Diabetes Mellitus Type 2 and Cardiovascular Diseases-Risk Assessment

Mirsada Avdagic-Terzic1, Zarina Babic1, Azra Burekovic2

ABSTRACT

Background Uncontrolled type 2 diabetes mellitus (T2DM) is widely recognized as a significant risk factor for the emergence of cardiovascular events. Early risk assessment, especially for coronary artery disease, is crucial to starting therapeutic strategies to lower cardiovascular risk. Objective To assess cardiovascular risk in patients with type 2 diabetes mellitus. Methods 64 patients were divided into groups according to age, gender, disease duration, glucoregulation, and applied treatment. The SCORE table was used to quantify cardiovascular risk. Results Our research showed that cardiovascular risk in patients with diabetes mellitus increases with age (rho = 0.458; p = 0.0001; p <0.05) and is higher in men (rho = -0.417; p <0.0001). It has been found that patients with a longer duration of diabetes mellitus have a higher cardiovascular risk (rho = 0.266; p = 0.032). Patients with better glucoregulation had a slightly lower cardiovascular risk, but correlation was statistically insignificant. No statistically significant correlation was observed between applied therapy and cardiovascular risk. Conclusion Good control and treatment of T2DM is of crucial importance for reducing cardiovascular risk. Key words: cardiovascular diseases, risk assessment, diabetes mellitus

1. BACKGROUND

Cardiovascular diseases (CVD) represent a group of diseases of the heart and blood vessels and are the leading cause of death in the world. An estimated 17.9 million people died from CVD in 2019, representing 32% of all deaths worldwide. Of these deaths, 85% were due to heart attacks and strokes. More than three-quarters of CVD deaths occur in middle and underdeveloped countries of the world (1).

It is well known that uncontrolled type 2 diabetes mellitus (T2DM) is a major risk factor for the development of major cardiovascular events such as acute coronary events, ischemic stroke, and peripheral ischemic disease of the extremities. However, T2DM also leads to diseases of the microvascular arterial network of the kidneys, eyes, nerves and other organs. In 2014, 8.5% of adults over the age of 18 had T2DM. Complications of diabetes mellitus significantly reduce the quality of life and life expectancy, on average from 4 to 8 years. In 2019, T2DM was the ninth direct cause of death worldwide with 1.5 million people, and 48% of deaths occurred before the age of 70 (2).

The challenge associated with treating DM and reducing CV events is the complex and multifaceted nature of the relationship between DM and CVD. CV risk factors, including obesity, hypertension, and dyslipidemia are common in patients with DM, especially those with T2DM. In addition, studies have shown that several factors including increased oxidative stress, increased coagulability, endothelial dysfunction, and autonomic neuropathy are often present in patients with DM and may directly contribute to the development of CVD (3). Together, the high rates of CVD risk factors and the direct biological effects of diabetes on the CV system place patients with diabetes at increased risk of developing CVD and contribute to an increased prevalence of myocardial infarction, stroke, and chronic heart failure (3, 4).

Great progress has been made in the prevention of cardiovascular diseases in patients with T2DM, in developed countries, primarily through better control of diabetes mellitus,
but cardiovascular diseases still remain very prevalent in this group of patients, especially in medium and underdeveloped countries. Good control and treatment of T2DM is of crucial importance for reduced economic costs of the health system, because the complications of this disease bring long-term disability (5).

2. OBJECTIVE
To examine the cardiovascular risk in patients with diabetes mellitus in relation to age, sex, disease duration, glucoregulation and applied therapy.

3. PATIENTS AND METHODS
Examinees and study design
A cross-sectional study was conducted with 65 subjects of both sexes (55 female and 10 male), aged between 37 and 84 years, who were examined in the Endocrinology outpatient clinic from 15.06.2019. until 05.07.2019. with a previously established diagnosis of diabetes mellitus type 2.

Inclusion criteria were: a) Patients who were examined in the Endocrinology outpatient clinic with a previously established diagnosis of diabetes mellitus type 2. b) Patients with complete data (duration of the disease, glucoregulation, therapy, blood pressure and total cholesterol values and smoking status). Excluding criteria were: a) Patients with incomplete data.

4. METHODS
According to the previously mentioned criteria, the following data were taken: gender, age, history of diabetes mellitus (duration of the disease, glucoregulation, therapy, blood pressure and total cholesterol values and smoking status). Based on the criteria of disease duration, patients are divided into four groups: up to one year, from 1 to 5 years, from 6 to 10 years, and over 10 years of disease duration. Based on glucoregulation criteria, patients were divided into five groups according to HbA1c values: below 7, from 7.1 to 8, from 8.1 to 9, from 9.1 to 10 and over 10.

Based on therapy, patients were divided into five groups: oral antidiabetic drugs (OAD), insulin therapy, combination of OAD and insulin therapy, combination of GLP 1 and OAD, and combination of GLP1 and insulin therapy.

Cardiovascular risk was calculated according to the SCORE cardiovascular risk assessment table.

Statistical analysis
Results are presented as absolute number, percentage, arithmetic mean with standard deviation and range of values.

Testing the influence of individual variables on cardiovascular risk was performed using Spearman’s rank correlation coefficient. The results of the analysis were considered statistically significant at the confidence level of 95% or with p<0.05. The analysis was carried out using the statistical package IBM Statistics SPSS v25.0.

5. RESULTS
Total number of 65 patients were included in the study. Table 1 shows the basic overview of the sample.

The average age of the examinees was 64.08±10.3 years, with the youngest examinee at the age of 37 and the oldest at the age of 84.

In relation to gender, women are more represented in 55 or 84.6% of cases. The duration of the disease (T2DM) was most often over 10 years in 28 or 43.1% of cases.

Glucoregulation according to HbA1c values was most often 9.1-10% in 15 or 23.5% of cases. The average cardiovascular risk calculated using the SCORE table was 3.17±2.33.

Association of patients’ average age and cardiovascular risk
Table and graphs show the relationship between the average age of patients with cardiovascular risk.

Data analysis revealed that older patients had a higher cardiovascular risk. Patients with a CV risk of up to 1 had an average age of 45-6.06 years, while patients with a CV risk greater than 10 had an average age of 69 years.

A statistically significant association was found in a positive direction, that is, older patients had a higher cardiovascular risk (r=0.458; p=0.0001; p<0.05).

Association of patients’ gender with cardiovascular risk
Analysis of the data found that men have a higher cardiovascular risk. The difference is statistically significant with rho = -0.417 and p>0.0001.

Association of disease duration (T2DM) with car-

| Age (Mean±SD) (range) (years) | 64.08±10.3 (37-84) |
|-----------------------------|----------------------|
| Gender (No) (%)             | Male 10 (15.4%)      |
|                            | Female 55 (84.6%)    |
| Disease duration (No) (%)   | Up to one year 3 (4.6%) |
|                            | from 1 to 5 years 16 (24.6%) |
|                            | from 6 to 10 years 18 (27.7%) |
|                            | >10 years 28 (43.1%) |
| Glucoregulation (No) (%)    | below 7 11 (17.2%) |
|                            | 7.1-8 13 (20.3%)     |
|                            | 8.1-9 12 (18.8%)     |
|                            | 9.1-10 15 (23.5%)    |
|                            | over 10 13 (20.3%)   |
| Therapy (No) (%)            | GLP 1 + insulin 4 (6.2%) |
|                            | GLP 1 + OAD 2 (3.1%) |
|                            | Insulin 13 (20.0%)   |
|                            | Insulin + OAD 36 (55.4%) |
|                            | OAD 10 (15.4%)       |
| CVR (No) (%)                | Up to 1 6 (9.2%)     |
|                            | from 1 to 5 49 (75.4%) |
|                            | from 6 to 10 9 (13.8%) |
|                            | >10 1 (1.5%)         |

Table 1. Basic overview of the sample
The duration of the disease (T2DM) shows a statistically significant positive, weak correlation ($r=0.266$; $p=0.032$) with cardiovascular risk. That is, patients with longer duration of T2DM have a higher cardiovascular risk.

**The association of glucoregulation with cardiovascular risk**

Glucoregulation shows a small, statistically insignificant negative correlation with cardiovascular risk. That is, patients with better glucoregulation have a slightly lower cardiovascular risk.

**Correlation of therapeutic choice with cardiovascular risk**

No statistically significant correlation was recorded between therapeutic choices and cardiovascular risk.

**6. DISCUSSION**

Many studies have been conducted worldwide that examined cardiovascular risk in patients with diabetes mellitus. Age represents one of the most important non-modifiable risk factors for CVD. The increase in cardiovascular risk is continuous and progressive in both men and women.
increases blood glucose levels, body mass index, dyslipidemia, and the level of blood pressure control, thereby increasing the risk of cardiovascular diseases (7).

In our study, data analysis found that men have a higher cardiovascular risk. The opposite results were obtained by Sanne A. E. Peters and associates. The results of their study suggest that type 2 diabetes confers a higher risk of cardiovascular disease in women than in men; women have a 27% higher relative risk of stroke and a 44% higher relative risk of coronary heart disease compared to men. Further studies addressing the mechanisms responsible for gender differences in the increased risk of cardiovascular disease associated with diabetes are needed to improve the prevention and management of diabetes in clinical practice (8).

Duration of diabetes is a key determinant of cardiovascular and diabetes risk. Patients with a duration of diabetes longer than 10 years can be considered patients with a particularly increased risk (9). In our study, the duration of the disease showed a statistically significant positive weak correlation with cardiovascular risk. Similar results were obtained by Wannamethee SG et al. They conducted a prospective observational study with the aim of assessing the incidence of coronary heart disease and cardiovascular mortality according to the time of T2DM diagnosis. Out of 4045 men, aged 60-79 years, were followed for an average of 9 years and were divided into 4 groups: a) no AMI/no T2DM, b) no AMI/T2DM with late onset (diagnosis after age 60), c) no AMI/T2DM with early onset (before age 60) and d) previous AMI/no T2DM. Patients with AMI and T2DM were excluded. There were a total of 372 major coronary heart disease events and 455 deaths. Compared with people without diabetes, T2DM had a higher mean risk for CV events and mortality, however, only patients with T2DM diagnosed before 60 years with a mean duration of 16.7 years showed a similar risk of CHD as those with previous MI without diabetes. Adjusted Hazard ratios (95% CI) for conventional risk factors and novel risk markers compared to group 1 were: 1.54 (1.07–2.11), 2.39 (1.41–4.05) and 2.51 (1.88–5.06), for groups 2, 3 and 4, respectively (10).

In our study, glucoregulation showed weak, statistically insignificant negative correlation with cardiovascular risk. That is, patients with better glucoregulation had a slightly lower cardiovascular risk. Similar results were obtained by Dizdarević-Bostandić et al. They found that patients with poorly controlled diabetes mellitus had a higher cardiovascular risk and that HbA1c could be a valuable parameter in the equation for calculating cardiovascular risk. This would lead to a more accurate clinical assessment of cardiovascular risk and guidance of therapeutic measures (11).

In our study, there was no statistically significant correlation between therapeutic choices and cardiovascular risk. However, in several recently reported clinical trials, insulin therapy was found to increase cardiovascular (CV) risk and mortality among patients with type 2 diabetes (T2D). Insulin therapy causes weight gain, recurrent episodes of hypoglycemia, and other potential adverse effects, including iatrogenic hyperinsulinemia. This excessive insulinization through the use of injected insulin predisposes to inflammation, atherosclerosis, hypertension, dyslipidemia, heart failure, and arrhythmias. These findings strongly suggest that insulin therapy has a worse short- and long-term safety profile than that found with many other T2D therapies. The potential adverse effects of insulin therapy should be weighed against the proven benefits of selected other therapies for T2D (12).

7. CONCLUSION

All the presented results indicate the need for detailed monitoring of patients with diabetes mellitus as well as better glucoregulation in order to reduce cardiovascular risk in these patients.

REFERENCES

1. Available at: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds). Accessed on: July 15th, 2022.
2. Sarwar N, Narula P, Seshasai SR, Gohil R, Kaptoge S, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010 Jun 26; 375(9733): 2215-2222. doi: 10.1016/S0140-6736(10)60484-9. Erratum in: Lancet. 2010 Sep 18; 376(9745): 958. Hillage, H L [corrected to Hillege, H L]. PMID: 2069967; PMCID: PMC2904878.
3. Matheus AS, Tannus LR, Cobas RA, Palma CC, Negrato CA, Gomes MB. Impact of diabetes on cardiovascular disease: an update. Int J Hypertens. 2013; 2013: 63789.
4. Li YW, Aronow WS. Diabetes mellitus and cardiovascular disease. J Clin Experiment Cardiol. 2011; 2: 2.
5. Duncan BB, Schmidt MI, Pankow JS, Ballantyne CM,Couper D, Vigo A, Hoogeveen R, Folsom AR, Heiss G. Atherosclerosis Risk in Communities Study. Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. Diabetes. 2005; 52: 1799–1805.
6. Tamiru S, Alemsged F. Risk Factors for Cardiovascular Diseases among Diabetic Patients In Southwest Ethiopia. Ethiopian journal of health sciences. 2010; 20(2), 121–128.
7. Rana JS, Liu JY, Moffet HH, Jaffe M, Karter AJ. Diabetes and prior coronary heart disease events and mortality, however, only patients with T2DM diagnosed before 60 years with a mean duration of 16.7 years showed a similar risk of CHD as those with previous MI without diabetes. Adjusted Hazard ratios (95% CI) for conventional risk factors and novel risk markers compared to group 1 were: 1.54 (1.07–2.11), 2.39 (1.41–4.05) and 2.51 (1.88–5.06), for groups 2, 3 and 4, respectively (10).
8. Peters SA, Huxley RR, Sattar N, Woodward M. Sex Differences in the Excess Risk of Cardiovascular Diseases Associated with Type 2 Diabetes: Potential Explanations and Clinical Implications. Curr Cardiovasc Risk Rep. 2015; 9(7): 36. doi:10.1007/s12170-015-0462-5.
9. Rana JS, Liu JY, Muflet HH, Jaffe M, Karter AJ. Diabetes and prior coronary heart disease are not necessarily risk equivalent for future coronary heart disease events. J Gen Intern Med. 2016; 31(4): 387–393.
10. Wannamethee SG, Shaper AG, Whincup PH, Lennon L, Sattar N. Impact of diabetes on cardiovascular disease risk and all-cause mortality in older men: influence of age at onset, diabetes duration, and established and novel risk factors. Arch Intern Med. 2011; 171(5): 404–410.
11. Dizdarevic-Bostandzic A, Begovic E, Burekovic A, Veljic-Asimi Z, Godzinjak A, Karlovic V. Cardiovascular Risk Factors in Patients with Poorly Controlled Diabetes Mellitus. Med Arch. 2018 Feb; 72(1): 13-16. doi: 10.5455/medarch.2018.72.13-16.
12. Mary E. Herman, James H. O’Keefe, David S.H. Bell, Stanley S. Schwartz. Insulin Therapy Increases Cardiovascular Risk in Type 2 Diabetes. Progress in Cardiovascular Diseases. 2017; 60(3): 434, https://doi.org/10.1016/j.pcad.2017.09.001.