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Long-term complications in youth-onset type 2 diabetes: the TODAY Study

Phil Zeitler MD, PhD
Professor and Head, Section of Pediatric Endocrinology
University of Colorado School of Medicine

The incidence of youth-onset type 2 diabetes (T2D) is increasing in parallel with the rise in childhood obesity in the United States. Compounding this increase, youth-onset T2D exhibits a more pernicious metabolic phenotype, with worse glycemic control, greater insulin resistance and more rapid deterioration of β-cell function than adult-onset T2D, raising the possibility of increased risk for early complications and comorbidities. The TODAY study group reported the prevalence, incidence, and clustering of complications and their association with risk factors in youth with T2D transitioning to young adulthood in the observational follow-up study (TODAY2).

In 2011, 82% of TODAY participants enrolled in the TODAY follow-up study (TODAY2) and the combined TODAY and TODAY2 studies provided up to 15 years of follow-up, with an average length of follow-up of 10.2 years since initial randomization. Assessment for complications began during the TODAY randomized trial and continued through TODAY2.

The prevalence of hypertension at baseline was 19.2% with a cumulative incidence of 65.7% over 15 years. Dyslipidemia was present in 20.8% of participants at baseline with a 15-year cumulative incidence of 51.6%. The prevalence of kidney disease at entry into TODAY was 8.0% with a 15-year cumulative incidence of 54.8%. The prevalence of nerve disease at entry into TODAY was 1.0 % with a 15-year cumulative incidence of 32.4%. Unlike kidney and nerve disease, which were assessed at least annually, retinal disease was assessed only twice during TODAY and TODAY2, thereby preventing determination of cumulative incidence. During

TODAY, 13.7% of participants had retinopathy, all cases being very mild NPDR. In TODAY2, after an additional 7 years of diabetes duration, 51.0% of participants had evidence of either retinopathy or macular edema, including 8.8% with moderate to severe retinal changes and 3.5% with macular edema. The cumulative incidence of any microvascular complication rose steadily from early in the course of disease and affected 50.0% of participants by 9 years and 80.1% by 15 years

Increased risk for development of any microvascular complication was associated with minority race/ethnicity, higher HbA1c, lower insulin sensitivity, hypertension, and dyslipidemia in unadjusted models, as well as multivariable models adjusted for sex, race/ethnicity and age at randomization.

Participants in TODAY and TODAY2 exhibited clustering of complications affecting the kidney, nerve, and retina. At the time of last visit, only 39.9% of all participants enrolled in TODAY were free of any complications, 31.8% had one complication, 21.3% had two, and 7.1% three complications. The risk factors for clustering of complications include minority race/ethnicity, glycemia, lower insulin sensitivity, hypertension, and dyslipidemia.

TODAY also collected and adjudicated diabetes-related events identified by participants' regular medical providers. These adjudicated events include rare but serious events such as myocardial infarction (MI), stroke (CVA), amputations, advanced eye disease, and end-stage kidney disease. In addition, there were 6 deaths among participants, due to myocardial infarction, kidney failure, sepsis, post-operative sepsis with multi-organ failure, and drug overdose.

Taken together, these data paint a picture of youth-onset T2D as a serious disease with early impacts for patients and public health implications for society. These grave findings suggest the

need for more aggressive management of glycemic and non-glycemic targets. Better understanding of health care needs and usage patterns of young adults with youth-onset type 2 diabetes will help ensure that the health care systems in the US and other countries with large populations of individuals with youth-onset T2D are fully prepared for the anticipated needs of these individuals.