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Urinary biomarkers in autosomal dominant polycystic kidney disease: is there no prognostic value?

To the Editor: We read with interest the article by Parikh *et al*, in which they showed that levels of neutrophil gelatinase-associated lipocalin (NGAL) and interleukin (IL)-18 did not correlate with changes in kidney volume or estimated glomerular filtration rate (eGFR) during follow-up in autosomal dominant polycystic kidney disease (ADPKD) patients relatively early in their disease.[1] Therefore, it was suggested that urinary biomarkers of kidney injury have no clinical prognostic utility.

Recently, we measured several biomarkers (glomerular, tubular, and inflammatory) in urine samples (stored for 0.7 years at −80 °C) of 102 ADPKD patients and found in a cross-sectional study significant associations between several urinary biomarkers, including NGAL, and measures of ADPKD severity.[2] After having read the publication by Parikh *et al*, we investigated the association of these markers with decline in eGFR (Chronic Kidney Disease Epidemiology Collaboration) in patients whose follow-up data were available without experimental intervention ($N = 46$, age 40 ± 14 years, 48% male, baseline eGFR 73 ± 37 ml/min per 1.73 m^2, eGFR change during 2.6 years follow-up: -2.6 ± 3.2 ml/min per 1.73 m^2/year). We found significant inverse associations between baseline urinary biomarker excretion of albumin, IgG, KIM-1, and MCP-1 and change in eGFR during follow-up (Table 1). These associations remained significant after adjustment for age, gender, and baseline eGFR. Similar to Parikh *et al*, we found no significant association between NGAL and change in eGFR, neither crude ($P = 0.07$) nor adjusted for age, sex, and baseline eGFR ($P = 0.47$). Urinary IL-18 was not measured.

Importantly, we have previously shown that frozen storage decreases the measured concentration of urinary biomarkers, such as NGAL, and induces more variability, especially after longer storage.[3] The decline or increased variability in marker concentration that is induced by frozen storage can therefore reduce the association that, in reality, is present. We have shown this latter phenomenon for urinary albumin concentration in non-ADPKD subjects.[4]

Table 1 | Association between slope of eGFR (CKD-EPI) and log-transformed urinary biomarker excretion

	Crude		Adjusted for age, gender, and baseline eGFR	
	Std. B	*P*-value	Std. B	*P*-value
Albumin (mg/24 h)	−0.542	<0.001	−0.474	0.005
IgG (mg/24 h)	−0.419	0.004	−0.310	0.044
KIM-1 (μg/24 h)	−0.347	0.018	−0.447	0.001
MCP-1 (μg/24 h)	−0.483	0.001	−0.390	0.006

Abbreviations: CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; IgG, Imunoglobulin G; KIM-1, kidney injury molecule 1; MCP-1, monocyte chemotactic protein 1.

Given these findings, we caution against a too skeptical view toward the utility of urinary biomarkers to predict disease progression in ADPKD. Our data indicate that some of these markers may be useful. More research investigating their prognostic value in ADPKD is definitely needed.

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Reappraisal of melamine exposure and adult calcium urolithiasis

To the Editor: In reference to Lopez and Quereda's comments to our recent article and questions about source of low-dose melamine exposure and change in incidence in urolithiasis in adults in Taiwan,[1,2] since the melamine-tainted formula incident in China in 2008, melamine has been detected in a few daily food products such as eggs, wheat gluten, and meats. Our recent study found that some melamine could migrate from daily-used melamine-made tableware even at room