

ASIAN CARDIOVASCULAR LANDSCAPE

Inter-Ethnic Differences in Cardiovascular Disease

Impact on Therapies and Outcomes



Rebecca T. Hahn, MD,^a Elaine Y. Wan, MD,^b Martin B. Leon, MD^a

The prevalence of cardiovascular disease varies among countries and reflect multifactorial differences such as genetic predisposition, diet, and social activity. The Asian population accounts for 60% of the global burden in cardiovascular disease, and there has been growing evidence that there are specific differences in coronary artery disease (CAD), statin usage, thrombosis, and risk of heart failure factors in this population. Contemporary cardiovascular trials have shown that East Asian populations have a higher risk for statin-induced myopathy and bleeding, specifically gastrointestinal bleeding and hemorrhagic stroke. Despite these observations, most guidelines for cardiovascular disease are based on American or European guidelines. This paper reviews the areas of opportunity for future research in Asian cardiovascular health and further understanding of inter-ethnic variabilities.

INTERETHNIC DIFFERENCES IN CAD

The UNICORN (UNited CORoNary) cohort study found distinct inter-ethnic differences in cardiovascular risk factors by enrolled parallel populations of consecutive patients undergoing coronary angiography or intervention for suspected CAD in the Netherlands and Singapore (1). Gijsberts et al. (1) found Chinese and Malay were independently associated with more severe CAD than white ethnicity. Furthermore, when divided for diabetes status, CAD was more severe in all Chinese, Indian, and Malay ethnic groups than in white ethnicity. A national population-based study of

Koreans confirmed the high prevalence and incidence of atherosclerotic cardiovascular disease (ASCVD) and its risk factors in the adult population of South Korea, highlighting the need for more intensive treatment and prevention (2). Despite the increased need for prevention, another study reported a high rate of permanent discontinuation of statin therapy, possibly related to statin intolerance in South Korean patients with ASCVD (3).

DIFFERENCES IN VALVULAR HEART DISEASE

Valvular heart disease offers another example of inter-ethnic differences in cardiovascular disease. Current societal guidelines emphasize the inconsistencies of aortic valve area calculations and mean gradients in patients with small body size. Chew et al. (4) showed that the current guidelines indeed overestimate the severity of aortic stenosis in the Asian cohort and suggest that an aortic valve area cutoff of 0.8 cm² in this population would improve the concordance of measurements for patients with small left ventricular outflow tracts (4). The OCEAN-TAVI (Optimized CathETER vAlvular iNtervention-Transcatheter Aortic Valve Intervention) registry studied Japanese patients with severe aortic stenosis, small annulus and small body surface area (5). This study found comparable high device success for the self-expanding and balloon-expandable valves, superior echocardiographically-derived hemodynamic performance for the self-expanding valve but no differences in 1-year all-cause mortality. Bicuspid aortic

From the ^aNew York-Presbyterian/Columbia University Irving Medical Center, and Cardiovascular Research Foundation, New York, New York, USA; and the ^bDivision of Cardiology, Section of Cardiac Electrophysiology, Department of Medicine, Vagelos College of Physicians and Surgeons, Columbia University, New York, New York, USA.

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**ABBREVIATIONS
AND ACRONYMS****AF** = atrial fibrillation**ASCVD** = atherosclerotic cardiovascular disease**CAD** = coronary artery disease**HF** = heart failure**HFpEF** = heart failure preserved ejection fraction**HFrEF** = heart failure reduced ejection fraction**TAVR** = transcatheter aortic valve replacement

valve morphology also appears to differ in the Asian population. Although the prevalence of the disease may be similar to that of Western populations (0.43%), associated valve abnormalities (aortic valve stenosis or aortic valve regurgitation) as well as complications (infective endocarditis and aortic dissection) were more common (6). Kong et al. (7) showed that Asians had a higher prevalence of type 1 bicuspid aortic valve with raphe between right and noncoronary cusps than Europeans (19.7% vs. 13.6%, respectively; $p < 0.001$), whereas Europeans

had a higher prevalence of type 0 bicuspid aortic valve (2 commissures, no raphe) than Asians (14.5% vs. 6.8%, respectively; $p < 0.001$) with significantly larger aorta dimensions (7). Computed tomography core laboratory assessment of patients presenting for transcatheter aortic valve replacement in China showed a high frequency of congenital aortic valve morphologies (47.5% bicuspid and 1.7% unicuspid) (8) and distinct regional variability.

**DIFFERENCES IN ARRHYTHMIA PREVALENCE
AND ANTITHROMBOTIC THERAPY**

As the Asian population grows and the number of aging Asian patients increases, the risk of cardiac arrhythmias continues to rise. Despite a higher incidence of hypertension, stroke, peripheral vascular disease, renal disease or increased alcohol intake, there is a lower prevalence of atrial fibrillation (AF) among Singaporean-Asians than among New Zealand-European patients with heart failure (HF) even after adjusting for age, clinical echocardiographic findings, and body mass index (9). Inter-ethnic differences, however, have been demonstrated in the ASIAN-HF (Asian Sudden Cardiac Death in HF) study. Author: in the sentence..." the terms connected with a slash, "Japanese/Koreans" are not clear; if you are referring to "Japanese and Koreans" please revise throughout for clarity. Although the clinical correlates of AF were similar across Asian ethnicities in 11 different regions (Hong Kong, Taiwan, China, Japan, Korea, India, Malaysia, Thailand, Singapore, Indonesia, and Philippines), Japanese/Koreans had higher odds of AF in HF with reduced ejection fraction (HF_rEF) than Chinese, whereas Indians had lower odds of AF in HF_rEF and HF preserved ejection fraction (HF_pEF) (10). Interaction between ethnicity and region was also seen in the Indian population, where Southeast Asian Indians had higher odds of AF than South Asian Indians. However, in all cases, AF was associated with poor quality of life and increased risk of mortality.

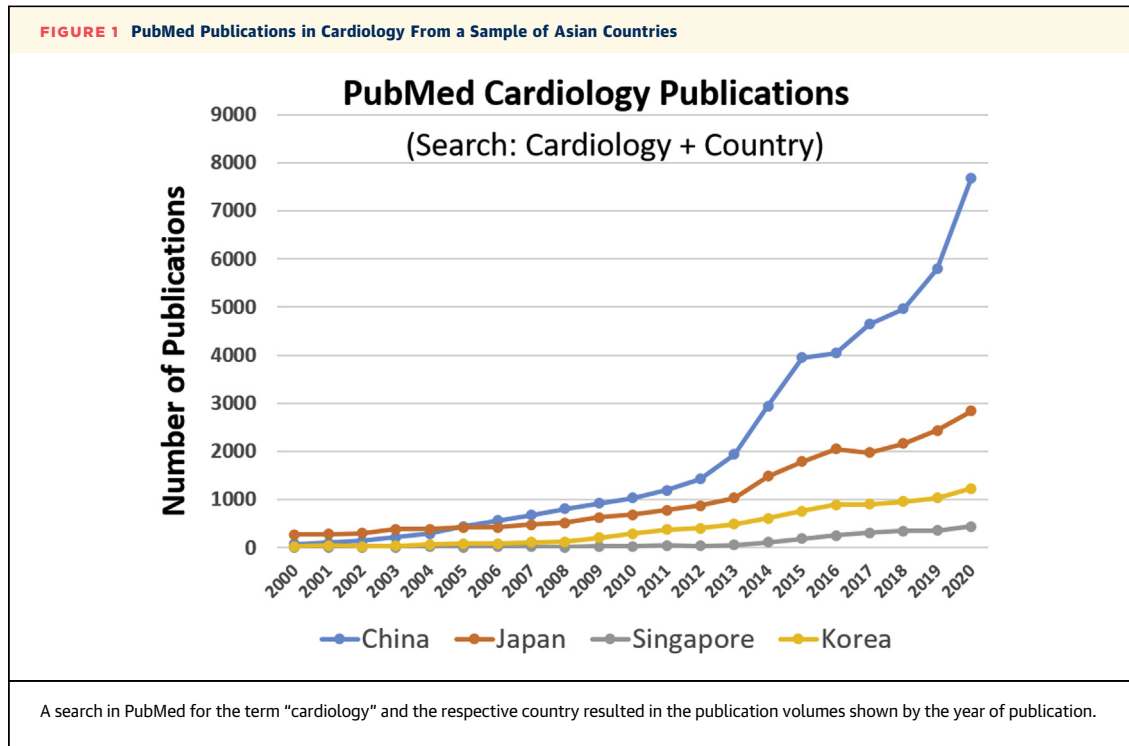
No doubt, the greatest cardiovascular morbidity associated with cardiac arrhythmias such as AF is stroke. Despite the clear benefit of oral anticoagulation, the concerns for bleeding remain, especially among the Asian population because of the risk of intracranial hemorrhage in comparison with non-Asians, especially with the usage of warfarin (11). Novel oral anticoagulants, however, seem to have a greater relative risk reduction of intracranial hemorrhage, even in those with a history of nonvalvular AF and intracranial hemorrhage, and require further study in the Asian population.

**THE "OBESITY PARADOX" IN ASIANS
WITH HEART FAILURE**

The ASIAN-HF registry studied both inpatient and outpatient populations and divided patients into 5 multimorbidity groups: elderly with more AF, metabolic, ischemic, lean diabetic, and young (12). They found that patients who were in the lean diabetic group had the worse quality of life, more severe signs and symptoms of HF, and a high rate of the all-cause mortality or HF hospitalization within 1 year. This "obesity paradox" has been well described in Western populations but may be better characterized as a "lean paradox" in which individuals who have normal weight or are underweight may have a poorer prognosis with respect to cardiovascular disease, as a result of a progressive catabolic state and lean mass loss (13). An additional cohort analysis of the ASIAN-HF study takes this concept one step farther, showing that individuals with a combination of low body mass index and high weight-to-height ratio (a "lean-fat" group) were more likely to be women (35.4%) and to be from low-income countries (47.7%) (predominantly in South and Southeast Asia) and had higher prevalence of diabetes (46%), worse quality of life scores (63.3 ± 24.2), and a higher rate of composite outcome (51 of 232; 22%), compared to the other groups ($p < 0.05$ for all) (14). They concluded that, in Asians, looking only at body mass index was not sufficient given the direct correlation of increased weight-to-height ratio and worsened outcomes in patients with HF_rEF and HF_pEF. Other studies have suggested that Southeast Asians may have the worse outcomes due to differences in health care infrastructure, as well as genetic, cultural, and environmental factors (15).

**FUTURE OF RESEARCH PUBLICATIONS ON
CARDIOVASCULAR DISEASE RISK AND
OUTCOMES IN ASIAN POPULATIONS**

When one searches PubMed for cardiology publications from various Asian countries (Figure 1), there is



a growing body of studies highlighting risk of cardiovascular disease and outcomes in Asian populations. To address the many differences in inter-ethnic prevalence of cardiovascular disease and to harness the growing Asian interest in clinical research, the editors of the *JACC* thought to initiate this open access journal which encourages Asian-focused research topics to facilitate the understanding, prevention, diagnosis, and treatment of cardiovascular diseases among Asian populations. This issue of *JACC: Asia* focuses on clinical research which includes randomized clinical trials, cohort studies, and registries studying Asian population-focused cardiovascular problems, cross-disciplinary studies where Asia holds a competitive edge, and comparative studies between Asia and the rest of the world. In addition, this issue of *JACC: Asia* will specifically feature studies dealing with cutting-edge technology to encompass newly developed clinical devices and techniques, as well as translational medicine and management guidelines relevant to Asian

populations. Most importantly, this new journal will promote a greater understanding of cardiovascular disease in Asian populations which may change management and outcomes.

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Dr. Hahn is a speaker and consultant for Edwards Lifesciences, Abbott Vascular, Gore & Associates, and Philips Healthcare; and she holds equity for Navigate; and is the Chief Scientific Officer for the Echocardiography Core Laboratory at the Cardiovascular Research Foundation for multiple industry-sponsored trials, for which she has received no direct industry compensation. Dr. Leon has received institutional clinical research grants to Columbia University from Abbott, Boston Scientific, Edwards Lifesciences, and Medtronic. Dr. Wan has reported that he has no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr. Rebecca T. Hahn, Columbia University Medical Center, New York-Presbyterian Hospital, 177 Fort Washington Avenue, New York, New York 10032, USA. E-mail: rth2@columbia.edu. Twitter: [@hahn_rt](https://twitter.com/hahn_rt).

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