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Editorial

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Can Genetic Risk Scoring Predict Atrial Fibrillation Ablation Outcomes?

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▸ See the article "A Genetic Risk Score for Atrial Fibrillation Predicts the Response to Catheter Ablation" in volume 49 on page 338.

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The importance of atrial fibrillation (AF) as an atrial arrhythmia is emphasized by its worldwide prevalence, associated morbidity, and mortality, and corresponding increase in health-care costs.[1] Genetic association studies of common genetic variants have proved a polygenic basis for AF.[2] Ablation is a widely recognized intervention that has been proven to be associated with improvement in quality of life in patients with AF.[1] However, despite their established efficacy, both catheter ablation and cryoablation of AF are associated with a substantial risk of recurrence necessitating careful risk and benefit assessment for each patient to identify preprocedural characteristics.[1] Various risk factors, including advancing age, male sex, hypertension, obesity, ischemic heart disease, myocardial infarction, valvular diseases, hyperthyroidism, and genetic predisposition, have been identified to influence the development of AF and its response to ablation therapy.[1][3]

Since the identification of the first AF gene in 2003,[4] interests in the role of genetics in predicting AF onset, risk stratification of AF outcomes, and treatment response to antiarrhythmic medications or catheter ablation procedures have been explored.[1] Fourteen genetic loci associated with AF in European and Asian ancestry groups have been identified in genome-wide association studies (GWASs).[5] The ability of genetics to predict the outcome of an ablation procedure has been investigated in several studies with differing results in different populations.

In 2010, Husser et al.[6] first suggested the potential role of genetic results in the stratification of patients for AF ablation therapy. In their study of 195 Caucasian patients of German descent, polymorphisms on chromosome 4q25 were reported to modulate the risk of AF recurrence after catheter ablation. This study paved the way for subsequent studies on the role of these polymorphisms in the genetic risk prediction of catheter ablation outcome. The association between the specific chromosome 4q25 variant and AF recurrence after ablation was reproduced.[7] Hu et al.[3] reported the genetic analysis of 189 Taiwanese patients who underwent AF catheter ablation. In this study, the chromosome 16q22 variant (rs7193343) was independently associated with AF recurrence after catheter ablation in the paroxysmal AF (PAF) group but not in the non-PAF group. In a report from the Korean population by Choi et al.,[8] the data showed that none of those previously reported top AF-susceptibility single nucleotide polymorphisms (SNPs) predicted clinical recurrence after catheter ablation with a follow-up duration of 18.3±13.9 months.

Conflict of Interest
The authors have no financial conflicts of interest.

Author Contribution
Conceptualization: Lin CY; Data curation: Lin CY; Resources: Lin CY; Supervision: Hu YF, Lin YJ, Chen SA; Writing - original draft: Lin CY; Writing - review & editing: Lin CY, Chen SA.

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In this issue of the *Korean Circulation Journal*, Choe et al.[9] investigated the prediction of the outcomes of AF ablation in a Korean population using a genetic risk score (GRS) constructed from a candidate polymorphism study of 20 pre-selected SNPs from previous GWASs as common genetic markers associated with AF incidence.[9] A GRS was calculated by summing the number of risk alleles for each of the 5 selected SNPs and resulted in a score ranging from 1 to 10, which was further divided into 3 groups with an incremental risk of recurrence in the higher GRS.

These studies presented inconsistent genetic associations in different populations and highlights the limitations of the use of SNPs, which varies between human populations such that a SNP allele that is common in 1 geographical or ethnic group may be much rarer in another. Replication studies in different populations are necessary to validate associations and their generalizability. Several studies have tried to incorporate genetic data by proposing cumulative GRS and providing predictive models for reliable assessment of AF risk.[2] Choe et al.[9] first reported the association between GRS and AF recurrence after catheter ablation. Although the clinical association between GRS and AF recurrence could be identified, the causal relationship between the specific SNPs and mechanism of AF recurrence or documented predictors was not established.

The task of sorting out relevant genetic information for ablation outcome is not easy and it is further complicated by clinical risk factors, variations in AF types, method of ablation, type of recurrence, and genetic variations in different populations and ethnicities.[1][2] Our experience showed that the contributions of genetic predisposition and clinical risk to the development of AF recurrence are substantial.[3] Genetic risk stratification may be used in clinical practice after considering basic clinical risk factors. The innovation and identification of AF genes offer cardiologists and electrophysiologists the opportunity to create unique patient profiles that can guide personalized treatment decisions and to achieve an era of "precision medicine." Choe et al.[9] demonstrated the feasibility of assessing AF recurrence risk by using the GRS within the Korean population. Future studies are warranted to further refine polygenic and clinical risk estimates in additional races and populations.

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