

**N. S. Lisyutenko*¹, N. A. Morova¹,
V. N. Tsekhanovich^{1, 2}**

¹— Omsk State Medical University of Ministry of Health of Russia, Omsk, Russia

²— Budgetary Healthcare Institution of Omsk Region "Regional Clinical Hospital"
Omsk, Russia

HEMOSTASIS PARAMETERS IN PATIENTS AFTER CORONARY ARTERY BYPASS SURGERY FOR STABLE ANGINA

Abstract

The objective of research is to assess the significance of hemostatic profile in the postoperative period after coronary artery bypass surgery for predicting the one-year functioning of the grafts.

Materials and methods. 46 men, who had coronary artery bypass surgery (CABS) for stable angina, were examined. 23 of them had 2 type diabetes mellitus (DM2), 23 of them did not have diabetes mellitus. All patients underwent fibrinogen, soluble fibrin monomer complex, D-dimer, induced platelet aggregation and lupus anticoagulant blood tests on the 14th day after surgery. The patients had coronary and bypass graft angiography for the assessment of graft patency a year after surgery.

Results. During the postoperative period, there were no statistically significant differences between patients with DM2 and patients without DM2 in the results of the above hemostatic profile tests (p value for the Mann-Whitney test is >0.05). Lupus anticoagulant was detected in 9 patients with DM2 and in 12 patients without DM2 (p value for Fisher's exact test is 0.554). 10 patients with DM2 and 6 patients without DM2 had graft occlusions a year after surgery; the differences for this sign were not statistically significant (p value for Fisher's exact test is 0.18). Fibrinogen, soluble fibrin-monomer complex, D-dimer, and induced platelet aggregation tests did not demonstrate prognostic significance in relation to graft occlusions in both groups of patients (p for χ^2 in the logistic regression model is >0.05). The factors associated with higher risk of graft occlusion in patients with DM2 were high ratio between screening and confirmatory test for the detection of lupus anticoagulant (odds ratio 2.27; 95% -confidence interval 1.119–1.238; $p < 0.05$).

Conclusion. After coronary bypass surgery, the one-year risk of graft thrombosis is higher in patients with DM2 and high positive LA activity

Key words: coronary artery bypass surgery, diabetes mellitus, lupus anticoagulant, hemostasis parameters, prognosis

Conflict of interests

The authors declare that this study, its theme, subject and content do not affect competing interests

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*Contacts: Natalia S. Lisyutenko, e-mail: n.labuzina@mail.ru

ADP — adenosine diphosphate, Ab — antibodies, LA — lupus anticoagulant, CAD — coronary artery disease, MI — myocardial infarction, CABS — coronary artery bypass surgery, SFMC — soluble fibrin monomer complexes, T2DM — type 2 diabetes mellitus, LA1 — lupus anticoagulant screening test (dilute Russell's viper venom time), LA2 — lupus anticoagulant confirmatory test (phospholipid-enriched dilute Russell's viper venom time), LA ratio — the ratio between the lupus anticoagulant screening and confirmatory tests (LA1/LA2).

Introduction

The need for cardiac surgery among the population in our country grows year by year due to the increase in the number of patients with coronary artery disease (CAD) [1]. Without diminishing the successes of modern interventional cardiology, it should be noted that coronary artery bypass surgery (CABS) is the preferred method of revascularization in multivessel hemodynamically significant coronary artery disease.

Among the most important issues in coronary surgery is post-CABS relapse of myocardial ischemia (angina relapse, myocardial infarction (MI)), due to which there is a need for coronary reinterventions [2]. Morphological background for these outcomes is generally based on the insufficiency of grafts due to their thrombosis, intimal hyperplasia, atherosclerosis progression [3]. In this case, patients with T2DM have a worse post-CABS prognosis as compared to people without carbohydrate metabolism disorders [4].

Identification of coronary graft occlusion predictors would make it possible to form risk groups among patients who have undergone CABS, and work out an effective strategy of secondary prevention for said patients.

According to the available literary data, the post-CABS activation of the hemostatic system affects the possibility of adverse clinical outcomes. In particular, higher D-dimer levels one month following CABS are associated with angina relapse [5]. In their study, B. Yanagawa et al. confirmed the significance of fibrinogen as a biochemical predictor of coronary graft occlusion in the long post-operative term [6].

The understudied issue is the impact of antiphospholipid antibodies (Ab) on the prognosis in patients with CAD in cases when there are no grounds for

making a diagnosis of antiphospholipid syndrome (asymptomatic carriage or transient occurrence of Ab to cardiolipin, Ab to β 2-glycoprotein-1, or Ab with lupus anticoagulant (LA) properties). The question of the predictive value of LA identification for patients who have undergone CABS remains open.

The **objective** of our study was to assess the existence of the relationship between the hemostatic system parameters in the post-CABS period and the development of coronary graft occlusions within one post-operative year.

Materials and Methods

The prospective cohort study was conducted in 2016–2018. The study design was approved by the local ethics committee. Voluntary informed consents were obtained from all the patients participating in the study.

The study included 46 males who had undergone coronary bypass surgery for grade III–IV stable angina according to the Canadian classification. The surgery was indicated for two- and three-vessel coronary artery disease with 50% and over stenosis [7]. Among 46 patients, 23 had T2DM, and 23 did not have diabetes. Clinical profiles of the patients are presented in Table 1.

Patients with T2DM and patients without T2DM were not significantly different in age, body mass index, smoking status, and cardiovascular comorbidity. However, the patients with T2DM had much greater waist circumference.

The inclusion criteria: male, CABS undergone under cardiopulmonary bypass for grade III–IV stable angina.

The exclusion criteria: MI experienced less than 12 weeks before the surgery, perioperative MI,

Table 1. Clinical characteristics of patients

Clinical sign	Patients with DM2 (n = 23)	Patients without DM2 (n = 23)	ρ for Mann—Whitney test, $\rho(U)/\rho$ for Fisher test, $\rho(F)$
Age, years. Me (P25; P75)	59 (53; 74)	58 (51; 65)	$\rho(U) = 0.221$
Body mass index, kg/m ² Me (P25; P75)	28.8 (25.3; 33.3)	26.8 (25.8; 30.7)	$\rho(U) = 0.175$
Waist circumference, cm Me (P25; P75)	103 (95; 112)	89 (80; 95)	$\rho(U) = 0.000$
One myocardial infarction, ($\% \pm S_p$)	14 (61 \pm 10%)	19 (83 \pm 8%)	$\rho(F) = 0.189$
Second myocardial infarction, ($\% \pm S_p$)	3 (13 \pm 7%)	2 (8.7 \pm 6%)	$\rho(F) = 1.000$
Arterial hypertension, ($\% \pm S_p$)	19 (83 \pm 8%)	20 (86.9 \pm 8%)	$\rho(F) = 0.189$
III functional class of angina pectoris, ($\% \pm S_p$)	19 (83 \pm 7.8%)	20 (86.9 \pm 7.8%)	$\rho(F) = 189$
IV functional class of angina pectoris, ($\% \pm S_p$)	4 (17.4 \pm 8%)	3 (13 \pm 7%)	$\rho(F) = 1.000$
Smoking status, ($\% \pm S_p$)	13 (56.5 \pm 10%)	16 (69.6 \pm 10%)	$\rho(F) = 0.542$
Hemodynamically significant atherosclerosis of the internal carotid arteries, ($\% \pm S_p$)	5 (21.7 \pm 9%)	6 (26.1 \pm 9%)	$\rho(F) = 1.000$
Hemodynamically insignificant atherosclerosis of the internal carotid arteries, ($\% \pm S_p$)	14 (60.9 \pm 11%)	9 (39 \pm 10%)	$\rho(F) = 0.238$

Note: AH — arterial hypertension, BMI — body mass index, Me (P25; P75) — median, upper and lower quartiles, ICA — internal carotid arteries, abs. — absolute number, S_p — standard error of the proportion, G — grade, DM2 — type 2 diabetes mellitus. P-values in bold indicate that there are statistically significant differences among the groups

diseases and conditions requiring prescription of oral anticoagulants, suppurative-septic complications that occurred due to the undergone CABS.

All the patients underwent CABS under cardiopulmonary bypass. A conduit and its application technique were selected by an operating surgeon on a case-by-case basis, depending on the clinical situation. Table 2 provides information of what conduits and in what combinations they were used in both groups of patients.

On Day 10–14 following the operation, blood sampling was conducted in all patients for the assaying of fibrinogen, soluble fibrin monomer complexes (SFMC), D-dimers, lupus anticoagulant (LA) and induced platelet aggregation. As antiplatelet therapy, all the patients received only acetylsalicylic acid at a dose of 100 mg. Low molecular heparins were discontinued on Day 4 following the operation.

Fibrinogen was assayed by the Sysmex 560 automatic coagulometer using Siemens reagents. D-dimer level was measured by NycoCard diagnostic kits manufactured by Nicomed using

NycoCard Reader II reflectometer. To detect SFMC, reagents manufactured by Tekhnologiya-standart were used. LA was assayed by the Sysmex ca-560 automatic coagulometer using Siemens reagents LA1 Screening Reagent and LA2 Confirmation Reagent. The screening test (LAC Screen) contains diluted Russell's viper venom and is intended for the screening assay of lupus anticoagulant. The confirmatory test (LAC Confirm) contains phospholipid-enriched diluted Russell's viper venom and is intended for the LA confirmation. Following the testing, the ratio between the screening and confirmatory tests (LA ratio) was calculated. With the LA ratio of 1.2–1.5, the LA content was considered as low, with the LA ratio within 1.5–2 — as moderate. If the LA ratio exceeded 2, the LA content was considered as high.

Platelet aggregation was assayed by the Chronolog model 490 optical c using inductors (ADP, Epinephrine) manufactured by Chrono-log. The induced aggregation parameters were determined by the light transmission curve. Epinephrine (5 μ g/ml) and ADP (5 μ g/ml) were used as aggregation inductors.

Table 2. The main strategies for coronary artery bypass surgery and the types of grafts used

Grafts used	Patients with DM2 (n = 23)	Patients without DM2 (n=23).	ρ for the Fisher test, $\rho(F)$.
LITA + SV ($\% \pm S_p$)	14 (60.9 \pm 10.9%)	12 (52.2 \pm 10.4%)	$\rho(F) = 0.766$
LITA + RA + SV ($\% \pm S_p$)	0	3 (13 \pm 7%)	$\rho(F) = 1.000$
LITA + RA ($\% \pm S_p$)	0	1 (4.3 \pm 4.3%)	$\rho(F) = 1.000$
RA + SV ($\% \pm S_p$)	1 (4.3 \pm 4.3%)	1 (4.3 \pm 4.3%)	$\rho(F) = 1.000$
Only SV, ($\% \pm S_p$)	8 (34.8 \pm 9.9%)	5 (21.7 \pm 8.6%)	$\rho(F) = 0.513$
Sequential venous grafts, ($\% \pm S_p$)	12 (52.2 \pm 10.4%)	8 (34.8 \pm 9.9%)	$\rho(F) = 0.373$
Two grafts, ($\% \pm S_p$)	19 (83 \pm 7.8%)	15 (65.2 \pm 9.9%)	$\rho(F) = 0.314$
Three grafts, ($\% \pm S_p$)	4 (17.4 \pm 7.9%)	7 (30.4 \pm 9.6%)	$\rho(F) = 0.314$
The total number of grafts, ($\% \pm S_p$)	50	51	$\rho(F) = 1.000$

Note: CV — calf vein; abs.— absolute number, S_p — standard error of the proportion. DM2 — type 2 diabetes mellitus; LITA — left internal thoracic artery; RA — radial artery; SV -saphenous vein

Within one year following the surgery, the patients were in real-life clinical practice settings: they were followed up by a cardiac rehabilitation professional, cardiovascular surgeon, as well as general practitioner in their home area. All the patients received acetylsalicylic acid at a dose of 100 mg/day, as well as beta-blockers and statins at individually adjusted doses. Nineteen patients with T2DM and 19 patients without diabetes received ACE inhibitors. Angiotensin receptor blockers were prescribed to two patients with T2DM and three patients without T2DM. The patients who received Clopidogrel for the experienced MI before the surgery continued its administration up to 12 months after the MI (10 patients with T2DM and 9 patients without diabetes). Seventeen patients with T2DM received oral anti-diabetic drugs as a monotherapy or combination therapy, 4 patients received therapy with insulin, and 2 patients controlled the glycemia through a low carbohydrate diet.

One year after the surgery, coronary graft angiography was performed in all of the patients to assess the graft patency.

Statistical methods. The type of distribution of continuous quantitative data was assessed by calculating the Shapiro—Wilk test. To compare two groups by quantitative measures, the Mann—Whitney U-test was applied. The two-tailed Fisher's test was used to compare the groups by qualitative binary features. Four subgroups were compared by quantitative

features using the Kruskal—Wallis test. The potential occlusion of coronary grafts was predicted by the logistic regression analysis. The critical value of the significance level is $\rho < 0.05$.

Results

Diabetes mellitus is a disease that contributes to the activation of hemostasis, therefore, first of all, the diabetic and non-diabetic patients were compared on all tested hemostatic parameters. The results are presented in Table 3.

No significant differences in the mentioned hemostatic parameters were revealed between the groups. The borderline difference was observed in the ADP-induced platelet aggregation: this aggregation was somewhat higher in the patients with T2DM.

Lupus anticoagulant was detected in 9 patients with T2DM and 12 patients without DM (ρ -value for the Fisher's test is 0.554). Among the tested diabetic patients, LA was detected in small amounts in 8 patients, and in a moderate quantity in 1 patient. In the non-diabetic patients, the small quantity of LA was reported in 9 cases, and the moderate one — in 3 cases. There were no cases of significant quantities of LA.

Table 4 presents values of the screening and confirmatory tests for lupus anticoagulant, as well as their ratios in both groups of patients.

Table 3. Comparison of hemostasis in the postoperative period in patients with and without type 2 diabetes mellitus

The studied parameter of hemostasis	Reference Values	Patients with DM2 (n=23), Me (P25; P75)	Patients without DM2 (n=23). Me (P25; P75)	p for the Mann—Whitney test
Fibrinogen, g/l	2–4	4.65 (3.7; 5.5)	3.9 (3.6; 5.3)	0.398
Soluble fibrin monomer complexes, mg/100 ml	3.5–15	19 (12; 26)	24 (14; 26)	0.899
D-dimer, mg/ml	≤0,3	0,5 (0.3; 1.3)	0,5 (0.4; 0.9)	0.499
Epinephrine-induced platelet aggregation, 5 µg/ml, %	78–88 *	40 (29; 56)	46 (31; 52)	0.955
ADP-induced platelet aggregation, 5 µg/ml, %	69–88 *	62 (51; 72)	58 (31; 62)	0.054

Note: * — reference values are provided for persons who do not receive antiplatelet therapy
Me — median, P25; P75 — upper and lower quartiles. ADP — adenosine diphosphate; DM2 — type 2 diabetes mellitus

Table 4. The significance of screening and confirmatory tests for the determination of lupus anticoagulant and LA ratio in patients with and without diabetes mellitus

Parameter	Patients with DM2 (n=23), Me (P25; P75)	Patients without DM2 (n=23). Me (P25; P75)	p for the Mann—Whitney test
LA1 screening, Dilute Russell's viper venom time, s	61 (56.3; 66.4)	60 (55.9; 72.2)	0.811
LA2 confirmative, phospholipid-rich dilute Russell viper venom time, s	44.8 (40.1; 47.0)	42,3 (39.5; 47)	0.238
LA ratio	1.27 (1.19; 1.35)	1.31 (1.16; 1.46)	0.451

Note: Me — median, P25; P75 — upper and lower quartiles. DM2 — type 2 diabetes mellitus

Relapse of angina during a year following the surgery occurred in 9 patients with T2DM and 14 patients without DM. There were no significant differences in the pain syndrome relapse incidence (ρ -value for the Fisher's test is 0.119). Based on the coronary graft angiography results, graft occlusions were found in 16 of 46 patients. Ten coronary graft occlusions occurred in the diabetic patients and 6 — in the non-diabetic patients. No occlusions of 2 or more grafts in the same patient were found during the study. Twenty percent of grafts (10 of 50) failed in the patients with T2DM, and 12% of grafts (6 of 51) — in the non-diabetic patients. No significant differences were revealed between the groups by the number of failed grafts (ρ -value for the Fisher's test is 0.288). Among the patients with T2DM, the pain syndrome relapse in 5 cases was due to the graft occlusion, in 4 cases — was not due to that reason, and asymptomatic graft occlusion was found in 5 patients. That is, pain syndrome relapse in patients with T2DM was not associated with the graft occlusion (ρ -value for the

Fisher's test is 0.417). In the non-diabetic patients, all 6 cases of graft occlusions were associated with pain syndrome relapse, 8 cases of angina relapse were not related to graft occlusions, and no asymptomatic occlusions were found. That is, pain syndrome relapse in patients without T2DM is statistically related to graft occlusions (ρ -value for the Fisher's test is 0.048).

Coronary artery stenosis cases were revealed de novo in 6 patients with T2DM and 7 patients without DM (ρ -value for the Fisher's test). However, angina relapse with the normal bypass patency was due to exclusively this phenomenon only in one patient with T2DM and one non-diabetic patient. In other cases, there was a combination of graft occlusion and atherosclerosis progression (3 cases in each group, respectively), or asymptomatic atherosclerosis progression (2 and 3 cases, respectively).

A fair question is the impact of medication therapy on the post-operative prognosis. Of particular

interest is the influence of Clopidogrel on the post-CABS prognosis. Among the patients with T2DM, coronary graft occlusions were found in 5 patients who received Clopidogrel and in 5 patients who did not receive Clopidogrel (ρ -value for the Fisher's test is 0.675). In the non-diabetic patients, these values were 2 and 7, respectively (ρ -value for the Fisher's test is 1.000). That is, the administration of Clopidogrel did not affect the probability of graft occlusions. The patients who continued to take Clopidogrel following CABS received it for different periods of time (1 to 9 months) up to 1 year after the experienced MI. In the group of patients with T2DM, the median course of the drug administration in the patients with graft occlusions was 1 month; ($P_{25} = 1$ month; $P_{75} = 5$ months); and in the patients without graft occlusions — 6 months; ($P_{25} = 5$ months; $P_{75} = 6$ months). Nevertheless, no association between the course of Clopidogrel administration and the probability of graft occlusions was revealed in the patients with T2DM (ρ -value for the Mann—Whitney test is 0.605). A similar situation is observed in the non-diabetic patients: the median course of the drug administration in the

patients with graft occlusions was 6 month; ($P_{25} = 2$ months; $P_{75} = 7$ months); and in the patients without graft occlusions — 5 months; ($P_{25} = 5$ months; $P_{75} = 10$ months) (ρ -value for the Mann—Whitney test is 0.858).

According to the data obtained, prescription of ACE inhibitors, angiotensin receptor blockers, as well as peculiarities of hypoglycemic therapy, did not affect the probability of coronary graft occlusions (ρ -value for the Fisher's test is ≥ 0.05).

In order to find out whether values of the hemostatic system parameters in the post-CABS period are associated with the probability of coronary graft occlusions, hemostatic parameters in the patients with graft occlusions were compared to those in the patients with properly functioning grafts, taking into account the existence of diabetes mellitus. The results are presented in Table 5.

As can be seen, no statistically significant differences in the hemostatic system parameters during the post-surgery period were revealed between the

Table 5. Patients with and without graft occlusions according to the hemostasis parameters level in the postoperative period, considering presence or absence of diabetes mellitus: Comparison

Parameter	Patients with DM2 without graft occlusion (n = 13), Me (P25; P75)	Patients with DM2 with graft occlusion (n = 10), Me (P25; P75)	Patients without DM2, without graft occlusion (n = 17), Me (P25; P75)	Patients without DM2 with graft occlusion (n = 6), Me (P25; P75)	Kruskal—Wallis test, ρ
Fibrinogen, g/l	4.25 (3.65; 4.95)	5.45 (4.5; 6)	4 (3.7; 5.3)	3.8 (3.1; 5.1)	3.697 $\rho = 0.296$
Soluble fibrin monomer complexes, mg/100 ml	17 (12; 26)	21 (18; 26)	24 (17; 26)	12 (4; 21)	6.222 $\rho = 0.101$
D-dimer, mg/ml	0.5 (0.3; 0.8)	0.7 (0.4; 1.4)	0.5 (0.4; 0.9)	0.4 (0.2; 0.5)	4.181 $\rho = 0.243$
LA ratio	1.195 (1.16; 1.129)	1.345 (1.25; 1.39)	1.36 (1.18; 1.48)	1.23 (1.15; 1.27)	7.002 $\rho = 0.072$
ADP-Induced platelet aggregation, 5 μ g/ml, %	62 (57; 72)	63 (40; 71)	58 (33; 61)	59.5 (29; 65)	4.085 $\rho = 0.254$
Epinephrine-induced platelet aggregation, 5 μ g/ml, %	43 (29; 61)	32 (30; 55)	48 (31; 53)	39.5 (33; 47)	0.738 $\rho = 0.864$

Note: Me — median, P25; P75 — upper and lower quartiles. DM2 — type 2 diabetes mellitus

patients with coronary graft occlusions and the patients without occlusions. However, the borderline differences were observed for LA ratios.

Lupus anticoagulant was previously found in 6 of 10 diabetic patients with graft occlusions; and only in 1 of 6 non-diabetic patients with graft occlusions (p -values for the Fisher's test are 0.102 and 0.069, respectively). That is, the fact of detecting the lupus anticoagulant following CABS was not associated with graft occlusions in the long term.

To give a final answer to the question of the impact of hemostatic parameters on the probability of graft occlusions, logistic regression analysis was performed.

There were 10 blocked grafts among the patients with T2DM ($n = 23$). Based on the logistic regression analysis, the only hemostatic parameter affecting the probability of coronary graft occlusions was LA ratio. The logistic regression equation in this case was as follows: $Y = B_0 + B_1 \cdot LA_{ratio}$. χ^2 for the model as a whole — 6.676; $p = 0.009$; $B_0 = -15.827$; $B_1 = 12.279$; prognostic χ^2 — 4.542; odds ratio = 2.27; 95% CI — 1.119–4.238; $p = 0.033$. Having calculated Y , the graft occlusion probability for any specific patient can be calculated by the formula $P = e^Y / (1 + e^Y)$, where e — base of the natural logarithm that approximately equals to 2.72. Y in this case is a natural logarithm of the odds ratio for a graft occlusion.

Example calculations. 1) LA ratio = 1.17 in patient A with type 2 diabetes mellitus on Day 14 following CABS.

$$Y = -15.827 + 12.279 \cdot 1.17 = -1.461$$

The graft occlusion probability is calculated by the formula $P = e^Y / (1 + e^Y)$; $P = 2.72^{-1.461} / (1 + 2.72^{-1.461}) = 0.188$; i.e., according to the logistic regression equation, the graft occlusion probability in the patient with these baseline data will be 18.8%.

2) LA ratio = 1.39 in patient B with type 2 diabetes mellitus on Day 14 following the CABS.

$$Y = -15.827 + 12.279 \cdot 1.39 = 1.241$$

$P = 2.72^{1.241} / (1 + 2.72^{1.241}) = 0.775$; i.e., according to the logistic regression equation, the graft occlusion probability in the patient with these baseline data will be 77.5%.

In the non-diabetic patients, the logistic regression analysis did not show any association between the hemostatic parameters and the prospective graft occlusion probability (p -value for χ^2 in the logistic regression model is >0.05).

Discussion

No statistically significant differences in blood content of the tested hemostatic parameters were revealed between the patients with and without T2DM in the post-CABS period. According to literary data, the patients with T2DM were expected to have more pronounced activation of both coagulative and vascular-platelet hemostasis [8]. The absence of significant differences in hemostasis status between the patients with T2DM and non-diabetic patients is likely due to that traumatic intervention under cardiopulmonary bypass is a strong activator of blood coagulation. At the same time, the patients with T2DM showed a tendency to higher ADP-induced platelet aggregation, which was fully consistent with hemostatic features described for patients with T2DM [9].

According to the data obtained, the content of fibrinogen, SFMC, D-dimer, as well as the induced platelet aggregation, was not related to graft occlusions within a post-operative year. This is partly confirmed by literary data: hypercoagulable state in the CABS perioperative period increases the probability of thrombotic events, but the impact of activated hemostasis on the coronary graft patency has not yet been proven. Based on the results of Study BARI 2D, high levels of fibrinogen and D-dimer following revascularization in patients with T2DM were associated with the risk of MI, stroke and total mortality within 5 years after the intervention [10]. The study conducted by M. Zacho et al. confirms the existence of a statistical relationship between the hypercoagulable state (based on thromboelastography findings) and the development of post-CABS thrombotic events. At the same time, the hypercoagulable state was not associated with

impaired coronary graft patency in the first post-operative months [41].

Based on the findings of this study, the patients with T2DM, unlike non-diabetic patients, showed no association between the pain syndrome relapse and the impaired coronary graft patency, the graft occlusions were asymptomatic in 5 of 40 cases. The most probable cause of this feature is silent myocardial ischemia as a manifestation of autonomic neuropathy (cardiovascular form). Among patients with CAD and T2DM, silent ischemia occurs at a frequency of up to 50%, and is an adverse prognostic factor [42]. Therefore, instrumental methods for diagnosis of myocardial ischemia (loading tests, 24-hour ECG monitoring) should be an integral part of the follow-up of patients with T2DM following CABS.

For the first time, the prospective study has demonstrated the negative impact of antibodies with LA potency on the prognosis of coronary graft operation in patients with T2DM. K. E. Morton et al. earlier established the association between the carriage of anti-cardiolipin antibodies and the high probability of coronary graft occlusions [43]. Following CABS, LA is found in a large number of patients ($46 \pm 7\%$). The identification of LA in the tested patients can include the following clinical situations:

1. Antiphospholipid syndrome — if LA remains in blood for more than 12 weeks, and there is a history of confirmed thrombosis (in particular, MI). Secondary thromboprophylaxis and hematologist follow-up are certainly indicated for such patients [44].
2. Asymptomatic LA carriage — if LA remains in the blood of patients without a history of thrombosis for more than 12 weeks [44].
3. Transient LA occurrence — occurs when LA is not found in blood in 12 weeks after the first identification. The occurrence of antibodies with LA potency can be a manifestation of systemic inflammation in response to major surgery under cardiopulmonary bypass [45].

The relevant objective is further study of the clinical significance of anti-phospholipid antibodies for the development of cardiovascular morbidity associated with atherosclerosis and atherothrombosis.

Conclusions

1. No significant differences in the blood content of fibrinogen, SFMC, D-dimer were revealed between diabetic and non-diabetic patients during the post-CABS period. The groups also had no differences in the induced platelet aggregation and the LA identification rate.
2. Coronary graft occlusions in the patients without T2DM manifested as angina relapse in all cases for a year following the surgery, but were not observed in the patients with T2DM.
3. Within one year following CABS, the patients with T2DM and high LA ratio are at an increased risk of coronary graft occlusions.

Contribution of Authors

Lisyutenko N.S. — collection and analysis of primary clinical data, manuscript writing

Morova N.A. — development of the concept and design, formulation of conclusions, interpretation and critical analysis of the results

Tsekhanovich V.N. — collection and analysis of primary clinical data, interpretation and critical analysis of results

All authors read the manuscript, approved its final version, and consented to publication

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