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A Rising Tide: The Global Epidemic of Atrial Fibrillation

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In his seminal lecture to the Massachusetts Medical Society in 1997, Dr. Eugene Braunwald pointed to atrial fibrillation (AF) as an emerging epidemic of cardiovascular disease.¹ At that time, information on the burden—prevalence, incidence, and associated outcomes—of AF in the general population was limited to a few epidemiologic studies, most of them conducted in the United States and Western Europe. Since then, dozens of publications have contributed to provide a clearer picture of the real impact of AF. These publications confirmed Dr. Braunwald's prediction, demonstrating that AF is the most common sustained arrhythmia in clinical practice and a major public health concern. In the last couple of years, two systematic reviews of the literature on global epidemiology of AF have provided concrete evidence of our increasing knowledge in this area.^{2, 3} Both reviews highlighted the growing prevalence and incidence of this arrhythmia globally, but also called attention to the limited information on AF epidemiology in developing countries. One of the reviews, for example, only identified six publications reporting the incidence of AF outside North American and Western Europe.²

In this issue of *Circulation*, Chugh and colleagues aim to provide a more comprehensive assessment of the burden of AF worldwide.⁴ In the context of the Global Burden of Disease 2010 Study, an international collaborative effort to systematically assess global data on all diseases and injuries, the authors reviewed the literature on the epidemiology of AF published between 1980 and 2010 to determine the incidence and prevalence of AF, as well as the AF associated disease burden. Using evidence from 184 different publications, they concluded that in 2010 approximately 33.5 million individuals have AF worldwide, with close to 5 million new cases occurring each year; that both the prevalence and incidence of the disease have increased meaningfully over the last 2 decades; and that, as a consequence, the life years lost to AF also have increased, with a striking doubling of the AF-associated mortality in the study period. Additionally, this study confirms previous observations, including the direct association between older age and AF burden, and the higher incidence and prevalence of AF in men than in women.⁵ Of note, the authors observed marked between-region variability in prevalence and incidence of AF, with the lowest burden in the Asia Pacific region, and the highest in North America.

The major strengths of the manuscript by Chugh and colleagues, compared with previous efforts to review the global epidemiology of AF, are the strict methodological approach and

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the use of the Global Burden of Disease framework. This approach standardizes the pooling of evidence from different studies, makes explicit assumptions about the modeling process, and, importantly, facilitates comparing the burden attributable to AF across regions and with that of other diseases. Nonetheless, some caveats need to be mentioned. First, although the systematic review included more than 180 original publications, fewer than 30% of them were from studies outside of North America and Western Europe. This indicates that data for most developing regions are quite sparse and probably based on single studies. Second, the burden associated with AF expressed as disability adjusted life-years (DALYs) requires assumptions about the weight assigned to AF sequelae. In this case, the authors assigned a weight of 0.031 (with 0 corresponding to total health, and 1 to total disability), which may seem low for a condition associated with considerable symptomatology in many patients, a 20% mortality in the first year after diagnosis,⁶ and a substantial increase in the risk of stroke, heart failure, and dementia.⁷ Highlighting this point, a recent analysis from the Framingham Heart Study reported that incident AF was associated with development of significant physical disability, even after accounting for the higher prevalence of cardiovascular disease in AF patients.⁸ Using a range of plausible disability weights for DALY estimates might have provided a more realistic assessment of the true burden of AF.

An important finding in this Global Burden of Disease assessment is the notable heterogeneity in prevalence and incidence estimates across regions. North America had the highest burden of AF, while the Asia Pacific region, particularly Japan, the Koreas and China, had the lowest. The factors underlying these differences are not known precisely, but several explanations can be offered. First, higher detection rates of AF in North America than in other regions, even if true rates were similar, would lead to this observation. Second, diversity in the prevalence of risk factors for AF, such as obesity or hypertension, could be responsible for between-region variability. Finally, differences in the underlying risk due to genetic factors might justify this regional heterogeneity. Several previous studies, predominately in the United States, reported lower risk of AF in non-whites compared to whites,^{9, 10} which could translate to higher risk of AF in North America than in East Asia or Sub-Saharan Africa. This hypothesis, however, does not explain the lower prevalence of AF in Europe compared to North America observed by Chugh and colleagues.

What to expect in the future?

In addition to providing a state-of-the-art summary of the current global AF burden, the article by Chugh and colleagues implies that this burden will continue to increase. The aging of the population, the improved survival of individuals with coronary artery disease and heart failure, major risk factors for the arrhythmia, and the growing ability to identify AF are factors that have contributed to the upward trend in AF burden over the last decades and will continue to do so, particularly in developing regions. Furthermore the obesity epidemic in the United States and other countries may contribute to further rises in the incidence of AF.

These trends would be less worrisome if we had established interventions for primary prevention of AF. Unfortunately, we lack strong evidence supporting any specific intervention for this purpose, beyond appropriate control of cardiovascular risk factors. More research aimed to develop and test strategies for the primary prevention of AF is desperately needed.

Where do we go next?

The work by Chugh and colleagues underscores existing gaps in our knowledge on the global epidemiology of AF and, therefore, provides a blueprint for action. First, more research on the prevalence and incidence of AF in developing countries, using standardized methods, is necessary in order to have a more complete and accurate picture of the AF

burden. Second, studies of the effect of AF on mortality, stroke, and other complications need to be conducted, mostly in developing regions, to understand the impact of the arrhythmia and the associated treatment needs. Third, we need a better understanding of the disability associated with AF, so calculations of AF-related DALYs reflect the true burden of the condition. Finally, as mentioned above, development of primary prevention interventions and strategies is a must if we want to reduce the global burden of AF in both developed and developing countries.

In conclusion, Chugh and colleagues confirm, on a global scale, Dr. Braunwald's prophetic words almost 20 years ago and serve as a call to action for investigators, clinicians, and policymakers interested in reducing the population burden of cardiovascular disease.

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