Glomerular Filtration Rate and Albuminuria: Twin Manifestations of Nephropathy in Diabetes

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In the past three decades, urinary albumin excretion has assumed a central role in the diagnosis and management of kidney disease among people with diabetes, both type 1 and type 2. Microalbuminuria was initially found to predict subsequent overt albuminuria (dipstick positive, or ≥300 mg/24 h), which in turn predicted loss of GFR (1–3). From the strength of these relationships, it has frequently been assumed that microalbuminuria and overt albuminuria are requisite first and second steps along a single pathway that leads to loss of GFR and ESRD.

In recent work, Perkins et al. (4) challenged these assumptions by demonstrating that microalbuminuria can regress to normoalbuminuria among people with type 1 diabetes. In this issue of the Journal of the American Society of Nephrology (JASN), these authors build on their previous work by examining change in GFR (estimated as 100/serum concentration of cystatin C) among patients from the same cohort (5); 578 patients with urine albumin excretion rates that were consistently ≤300 µg/24 h, which in turn predicted loss of GFR (1–3). From the strength of these relationships, it has frequently been assumed that microalbuminuria and overt albuminuria are requisite first and second steps along a single pathway that leads to loss of GFR and ESRD.

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cystatin C with GFR as measured using clearance of radiolabeled or unlabeled compounds does not depend on age or gender (12). Moreover, serum cystatin C may more reliably detect differences in GFR when GFR is >60 ml/min per 1.73 m² (13–16). When cystatin C concentrations are expressed as 100/cystatin C or transformed using prediction equations, they have the potential to improve the accuracy of eGFR (17). However, most studies that have assessed serum cystatin C as a measure of GFR have been cross-sectional in nature, and longitudinal studies are needed to define further the potential role of cystatin C in clinical care. In a previous issue of JASN, Perkins "et al." (18) reported the first such longitudinal study. Changes over time in GFR (measured by clearance of iothalamate), serum creatinine eGFR, and cystatin C eGFR were compared among 30 Pima Indians with a mean baseline GFR 153 ml/min per 1.73 m². The change in 100/cystatin C correlated with the change in iothalamate-GFR more accurately than did the change in eGFR as calculated from serum creatinine.

We agree with Perkins "et al." and with the National Kidney Disease Education Program that improved measurements/estimates of GFR must become a component of routine clinical care for people with diabetes. Serum cystatin C is an excellent candidate for this measurement. As stated previously (19), the much greater costs of cystatin C assays currently reduce their application in clinical medicine. However, when cystatin C is added to the menus of random access analyzers that are ubiquitous in clinical laboratories, it may be more readily used in general medical practice and in clinical nephrology.

The study by Perkins "et al." in this issue of JASN was restricted to people with type 1 diabetes. However, it is important to note that early loss of GFR also has important consequences in the general population (20). Cystatin C shows promise as a valuable tool to describe the pathophysiologic, diagnostic, prognostic, and therapeutic implications of GFR loss, independent of and together with albuminuria, among people with and without diabetes.

Disclosures

None.

References


See the related article, "Microalbuminuria and the Risk for Early Progressive Renal Function Decline Type 1 Diabetes,” on pages 1353–1361.