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Editorial Comment
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Reappraisal of the Worldwide Prevalence of Brugada Syndrome and Brugada Phenotype: From the Old to the New Diagnostic Criteria

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Given the risk of life-threatening ventricular tachyarrhythmias and sudden cardiac death (SCD) of Brugada syndrome (BrS), there are growing literature and investigations exploring the epidemiology and mechanism of the associated phenotype, clinical managements, and the outcome through long-term follow-up.[1] Previously, identification of the specific Brugada electrocardiographic (ECG) characteristics, including coved type (type 1) or saddleback (type 2 and type 3) within the leads overlying the right ventricular outflow tract spontaneously and/or enhanced by fever or sodium channel blockers, leads to the diagnosis of BrS.[2] Emerging the possibility of over-diagnosis, a Shanghai BrS scoring system has been proposed to refine BrS according to different weighted coefficients based on expert opinions.[3] Of the Shanghai scoring system, the updated diagnostic criteria exclude patients presenting with type 2 and type 3 BrS ECG without the presence of type 1 BrS morphology documented clinically or after drug provocative test. Moreover, different weighted scores will be given to the individuals with type 1 BrS ECG spontaneously, by fever, or by class I antiarrhythmic drugs.[3,4] With consideration of the above changes, the accurate worldwide prevalence of BrS requires a delicate systematic review and reappraisal.

In this issue of *Acta Cardiologica Sinica*, the authors et al.[5] sought to re-assess the worldwide prevalence of BrS under the hurdles from non-uniform literature, heterogenous situations causing BrS, different study populations and methodologies, and unequal publication from each region. A total of 28 cohort or cross-sectional observational studies were included. In order to fulfill the diagnostic criteria of Shanghai scoring system, only patients with spontaneous type 1 BrS ECG and 7 patients with type 2/3 Brugada ECG phenotype confirmed as BrS were included to evaluate the worldwide prevalence. There were 218 patients confirmed to be BrS, which was translated into a pooled worldwide prevalence of 0.5 per 1000. It makes sense that the above prevalence of BrS was much lower than the mean prevalence of the Brugada ECG pattern from the previous report (0.4%).[6] The highest pooled prevalence of BrS was up to 6.8 per 1000 in Thailand, which was 14 times higher than the worldwide prevalence. Among the different regions, the highest prevalence was found in Southeast Asia (3.7 per 1000), followed by the Middle East, South Asia, East Asia, Europe, and North America. Notably, the distribution pattern of BrS between different regions was comparable to that of the BrS ECG pattern as the previous report.[6] Provided the highest regional prevalence of BrS in Asia, it is not surprising that BrS is more common in Asian (1.8 per 1000), followed by Caucasian and Hispanic subjects with high heterogeneity between different ethnicities. Furthermore, the worldwide prevalence of type 2/3 Brugada ECG phenotype was 6.1 per 1000. Similar to the distribution pattern of BrS, the highest prevalence of type 2/3 Brugada ECG was found in Thailand (60.1 per 1000), whilst Asian population (8.3 per 1000) had a higher prevalence between different ethnicities, especially for Southeast Asian (35.5 per 1000).

In general, emerging the new proposed Shanghai scoring system, this fascinating systematic review demonstrated a comparable heterogeneity of the worldwide prevalence of BrS and type 2/3 Brugada ECG phenotype between different regions and ethnicities. Several ques-

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tions remain unsolved from the above. First of all, lots of the selected articles did not well address the prevalence of BrS for those with initial manifestations of type 2/3 Brugada ECG phenotype, which can therefore result in the underestimation of the worldwide prevalence. Second, despite that the authors aimed to standardize the study population, it is still unknown whether the prevalence will vary between heterogeneous populations, such as patients with palpitation, the hospital-based group, the pre-operation group, athletes, the military group, and the emergency room-based group. The presence of BrS in a specific population may not accurately reflect the worldwide prevalence.[7,8] The above is also evidenced by the fact that type 1 Brugada phenotype could be documented in 2% of consecutive patients presenting with fever in Israeli Emergency Department, while 4% of healthy individuals with atrioventricular nodal reentrant tachycardias would develop type 1 Brugada phenotype after ajmaline provocative test in Turkey.[9,10] Hence, confounding effects on the worldwide prevalence of BrS owing to certain selected subjects are hard to evaluate. It also re-emphasizes the importance on recognizing other clinical manifestations, such as the history of unexplained SCD or documented ventricular tachyarrhythmias, the underlying family history from the first- or second-degree relative and the presence of susceptible genes responsible for the pathogenesis of BrS.[3] In addition, seeking arrhythmia-related syncope or syncope with/without identifiable etiology (such as hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, pulmonary embolism, or ischemic heart disease) by imaging is essential before BrS is ascertained.[11-13] As the recommendation by current guidelines, acquisition of the above information could prevent the over-diagnosis of BrS, especially for patients with the manifestation of ECG phenotype only.

Last but not least, the previous meta-analytic review demonstrated that the presence of Brugada ECG phenotype may not be well correlated to all-cause death and cardiac death.[6] Whether the differences with regard to the incidence of ventricular tachyarrhythmias and long-term prognosis between different geographic regions, ethnicities, and specific population in BrS display in a various distribution is still uncertain. In spite of the low incidence of event rate in those with Brugada phenotype without fulfilling the diagnosis of BrS, what is the best clinical strategy and the appropriate risk stratification to prevent future occurrence of fatal arrhythmias? Before we come to the next step, a robust global registration with long-term follow up of subjects with Brugada phenotype and BrS is certainly required.

CONFLICT OF INTEREST

None to declare.

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