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Genome-wide association studies identify genetic loci related to incident chronic kidney disease

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Objectives : Chronic kidney disease (CKD) is common, affecting about 10% of the genetic population. The genetic component about CKD incidence is not well known.

Methods : We conducted a genome-wide association (GWA) studies regarding the CKD incidence based on two population-based prospective cohorts, Korean Genome Epidemiology Study (KOGES). 3617 Koreans from two different cohorts, aged 40 to 49 years without CKD at initial visit, were included in our analysis. To explore genetic loci associated with the CKD incidence, we used 2510 person in an urban population-based cohort as a discovery set. Another sample that comprised 1107 who were from an independent cohort enrolled in a rural area served as a resource for replication. At baseline (June 2001 through January 2003), members of both cohorts provided information on baseline creatinine, and their DNA samples were collected for genotyping. Single nucleotide polymorphisms (SNPs) that surpassed a significance threshold of $P < 1 \times 10^{-3}$ for association with incident CKD were selected

Results : Mean age was 44.2 ± 2.8 years and 1809(50.0%) were male. Total 282 among 3617 developed incident CKD during follow up period. Incident CKD group was older (45.0 ± 2.7 vs 44.1 ± 2.7 , $P < 0.001$), more female (61.9% vs 49.0%, $P < 0.001$), had more hypertension (13.2% vs 7.5%) and diabetes (9.3% vs 2.9%, $P < 0.001$). Initial estimated glomerular filtration rate was lower in incident CKD group (83.4 ± 13.0 vs 94.0 ± 15.8 , $P < 0.001$). We identified 12 SNPs (rs2025936, rs11166378, rs10783124, rs1505141, rs2777732, rs1146883, rs1146888, rs2657128, rs1700826, rs2657132, rs1146890, rs236586) were associated with incident CKD in GWA studies and made genetic risk score using these SNPs. In multiple Cox regression analysis adjusted for age, gender, diabetes, hypertension, estimated glomerular filtration rate at initial visit, and body mass index, genetic risk score was still a significant associated factor for incident CKD (HR 1.311, CI 1.201, 1.431, $P < 0.001$).

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Conclusions : In a GWA study, we identified several loci highly associated with incident CKD. The findings suggest the need for further investigations on the genetic propensity for CKD.

Keywords : chronic kidney disease, Genome-wide association studies