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Diabetes Care®

In This Issue of *Diabetes Care*

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Predicting High-Risk Type 1 Diabetes Drivers to Reduce Accidents

Up until now no specific clinical screening tool has existed to identify type 1 diabetes patients who drive and who may have heightened risk for driving accidents due in particular to hypoglycemia. Cox et al. (**p. 742**) report the development and validation of a short questionnaire specifically designed to achieve this. In a series of studies the authors initially report that they could identify a number of factors that predicted low and high risk for accidents, which they subsequently assembled into the Risk Assessment of Diabetic Drivers (RADD) scale. To then validate the approach, they recruited just over 1,700 drivers with type 1 diabetes and asked them to complete the RADD over the Internet to eventually identify groups at low or high risk for driving mishaps. Following treatment with either regular care alone or in combination with the Internet intervention, they found that high-risk drivers did indeed have more accidents and that the intervention reduced the rate of accidents in comparison to regular care alone. Commenting more widely on the studies, author Daniel J. Cox said: "There are many conditions that increase the risk of vehicular collisions. These include adolescence, attention deficit/hyperactivity disorder, depression, sleep apnea, narcolepsy, along with diabetes. The advantage to drivers with diabetes is that they can determine if they are at elevated risk and then take steps to prevent such mishaps. Avoiding driving mishaps has major benefits in terms of medical, financial, legal, social, and psychological impacts, affecting the driver with diabetes, their loved ones, and others on the road. Just like diabetes caretakers should routinely check the feet of their patients for lesions, they should also check the vulnerability of their patients for driving mishaps. However, it is important to note that drivers with diabetes who are not identified as high risk still have the possibility of experiencing acute driving impairment either due to hypoglycemia or extreme hyperglycemia."

Cox et al. Predicting and reducing driving mishaps among drivers with type 1 diabetes. Diabetes Care 2017;40:742–750

Early HbA_{1c} Response to Metformin in Type 2 Diabetes Is Predictive of Later Cardiovascular Complications and Death

Achieving large initial reductions and low levels of HbA_{1c} within 6 months of metformin initiation is associated with lower risk of cardiovascular disease and death in type 2 diabetes. This is according to Svensson et al. (**p. 800**) who report the outcome of a large population-based cohort study based in northern Denmark that classified patients according to HbA_{1c} achieved and subsequent rates of acute myocardial infarction, stroke, or death. According to the authors, while previous studies have pointed toward some benefit for early intensive glycemic control on cardiovascular outcomes, the definitive relationship between early achieved HbA_{1c} level or the magnitude of HbA_{1c} reduction and subsequent long-term risk in a real-world setting has never been investigated thoroughly. Compiling data from 24,752 type 2 diabetes patients taking metformin, they found that risk for a combined measure of death, myocardial infarction, and stroke gradually increased with rising levels of achieved HbA_{1c} compared with a target of 6.5%. Individual outcome events followed a similar pattern. The magnitude of reduction of HbA_{1c} from baseline also predicted reduced risk of adverse outcomes in comparison to no change at all. According to author Reimar W. Thomsen: "Our findings clearly show that achievement of good glycemic control early in type 2 diabetes—as recommended in current treatment guidelines—predicts beneficial long-term prognosis. Of importance, we observed this association also in elderly people with type 2 diabetes. We cannot say from our data if the decreased risk of cardiovascular outcomes and mortality is related to more intensive and compliant early glucose-lowering therapy or rather if rapid glycemic responders to therapy may have a milder variant of type 2 diabetes than patients that are poor responders. No matter what, poor early glycemic response provides an important prediction tool for doctors to identify patients who have increased risk for cardiovascular complications and death."

Svensson et al. Early glycemic control and magnitude of HbA_{1c} reduction predict cardiovascular events and mortality: population-based cohort study of 24,752 metformin initiators. Diabetes Care 2017;40:800–807

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No Relation Between Daily Glycemic Variability and Microvascular Outcomes After Accounting for Missing Data in the DCCT

The Diabetes Control and Complications Trial (DCCT) revealed that intensive treatment markedly reduced the risk of the microvascular complications of type 1 diabetes compared with conventional therapy. In subsequent analyses, it became clear that lifetime exposure to hyperglycemia (mean HbA_{1c} levels) almost totally explained the difference in risk between groups. However, the level of HbA_{1c} alone did not explain the majority of the risk among all patients in the study. Thus, it appears that factors other than HbA_{1c} could explain some of the risk of these complications. A particular focus has been on glycemic variability and specifically whether daily swings in glucose levels might explain the risk of developing microvascular complications. Other investigators have attempted to explore the role of glucose variation using the DCCT data because it includes quarterly 7-point blood glucose profiles and careful assessment of complications over an average of 6.5 years. However, according to Lachin et al. (**p. 777**), those analyses may be flawed due to a modest fraction (almost 20%) of missing blood glucose profile values. To solve this issue, the authors report a reanalysis that crucially deals with the missing data before statistically testing the relationship in question. The method they report is multiple imputation, which, at least in theory, can provide an objective estimate of the associations in question from data sets with complete glucose profile values. Overall, their results suggest that within-day glycemic variability likely does not play a role in the development of microvascular complications beyond that of the influence of mean blood glucose levels. As outlined by author John M. Lachin to *Diabetes Care*: "The variance of the values within profiles is modestly correlated with the mean glucose within profiles. So the question is whether the level of glucose variation provides additional information about processes that determine complications than does the mean itself. In our results it does not appear to do so."

Lachin et al. Association of glycemic variability in type 1 diabetes with progression of microvascular outcomes in the Diabetes Control and Complications Trial. Diabetes Care 2017;40:777–783

Preventing Hypoglycemia With a Predictive Insulin Pump and Continuous Glucose Monitoring

A predictive low glucose management approach to insulin delivery via a pump and continuous glucose monitoring can significantly reduce numbers and severity of hypoglycemia events in children with type 1 diabetes. This is according to Battelino et al. (**p. 764**) who report an investigator-led randomized controlled trial of the device with the algorithm system turned on versus off as the control. According to the authors, the system is designed to stop insulin delivery when glucose levels are predicted to hit a certain level—and to do this 30 min before to allow glucose levels to rise. After recovering to a target range, the system then resumes insulin delivery. The trial involved 100 children (aged 8–18 years) with type 1 diabetes who were then randomized to either the intervention group or the control group. All used the same sensor-augmented insulin pump (from Medtronic). According to the authors, the number of hypoglycemia events in the treatment group was significantly reduced in comparison to the control group over the 2-week intervention period. The mean number of events in the treatment group was 4.4 ± 4.5 while the control group experienced 7.4 ± 6.3 events over the 14-day trial. The authors highlight that while there were no serious adverse events during the trial, many patients did experience moderate hyperglycemia, which, in the long run, will presumably need addressing. Commenting on the study, author Tadej Battelino said: "Despite accumulating data that sensor-augmented insulin pumps, particularly with the predictive low glucose management function, are safe and effectively reduce the number and duration of hypoglycemia in young patients with type 1 diabetes, their use in routine clinical practice remains surprisingly low. I hope the positive results from the current study will translate into a more widespread use of continuous glucose monitoring and sensor augmented insulin pumps in pediatric populations with type 1 diabetes."

Battelino et al. Prevention of hypoglycemia with predictive low glucose insulin suspension in children with type 1 diabetes: a randomized controlled trial. Diabetes Care 2017;40:764–770

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