Retinopathy Predicts Future Cardiovascular Events Among Type 2 Diabetic Patients

The Valpolicella Heart Diabetes Study

We read with interest the recent article by van Hecke et al. (1) showing that diabetic retinopathy is associated with an increased risk of mortality and cardiovascular disease (CVD) incidence among type 1 diabetic patients.

Because the available data on associations between retinopathy and incident CVD in large population samples of type 2 diabetic patients are limited and conflicting (2–4), we would like to offer recent findings from our large observational study. We carried out a prospective, nested, case-control study in 2,103 type 2 diabetic outpatients, who were free of diagnosed CVD at baseline. More details of study design and methods have been published elsewhere (5).

During 5 years of follow-up, 248 participants (62% men; age 66 ± 4 years; diabetes duration 14 ± 3 years) subsequently developed nonfatal coronary heart disease (myocardial infarction and coronary revascularization procedures), ischemic stroke, or cardiovascular death. Using risk-set sampling, 496 control subjects, among those who remained free of diagnosed CVD during follow-up, were randomly selected in a 2:1 ratio, matched for age and sex to the case patients. At baseline, a single ophthalmologist diagnosed retinopathy after pupillary dilation, according to a clinical disease severity scale (6). Overall, 364 (48.9%) participants had retinopathy, 285 of whom had nonproliferative retinopathy and 79 proliferative retinopathy (as also confirmed by fluorescein angiography). After adjustment for age, sex, BMI, smoking history, plasma lipids, HbA_{1c}, and diabetes duration and treatment, those with nonproliferative (odds ratio 1.7 [95% CI 1.2–2.3]; $P < 0.001$) or proliferative (4.1 [2.0–8.9]; $P < 0.001$) retinopathy had a higher risk of incident CVD than those without retinopathy. Additional adjustment for hypertension (defined as blood pressure ≥130/85 mmHg or treatment) and macroalbuminuria (defined as urinary albumin-to-creatinine ratio ≥25 mg/mmol) considerably attenuated these associations, particularly among those with nonproliferative retinopathy (1.1 [0.7–1.5]; P = NS); the risk of incident CVD remained twofold greater, but statistically nonsignificant, among those with proliferative retinopathy (2.04 [0.9–5.8]; $P = 0.08$).

These results show that retinopathy is associated with a moderately increased risk of incident CVD among type 2 diabetic individuals, thus suggesting that retinopathy and CVD may have similar pathophysiological backgrounds. However, this association seems to be largely explained by occurrence of classical risk factors, especially hypertension and nephropathy. Thus, our data emphasize the importance of evaluating the CVD risk among diabetic patients with retinopathy; these patients could be candidates not only for aggressive treatment of their eye disease but also for blood pressure lowering, as well as aggressive treatment of underlying CVD risk factors.

GIOVANNI TARGHER, MD
LORENZO BERTOLINI, MD
ROBERTO TESSARI, MD
LUCIANO ZENARI, MD
GUIDO ARCARO, MD

From the Diabetes Unit, "Sacro Cuore" Hospital of Negrar, Negrar (VR), Italy.

Address correspondence to Giovanni Targher, MD, Diabetes Unit, Ospedale "Sacro Cuore–don Calabria," Via Sempreboni, 5, 37024 Negrar (VR), Italy. E-mail: targher@sacrocuore.it.

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Prostatic Cancer, Hypogonadism, and Insulin Resistance

A case report

A 47-year-old Greek diabetic man presented with erectile dysfunction and a decrease in sexual desire. The patient had type 2 diabetes for the previous 8 years and was on treatment with rosiglitazone and metformin with strict glycemic control (HbA_{1c} 5.8%). No symptoms or signs of neuropathy were present. Hypogonadotrophic hypogonadism was found.

His plasma testosterone level was very low (100 ng/dl [reference range 300–1,000]) and there was no luetinizing hormone response to luetinizing hormone–releasing hormone (LHRH) test. Further work-up with a magnetic resonance imaging scan and hypophyseal function tests did not reveal any space-occupying lesions of the hypothalamic pituitary site.

The process led to the diagnosis of idiopathic hypogonadotropic hypogonadism. On further work-up, the patient was found to have a prostatic carcinoma. There was no evidence of metastatic disease (his plasma prostate specific antigen [PSA] level was 1.9 ng/ml).

Six years earlier, the patient was treated with finasteride for benign prostatic hypertrophy. A radical prostatectomy was performed and a poorly differentiated adenocarcinoma was found (Gleason grade 10, T3N1Mx).

Postoperatively his plasma testosterone rose to normal levels (530 ng/dl), and there was no need for diabetes medica-