Comparative analysis of oral anticoagulation therapy in Asian patients with atrial fibrillation and end-stage renal disease: a nationwide population-based cohort study

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Background: The efficacy and safety of direct oral anticoagulants (DOACs) in patients with end-stage renal disease (ESRD) on dialysis is unclear. Although the RENAL-AF trial (Renal Hemodialysis Patients Allocated Apixaban Versus Warfarin in Atrial Fibrillation), a prematurely stopped randomized controlled trial, has been recently reported, the risks of clinical outcomes comparing DOAC and warfarin in patients with AF and ESRD is still inconclusive.

Purpose: To analyze comparative effectiveness and safety of oral anticoagulant therapy including warfarin, rivaroxaban, apixaban, and edoxaban in Asian patients with AF and ESRD

Methods: Using a Korean nationwide claims database, anticoagulated patients with AF and ESRD between 2014 and 2020 were included. The occurrence of ischemic stroke, major bleeding, all-cause death, and the net clinical outcome (NCO, the composite of all clinical outcomes) were evaluated. We firstly compared between pooled DOAC and warfarin, and also compared each DOAC (rivaroxaban, apixaban, and edoxaban) to warfarin. Inverse probability of treatment weighting using propensity scores were used to balance difference in baseline characteristics of each group.

Results: A total of 5503 patients were included (3484 with warfarin, 407 with rivaroxaban, 1273 with apixaban, and 339 with edoxaban). During a median 1.4-year (interquartile ranges 0.5-3.0 years) of follow-up, 345, 376, 2321, and 2617 of ischemic stroke, major bleeding, all-cause death, and the NCO were occurred (incidence rate, 3.44, 3.77, 22.11, and 27.35 per 100 person-years, respectively). to warfarin, DOAC was associated with significantly lower risks of major bleeding (hazard ratio, 95% confidence interval: 1.159, 0.929-1.440, p=0.187), all-cause death (0.667, 0.520-0.847, p<0.001), and NCO (0.816, 0.748-0.889, p<0.001), with a comparable risk of ischemic stroke (1.159, 0.299-1.440, p=0.001) (Figure A). For the comparison between each DOAC and warfarin (Figure B), apixaban showed a comparable risk of ischemic stroke with warfarin, however, rivaroxaban and edoxaban were associated with a higher risk of ischemic stroke than warfarin. Among 3 DOACs, only apixaban associated with a lower risk of major bleeding than warfarin (0.600, 0.434-0.812, p=0.001). All DOACs were associated with a lower risk of all-cause death than warfarin. Overall, apixaban and rivaroxaban showed a significantly lower risk of NCO than warfarin (0.799, 0.719-0.887, p<0.001 for apixaban vs. warfarin; 0.842, 0.732-0.963, p=0.013 for rivaroxaban vs. warfarin). The results were consistent in a competing risk analysis.

Conclusion: In this large-scale observational cohort study, DOAC might be associated with a lower NCO than warfarin in Asians patients with AF and ESRD on dialysis. In line with current guidelines, apixaban and rivaroxaban could be a reasonable choice to achieve better net clinical benefit than warfarin in patients with AF and ESRD who are needed anticoagulation therapy.