Introduction: Obesity and obstructive sleep apnea (OSA) are associated with the atrial fibrillation (AF) risk. However, the study of causal relationship of obesity on risk of OSA in patients with AF is limited. The aim of study was to examine the causal effect between obesity and OSA in patients with AF using a Mendelian randomization study design.

Methods: 546 patients with AF (mean age 59.9±10.5 years, 74.2% male) who underwent radiofrequency catheter ablation were used for Mendelian randomization analysis from GWAS dataset. To use the genetic instrumental variables (IVs), we choose the 6 SNPs (p value < 0.05) associated with the increasing level of body mass index (BMI; mg/kg). In addition, we also constructed the weighted genetic risk score (wGRS) by using selected 6 SNPs as an IV.

Result: We found the significant association (p < 0.001) of BMI on OSA after adjusting age and gender. Additionally, a BMI levels in the upper quartile associated with a 4.84 fold increased risk of apnea/hypopnea index compare to lower quartile (95% CI = 2.62–8.93, p < 0.001). The top SNP rs2535633 on ITIH4 (0.65 mg/kg per allele change, p < 0.001) and wGRS (0.86 mg/kg per 1SD change, p < 0.001) were significantly associated with increase the BMI level. In Mendelian randomization analysis, the estimated the causal effect (beta coefficient) of OSA risk was 4.97 (95% CI = 1.75 to 8.18, p = 0.003) and 5.06 (95% CI = 2.25 to 7.88, p < 0.001) using ITIH4 and wGRS, respectively.

Conclusion: Our finding suggests that increasing OSA risk in patients with AF is causally associated obesity at the genetic levels. It may valuable finding in order to reduce the AF risk.