Gender Differences in the Control of Cardiovascular Risk Factors in Patients with Type 2 Diabetes — A Cross-Sectional Study

Mario Šekerija¹, Tamara Poljičanin¹, Katja Erjavec², Ana-Marija Liberati-Čizmek¹, Manja Prašek¹ and Željko Metelko¹,²

Abstract

Objective Trends in diabetes and cardiovascular mortality rates are considerably different between women and men; this can be partially explained by differences in diabetes control. The aim of this cross-sectional study was to assess whether sex differences exist in effective control of cardiovascular risk factors among persons with type 2 diabetes treated at the Vuk Vrhovac University Clinic in 2008.

Materials and Methods We performed a cross-sectional analysis including 8,775 patients who attended the clinic in 2008. Levels of HbA1c, systolic and diastolic blood pressure (SBP, DBP), LDL-cholesterol (LDL) and triglycerides (TG) were analyzed. Multiple adjusted odds-ratios were calculated for categories of cardiovascular risk factors considered not being in control (HbA1c ≥ 7%, SBP ≥ 130 mmHg, DBP ≥ 80 mmHg, LDL ≥ 2.5 mmol/L, TG ≥ 1.7 mmol/L).

Results Women had higher levels of HbA1c (7.05 vs. 6.86%; p<0.001), despite the fact that a larger proportion of women were receiving insulin therapy than men (51.3% vs. 44%). Women also had higher mean values of SBP (144.7 vs. 141.9 mmHg; p<0.001) and LDL (2.92 vs. 2.84 mmol/L). There were no differences in DBP (86.1 vs. 86.0 mmHg; p=0.748) and only triglyceride levels were higher in men (2.04 vs. 1.94 mmol/L; p=0.003). In multi-adjusted logistic regression model female sex was associated with a higher odds ratio of having uncontrolled values of HbA1c (OR=1.21; 95%CI 1.11-1.32), SBP (OR=1.21; 95%CI 1.07-1.37) and LDL (OR=1.13; 95%CI 1.04-1.23).

Conclusion Women with diabetes have poorer control of main potentially modifiable cardiovascular risk factors than men. This could contribute to disparities in trends in cardiovascular mortality and it demands clinicians’ and public health awareness.

Key words: gender, diabetes mellitus, risk factors, cardiovascular diseases

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Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both (1), and type 2 DM results from a progressive insulin secretory defect on the background of insulin resistance as opposed to type 1 DM which results from β-cell destruction, usually leading to absolute insulin deficiency (2). Diabetes mellitus continues to increase in numbers and significance, thus becoming a growing burden in public health (3). It is estimated that there are 235 million people with diabetes in 2010 (6.4% of the world population) and this number is expected to increase to 438 million by 2030 (7.7%) (4). The number of persons with glucose intolerance worldwide is estimated to be 344 million in 2010 and is expected to rise to 472 million by 2030 (8.4% of adult population) (5). The prevalence of DM in Croatia is 6.1% in the 18-65 age group (6), with...
total prevalence in the age group 18+ estimated to be around 9% (5).

The burden of risk factors for cardiovascular disease (CVD) in persons with diabetes is high, with 75% of diabetic patients suffering from hypertension and 64% from high cholesterol (7). The relative risk of fatal coronary heart disease (CHD) associated with diabetes is 50% higher in women (8). During the past 30 years, there has been a decline in both total and CVD-related mortality among men and women without diabetes (9). Furthermore, a decline has also been observed in men with diabetes, while their female counterparts did not show this decline, with study of independent samples of U.S. population aged 35-74 from the National Health and Nutrition Surveys showing that in men with diabetes CVD mortality rates decreased from 26.4/1,000 person-years in 1971-1986 period to 12.8/1,000 person-years in 1988-2000, while in women with diabetes the CVD mortality rate did not decline between 1971-1986 (10.5/1,000 person-years) and 1988-2000 (9.4/1,000 person-years) (9, 10). While the mortality rates of persons with DM are still higher in men, the difference is now much smaller than it was a few decades ago.

This sex difference in mortality trends in patients with diabetes has been attributed to physiological, biological (11) and behavioral (12) sex-based differences but may also be attributed to differences in the treatment of CVD risk factors (13). Disparities in quality and accessibility of medical care (14, 15) are a further disadvantage of diabetic women, with insufficient data on these matters in Croatia and similar countries. An inappropriate regulation and treatment of cardiovascular disease risk factors may increase complications and mortality among patients. It has been shown that women are less aggressively treated for many CHD factors (8) and are more likely to have poorer control of HbA1c, systolic blood pressure as well as LDL cholesterol (16, 17). In a recent study conducted on the US population women were also less likely than men to have HbA1c <7% (13), which is an established risk factor for the development of diabetic complications (18).

In Croatia, according to official mortality statistics for 2008, diseases of the circulatory system (International Classification of Diseases 10, codes I00-I99) were the main cause of death in 57.2% of Croatian women (crude mortality rate 644/100,000), as opposed to 43.5% of Croatian men (crude mortality rate 534/100,000) (19). Furthermore, proportional diabetes mortality rates have constantly been higher in women than in men, with death certificate data from 2008 pointing to diabetes as an underlying cause of death in 2.92% of women (crude mortality rate 32.9/100,000) and 2.05% of men (crude mortality rate 25.2/100,000) (19).

Since the majority of persons with diabetes are dying of cardiovascular causes, associated with macrovascular complications of diabetes, the sex inequalities in cardiovascular and diabetes mortality in Croatia could be, at least in part, explained by the differences in quality of diabetes care, including the control of blood pressure and serum cholesterol. Therefore, the aim of this study was to investigate the differences in reaching the treatment goals in men and women with diabetes according to the existing guidelines in order to identify fields of possible improvement of diabetes care.

### Materials and Methods

This study is a cross-sectional trial with data on patients with type 2 diabetes attending the Outpatient Department of Vuk Vrhovac University Clinic from January 1st to December 31st, 2008. The Outpatient Department of the Clinic annually covers around 20,000 patients from the area of Zagreb, the capital of Croatia.

Diabetologists at the Clinic use CroDiabNET (20), a software developed to assist with patient examination and data collection for the Croatian National Diabetes Registry. Laboratory parameters and data on diabetes complications, education, and therapy are entered in CroDiabNET in a way that constitutes a basic informatic sheet (BIS), recognized by the international diabetology community as the optimal data collection form for the follow-up and improvement of diabetes care (21). The approval for usage and analysis of depersonalized data was obtained from Croatian Diabetes Registry.

In 2008 there were 16,984 patients with diagnosed diabetes and at least one visit to the Vuk Vrhovac University Clinic Outpatient Department. Of these patients, 15,311 were type 2 diabetics as defined by the attending diabetologist according to the criteria of World Health Organization (1), and 8,775 (57%) had all study endpoints measured at least once during the study period: HbA1c, systolic and diastolic blood pressures and blood lipids, with data on age, sex, body mass index and duration of diabetes available. The studied group (n=8,775) was compared by sex and age to the group of type 2 diabetics that did not have all of the study parameters present and was excluded from the study. The sex distribution did not differ significantly (p=0.271, chi-square), while the patients in our study group were older than those excluded from the study (63.83 ± 10.28 vs. 61.31 ± 13.69; p<0.001). For the purpose of this study, if more than one visit was recorded, the latest recorded data in 2008 on each parameter were taken.

To investigate whether there were any differences in the studied cardiovascular risk factors between female and male patients, the mean values of these parameters were compared according to sex. In addition, data were analyzed to establish the proportion of women and men who reached recommended target values of these risk factors, as defined by The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD) (22) (SBP <130 mmHg, DBP <80 mmHg, LDL <2.5 mmol/L, TG<1.7 mmol/L) and American Diabetes Association (23) (HbA1c <7%).

Prescribed diabetes therapy was defined as diet only, oral hypoglycemic agents (OHA), a combination of insulin+
Table 1. Descriptive Characteristics of the Study Participants

<table>
<thead>
<tr>
<th></th>
<th>Men (n=4,578)</th>
<th>Women (n=4,197)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>6.86 ± 1.25</td>
<td>7.05 ± 1.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;7.0 (%)</td>
<td>58.0</td>
<td>53.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>141.94 ± 18.92</td>
<td>144.73 ± 19.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;130 (%)</td>
<td>19.8</td>
<td>15.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>86.03 ± 10.91</td>
<td>86.11 ± 10.71</td>
<td>0.748</td>
</tr>
<tr>
<td>&lt;80 (%)</td>
<td>14.6</td>
<td>13.7</td>
<td>0.270</td>
</tr>
<tr>
<td>LDL-cholesterol (mmol/L)</td>
<td>2.84 ± 0.95</td>
<td>2.92 ± 0.94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;2.5 (%)</td>
<td>37.2</td>
<td>34.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>2.04 ± 1.72</td>
<td>1.94 ± 1.35</td>
<td>0.003</td>
</tr>
<tr>
<td>&lt;1.7 (%)</td>
<td>52.9</td>
<td>53.8</td>
<td>0.427</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>62.34 ± 10.35</td>
<td>65.45 ± 9.96</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.83 ± 4.02</td>
<td>29.89 ± 4.72</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration (yrs)</td>
<td>10.90 ± 8.29</td>
<td>11.61 ± 8.47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type of therapy (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet only</td>
<td>1.6</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>Oral hypoglycaemic agents (OHA)</td>
<td>54.4</td>
<td>47.5</td>
<td></td>
</tr>
<tr>
<td>OHA + insulin</td>
<td>18.1</td>
<td>23.3</td>
<td></td>
</tr>
<tr>
<td>Insulin only</td>
<td>25.9</td>
<td>28.0</td>
<td></td>
</tr>
</tbody>
</table>

*Data are shown as mean±standard deviation unless noted otherwise.

OHA and insulin only.

**Statistical analyses**

Sex differences between levels of CVD risk factors were analyzed using Student’s t-test. We used logistic regression models to estimate differences in the levels of CVD risk factors, with patient sex as an explanatory variable. The models were adjusted for age, duration of diabetes and BMI. Statistical significance was defined as p<0.05. All statistical analyses were performed using SAS (version 9.1.3).

**Results**

Subject characteristics are shown in Table 1. Approximately 56% of patients had good glycemic control (HbA1c<7.0%). Triglyceride levels were in control in 53%, while LDL levels were good in 36% of patients. Recommended levels of systolic and diastolic blood pressure were achieved in 18% and 14% of cases, respectively. More men than women were treated with OHA (54% vs. 48%), while women were more likely to be treated with insulin+OHA combination (23% vs. 18%) and insulin alone (28% vs. 26%).

Female persons with diabetes were found to have significantly higher levels of HbA1c, systolic blood pressure and LDL-cholesterol, while male patients had higher triglyceride levels. No sex differences were observed in diastolic blood pressure. Women were also found to be older, with longer diabetes duration and higher BMI. A significantly higher proportion of women did not reach recommended target levels of HbA1c, SBP and LDL in comparison with men, while there were no sex differences in the proportion of patients reaching target levels of DBP and TG.

In the unadjusted logistic regression model, women were more likely than men to have HbA1c ≥7.0%, systolic blood pressure ≥130 mmHg and LDL-cholesterol ≥2.5 mmol/L. The largest odds ratios between women and men were observed regarding systolic blood pressure control. The association of diastolic blood pressure and triglyceride levels with the patients’ sex was not statistically significant. However, after adjusting for possible confounders (age, duration of diabetes and BMI) the odds ratio for women to have increased systolic blood pressure has somewhat decreased (OR=1.21; 95% CI 1.07-1.37) to a level similar to that for HbA1c (OR=1.21; 95% CI=1.11-1.32). Unadjusted and adjusted odds ratios are shown in Table 2.

In addition to multivariate analysis, we categorized the patients by age and compared the levels of cardiovascular risk factors by sex (Table 3). The results showed improvement in the levels of CVD risk factors with age (except for systolic blood pressure), and the sex differences were similar to those in the multivariate analysis.

**Discussion**

In this sample of persons with type 2 diabetes from the hospital outpatient department, the overall percentage of patients reaching target levels of HbA1c was comparable to that from other studies (24-26). Women, however, had significantly higher mean values of HbA1c than men, reaching target levels (<7%) to a lesser extent, in spite of the more intense therapy for diabetes. This could be associated with longer diabetes duration, higher age and BMI observed in women.

While as much as over a half of the study population reached recommended targets for diabetes treatment, only
group 65+ had higher levels of LDL than the 45-64 age

The analysis stratified by age groups revealed that the age

women. While we did not have data on menopausal status,

treating LDL-cholesterol levels are the same in men and

significant in perimenopause (32); however, the goals of

premenopausal women (31), and this increase is especially

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for poor SBP and HbA1c control. Literature shows that

to men (30), women were found to be at an even higher risk

to have poor control of LDL-cholesterol levels as compared

vious investigation reporting that women were more likely

18% and 14% of patients reached the recommended levels

of systolic and diastolic blood pressure, respectively. This is

consistent with the previous research, showing that among

patients with diabetes, physicians tend to focus more on an-
tihyperglycemic treatment, although lipid and blood pressure

control might be more effective in preventing patient-related

endpoints (27). The prevalence of hypertension is already re-

ported to be greater in diabetic women than in diabetic

men (28, 29), and the women in the present study also had

higher mean systolic blood pressure and reached target val-

ues less frequently.

Although the present study was in agreement with a pre-

vious investigation reporting that women were more likely to

have poor control of LDL-cholesterol levels as compared to

men (30), women were found to be at an even higher risk for

poor SBP and HbA1c control. Literature shows that

postmenopausal women have higher levels of LDL-

cholesterol, even after adjusting for age in comparison to

premenopausal women (31), and this increase is especially

significant in perimenopause (32); however, the goals of

treating LDL-cholesterol levels are the same in men and

women. While we did not have data on menopausal status,

the analysis stratified by age groups revealed that the age

group 65+ had higher levels of LDL than the 45-64 age

group (p<0.001; Scheffe’s post hoc) and 20-44 age group

(p<0.001), while the two younger groups had similar levels of

LDL-cholesterol (p=0.192). It seems that the elderly dia-
betic women had more favourable lipid profiles, however

without the data on statin therapy we cannot make further

judgments on this issue. Interestingly, mean triglyceride lev-
els were higher in men, while a similar proportion of males

and females reached recommended target levels. It may be

explained by the fact that a larger percentage of men have

more significantly uncontrolled levels of TG (>4 mmol/L;

7.6% vs. 5.4%; p<0.001).

Previous research has shown that in patients with diabetes

clinicians focus on antihyperglycemic treatment (7). Al-

though achieving optimal blood glucose regulation is an im-

portant treatment goal, especially for the prevention of mi-

crovascular complications of diabetes, such an approach,

may, given the limited time and human resources, lead to in-
sufficient control and treatment of other CVD risk factors

like blood pressure or serum cholesterol. Future research

should be undertaken to clarify whether or not clinicians

have different ways of reasoning in terms of CVD risk fac-
tors in diabetic men and women.

This study has several limitations - data on hypertension

dyslipidemia therapy were not available, which made

| Table 2. Odds Ratios, Adjusted Odds Ratios and 95% Confidence Intervals between Diabetic Women vs. Men for Having Poorly Controlled CVD Risk Factors* |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                   | Odds ratio      | 95% Confidence interval | p         |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| HbA1c (%)                        | 1.218           | 1.118-1.326     | <0.001         |
| Systolic blood pressure (mmHg)   | 1.208           | 1.106-1.319     | <0.001         |
| Diastolic blood pressure (mmHg)  | 1.387           | 1.231-1.563     | <0.001         |
| LDL-cholesterol (mmol/L)         | 1.210           | 1.070-1.369     | 0.002          |
| Triglycerides (mmol/L)           | 0.925           | 0.812-1.053     | 0.240          |
|                                  | 1.009           | 0.882-1.155     | 0.891          |
|                                  | 1.129           | 1.035-1.230     | 0.006          |
|                                  | 1.168           | 1.069-1.275     | 0.001          |
| Triglycerides (mmol/L)           | 0.931           | 0.855-1.014     | 0.102          |
|                                  | 0.916           | 0.838-1.002     | 0.054          |
| * Text in bold shows multiple-adjusted (adjusted for age, duration of diabetes and BMI) odds ratios |

| Table 3. Cardiovascular Risk Factors Stratified by Age Groups |
|-------------------|-------------------|-------------------|-------------------|-------------------|
|                   | 20-44             | 45-64             | 65+               |
|                   | Men (n=199)       | Women (n=111)     | Men (n=2,387)     | Women (n=1,725)   | Men (n=1,992)     | Women (n=2,361)   | p         |
| HbA1c (%)         | 7.14 ± 1.53       | 7.19 ± 1.34       | 0.755             | 6.94 ± 1.31       | 7.15 ± 1.32       | <0.001         |
| Systolic blood pressure (mmHg) | 137.64 ± 18.17    | 134.37 ± 18.98    | 0.136             | 142.16 ± 19.19    | 144.06 ± 19.10    | 0.002          |
| Diastolic blood pressure (mmHg) | 88.84 ± 11.66     | 87.52 ± 11.38     | 0.335             | 87.97 ± 10.93     | 87.68 ± 10.68     | 0.399          |
| LDL-cholesterol (mmol/L)         | 3.03 ± 1.14       | 3.04 ± 0.86       | 0.965             | 2.90 ± 0.94       | 2.97 ± 0.96       | 0.012          |
| Triglycerides (mmol/L)           | 2.63 ± 2.61       | 2.03 ± 1.54       | 0.026             | 2.22 ± 1.81       | 2.09 ± 1.57       | 0.010          |
| BMI (kg/m²)                   | 29.86 ± 4.19      | 30.24 ± 5.74      | 0.534             | 29.33 ± 4.21      | 30.39 ± 5.00      | <0.001         |

* Data are shown as mean±standard deviation
estimates of the proportion of patients treated for these disorders impossible. Secondly, data on patients’ smoking status, a known cardiovascular risk factor, were also not included because of their low availability. The strengths of this study are in its size, larger than most of the studies published in this field, and in the fact that this was the first research set to explore possible differences in CVD risk factors between women and men with diabetes in Croatia.

In conclusion, our data implicate that diabetic women have poorer control of the main potentially modifiable CVD risk factors than diabetic men. Since the current guidelines for CVD risk factors do not differentiate between men and women, efforts should be made to reach therapeutic targets in women and men alike. Moreover, diabetes control in women is worse despite the more intensified drug therapy, calling for greater inclusion of other types of treatment such as physical activity, education and psychological counseling. Further prospective research is needed to clarify the importance of CVD risk factor control in diabetic women and the differences in trends in overall and cardiovascular mortality in men and women with diabetes.

The authors state that they have no Conflict of Interest (COI).

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