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CUMULATIVE AND INDIVIDUAL EFFECTS OF SINGLE NUCLEOTIDE POLYMORPHISMS FOR ATRIAL FIBRILLATION BY META-ANALYSIS OF GENOME-WIDE ASSOCIATION STUDIES IN PATIENTS WITH HEART FAILURE

Poster Contributions
Poster Hall B1
Monday, March 16, 2015, 9:45 a.m.-10:30 a.m.

Session Title: Risks for Atrial Fibrillation: Where Do We Look?
Abstract Category: 4. Arrhythmias and Clinical EP: AF/SVT
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Background: In patients with heart failure (HF), atrial fibrillation (AF) is a common arrhythmia and has a significant association with an increased risk for mortality. The cumulative effects of ten genotypes susceptible to AF identified by meta-analysis of genome-wide association studies (GWAS) were reported to confer AF risk. However, little is known about genetic pathogenesis related to HF. The purpose of our study was to clarify the cumulative effects of 10 GWAS-proven single nucleotide polymorphisms (SNPs) in AF patients with HF, and to examine the influences of genetic pathogenesis in two clinical forms of HF.

Methods: Two hundred seventy-eight patients with HF (200 with HF with preserved Ejection Fraction (EF) (HFPEF), 78 with HF with reduced EF (HFREF)) were enrolled in this study. Of these patients, 184 were diagnosed with AF and 93 were diagnosed with sinus rhythm (SR). We genotyped 10 SNPs validated by meta-analysis of GWAS for AF. The 10 SNPs were KCNN3-PMVK (rs6666258), PRRX1 (rs3903239), PITX2 (rs6817105), WNT8A (rs2040862), CAV1 (rs3807989), C9orf3 (rs10821415), SYNPO2L (rs10824026), SYNE2 (rs1152591), HCN4 (rs7164883), and ZFHX3 (rs2106261). Cumulative effects were calculated as a genotype risk score by summing the number of risk alleles from the 10 SNPs for each patient.

Results: In all HF patients, the total genotype risk score was significantly higher in patients with AF than in those with SR (7.1±0.9 vs 6.4±0.7, P= 0.001). However, this cumulative genetic relationship with AF was not identified in patients with HFREF. The frequency of the risk allele in HCN4 gene was significantly higher in HFREF patients with AF than those with SR (p=0.012). On the other hand, this frequency tended to be lower in patients with AF than in those with SR (P=0.062) in HFPEF.

Conclusion: We found that the genotype risk score based on 10 GWAS-proven SNPs for AF was significantly associated with AF in patients with heart failure. Additionally, HCN4 gene might play an inverse role in pathogenesis of AF between the two clinical forms of HF.