The effect of non-vitamin K antagonist oral anticoagulants in high frail patients with atrial fibrillation

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**Introduction:** The non-vitamin K antagonist oral anticoagulants (NOACs) have all been shown to be at least as effective and safe as warfarin in large randomised controlled trials. However, there is a paucity of data evaluating the NOAC to warfarin in frail AF patients. Therefore, we sought to assess the effectiveness and safety of NOAC versus warfarin in frail non-valvular AF (NVAF) patients treated in routine practice.

**Methods:** Using the Korean national health insurance service database, we identified patients with non-valvular AF who initiated NOAC or warfarin in 2013–2016. For each patient, the Hospital Frailty Risk Score was calculated retrospectively using all available ICD-10 diagnostic codes. According to the aggregate score, patients were divided into the three frailty risk categories: low risk (<5 points), intermediate risk (5–15 points) and high risk (>15 points) as recommended. We compared the outcome between NOAC and propensity score matched warfarin users.

**Result:** NOAC was associated with significantly reduced hazards of all-cause death (hazard ratio [HR] 0.22, 95% confidence interval [CI] 0.20–0.25, P<0.001), SSE (HR 0.78, 95% CI 0.66–0.92, P<0.001) or major bleeding (HR 0.78, 95% CI 0.67–0.93, P<0.001) compared with warfarin in patients with high frailty risk. NOAC were associated with reduced hazards of ischemic stroke in patients with intermediate and low frailty risk, but not in those with high frailty risk after the adjustment of competing risk of mortality. After multivariable adjustment, dabigatran was associated with lower hazards of developing ischemic stroke/SE (HR 0.67, 95% CI 0.53–0.86, P=0.002), rivaroxaban was associated with lower risk of major bleeding than warfarin in high frail risk group (HR 0.55, 95% CI 0.32–0.95, P=0.031). No significant differences were observed between any NOAC and warfarin in rates of major bleeding or in any major bleeding subtype including haemorrhagic stroke, intracranial haemorrhage and gastrointestinal bleeding in high frail risk population.

**Conclusion:** Our study found that compared with warfarin, NOAC is associated with reduced mortality and SSE in NVAF patients with high frail risk. The relative effectiveness and safety of NOACs compared with warfarin appears maintained in frail NVAF patients treated in routine clinical practice.