COMMENTS AND RESPONSES

Retinopathy Predicts Cardiovascular Mortality in Type 2 Diabetic Men and Women

Response to Juutilainen et al.

We read with interest the recent article by Juutilainen et al. (1) showing that proliferative retinopathy in both sexes and nonproliferative retinopathy in women independently predict all-cause and cardiovascular disease (CVD)-associated death. The authors have cautiously concluded that the sex difference observed in the association between nonproliferative retinopathy and cardiovascular death needs to be confirmed in larger studies. Indeed, I think the relatively low frequency of retinopathy (23%) and the relatively high cut-off chosen for diagnosing hypertension (blood pressure ≥160/95 mmHg or treatment) could be some possible explanations for these apparently unexpected results.

Previously, we found that retinopathy is associated with an increased CVD incidence among 744 type 2 diabetic patients followed for 5 years (2). This association was largely explained by occurrence of traditional risk factors, especially hypertension (defined as blood pressure ≥130/85 mmHg or treatment) and proteinuria. However, in this study no separate statistical analyses had been made for men and women (2).

Recently, we have reevaluated the CVD outcomes among 2,103 type 2 diabetic participants of the Valpolicella Heart Diabetes Study during an extended follow-up of 6.5 years. A total of 384 participants (63% men, mean age 62 ± 4 years, with diabetes duration 16 ± 3 years) developed incident CVD events (myocardial infarction, ischemic stroke, coronary revascularization, or cardiovascular death), whereas 1,719 participants remained free of diagnosed CVD during follow-up. At baseline, a single ophthalmologist diagnosed retinopathy after pupillary dilation, according to a clinical disease severity scale (3).

Overall, 987 (46.9%) participants had retinopathy, of whom 798 had nonproliferative and 189 had proliferative retinopathy (confirmed by fluorescein angiography). After adjustment for age, BMI, smoking status, lipids, A1C, and diabetes duration and treatment, those with nonproliferative or proliferative retinopathy had a higher risk ($P < 0.001$) of incident CVD than those without retinopathy (hazard ratio 1.57 [95% CI 1.18–2.51] and 3.72 [2.11–7.58] for men; 1.63 [1.23–2.56] and 3.77 [2.15–7.83] for women, respectively). Further adjustment for hypertension (blood pressure ≥130/85 mmHg or treatment) and macroalbuminuria (urinary albumin-to-creatinine ratio ≥25 mg/mmol) considerably attenuated these associations, particularly among those with nonproliferative retinopathy; the risk of incident CVD remained approximately twofold greater—but statistically nonsignificant ($P > 0.07$)—among men (1.95 [0.89–4.41]) and women (1.99 [0.94–4.82]) with proliferative retinopathy.

These results extend our previous findings showing that retinopathy is associated with an increased CVD incidence in people with type 2 diabetes. However, this association appears to be principally explained by occurrence of hypertension and proteinuria. Moreover, our results do not support any significant sex difference in the adverse impact of retinopathy on incident CVD events.

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DOI: 10.2337/dc07-0265

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