Gender Disparities in the Treatment and Control of Cardiovascular Risk Factors in Type 2 Diabetes

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Objective—To assess whether gender differences exist in the effective control and medication treatment intensity of cardiovascular disease (CVD) risk factors.

Research Design and Methods—Cross-sectional analysis including 44,893 patients with type 2 diabetes (51% women). Endpoints included uncontrolled CVD risk factors [LDL-C ≥130 mg/dl; systolic blood pressure (SBP) ≥140 mmHg; and hemoglobin-A1c (HbA1c) ≥8%] and the intensity of medical management in patients with uncontrolled CVD risk factors. Multiple-adjusted odds ratios were calculated after stratification for the presence of CVD (present in 39% of the patients).

Results—Women with CVD were less likely to have SBP, LDL-C and HbA1c controlled and less likely to receive intensive lipid-lowering treatment. Women without CVD were less likely than men to have LDL-C controlled with no differences in SBP or HbA1c control.

Conclusions—Women with diabetes and CVD have poorer control of important modifiable risk factors compared to men and receive less intensified lipid-lowering treatment.
Mortality rates from cardiovascular disease (CVD) have been declining during the last years in both men and women in the U.S. and Europe (1,2). However, in patients with diabetes a decrease has been observed only in men (2). Furthermore, the relative risk for fatal diabetes-associated CHD is 50% higher in women than in men (3). More adverse cardiovascular risk profiles among women with diabetes have been postulated as reasons, combined with possible disparities in treatment, which may favor men (3-5). A study from U.S. managed care health plans found poorer control of blood pressure and LDL-cholesterol in female compared to male patients and suggested that these findings may contribute to the gender disparity in CVD mortality trends (6). No study in Europe has investigated gender disparities in the main cardiovascular risk factors in patients with diabetes and/or has put them into perspective with treatment intensity.

RESEARCH DESIGN AND METHODS
This study is a cross-sectional trial in outpatients with type 2 diabetes using data of the DUTY registry (7). Data of 44,893 patients were obtained from 3,096 office-based physicians. Endpoints included levels of modifiable CVD risk factors, i.e. most recent levels of systolic blood pressure (SBP), LDL-C and HbA1c (intermediate outcomes). These outcomes were analyzed as binary variables according to the levels considered not in control and therefore requiring more action, as recommended by the ADA (8). A second set of endpoints was defined to reflect the intensity of medication management strategies of the three outcomes for subjects with risk factor values at or above these cutpoints. For each CVD risk factor, we calculated the gender-specific proportion of the patients with levels not in control who were currently receiving more intensive medication, presumably reflecting a greater effort to manage the outcome.

Stratified by the presence or absence of CVD, we used logistic regression models to estimate differences in the levels and treatment of CVD risk factors by gender. We estimated the probability of having CVD risk factors not under control or of receiving more intense medication for those with poorly controlled risk factors and modeled the risk differences between men and women and their confidence intervals. The main explanatory variable was patient gender. The covariates included age, body mass index, duration of diabetes, and current smoking.

RESULTS
Subject characteristics are shown in Online Appendix Table-A1. Approximately 63% of the patients had SBP ≥ 140 mmHg, 48% had LDL-C ≥ 130 mg/dl, and 24% had HbA1c levels ≥ 8.0%. Intensive treatment with antihypertensive agents was done in 39% of the patients, with lipid-lowering drugs in 32% and with antihyperglycemic agents in 39%. Unadjusted risk differences were larger in women than in men throughout (Online Appendix Table-A2).

The upper part of Table 1 shows the calculated odds ratios for risk factors not under control. After multiple adjustments, among patients with a CVD history women were significantly more likely than men to have SBP ≥ 140 mmHg, LDL-C ≥ 130 mg/dl and HbA1c levels ≥ 8.0%. The largest differences observed between men and women were in LDL-C control. Among patients without a history of CVD, women were significantly more likely than men to have LDL-C ≥ 130 mg/dl, while there was no difference in SBP and HbA1c.

The lower part of Table 1 reports the estimated probabilities of the intensity of medication management. In adjusted models, among those with a history of CVD, the
medication intensity was similar in men and women with respect to antihypertensive and antihyperglycemic medications, but women received significantly less lipid-lowering medications. Among patients without a history of CVD, there were no significant differences.

CONCLUSIONS
In this large German population of patients with type 2 diabetes women with a history of CVD were more likely to have all three risk factors uncontrolled, the differences in lipid-control being the most pronounced. Women were also less likely to receive lipid-lowering medications. Among patients without a history of CVD, women were more likely to have uncontrolled LDL-C. These results are of particular interest, since it has been shown that the stronger effect of type 2 diabetes on the risk of CHD in women is in part explained by a greater effect of atherogenic dyslipidemia and blood pressure in diabetic women (9). Our findings are consistent with previous reports (5,10) albeit supported by a much larger data source. A cross-sectional analysis in American patients with diabetes found that women were less likely than men to have Hba1c<7%, less likely to be treated with lipid-lowering medications and, when treated, less likely to have LDL-C<100 mg/dl (4). We extend the above data by showing that lack of control is even more pronounced among patients with CVD, a finding with obvious clinical implications.

We have recently shown that among patients with diabetes physicians focus more on antihyperglycemic treatment, although blood pressure and lipid control are more effective in affecting patient-related endpoints (7).

A limitation of the study is its cross-sectional design. The strengths include its large size, >10-times higher than previously published study in this field. It has been shown that a target-driven, long-term, intensified intervention aimed at multiple risk factors in patients with type 2 diabetes reduces the risk of cardiovascular events (11). The present study shows that women with diabetes have poorer control of important modifiable risk factors compared to diabetic men and receive less intensified lipid-lowering therapy. More intensive treatment of women with diabetes may improve the gender disparity in CVD mortality.

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Author Contributions: Drs. Berthold and Gouni-Berthold had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Böhm, Krone.

Acquisition of data: Böhm, Krone.

Analysis and interpretation of data: Berthold, Mantzoros, Gouni-Berthold.

Drafting of the manuscript: Berthold, Mantzoros, Gouni-Berthold.

Critical revision of the manuscript for important intellectual content: Böhm, Mantzoros, Krone.

Statistical analysis: Berthold, Gouni-Berthold.

Administrative, technical, or material support: Böhm, Krone.

Study supervision: Böhm, Krone.

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REFERENCES


Table 1: Odds ratios and 95% CI between diabetic men and women for CVD risk factors not under control as well as for intensity of medication management* for each CVD risk factor among patients with levels not under control (unadjusted and adjusted estimates using the male gender as the referent).

<table>
<thead>
<tr>
<th></th>
<th>With CVD (n = 9,521 men and n = 8,050 women)</th>
<th>Without CVD (n = 12,417 men and n = 14,905 women)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
<td>P value</td>
</tr>
<tr>
<td>CVD risk factors not in control (unadjusted)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP ≥ 140 mmHg</td>
<td>1.20</td>
<td>1.12 to 1.27</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDL-C ≥ 130 mg/dl</td>
<td>1.33</td>
<td>1.25 to 1.42</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HbA1c ≥ 8%</td>
<td>1.04</td>
<td>0.97 to 1.11</td>
<td>0.32</td>
</tr>
<tr>
<td>CVD risk factors not in control (multiple-adjusted)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP ≥ 140 mmHg</td>
<td>1.19</td>
<td>1.11 to 1.29</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDL-C ≥ 130 mg/dl</td>
<td>1.44</td>
<td>1.33 to 1.55</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HbA1c ≥ 8%</td>
<td>1.15</td>
<td>1.06 to 1.25</td>
<td>0.0009</td>
</tr>
<tr>
<td>Intensity of medication management (unadjusted)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 2 antihypertensive agents</td>
<td>1.09</td>
<td>1.02 to 1.16</td>
<td>0.014</td>
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<tr>
<td>≥ 1 lipid-lowering drug</td>
<td>0.76</td>
<td>0.72 to 0.81</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>≥ 2 oral antihyperglycemic agents or insulin</td>
<td>1.11</td>
<td>1.03 to 1.18</td>
<td>0.003</td>
</tr>
<tr>
<td>Intensity of medication management (multiple adjusted)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 2 antihypertensive agents</td>
<td>0.998</td>
<td>0.92 to 1.08</td>
<td>0.97</td>
</tr>
<tr>
<td>≥ 1 lipid-lowering drug</td>
<td>0.85</td>
<td>0.79 to 0.91</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>≥ 2 oral antihyperglycemic agents or insulin</td>
<td>1.04</td>
<td>1.05 to 1.13</td>
<td>0.40</td>
</tr>
</tbody>
</table>

*These outcomes were analyzed as binary variables (≥ 140 vs. < 140 mmHg for SBP; ≥ 130 vs. < 130 mg/dl for LDL-C; and ≥ 8.0 vs. < 8.0% for HbA1c) according to the levels considered not in control and therefore requiring more action as recommended by the ADA. More intense medication management was defined as the use of two or more drug classes of antihypertensive agents for hypertension; of one or more lipid-lowering agents for lipid management; and of two or more oral agents or insulin for antihyperglycemic treatment.