Editorial Commentary

Risk factors for long-term diabetic retinopathy in type 1 diabetes: evaluation of evidence from the Vascular Diabetic Complications in Southeast Sweden study

Jakob Grauslund[1,2,3], Ulrik Frydkjaer-Olsen[1,2], Thomas Lee Torp[1,2]

[1]Department of Ophthalmology, Odense University Hospital, Odense, Denmark; [2]Department of Clinical Research, Faculty of Health Science, University of Southern Denmark, Denmark; [3]Steno Diabetes Center Odense, Odense University Hospital and Svendborg Hospital, Odense, Denmark

Correspondence to: Professor Jakob Grauslund, PhD, DMSci. Department of Ophthalmology, Odense University Hospital, Sdr. Boulevard 29, 5000 Odense, Denmark. Email: jakob.grauslund@rsyd.dk.

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Diabetic retinopathy (DR) is by far the most common long-term complication in diabetes, and it is estimated that 95–97% of patients with type 1 diabetes will be affected in time (1,2). Given that blindness is expected to affect 3–8% of type 1 diabetes patients (3,4), it is vital to perform eye screening in order to treat sight-threatening complications prior to irreversible visual loss (5,6).

While ocular treatment of DR by laser photocoagulation, intravitreal therapy and vitrectomy is only indicated at the advanced stages of proliferative DR (PDR) (7) and diabetic macular edema (8,9), early prevention or arrest of DR has been tested systemically and topically with mixed results. Potential targets for preventive oral treatment have been general blood pressure lowering (10,11), inhibition of the renin-angiotensin system (12-14), and lipid lowering with fenofibrate (11,15). Likewise, topically neuroprotection has been tested with limited short-term effects (16).

So far, strict glycemic control has constantly been confirmed as the most important preventer of DR. This was first demonstrated in the Diabetes Control and Complication Trial (DCCT), which was a 6.5 years randomized trial of patients with type 1 diabetes aimed to evaluate the effect of strict glycemic control with incident and progressive DR as principal endpoints (17). In brief, DR did not differ between groups for the first two or three years, but afterwards a stunning reduction of 75% and 54% for incident and progressive DR, respectively, was demonstrated in the strict glycemic control group. Similar results were confirmed for patients with type 2 diabetes in the United Kingdom Prospective Diabetes Study (UKPDS) (18). In this study, patients randomized to strict glycemic control had a 21% lower 12-year risk of a 2-step DR progression.

For practical reasons, hemoglobin A1c (HbA1c) is used to indicate glycemic control. However, HbA1c only reflects blood sugar levels within the last three months. Therefore, it is vulnerable to differences in glycemic control over time (19). A potential approach to account for this was presented in the Vascular Diabetic Complications in Southeast Sweden (VISS) study, in which the term long-term mean weighted HbA1c (wHbA1c) was introduced (20). In brief, the VISS study was a population-based observational study of 451 patients diagnosed with diabetes prior to the age of 35 between 1983 and 1987. Patients were followed for 18–24 years and level of DR has been determined by fundus photography and evaluated in association with wHbA1c.

Interestingly, lower wHbA1c was the only independent predictor of long-term PDR. Weighted HbA1c was also highly predictive of incident DR illustrated by the fact that 20 of 36 patients with wHbA1c ≤ 50 mmol/mol (6.7%) did not have DR at follow-up as opposed to none of 49 patients with wHbA1c > 80 mmol/mol (9.5%).

In addition to weighted glycemic control, onset of diabetes prior to the age of 6 years also associated with longer duration before development of DR. In contrast to

the present study, a 25-year follow up of 995 patients with type 1 diabetes from the Wisconsin Epidemiologic Study of Diabetic Retinopathy did not identify young age at onset (defined as age 0–9 years) as a predictor of progression of DR, incident PDR, or 2-step or more improvement in DR, respectively (21). While it is well known that PDR is extremely seldom in children (22), the concept of young age at onset as a protective factor for long-term DR is an interesting finding that warrants further investigation.

The VISS study strengthens the evidence identifying glycemic control as the most important modifiable risk factor of DR. Patients with diabetes and treating physicians should be aware of the essential potential to prevent or delay DR by optimizing glycemic control. In addition, life-long diabetic eye screening should be encouraged to prevent vision loss and blindness in diabetes.

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