中文題目:利用尿液脂肪酸和視黃醇結合蛋白-4 預測嚴重非酒精性脂肪肝病合併高血壓病人的慢性腎臟性疾病進展

英文題目: Urinary fatty acid and retinol binding protein-4 predict CKD progression in severe NAFLD patients with hypertension

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Background*:* High prevalence of CKD and hypertension had been reported among non-alcoholic fatty liver disease (NAFLD) patients. Detection of the chronic kidney disease (CKD) progression can begin early intervention to improve the prognosis of severe NAFLD. Serum and urine biomarkers including intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), adhesion molecules, fatty acid-binding protein (FABP) and retinol binding protein (RBP4), which are produced from inflamed liver, adipose tissue and immune cells, had been reported to predict the CKD progression.Moreover, apoptosis is one important pathway to induce the CKD progression. Accumulation of albumin in kidney leads to accumulate misfolded proteins within endoplasmic reticulum (ER) and induction of ER stress. Prolonged ER stress induced protein that promoting apoptosis. This bi-directional cross-sectional study evaluates the roles of fatty acid-binding protein (FABP) and retinol binding protein (RBP4) for the prediction of CKD progression in severe NAFLD patients with hypertension and proteinuria. The direct effects of newly screened biomarkers on the albumin-induced kidney injury will evaluate on the *in vitro* experiments.

Method*:* This study prospectively screened 330 severe NAFLD patients with abnormal liver and renal function tests from the medical records from October 2014 to March 2019. Then, 120 severe NAFLD patients met the inclusion criteria of hypertension and proteinuria ($NAFLD^+$ HTN^+). After excluding cases with excluding criteria, 90 severe NAFLD patients with hypertension and proteinuria ($NAFLD^+HTN^+$) were enrolled and divided into CKD (n=39) and non-CKD groups (n=51) according to the eGFR data within 24 months before time of inclusion. Finally, 39 $NAFLD^+$ HTN^+ patients with CKD were included for clinical serologic and urinary measurements.

Results: Among 39 NAFLD+HTN+ patients, 18 cases were categorized as CKD progression group according to the slope or reciprocal serum creatinine across 24 month before and 24 month after inclusion. Surrogate markers for hypertension, major risk factor for CKD, including serum CRP, sICAM-1, sVCAM-1 and urine VCAM-1 were significantly increased in CKD progression group. FABP1, FABP4, RBP4 levels, both in serum and urine, were elevated in CKD progression group compared with CKD stable groups. In comparison with CKD stable group (n=21), the positive correlation between fold change values of hepatic fibrotic score (KPa), urinary FABP4 or urinary RBP4 versus severity of albuminuria were noted among CKD progression group. On multivariate analysis, high BMI (>25 kg/m2), high hepatic fibrosis score (>9.5KPa), high urinary level of VCAM-1 (>2239μg/g.cr), high urinary level of FABP4 (>115 ng/g.cr) and high urinary level of RBP4 (>33.5 mg/g.cr) are five independent predictors for progressive CKD during 24 months of follow-up.

Conclusion: Through clinical approaches, this study revealed high levels of liver and adipose tissue-derived inflammatory markers including uVCAM-1, uFABP4 and uRBP4, which were new predictors for the CKD progression in severe NAFLD patients with hypertension and proteinuria.

Keywords: Non-alcoholic fatty liver disease, Chronic kidney disease, Fatty acid-binding protein, Retinol binding protein, Albuminuria