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CVD Risk Factors Only Explain ~50% of the Effect of Glycemia on CVD Risk in DCCT/EDIC

A further analysis of the Diabetes Control and Complications Trial and its follow-up, the Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study suggests that HbA_{1c} is associated with the risk of cardiovascular disease (CVD) and also with a series of traditional CVD risk factors in type 1 diabetes. However, when considered together, the traditional CVD risk factors only account for ~50% of the effect of glycemia on the risk of CVD. As a consequence of this, the authors of the study, Bebu et al. (p. 1284), suggest that aggressive management of nonglycemic CVD risk factors is needed in addition to aggressive glycemic management in type 1 diabetes. Using data from the DCCT/EDIC study, the authors estimate the degree to which the effect of glycemia on CVD risk is mediated (explained) by traditional CVD risk factors, individually and grouped together. Cardiovascular outcomes included a composite CVD outcome as well as major atherosclerotic cardiovascular events (MACE). After adjusting for age, they found that only a few individual factors (mean pulse, total and LDL cholesterol, triglycerides, and albumin excretion rate) explained more than 10% of the effect of glycemia on CVD risk. When considered together in multivariable models, the traditional CVD risk factors only explained up to ~50% of the effect of glycemia on CVD risk. Commenting further, author Ionut Bebu told *Diabetes Care*: “With standardized assessments of putative risk factors and CVD outcomes and outstanding follow-up for nearly three decades, the DCCT/EDIC study provides a unique opportunity to evaluate mechanisms underlying the effect of glycemia on the risk of CVD in type 1 diabetes. Our findings show that the effect of cumulative glycemic exposure on the subsequent risk of CVD is not completely explained by its association with traditional CVD risk factors in this population. Therefore, aggressive glycemic management, coupled with strong control of nonglycemic traditional CVD risk factors are indicated for individuals with type 1 diabetes.”

Bebu et al. Mediation of the effect of glycemia on the risk of CVD outcomes in type 1 diabetes: the DCCT/EDIC study. *Diabetes Care* 2019;42:1284–1289

Cognitive Behavioral Therapy and Exercise for Remission of Depression in Type 2 Diabetes

A behavioral intervention approach can result in clinically meaningful improvements in depression outcomes in adults with type 2 diabetes and major depressive disorder, according to de Groot et al. (p. 1185). The controlled trial, Program ACTIVE, involved patients with type 2 diabetes for >1 year and depression who were then randomized to receive one of four treatments. The treatments were 10 sessions of cognitive behavioral therapy (CBT) over 12 weeks, 12 weeks of community-based exercise including six sessions with a personal trainer, a combination of CBT and exercise, or usual care as the control. Primary outcomes were depression remission and change in HbA_{1c}. The study was performed in community settings in three U.S. states through partnerships with community-based fitness and mental health providers. The authors found that the odds of achieving depression remission with CBT, exercise, or both were 5.0–6.8 times higher than usual care. The combination of CBT and exercise also resulted in improved HbA_{1c}. In addition, an exploratory post hoc analysis revealed that participants with HbA_{1c} >7.0% at baseline experienced a 1.1% reduction in HbA_{1c} following completion of the combination of CBT and exercise. The results, they suggest, are clinically meaningful and means that these approaches (CBT and exercise) can effectively be delivered using existing community resources and providers in regions with restricted access to specialist care resources. They note a number of limitations with the study including the possibility that the small sample size may have precluded observing reductions in HbA_{1c} in the arms with just one intervention (i.e., CBT or exercise alone). According to author Mary de Groot: “The findings from Program ACTIVE show that people who struggle with type 2 diabetes and depression can find relief from talk therapy and exercise. When talk therapy and exercise are combined, both depression and HbA_{1c} are improved resulting in better quality of life. Our hope as a research team is that these interventions will become widely available to patients and their providers.”

de Groot et al. Program ACTIVE II: outcomes from a randomized, multistate community-based depression treatment for rural and urban adults with type 2 diabetes. *Diabetes Care* 2019;42:1185–1193

Young Children With Type 1 Diabetes Have Much Higher Insulin Variability Than Adults or Adolescents

Young children with type 1 diabetes have a higher variability in insulin requirements than adults or adolescents, according to Dovc et al. (p. 1344). As a result, they suggest the finding may complicate the attainment of glucose control in this group particularly through higher risk of dysglycemia. They also suggest, on the basis of the result, that young children may benefit from using hybrid closed-loop insulin delivery to help control glucose levels. The conclusions come from an analysis of data from trials with closed-loop insulin delivery systems where the authors compared thousands of days and nights worth of data collected over a 3-week period. The 114 participants involved in the study used the systems in closed-loop mode under unrestricted-living conditions (20 individuals aged 1–6 years, 21 individuals aged 7–12 years, 15 individuals aged 13–17 years, and 58 adults aged >18 years). The authors found that compared with adults, the coefficient of variation in insulin delivery was 10.7% higher in young children at night and 6.4% higher during the day. A similar pattern emerged when comparing young children with adolescents; nighttime variation was 10.2% higher while daytime variation was 7.0% higher. They suggest the observations might well inform clinical practice and explain in part why, despite frequent insulin dose adjustments, dysglycemia and risk of hypoglycemia remains a significant issue in this population. They propose that varying spontaneous activity levels, growth and development, and lifestyle as reasons for this age-group having particular issues meeting glycemic targets. On that basis, they suggest that closed-loop insulin systems might offer real benefits in this age-group. Author Roman Hovorka commented further: “Closed-loop systems are the future of type 1 diabetes therapy and more so for the very young children who have particular difficulties in attaining desirable glucose levels due to, at least in part, highly variable insulin needs.”

Dovc et al. Young children have higher variability of insulin requirements: observations during hybrid closed-loop insulin delivery. *Diabetes Care* 2019;42:1344–1347

Diabetes, Poor Glycemic Control Linked to Cognitive Impairments in Older Age

Further analysis from the Atherosclerosis Risk in Communities (ARIC) Study suggests that poor glycemic control, diabetes status, and longer diabetes duration are associated with poor cognitive outcomes in older adults. As a result, the authors of the study, Rawlings et al. (p. 1248), suggest that maintaining good glycemic control in older adults with diabetes is important for mitigating cognitive impairments that might appear with age. The conclusions come from a prospective analysis of ~5,000 participants in the ARIC Study and specifically data collected at the fifth (2011–2013) and sixth (2016–2017) examinations. Among a series of outcomes, they report that diabetes was not associated with incident dementia but was associated with incident mild cognitive impairment. HbA_{1c} level in individuals with diabetes was also linked to cognitive outcomes; well-controlled individuals with HbA_{1c} <7% did not have higher risk of cognitive impairment compared with individuals without diabetes, while individuals >7% had 1.73 times higher risk. Longer duration of diabetes was also associated with incident dementia and cognitive impairment. The link between diabetes and dementia is widely documented but progression in cognitive function, from normal cognition to mild cognitive impairment and then on to dementia, has been less studied, according to the authors. On the basis of the outcomes, they suggest that good glycemic control in this population may reduce cognitive impairment development in older age. Commenting more widely on the research, author Elizabeth Selvin said: “These results, coupled with existing literature, suggest diabetes and poor glycemic control have important implications for short- and long-term changes. There is a substantial cognitive decline associated with diabetes and poor glucose control in people with diabetes. And we know how to prevent or delay the diabetes associated with this decline. We hope that the message that better diabetes control and prevention of diabetes and its risk factors can help stave off cognitive decline will help motivate people to make lifestyle changes.”

Rawlings et al. The association of late-life diabetes status and hyperglycemia with incident mild cognitive impairment and dementia: the ARIC Study. *Diabetes Care* 2019;42:1248–1254

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