

# The Toll of Diabetes



By *Chuck Dinerstein* — August 14, 2018



Courtesy of Bess Hemeti [1]

As a vascular surgeon many of my patients had diabetes and in evaluating their surgical risk I was taught a rough rule of thumb: the chronologic age of a patient with diabetes added to the duration of their diabetes was a good measure of their physiologic age, e.g., a 65-year-old with a 20 year history of diabetes was physiologically 85. A paper in *The Lancet* demonstrates the truth of that heuristic in Type 1 diabetes.

Type 1 diabetes represents a significant chronic disease of childhood and results in a lower life expectancy, primarily from cardiovascular disease. While Type 1 diabetes represents an autoimmune disease in which the insulin-producing cells of the pancreas are destroyed there is increasing evidence that it is not one monolithic process. Varying biomarkers suggest the “insulinitis” of Type 1 diabetes has differing severity and as a consequence places different stresses on our physiology. When we characterize the phenotype, Type 1 diabetes, our aggregation may ignore some of the nuances. The study looks for a bit of that subtlety in the age of onset and subsequent duration.

## **The Study**

The researchers made use of the Swedish National Diabetes Register which records health information on all patients, 18 or older, with diabetes; and linked this information to other Swedish registries to capture sociodemographic details. For this study, a patient was considered a Type 1 diabetic if they were treated solely with insulin and had an age of onset before 30. About 27,000 patients were identified, mean age 29, with slightly more men than women and matched against multiple control populations; longitudinal information spanned a median of 10 years. The age of onset was stratified into groups.

- There was little difference in education, income or marital status between patients with Type 1 and controls.
- Cardiovascular disease was more common in the patients with diabetes, although the incidence was quite low in both populations. [1]
- HbA1c levels were highest in those with the youngest age of onset
- Incidence rates of an elevated BMI, high blood pressure, elevated cholesterol and smoking increased with age of onset.

So roughly speaking, there were no apparent differences in socioeconomic (and how that may relate to health care access and treatment) between the two groups. And as we would guess, cardiovascular disease, the well recognized “complication” of diabetes was elevated in that group. The elevation of HbA1c reflects both the chronicity of the disease as well as the difficulties in mimicking physiologic ranges. But the higher incident rates for BMI, hypertension, and elevation of cholesterol, in the presence of relatively lower HgA1c values, in those with late-onset Type 1 diabetes suggests, there may be a subclinical period of metabolic changes that may cause damage but are phenotypically insufficient to meet our diagnostic criteria - and indeed demonstrates that Type 1 diabetes is not a monolithic grouping. The researchers went on to calculate hazard ratios, measures of increased risk. Earlier onset compared with later onset of Type 1 diabetes, was associated with

- Threefold greater risk of cardiovascular disease
- A loss of 16 years of life compared to a 10-year loss in older-onset patients [2]
- Women had greater hazard ratios and loss of life expectancy than men in all age groups and for all outcomes. For example, onset between birth and age ten was associated with a 30-fold increase in heart attacks, in aggregate, but for women, it was 90-fold greater.

### **Duration and gender matters**

The study makes it clear that the duration of Type 1 diabetes matters, merely recording whether a patient has diabetes or not, poorly reflects the impact of the phenotype on the diseases, or what we term co-morbidities, that accompany diabetes. Even more importantly, the cumulative physiologic damage from Type 1 diabetes is much different between men and women. It is not that women have atypical symptoms, they have a different form of heart disease with its own prognosis despite the phenotypic similarities.

The real problem given this new information is how we might intervene. The authors point out that the American Heart Association and American Diabetes Association guidelines acknowledge the increased risk for those with Type 1 diabetes but do not alter their recommendations based upon duration. While the authors are quick to move away from treating children with blood pressure and cholesterol medications they do raise the question of whether they should be prescribed to those with Type 1 diabetes at an earlier age before the phenotype of the coronary disease appears.

The study has limitations, it reflects the Swedish population, it has no information on the quality of glucose management (beyond HgA1c) in these patients, and one might argue about their diagnostic criteria for Type 1 diabetes. The loss of glucose control, our hallmark for diabetes, has

many underlying causes and the trajectory of our health is more influenced by those underlying causes – diabetes is more than type 1 or 2, understanding the nuance may well help to personalize our care and improve our outcomes.

[1] Outcome measures were all-cause mortality, cardiovascular mortality, acute myocardial infarction (heart attack), stroke, coronary artery disease, heart failure and atrial fibrillation.

[2] If you play with the math the heuristic is in the right ballpark, age adding about .6 years for every year diabetes was present.

Source: Excess mortality and cardiovascular disease in young adults with Type 1 diabetes in relation to age of onset: a nationwide, register-based cohort study. The Lancet DOI: 10.1016/S0140-6736(18)31506-X

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