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The Effect of Glycemia for Complications Development after Coronary Revascularization in Patients with Coronary Heart Disease and Diabetes

ABSTRACT

The aim of our study was to evaluate the relationship of hyperglycemia and postoperative hospital complications after coronary artery bypass surgery in diabetic patients. The study included 482 patients who underwent coronary artery bypass surgery (CABG) in the period from 2003 to 2008 in The Bakoulev Scientific Center for Cardiovascular Surgery. In our study DM is not associated with an increased risk of major cardiovascular events (death, stroke, myocardial infarction) after CABG. However, the presence of diabetes is associated with an increase in the number of postoperative infectious complications. Hyperglycemia more than 200 mg / dL is a risk factor that increases the risk of postoperative complications such as death, stroke, acute renal failure, arrhythmias, and infectious complications.

Keywords: coronary artery disease, diabetes mellitus, hyperglycemia, coronary artery bypass grafting.

INTRODUCTION

The prevalence of diabetes mellitus (DM) among patients with coronary heart disease has led to a sharp increase in their numbers among the contenders for coronary revascularization. According to the literature, from 30 to 40% of diabetic patients in need of surgical treatment of concomitant coronary artery disease [1].

However, the results of the study suggest that the results of coronary artery bypass grafting (CABG) in patients with diabetes, in general, worse than others [5,6]. Szabó Z. et al. evaluated early and 30-day results of CABG in patients with diabetes (540 patients) and patients without diabetes (2,239 patients). Thirty-day mortality in the group of diabetics was 2.6% and in the control group was 1.6% ($p = 0.15$). However, the presence of diabetes was accompanied by a 1.9-fold increased risk of long-term mortality compared to patients without diabetes [15]. In recent studies more and more authors began to point to comparable levels of postoperative mortality between patients with and without diabetes mellitus [3, 11]. In addition, it points to an increased risk of neurological, renal complications and increased wound infections [2, 8, 9, 10]. In recent years, the glycemic control during CABG surgery and other cardiac surgery has become the object of intense study. According to most researchers, hyperglycemia that occurs in the postoperative period is

associated with increased morbidity in the postoperative period. Several authors indicated the need for careful control of intraoperative glucose, in order to correct the violations and prevent the adverse effects of hyperglycemia on the cardiovascular system. The **aim** of our study was to evaluate the correlation of hyperglycemia and postoperative hospital complications after coronary artery bypass surgery in diabetic patients.

MATERIALS AND METHODS

The study included 482 patients who underwent coronary artery bypass surgery (CABG) in the period from 2003 to 2008 in the Bakoulev Scientific Center for Cardiovascular Surgery. Patients were divided into 2 groups: group 1 included 282 patients with coronary artery disease with diabetes, the second group (control) - 200 CHD patients without diabetes. In both groups of patients are male dominated. By the number of women groups did not differ. The age of patients in group 1 averaged $57 \pm 7,5$ years, which is significantly lower than in the control group 2 ($62 \pm 11,2$ years.), $P < 0.01$. Also, most patients' in-group 1 had a history of myocardial infarction, clinically more severe angina, hemodynamically significant atherosclerosis of brachiocephalic arteries, chronic renal failure. Average EuroScore in Group 1 was 4.2, in comparison with the group 2 was significantly higher ($p = 0.019$). In addition, patients with diabetes had a higher body mass index, more frequent hypertension and hyperlipidemia. Overall, the survey results indicated an objectively more severe clinical condition of patients in group 1 patients underwent bypass surgery on a beating heart or cardiopulmonary bypass (no significant differences between groups). Index revascularization in group 1 was 2.9, group 2 - 3.0 and was not significantly different. All patients in Group 1 ($n = 282$) suffering type 2 diabetes. Thus, patients with type 2 diabetes, lung flow (available only on the hypoglycemic diet) were excluded. 31 patients (11%) had a severe course of type 2 diabetes require regular insulin. The remaining 251 (89%) patients with hypoglycemic effect turned out to be using oral antidiabetic drugs, including drugs sulfonylurea - 53% biguanides - 34%, thiazolidinediones - 8%, other - 5%. Use of oral hypoglycemic agents in diabetic patients discontinued for 12-48 hours prior to surgery. At the stage of preoperative preparation for readings of planned changes the hypoglycemic therapy and transfer patients to insulin. Excess fasting glucose above 180 mg / dL (10 mmol / L) is an indication for transfer to insulin. The average fasting blood glucose level in the diabetic group was 134 mg / dl (7.44 mmol / l), which expectedly higher in comparison with the control group 83 mg / dl (4.6 mol / l), $p < 0.001$. On preoperative criteria for compensation of carbohydrate metabolism as measured by the level of glucose, consistent with 54% of patients, 28% were subcompensation patients. In 18% of

patients failed to achieve the level of compensation or subcompensation.

For the assessment of postoperative glycemic glucose monitoring was conducted at baseline (before surgery), the day of surgery and for the next 10 days after the operation. Repeated daily blood sampling result is determined by calculating the average daily figure.

The primary study endpoint in the hospital stage was considered fatal outcome, nonfatal myocardial infarction (MI), nonfatal stroke. The secondary endpoints carried infectious-inflammatory complications (including mediastinitis), bleeding, pulmonary complications, acute renal failure, supraventricular arrhythmias, and the duration of postoperative stay.

Statistical analysis of the data

The study used a statistical analysis performed using the software package «Statistica 8.0». For compare two groups of high-quality binary features used double-sided version of Fisher's exact test. For compare two groups in quantity normally distributed attributes used Student's t test. Differences were considered statistically significant at $p < 0,05$. To quantify the probability of the outcome associated with the presence of risk factors was carried out calculation of the relative risk with 95% confidence intervals (CI). Calculation of the confidence interval for the odds ratio was conducted by the method of Woolf.

RESULTS

In group 1 to achieve the primary end point (death, MI, stroke) were observed in 24 patients (8.5%) in group 2 - 14 patients (7%), $p > 0.05$. In-group 1, the incidence of atrial fibrillation, acute renal failure, and infectious-inflammatory complications was significantly higher in comparison with the control group. The duration of the postoperative period in the group with diabetes was also more. In general, despite the lack of significant differences on major cardiovascular postoperative complications (death, myocardial infarction and stroke), hospital results in patients with diabetes were generally worse than in the control group (Table. 1).

Table 1

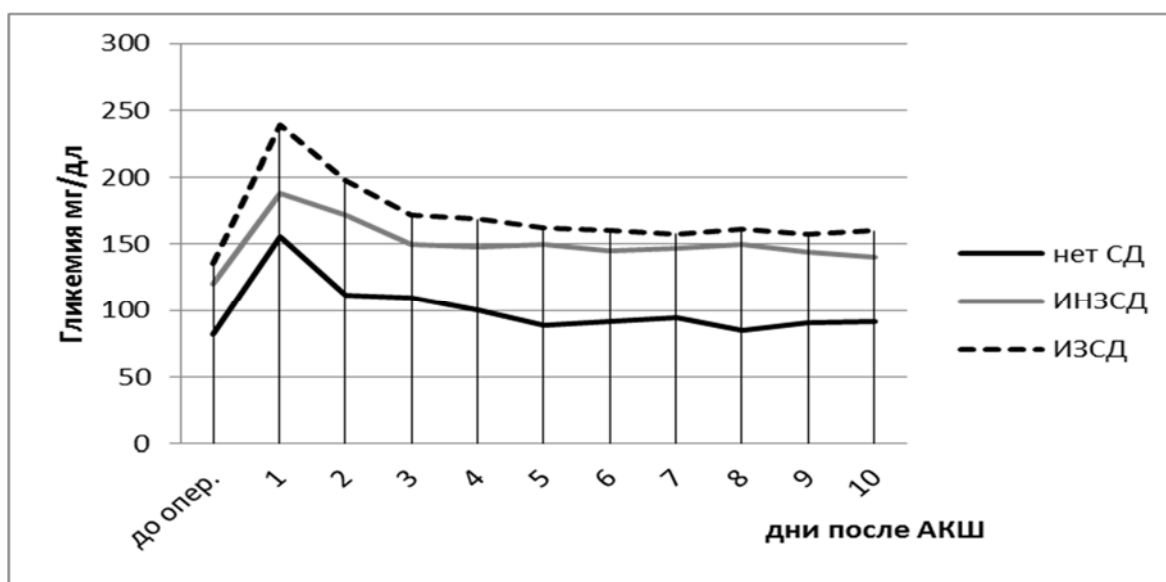
Postoperative complications at the hospital period

	1 group with diabetes	2 group control	p
Death	8 (2,84%)	4 (2%)	0.3
Myocardial infarction left ventricular	5 (1,77%)	4 (2%)	0.5
CVA	11 (3,9%)	6 (3 %)	0.3
Atrial fibrillation	25(9%)	10 (5%)	0,035
Postoperative bleeding	13 (4,6%)	7 (3,5%)	0.1
Pulmonary complications	10 (3,5%)	6 (3%)	0.5
Mediastinitis	15 (5,3%)	6 (3%)	0,037
Any infectious-inflammatory complications *	130(46%)	69(34,5%)	0,01
Acute renal failure	13 (4,6%)	5 (2,5%)	0,04
The duration of postoperative hospital stay of the day more than 10 days.	69 (24,5%)	30 (15%)	0,001

Note: * superficial wound complications, pneumonia, pleuritis, pericarditis, urinary tract infections, sepsis, mediastinitis.

As stated previously, all patients underwent perioperative monitoring of blood glucose at baseline and 1 to 10 days after CABG. Peak lift glucose accounted for 1-2 days after surgery, which is associated usually with a common perioperative stress, the influence of cardiopulmonary bypass, using contra insular hormones and other factors. Perioperative blood glucose among patients in-group 1 in all inspection points was significantly higher (p trend <0.001) in comparison with the group 2. When comparing the dynamics of glycaemia from diabetic patients initially treated with oral hypoglycemic agents and insulin-dependent diabetes patients, it was found that the degree hyperglycemia with insulin dependent diabetes in the perioperative period was greater ($p = 0.01$) (Fig. 1).

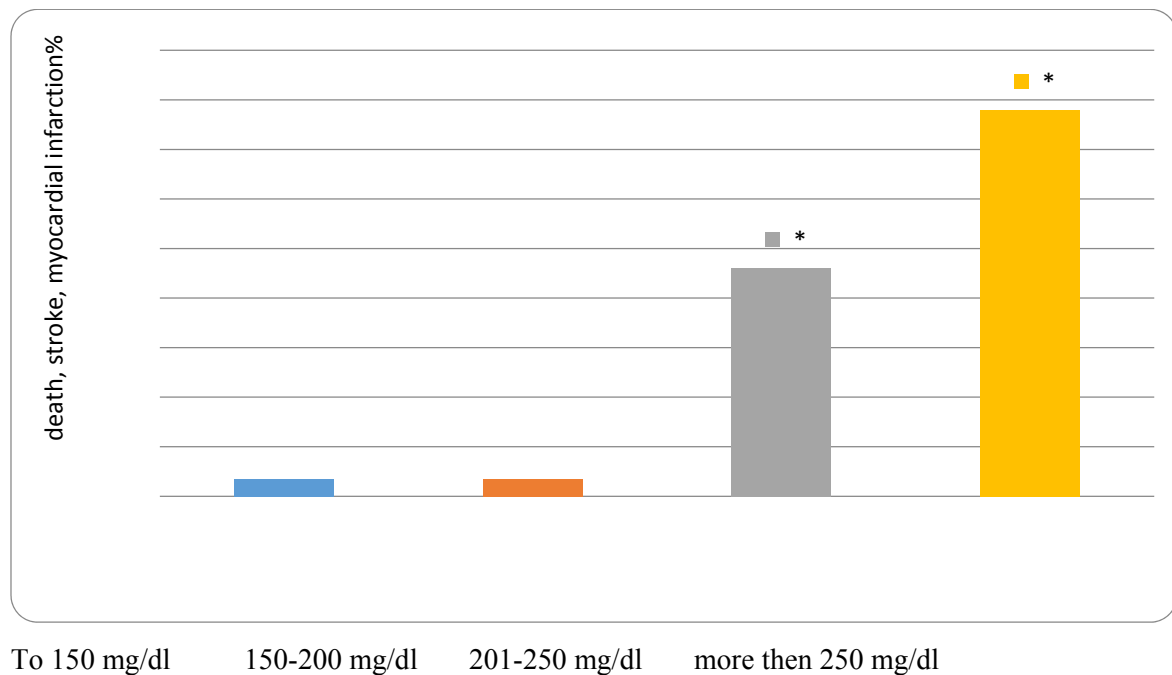
Figure 1. Dynamics of perioperative glycemias in patients with insulin-dependent diabetes and non-insulin dependent diabetes, compared with patients without diabetes



Abbreviations: СД – diabetes, ИНЗСД – non-insulin dependent diabetes, ИЗСД – insulin-dependent diabetes.

In identifying the correlation between glucose level and the onset of the primary endpoint was observed that blood glucose above 200 mg / dl during the first 48 hours after surgery in patients with diabetes was accompanied by a significant increase in the number of analyzed complications (Fig. 2).

Figure 2. Correlation of postoperative glucose level (first 48 hours) and the occurrence of postoperative complications (death, stroke, myocardial infarction) in patients with diabetes



We conducted a risk assessment of postoperative complications in patients allocated to CABG in the presence of diabetes (Table. 2, A) and in the presence of hyperglycemia greater than 200 mg / dl (in the first 48 hours after surgery) (Table. 2, B). Statistical analysis confirmed the absence of the correlation diabetes and increases the risk of the primary points in the immediate postoperative period. Also, there was no significant effect of diabetes on the development of acute renal failure, pulmonary complications, supraventricular arrhythmias and bleeding. However, it was found that the presence of diabetes increases the risk of mediastinitis (OR - 1.8, 95% CI 1,3-2,2, $p = 0.039$), and any infectious-inflammatory complications (OR, 2.3; 95% CI, 1.9-2.8, $p = 0.01$) and prolonged postoperative hospital stay (OR, 2.2; 95% CI - 1.5-2.7, $p = 0.001$).

Table 2

Correlation of diabetes (A) and perioperative hyperglycemia greater than 200 mg / dl (B) and the risk of hospital complications A.

Complications	Diabetes		
	OR	95% CI	p
Mortality	1,4	0,5 – 3,2	128
Myocardial infarction	0,8	0,2-1,7	0,42
Stroke	1,9	1.1 – 6.6	0,063
Acute renal failure	2,1	1.1 – 3.0	0,06
Pulmonary complications	1,2	0,4 – 2,2	0,15
Supraventricular arrhythmias	1,5	0,7 – 3,9	0.09
Mediastinitis	1,8	1,3 – 2,2	0,039
Any infectious-inflammatory complications	2,3	1,9-2,8	0,01
Bleeding	1,4	0,7 – 2,4	87
Prolonged postoperative stay	2,2	1,5-2,7	0,01
B.			
Complications	Hyperglycemia $\geq$ 200 mg/dl		
	OR	95% CI	p
Mortality	1,7	1,4 – 2,4	38
Myocardial infarction	2,3	1,2-3,7	0,6
Stroke	2,1	1.5 – 3,0	0,041
Acute renal failure	1,6	0,8 – 2.0	0,033
Pulmonary complications	2,8	0,7 – 4,2	0,26
Supraventricular arrhythmias	1,35	1,2 – 1,6	0.01
Mediastinitis	2,6	2,0 – 3,1	0,001
Any infectious-inflammatory complications	4,7	4,16 – 5,2	0,001
Bleeding	2,3	0,2 – 4,4	0.18
Prolonged postoperative stay	2,5	1,9-2,9	0,001

Radically different pattern was observed in the group of patients with postoperative hyperglycemia: the development of hyperglycemia after CABG was associated with significant

increased risk of mortality (OR, 1.7; 95% CI 1.4-2.4, $p = 0.038$), stroke (OR-2 1, 95% CI 1.5-3.0, $p = 0.04$), acute renal failure (OR, 1.6; 95% CI, 0.8 - 2.0, $p = 0.03$), supraventricular rate (OR, 1.35; 95% CI 1.2-1.6, $p = 0.01$), mediastinitis (OR, 2.6; 95% CI 2.0-1.6, $p = 0.001$, any infectious and inflammatory complications (OR - 4.7, 95% CI 4.2-5.2, $p = 0.001$), as well as an increase in the duration of postoperative hospital stay days (OR, 2.5; 95% CI: 1,9 2.9, $p = 0.001$). Thus, the development of hyperglycemia in the immediate postoperative period is more important and significant risk factor than the associated diabetes. Several studies have shown that hyperglycemia is the reason for the growth of morbidity and mortality in all patients undergoing CABG, regardless of the presence of diabetes. Thus, Dons T. et al. in the analysis of clinical outcomes of 6280 patients undergoing cardiac surgery showed that patients with high peak levels of glucose (20 mmol / L) during CABG had the highest rates of morbidity and mortality, regardless of the presence of diabetes [4]. Fish L. et al. discovered the following regularity - an increase of glycaemia in the postoperative period (more than 14 mmol / L) in 10 times increased risk of various complications [7]. Thus, these studies clearly show that, regardless of the presence of diabetes, increased levels of glucose in the perioperative period is associated with an increase in morbidity and mortality.

In our study, despite a comparable incidence of major cardiovascular events (death, myocardial infarction, stroke), immediate results after CABG in patients with diabetes have been worse, primarily due to increased infectious complications. Also, it was shown that postoperative hyperglycemia greater than 200 mg / dL had an increased risk of early cardiovascular events (death, stroke), and also, acute renal failure, arrhythmias, and infectious and inflammatory events (including mediastinitis). Our results are consistent with data presented in other studies [6,12,13,14], where it was shown that uncontrolled intraoperative hyperglycemia is a predictor of hospital mortality and increase the growth of post-operative complications, including infection. Similar results confirming growth complications of hyperglycemia presented and other publications.

CONCLUSION

The presence of diabetes in patients referred to CABG, is not accompanied by an increased risk of major cardiovascular events (death, stroke, myocardial infarction), but is associated with an increase in the number of infectious complications. Hyperglycemia more than 200 mg / dL is a risk factor that increases the risk of postoperative complications such as death, stroke, acute renal failure, arrhythmias, and infectious and inflammatory complications. In patients with insulin-dependent diabetes occurs more severe decompensation of carbohydrate metabolism in the postoperative period compared with patients with diabetes on medication hypoglycemic therapies, and therefore they have a higher risk of postoperative complications. Ensuring careful monitoring of blood glucose levels in the perioperative period reduces postoperative morbidity and improve the immediate results of the operation.

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