COMMENTARY

The Clinical Significance and Implications of Developing Diabetic Retinopathy During the 5 Years Following the Diagnosis of Type 1 Diabetes

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The landmark study the Diabetes Control and Complications Trial (DCCT), a randomized controlled clinical trial of tight glycemic control, and its observational follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC), once again provide important data regarding diabetic retinopathy (DR) in people with type 1 diabetes (T1D) in the current issue of *Diabetes Care* (1). In this analysis, the increased risk of developing vision-threatening DR in participants who were detected to have early DR within the first 5 years after the diagnosis of T1D and who had >30 years of follow-up was highlighted. Although there was increased risk of developing clinically significant macular edema (CSME) and proliferative diabetic retinopathy (PDR), only the development of PDR persisted in the adjusted analyses, with hazard ratios of 1.47–1.53 (P = 0.028). The DCCT/EDIC study established the role of tight glycemic control in reducing the risk of progression of DR (2) and the legacy effect in which the benefits of tight control persisted despite stopping the randomized trial of glycemic control (3). However, this early-onset DR within 5 years of diagnosis was not associated with the treatment allocation to glycemic control or to the glycosylated hemoglobin levels.

DR, a major microvascular complication of diabetes, is the leading cause of blindness in working-age Americans, and globally, the prevalence of diabetes is projected to increase by 46%, from 537 million in 2021 to 784 million in 2045 (4), with one-third of the population with diabetes having DR (5). In the U.S., T1D also was found to be increasing annually by 1.4% in youth and even more among Hispanic individuals than non-Hispanic White individuals (4.2% vs. 1.2%, $P < 0.001$) (6). The burden of treating people with diabetes and DR is indeed increasing.

A main barrier for receiving DR treatment is the lack of an effective screening program to detect the presence of DR. Recommendations from the various professional societies suggest schedules for the first dilated eye exam for people with T1D beyond the first 5 years of diagnosis of diabetes, while two organizations suggest scheduling an exam earlier (Table 1). Based on three decades of research on the risk of progression to PDR, the authors of the current DDCT/EDIC study (1) suggest that ". . . annual eye examination initiated at the time of diabetes diagnosis, as currently suggested for patients with T2D [type 2 diabetes], might be valuable for individuals with T1D."

Data that are relevant to this discussion regarding screening protocols for DR include previously published DCCT/EDIC data on the frequency of evidence-based screening for DR (7). Using Markov modeling and including the known risk factors for progression, the likelihood of progression to PDR or CSME in participants was determined to vary with initial severity of DR. Participants with milder DR and lower glycosylated hemoglobin level had a lower rate of progression to PDR or CSME. For example, the risk of progression from no retinopathy to PDR or CSME was 1.0% over 5 years among people who have glycosylated hemoglobin of 6% compared with 4.3% over 3 years among those with a glycosylated hemoglobin level of 10%. The probability of progressing to PDR or CSME was associated with a progressively shorter interval of time between visits, i.e., 5% between retinal screening examinations at 4 years among participants who had no retinopathy and 3 months among those with severe nonproliferative DR. There were 58% fewer exams for DR with this practical, evidence-based schedule rather than the annual examinations advocated by some organizations. They developed an online application (https://extapps.bsc.gwu.edu/shinypub/edic/retinopathy/) that provides the cumulative incidence of PDR and CSME based on the current level of

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Table 1—Recommended eye examination schedules for people with type 1 diabetes

Professional societies	Recommended initial evaluation time	Recommended follow-up time
American Academy of Ophthalmology Preferred Practice Pattern	5 years after diagnosis of diabetes	Yearly, while abnormal findings will dictate more frequent examinations
American Diabetes Association	5 years after diagnosis	If no evidence of DR then every 2 years, otherwise annually
International Society for Pediatrics and Adolescent Diabetes	At age 11 years, with 2–5 years' duration of diabetes	<10 years' duration of diabetes, every 2 years
American Academy of Pediatrics	At age >9 years, 3–5 years after diagnosis	Abnormal findings will dictate more frequent follow-up examinations

retinopathy and averaged glycosylated hemoglobin A_{1c}. Similar data and conclusions were seen for patients with T1D followed for a 30-year period in Australia (8).

How do these data reconcile with the recommendations proposed by the current study to perform initial eye exams at diagnosis, similar to what is recommended for people with T2D? Given the huge burden of screening and caring for patients with diabetes, starting the screening earlier may require a greater effort from all health care systems to accommodate the extra examinations. To accomplish this, one may need to consider telemedicine and the use of algorithms developed with artificial intelligence for the detection of referable DR. In U.S. health care systems in which there is a one-payer system, such as the Veterans Administration (9) and the Indian Health Service (10), robust screening programs are underway to improve the rates of screening of the patients of these health care systems. Although there is great promise with the availability of two U.S. Food and Drug Administration–authorized algorithms for this purpose, there is still a substantial journey prior to implementing such systems in health care networks, as there is a need to test them with real-world data (11).

This call to action to screen earlier was also discussed previously by other investigators who found youth with T1D and T2D were at considerable risk of developing DR and should undergo regular screenings by eye care professionals to ensure that timely diagnoses are determined when DR develops and to limit progression to vision-threatening ocular disease (12). Clearly, screening early may have a beneficial effect, as DR is a lifelong condition that will have a marked impact on quality of life.

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