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EDITORIAL

Understanding the global burden of atrial fibrillation and regional variations: we need improvement

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This editorial refers to 'Global variations in the prevalence, treatment, and impact of atrial fibrillation in a multinational cohort of 153,152 middle-aged individuals' by P.G. Joseph *et al.*, pp. 1523–1531.

The prevalence and incidence of atrial fibrillation (AF) are increasing rapidly, and thus, understanding the epidemiology of this common arrhythmia allows us to plan management and prevention strategies. This is important given the healthcare burden of stroke, morbidity, and mortality associated with AF. However, despite several large community-based studies that have been published thus far, the true prevalence of AF is possibly underestimated especially across different geographic regions of the world. Indeed, the study of epidemiology and AF associated outcomes have been widely studied in Europe and North America, whereas data on AF from the rest of the world beyond these regions are scanty.[1] Various studies have investigated the racial and ethnic differences in AF prevalence, finding a great variation across regions but these are considerably different with respect to specific design, baseline characteristic of population included and importantly, methods to detect AF.[2]

In the present issue of *Cardiovascular Research*, Joseph *et al.*[3] report on global variations in the prevalence, treatment and impact of AF in a large cohort of middle-aged individuals from two prospective population-based cohort studies, the Prospective Urban Rural Epidemiology study (PURE) and the Canadian Longitudinal Study of Aging (CLSA). First, the authors should be commended because their effort to use systemic population sampling for AF ascertainment.[3] Indeed, the variability of the AF prevalence across different areas of the world reported by previous studies, could be partially biased by the differences in the quality of healthcare systems leading to a lower systematic search and detection of AF.[2] The methods used by Joseph *et al.*[3] partially overcome this issue. Conversely, by using only 12-lead electrocardiograms, the prevalence of non-permanent forms of AF could be largely underestimated without the utilization of more sophisticated diagnostic tools such as 24-h Holter monitoring, handheld devices or other wearable technologies.

In their primary analysis, age- and sex-standardized AF prevalence varied greatly between regions being highest in North America, Europe, China, and Southeast Asia and lowest in the Middle East, Africa, and South Asia.[3] Surprisingly, these regional variations in AF prevalence were only partially attenuated by adjusting for traditional risk factors (i.e. diabetes mellitus, hypertension, heart failure, myocardial infarction etc.) suggesting that other elements may contribute to explain these differences and play a key role in the development of AF.[3] Additionally, the impact of risk factors on AF risk varied across regions, being more pronounced in North America and Europe while almost completely absent in China and South Asia.[3]

These observations contribute to enrich the debate on the determinants of AF. It is well established that modifiable cardiovascular risk factors and lifestyle are important in the development of AF, especially in the European countries or North American but in contrast, little is known about other several AF determinants such as environmental factors, genetics and diet that could be more important in other countries (*Figure 1A*). Additionally, Joseph *et al.*[3] reported that compared to low-income countries (LICs), AF prevalence was higher both in middle-income countries (MICs) and high-income countries (HICs) even after the adjustments for cardiovascular risk factors suggesting that also the economic development plays a key role. However, the precise reasons explaining these ethnic and regional variations in AF epidemiology remain poorly understood and further studies are warranted.

The hypothesis that European ancestry could be an independent predictor of a higher risk of AF is attractive and supported by other large observational studies.[4] For example, African American individuals from two large cohorts, the Cardiovascular Health Study (CHS) and the Atherosclerosis Risk in Communities (ARIC) study, had a lower incidence of AF despite a higher prevalence of several traditional risk factors for AF and notably, every 10% increase in European ancestry augmented the risk of AF by at least 10%.[4] The potential role of other novel risk factors, such as air pollution or diet, should also be better elucidated to explain the geographical variation in AF epidemiology. For example, it has been reported that a prolonged exposure to ambient particulate matter,

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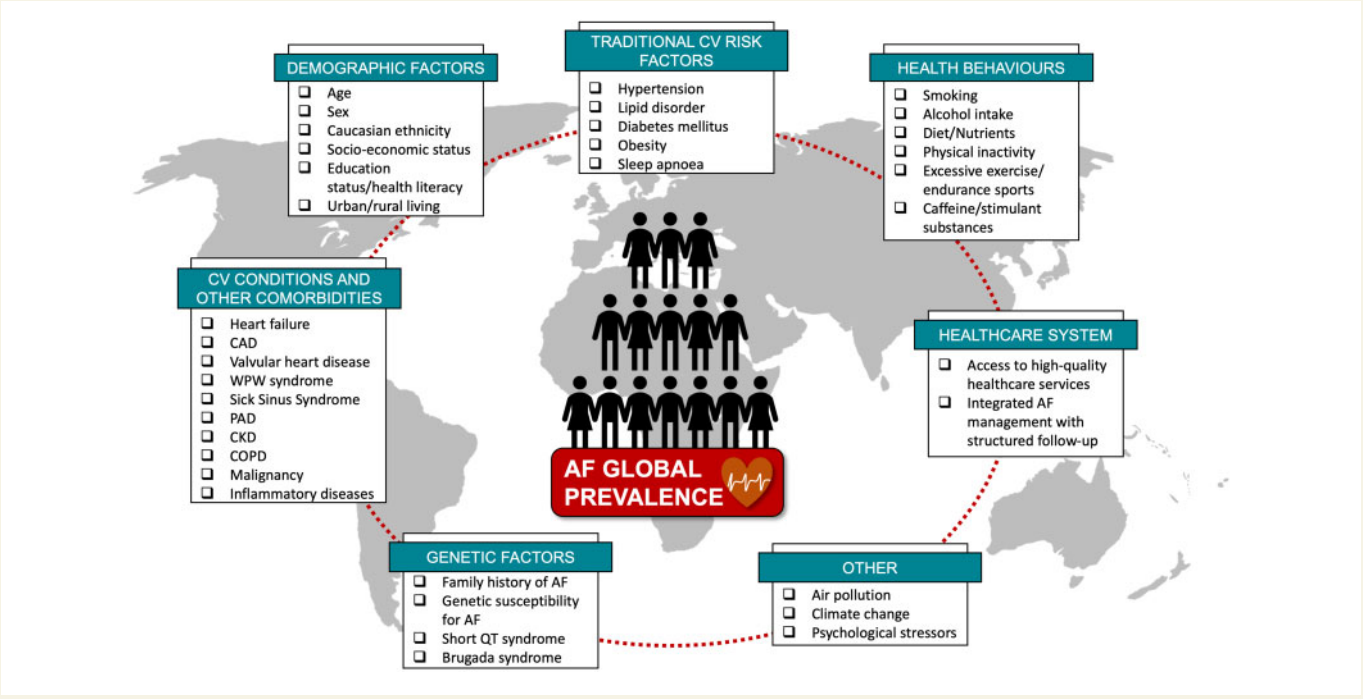

Figure 1 Determinants of variations in global AF prevalence. AF, atrial fibrillation; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; PAD, peripheral artery disease; WPW, Wolff-Parkinson-White.

increases the risk of cardiovascular diseases and indeed, some of the highest polluted cities are now in China, India, Indonesia, or Egypt.[5]

Another important issue raised by the authors, is the dramatic gap of thromboprophylaxis for stroke prevention delivered in the different regions of the world.[3] As reported by Joseph *et al.*,[3] the vast majority of patients in HICs (in Europe or North America) at high risk for stroke received thromboprophylaxis, compared to only 24% of LICs or MICs. Such regional differences in use of oral anticoagulants (OACs) for stroke prevention are evident from several prior studies. As highlighted by the Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation (GLORIA-AF) registry, OAC prescription ranged from nearly 90% in Europe to only 55% in Asia.[6] Altogether, the data reported by Joseph *et al.*[3] and other studies as GLORIA-AF,[6] underline the suboptimal OAC treatment for stroke prevention in LICs. Interventions to improve uptake of OAC are needed.[7]

This is a highly relevant ethical issue that should needs to be addressed. The high burden of death and stroke in AF population in HICs, has been ameliorated by the widespread use of OACs and by adherence to guidelines and the integrated care management of AF.[8] A similar integrated care management strategy should be encouraged in LICs and MICs but implementation of such an approach poses challenges. In a cluster randomized trial (the mAFA-II trial), a mobile health technology approach based on an AF App was associated with improved long-term clinical outcomes, compared to usual care.[9]

In conclusion, the relevance of the study by Joseph *et al.*[3] is two-fold. First, less than 20% of regional variances of AF prevalence was explained by traditional cardiovascular risk factors and this should warrant the search of novel determinants and characterization of this common arrhythmia.[10] Second, there is an urgent medical need to improve AF care and reduced inequalities in management globally. A joint integrated effort of clinicians and healthcare providers is required to reduce the global burden of AF and its associated adverse outcomes.

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