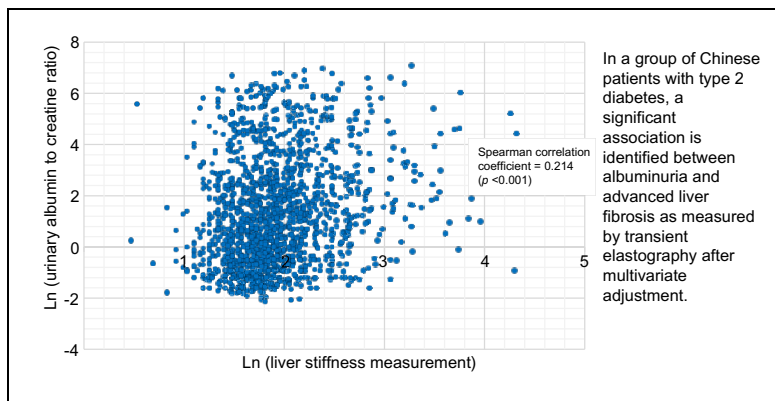


Advanced liver fibrosis but not steatosis is independently associated with albuminuria in Chinese patients with type 2 diabetes

Graphical abstract



Highlights

- Non-alcoholic fatty liver disease has been linked to chronic kidney disease in observational studies.
- In this cohort of 1,763 patients with type 2 diabetes, we show that liver fibrosis but not steatosis was associated with albuminuria.
- The association remains consistent using different liver stiffness cut-offs and adjusting for other metabolic factors and medications.

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Lay summary

In this study, we assessed the link between non-alcoholic fatty liver disease (NAFLD) and albuminuria in a cohort of 1,763 Chinese patients with type 2 diabetes. This study shows that advanced liver fibrosis, a severe form of NAFLD, was independently associated with increased risk of albuminuria. The risk of albuminuria increased with greater severity of liver fibrosis.



Advanced liver fibrosis but not steatosis is independently associated with albuminuria in Chinese patients with type 2 diabetes

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Background & Aims: Increasing evidence suggests that non-alcoholic fatty liver disease (NAFLD) may be an independent risk factor for chronic kidney disease (CKD). Given the high prevalence of NAFLD among patients with diabetes who are also at risk of CKD, we aimed to investigate the association between NAFLD and albuminuria, a marker commonly found in diabetic nephropathy.

Methods: This study included a cohort of Chinese patients with type 2 diabetes from the Hong Kong Diabetes Registry recruited between March 2013 and May 2014. Liver stiffness measurement (LSM), with probe-specific cut-offs, was used to detect advanced liver fibrosis. While controlled attenuation parameter (CAP) was used to assess liver steatosis using transient elastography.

Results: A total of 1,763 Chinese patients with type 2 diabetes were recruited in this analysis. The mean (standard deviation) age and duration of diabetes were 60.7 (11.5) years and 10.8 (8.5) years, respectively. The prevalence of albuminuria was higher in diabetic patients with liver steatosis and those with advanced fibrosis (no NAFLD vs. liver steatosis vs. advanced fibrosis: 41.4% vs. 46.2% vs. 64.2%, $p < 0.001$). After adjustment for potential confounders including glycated hemoglobin, hypertension and body mass index, advanced fibrosis, but not liver steatosis, was associated with increased risk of albuminuria (odds ratio [OR] 1.52; 95% confidence interval [CI] 1.02–2.28; $p = 0.039$) in patients with eGFR ≥ 60 ml/min/1.73 m². The odds of albuminuria increased with greater severity of liver

fibrosis in a dose dependent manner, with the highest odds observed in patients with LSM scores ≥ 11.5 kPa assessed by M probe or ≥ 11.0 kPa assessed by XL probe (adjusted OR 1.53; 95% CI 1.07–2.20; $p = 0.021$).

Conclusions: Advanced liver fibrosis, but not steatosis, is independently associated with albuminuria in Chinese patients with type 2 diabetes. Attention should be paid to liver fibrosis in patients with obesity and type 2 diabetes complicated with albuminuria.

Lay summary: In this study, we assessed the link between non-alcoholic fatty liver disease (NAFLD) and albuminuria in a cohort of 1,763 Chinese patients with type 2 diabetes. This study shows that advanced liver fibrosis, a severe form of NAFLD, was independently associated with increased risk of albuminuria. The risk of albuminuria increased with greater severity of liver fibrosis.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease, consisting of a spectrum of diseases, ranging from simple steatosis (accumulation of $>5\%$ of triglycerides without evidence of hepatocellular injury in the liver, a relatively benign condition), to non-alcoholic steatohepatitis (NASH) with inflammation and ballooning of the hepatocytes. NASH is an active and severe form of NAFLD which may progress to liver fibrosis, cirrhosis and hepatocellular carcinoma. Both simple steatosis and NASH are potentially reversible through lifestyle intervention and/or pharmacological treatments; whereas liver fibrosis is associated with significant clinical outcomes.^{1–3} This highlights the importance of early detection of NAFLD and the clinical need to identify at risk individuals for regular screening. Of note, patients with type 2 diabetes are at high risk of developing NAFLD, with 46–70% of patients with type 2 diabetes reported to have NAFLD worldwide.^{4–8} In comparison, NAFLD is detected in 6–35% of adults in the general population.^{9,10} Using non-invasive methods such

Keywords: Non-alcoholic fatty liver disease; Albuminuria; Diabetic nephropathies; Diabetes mellitus; Type 2; Liver fibrosis; Transient elastography.

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