Atrial Fibrillation (AF) - Clinical

Impact on outcomes in Europe: a cluster analysis from the ESC-EHRA EORP AF general long-term registry

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Introduction: Data derived from recent observational studies in atrial fibrillation (AF) show how the complexity of the clinical phenotype, beyond baseline thromboembolic risk, can increase risk of major adverse outcomes. Importantly, risk factors tend to occur in clusters, rather than occur individually in isolation.

Aims: To describe AF patients' clinical phenotypes among a large contemporary European AF cohort and to analyse the differential impact of these clinical phenotypes on the occurrence of major adverse outcomes.

Methods: We performed a hierarchical cluster analysis based on Ward's Method and using Squared Euclidean Distance using 22 clinical covariates. All variables were considered as binary. Examining the distances between cluster coefficients and by visual inspection of the dendrogram produced we identified the optimal number of clusters. Patients with data available for all 22 variables were included. We considered occurrence of cardiovascular events and all-cause death.

Results: Among the original 11096 patients included, 9363 (84.4%) were available for this analysis. The cluster analysis identified three clusters: Cluster 1 (n = 3634; 38.8%) characterized by older patients with prevalent noncardiac comorbidities; Cluster 2 (n = 2774; 29.6%) characterized by younger patients mainly admitted for first detected and paroxysmal AF with low prevalence of concomitant conditions; Cluster 3 (n = 2955; 31.6%) included patients with high prevalence of permanent AF, cardiac risk factors and comorbidities. Thromboembolic and bleeding risks were higher in Cluster 3 and progressively lower in Cluster 1 and Cluster 2 (both $p < 0.001$). Use of oral anticoagulant was significantly lower for Cluster 2 (83.2% vs. 86.5% and 86.7% in Cluster 1 and Cluster 3, respectively; $p < 0.001$). Over a mean follow-up of 22.5 (SD5.5) months, Cluster 3 had the highest rate of both cardiovascular events (10.0%) and all-cause death (13.2%), compared with Cluster 1 (6.6% and 9.4%, respectively) and Cluster 2 (3.7% and 3.8%, respectively) (both $p < 0.001$). Kaplan-Meier curves (Figure) show that Cluster 2 (green line) had the lowest cumulative risk of outcomes; risk was progressively higher in Cluster 1 (orange line) and Cluster 3 (yellow line). A Cox multivariable regression analysis, adjusted for type of AF, symptomatic status, CHA2DS2-VASc score and use of oral anticoagulants, showed that both Cluster 3 and Cluster 1 were associated with a significantly increased risk of cardiovascular events (HR: 1.80, 95%CI: 1.39-2.33 and HR: 1.40, 95%CI: 1.09-1.80, respectively) and all-cause death (HR: 1.80, 95%CI: 1.40-2.30 and HR: 1.66, 95%CI: 1.30-2.11) compared to Cluster 2.

Conclusions: In European AF patients, three main clinical clusters were identified, those with non-cardiac comorbidities, low risk and cardiac comorbidities. Both non-cardiac and cardiac comorbidities clusters were found to be associated with an increased risk of cardiovascular events and all-cause death.

Abstract Figure. Kaplan-Meier Curves for Outcomes