

*УДК 616.379-008.64*

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**MEASURES TO ELIMINATE THE RISK OF DIABETES IN MEN  
WITH RISK FACTORS FOR CARDIOVASCULAR DISEASES**

**Resume:** The paper considers potential ways in which the dynamics of risk factors for cardiovascular diseases over time could mediate the effect of glycosylated hemoglobin on the risk of developing cardiovascular diseases during a 28-year follow-up during a study on the control of diabetes and its complications of the Epidemiology of interventions and complications in diabetes mellitus.

**Keywords:** diabetes mellitus, risk factors, cardiovascular diseases, men, assessment, risk of development.

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**МЕРЫ ПО УСТРАНЕНИЮ РИСКА РАЗВИТИЯ ДИАБЕТА У  
МУЖЧИН С ФАКТОРАМИ РИСКА СЕРДЕЧНО-СОСУДИСТЫХ  
ЗАБОЛЕВАНИЙ**

**Резюме:** В работе рассмотрены потенциальные пути, с помощью которых динамика факторов риска сердечно-сосудистых заболеваний с течением времени могла бы опосредовать влияние гликозилированного гемоглобина на риск развития сердечно-сосудистых заболеваний в течение 28-летнего наблюдения в ходе Исследования по контролю диабета и его

осложнений Эпидемиологии интервенций и осложнений при сахарном диабете.

**Ключевые слова:** сахарный диабет, факторы риска, сердечно-сосудистая заболевания, мужчины, оценка, риска развития.

**Relevance.** Diabetes mellitus is one of the most powerful risk factors for the development of cardiovascular diseases. 50% of patients with type 1 diabetes and 80% of people with type 2 diabetes have early disability and premature death due to cardiovascular complications[3].

People suffering from diabetes are often at risk of strokes, heart attacks and high blood pressure. Problems with vessels in the extremities are also a frequent complication in diabetes mellitus. At the same time, the development of complications may be asymptomatic for several years.

It is a mistake to think that heart diseases develop in adulthood and old age. In diabetes mellitus, cardiovascular diseases can occur up to 30 years[7].

Diabetes mellitus (DM) is a severe endocrine disease in which the blood sugar level rises (hyperglycemia) as a result of a violation of the production of the hormone insulin by the pancreas or a decrease in the sensitivity of body tissues to it.

Today there are more than 40 different factors that, under appropriate conditions, can lead to diabetes mellitus.

Inheritance is characteristic of both types of diabetes, but it is more common with type 2 diabetes, it is inherited in 80% of cases through the mother and father. Type 1 diabetes is inherited on the maternal side in 3-7% of cases, on the paternal side - in 10% of cases. The development of diabetes is caused by certain defects in the genes responsible for the full synthesis of insulin. It can be transmitted not only to children! but also after a generation, increasing the risk of developing DM by 2-6 times. There is a very high probability of the disease in twins[4].

The main provoking factor of type 1 diabetes is considered to be viral infections: rubella, chickenpox, mumps, viral hepatitis. Viruses of these diseases selectively infect insulin cells, which lose the ability to synthesize full-fledged insulin. This leads to the appearance of pronounced symptoms of diabetes: thirst, increased urination, increasing weight loss, and if timely medical care is not provided, and to the development of diabetic coma with loss of consciousness.

Despite the progress made in treatment methods in recent years, the risk of developing cardiovascular diseases in type 1 diabetes remains higher compared to that in an age-comparable population without diabetes mellitus. During the average follow-up period (up to 17 years) during the Study on the Control of diabetes mellitus and its complications (Diabetes Control and Complication Trial) and the observation of its spread in the study of the Epidemiology of interventions and complications in diabetes (Epidemiology of Diabetes Interventions and Complications), it was found that on average 6.5 years of intensive antidiabetic therapy leads to a decrease in the average the level of glycosylated hemoglobin up to  $\approx 7\%$  (53 mmol/mol); to reduce the risk of developing cardiovascular diseases by 42%; and reducing the risk of nonfatal myocardial infarction, stroke or death from cardiovascular diseases (major atherosclerotic cardiovascular events) by 57% compared with traditional therapy, in which the average value of glycosylated hemoglobin is  $\approx 9\%$  (75 mmol/mol).

The reliability of the protective effect of the 6.5-year intensive care course was confirmed by at least another 10-year observation period. Over the entire period of both studies (28 years), intensive therapy reduced the incidence of cardiovascular diseases by 30% compared to traditional therapy, despite similar levels of glycemia during most of the follow-up period of the epidemiology of interventions and complications in diabetes.

The high frequency of cardiovascular complications in patients with diabetes mellitus (DM) is one of the most important problems not only of domestic, but also of world health. Expenses for the treatment of diabetes and its complications in the United States in 2017 amounted to \$ 327 billion, of which 71% accounted for complications associated with atherosclerosis [3]. According to the FORESIGHT-DM2 study, in the Russian Federation the cost of treatment of DM2 is more than 7 thousand. \$ per 1 patient per year, and 53.5% of this amount is the loss of GDP due to disability of patients, 37.7% is direct medical costs, of which 57% is for the treatment of complications of diabetes and concomitant diseases, and the share of antihyperglycemic therapy is only 10% [2]. Unfortunately, it is not yet possible to significantly reduce the mortality rate from coronary heart disease in patients with diabetes in any country in the world. Sudden death in DM develops in men by 50%, and in women by 300% more often than in persons of the corresponding sex and age without diabetes [6].

The prevalence of coronary heart disease among patients with DM 2 is 2-4 times higher than the average in the population and is about 70-80%. According to a large study by INTERHEART, DM is one of the three most important causes of AMI in middle-aged men (after lipid metabolism disorders and smoking), more significant than arterial hypertension (AH) [8]. By the age of 50, almost half of patients with diabetes have at least one of the complications of coronary heart disease: unstable angina, MI, life-threatening cardiac arrhythmias; rapid development of chronic heart failure (CHF) [4]. According to the PROGNOSIS-CHD registry, for 7.3 years of follow-up of 504 patients with a confirmed diagnosis of CHD, the relative risk of developing the primary endpoint (deaths from all causes, fatal and non-fatal cardiovascular events) in the presence of DM increased by 1.7 times, in the presence of a combination of DM with arterial hypertension - by 2.4 times [7].

The main risk factor for the development of cardiovascular complications in patients with DM 2 is hyperglycemia. The results of numerous studies have demonstrated that a decrease in the level of glycated hemoglobin (HbA1c) is accompanied by a decrease in the risk of specific vascular complications of diabetes. The most significant is the DCCT (Diabetes Control and Complications Trial) study conducted in 1982-1989 with the participation of a large group of patients with type 1 diabetes mellitus (DM 1), including adolescents. Improvement of glycemic control was shown during the transition from traditional to intensive insulin therapy regimen, which was accompanied by a reduction in the risk of development and progression of vascular complications [2]. The EDIC study (The Epidemiology of Diabetes Interventions and Complications Research Study), which was a continuation of the DCCT study, demonstrated that 4 years after the transfer of all patients to an intensified insulin therapy regimen against the background of achieving the same glycemic control in both groups of adolescents, the risk of retinopathy progression remained lower in the group that initially received intensive treatment [1]. This phenomenon is called "positive metabolic memory". The results of this study showed that it is important not only to ensure a decrease in glucose levels to target levels, but also to prevent hypoglycemia, as well as significant fluctuations in blood glucose levels, since all these conditions initiate oxidative stress, chronic inflammation, endothelial dysfunction in the vessels and play an important role in the development of diabetic complications [1,6].

The problem of high cardiovascular risk in patients with DM2 is fully reflected in the current Russian clinical guidelines for the diagnosis and treatment of diabetes mellitus [3].

Establishing a significant role of a cardiologist in the management of a patient with DM2 is a matter of clinical necessity. The WHO global report on diabetes mellitus (2016) indicates that in order to achieve better results, capacity-building efforts in the field of diagnosis and treatment of diabetes

should be undertaken in the context of a comprehensive fight against non-communicable diseases, in particular with the combination of treatment of diabetes and cardiovascular diseases.

In this regard, a cardiologist should have sufficient knowledge in the field of prevention, diagnosis, treatment of diabetes and its complications, including knowing not only the known effects of the main classes of antidiabetic drugs, but also their pleiotropic cardiovascular effects, as well as the possibility of using hypolipidemic and antihypertensive therapy in relation to patients with DM2.

The most important condition for modern treatment of DM2 is early diagnosis of this disease, since an increase in the duration of "untreated" diabetes significantly worsens the patient's prognosis. A cardiologist and a therapist are often "first contact" doctors who identify glucose metabolism disorders in people with cardiovascular pathology.

It is known that about 30% of patients admitted to specialized clinics with a diagnosis of "ACS" have a history of impaired glucose tolerance or recently diagnosed diabetes.

A cardiologist should have in-depth knowledge and skills on issues of rational nutrition, adequate physical activity, correction of CVD risk factors such as smoking, hypertension and dyslipidemia. In this regard, the treatment of a patient with DM2, along with the long-term maintenance of glycemic targets, should be aimed at managing the prognosis of patients in terms of the risk of developing cardiovascular complications.

**The purpose of the study.** To study the risk assessment of diabetes in men with a risk factor for cardiovascular diseases and implement it in practice.

**Materials and methods of research.** To select the task, we selected 65 men with a risk factor for cardiovascular diseases and assessed the risk factor for diabetes using modern methods.

**The results of the study.** Studies on the control of diabetes and its complications have not suffered any cardiovascular event. This benchmark was reached in 2021, after which a formal analysis of risk factors was carried out. In the multivariate Cox model, which was also adjusted for age, duration of diabetes mellitus, use of angiotensin converting enzyme inhibitors and family history of myocardial infarction, it was revealed that the average level of glycosylated hemoglobin was a stronger predictor of future cardiovascular events than the level of average systolic blood pressure, low-density lipoprotein cholesterol, circulating triglycerides and pulse rate.

However, this analysis did not allow to modulate covariance effects over time and did not take into account the possibility of the influence of glycosylated hemoglobin on other risk factors for the development of cardiovascular diseases.

The study used data from 65 participants with one or more cardiovascular diseases and complications as a result of the development of diabetes mellitus, noted over 27 years of observation. Data analysis showed that the effect of the average value of glycosylated hemoglobin on the risk of developing cardiovascular diseases was constant, regardless of the passage of time.

With elevated values of glycosylated hemoglobin, the increase in the incidence of cardiovascular etiology was approximately 3.3 cases per 1000 patients per year. The predicted value (area under the curve) of glycosylated hemoglobin for a 10-year period decreased from about 0.72 over a 10-20-year interval to 0.69 over a 20-30-year interval, whereas the same value for traditional risk factors for cardiovascular diseases (systolic blood pressure, pulse rate, triglyceride levels and low lipoprotein cholesterol density) slightly increased.

The level of risk associated with each of the covariants remained unchanged over time. However, there was an indirect effect of the level of glycosylated hemoglobin in the blood serum on the development of risk factors

for cardiovascular diseases. In fact, the effect of glycosylated hemoglobin on the risk of developing cardiovascular diseases is due to its indirect effect on systolic blood pressure, pulse rate, triglycerides or low-density lipoprotein cholesterol. At the initial stage of the Study to control diabetes and its complications, people with high blood pressure and hypercholesterolemia were excluded. Thus, the only major risk factor associated with the operant was hyperglycemia, which naturally prevailed. Hyperglycemia may have a significant impact on the early stages of the progression of cardiovascular diseases, for example, the atherosclerotic process.

These results are of clinical significance for further understanding of possible mechanisms of development of cardiovascular diseases in type 1 diabetes mellitus. For 20-30 years of observations (27-37 years of the course of the disease), the level of low-density lipoprotein cholesterol mediated 31% of the effect of glycosylated hemoglobin. Therapy in this case should be aimed at reducing the level of low-density lipoprotein cholesterol in the blood serum. The results obtained by the authors further enhance the value of intensive control of glycemia at the initial stages of diabetes mellitus, and then the management of other risk factors for the development of cardiovascular diseases, since their activity increases over time.

Men of working age in 40% of cases at the time of examination have a very high risk of developing DM. At the same time, in most cases, a high risk of developing diabetes is combined with the presence of risk factors such as hypertension, dyslipidemia, hyperuricemia and LV. "FIND THE SEARCH".

In the future, an extended diagnosis in the form of a glucose tolerance test will determine the tactics of prevention and drug correction to slow down and prevent diabetes among people with high and very high cardiovascular risk.

**Conclusion.** In diabetes mellitus, in order to prevent cardiovascular diseases, careful control of body weight, daily physical exercises, smoking and

alcohol cessation are necessary. It is necessary to maintain three main indicators in the norm:

-the level of glycated hemoglobin (must correspond to the individual goal);

-blood pressure (less than 140/80 mmHg)

-low-density lipoprotein cholesterol (less than 2.5 mmol/l or 1.8 mmol/L, depending on the risk of adverse cardiovascular events).

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