

Reply Letter

Reply: Sex-Based Differences in Outcomes of Oral Anticoagulation: Does the Antiplatelet Therapy Matter?

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We thank Dr. Mo and colleagues for their interest in our study and the opportunity for a discussion on the possible confounding of the sex-based differences in the risk of intracranial hemorrhage. First, we agree that the use of an antiplatelet may affect treatment outcomes and treatment choices between direct oral anticoagulants (DOACs) and warfarin (1). Over 70% of the patients in our study were treated with an antiplatelet within 90 days on or before the index date, which was defined as the start date of the first prescription of oral anticoagulants. To reduce confounding, antiplatelet was included in our propensity score model and the baseline characteristics between the comparison groups were well balanced with standardized differences less than 0.1 in both men and women. Although it was suggested in a previous study that high platelet reactivity was associated with a reduced risk of bleeding in women only, it was a post hoc analysis in which the target patient group and definition of bleeding outcomes were different from our study (2). Of note, the objective of our study was to compare the clinical outcomes of DOACs versus warfarin within men and within women, respectively. Further investigation into the understanding on the effect of antiplatelets on the clinical outcomes of DOACs versus warfarin in the specific sex is warranted.

Second, the aim of our study was to provide more evidence to inform the choice of oral anticoagulants within a specific sex. We concluded that DOACs were associated with a lower risk of intracranial hemorrhage and all-cause mortality in women only. Propensity score matching was performed between DOAC and warfarin groups, but not between men and

women. A different methodology will be required to balance any differences in baseline characteristics, including the CHA₂DS₂-VASc score, between sexes. This is a different study objective and beyond the scope of the current study. Further comparisons with a larger sample size are required to investigate the association between sex and intracranial hemorrhage within the specific oral anticoagulant.

References:

1. Gong X, Tang S, Li J, Zhang X, Tian X, Ma S. Antithrombotic therapy strategies for atrial fibrillation patients undergoing percutaneous coronary intervention: a systematic review and network meta-analysis. *PLoS One* 2017;12(10):e0186449.
2. Yu J, Mehran R, Baber U, Ooi SY, et al. Sex differences in the clinical impact of high platelet reactivity after percutaneous coronary intervention with drug-eluting stents: results from the ADAPT-DES Study (Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents). *Circ Cardiovasc Interv* 2017;10:e003577.