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Renin-independent aldosteronism and chronic kidney disease in diabetes: Observational and Mendelian randomization analyses

Background

Renin-independent aldosteronism (RIA) describes the spectrum of autonomous aldosterone secretion from mild to overt. We aimed to explore whether RIA is causally associated with chronic kidney disease (CKD) in patients with diabetes.

Methods

We cross-sectionally included 1027, 402 and 39,709 patients with any type of diabetes from cohorts of EIMDS, CONPASS and UK Biobank, respectively. In EIMDS, we defined RIA and renin-dependent aldosteronism based on plasma aldosterone and renin concentrations. We performed captopril challenge test to confirm renin-dependent or independent aldosteronism in CONPASS. In UK Biobank, we generated genetic instruments for RIA based on the genome-wide association studies (GWAS). We extracted the corresponding single nucleotide polymorphisms (SNPs) information from the GWAS data of CKD in diabetes. We harmonized the SNP-RIA and SNP-CKD data to conduct the two-sample Mendelian randomization analyses.

Findings

In EIMDS and CONPASS, when compared to subjects with normal aldosterone concentration or renin-dependent aldosteronism, participants with RIA had a lower estimated glomerular filtration rate, a higher prevalence of CKD, and a higher multivariate-adjusted odds ratio (OR) of CKD (OR 2.62 [95%CI 1.09–6.32] in EIMDS, and 4.31 [1.39–13.35] in CONPASS). The two-sample Mendelian randomization analysis indicated that RIA was significantly associated with a higher risk of CKD (inverse variance weighted OR 1.10 [95 % CI 1.05–1.14]), with no evidence of significant heterogeneity or substantial directional pleiotropy.

Interpretation

Among patients with diabetes, renin-independent aldosteronism is causally associated with a higher risk of CKD. Targeted treatment of autonomous aldosterone secretion may benefit renal function in diabetes.



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Key words: Renin-independent Aldosteronism, Diabetes, Chronic kidney disease, Mendelian randomization, Causal relationship

Biography

Yi Luo is a researcher in the Department of Endocrinology, Bishan Hospital of Chongqing Medical University, China. She has contributed to published research in the field of endocrinology, with a focus on diabetes and glucose metabolism.