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In This Issue of *Diabetes Care*

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Diabetes and Prediabetes Increase Risk of All-Cause Hospitalization

Having diabetes, prediabetes, or even undiagnosed diabetes is likely to significantly increase risk of all-cause and cause-specific hospitalization, and, as Schneider et al. (**p. 772**) suggest, preventing progression from prediabetes to diabetes could well have significant implications for health care systems in the U.S. The community-based longitudinal Atherosclerosis Risk in Communities (ARIC) study followed 13,522 individuals over a 20-year period and examined numbers of hospital admissions and reasons for admission. Participants were then categorized by diabetes/HbA_{1c} status via frozen blood assays. Rates of all-cause hospitalization increased according to the severity of diabetes diagnosis category (HbA_{1c}). For example, rates of hospitalization were 3.1 times higher when full diabetes was present, 1.6 times higher with undiagnosed diabetes, and 1.3 times higher with prediabetes (all in comparison with no diabetes). A standout reason for hospitalization with diabetes was admissions due to cardiovascular complications, which, the authors hypothesized, would be the case. However, other categories of the disease were all significantly increased in patients with diabetes. According to the authors, the magnitude of risk and the causes of hospitalization have previously been poorly characterized despite spiraling costs associated with the disease in the U.S. The total estimated health care costs in the U.S. for diabetes hit $245 billion in 2012, and ~43% of that total was inpatient hospital care. Commenting on the outcomes of the study, Dr. Schneider stated: "Our study found increased risk of total hospitalizations, and cardiovascular disease-related hospitalizations in particular, among those with prediabetes, undiagnosed diabetes, and diagnosed diabetes. These results suggest that prevention of prediabetes from progression to overt diabetes and improved glycemic control among those with diagnosed diabetes may reduce the burden of hospitalizations over the life span. We also found high rates of hospitalization due to endocrine, infection, and iatrogenic/injury causes among those with diagnosed diabetes, which suggests that increased efforts are needed to reduce the burden of potentially preventable hospitalization among individuals with diabetes."

Schneider et al. Diabetes and prediabetes and risk of hospitalization: the Atherosclerosis Risk in Communities (ARIC) study. Diabetes Care 2016;39:772–779

Type 2 Diabetes Is Reversible Following Very Acute Weight Loss

Type 2 diabetes is potentially reversible following acute weight loss and subsequent weight maintenance over 6 months, according to Steven et al. (**p. 808**). However, the diet only resulted in reversal of type 2 diabetes in 40% of the patients, with the balance seeing no benefit over the same period. The prospective longitudinal single-center study examined the physiological effects of weight loss in 30 individuals with type 2 diabetes. The study had three phases: weight loss via a very low-calorie diet, a return to an isocaloric diet, and then 6 months of intensive dietary weight management. A range of physiological markers were then assessed. The authors report significant underlying differences between the so-called responders and nonresponders in terms of physiological reaction to the very low-calorie diet. This included reductions in HbA_{1c} to near-normal healthy levels in the responders. However, perhaps the most telling finding was that all the responders returned to nondiabetic blood glucose levels and were also characterized as having a return to first-phase insulin response. Although the study is not controlled, the authors note that "the study was designed to define the durability over 6 months of the clinical and pathophysiological changes." They also report that a larger controlled investigation is already underway in terms of the DiRECT trial. This should, according to the authors, address whether such an approach has clinical utility. Commenting on the wider implications of the study, Prof. Taylor stated: "The major importance of these results lies in the durability of the return to nondiabetic levels of glucose control off all treatment. However, the demonstration that the levels of fat in liver and pancreas remained normal even though the volunteers would still be classified as obese or overweight is a dramatic confirmation of the personal fat threshold concept: individuals only develop type 2 diabetes if they exceed their personal fat threshold, and this is irrespective of BMI."

Steven et al. Very low-calorie diet and 6 months of weight stability in type 2 diabetes: pathophysiological changes in responders and nonresponders. Diabetes Care 2016;39:808–815

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Intensive Glucose Control Reduces Risk of End-Stage Kidney Disease in Type 2 Diabetes: Long-term Follow-up and Benefits

Intensive glucose control may produce long-term reductions in risk of end-stage kidney disease (ESKD) in type 2 diabetes, and it is likely that there is no increased risk of cardiovascular events or death, according to Wong et al. (**p. 694**) who report a 5.4-year post-trial follow-up of ~8,500 participants from the ADVANCE trial, which showed that intensive glucose control reduced the risk of a range of renal outcomes, including ESKD in patients with type 2 diabetes. According to the authors, the small number of ESKD events in that study limited the strength of the conclusions, and so, this lead them to follow-up with the ADVANCE-ON study that they now report a further analysis of. While the differences in HbA_{1c} achieved during the initial (ADVANCE) trial phase had disappeared by the first post-trial visit in ADVANCE-ON, in-trial reductions in risk of ESKD persisted after 10 years of overall follow-up. There were 29 ESKD events in the intensive treatment group compared with 53 events in the standard treatment group after 10 years. Subgroup analyses then showed that earlier stages of kidney disease and lower blood pressure at baseline were likely associated with the greatest reductions in risk of ESKD. Of note, there was no increased risk of cardiovascular complications or death associated with the intensive glucose control over the longer period of the study. Commenting more widely on the results, Prof. Zoungas stated: "Our findings highlight the importance of active and effective blood glucose management for long-term renal protection in patients with type 2 diabetes. Intensive glucose treatment is likely to have produced major long-term benefits for the kidneys without jeopardizing cardiac safety. The long-term renal benefits were more pronounced for patients with preserved kidney function and better blood pressure control."

Wong et al. Long-term benefits of intensive glucose control for preventing end-stage kidney disease: ADVANCE-ON. Diabetes Care 2016;39:694–700

Sleep Deprivation Worsens Cognitive Impairment in Recovery From Hypoglycemia

Sleep deprivation on top of hypoglycemia results in greater levels of cognitive dysfunction and a longer persistence of hypoglycemia symptoms in the recovery period in comparison with hypoglycemia alone, according to Inkster et al. (**p. 750**) who examined the effects in a small (n = 14) study of adults with type 1 diabetes. Significantly, hypoglycemia resulted in cognitive dysfunction, but additional sleep deprivation did not add to the effects before or during hypoglycemia. It was only in the recovery period, when normoglycemia was restored that sleep deprivation adversely affected cognition and extended persistence of hypoglycemia symptoms. To study the effects, the authors used a hyperinsulinemic, hypoglycemic clamp method to experimentally reduce blood glucose levels. They did this twice, with one session being conducted after no overnight sleep and the other following a good night of sleep. All participants were randomized and counterbalanced to the experimental condition, according to the authors. Throughout the clamp sessions they then applied a battery of sequential tests to assess a range of different cognition function–related variables. These included tests for attention, response times, and a variety of memory tests. According to the authors, although such investigations have taken place previously, they have focused on healthy adults and showed that full sleep deprivation did not add to cognitive dysfunction due to hypoglycemia. Commenting more widely on the study, Dr. Inkster stated: "This previously unrecognized effect of sleep deprivation on recovery from hypoglycemia is relevant to people with type 1 diabetes who encounter periods of sleep deprivation. For example, activities such as driving could be compromised for longer than the 45 min that is usually recommended to allow full recovery from hypoglycemia. Similarly, symptoms of hypoglycemia continued to be scored higher when subjects were sleep deprived. That is something that people with type 1 diabetes should be aware of to prevent overtreatment of hypoglycemia occurring overnight or at other times of sleep deprivation."

Inkster et al. Effects of sleep deprivation on hypoglycemia-induced cognitive impairment and recovery in adults with type 1 diabetes. Diabetes Care 2016;39:750–756

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