COMMENT ON NIEWCZAS ET AL.

Circulating Modified Metabolites and a Risk of ESRD in Patients With Type 1 Diabetes and Chronic Kidney Disease. Diabetes Care 2017;40:383–390

Kaiping Luo,[1] Weidong Fang,[1] and Gaosi Xu[2]

Diabetes Care 2017;40:e108 | https://doi.org/10.2337/dc17-0157

Niewczas et al. (1) reported the associations between metabolomic determinants and the risk of end-stage renal disease (ESRD) in participants with type 1 diabetes. The study concluded that patients with elevated circulating levels of certain modified metabolites experienced faster renal function decline than other participants. The research is exciting. However, we have several concerns about the study.

Niewczas et al. determined the estimated glomerular filtration rate (eGFR) by using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Concerns have been raised about the use of the CKD-EPI equation because of the high prevalence of ESRD that had been estimated in the elderly compared with younger people and because the equation was more suitable for patients with eGFR $>$60 mL/min/1.73 m^2 (2). However, the observational end point of the study by Niewczas et al. is ESRD, which means the eGFR is $<$15 mL/min/1.73 m^2 and the participants' eGFR could be overestimated.

Data in the study on demographic and fundamental characteristics, blood pressure and glycemic control, and medication were incomplete. LeCaire et al. (3) showed that sex, age, period of diagnosis, diabetes duration, presence of proteinuria, baseline eGFR, glycosylated hemoglobin level, systolic and diastolic blood pressure, antihypertensive medication use, and prevalent proliferative retinopathy were significantly associated with the development to ESRD. For example, intensive diabetes management may delay the progress to ESRD. However, the glycosylated hemoglobin target and blood pressure target were not mentioned in the current study (1). Furthermore, Niewczas et al. did not perform kidney biopsy, which is the diagnostic gold standard for these patients.

The study (1) monitored the occurrence of persistent proteinuria by using routinely measured albumin-to-creatinine ratios (ACR). However, there are still several issues of concern about ACR. First, the definition of "persistent proteinuria" was missing. Given the high day-to-day variability, many factors may influence the appearance of albumin in the urine, e.g., dietary protein intake, physical exercise, diuresis, metabolic perturbations such as ketosis and hyperglycemia, the presence of urinary tract infection, fever, pregnancy, and hypertension. In addition, the confirmation of elevated ACR requires two additional tests during the subsequent 3 to 6 months on first-voided urinary specimens (4). Second, de Boer et al. (5) showed that some patients with diabetes without abnormalities in urinary albumin excretion had a decline in GFR, suggesting that patients with negative urinary albumin may also suffer from diabetic kidney disease. Third, we regret that diabetic retinopathy was not considered in the study by Niewczas et al. (1). According to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) guidelines, diabetic retinopathy is one of the diagnostic criteria for diabetic nephropathy (4). To avoid missing the subjects with normal albuminuria but decreased GFR in the study group of this prospective research, screening for diabetic retinopathy should be considered in these subjects.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

1. Niewczas MA, Mathew AV, Croall S, et al. Circulating modified metabolites and a risk of ESRD in patients with type 1 diabetes and chronic kidney disease. Diabetes Care 2017;40:383–390
2. Levey AS, Stevens LA, Schmid CH, et al.; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–612
3. LeCaire TJ, Klein BE, Howard KP, Lee KE, Klein R. Risk for end-stage renal disease over 25 years in the population-based WESDR cohort. Diabetes Care 2014;37:381–388
4. James M, Bouchard J, Ho J, et al. Canadian Society of Nephrology commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. Am J Kidney Dis 2013;61:673–685
5. de Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal trends in the prevalence of diabetic kidney disease in the United States. JAMA 2011;305:2532–2539

[1]*Department of Nephrology, People's Hospital of Ganzhou, Ganzhou, China*
[2]*Department of Nephrology, The Second Affiliated Hospital of Nanchang University, Nanchang, China*

Corresponding author: Gaosi Xu, gaosixu@163.com.