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Effect of newly detected hyperglycemia on the course of coronary heart disease

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ABSTRACT

Mechanisms and causes of hyperglycemia (HG) during coronary heart disease (CHD), particularly in its unstable forms, remain not fully investigated. The study aimed to determine the effect of newly detected HG on the course of CHD and examine the features of carbohydrate metabolism in patients with CHD. The study was conducted in Moscow (Russia) in 2018-2021. A total of 139 patients with CHD aged 43 to 79 years were examined. All participants were divided into comparison groups, including 34 patients with average glucose levels, 28 patients with fasting HG, 46 patients with impaired glucose tolerance (IGT), and 31 patients with newly diagnosed type 2 diabetes. The range of laboratory examinations included general clinical tests of blood and urine, determination of blood urea, creatinine, C-reactive protein, bilirubin and its fractions, the activity of hepatic transaminases, the study of carbohydrate metabolism, lipidogram, ionogram, and coagulogram. First-time diagnosed HG was a fairly frequent diagnosis in CHD patients (in 105 (75.5%) of 139 patients examined). IGT and type 2 diabetes mellitus recently detected in CHD patients have common disease-causing factors: insulin resistance, lipid metabolism disorders, and sympathetic nervous system activation against the background of reduced parasympathetic effects. All of this should be considered in developing treatment regimens for CHD patients and controlling risk factors.

Keywords: hyperglycemia, coronary heart disease, insulin resistance

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death, accounting for nearly one-third of deaths globally [1, 2]. The most common CVD is coronary heart disease (CHD), affecting nearly 126 million people worldwide (1.72% of the world population). Its prevalence amounts to 1,655 people per 100,000 population [3, 4]. In the USA, over 15.5 million people over the age of 20 are suffering from CHD, and every 42 seconds, one resident of this country has a heart attack (myocardial infarction [MI). In the European Union, CHD causes half of all deaths from cardiovascular pathology. CVDs account for 16% of all deaths in the world. The first place among the causes of death is CHD, according to WHO. WHO data shows that from 2000 to 2019, diabetes mortality increased by 70% worldwide, while 80% of the disease cases were men. In the Eastern Mediterranean, diabetes mortality has increased by almost two times, and the estimated percentage indicates the highest increase in diabetes mortality in this region.

Due to its nature, CHD is a myocardial disorder caused by decreased blood flow into the coronary arteries, leading to an imbalance between the oxygen demand of the myocardium and actual oxygen consumption [5-7]. The major risk factors for CHD and its progression are family history, age, gender, high BP, high blood cholesterol levels, diabetes mellitus (DM), obesity, low physical activity, and smoking [8-12]. A diet that includes a lot of fried foods, fats, eggs, and sweetened beverages increases the probability of CHD by 56% [10]. Hyperglycemia (HG) is a predictor of DM. Prediabetes is more common in men and can turn into diabetes in the period from several months to several years. The heredity of DM is 30-70% [11, 12]. United Kingdom Prospective Diabetes Study (UKPDS) presented an assessment of risk factors for CHD in DM. It is the largest prospective observation of type 2 DM [13]. Gender and age data revealed that the risk factors for CHD in DM are (in order of importance) an increased concentration of low-density lipoprotein (LDL) cholesterol, a reduced concentration of high-density lipoprotein (HDL) cholesterol, HG, hypertension, and smoking. Men are more likely to have CHD at 40-45 years since they are in a larger number of risk groups (smoking and alcohol).

It is difficult to overestimate the role of HG as an independent predictor of the adverse course and prognosis of acute coronary syndrome (ACS) in people with DM and without it. The incidence and mortality from CHD in patients with DM exceed the expected levels with a simple summation of risks, indicating the direct effect of HG on the atherosclerotic process. Nevertheless, HG in patients without DM is associated with worse clinical outcomes and higher mortality from all causes compared to patients with DM [14]. An increase in blood sugar at the time of intake is usually perceived as a reaction to stress in an acute condition. However, in some cases, it can serve as a marker of an existing but not yet diagnosed type 2

DM or impaired glucose tolerance (IGT). According to observational studies, HG occurs in 32-38% of patients in hospital, in 41% of severe patients with ACS, in 44% of patients with heart failure, and in 80% of patients after coronary artery surgery [15].

Atherosclerotic injury of the coronary arteries is the primary cause (95% of cases) and the basis of CHD pathogenesis [16]. The key metabolic precondition for CHD progression is atherogenic dyslipidemia [17, 18]. There is a direct correlation between CHD incidence and mortality, on the one hand, and blood cholesterol level, on the other. In addition, hypercholesterolemia, along with smoking, obesity, hypertension, DM, and age, is the main predictor of atherosclerosis and its complications. A high rate of proactive lipids is associated with an increased risk of MI in the population (approximately 50%) [19].

Essential CHD pathogenesis factors also include reduced dilatation ability of coronary arteries; production of biologically active substances by endothelium, facilitating platelet hyperaggregation, blood hypercoagulation and having a vasoconstrictive effect; the coronary steal phenomenon; increase in myocardial oxygen demand; lack of collateral circulation; free radical oxidation of lipid, and others [20-22].

Over the past few years, there has been a growing interest in HG relative to the pathogenesis of CHD [23, 24]. HG is an early manifestation of insulin resistance (IR) to which CHD has an inextricable link [25, 26]. HG enhances atherogenic processes in blood vessels through generalized endothelial dysfunction, increased oxidative stress, and a high content of glycolysis products in the blood [27]. All this promotes the adherence of monocytes to the endothelium of blood vessels and their penetration into the vascular wall [23]. This monocyte-endothelial interaction as one of the principal triggering mechanisms of atherogenesis is directly related to free radical oxidation of lipids and oxidative stress. By penetrating the vascular intima, monocytes accumulate oxidized lipids and become foamy cells that secrete some biologically active substances that are critical atherogenesis processes [28, 29]. These are, in particular, such proinflammatory mediators as E-selectin, endothelial cell adhesion molecules-1, intercellular adhesion molecules-1, and others. Furthermore, they improve the adhesion capacity of the monocytes and their penetration into the vascular intima. Thus, HG promotes the formation of a specific atheroma cell component, leading to atheromatous lesions of the vascular walls [23, 30].

Research data suggest that HG has a negative predictive value in CHD, particularly in its unstable forms [31, 32]. In CHD, HG may be a consequence of stress response, prediabetes, or early DM. In any case, this pathology requires special attention from physicians due to its adverse effect on the course and outcomes of CHD [25, 33]. However, HG is not considered an obligatory symptom in the clinical course of CHD and its complications [23-25].

Despite numerous studies on this problem, the mechanisms and causes of HG during CHD, particularly in its unstable forms, remain not fully investigated. Furthermore, the diagnostic importance of HG in CHD is not fully understood. Consequently, there are some difficulties in choosing therapeutic tactics, which determines the relevance and the need to continue research on HG in CHD patients.

Aim of the Study

This study aimed to determine the effect of newly detected HG on the course of CHD and examine the features of carbohydrate metabolism in patients with CHD. Research objectives are, as follows:

a. conducting general clinical tests of blood and urine,
b. determining blood urea, creatinine, C-reactive protein, bilirubin, and its fractions,
c. studying the activity of hepatic transaminases, and
d. studying carbohydrate metabolism, lipidogram, ionogram, and coagulogram.

MATERIAL AND METHODS

Sample

The study was conducted at Lomonosov Moscow State University between October 2018 and June 2021.

The study enrolled 139 patients diagnosed with CHD, including 62 (44.6%) females and 77 (55.4%) males aged 43 to 79 years (mean age 61.37±5.12 years). Based on the reported impaired glucose metabolism, patients with CHD were divided into comparison groups, comprising 34 patients with normal blood sugar (glucose) levels, 28 patients with fasting hyperglycemia (FHG), 46 patients with IGT, and 31 patients with recently diagnosed type 2 DM. Of all CHD patients, 59 (42.4%) had a stable CHD, and 80 (57.6%) had an ACS. The control group included 30 healthy individuals (14 (46.7%) females and 16 (53.3%) males) aged from 40 to 67 years (mean age 48.03±4.06 years). In this study, practically healthy people are citizens who do not need dispensary observation.

Inclusion and Exclusion Criteria

Inclusion criteria

Diagnosis of CHD, blood glucose content ≥5.6 mmol/l, patient's aged 40-80 years, and informed signed consent to participate in the study.

Exclusion criteria

Type 1 or 2 DM, endocrine disorders, intake of drugs that affect carbohydrate metabolism, obesity degree I-III (30 and more kg per $1m^2$), acute or chronic somatic pathology at an acute stage or sub/decompensation, mental illness,oncological pathology, pregnancy/lactation, drug and alcohol abuse, smoking less than three years before inclusion in the study, patient reluctance to participate in the study, lack of adherence to the research algorithm and prescribed procedures.

Obesity was an exclusion criterion because it is a predictor of DM and CVDs. The status of type 2 DM: type 2 DM is excluded whereas recently diagnosed type 2 DM patients are included in the study.

Research Methods

The examination of each patient included a comprehensive review of complaints, medical history, physical examination, and laboratory and instrument investigation methods. The physical examination required anthropometric measurement of blood pressure.

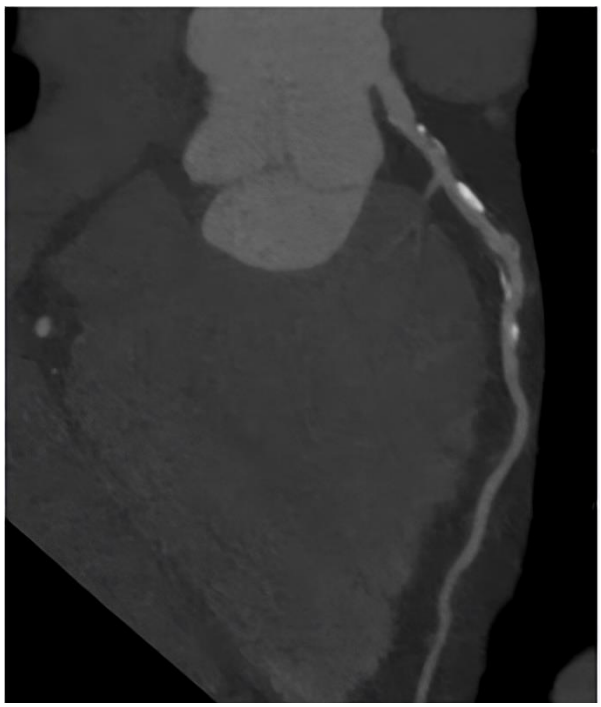

Figure 1. Complications arising from ACS & stable CHD (Source: Authors' own elaboration)

The range of laboratory examinations included general clinical tests of blood and urine, determination of blood urea, creatinine, C-reactive protein, bilirubin and its fractions, the activity of hepatic transaminases, the study of carbohydrate metabolism, lipidogram, ionogram, and coagulogram.

The state of carbohydrate metabolism was studied for fasting glucose levels and two hours following loading of blood insulin and C-peptide with glucose by the glucose oxidation technique (by immunoenzymatic analysis using standard kits DRG Instrumentals GmbH, Germany), and of glycosylated hemoglobin (HbA1c) by ion-exchange chromatography technique (HUMAN, Germany). The degree of IR was assessed by the HOMA2-IR index using HOMA CalculatorVersion 2.2.3 Diabetes Trials Unit, University of Oxford (UK). A HOMA2-IR value >1.80 was considered to indicate the presence of IR.

The blood lipid spectrum was examined for the content of total cholesterol (TC), LDL, HDL, triglycerides (TG) in blood using standard ACCENT-200 kits (PZ CORMAY S.A., Poland). The atherogenicity index (AI) was determined as (TC-HDL)/HDL.

Instrumental examination included electrocardiography (ECG), Holter ECG monitoring, and EchoCG.

Statistical Analysis

Statistical data processing was performed using Statistica software for Windows 10 Pro (Stat Soft inc., USA) and Microsoft Excel 2013 (Microsoft, USA). Mann-Whitney U-test was used to compare quantitative indices. Values were presented as mean (M)±standard deviation (SD). The differences were considered statistically significant at $p<0.05$. In comparing the frequency of the indicators, the odd ratio (OR) was calculated (using the Past software, version 4.08).

Compliance With Ethical Standards

The study was undertaken following the key points of international guidance on Good Clinical Practice (1996), the Helsinki Declaration (1964-2013), and other international regulations.

Table 1. Gender & age differences, anthropometric parameters, & heart performance indicators in patients with CHD in terms of glucose metabolism disorders

Glycemic status	Age vs. gender (years [M±SD])	
	Female (n=62)	Male (n=77)
Normal blood sugar	69.51±6.70	57.09±4.83*
FHG	67.45±4.62	56.61±5.48*
IGT	66.73±5.08	63.59±6.10
Type 2 DM	61.07±6.21**	64.20±5.75
Average blood pressure (mmHg)	147/92	150/94
Heart rate	89±4	90±3
Body weight (kg)	79.00±3.60	80.10±1.40
Chest circumference (cm)	84.00±0.70	85.00±0.90

Note. *Differences are statistically significant when compared to women ($p<0.05$); **Differences are statistically significant when compared to women in group with normal blood sugar levels ($p<0.05$); FHG: Fasting hyperglycemia; IGT: Impaired glucose tolerance; & DM: Diabetes mellitus

RESULTS

Among CHD patients examined, only 34 (24.5%) had normal blood sugar levels. First-diagnosed FHG was present in 28 (20.1%) patients with CHD, IGT was observed in 46 (33.1%) patients, type 2 DM–in 31 (22.3%) patients. In analyzing the structure of CHD, the newly detected HG was found to be 1.76 times ($p<0.05$) more common in ACS patients than those with stable CHD (**Figure 1**). Moreover, FHG was significantly more common in patients with stable forms of CHD (in 47.4% versus 14.9% of cases, $p<0.0001$), and IGT was more typical for ACS patients (in 50.8% versus 28.9% of cases, $p=0.0322$). Type 2 DM was also most prevalent in ACS patients (in 28.3% of cases versus 13.6% of cases, $p=0.0371$).

When studying gender and age-specific features of carbohydrate metabolism disorders in patients with CHD, the mean age of women with CHD and normal blood sugar level or CHD with FHG were found to be significantly higher compared to that of men ($p<0.05$). No statistically significant difference was revealed in age between men and women with CHD accompanied by IGT and type 2 DM ($p>0.05$). There was also a statistically significant difference in age between women with CHD and type 2 DM ($p<0.05$) (**Table 1**).

The study showed that incidence of arrhythmias increased with the aggravation of metabolic disorders of glucose: in 12 (34.5%) patients with normal blood sugar level, in 11 (39.3%) patients with FGH, in 29 (63.0%) patients with ITG (versus normal blood sugar level, OR=3.12, 95% CI [1.24-7.88], $p=0.0155$; versus FHG, OR=2.64, 95% CI [1.00-6.93], $p=0.0492$), in 24 (77.4%) patients with type 2 DM (versus normal blood sugar level, OR=6.29, 95% CI [2.10-18.83], $p=0.0010$; versus FHG, OR=5.30, 95% CI [1.71-16.46], $p=0.0039$; vs. ITG, OR=2.01, 95% CI [0.72-5.65], $p>0.05$). Patients with newly diagnosed type 2 DM had a higher incidence of stage IIB-III heart deficiency (HD) (23 [74.2%] vs. 8 [28.6%] patients; OR=10.06, 95% CI [3.27-30.98], $p<0.0001$) compared with ITG (in 23 (74.2%) vs. 17 (37.0%); OR=4.90, 95% CI [1.80-13.37], $p=0.0019$) and those with normal blood sugar level (in 23 (74.2%) vs. 8 (23.5%); OR=9.35, 95% CI [3.02-28.90], $p=0.0001$).

All patients with CHD had stage 1-3 arterial hypertension (AH). There were no statistically significant differences in the incidence of the AH crisis course in both males and females between the comparison groups ($p>0.05$). The mean values of systolic/diastolic blood pressure and heart rate (HR) did not

Table 2. Carbohydrate metabolism indicators in patients with ACS a& stable CHD (M±SD)

Indicator	Control group (n=30)	CHD patients (n=139)			
		Normal blood sugar (n=34)	FHG (n=28)	IGT (n=46)	DM (n=31)
Fasting glucose (mmol/l)	4.51±0.32	4.60±0.27	6.38±0.36*/**	6.42±0.41*/**	7.89±0.35*/**/***/#
Glucose h/2 hours after meal (mmol/l)	6.05±0.46	6.08±0.39	6.24±0.50	8.57±0.61*/***	12.70±0.62*/**/***/#
HbA1c (%)	4.18±0.29	4.35±0.26	5.06±0.21*/**	5.76±0.30*/***	6.34±0.35*/**/***/#
Insulin (units/l)	7.57±0.60	8.19±0.94	18.38±1.72*/**	17.40±1.54*/**	13.56±1.08*/**
HOMA2-IR	0.71±0.10	1.04±0.15	2.48±0.18*/**	2.36±0.20*/**	1.92±0.16*/**

Note. *Differences are statistically significant compared to control group (p<0.05); **Differences are statistically significant compared to group with normal blood pressure (p<0.05); ***Differences are statistically significant compared to FHG group (p<0.05); #Differences are statistically significant compared to IGT group (p<0.05); HbA1: Glycosylated hemoglobin; FHG: Fasting hyperglycemia; IGT: Impaired glucose tolerance; & DM: Diabetes mellitus

Table 3. Lipidogram parameters in patients with CHD & newly diagnosed HG (M±SD)

Indicator	Control group (n=30)	CHD patients (n=139)			
		Normal blood sugar (n=34)	FHG (n=28)	IGT (n=46)	DM (n=31)
TC(mmol/L)	4.19±0.31	6.15±0.42*	6.22±0.40*	6.08±0.37*	6.41±0.45*
TG (mmol/l)	1.10±0.12	1.96±0.27*	2.07±0.25*	1.92±0.19*	2.30±0.24*/#
LDL (mmol/l)	1.96±0.17	3.38±0.31*	3.53±0.39*	3.60±0.25*	3.75±0.28*
HDL (mmol/l)	1.83±0.22	1.29±0.16*	1.24±0.16*	1.27±0.20*	1.06±0.09*/**/***/#
AI	1.29±0.08	3.77±0.31*	4.05±0.31*	3.78±0.33*	5.05±0.41*/**/***/#

Note. *Differences are statistically significant compared to control group (p<0.05); **Differences are statistically significant compared to group with normal blood pressure (p<0.05); ***Differences are statistically significant compared to FHG group (p<0.05); #Differences are statistically significant compared to IGT group (p<0.05); TC: Total cholesterol; TG: Trygliceride; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; FHG: Fasting hyperglycemia; IGT: Impaired glucose tolerance; & DM: Diabetes mellitus

statistically differ between the studied groups (patients with normal blood sugar, FHG, IGT, type 2 DM) (p>0.05). However, HR was significantly higher in women with newly diagnosed type 2 DM compared to those with FHG (87.29±4.51 bpm vs. 69.72±3.16 bpm, p<0.05).

In patients with CHD with newly diagnosed type 2 DM, the index of sympathetic activation was significantly higher compared to patients with FHG (64.48±4.83% vs. 52.37±3.06%, p<0.05) and normal blood sugar levels (64.48±4.83% vs 55.19±3.61%, p<0.05). No statistically significant differences were observed between patients with FHG and IGT for the same index (p>0.05). In contrast, in patients with CHD with newly detected HG, a parasympathetic activation was found to be decreased. Thus, this index was 47.63±3.85% in FHG patients, 44.81±3.40% in those with normal blood sugar levels, and 35.52±2.76% in type 2 DM.

Statistically significant intergroup differences of the index p<0.05 between type 2 DM and FHG, as well as type 2 DM and IGT (p<0.05). It is noteworthy that in all groups of CHD with newly detected HG, the decrease in parasympathetic activation was significantly higher in women than in men (p<0.05). For anthropometric parameters (body weight, chest circumference), the comparison groups did not show any differences (p>0.05).

The results of the study of key carbohydrate metabolism endpoints in CHD patients are presented in **Table 2**.

The highest post-prandial and fasting blood glucose values were found in patients with CHD and type 2 DM. In all groups of CHD patients with newly detected HG (FHG, IGT, and type 2 DM), HbA1c levels were significantly higher compared to the control group (p<0.05), and the maximum value was recorded for patients with CHD and newly detected type 2 DM (**Table 2**).

In all CHD groups with newly detected HG, there was a significant increase in insulin content in the blood, namely, by 2.43 times for FHG patients (p<0.05), by 2.30 times in group with normal blood sugar (p<0.05), and by 1.79 times in type 2 DM patients (p<0.05). No statistically significant intergroup difference of the index (p>0.05) was recorded. The HOMA2-IR index was similarly increased. The group of patients with CHD and normal blood sugar did not differ from the control in insulin and HOMA2-IR indices (p>0.05) (see **Table 2**).

Following this study, it was found that all CHD patients had dyslipidemia. All comparison groups showed statistically significant increases (p>0.05) in blood levels of TC, TG, LDL, AI, and decreased HDL in the blood compared to the control group. At the same time, the largest changes in lipidograms were observed in newly diagnosed CHD and type 2 DM patients (**Table 3**).

DISCUSSION

High glucose concentrations have a direct toxic effect on the vascular endothelium. This, in turn, causes an increase in muscle spasms, hyperplasia of smooth muscle fibers and leads to atherosclerosis. There is also a reverse connection when AH leads to IR. The main feature of this mechanism is the closure of small capillaries and decreased blood flow in skeletal muscles, reducing their utilization of glucose, that is, IR of muscle tissue. A pre-diabetic state, preceding diabetes, may increase the possibility of a CHD case. In most people, prediabetes turns into type 2 diabetes within 10 years if their lifestyle does not change. When prediabetes is diagnosed, continued loss of beta cell function usually leads to type 2 DM. The use of SGLT2-i may be associated with a lower risk of new arrhythmic events. Thus, studies have revealed the cardioprotective effects of SGLT2-i in patients with acute myocardial infarction (AMI) beyond glycemic control [34]. Based on a sample of 646 patients with MI, it was found that the rates of cardiovascular mortality and hospitalization for heart failure were significantly lower in the sample using SGLT2-i [35]. Similar results were obtained for patients with MI and type II diabetes using SGLT2-i. They had a reduced inflammatory response and a smaller infarction size. These facts confirm the effectiveness of SGLT2-i in states of CHD [36].

The main tasks and objectives of the study were to estimate the influence of newly detected glucose metabolic disorders such as FHG, ITG, and type 2 DM on the course of CHD, determine risk factors, and study the features of carbohydrate metabolism parameters. According to the study results, prediabetes and type 2 DM were fairly common among CHD patients (in 105 [75.5%] out of 139). However, ITG occurred significantly more frequently in patients with ACS (in 50.8% versus 28.9% in patients with stable ACM, p=0.0322). Furthermore, among ACS patients, there was a higher incidence of newly diagnosed type 2 DM (in 28.3% of cases compared to 13.6% of cases, p=0.0371). Stable CHD forms were characterized by a milder glucose metabolism disorders–FHG (in 47.4% versus 14.9% of cases in ACS patients, p<0.0001). In the authors' opinion, it indicates that disorders of carbohydrate metabolism negatively affect the course of CHD and lead to its destabilization. The negative influence of glucose metabolism disorders on CHD course is also confirmed by increased frequency of heart rhythm disorders: in 12 (34.5%) patients with normal blood sugar, in 39.3% of patients with FHG, in 63.0% of patients with ITG, and 77.4% of patients with type 2 DM. The stage of heart failure (NYHA II-III) was noted in 74.2% of patients with type 2 DM versus 23.5% of patients with normal blood sugar levels, in 28.6% of patients with FHG, and 37.0% of patients with ITG.

Significantly higher values of sympathetic activation against inhibition of parasympathetic one were typical for patients with CHD and newly diagnosed type 2 DM compared to FHG, ITG, and normal blood sugar levels. These differences were more pronounced in women than men (p<0.05), indicating that parasympathetic inhibition is one of the mechanisms that inhibit insulin secretion. The hyperactivation of sympathetic effects as one of the most important mechanisms of CD and AH confirms the necessity of metabolically neutral β-adrenoblockers (e.g., bisoprolol, metoprolol, carvedilol, and nebivolol).

In analyzing the study results, it was found that the mean age decreased in women as carbohydrate metabolic disorders increased (see **Table 2**). It indicates that carbohydrate metabolic disorders are an early CHD risk factor in women. Generally, this pathology develops 10 years later than in men in other circumstances due to the protective effect of estrogen [37, 38].

All patients studied with CHD had lipid metabolism disorders, which manifested as increased levels of TC, TG, LDL, and AI in the context of decreased anti-atherogenic HDL. The greatest lipidogram changes were observed in CHD patients with newly detected type 2 DM. Maximum fasting and post-prandial HG were also characteristic of newly diagnosed type 2 MD patients (see **Table 3**). A significant increase (p<0.05) in blood insulin content and progression of IR manifested by the rise in HOMA-IR2 index was recorded in all investigated patients with CHD and newly detected HG (FHG, ITG, and type 2 DM) compared to controls and those with normal blood sugar. In the type 2 DM group, the blood insulin level was lower than FHG and ITG patients. However, the difference was not statistically significant (p>0.05) since it was the first diagnosis of type 2 DM when insulin secretion may be within the normal range or reduced slightly at the early stages. Changes in carbohydrate metabolism can indicate that one of the important and common pathogenic mechanisms of carbohydrate metabolism disorders and CVD is IR. This needs to be considered to reduce cardiovascular risk and prevent the development of type 2 DM.

The findings of this study are consistent with data from other studies investigating hyperglycemic disorders in CHD patients [24, 34, 39]. Thus, the study [24], including 6,764 patients with CHD (type 2 DM was present in 996 patients), found that glycemic control status and HbA1C levels were independently associated with CHD. The prevalence of obstructive CHD was higher among patients with type 2 DM than those without DM (15.0% vs. 6.6%, respectively, p<0.001) [24].

It was evaluated their study the association of blood HbA1c with the severity and short-term results of AMI with ST-segment elevation in nondiabetic patients [33]. The study involved AMI 290 patients with elevated ST-segment without diabetes. The study found that patients with blood HbA1c>5.8% had a higher CHD severity than the low-HbA1c group (7.7±2.7 vs. 5.5±2.6 Kaliff's score, p=0.001). Moreover, the mortality rate at 12 months was much higher (7.7% vs. 2.7%, p=0.043) [34]. The meta-analysis in [39], which included 20 studies involving 22,428 patients, showed that high HbA1c levels in CHD patients without DM were associated with higher rates of long-term death (OR=1.76, 95% CI [1.44-2.16], p<0.001) and MI (OR=1.69, 95% CI [1.07-2.67], p=0.026).

The study by Mossmann et al. [40] reported that in patients who underwent coronary angiography and did not suffer from DM and obesity, an increase in HOMA-IR index above 4.21 indicates a high risk of clinically significant CHD.

CONCLUSIONS

Thus, newly detected HG is a fairly frequent finding in CHD (in 105 [75.5%] patients with CHD out of 139 examined) and is more common in ACS (83.3% versus 64.4% of cases with stable CHD, OR=2.85 95% CI [1.28-6.32], p=0.0101), with the prevalence of glucose tolerance disorders and type 2 DM. HG in CHD patients negatively affects the course of the disease, contributing to more frequent arrhythmias and early CHD in women.

In patients with CHD with newly diagnosed type 2 DM, the index of sympathetic activation was significantly higher compared to patients with FHG (64.48±4.83% vs. 52.37±3.06%, p<0.05) and normal blood sugar levels (64.48±4.83% vs 55.19±3.61%, p<0.05). No statistically significant differences were observed between patients with FHG and IGT for the same index (p>0.05). In contrast, in patients with CHD with newly detected HG, a parasympathetic activation was found to be decreased. Thus, this index was 47.63±3.85% in FHG patients, 44.81±3.40% in those with normal blood sugar levels, and 35.52±2.76% in type 2 DM. Statistically significant intergroup differences of the index p<0.05 between type 2 DM and FHG, as well as type 2 DM and IGT (p<0.05).

IGT and newly detected type 2 DM in CHD have common pathogenetic factors, including IR, lipid metabolism disorders, sympathetic nervous system activation against the background of reduced parasympathetic effects. These factors must be considered when controlling risk factors and developing treatment regimes for CHD patients. A reliable and safe method of verifying glucose tolerance disorder and DM is an oral glucose tolerance test, which must be carried out in all CHD patients.

Limitations

It is necessary to conduct a study on a larger sample of patients. It is also important to consider the indicators of younger patients with a similar diagnosis, as well as with supraventricular or ventricular arrhythmias, since the latter can affect the autonomic nervous system, and, as a consequence, lead to arrhythmias.

Prospects for Further Research

Developing a complex pathogen scheme for correcting newly detected HG in CHD patients.

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Ethical statement: Authors stated that the study was conducted with the approval of the Ethics Committee (Protocol No. 443) of Lomonosov Moscow State University. All participants signed a written consent to participate in the study. The study participants were guaranteed anonymity and confidentiality of the information received.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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