

## Genetically, dietary sodium intake is causally associated with salt-sensitive hypertension risk in a community-based cohort study: a Mendelian randomization approach

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Excessive dietary salt intake is associated with an increased risk of hypertension. Salt sensitivity, i.e., an elevation in blood pressure in response to high dietary salt intake, has been associated with a high risk of cardiovascular disease and mortality. We investigated whether a causal association exists between dietary sodium intake and hypertension risk using Mendelian randomization (MR). We performed an MR study using data from a large genome-wide association study comprising 15,034 Korean adults in a community-based cohort study. A total of 1,282 candidate single nucleotide polymorphisms associated with dietary sodium intake, such as rs2960306, rs4343, and rs1937671, were selected as instrumental variables. The inverse variance weighted method was used to assess the evidence for causality. Higher dietary sodium intake was associated with salt-

sensitive hypertension risk. The variants of SLC8E1 rs2241543 and ADD1 rs16843589 were strongly associated with increased blood pressure. In the logistic regression model, after adjusting for age, gender, smoking, drinking, exercise, and body mass index, the GRK4 rs2960306TT genotype was inversely associated with hypertension risk (OR = 0.356, 95% CI = 0.236–0.476). However, the 2350GG genotype (ACE rs4343) exhibited a 2.11-fold increased hypertension risk (OR = 2.114, 95% CI = 2.004–2.224) relative to carriers of the 2350AA genotype, after adjusting for confounders. MR analysis revealed that the odds ratio for hypertension per 1 mg/day increment of dietary sodium intake was 2.24 in participants with the PRKG1 rs12414562 AA genotype. Our findings suggest that dietary sodium intake may be causally associated with hypertension risk.