Glycemic Control and Cardiovascular Disease in Patients With Type 1 Diabetes

Reviewed by K.M. Venkat Narayan, MD, MPH, FRCP, FACP

STUDY

The DCCT/EDIC Study Research Group: Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 353:2643–2653, 2005

SUMMARY

Objective. To investigate whether the use of intensive glycemic control versus conventional therapy during the Diabetes Control and Complications Trial (DCCT) affected the long-term incidence of cardiovascular disease (CVD).

Design. The DCCT randomly assigned 1,441 patients with type 1 diabetes to intensive or conventional therapy, treating them for a mean of 6.5 years. Ninety-three percent were subsequently followed for CVD in the Epidemiology of Diabetes Interventions and Complications (EDIC) study.

Setting. Multicenter study in the United States.

End points. CVD was defined as nonfatal myocardial infarction, stroke, death from CVD, confirmed angina, or the need for coronary artery revascularization.

Results. At the end of the DCCT, after 6.5 years of treatment, mean hemoglobin A_{1c} (A1C) was 7.4% in the intensive group and 9.1% in the conventional group. After an additional 11 years of follow-up, during which the conventional group received more intensive therapy, A1C levels were 7.9 and 7.8% in the DCCT intensive and conventional groups, respectively. Intensive treatment reduced the risk of any CVD event by 42% (95% CI 9–63) and the risk of nonfatal myocardial infarction, stroke, or death from CVD by 57% (12–79). The change in A1C during 6.5 years of treatment in the DCCT was significantly associated with most of the positive effects of intensive treatment on CVD.

Conclusion. Intensive glycemic therapy reduces the risk of CVD in patients with type 1 diabetes.

COMMENTARY

CVD is the leading cause of death among people with diabetes, who have a two to three times greater risk of CVD than those without diabetes.[1] Prevention of CVD among people with diabetes is, therefore, important. Several CVD risk factors (e.g., dyslipidemia, smoking, and hypertension) are well established. Epidemiological studies have shown a relationship between glycemia and CVD, but until recently this had not been definitively confirmed in a randomized controlled trial.

These recently published results of the DCCT/EDIC study make a very important contribution to our knowledge on this topic by confirming the link between glycemia and CVD in people with type 1 diabetes. The DCCT/EDIC study is the follow-up of the classic DCCT of 1,441 people with type 1 diabetes. The participants were, on average, 27 years old when they enrolled in the DCCT and 45 at the conclusion of EDIC in 2005. At the start of the DCCT, participants were randomized to receive either intensive or conventional glycemic control, and the mean A1C in both groups was identical (9.1%). Randomization ensured that all known CVD risk factors (smoking, hypertension, and dyslipidemia) were evenly distributed between the two groups.

At the end of the DCCT, after an average treatment duration of 6.5 years, the mean A1C 7.4% in the intensive group and 9.1% in the conventional group. This difference resulted in major benefits in reducing microvascular complications. The DCCT cohort was then followed up in EDIC for 11 years, and the average A1C at its conclusion in February 2005 was 7.9% in the intensive group and 7.8% in the conventional group. During 11 years of post-DCCT follow-up, the intensive group worsened by only 0.5 of a percentage point, but the conventional group benefited from switching to intensive treatment, and the gap between the two groups almost disappeared. Although glycemia tends to worsen with age, the experience from the DCCT/EDIC study demonstrates that it is possible to achieve average levels of A1C < 8% at 17 years of follow-up.

By the conclusion of the EDIC, the risk of any CVD was 42% lower in the group treated intensively in the DCCT for 6.5 years than in those treated conventionally. Although the mean A1C in the two groups converged, the DCCT intensive group benefited in terms of CVD. All other risk factors (blood pressure, lipids, and smoking) were similar in the two groups. This study has thus demonstrated conclusively for the first time that CVD can be reduced substantially and independently by intensive glycemic control.

The study has two important limitations. First, the numbers of events were

small. Second, the interventions were unmasked at the end of the DCCT. Despite these limitations, this rigorously conducted study provides the best evidence yet of a link between glycemia and CVD.

An obvious question is whether these results will apply to people with type 2 diabetes. The Action to Control Cardiovascular Risk in Diabetes trial is addressing this question, and so is the Veterans Affairs Glycemic Control and Complications in Diabetes Type 2 trial. Evidence for reduction in microvascular complications from tight glycemic control among people with type 2 diabetes already exists.

One concern about tight glycemic control in people with diabetes is the risk of hypoglycemia. In the past 5–10 years, however, innovations in glycemia testing, drugs, and delivery methods mean that the risk of hypoglycemia, while serious, should be manageable through good evidence-based protocols.

The results of the DCCT/EDIC study provide stronger justification for tight control of glycemia among people with diabetes. The challenge will be to translate these findings into practice. This will require a different mindset and a corresponding set of new strategies to implement aggressive diabetes control while keeping side effects low.

REFERENCES

[1]Saydah SH, Eberhardt MS, Loria CM, Brancati FL: Age and the burden of death attributable to diabetes in the United States. *Am J Epidemiol* 156:714–719, 2002

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