

# Questions of the mathematical modeling of the progression of coronary heart disease in patients with type 2 diabetes mellitus

## Abstract

In 2017-2019, 40 patients were examined (16 of them men, 24 women) with type 2 diabetes mellitus in combination with IHD, of which 38 patients had a favorable course and 8 with an unfavorable course. For an unfavorable profile, the presence of strokes, myocardial infarction (fatal, nonfatal), repeated hospitalizations for worsening chronic heart failure (decrease in ejection fraction), repeated surgical interventions (percutaneous coronary intervention, coronary artery bypass grafting) for the current 3 years was taken into account. The average age of patients was 65.5 years. In total, 119 signs recorded in the first three days from the moment of patient's arrival were analyzed as possible predictors of an unfavorable prognosis. From this whole set, a number of parameters with corresponding values were selected as markers of coronary heart disease, which showed the highest incidence rate in the group of patients with adverse course (NBT) and the highest in the group of patients with favorable course (BT). The most pathognomonic predictors of IHD progression in patients with type 2 diabetes were systolic LV dysfunction ( $fv < 40\%$ ),  $SBP > 160$  mm Hg and/or  $DBP$  above 100 mm Hg. Art., severe angina pectoris, LVH and ECG signs of myocardial ischemia, persisting upon discharge from the hospital, history of ACVA comorbidity plus DM-2.

**Keywords:** diabetes mellitus type 2, ischemic heart disease, modeling

Volume 7 Issue 5 - 2020

Yulduz Makhkamovna Urmanova, Shakhnoza Shokirjonovna Mukhtarova, Tursunkulov Ortikali, Margarita Zairganovna Mukhtarova, Kholikov Farkhod Jamoliddin Ugli

Endocrinology department, Tashkent Pediatric Medical Institute, Tashkent Medical Academy, Republic of Uzbekistan

**Correspondence:** Yulduz Makhkamovna Urmanova, Endocrinology department, Tashkent Pediatric Medical Institute, Tashkent Medical Academy, Republic of Uzbekistan, Tashkent, 100140, Bogishamol str, 223, Email: [Yulduz.urmanova@mail.ru](mailto:Yulduz.urmanova@mail.ru)

**Received:** June 18, 2020 | **Published:** September 07, 2020

## Introduction

Type 2 diabetes mellitus (T2DM) is a rapidly growing medical and social problem in all industrialized countries, due to early disability and high mortality, most often from cardiovascular complications. The number of people with diabetes is expected to increase from 135 to 300 million people by 2025.<sup>1-3</sup> Most cases of diabetes mellitus (up to 90%) will be type 2 diabetes mellitus. Despite the successful development of medical technologies in the diagnosis of coronary heart disease, mortality from coronary heart disease in the diabetes population is not reduced. Acute coronary syndrome in people with type 2 diabetes often develops in the absence of significant stenosis of the arteries of the heart.<sup>4-6</sup> Therefore, the identification of coronary insufficiency in the preclinical stage of coronary heart disease in the diabetes population acquires special social significance.<sup>7-10</sup> The American Heart Association and the European Society of Cardiology are currently treating T2DM as the equivalent of IHD in relation to the risk of subsequent cardiovascular events. The high frequency of coronary death among patients with diabetes is primarily due to objective difficulties in the early diagnosis of coronary artery disease.<sup>11-13</sup> The asymptomatic nature of myocardial ischemia in the presence of proven coronary artery disease is recorded in more than 1/3 of them: according to different researchers, from 30 to 48%. A frequent development of the cardiac form of autonomic neuropathy makes it impossible to accurately use the standard criterion for achieving a diagnostic level of stress test for heart rate recommended by the American Heart Association and the American College of Cardiology. In recent years, special attention of world studies is aimed at improving the methods for assessing the risk of coronary heart disease individually in each patient with diabetes in order to identify people who need "aggressive" therapy.<sup>3,14-17</sup> The development of an algorithm for the early diagnosis of coronary heart disease and ways

of its correction are actual problems of endocrine cardiology.<sup>2</sup> All of the above served as the reason for the present study. The purpose of the study-to determine the prognostic signs of an unfavorable course of coronary heart disease with the development of a table of test probabilities to enhance the effectiveness of risk stratification in patients with type 2 diabetes.

## Methodology

Under our supervision for 2017-2019, 40 patients (including 16 men, 24 women) with type 2 diabetes mellitus in combination with coronary heart disease, including 38 patients with a favorable course and 8 with an unfavorable course of the disease, were in the Center of Cardiology of the Ministry of Health of the Republic of Uzbekistan. For the adverse profile, the presence of acute myocardial infarction (AMI: fatal, nonfatal), acute cerebrovascular accident (ACVA), repeated hospitalizations for worsening of chronic heart failure (decrease in ejection fraction), repeated surgical interventions (percutaneous coronary intervention, aorto-coronary artery bypass grafting) were taken into account. For the current 3 years. The average age of patients was 65.5 years. 20 healthy individuals of the corresponding gender and age constituted the control group.

The research methods included:

1. General clinical and biochemical studies (fasting glycemia, postprandial hyperglycemia, glycemic profile, glycosylated hemoglobin, coagulogram, lipid profile, C-reactive protein, creatinine, glomerular filtration rate),
2. Study of endocrine, cardiological status (heart rate - heart rate, systolic blood pressure - SBP, diastolic blood pressure - DBP),
3. Anthropometry - height, weight, BMI),

- Instrumental (fundus, visual acuity I, ECG dynamics Echo ECG, ultrasound viscera, daily monitoring, veloergometriya, coronarography and others, if necessary.),
- Tumor necrosis factor study, troponin.

Statistical analysis was performed using the free statistical software “R” version 3.5.2. When comparing the average values in normally distributed sets of quantitative data, the Student t-test was calculated. When comparing the nominal data, the Pearson criterion method  $\chi^2$ , Kullback-Leibler divergence was used. The differences were considered statistically significant at a significance level of  $p < 0.05$ .

Inclusion criteria: IHD (NS) with type 2 diabetes (WHO, 2006). By classification (Braunwald E.) IIA; IIB.

Exclusion criteria: type 1 diabetes, myocardial infarction with Q wave  $< 3$  months. prescription, patients with chronic heart failure III-IV FC, severe violations of the liver and kidneys, complex rhythm disturbances, etc.

## Discussion

Diabetes has long been considered the “equivalent of cardiovascular risk.” This statement was substantiated on the basis of the results of a study<sup>1</sup> conducted in patients with type 2 diabetes who did not had registered cases of coronary artery disease and showed same coronary mortality as in patients without diabetes who previously had coronary artery disease. The presence of type 2 diabetes also increased coronary mortality, worsening the prognosis in patients with newly diagnosed coronary artery disease.<sup>2</sup> These arguments led to the fact that in 2001, NCEP-ATP III<sup>3</sup> recommended treating patients with diabetes as a separate high-risk category without stratification. But recent evidence suggests that the risk of coronary heart disease in type 2 diabetes is not always similar to the risk of patients with previous CVD, and is very heterogeneous. In particular, a meta-analysis of 13 epidemiological studies (45,108 patients with and without diabetes) showed that in patients with type 2 diabetes without coronary artery disease, the risk of coronary artery disease is 43% lower than in patients without diabetes with previous myocardial infarction.<sup>4</sup> And in the cohort,<sup>5</sup> including 1,586,061 people aged 30–90 years (observation of 10 years), the risk of coronary heart disease was significantly lower among patients with type 2 diabetes without coronary artery disease than in patients with coronary artery disease without diabetes. In another meta-analysis of studies with patients with type 2 diabetes,<sup>6</sup> in which the cardiovascular risk was assessed by the value of coronary calcium, it was shown that 5-year survival in patients with type 2 diabetes was the same as in patients without diabetes.<sup>7</sup> Thus, it is likely that a subgroup with a lower risk of coronary heart disease also exists in type 2 diabetes, especially in patients under the age of 40 years with a shorter duration of the disease.

Currently, the 2016 ADA guidelines for diabetes care<sup>8</sup> and the 2019 ESC<sup>9</sup> diabetes guidelines are no longer considered equivalent to coronary risk. Now with risk stratification for patients with diabetes aged 40 to 75 years, it is recommended to use a global risk assessment calculator with a division into two risk categories.<sup>10</sup> The ESC guidelines say that the risk of diabetes approaches the risk of coronary heart disease if patients have had a history of illness for more than 10 years or in the presence of renal dysfunction or microalbuminuria.<sup>9</sup> Patients younger than 40 years with a shorter duration of diabetes are currently identified as part of the low-risk group. This distribution of patients with type 2 diabetes in different groups of cardiovascular risk

allows you to distribute to those who can get more benefit from more intensive prevention of CVD. What are the options for stratifying CVD risks in type 2 diabetes? If we consider the proposals of the American Heart Association and the American College of Cardiology (AHA/ACC), they propose an approach based on global risk assessment.<sup>10</sup> ACC/AHA designed calculator to evaluate 10-le.

## Findings

For the prognosis, 40 patients with coronary heart disease in combination with type 2 diabetes were analyzed. The observation period was 3 years, with 32 patients (80%) with a favorable course, 8 (20%) with an unfavorable disease. As can be seen from Table 1, the average duration of diabetes was 5.2 years, 16 patients had a history of AMI (40%), 20 patients (40%) abused smoking, 37 patients (93%) had left ventricular hypertrophy, and 24 patients (60%) found stenosis of the common carotid artery. In total, 119 signs recorded in the first three days from the patient's arrival were analyzed as possible predictors of an unfavorable prognosis:

- Clinical anamnestic (demography, bad habits, experience of cardiovascular disease, experience of diabetes mellitus, the presence of post-infarction cardiosclerosis, arterial hypertension, pain syndrome, LDCs, acute cerebrovascular accident or transient ischemic attack) - a total of 14 signs,
- Instrumental (resting ECG on the day of receipt and discharge, 9 ka categories of ST/T changes and their combination Holter ECG monitoring: episodes of ischemia, arrhythmia, HRV Echo-ECG: TMP, TZS, KDO, KSO, UO, MO, FV, E/A. Doppler SA TIM. Ultrasound of the brachiocephalic arteries-the presence of plaques in the carotid artery. Coronarography - coronary vascular lesion. Veloergometry. Implantation tonometry - only 80 signs. 3) Biochemical: lipid spectrum (total cholesterol, high density lipoproteins, low density lipoproteins, triglycerides), carbohydrate metabolism (fasting glucose postprandial difference, glycated hemoglobin), creatinine, urea, glomerular filtration rate, ALT, AST, C-reactive protein, troponin, potassium, sodium, TSH, free T4 - only 25 signs.
- The most common in patients was arterial hypertension (95%), heart failure (92.5%) in second place, chest pain (90%) in third, and atherosclerosis in fourth (82.5 %), in the fifth - myocardial infarction (40%), in the sixth - kidney disease (32.5%).

The dynamics of adverse events during the observation period; A study of medical history revealed that over the past 3-6 months, the combination of transferred 1-ONMK and 1-AMI was observed in 5 (12.5%) patients, while 1 patient died in the last 12 months, and 1 AMI and 2 in 36 months ONMK was also noted in 5 patients (12.5%). From this whole set, a number of parameters with corresponding values were selected as markers of coronary heart disease, which showed the highest incidence in the group of patients with adverse course (NBT) and the highest in the group of patients with favorable course (BT). Table 2 gives a comparative characteristic of the frequency of adverse factors in patients with coronary artery disease with a favorable and unfavorable outcome. As can be seen from Table 2, the most pathognomonic predictors of IHD (ischemic heart disease) progression in patients with type 2 diabetes were systolic LV dysfunction (fv  $< 40\%$ ), SBP  $> 160$  mmHg / or DBP above 100 mmHg. Art, severe angina pectoris, LVH (left ventriculium hypertrophy) and ECG-signs of myocardial ischemia, persisting upon discharge from the hospital, history of ACVA comorbidity plus DM-2.

**Table 1** General characteristic of patients

Sign to be analyzed	N, abs	%
Men	16	40
Women	24	60
The average age, years	65.5±0.21	
The average duration of diabetes, years	5.2±0.26	
History of Acute Myocardial Infarction	16	40
History of Hypertension	35	87.5
sBP ≥ 140 mm RT.Art.	28	70
dBP ≥ 90 mm RT.Art.	20	50
Smoking	20	50
Heart rate	73.9±0.43	
Overweight + obesity	32	80
Cholesterol	197.4±1.39	
Left ventricular hypertrophy	37	92.5
Low density lipoproteins	110.4±1.21	
Triglycerides	248.7±4.24	
Fasting glycemia	8.1±0.08	
Postprandial glycemia	12.4±0.15	
Glycated hemoglobin	9.0±0.07	
Ejection fraction	57.1±0.21	
The presence of plaques in the carotid artery	24	60
Surgical interventions (percutaneous coronary intervention, coronary Artery bypass grafting - CABG)	21	52.5
Total	40	19.2

Note: DM, diabetes mellitus; AMI, acute myocardial infarction; CAD, systolic blood pressure; dAD, diastolic blood pressure; heart rate, heart rate; LDL, low-density lipoproteins; TG, triglycerides; CABG, aorto-coronary artery bypass grafting

**Table 2** Comparative characteristics of the frequency of adverse factors in patients with coronary artery disease with a favorable and unfavorable outcome

Name of the characteristic	N=40		BT		NBT		BT и NBT	χ <sup>2</sup>	p				
	Abs	%	Abs	%	Abs	%							
sBP>160	16	40	11	34.4	5	62.5	1.8	2.64	0.1	11	21	5	3
dBP>90	115	81.6	96	80.7	19	86.4	1.1	0.1	0.7	96	-64	19	-11
Postinfarction atherosclerosis	102	72.3	83	69.7	19	86.4	1.2	1.8	0.2	83	-51	19	-11
Fasting glycemia≥14.8	28	19.9	21	17.6	7	31.8	1.8	1.5	0.2	21	11	7	1
Fasting glycemia≤6.1	73	51.8	58	48.7	15	68.2	1.4	2.1	0.1	58	-26	15	-7
Triglycerides≥306	37	26.2	32	26.9	5	22.7	0.8	0	0.9	32	0	5	3
Postprand. glycemia≤8.1	43	30.5	32	26.9	11	50	1.9	3.6	0.06	32	0	11	-3
Postprand. glycemia≥6.0	29	20.6	20	16.8	9	40.9	2.4	5.21	0.02	20	12	9	-1
Ejection fraction ≤40	39	27.7	29	24.4	10	45.5	1.9	3.14	0.1	29	3	10	-2
Heart rate≥90	1	0.7	1	0.8	0	0	0	0	0	1	31	0	8
Insulin therapy	40	100	32	100	8	100				32	0	8	0

## Conclusion

1. The characteristics of the profile of patients with coronary heart disease with type 2 diabetes, without signs of LV systolic dysfunction, life-threatening cardiac arrhythmias and complications in the acute period, but with a high long-term risk of an adverse outcome that has remained, are: long-term (5 years or more) history of type 2 diabetes, ACVA in history, LVH, anatomical signs of vascular endothelial damage, severe disorders of carbohydrate and lipid metabolism, detected upon admission to the clinic.
2. Clinical markers of the adverse course of coronary heart disease in patients
3. With DM-2 are: uncontrolled hypertension with SBP more than 160 mm Hg and/or DBP above 100 mm RT. Art.) detected during the first examination at the time of the first contact with the patient, severe angina pectoris, LVH and ECG signs of myocardial ischemia, persisting upon discharge from the hospital, a history of ACVA comorbidity plus DM-2.
4. Criteria that negatively affect the long-term outcome of coronary heart disease in patients with type 2 diabetes are: hyperglycemia, in particular, a high level of fasting skin ( $>13\text{mmol/l}$ ), or PPPG ( $>54\%$  or more), as well as an increase in the level of OH  $\geq 200$  mg/dl and LDL cholesterol  $>193$  mg/dl.

## Acknowledgments

None.

## Funding

None.

## Conflicts of interest

Author declares that there is no conflict of interest.

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