Renal Impairment, Normal Albumin Seen in Type 1

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WASHINGTON — Renal insufficiency in the absence of elevated urinary albumin excretion can occur in patients with type 1 diabetes and may be associated with elevated urinary levels of some inflammatory markers in patients with type 2 diabetes, Dr. Mark E. Molitch and Dr. Monika Niewczas said in separate presentations at the annual scientific sessions of the American Diabetes Association.

Although it was once thought that urinary albumin excretion levels always rose before the decline in glomerular filtration rate (GFR) in patients who went on to develop diabetic nephropathy, recent studies have shown that a significant proportion of diabetic patients have renal insufficiency even in the absence of elevated urinary protein. In one analysis of data from the Third National Health and Nutrition Examination Survey, 30% of 171 adults older than 40 years with type 2 diabetes had chronic renal insufficiency—defined as a GFR of less than 60 mL/min per 1.73 m² of body surface area—despite the absence of microalbuminuria or macroalbuminuria and retinopathy (JAMA 2003;289:3273-7).

Those authors concluded, and clinical guidelines since have concurred, that all patients with diabetes should have annual assessments of GFR as part of their routine kidney assessment. But few data have been collected in patients with type 1 diabetes, said Dr. Molitch, professor of medicine and director of the endocrinology clinic at Northwestern University, Chicago.

Serum creatinine and urine albumin measurements were analyzed among approximately 1,300 adults with type 1 diabetes who had participated in the landmark Diabetes Control and Complications Trial (DCCT) and are now being followed longitudinally in the Epidemiology of Diabetes Interventions and Complications (EDIC) study.

Serum creatinine and urine albumin measurements in 4-hour collections are obtained from the subjects every other year, and the GFR is estimated. The proportion with renal insufficiency (estimated GFR of less than 60) increased steadily with time since DCCT ended and EDIC began, from 1.59% during the first 2 years up to 4.22% at EDIC years 9 and 10. Among those individuals, the proportion with normal albumin excretion rates, defined as less than 30 mg per 24 hours, ranged from 52% during years 1 and 2 to 29% at years 5 and 6, said Dr. Molitch.

Of the 55 patients with renal insufficiency at years 9 and 10, 40% had albuminuria (greater than 300 mg/24 hours). As expected, the rate of renal insufficiency rose with increasing albumin excretion. Of the total 172 patients with microalbuminuria at year 9 and 10, 7% had estimated GFR less than 60, rising to 30.4% of those with albuminuria.

Dr. Niewczas of the Joslin Diabetes Center, Boston, reported that of a total of 5,627 patients with type 2 diabetes seen at her institution, 64% had normoalbuminuria. Of those 3,623 patients, 11% (398) had an estimated GFR less than 60. That proportion increased to 21% of the 1,542 with microalbuminuria and 58% of the 462 with albuminuria. In the general U.S. population, only about 3% have a GFR less than 60, she noted.

The patients who had renal decline in the absence of an impaired glomerular filtration barrier (no elevated levels of albumin, IgG, or fibronectin) did not differ from the patients with stable renal function with regard to clinical characteristics such as hemoglobin A₁c, systolic blood pressure, or use of antihypertensive medications, she said.

Elevated urinary excretion of the inflammatory markers interleukin-8 and monocyte chemotactic protein 1 were associated with declining renal function in patients with normalalbuminuria, microalbuminuria, and proteinuria, whereas levels of interleukin-6, interferon-inducible protein 10, and regulated upon activation, normal T cell expressed and secreted did not differ. ■