

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Table 1. Characteristics of the patients with myocardial infarction

Parameters	DM group *n* = 76	Non-DM group *n* = 115	*p*
Age, years M (SD)	53 ± 5	52 ± 5	0.2822
Sex, m/f, *n*	59 / 17	101 / 14	no data
BMI kg/m^2, M (SD)	29.1 ± 4.6	27.7 ± 4.7	0.0855
DM duration, *n* (%) up to 12 months 1–5 years > 5 years	 16 (21.1%) 24 (31.6%) 36 (47.4%)		no data
History of MI, *n* (%)	24 (31.6%)	20 (17.4%)	0.3829
Anterior MI, *n* (%)	35 (46%)	56 (48.7%)	no data
Non-anterior MI, *n*. (%)	41 (54%)	59 (51.3%)	no data
Arterial hypertension, *n* (%) Grade 1 Grade 2 Grade 3	 32 (42.0%) 10 (13.3%) 34 (44.7%)	 72 (62.6%) 25 (21.7%) 18 (15.7%)	no data
Acute cardiac failure by Killip classification, *n* (%) Class I Class II Class III	 48 (63.2 %) 27 (35.5 %) 1 (1.3 %)	 85 (73.9 %) 28 (24.3 %) 2 (1.8 %)	no data
Troponin I, pg/mL, *Me* (IQR)	73.0 (4.0 – 50000)	67.0 (3.0 – 50000)	0.0015
Total cholesterol, mmol/l, (*M* ± *m*)	5.58 ± 1.53	5.03 ± 1.45	0.0141
Triglycerides, mmol/l, (*M* ± *m*)	2.18 ± 1.31	1.71 ± 1.01	0.0012
High-density lipoprotein cholesterol mmol/L, (*M* ± *m*)	1.30 ± 0.42	1.15 ± 0.32	0.0046
Low-density lipoprotein cholesterol mmol/L, (*M* ± *m*)	4.14 ± 1.45	3.66 ± 1.26	0.0334
Glycated hemoglobin, % (*M* ± *m*)	7.9 ± 1.78	5.26 ± 0.56	0.0001
Creatinine, μmol/L, (*M* ± *m*)	90.7 ± 14.5	89.5 ± 16.7	0.5158
GFR by MDRD mL/min/1.73 m^2, (*M* ± *m*)	66.0 ± 15.0	78.0 ± 18.0	0.0001

Differences between groups were assessed by the Mann–Whitney *U*-test, and a *p* value lower than 0.05 was considered significant. Spearman's coefficient was used to assess the correlation between NT-proBNP values and HM parameters.

Receiver operating characteristic (ROC) analysis indicating the area under the ROC curve (AUC) was performed to obtain the operational characteristics of event predictors. Based on the median of the initial NT-proBNP levels obtained on day 1 after PCI, the maximum sensitivity, and specificity of the biomarker were determined after 12 months.

RESULTS

HM parameters were analyzed in 37 patients with LVEF of 42% (27%–45%) in the DM group and 42 patients with LVEF of 46% (37%–49%) in the non-DM group (Table 2).

Furthermore, 3 of 37 patients in the DM group and 17 of 42 patients in the non-DM group did not have ventricular ectopic activity on day 1 after PCI. Ten patients in the DM group and five in the non-DM group had grade I ventricular extrasystole (VES) (< 30/h). In three patients in the DM group, VES grade II (> 30/h) was detected.

Most often, in patients with MI in the DM group on day 1 after PCI, VES grades III–V were detected in 21 of 37 (56.7%) patients. In 12 of 37 patients in the DM group and 17 of 42 patients in the non-DM group, single polytopic VESs of ⩾ 3 morphological types were recorded. In five patients in the DM group and three patients in the non-DM group, paired monomorphic (grade IVa) and paired polymorphic (grade IVb) VES with a shortening coupling interval were detected. Moreover, four DM patients in the DM group had unstable paroxysms of monomorphic ventricular tachycardia (VT) (< 30 s). In the non-DM group, no paroxysms, and runs of VT were recorded. In general,

Table 2. Dynamics of Holter monitoring indicators in patients with myocardial infarction on day 1 after PCI and after 12 months.

Me indicator (IQR)	Day 1 after PCI			After 12 months		
	DM group *n* = 37	Non-DM group *n* = 42	*p*	DM group *n* = 37	Non-DM group *n* = 42	*p*
Daytime heart rate, bpm	72 (68–76)	69 (62–74)	p_1 = 0.0705	64 (58–71)	69 (62–74)	p_2 = 0.2286
HR at night, bpm	66 (62–73)	62 (56–67)	p_1 = 0.0235	55 (50–65)	64 (59–66)	p_2 = 0.2281
VES grade III	*n* = 12 38 (11–730)	*n* = 17 12 (5–19)		*n* = 6 1770 (4-10890)	*n* = 4 38 (20-77)	
VES grade IV	*n* = 5 19 (13–57)	*n* = 3 1 (1.1)		*n* = 2 539 (5–1073)	*n* = 3 1 (1–1)	
VES grade V	*n* = 4 4 (1–41)			*n* = 1 59 (59–59)		
Ischemia index, μV · min	33 775 (20210–94475)	17 317 (10185–55712)		32 078 (8144–40782)	3041 (1358–30075)	p_2 = 0.0196 p_3 = 0.0050 p_4 = 0.0329
Ischemia duration, min	417 (228–942)	305 (203–705)		355 (271–503)	57 (9–189)	p_2 = 0.0111 p_3 = 0.0050 p_4 = 0.0033

Note: p_1 — is the significance of differences between groups on day 1 after PCI; p_2 — is the significance of differences between groups after 12 months; p_3 — is the significance of differences between the indicator on day 1 and after 12 months in the DM group, and p_4 — is the significance of differences between the indicator on day 1 and after 12 months in the non-DM group.

Таблица 3. Динамика эхокардиографических показателей и содержания в крови NT-proBNP у больных с инфарктами миокарда и желудочковой экстрасистолией III–V градаций

Parameters	Day 1 after PCI		After 12 months		*p*
	DM group *n* = 37	Non-DM group *n* = 42	DM group *n* = 37	Non-DM group *n* = 42	
NT-proBNP pg/mL, Me (IQR)	1127 (790–2530)	614 (421–1397)	938 (497–1294)	517 (118–989)	p_1 = 0,0010 p_2 = 0,0054 p_3 = 0,0004 p_4 = 0,0001
LVEF, % Me (IQR)	42 (27–45)	46 (37–49)	33 (28–35)	49 (44–58)	p_1 = 0,0014 p_2 = 0,0001 p_3 = 0,0227 p_4 = 0,0184
WMSI Me (IQR)	1,65 (1,56–2,0)	1,34 (1,25–1,80)	1,75 (1,63–1,93)	1,31 (1,13–1,81)	p_1 = 0,0008 p_2 = 0,0003 p_3 = 0,1687 p_4 = 0,0072

20 of 42 (47.6%) patients in the non-DM group had high-grade VESs.

The ischemia index, that is, an indicator of the depth of the ST segment depression in patients with DM ranged from 20 210 to 94 475 μV·min (on average, 33 775 μV · min), which was almost twice as high as in patients with MI in the non-DM group (17 317, 10 185–55 712 μV · min).

On day 1 after stenting of the infarct-associated CA in the DM group, myocardial ischemia persisted, whereas the ischemia duration ranged from 228 to 942 (average, 417)

min. In the non-DM group, the ischemia duration after PCI was shorter and averaged 305 (203–705) min.

The NT-proBNP level in the blood serum of the DM group was two times higher than that in the non-DM group (p_1 = 0.0010). WMSI in the DM group was high, that is, 1.65 (1.56–2.0) in patients with grade 3–4 lesions, whereas in the non-DM group, the WMSI was 1.34 (1.25–1.80) in those with grades 2–3 lesions (p_1 = 0.0008). In patients of the DM group with VES grades III–V, the LVEF was significantly lower than that in patients without diabetes (p_1 = 0.0014) (Table 3).

In the DM group, in young, and middle-aged patients with MI, large lesion area, and persistent myocardial ischemia after PCI, high NT-proBNP levels, and VES grades III–V were recorded. In the non-DM group, in the presence of WMSI grades 2–3, persistent myocardial ischemia, but of a shorter duration, VES grades III–V were registered less frequently and NT-proBNP levels were significantly lower.

After 12 months, the number of high-grade VESs in the DM group decreased and was recorded in 9 of 37 (24.3%) patients. Thus, in 6 of 37 patients, single polytopic polymorphic VES were recorded, with 4–10 890 (average, 1770) per day. Two patients had a paired polymorphic VES with a shortening coupling interval, with 5–1073 (average, 529) per day. Unsustainable (< 30 s) and sustained (⩾ 30 s) VT paroxysms of 59 per day were recorded in one patient, whereas the ventricular contraction rate reached 160–196 beats/min (grade V).

The duration of ischemic displacement of the ST segment decreased from 417 to 355 min (p_3 = 0.0050) and the ischemia index from 33775 to 32 078 μV · min (p_3 = 0.0050).

After 12 months, 7 of 42 patients in the non-DM group (16.7%) also showed an improvement. Of 42 patients, 4 had grade III VESs with a frequency of 38 (20–77) per day. Three patients had VES grade IV. Unlike the DM group, no VT paroxysms were recorded in this group. The ischemia duration was 57 (9–189) min (p_4 = 0.0033), and the ischemia index decreased by more than five times (3041, 1358–30075, μV · min) (p_4 = 0.0329).

In general, after 12 months, the ischemia index in the DM group was 10.5 times higher than that in the non-DM group (p_2 = 0.0196), and the duration of myocardial ischemia was six times longer than that in the non-DM group (p_2 = 0.0111). Probably, prolonged postinfarction myocardial ischemia in patients with low LVEF in the DM group was the cause of life-threatening ventricular arrhythmias.

After 12 months in the DM group, LVEF decreased to 33% (28%–35%) (p_3 = 0.0227), whereas in the non-DM group, the EF increased to 49% (44%–58%) (p_4 = 0.0184). The blood serum levels of NT-proBNP in the DM group decreased to 938 (497–1294) pg/mL (p_3 = 0.0004), which exceeded significantly the normal value (< 125 pg/mL) and was higher than that in the non-DM group (p_2 = 0.0054). Moreover, in the non-DM group, the NT-proBNP level decreased to 517 (118–989) pg/mL (p_4 = 0.0001) and was almost normalized in some patients.

To assess the NT-proBNP level in predicting ventricular arrhythmias in patients with MI and ST-segment elevation, Spearman's rank correlation was employed. Table 4 presents the results of the correlation analysis.

In the DM group, patients with MI were found to have a high-level positive correlation between the NT-proBNP level on day 1 after PCI and the number of VESs (r = 0.5796; p = 0.0117),

Table 4. Correlation dependence of NT-proBNP levels on day 1 of myocardial infarction after PCI with Holter monitoring indicators after 12 months

Parameters	DM group		Non-DM group	
	r	*p*	*r*	*p*
Number of VES grades III–V	0.5796	0.0117	0.6010	0.0051
Ischemia index (μV · min)	0.5814	0.0003	0.5235	0.0004
Ischemia duration (min)	0.6101	0.0001	0.6458	0.0001

Table 5. Correlation dependence of NT-proBNP levels taken 12 months after myocardial infarction with Holter monitoring indicators after 12 months

Parameters	DM group		Non-DM group	
	r	*p*	*r*	*p*
Number of VES grades III–V	0.7685	0.0001	0.5149	0.0084
Ischemia index (μV · min)	0.8108	0.0001	0.3946	0.0097
Ischemia duration (min)	0.8681	0.0001	0.6901	0.0001

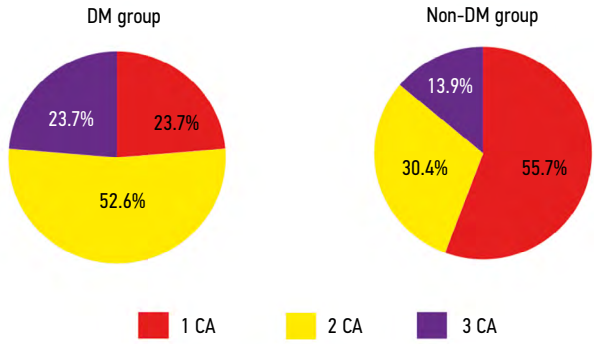

Fig. 1. Incidence of atherosclerotic coronary arteries in young and middle-aged patients with myocardial infarction with and without DM

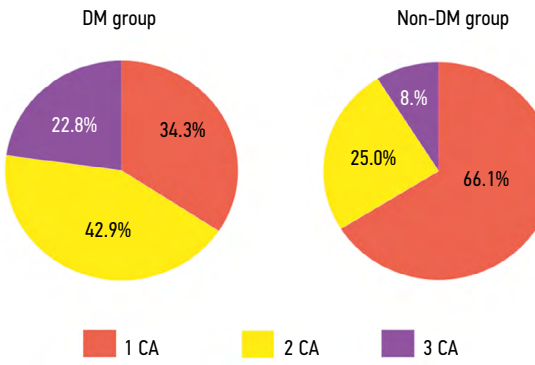

Fig. 2. Incidence of atherosclerotic lesions of the coronary arteries in patients with anterior myocardial infarction

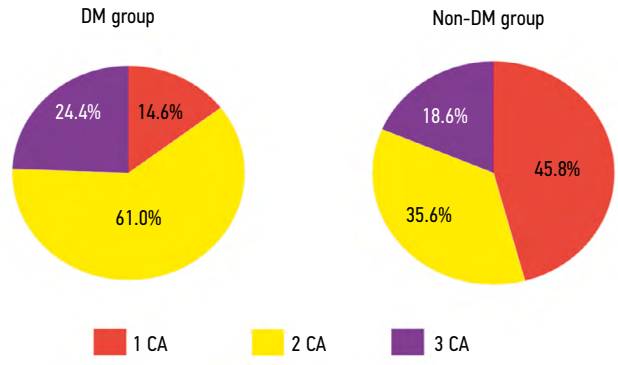

Fig. 3. Incidence of atherosclerotic lesions of the coronary arteries in patients with non-anterior myocardial infarction

ischemia index (r = 0.5814; p = 0.0003), and myocardial ischemia duration (r = 0.6101; p = 0.0001) after 12 months.

By analogy in the DM group, in patients with MI in the non-DM group, a positive correlation dependence of a high significance was also noted between the NT-proBNP level and the number of VESs (r = 0.6010; p = 0.0051), ischemia index (r = 0.5235; p = 0.0004), and myocardial ischemia duration (r = 0.6458; p = 0.0001) after 12 months.

Correlations between NT-proBNP levels taken after 12 months and HM parameters after 12 months in the DM group become comparable (Table 5). Thus, a high significantly positive dependence increased between the NT-proBNP level and VES grades III–V (r = 0.7685; p = 0.0001), ischemia index (r = 0.8108; p = 0.0001), and myocardial ischemia duration (r = 0.8681; p = 0.0001).

After 12 months in the non-DM group, the correlation between serum NT-proBNP levels and HM parameter values after 12 months, compared with an acute MI period, decreases while maintaining significance. This is most noticeable in the ratio with VES grades III–V (r = 0.5149; p = 0.0084) and ischemia index (r = 0.3946; p = 0.0097).

Probably, this recorded difference is due to numerous arrhythmias in the postinfarction period in the DM group and to deeper and more prolonged myocardial ischemia associated with the peculiarities of CA lesions in diabetes (Fig. 1).

According to the coronary angiography (CAG) results, the incidence rates of lesions of CAs 2 and 3 were 52.6% and 23.7% (73.6%) in the DM group and 30.4% and 13.9% (44.3%), respectively, in the non-DM group.

In anterior and non-anterior MI in patients with DM, the incidence rates of multivessel CA lesions were 65.7% and 85.4%, respectively (Fig. 2, 3).

In the non-DM group of patients with anterior and non-anterior MI, the incidence rates of multivessel CA lesions were 34.9% and 54.2%, respectively, which was less than that in the DM group.

Apparently, after PCI with CA stenting, young, and middle-aged patients in the DM group, low LVEF, and high-grade ventricular arrhythmias require the most complete myocardial revascularization in the postinfarction period.

To confirm the NT-proBNP levels in the DM group, taken on day 1 after PCI, the ROC analysis was used to predict ventricular arrhythmias 12 months later (Fig. 4).

In the plotted graph, the AUC value was 0.8429, which indicates that the model is effective and has high predictive power. Serum NT-proBNP levels higher than 898 pg/mL on day 1 of MI after PCI in the DM group were a predictor of high-grade VES after 12 months with a sensitivity of 100% and a specificity of 80%.

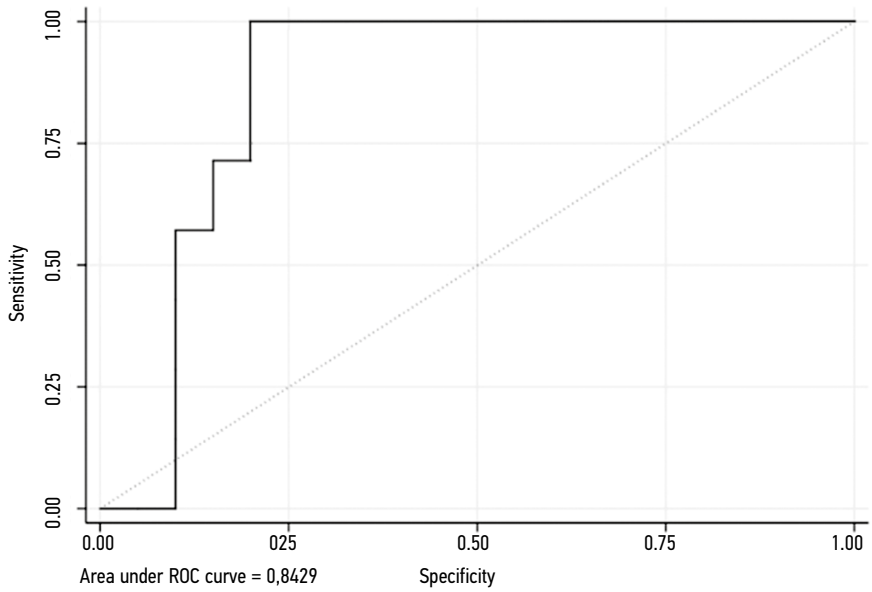

Fig. 4. ROC curve. Model of sensitivity and specificity of NT-proBNP, taken on day 1 after PCI in patients with diabetes mellitus, as a predictor of VES grades III–V in 12 months

In the non-DM group, the AUC value was 0.5000, indicating that this model is non-functional, and the predictive value of NT-proBNP is low.

DISCUSSION OF RESULTS

According to Katritsis et al. (2013), after myocardial reperfusion, and treatment with beta-blockers, runs, and unstable paroxysms of VT were detected in 56.4% of the patients with HM, which greatly increased the risk of sudden death [15]. This is consistent with the results of our study that the incidence rates of grade III–V VESs after PCI were 56.7% in the DM group and 47.6% in the non-DM group. After 12 months, the frequency of VESs decreased to 24.3% in the DM group and up to 16.7% in the non-DM group.

A study supervised by Lekston et al. (2014) proved that reperfusion is not always successful in patients with DM and ACS, compared with patients without DM. This occurred because at least two CAs are affected more often in DM; thus, repeated PCI or coronary artery bypass grafting was performed [16]. According to our data, on day 1 after reperfusion, myocardial ischemia persisted in the DM group, which duration was significantly longer than that in the non-DM group. After 12 months, both groups showed improvement as a decrease in the ischemia index and myocardial ischemia duration; however, in the DM group, the ischemia index was 10.5 times greater, and the myocardial ischemia duration was six times longer than that in the non-DM group.

The mortality analysis performed by Denisova et al. (2016) revealed that fatal arrhythmias were more common in patients with type 2 DM, who died from ACS, than in patients with normal carbohydrate metabolism [17].

Maggioni et al. (1993) followed up 8676 patients after MI for 6 months. In 64.1% of the patients, ventricular arrhythmias were recorded, and 19.7% of them had high-grade VES and 6.8% of them had VT paroxysms. Moreover, 2% of deceased patients had rhythm disorders in the postinfarction period [18]. With follow-up periods of up to 4 years, the prognosis is relatively favorable. With long follow-up periods, including the registration of VT paroxysms, LV dysfunction decreased with EF [19]. In the present study, with a follow-up period of up to 12 months, the dynamics of LVEF was multidirectional in the DM group and non-DM group with VES grades III–V. Thus, in the DM group, by the end of year 1 after MI, the LVEF decreased; in the non-DM group, normal, and moderately reduced EF values were recorded.

Ephrem et al. (2013) followed up 222 patients during the rehabilitation period after ACS for 2.3 years. According to the results of HM, 48% of the patients had VESs, which were complicated by the aggravation of HF, palpitations, and syncope in 17.6% of cases. They concluded that polymorphic VESs occurring at a frequency of < 4/h are prognostically unfavorable [20].

Structural changes in the heart in the DM group and those who died from MI were studied by Mayorova et al. (2011). In the presence of severe atherosclerosis of the CAs, postinfarction and diffuse small-focal cardiosclerosis, 17.9% of the patients have metabolic myocardial damage with the formation of diabetic cardiomyopathy, namely, an increase in heart mass, sharp dilatation of the cavities, signs of microangiopathy, cardiomyocyte damage, and

myocardial stroma [21]. According to Akhmedov et al. (2015) and Elsukov et al. (2015), diabetic autonomic cardioneuropathy is characterized by the early degeneration of nerve fibers of both the sympathetic and parasympathetic systems and may be complicated by the development of fatal ventricular arrhythmias, sudden cardiac arrest, and painless MI [22, 23].

Skranes et al. (2016), based on the analysis of 24-h HM records in 498 patients, revealed that NT-proBNP levels are significantly higher in patients with VES and complex ventricular arrhythmias than in those without ventricular arrhythmias [8]. Using multivariate regression analysis, Omland (2008) concluded that an increase in the NT-proBNP level after ACS is associated with a high risk of fatal ventricular arrhythmias (OR 1.50 [95% OR 1.07–2.12], $p = 0.020$) [24].

According to our data, on day 1 after PCI in young and middle-aged patients with DM and MI associated with a large lesion area and persistent myocardial ischemia, high levels of NT-proBNP, and grades III–V VES were recorded. In the non-DM group, after reperfusion, myocardial ischemia also persisted; however, the frequency of grades III–V VES was lower. The blood serum level of NT-proBNP was significantly lower in them.

The NT-proBNP level is a significant factor in assessing the long-term prognosis of patients with DM after ACS. Thus, Salama et al. (2011), as a result of long-term follow-up of 62 diabetic patients after ACS, proved that the blood concentration of NT-proBNP in predicting long-term mortality is more accurate than other markers [25].

In patients with MI in the DM group, we revealed a high-significance positive correlation between the NT-proBNP level taken on day 1 after PCI and the number of VESs, ischemia index, and myocardial ischemia duration after 12 months. The prediction of high-grade VESs in the early period of MI with NT-proBNP levels > 898 pg/mL is performed with a sensitivity of 100%.

CONCLUSION

The blood serum levels of NT-proBNP in young and middle-aged patients with DM, and MI on day 1 after PCI is a reliable prognostic biomarker of ventricular arrhythmias over the next 12 months. To finally resolve the issue of which parameters, in addition to myocardial ischemia and LVEF, are closely associated with a high NT-proBNP prediction, and require additional studies in the context of groups of revascularized and non-operated patients.

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