Apolipoprotein E and Progression of Chronic Kidney Disease

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Context Apolipoprotein E (APOE) genetic variation has been implicated in diabetic nephropathy with the 2 allele increasing and the 4 allele decreasing risk. APOE allelic associations with chronic kidney disease beyond diabetic nephropathy are unknown, with no studies reported in high-risk African American populations.

Objective To quantify the risk of chronic kidney disease progression associated with APOE in a population-based study including white, African American, diabetic, and nondiabetic individuals.

Design, Setting, and Participants Prospective follow-up (through January 1, 2003) of Atherosclerosis Risk in Communities (ARIC) study participants, including 3859 African American and 10 661 white adults aged 45 to 64 years without severe renal dysfunction at baseline in 1987-1989, sampled from 4 US communities.

Main Outcome Measures Incident chronic kidney disease progression, defined as hospitalization or death with kidney disease or increase in serum creatinine level of 0.4 mg/dL (35 µmol/L) or more above baseline, examined by APOE genotypes and alleles.

Results During median follow-up of 14 years, chronic kidney disease progression developed in 1060 individuals (incidence per 1000 person-years: 5.5 overall; 8.8 in African Americans and 4.4 in whites). Adjusting for major chronic kidney disease risk factors, 2 moderately increased and 4 decreased risk of disease progression (likelihood ratio test, \( P = .03 \)). Further adjustment for low- and high-density lipoprotein cholesterol and triglycerides did not attenuate relative risks (RRs) (2: 1.08 [95% CI, 0.93-1.25] and 4: 0.85 [95% CI, 0.75-0.95] compared with 3; likelihood ratio test, \( P = .008 \)). 4 decreased risk of end-stage renal disease (RR, 0.60 [95% CI, 0.43-0.84]). 2 was associated with a decline in renal function (RR, 1.25 [95% CI, 1.02-1.53]), though not with events, such as hospitalizations or end-stage renal disease. Risks were similar stratified by race, sex, diabetes, and hypertension (all \( P \) values for interaction >.05). Excess risk of chronic kidney disease in African Americans was not explained by APOE alleles.

Conclusions APOE variation predicts chronic kidney disease progression, independent of diabetes, race, lipid, and nonlipid risk factors. Our study suggests that nonlipid-mediated pathways, such as cellular mechanisms of kidney remodeling, may be involved in the association of APOE alleles and progression of chronic kidney disease. JAMA 2005; 293(23):2892-9

Incidence Rates of Chronic Kidney Disease Progression by APOE Genotype and Race

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