Clonal hematopoiesis of indeterminate potential in atrial fibrillation: prevalence and an association with progression


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Background: Both clonal hematopoiesis of indeterminate potential (CHIP) and atrial fibrillation (AF) are age-related conditions. Also, CHIP is associated with an increased risk of cardiovascular disease which might contribute to the development of AF. However, the direct association between CHIP and AF is unknown.

Objective: To evaluate the potential role of CHIP in the development and progression of AF.

Methods: Deep-targeted sequencing of 24 CHIP mutations was performed in 1,004 patients with AF and 3,341 non-AF healthy adults. Variant allele fraction (VAF) ≥2.0% indicated the presence of CHIP mutations. The association between CHIP and AF was evaluated by the comparison of (1) the prevalence of CHIP mutations between AF and non-AF adults and (2) clinical characteristics discriminated by CHIP mutations within AF patients.

Results: The mean age was 67.6 ± 6.9 vs. 58.5 ± 6.5 years in AF (paroxysmal, 39.0%; persistent, 61.0%) and non-AF cohorts, respectively. Twenty-four CHIP mutations with a VAF of at least 0.02 were found in 237 (23.6%) AF patients and 356 (10.7%) non-AF adults (p < 0.001). The most common CHIP mutation genes in AF were DNMT3A (13.5%), TET2 (6.6%), and ASXL1 (1.5%). After multivariable adjustment, detected CHIP mutations were 1.4-fold higher in AF patients than in non-AF adults [odds ratio (OR), 1.38 and 95% confidence interval (CI), 1.10-1.73, p < 0.01 for all AF; OR (95% CI), 1.50 (1.14-1.99), p < 0.01 for long-standing persistent AF]. In gene-specific analyses, TET2 somatic mutation presented the highest association with AF (OR, 1.63; 95% CI, 1.03-2.56, p = 0.036). AF patients with CHIP mutations were older and had more diabetes, a longer AF duration, and a higher E/E' than those without CHIP mutations (all p < 0.05).

Conclusion: CHIP mutations, primarily DNMT3A or TET2, are 1.4-fold more prevalent in AF than non-AF adults and might contribute to the progression of AF. Further studies are required to elucidate the underlying pathophysiologic role of CHIP in AF.