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Significant urinary metabolites in the progression of chronic kidney disease

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Objectives: Despite the development of diagnostic techniques, methods for predicting changes in renal function or outcomes are still insufficient. Metabolomics is considered to be a breakthrough method to address the shortage of tools by analyzing the end metabolites, reflecting genetic and environmental factors. Herein, we would like to propose the metabolites which significantly associated with development and progression of chronic kidney disease (CKD).

Methods: We measured urinary metabolites from 1,274 urine samples at the time of renal biopsy and 147 urine samples from healthy subjects using nuclear magnetic resonance (NMR). The clinical outcome was defined as a decrease in estimated glomerular filtration ≥ 30%, doubling of serum creatinine, or development of an end-stage renal disease. The survival analysis was performed by median concentration of metabolites.

Results: Initial partial components analysis and partial least squares-discriminant analysis score plots showed discriminated cluster between CKD and control, and according to the stage of CKD. Among the 41 candidate metabolites, 30 metabolites were initially selected by descriptive measurement using peak velocity. There were 10 metabolites (acetone, betaine, choline, dimethylamine, fumarate, glycerol, Isoleucine, lactate, leucine, trimethylamine-N-oxide) which showed significantly increased risk of developing clinical outcomes according to increasing concentration. In contrary, citrate, indoxyl-sulfate, and formate showed decreased risk according to increasing concentration for developing clinical outcomes. Total of 4 metabolites (betaine, choline, fumarate, trimethylamine-N-oxide) revealed significantly different level in concentration in CKD compared to control, moreover this difference maintained with same way in a different stage of CKD.

Conclusions: Metabolites which inform the disease progression or development can be a noble biomarker. In our study, betaine, choline, fumarate, trimethylamine-N-oxide, fumarate was revealed as a significant predictor in the progression of CKD. Although additional study for validation should be performed, we could find significant metabolites associate with CKD. And these results could be an instrumental keynote to moving ahead.