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Urine myo-inositol, the novel prognostic biomarker for diabetic kidney disease: a targeted metabolomics study using NMR

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Objectives: Diabetic kidney disease (DKD) is a leading cause of CKD and ESRD. Metabolomics has been increasingly applied to identify new biomarkers to specify the cause of chronic kidney disease (CKD), as it can more precisely predict outcomes and identify treatment options. We investigated the association between urine metabolites and end-stage kidney disease (ESRD) progression in DKD, using NMR based targeted metabolomics.

Methods: Prospectively stored urine samples from consecutive patients with DKD stage 1 to 5 (n=208) and their healthy controls (n=26) were analyzed. Cross-sectional associations were evaluated between eGFR or UPCR (urine protein creatinine ratio) and 26 urinary metabolites. Cox models were conducted for the risk of ESRD and mortality. Also, C statistics was used to assess the additive effect of each metabolite to predict ESRD progression

Results: ESRD occurred in 103 (44.0%) patients and 65 (27.8%) deaths occurred. The median fold change in 9 metabolites (glucose, mannose, myo-inositol, glycerol, lactate, fumarate, creatine, taurine and choline) revealed a trend according to DKD stages. Myo-inositol has the strongest association with eGFR, the principal predictive marker of ESRD. The relationship between the competitive metabolites and outcomes (ESRD and mortality) was investigated by Cox models. Of these, 4 metabolites (myo-inositol, glycerol, fumarate, oxoisocaproate) had predictive values for ESRD and among them, only myo-inositol retained predictive significance in mortality (adjusted HR 1.004, 95% confidence interval 1.002–1.006, p-value <0.001).

Conclusions: Our results suggest that myo-inositol can be a predictive biomarker for the risk of ESRD progression in DKD. Further mechanistic studies are needed on myo-inositol.