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DIABETES

Intensive glucose control in type 1 diabetes mellitus reduces risk of GFR loss

Intensive early control of glucose levels in patients with type 1 diabetes mellitus (T1DM) reduces the long-term risks of developing an impaired glomerular filtration rate (GFR), according to new research. Investigators involved in the Epidemiology of Diabetes Interventions and Complications (EDIC) study—an observational extension of the interventional Diabetes Control and Complications Trial (DCCT)—found that patients who received intensive diabetes therapy early in the course of disease had a 50% lower risk of developing an impaired GFR over a median follow-up of 22 years than patients who received conventional diabetes therapy. "This study demonstrated for the first time that impaired GFR can be prevented in T1DM," explains Ian de Boer of the study group. "Combined with the previously published beneficial effects of DCCT intensive diabetes therapy on albuminuria, retinopathy, neuropathy, and cardiovascular disease, this study reinforces current American Diabetes Association and National Kidney Foundation guidelines to target a glycated hemoglobin level of less than 7% in the care of people with T1DM."

Patients with T1DM are at risk of developing kidney disease, as manifest by the presence of albuminuria or impaired GFR. The DCCT, a multicenter, randomized, controlled trial of 1,441 patients with T1DM, demonstrated that intensive glucose control was associated with lower glycated hemoglobin levels and a reduced risk of microalbuminuria and macroalbuminuria compared with conventional therapy. In the DCCT, patients were randomly assigned to receive either intensive diabetes therapy, which consisted of three or more insulin injections per day or use of an insulin pump and aimed to achieve a glycated hemoglobin level of <6.05%, or conventional therapy, which consisted of one or two insulin injections per day and aimed to prevent symptoms of hyperglycemia and hypoglycemia. Patients were followed for a mean of 6.5 years. Following the termination of DCCT in 1993, all participants were invited to participate in the EDIC study, an observational follow-up study that aimed to investigate the effects of the different regimens on long-term diabetes complications, including GFR loss. "There is increasing recognition that albuminuria and GFR loss do not always track together," comments de Boer. In the EDIC study, we tested whether DCCT intensive diabetes therapy, which had previously been shown to reduce risks of albuminuria, also reduced the risk of impaired GFR. Because GFR is generally lost over many years, this study required very long-term follow-up".

In total, 1,375 DCCT participants agreed to participate in the EDIC extension study. During follow-up, 24 patients who had received intensive therapy in DCCT and 46 patients who had received conventional therapy in DCCT developed an impairment in GFR, defined as an estimated GFR of <60 ml/min/1.73 m^2 at two consecutive visits, generally 1 year apart. The cumulative incidence of developing impaired GFR 20 years after randomization was 2.0% for patients who had received intensive therapy and 5.5% for patients who had received conventional therapy.

The researchers also found that patients who received intensive therapy had a 37% lower risk of the composite outcome of an impaired GFR or death than those who received conventional therapy. In addition, adjustment for between-group differences in mean glycated hemoglobin level or albumin excretion rate attenuated the beneficial effect of intensive glucose control on risk of impaired GFR, which de Boer believes indicates that hyperglycemia is an initiating factor in the pathogenesis of GFR loss in patients with T1DM.

The researchers will continue to collect data on the study participants. "We plan to use these data to identify additional risk factors for kidney disease in patients with T1DM that might lead to new treatment approaches. Intensive diabetes therapy is a critical intervention for preventing kidney disease in T1DM, but intensive diabetes control can be hard to implement and may not prevent all diabetes complications," states de Boer. They also hope that extended follow-up of these patients will help elucidate the long-term effects of early intensive glucose control. "We will continue to follow these participants for the development of more advanced renal complications, including end-stage renal disease, as well as other causes of diabetes-related morbidity and mortality, and we will determine the effects of intensive diabetes therapies on these outcomes," concludes de Boer.

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