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ASSOCIATIONS OF NON-INVASIVE PARAMETERS OF LIVER STEATOSIS AND FIBROSIS WITH RENAL IMPAIRMENT IN TYPE 2 DIABETES: A 6-YEAR LONGITUDINAL ANALYSIS

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OBJECTIVES

We examined the associations of non-invasive parameters of liver steatosis and fibrosis with renal impairment, and the mediatory role of the pro-angiogenic factor leucine-rich α-2 glycoprotein 1 (LRG).

METHODOLOGY

Adults with type 2 diabetes (T2D; n = 2,057) were recruited by the Singapore study of macroangiopathy and microvascular reactivity in type 2 diabetes (SMART2D) study and followed up for 6 years. Baseline liver steatosis [(hepatic steatosis index (HSI) and Zhejiang university index (ZJU)] and liver fibrosis [aspartate transaminase/alanine transaminase ratio (AAR) and bard] scores were calculated. Plasma LRG1 levels were quantified using immunoassay. Study outcomes were estimated glomerular filtration rate (eGFR) decline of ≥40% and albuminuria progression. In an independent T2D group (n = 47), cross-sectional correlations between transient elastography readings and renal markers were explored.

RESULTS

In the cross-sectional study, liver steatosis and fibrosis parameters derived from either composite scoring systems or elastography were associated with increased albuminuria and reduced renal function, respectively. Among individuals with follow-up data, 32.4% (n = 481/1484) developed eGFR decline, while 38.3% (n = 503/1312) had albuminuria progression. Multivariable cox regression analyses revealed that AAR (hazard ratio:1.56; 95% CI:1.15–2.11, p=0.004) and bard (hazard ratio:1.16, 95% CI:1.04–1.28, p=0.005) predicted eGFR decline. Binary mediation showed that LRG1 accounted for 34.2% and 28.1% of the effects of AAR and bard scores on the risk of eGFR decline, respectively. In contrast, liver steatosis but not liver fibrosis indices (HSI, ZJU) independently predicted albuminuria progression.

CONCLUSION

Liver steatosis is associated with worsening of albuminuria. Similarly, liver fibrosis is associated with renal function decline, potentially driven by increased inflammation and angiogenesis.