Sex Difference in Clinical Recurrence After Catheter Ablation in Young Patients With Atrial Fibrillation — What Is the Underlying Mechanism? —

Hiroya Mizuno, MD

Many reports have focused on the sex difference in epidemiology, comorbidity and medical access of atrial fibrillation (AF), which has led to wide recognition of the importance of understanding the disparities of therapeutic impact of AF between males and females. Although the incidence of AF increases with age and is lower in females than males,1,2 over the age of 75 years, more than half of AF patients are women because of their increased life expectancy.3 Compared with men, women with AF are symptomatic and have more comorbidities. Furthermore, delayed consultation by women results in longer disease duration and frequent long-lasting persistent AF.4,5 Female sex is taken into account in CHADS2-VASc scoring system for stroke, so women have increased risk of stroke and systemic embolism.6 Despite having more severe symptoms, women are less likely to have therapies such as cardioversion, catheter ablation and antiarrhythmic drugs.7,8 There seems to be no consensus about the disparity in anticoagulation: insufficient NOAC dosing was more common among woman in the South Korean CODE-AF registry,7 but the prevalence of anticoagulant use was similar in women and men in the global GLORIA-AF registry.8

Some studies suggest sex-specific risk factors. In the AFFIRM trial, left atrial (LA) diameter enlargement was an independent risk factor of cardiovascular death only in females.9 Yoshida et al showed a significant negative association between global LA function and CHADS2 score only among women.10

Nowadays, catheter ablation is a mainstream nonpharmacological therapy for AF. There is also a sex difference in clinical outcome after catheter ablation. In a national population-based cohort study in the USA, 16.5% of the 37,360 patients who had catheter ablation against AF were readmitted within 90 days. Female sex was the independent predictor of recurrence after catheter ablation, despite women being less likely to receive catheter ablation for AF.11 The FIRE and ICE trial also revealed significantly high recurrence and readmission rates in women after ablation.12 Tripathi et al reported frequent ablation-related complications among woman in a survey of the Nationwide Inpatient Sample database.13

As shown, many studies have clarified the presence of a sex difference in the efficacy and safety of catheter ablation therapy. However, the results were more or less affected by confounders such as patient characteristics, disease duration and social background.14 In the study published in this issue of the Journal, Yu et al15 evaluate the association between sex and clinical recurrence after catheter ablation in relatively young (<60 years old) AF patients who had been exposed to fewer modifying factors. Even in their study, there were differences in patient profiles between the sexes: women were older, smaller and had more heart failure but less hypertension, diabetes and vascular disease. CHADS2VASc scores for the women were higher by 1 point than those for the men, which means the number of risk factors was identical. The recurrence rate after initial ablation was significantly higher in women and this positive association was seen in the comparison between propensity score-matched groups. They applied Cox regression analysis with 2 different models to find that female sex was an independent predictor of recurrence. Moreover, they compared the outcome of second ablation in 111 patients with AF recurrence and showed again that women had higher recurrence even after a second procedure, despite no difference between sexes for procedural success such as pulmonary vein isolation and completion of bidirectional block in the first ablation.

This study is unique and important for the following reasons: it focused on young AF patients and added the propensity score-matched comparison to eliminate confounding factors. Furthermore, they showed that procedural success is not associated with recurrence by comparing the recurrence rate after a second session. The results suggest the presence of unexplained mechanisms directly involved in recurrence after ablation.

The authors speculate about the potential role in recurrence of the autonomic nervous system, remodeling of atria by increased inflammation and large volumes of pericardial fat. In this study, women had increased vagal tone and a larger LA corrected by body mass index. Further study is strongly expected to identify the mechanism
Intervening between sex and clinical recurrence. It will elucidate the critical stages of the onset and progression of AF, then provide new therapeutic strategies to improve the outcome of AF.

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References