



## Screening for Diabetic Retinopathy in Youth-Onset Diabetes

Emily Y. Chew, MD - Bethesda, Maryland

The incidence of diabetes is on the rise in the youth of the United States. Although in the past, type 1 diabetes (T1DM) was diagnosed more commonly in adolescents and young adults, the incidence of type 2 diabetes (T2DM) has increased dramatically over the last 2 decades in the United States as rates of obesity also have soared.<sup>1</sup> Accompanying the increase in diabetes is an increase in diabetic retinopathy, a microvascular complication that potentially can lead to blindness. In this issue of *Ophthalmology*, Wang et al<sup>2</sup> used data from records of beneficiaries in a large, nationwide managed care network in the United States to identify risk factors associated with the risk of diabetic retinopathy developing in youths with either T1DM or T2DM (see page 424). The investigators also examined whether the screening guidelines for detecting diabetic retinopathy recommended by organizations such as the American Academy of Ophthalmology, the American Diabetes Association, and the American Academy of Pediatrics can identify individuals affected with diabetic retinopathy appropriately and in a timely fashion.

Using insurance claims in a population of nearly 4000 individuals 21 years of age or younger with newly diagnosed diabetes, the analyses showed that

the median ages of onset of diabetes were 12 and 18 years for T1DM and T2DM, respectively. The median follow-up after the initial diagnosis of diabetes was approximately 3 years. The demographic studies showed that 85% were white among those with T1DM and that 72% were white and 83% were female among those with T2DM. Approximately 20% and 7% of the patients with T1DM and T2DM, respectively, were detected to have diabetic retinopathy by clinical examinations by eye-care providers of various expertise.

Risk factors evaluated in this study included glycemic control (glycosylated hemoglobin), age, gender, and socioeconomic status. Increasing age was correlated with increasing risk of diabetic retinopathy (4.5%/year) in T1DM, whereas men had double the risk and those in the highest income group compared with the lowest income group had 50% reduction of the risk in T2DM. Not surprisingly, increasing glycosylated hemoglobin was associated with greater risk of diabetic retinopathy. With every 1-point increase in glycosylated hemoglobin, there was a 20% and a 30% increase diabetic retinopathy diagnosis in T1DM and T2DM, respectively.

The current guidelines recommend that persons with T2DM should undergo an eye examination at the time of initial diagnosis of diabetes for early detection of diabetic retinopathy regardless of age. However, for those with T1DM, the American Academy of Ophthalmology recommends eye examinations 5 years after initial diagnosis of

diabetes for persons of all ages. The American Diabetes Association and American Academy of Pediatrics suggest that the eye examinations be performed 3 and 5 years after diagnosis of diabetes for subjects 9 years of age and older and those 10 years of age and older, respectively. The data from the current study suggested that up to one quarter of those with any diabetic retinopathy detected by clinical examinations would be missed by using the current guidelines. The severity of the retinopathy at the time of detection was noted as nonspecific diabetic retinopathy in most cases. Did these recommendations miss vision-threatening lesions that required prompt treatment? Only 5 patients were diagnosed with macular edema, and 13 patients were detected clinically to have proliferative diabetic retinopathy, but yet none received standard therapies, including intravitreal injections of anti-vascular endothelial growth factor agents, laser photocoagulation, and so forth. This may be because of potential misclassification, as suggested by the authors. Advanced imaging with optical coherence tomography and fundus photographs was included among the data.

Would it be important to detect the presence of diabetic retinopathy even if it indeed were not vision threatening? Data from numerous studies suggest

that detecting diabetic retinopathy early results in enormous benefits. This is especially relevant for adolescents and young adults whose diabetic retinopathy would pose a high burden of disease simply because of their many more anticipated years of life and, potentially, because of life-long care. Patients with diabetic retinopathy would be encouraged to be followed up for further monitoring and timely delivery of highly effective therapies.

It is not surprising that adolescents with diabetic retinopathy were found to have higher glycosylated hemoglobin. Randomized controlled clinical trials of glycemic control have demonstrated the marked impact of tight glycemic control on the course of all diabetic complications, not only diabetic retinopathy. In both T1DM and T2DM, tight glycemic control has reduced the development and progression of diabetic retinopathy. When the randomized trial was completed, the beneficial effects of intensive glycemic control persisted many years later, although the glycosylated hemoglobin levels were similar in both treatment groups. In T1DM, the tight glycemic control in the Diabetes Control and Complications Trial continued to have a persistent effect 10 to 25 years after the randomized controlled trial had stopped.<sup>3</sup> In persons with T2DM, the same persistent effect of tight glycemic control in reducing the development and progression of diabetic retinopathy also was seen in the United Kingdom Prospective Study of Diabetes<sup>4</sup> and the Actions to Control Cardiovascular Risk in Diabetes Eye Study.<sup>5</sup>

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In the United Kingdom Prospective Study of Diabetes, intensive blood pressure control (from systolic blood pressure of 180–140 mmHg) was demonstrated to be effective in reducing the progression of diabetic retinopathy and reducing the vision loss secondary to diabetic macular edema.<sup>6</sup> However, reducing the blood pressure to 140 to 120 mmHg in the Actions to Control Cardiovascular Risk in Diabetes Eye Study had no effect on the progression of diabetic retinopathy.<sup>5</sup> Management of dyslipidemia, specifically with fenofibrate, reduced the risk of progression of diabetic retinopathy by as much as one third in 2 studies in T2DM, especially in persons with existing diabetic retinopathy.<sup>5,7</sup> Fenofibrate has not been used widely because of the failure of these randomized trials to show a benefit effect of fenofibrate in reducing cardiovascular diseases.

The authors of the current study have stated eloquently some of the limitations of the data collected from a managed care system. This population is less generalizable to the population with diabetes in the United States given that this population had access to health care and did not demonstrate a particularly diverse range of racial and ethnic groups. The prevalence of youth-onset type 2 diabetes was higher in nonwhite populations, as reported in the consensus article on youth-onset diabetes initiated by the American Diabetes Association.<sup>8</sup> Diabetic retinopathy in adolescents with either T1DM or T2DM was more prevalent in nonwhite racial and ethnic groups.<sup>9</sup> In addition to having the highest rates of youth-onset diabetes in the United States, approximately half of the American Indian youth with diabetes had an A1C level greater than 9.5%.<sup>10</sup> Thus, this current study population from a managed care network may underestimate the incidence of diabetic retinopathy given the differences in some of the associated risk factors in some of the other groups with youth-onset diabetes.

The study provides very important data that our professional societies should consider when determining the guidelines for screening for diabetic retinopathy in those with youth-onset diabetes. Changes in the timing of screening for those with T1DM, as suggested by the investigators, should be considered. Screening for diabetic retinopathy takes on more urgency as the number of adolescents who demonstrate diabetes increases dramatically in the United States. Technologies such as telemedicine using nonmydriatic fundus cameras associated with primary care physicians' and pediatricians' offices may provide the necessary tools for screening diabetic retinopathy.<sup>11,12</sup> This may be necessary to accommodate the increase in persons at risk of developing diabetes. However, such screening does not entirely replace the ocular examination to rule out other ocular conditions such as uncorrected refractive errors and other less common eye diseases in the adolescent population. In addition, it provides an opportunity to educate the patient on the importance of

medical therapies, including tight glycemic control, maintaining optimal blood pressure, and treating dyslipidemia. Ultimately, the most important part in fighting this epidemic of youth-onset diabetes may be preventive measures to reduce the rates of obesity nationally and globally. We need to redouble our efforts to achieve this goal.

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## Footnotes and Financial Disclosures

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### Correspondence:

Emily Y. Chew, MD, National Eye Institute/National Institutes of Health, Division of Epidemiology and Clinical Applications, NIH, Building 10, CRC, Room 3-2531, 10 Center Dr, MSC 1204, Bethesda, MD 20892. E-mail: [echew@nei.nih.gov](mailto:echew@nei.nih.gov).