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Cardiovascular Risk Factors in Patients with Poorly Controlled Diabetes Mellitus

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ABSTRACT

Introduction: Diabetes mellitus(DM) is considered an independent cardiovascular risk factor. Having in mind concomitant occurence of diabetes and other cardiovascular risk factors, it is expected that patients with poor glucoregulation will have more cardiovascular risk factors and higher cardiovascular risk than patients with good glucoregulation. **Aim:** To compare cardiovascular risk and cardiovascular risk factors between patients with poorly controlled and patients with well-controlled Diabetes mellitus. **Material and Methods:** Hundered ten patients aged 40-70 years suffering from Diabetes mellitus type 2 were included. Research is designed as a retrospective, descriptive study. Patients with glycosylated hemoglobin (HbA1c) > 7% were considered to have poorly controlled diabetes. The following data and parameters were monitored: age,sex, family history, data on smoking and alcohol consumption, BMI (body mass index), blood pressure, blood glucose, total cholesterol, triglycerides, LDL, HDL, fibrinogen, uric acid. For the assessment of cardiovascular risk, the WHO / ISH (World Health Organization/International Society of hypertension) tables of the 10-year risk were used, and due to the assessment of the risk factors prevalence, the optimal values of individual numerical variables were defined. **Results:** Differences in the mean values of systolic, diastolic blood pressure, fasting glucose, total cholesterol, LDL cholesterol are statistically significant higher in patients with poorly controlled diabetes. Hypertension more frequently occurre in patients with poorly controlled DM. The majority of patients with well-controlled DM belong to the group of low and medium cardiovascular risk, while the majority of patients with poorly controlled DM belong to the group of high and very high cardiovascular risk. In our research, there was a significant difference in cardiovascular risk in relation to the degree of DM regulation, and HbA1c proved to be an important indicator for the emergence of the CVD. **Conclusion:** There are significant differences in certain risk factors between patients with poorly controlled and well controlled DM. Patients with poorly controlled diabetes mellitus have a higher cardiovascular risk than patients with well controlled diabetes. The value of HbA1c should be considered when assessing cardiovascular risk.

Keywords: cardiovascular risk, cardiovascular risk factors, poorly controlled diabetes mellitus.

1. INTRODUCTION

Cardiovascular diseases (CVD) are a group of heart and blood vessel disorders, including: coronary heart disease, cerebrovascular disease, peripheral artery disease. Heart diseases and circulatory system diseases are the leading cause of mortality in Europe as a whole, responsible for more than 3.9 million deaths per year, or 45% of all deaths (1). Most cardiovascular diseases are caused by a risk factors that can be controlled, treated or modified, but there are certain risk factors that can't be affected. We are talking about changeable and unchangeable cardiovascular risk factors. Cardiovascular (CV) risk is the likelihood of developing a cardiovascular disease within a defined time period, whilst taking into account several risk factors. Identification of cardiovascular risk and risk factors leading to its increase, enables the prevention of cardiovascular diseases and their consequences. Unchangeable risk factors are: genetic predisposition, age, gender, and race. Changeable risk factors are: high blood pressure, elevated cholesterol, elevated LDL, elevated triglycerides, reduced HDL, elevated blood glucose, physical inactivity, increased body weight, smoking, alcohol, stress. Total cardiovascular risk is assessed by tables that take into account the coexistence of several factors, such as age, gender, smoking, BMI, diabetes, high blood pressure and certain biochemical parameters.

Using tables in clinical assessment of cardiovascular risk, patients are classified into groups with low (<10%), medium (10-20%), high (20-30%) and very high risk (≥30) (2). Diabetes mellitus type 2 as well as other types of glucose metabolism disorders are the risk factors for the emergence of CVD. The most convincing evidence for this comes from the DECODE study, which analyzed several European cohort studies with basic OGTT data (3, 4). Several studies have shown that the increase in HbA1c is associated with an increase in the risk for CVD. (3, 5, 6).

Having in mind concomitant occurrence of diabetes and other cardiovascular risk factors, it is expected that patients with poor glucoregulation will have more cardiovascular risk factors and higher cardiovascular risk than patients with good glucoregulation.

2. AIM

The aim of our study is to compare cardiovascular risk factors between patients with poorly controlled diabetes and patients with well controlled diabetes. Second aim is to assess the cardiovascular risk of the patients and to compare the cardiovascular risk between patients with poorly controlled diabetes and patients with well controlled diabetes.

3. METHODS

The study was conducted at the Department of Clinical Endocrinology, Clinical Center University of Sarajevo. Hundered ten patients aged 40-70 years suffering from Diabetes mellitus type 2 were included. Research is designed as a retrospective, descriptive study. Data were provided from the patient medical histories. Patients with glycosylated hemoglobin (HbA1c) > 7% were considered to have poorly controlled diabetes.The following data and parameters were monitored: age, gender, data on smoking and alcohol consumption, BMI (body mass index), blood pressure, cholesterol, triglycerides, LDL, HDL, fibrinogen, uric acid. For the assessment of cardiovascular risk, the WHO/ISH (World Health Organization/International Society of hypertension) tables of the 10-year risk were used, and due to the assessment of the risk factors prevalence, the optimal values of individual numerical variables were defined. Hypertension is defined as values of systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg or presence of antihypertensive therapy. Hypercholesterolaemia is defined as total cholesterol value > 5 mmol/l or lower total cholesterol with the presence of lipid lowering agents. The hypertriglyceridaemia is defined as value > 1.7 mmol/l, low HDL cholesterol is defined as <1 mmol/l in men, <1.3 mmol/l in women. High LDL cholesterol is defined as value of > 2.5 mmol/l. Hyperuricemia is defined as uric acid value > 506 mmol/l for men and a value of > 393 mmol/l for women. The elevated fibrinogen is defined as > 3.5 g/l. The cigarette smoking is defined as the currently active smoking or if someone stopped smoking less than a year ago of the assessment of cardiovascular risk. Consuming alcohol is defined as active drinking of any type of alcohol in any quantity. A positive family history

is defined as the presence of cardiovascular diseases and cardiovascular events in the patient's immediate family.

Obesity is defined as BMI value > 30 kg/m2 calculated from anthropometric measures, body height and body weight using the standardized formula (BMI = weight in kg/height in m2. The statistical data analysis was done by software SPSS v. 22.0 (IBM) and Excell 2007 (Microsoft Corporation).

4. RESULTS

Out of total number of 110 patients, 57 were with poorly controlled DM and 53 with well controlled DM. There are no statistically significant differences in the men and women ratio between the groups (p=0,483).

The mean age of patients with poorly controlled and patients with well controlled DM is approximately equal (0.496).

	Diabetes mellitus control		
	well	poor	
	X (SD)	X (SD)	p
Systolic blood pressure (mmHg)	135.28 (23.583)	152.28 (26.340)	0.0006
Diastolic blood pressure (mmHg)	79.06 (13.085)	87.98 (12.708)	0.0004
Glucose (mmol/L)	7.204 (2.0951)	15.954 (7.0142)	0.0001
HbA1c (%)	6.521 (.6766)	10.279 (1.5946)	0.0001
Total cholesterol (mmol/L)	4.526 (1.2121)	5.244 (1.5732)	0.0089
Triglycerides (mmol/L)	2.2683 (1.85658)	2.8863 (2.26334)	0.1219
HDL cholesterol(mmol/L)	0.9900 (.28073)	1.0411 (.26852)	0.3318
LDL cholesterol (mmol/L)	2.8223 (1.13597)	3.3782 (1.46278)	0.0289
Acidum uricum (mmol/L)	341.70 (131.078)	270.30 (96.387)	0.0014
Fibrinogen (g/L)	4.119 (1.1641)	4.423 (1.7474)	0.2891

Table 1. Mean values of parametars according to glucoregulation statistically significant if p <0.05.

Differences in the mean values of systolic, diastolic blood pressure, fasting glucose, total cholesterol, LDL cholesterol are statistically significant higher in patients with poorly controlled diabetes.

	Diabetes mellitus control		
hypertension	well N (%)	poor N (%)	total N (%)
no	28 (70.0)	12 (30.0)	40 (36.4)
yes	25 (35.7)	45 (64.3)	70 (63.6)
total	53 (48.2)	57 (51.8)	110 (100.0)

Table 2. Hypertension according to glucoregulation (p=0,001)

Out of total number of patients (n=110), 70 are with hypertension. In the group of patients with poorly controlled DM, 45 of them have hypertension, 12 do not have , and in the group of patients with well controlled DM 25 have hypertension, and 28 are without hypertension (p=0,001).

	Diabetes mellitus control p		
	well	poor	
M:F ratio	0.77	0.84	0.483
	X (SD)	X (SD)	p
Age (years)	60.038 (6.5102)	59.193 (6.4654)	0.496
Duration of diabetes DM (years)	8.36 (5.558)	6.75 (6.200)	0.157
Total number of cardio-vascular risk factor	6.792 (1.8642)	7.456 (1.8523)	0.064
	% patients	% patients	p
Age >60 god.	60.4	52.6	0.266
Men	43.4	45.6	0.483
Obesity (BMI>30kg/m2)	34.0	54.4	0.025
Systolic blood preasure >140mmHg	58.5.	75.4	0.045
Diastolic blood preasure >90mmHg	30.2	57.9	0.003
Positive family history	34.0	47.4	0.108
Smoking	20.8	31.6	0.142
Alcohol comsumption	11.3	15.8	0.344
Total cholesterol >5mmol/L	45.3	50.9	0.346
Triglycerides >1,7mmol/L	49.1	63.2	0.097
HDL <1mmol/L (M), HDL <1.3mmol/L (F)	79.2	63.2	0.049
LDL >2,5 mmol/L	60.4	71.9	0.140
Acidum Uricum >393mmol/L (F), >506mmol/L (M)	18.9	7.0	0.057
Fibrinogen >3.5 g/L	73.6	73.7	0.580

Table 3. Risk factors according to glucoregulation. Statistically significant if p <0.05.

There are no significant differences in men and women ratio, age, and the duration of DM between the groups. For the most risk factors, the percentage of patients is higher in the group of patients with poorly controlled DM, for obesity and blood pressure (systolic and diastolic) differences among patients are statistically significant.
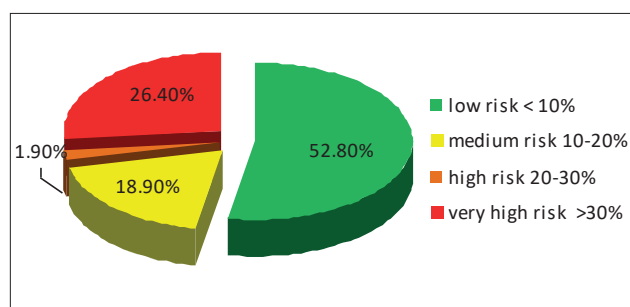

Chart 1. Distribution of patients with well-controlled DM according to the CVR categories

WHO/ISH Ten-year cardiovascular risk (CVR)

The majority of patients with well-controlled DM belong to the group of low and medium cardiovascular risk, while 14 patients belong to the group of very high cardiovascular risk. Only one patient belong to the high risk group. The majority of patients with poorly controlled DM belong to the group of high and very high
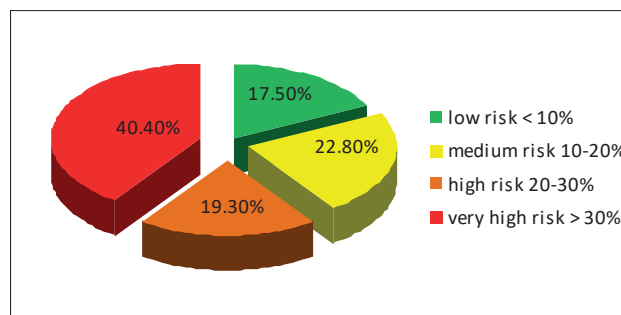

Chart 2. Distribution of patients with poorly controlled DM according to the CVR categories

cardiovascular risk. 13 patients belong to the group of medium risk, and the smallest number of patients with poorly controlled DM belong to the low risk group.

5. DISCUSSION

We have showed in our study that there is a difference in the most examined cardiovascular risk factors in patients with well-controlled DM compared to patients with poorly controlled DM. Differences in the mean values of systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, LDL cholesterol are statistically significant, while differences in the mean values of triglycerides, HDL cholesterol, and fibrinogen didn't reach statistical significance, but have for sure clinical relevance. Numerous studies have shown a positive effect of lowering blood pressure to the cardiovascular outcome when systolic blood pressure is below 140 mmHg and diastolic below 85 mmHg. Lowering blood pressure leads to a decrease in cardiovascular risk (3, 7, 8). Total cholesterol in our study is higher in patients with poorly controlled DM compared to patients with well controlled DM (p= 0.0089). The importance of lowering total cholesterol in lowering overall cardiovascular risk is also demonstrated by AHA and ACC guidelines (9). LDL cholesterol is higher in patients with poorly controlled DM compared to patients with well controlled DM (p=0.0289). There is plenty of evidence for the benefit of lowering LDL cholesterol following the lowering of CV risk (3, 10, 11). In a meta-analysis involving 18.686 DM patients for 4.3 years with 3247 large vascular incidents 9% reduction was reported in all causes of mortality and 21% decreased incidence of major vascular outcomes by mmol /l lowering LDL cholesterol. Absolute reduction of LDL cholesterol, shows a positive relationship between LDL cholesterol and cardiovascular risk, and is observed at a LDL cholesterol value of 2.5 mmol /l (3).

Fibrinogen was higher in patients with poorly controlled DM, 4,423 g/l compared to the group with well controlled diabetes, 4,119 g/l. Although we did not find a statistically significant difference (p=0.2891) we considere every raise in levels of fibrinogen clinical relevant as increased coagulability, and the increase in fibrinogen levels contributes to the formation of CVD, in particular incidents such as myocardial infarction and stroke (3, 12, 13). We have come to the conclusion that obesity, increase in systolic and diastolic blood pressure, positive family history, smoking, alcohol consumption, total cholesterol, LDL cholesterol and triglyceride values are more

present in patients with poorly controlled DM compared to patients with well controlled DM. Statistically significant difference was found for obesity, as well as blood pressure, systolic and diastolic (p=0.025, p=0.045, p= 0.003). Obesity is considered to be a significant independent cardiovascular risk factor, but both, obesity and DM are not included in the equation of cardiovascular risk assessment, but only as additive variable. A link between obesity and cardiovascular risk in DM patients is shown by a study which concluded that patients with poor nutrition, lack of physical activity have higher HbA1c values and that they constitute the largest number of patients with very high cardiovascular risk (14). "Look AHEAD (Action for Health in Diabetes)" is a great clinical study of the effects of persistent weight loss on glycemia and the prevention of CVD and vascular incidents in patients with DM type 2. One-year results of an intensive intervention over the lifestyle show 8.6% weight loss, a significant reduction in HbA1c and a reduction in several risk factors for CVD (3,15). According to the data from our study, smoking is more prevalent in a group of patients with poorly controlled DM. In this group of patients 18 patients smoke, while in the group of patients with well controlled DM 11 patients smoke. According to literature, smoking in any quantity increases the risk of CVD occurrence and early death. Smoking cessation reduces the risk of developing CVD (3). Each patient within the examined groups was assessed a 10-year cardiovascular risk according to WHO/ISH tablets. Other studies using WHO/ISH tables in their methodology recognize the usefulness of these in clinical work but also in the work of family doctors, even in comparison with other significant methods of cardiovascular risk assessment (16, 17). Statistically significant higher (p=0.001) hypertension is present in the group of patients with poorly controlled DM. This is important data because the literature agree that hypertension causes a four-fold increase in cardiovascular risk in people with DM (3, 18). Our results indicate that the HbA1c could be a valuable parameter in the equations for calculating cardiovascular risk. This would lead to a more precise clinical assessment of cardiovascular risk and the direction of therapeutic measures. This is confirmed by literature that recognizes the permanent relationship between the increase in HbA1c and the occurrence of CVD (3).

6. CONCLUSION

Patients with poorly controlled diabetes have significantly higher systolic and diastolic blood pressure than patients with well controlled diabetes. Total cholesterol and LDL cholesterol levels are significantly higher in patients with poorly controlled diabetes than in patients with well controlled diabetes. Obesity and hypertension are more prevalent in patients with poorly controlled diabetes compared to patients with well controlled diabetes. Patients with poorly controlled diabetes have a higher cardiovascular risk than patients with well controlled diabetes. It would, of course, be useful in some future research to examine correlations, as well as causation-related links among particular risk factors.

Further long-term prospective clinical trials with more patients included are needed to investigate intervention strategies to diminish cardiovascular risk in type 2 diabetes mellitus.

- **Conflict of interest:** Authors declare no conflicts of interest.

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