Clinical phenotypes of atrial fibrillation and risk of mortality: a cluster analysis

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Background: Patients with atrial fibrillation (AF) experience a high mortality rate despite optimal antithrombotic treatment. Characteristics of AF patients at higher mortality risk have been barely described so far and no risk score has been specifically developed at this aim. Furthermore, a clinical approach based on risk scores present some limits such as to not consider some important risk factors for mortality, and many available scores have poor predictive value. Cluster analysis may play a role in overcoming limitations of risk scores, especially in the case of overlapping risk factors.
Purpose: To identify of clinical phenotypes by using an unbiased statistical approach, such as the cluster analysis.
Methods: Cluster analysis was used to identify clinical phenotypes of AF patients associated with all-cause mortality in 5,171 AF patients from the START registry. Clinical variables used for the analysis were age, sex, diabetes, previous cerebrovascular events, previous cardiovascular events, heart failure, peripheral artery disease, use of non-vitamin K oral anticoagulants, cancer, pulmonary disease, smoking habit, previous major bleeding. The risk of all-cause mortality in each cluster was analyzed.
Results: We identified 4 clusters (Figure 1). Cluster 1 was composed by youngest patients, with obesity and paroxysmal AF; Cluster 2 by patients with low cardiovascular risk factors and high proportion of cancer; Cluster 3 by men with diabetes and coronary and peripheral artery disease, a high proportion of thrombocytopenia, and a high use of aspirin, proton pump inhibitors, and statins; Cluster 4 included the oldest patients, mainly women, with previous cerebrovascular disease, persistent/ permanent AF, heart failure, kidney disease and anemia. In this cluster there was the highest use of digoxin and NOACs.
During 9856,84 patient/years of observation, 386 deaths (3.92%/year) occurred. Mortality rates significantly increased across clusters: 0.42%/year (cluster 1, reference group), 2.12%/year (cluster 2, adjusted hazard ratio [aHR] 3.306, 95% confidence interval [CI] 1.204–9.077, p=0.020), 4.41%/year (cluster 3, aHR 6.702, 95% CI 2.433–18.461, p<0.001) and 8.71%/year (cluster 4, aHR 8.927, 95% CI 3.238–24.605, p<0.001).
Conclusions: We identified different clinical phenotypes of AF patients by cluster analysis which were specifically associated with mortality. This approach may help identify patients at higher risk of mortality.

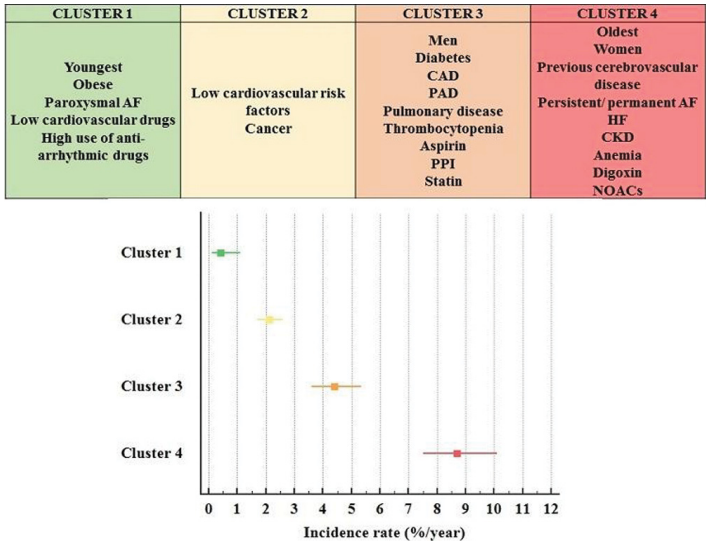

Figure 1