Abstract: P4797

Genetic testing in 101 consecutive lone atrial fibrillation patients is able to identify a subgroup with increased severity

Authors:
G D’Arezzo Pessente¹, FD Darieux¹, LS Sacilotto¹, NO Olivetti¹, FW Wulkan¹, TO Oliveira¹, DH Hachul¹, TW Wu¹, MS Scavacca¹, JK Krieger¹, AP Pereira¹, ¹Heart Institute of the University of Sao Paulo (InCor) - Sao Paulo - Brazil,

On behalf: GenBrA

Topic(s):
Genetic Causes of Atrial Fibrillation

Citation:

Funding Acknowledgements:
National Council for Scientific and Technological Development (CNPq)

Introduction: Atrial fibrillation (AF) is the most common arrhythmia and the cause of 15% of all strokes and up to 6% of medical admissions. It is estimated that currently about 2.0 million Brazilians, and 30 million individuals worldwide, are affected by the disease. It is a complex and multifactorial disease, and the mechanisms are still not well understood. Between 10-20% of AF patients do not have any known predisposing factors, a condition once called "lone AF". The role of genetic testing still remains controversial in this clinical scenario. Purpose: The aim of this study was to identify the occurrence of pathogenic genetic variants in patients with atrial fibrillation without known risk factors. Methods: In a tertiary hospital, 101 young patients with apparent "lone AF" were screened with genetic testing by NGS using a custom genetic panel with 159 channelopathy and cardiomyopathy related genes. Variants found were classified according to the American College of Genetic and Genomic (ACMG) criteria. Subjects were evaluated with clinical and familial history, electrocardiogram, 24 hours Holter monitoring, echocardiogram, cardiac MRI and treatment response. Multivariate analyses were performed by logistic linear regression model. Results: During an inclusion period of 4 years, 101 consecutive patients, with mean age of 38.6 years old, were classified as "lone AF" (78% male); 76% presented paroxysmal AF and 24% persistent/permanent AF. Family history of early sudden death (bellow 60 years old) was reported in 37% of cases (78% below 50 years old); 10% had family members with pacemakers; and 44% reported having family members with early AF onset. Genetic testing demonstrated that 14/101 (13.8%) of patients presented genetic variants classified as pathogenic or likely pathogenic (P/LP) according to ACMG criteria. The genes most frequently affected were LMNA (3/101), ANK2 (3/101) and truncating variants in TTN (3/101). Two variables were significantly associated with harboring a pathogenic mutation: family history of sudden death (OR:5.58; 1.19-26.12 CI; p=0.029) and pacemaker reported in the family history (OR:6.83; 1.11-42.04 CI; p=0.038). Conclusion: Our data showed that approximately 15% of "lone AF" patients are carriers of known pathogenic mutations in genes associated with inherited cardiomyopathy. In addition, we show that being a carrier is potentially associated with a more severe phenotype. These findings suggest that genetic testing in "lone AF" patients may be able to identify a subgroup with a more severe phenotype are for whom a different management strategy might be indicated.