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Editorial

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A 'Gender Paradox' of Female as a Stroke Risk in Atrial Fibrillation: Do Women Live Longer Than Men?

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▸ See the article "Association of Gender With Clinical Outcomes in a Contemporary Cohort of Patients With Atrial Fibrillation Receiving Oral Anticoagulants" in volume 52 on page 593.

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Embolic stroke is the most important sequalae of atrial fibrillation (AF), which is substantially preventable with thorough evaluation and appropriate measures of anticoagulation. Major risk factors have been identified from landmark randomized controlled trials during the past two decades and was refined as CHA_2DS_2-VASc (Congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke, vascular disease, age 65–74 years, sex category [female]) score.[1] Although male gender is known to have poorer cardiovascular health, it is not the case in terms of AF-related thromboembolism.[2] Female gender is an established risk factor for stroke and thromboembolism in patients with AF without oral anticoagulant (OAC) therapy, with variation across age and ethics.[3] Before introduction of non-vitamin K antagonist oral anticoagulants (NOAC), warfarin had been mainstream therapy of anticoagulation for stroke prevention with various limitations on efficacious utilization in clinical field. Treatment effectiveness of warfarin is quantified by time in therapeutic range (TTR), which correlates with thromboembolic event as well as hemorrhagic events.[4] It is also associated with several factors, including female sex, which implies less likelihood to achieve sufficient TTR. Previous studies with anticoagulation with warfarin showed higher risk of stroke event in female compared to male, which led to suggestion of more active anticoagulation for female to reduce the risk of stroke.[5][6]

NOAC has become a 'game-changer' in anticoagulation for stroke prevention with AF, and is recommended as first-line therapy for patients with non-valvular AF when eligible. NOAC with standard-dosing has also resulted better efficacy and safety in Asian population compared with non-Asian population, which favors its widespread use in Asian AF patients.[7] However, less is known about the sexual difference of efficacy and safety outcome in the era of NOAC, especially in Asian population.

In this issue, Kim et al.[8] investigated clinical outcomes of patients with non-valvular AF treated with OAC and reported relationship with gender. This study which was based on prospective cohort of Korean AF patients reported no significant difference in primary outcome of stroke or systemic embolism as well as safety endpoint of major bleeding between sex, regardless of type of OAC (warfarin or NOAC) used. Although women with intermediate to high risk of stroke were older compared to male counterpart, women have also showed lower rate of adjusted all-cause mortality, without significant difference of cardiovascular death.

Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

Author Contributions

Conceptualization: Choi JI; Supervision: Choi JI; Writing - original draft: Jeong JH, Choi JI; Writing - review & editing: Jeong JH, Choi JI.

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Female sex has been known as a robust risk of embolic stroke in AF, even with appropriate anticoagulation with warfarin. Kim et al.[8] provided a valuable insight on the effect of sex on clinical outcomes, regarding contemporary anticoagulation use patterns. In Asian population, predominant usage of NOAC in real-world resulted in no longer higher risk of stroke in female sex group. However, there are several issues that are yet investigated, such as the dosage of NOAC used, which is also linked to potential hemorrhagic event. Inappropriate dose reduction of NOAC is frequent in Korean AF population.[9]

Although detailed information of inappropriate dosage regarding sex is not provided in the study, female who represented elderly population as well as lower body weight compared to male might have included higher proportion of patients with use of low dose NOAC. Further gender-specific differences should be encompassed, such as discrete risk factors that affect expression of AF in elderly women.[10] In addition, studies regarding prescription type and dose of NOACs may provide more profound insight into gender-related differences in major outcomes of thromboembolic event in patients with AF.

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