

Abstract Type : Oral

Abstract Submission No. : OR-1092

Plasma RIPK3 as a biomarker of diabetic nephropathy in type 2 diabetes

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Objectives: RIPK3 acts as a critical regulator of necroptosis and play an important role in kidney injuries. We investigated the role of circulating RIPK3 as a biomarker of diabetic nephropathy.

Methods: Study subjects were collected from a prospective observational cohort for diabetic nephropathy. A total of 140 type 2 diabetic patients and 19 healthy control subjects were enrolled. They were followed-up with estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (UACR). Circulating RIPK3 concentrations were assessed by ELISA.

Results: Plasma RIPK3 levels were elevated in type 2 diabetic patients compared to non-diabetic control ($P = 0.029$). In type 2 diabetic patients, as albuminuria worsened, plasma RIPK3 levels were increased accordingly ($P = 0.006$). After adjusting confounding variables, participants with the highest tertile of plasma RIPK3 had higher annual increase of UACR in type 2 diabetic patients ($\beta = 0.210$, $P = 0.012$) and in normoalbuminuric subgroup ($\beta = 0.214$, $P = 0.007$). These participants with the highest tertile of plasma RIPK3 were associated with higher incidence of renal progression (Hazard ratio [HR]: 2.29 [1.05–4.98]) and incident chronic kidney disease (CKD) (HR: 4.08 [1.10–15.13]).

Conclusions: Circulating RIPK3 can reflect the severity of diabetic nephropathy and predict the deterioration of albuminuria and renal function. These results highlight that circulating RIPK3 could be a novel predictor for diabetic nephropathy.