

“On the Importance of Risk Factors for the Progression of Coronary Heart Disease in Patients with Type 2 Diabetes Mellitus”

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SUMMARY

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, heart attacks 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 the 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 CHD 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 AMI comorbidity plus SD-2.

Keywords: Diabetes Mellitus Type 2; Ischemic Heart Disease; Modeling

Abbreviations: DM 2: 2 Diabetes Mellitus; HF: Heart Failure; QoL: Quality of Life; AHA: American Heart Association; ESC: European Society of Cardiology; DKD: Diabetic Kidney Disease; SGLT2: Sodium-Glucose Cotransporter-2; LoE: Level of Evidence; T2DM: 2 Diabetes Mellitus; RCTs: Randomized Controlled Trials; CKD: Chronic Kidney Disease; CAD: Coronary Artery Disease; PCI: Percutaneous Coronary Intervention; MRA: Mineralocorticoid Receptor Antagonist

Background

Type 2 diabetes mellitus (DM 2) is a rapidly growing medical and social problem in all industrialized countries due to early disability and high mortality, most often from cardiovascular complications. (I.I. Dedov, M.V. Shestakova, 2003). The number of people with diabetes is expected to increase from 135 to 300 million by 2025. The majority of cases of diabetes mellitus (up to 90%) will be type 2 diabetes mellitus (J.J./ Bakh and E.E. van der Wall, 2006). Heart failure (HF) is defined as a clinical syndrome with symptoms and/or signs caused by a structural and/or functional abnormality of the heart, confirmed by elevated natriuretic peptides and/or objective evidence of pulmonary or systemic congestion [1]. It remains a leading global cause of mortality, morbidity and poor quality of life (QoL), with high use of health care resources and costs. [2]. Therefore, this is an area of active research. [3] Currently, the American Heart Association (AHA, SC Smith et al., 2016) and the European Society of Cardiology (ESC, L. Rydén et al., 2017) consider T2DM to be equivalent to CHD in terms of the risk of subsequent cardiovascular events. Diabetic cardiomyopathy is a form of stage B HF with a high risk of progression to overt disease. Diabetic kidney disease (DKD) is also an important risk factor for developing HF. [4-7]. Sodium-glucose cotransporter-2 (SGLT2) inhibitors and finerenone, a non-steroidal and selective mineralocorticoid receptor antagonist (MRA), are currently recommended [class of recommendation (CoR) I, level of evidence (LoE) A] for the prevention of HF in patients with type 2 diabetes mellitus (T2DM) and CKD [8].

SGLT2 inhibitors also reduce cardiovascular mortality in these patients. The indications for the use of SGLT2 inhibitors are based on the results of the DAPA-CKD and EMPA-KIDNEY trials and a subsequent meta-analysis of 13 large randomized controlled trials (RCTs), including the CREDENCE, SCORED, and CHF trials. [9] The FIDELIO-DKD and FIGARO-DKD studies, and a pre-specified individual patient-level analysis, a pooled analysis of these two studies (the FIDELITY pooled analysis) demonstrated benefits of finerenone in cardiovascular and renal outcomes compared with placebo across the spectrum of chronic kidney disease (CKD) in patients with T2DM. Among patients hospitalized for acute decompensated HF, obstructive coronary artery disease (CAD) was more common in HF with reduced left ventricular ejection fraction (HFrLVEF) than in HF with preserved LVEF (HFpLVEF). The role of percutaneous or surgical coronary revascularization remains uncertain in patients with HFrLVEF and chronic coronary syndromes. Percutaneous coronary intervention (PCI) was not more effective in reducing all-cause death or CVD than medical therapy alone in the REVIVED-BCIS trial. Iaconelli A. et al. conducted a meta-analysis of five RCTs (some of them unblinded) with a total of 2842 patients to examine the effect of coronary revascularization on morbidity and mortality in patients with chronic HF due to CAD.

Coronary revascularization was associated with a lower risk of all-cause mortality compared with medical therapy [hazard ratio (HR) 0.88, 95% confidence interval (CI) 0.79–0.99] and cardiovascu-

lar mortality (HR 0.80, 95% CI 0.70–0.93), but not with the composite of HF hospitalization or all-cause mortality [10]. In recent years, special attention of world research is directed to improving methods of assessing the risk of coronary heart disease individually for each patient with diabetes in order to identify people who need “aggressive” therapy. The development of an algorithm for early diagnosis of coronary heart disease and ways of its correction are urgent problems of endocrine cardiology.

Purpose of the Study

determination of prognostic signs of an unfavorable course of ischemic heart disease with the development of a table of test probabilities to enhance the effectiveness of risk stratification of patients with type 2 diabetes mellitus.

Material and Methods

Under our observation at the RSNPMC of Cardiology of the Ministry of Health of the Republic of Uzbekistan there were 40 patients (including 16 men and 24 women) with type 2 diabetes mellitus combined with coronary heart disease, of which 38 patients had a favorable course and 8 had an unfavorable one. The presence of strokes and heart attacks over the past 3 years was taken into account for an unfavorable profile. The average age of the patients was 65.5 years. The control group consisted of 20 healthy individuals of the corresponding gender and age. The research methods included:

- 1) General clinical and biochemical studies (fasting blood glucose, postprandial hyperglycemia, glycemic profile, glycated hemoglobin, coagulogram, lipid profile, C-reactive protein, creatinine, glomerular filtration rate),
- 2) Research endocrine science, cardiological status (heart rate - HR, systolic blood pressure - SBP, diastolic blood pressure - DBP),
- 3) Anthropometry - height, weight, BMI),
- 4) Instrumental (echocardiography, visual acuity, ECG dynamics, Echo-ECG, Ultrasound internal organs, daily monitoring, veloergometry, coronary angiography if necessary, etc.),
- 5) Tumor necrosis factor assay, troponin, total CPK.
- 6) Study of quality of life (QOL) using a questionnaire from IDF (2017) “Taking diabetes to heart”. Statistical analysis was performed using free statistical programs “R” version 3.5.2. When comparing average values in normally distributed sets of quantitative data, Student’s t-test was calculated. When comparing nominal data, the Pearson χ^2 criterion method and the Kullback-Leibler divergence were used. Differences were considered statistically significant at a significance level of $p < 0.05$. Inclusion criteria: coronary heart disease (CHD) with type 2 diabetes (WHO, 1999). According to the classification (Braunwald E.) IIA; IIB. Exclusion criteria: type 1 diabetes, Q-wave MI < 3 months ago,

patients with CHF III-IV FC, severe liver and kidney dysfunction, complex rhythm disturbances, etc.

Research Results

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 one. As can be seen from Table 1, the average duration of diabetes was 5.2 years, 16 patients had a history of myocardial infarction (40%), 20 patients (40%) abused smoking, 37 patients (93%) had left ventricular hypertrophy, and 24 patients (60%) had stenosis of the common carotid artery. In total, 119 signs recorded in the first three days from the moment of patient admission were analyzed as possible predictors of an unfavorable prognosis:

clinical and anamnestic data (14 signs), instrumental (80 signs), and biochemical (25 signs). The most common comorbidity among patients was arterial hypertension (95%), followed by heart failure (92.5%), chest pain (90%) in third place, atherosclerosis (82.5%) in fourth place, myocardial infarction (40%) in fifth place, and kidney disease (32.5%) in sixth place. A study of the anamnestic data revealed that over the past 3-6 months, a combination of 1 stroke and 1 acute myocardial infarction was observed in 5 (12.5%) patients, with 1 patient dying over the past 12 months, and over 36 months, 1 acute myocardial infarction and 2 strokes were also observed in 5 patients (12.5%). The number of parameters with corresponding values were identified as markers of coronary heart disease, which demonstrated the highest frequency of occurrence in the group of patients with an unfavorable course (nBC) and the highest in the group of patients with a favorable course (BC).

Table 1: General characteristics of patients.

Analyzed Feature	N (abs)	%
Male	16	40.0
Female	24	60.0
Average Age, Years	65,9±5,67	
Average Duration Of Illness	7,5±2,5	
Documented Acute Myocardial Infarction	16	40
History Of Arterial Hypertension	36	87.5
Systolic Arterial Pressure (SAP)	28	70.0
Dyastolic Arterial Pressure (DAP)	20	50.0
Smoking	25	50.0
Puls	75,6±8,45	
Obesity	34	80.0
Cholesterol	198,9±8,39	
Hypertrophy of left Ventricle	37	92.5
Low Density Lipoproteins	110,6±5,27	
Triglycerides	249,7±6,5	
Fasting Glycemia	8,6±1,27	
Postprandial Hyperglycemia	12,4±0,34	
HbA1C, %	23	57.6
ejection fraction	57,2±9,35	
Presence Of Plaques in The Carotid Artery	25	60.0
Surgical Interventions (Stenting, Shunting)	17	42.5
Total	43	19.2

Note: DM - diabetes mellitus, AMI - acute myocardial infarction, SBP - systolic BP, DBP - diastolic BP, HR - heart rate, LDL - low density lipoproteins, TG - triglycerides, CABG - coronary artery bypass grafting.

Table 2 shows comparative characteristics of the frequency of occurrence of factors of unfavorable course in patients with coronary heart disease with favorable and unfavorable outcome. As can be seen from Table 2, the most pathognomonic predictors of the progression of coronary heart disease in patients with type 2 diabetes were:LV

systolic dysfunction (EF<40%), SBP>160 mmHgand/or DBP above 100 mmHg,severe angina, LVH and ECG signs of myocardial ischemia that persist upon discharge from hospital, comorbidity of AMI in the anamnesis plus type 2 diabetes.

Table 2: Comparative characteristics of the frequency of occurrence of factors of unfavorable course in patients with coronary heart disease with favorable and unfavorable outcome.

Sign	N=40		BT		nBT		BT and nBT	χ ²	r				
	Abs	%	Abs	%	Abs	%							
Documented History of MI√	16	40.0	11	34.4	5	62.5	1.8	2.64	0.10	11	21	5	3
Dyslipidemia√	115	81.6	96	80.7	19	86.4	1.1	0.1	0.7	96	-64	19	-11
Smoking√	102	72.3	83	69.7	19	86.4	1.2	1.8	0.2	83	-51	19	-11
Age>60√	28	19.9	21	17.6	7	31.8	1.8	1.5	0.2	21	11	7	1
Documented Diabetes Mellitus√	73	51.8	58	48.7	15	68.2	1.4	2.1	0.1	58	-26	15	-7
Obesity (BMI>30)√	37	26.2	32	26.9	5	22.7	0.8	0.0	0.9	32	0	5	3
Left Ventricular Hypertrophy (ECG/EchoCG signs)	43	30.5	32	26.9	11	50.0	1.9	3.6	0.056	32	0	11	-3
SBP>160 mmHg on admission√	29	20.6	20	16.8	9	40.9	2.4	5.21	0.02	20	12	9	-1
DBP>100 mmHg on admission√	39	27.7	29	24.4	10	45.5	1.9	3.14	0.1	29	3	10	-2
LV Systolic Dysfunction (EF<40%)	1	0.7	1	0.8	0	0.0	0	0	0	1	31	0	8
Total patients with coronary heart disease combined with type 2 diabetes	40	100.0	32	100.0	8	100.0				32	0	8	0

Note: BT – patients with a favorable course of the disease, nBT – patients with an unfavorable course of the disease. P – reliability of differences in comparison with the control, χ² – Pearson criterion.

Conclusions

1. The characteristics of the profile of patients with coronary heart disease and type 2 diabetes who do not have signs of LV systolic dysfunction, life-threatening heart rhythm disturbances and complications in the acute period, but with a persistent high long-term risk of an unfavorable outcome are: a long (5 years or more) history of type 2 diabetes, a history of myocardial infarction, LVH, anatomical signs of vascular endothelial damage, severe disorders of carbohydrate and lipid metabolism detected upon admission of the patient to the clinic.
2. Clinical markers of an unfavorable course of coronary heart disease in patients with type 2 diabetes are: uncontrolled hypertension with SBP over 160 mm Hg and/or DBP over 100 mm Hg, detected during the first examination at the time of first contact with the patient, severe angina, LVH and ECG signs of myocardial ischemia that persist upon discharge from the hospital, and a history of comorbidity with AMI plus type 2 diabetes.

3. Criteria that negatively affect the long-term outcome of coronary heart disease in patients with type 2 diabetes are: hyperglycemia, in particular high levels of fasting (>13 mmol/l) or PPPG (>54% or more), as well as an increase in the level of TC ≥ 200 mg/dl and LDL-C > 193 mg/dl.

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