A Mendelian randomization analysis: The causal association between serum uric acid and atrial fibrillation

Myunghee Hong
Pil-Sung Yang
Inseok Hwang
Tae-Hoon Kim
Hee-Tae Yu
Jae-Sun Uhm
Boyoung Joung
Moon-Hyoung Lee
Hui-Nam Pak

**Introduction**: Observational studies were shown that high levels of serum uric acid (UA) were associated with the atrial fibrillation (AF). However, the causal effect of urate on risk of AF is still unknown. To clarify the potential causal association between uric acid and atrial fibrillation, we performed the Mendelian randomization analysis using genetic instrumental variables (IVs).

**Methods**: In Korean GWAS dataset consisting of 672 patients with AF (mean age 50.5±7.8 years, 81.0% male, Yonsei AF Ablation cohort) who underwent radiofrequency catheter ablation and 3,700 controls (Korea Genome Epidemiology Study), we selected the 10 SNPs with p value less than 0.05 associated with the increasing serum level of UA. Additionally, we also calculated the weighted genetic risk score (wGRS) using selected 10 SNPs in order to use as an instrumental variable. Mendelian randomization analysis was calculated by the 2-stage least square (2SLS) method.

**Result**: The conventional association between serum uric acid and AF was shown the significance level (p = 0.004) after adjusting the potential confounding factors. The SNP rs1165196 on SLC17A1 (F-statistics = 221.82, 0.18 mg/mL per allele change, p < 0.001) and wGRS (F-statistics = 237.27; 0.20 mg/mL per 1SD change, p < 0.001) were significantly associated with increase the UA level. Mendelian randomization analysis was shown the causally associated with rs1165196 only (estimated odds ratio (OR) = 0.25, 95% CI = 0.08–0.77, p = 0.016), but not wGRS (estimated OR =0.98, 95% CI = 0.54–1.76, p = 0.944).

**Conclusion**: In contrast to the observational studies, the increasing levels of serum UA are causally associated with decreasing AF risk at SLC17A1 gene. It is warranted to test the reproducibility in the higher number of population.