Stroke & Systemic Embolism and Other Adverse Outcomes of Heart Failure with Preserved and Reduced Ejection Fraction in Atrial Fibrillation: Results from the CODE-AF Registry

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**Introduction**: It is unknown whether different types of heart failure (HF) have similar risk of thromboembolic event and other adverse outcomes in patients with non-valvular atrial fibrillation (AF).

**Methods**: A 10,586 non-valvular AF patients enrolled in the prospective, multicenter outpatient CODE-AF (Comparison study of Drugs for symptom control and complication prevention of Atrial Fibrillation) registry from June 2016 to February 2019 were analyzed. The risk of ischemic stroke & systemic embolism, myocardial infarction, major bleeding, and all-cause mortality were evaluated in each type of HF.

**Result**: HF group included 941 (8.9%) patients, and the proportion of preserved (HFpEF), mid-range (HFmrEF), and reduced ejection fraction (HFrEF) was 43.5%, 26.7%, and 29.8%, respectively. Each of these 3 groups had significantly higher CHA2DS2-VASc risk score (HFpEF 4, IQR 3-5; HFmrEF 3, IQR 2-5; HFrEF 4, IQR 2-5; no-HF 2, IQR 1-3) and use of oral anticoagulation (HFpEF 84.8%; HFmrEF 86.9%; HFrEF 84.4%; no-HF 68.7%) than no-HF group (p<0.001, for each comparison with no-HF). Among them, HFpEF group was significantly older (p<0.001) and had significantly higher CHA2DS2-VASc risk score (p=0.005) than HFrEF group. During follow-up of median 1.21 years, incidence of ischemic stroke & systemic embolism was 1.80 events/100PYR in HFpEF group, and 0.71 events/100PYR in no-HF group; cumulative incidence was significantly higher in HFpEF group (p=0.006). The risk of thromboembolic events was significantly increased in HFpEF (adjusted HR 2.24, 95% CI 1.12-4.50, p=0.02), and consistently increased even in HFpEF with oral anticoagulation (adjusted HR 2.56, 95% CI 1.21-5.42, p=0.01). Compared to no-HF, cumulative incidence of myocardial infarction was significantly higher in HFmrEF (p=0.03), and all-cause mortality was significantly higher in HFpEF (p=0.02) and HFrEF (p=0.02); but, the risks of these adverse outcomes were not significantly higher in each type of HF compared to no-HF.
Conclusion: Patients with HFpEF were significantly older and higher risk of ischemic stroke compared to patients without HF, or even compared to patients with HFrEF. Compared to no-HF, the risk of ischemic stroke & systemic embolism was significantly higher in HFpEF, but not in HFmrEF and HFrEF. This result suggests that stricter use of oral anticoagulation is needed for patients with HFpEF.