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Heart failure clinical phenotypes and outcomes in patients with atrial fibrillation: an analysis from the eurobservational research programme in atrial fibrillation long-term general registry

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On behalf of EORP-AF Long-Term General Registry Executive Committee and Investigators

Introduction: Heart failure (HF) is a well-known risk factor for atrial fibrillation (AF). Moreover, HF is associated with worse clinical outcomes in patients with known AF. Recently, phenotypes of HF have been redefined according to the level of ejection fraction (EF). New data are needed to understand if a differential risk for outcomes exists according to the new phenotypes' definitions.

Purpose: To evaluate the risk of major adverse outcomes in patients with AF and HF according to HF clinical phenotypes.

Methods: We performed a subgroup analysis of AF patients enrolled in the EORP-AF Long-Term General Registry with a history of HF at baseline, available EF and follow-up data. Patients were categorized as follows: i) EF $<$40%, i.e. HF reduced EF [HFrEF]; ii) EF 40–49%, i.e. HF mid-range EF [HFmrEF]; iii) EF $\geq$50%, i.e. HF preserved EF [HFpEF]. Any thromboembolic event (TE)/acute coronary syndrome (ACS)/cardiovascular (CV) death, CV death and all-cause death were recorded.

Results: A total of 3409 patients were included in this analysis: of these, 907 (26.6%) had HFrEF, 779 (22.9%) had HFmrEF and 1723 (50.5%) had HFpEF. An increasing proportion with CHA2DS2-VASc $\geq$2 was found across the three groups: 90.4% in HFrEF, 94.6% in HFmrEF and 97.3% in HFpEF ($p<0.001$), while lower proportions of HAS-BLED $\geq$3 were seen (28.0% in HFrEF, 26.3% in HFmrEF and 23.6% in HFpEF, p=0.035). At discharge patients with HFpEF were less likely treated with antiplatelet drugs (22.0%) compared to other classes and were less prescribed with vitamin K antagonists (VKA) (57.0%) and with any oral anticoagulant (OAC) (85.7%). No differences were found in terms of non-vitamin K antagonist oral anticoagulant use. At 1-year follow-up, a progressively lower rate for all study outcomes (all $p<0.001$), with an increasing cumulative survival, was found across the three groups, with patients with HFpEF having better survival (all $p<0.0001$ for Kaplan-Meier curves). After full adjustment, Cox regression analysis showed that compared to HFrEF, HFmrEF and HFpEF were associated with risk of all study outcomes (Table).

Conclusions: In this cohort of AF patients with HF, HFpEF was the most common phenotype, being associated with a profile related to an increased thromboembolic risk. Compared to HFrEF, both HFmrEF and HFpEF were associated with a lower risk of all major adverse outcomes in AF patients.

Cox Regression Analysis

HR (95% CI)	Any TE/ACS/CV Death	CV Death	All-Cause Death
HFmrEF	0.65 (0.49–0.86)	0.53 (0.38–0.74)	0.55 (0.41–0.74)
HFpEF	0.50 (0.39–0.64)	0.42 (0.31–0.56)	0.45 (0.35–0.59)

ACS = Acute Coronary Syndrome; CI = Confidence Interval; CV = Cardiovascular; EF = Ejection Fraction; HF = Heart Failure; HR = Hazard Ratio.