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GLOBAL DISTRIBUTION OF AORTIC VALVE STENOSIS ACCORDING TO ETHNIC POPULATIONS: EPIDEMIOLOGY, GENETIC SUSCEPTIBILITY, AND CLINICAL IMPLICATIONS

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ABSTRACT:
Aortic valve stenosis (AS) represents the most frequent valvular heart disease requiring surgical or transcatheter intervention in developed countries and constitutes an increasing global health burden due to population aging and improved life expectancy. Although the prevalence of aortic stenosis has traditionally been associated with elderly Caucasian populations, accumulating evidence suggests significant ethnic variations in disease prevalence, age at presentation, pathological mechanisms, and clinical outcomes. These differences appear to result from complex interactions between genetic background, environmental exposure, socioeconomic factors, access to healthcare, and distribution of cardiovascular risk factors.
Caucasian populations, particularly those of European ancestry, demonstrate the highest reported prevalence of calcific aortic valve stenosis, partly related to increased longevity, higher frequency of bicuspid aortic valve disease, and genetic susceptibility involving pathways associated with lipid metabolism, inflammation, and valve calcification. In contrast, African populations appear to have lower rates of calcific aortic stenosis despite a higher prevalence of hypertension and other cardiovascular risk factors. Asian populations historically showed lower rates of severe aortic stenosis; however, rapid demographic aging and westernization of lifestyle have resulted in a substantial increase in disease burden. Hispanic and South Asian populations represent heterogeneous groups in which metabolic factors, healthcare disparities, and genetic admixture influence disease expression.
Understanding ethnic differences in aortic stenosis epidemiology is increasingly important for cardiovascular prevention, early diagnosis, surgical planning, and allocation of healthcare resources. This review summarizes current knowledge regarding global ethnic variations in aortic valve stenosis, emphasizing epidemiological patterns, genetic determinants, and implications for contemporary cardiac practice.

KEYWORDS: Aortic stenosis; ethnic differences; calcific aortic valve disease; epidemiology; genetics; bicuspid aortic valve; cardiovascular disparities.

1. INTRODUCTION

Aortic valve stenosis (AS) is a progressive disease characterized by thickening, fibrosis, and calcification of the aortic valve leaflets, leading to obstruction of left ventricular outflow and increased cardiovascular morbidity and mortality. It represents the most common valvular disorder in industrialized countries and is currently the leading indication for surgical aortic valve replacement (SAVR) and transcatheter aortic valve implantation (TAVI) worldwide (1).
The epidemiology of AS has changed considerably during the last century. Historically, rheumatic fever was the dominant cause of valvular disease globally; however, in high-income countries, degenerative calcific aortic stenosis has become the predominant phenotype because of increased life expectancy and reduced incidence of rheumatic heart disease (2). As populations continue to age, the prevalence of AS is expected to increase substantially, creating significant challenges for healthcare systems.
Although aging represents the strongest risk factor for calcific aortic valve disease, epidemiological studies demonstrate important differences among ethnic populations. These variations are observed not only in disease prevalence but also in age at diagnosis, severity of calcification, associated cardiovascular risk factors, genetic susceptibility, and outcomes after intervention (3).
Ethnicity represents a complex biological and social construct that includes genetic ancestry, environmental exposure, lifestyle characteristics, socioeconomic conditions, and access to healthcare. Therefore, differences in AS distribution among populations cannot be explained exclusively by genetic factors. Instead, they reflect the interaction between inherited susceptibility and external determinants throughout life (4).

Large population studies such as the Multi-Ethnic Study of Atherosclerosis (MESA) and the Atherosclerosis Risk in Communities (ARIC) study have provided important insights into racial and ethnic differences in aortic valve calcification, an early marker of future clinically significant AS. These investigations demonstrated that the burden and progression of valve calcification differ substantially among ethnic groups, suggesting underlying biological variability in disease development (5).

2. WORLDWIDE EPIDEMIOLOGY OF AORTIC VALVE STENOSIS

The global prevalence of AS is strongly age dependent. Mild aortic valve sclerosis is frequently detected in individuals older than 65 years, whereas clinically significant stenosis affects approximately 2–3% of adults over 65 years and more than 10% of individuals older than 80 years in Western populations (1,6).

The Global Burden of Disease (GBD) studies have demonstrated a continuous increase in AS-related morbidity and mortality during recent decades, primarily driven by population aging. Worldwide, deaths attributable to AS have increased despite advances in surgical and transcatheter treatment, reflecting the growing number of elderly individuals affected by the disease (7).

The epidemiological profile differs substantially between regions:

- **North America and Western Europe:** predominantly degenerative calcific AS associated with advanced age.
- **Low- and middle-income countries:** persistent contribution of rheumatic valve disease.
- **East Asia:** rapidly increasing prevalence due to demographic aging.
- **Sub-Saharan Africa:** lower documented rates of degenerative AS but significant underdiagnosis due to limited access to echocardiography and cardiac surgery.

In Europe, severe AS represents a major healthcare challenge, with thousands of valve replacements performed annually. The expansion of TAVI programs has further increased recognition of AS among elderly and high-risk patients (8).

3. ETHNIC DISTRIBUTION OF AORTIC VALVE STENOSIS

3.1 Caucasian Populations

Individuals of European ancestry demonstrate the highest reported prevalence of calcific aortic stenosis in population-based studies. This observation is partly explained by greater life expectancy, allowing more time for progressive leaflet calcification, but biological differences also appear to contribute.

Studies evaluating aortic valve calcium burden have consistently shown higher levels among White populations compared with other ethnic groups after adjustment for traditional cardiovascular risk factors (5,9). The reasons are multi-factorial and include differences in:

- genetic susceptibility,
- lipoprotein metabolism,
- inflammatory response,
- extracellular matrix remodeling,
- prevalence of bicuspid aortic valve.

A major genetic contributor is elevated lipoprotein(a) [L p (a)], which has a strong hereditary component and is associated with increased risk of calcific aortic valve disease. Variants within the LPA gene influence circulating Lp(a) concentration and appear to contribute significantly to ethnic differences in AS susceptibility (10).

Caucasian populations also demonstrate a relatively high prevalence of bicuspid aortic valve (BAV), occurring in approximately 1–2% of individuals. BAV is associated with accelerated valve degeneration and earlier development of clinically significant stenosis compared with tricuspid valves (11).

In European and North American populations, calcific AS commonly presents between 65 and 85 years of age, although patients with BAV frequently require intervention earlier, often between 50 and 70 years.

3.2 African and African-American Populations

African and African-American populations demonstrate a lower prevalence of calcific aortic stenosis compared with Caucasian populations despite a higher prevalence of several cardiovascular risk factors, including hypertension, obesity, diabetes mellitus, and chronic kidney disease (5).

Data from MESA demonstrated that African-American participants had significantly lower levels of aortic valve calcification compared with White participants after adjustment for age and cardiovascular risk factors (5). This finding suggests that mechanisms beyond traditional risk factors influence valve mineralization.

Several hypotheses have been proposed:

1. Genetic protection against calcification

Differences in genetic variants regulating mineral metabolism, inflammation, and lipid pathways may contribute to lower susceptibility.

2. Differences in Lp(a) distribution

Although Lp(a) levels vary considerably among individuals, population studies suggest differences in allele frequency and isoform distribution among ethnic groups.

3. Patterns of vascular and valvular remodeling

Biological differences in extracellular matrix regulation and inflammatory activation may influence progression from sclerosis to stenosis.

However, African populations face important healthcare challenges, including limited access to echocardiographic screening, cardiac surgery, and transcatheter therapies. Consequently, available epidemiological data may underestimate the true burden of AS.

3.3 Asian Populations

Historically, Asian populations have demonstrated a lower prevalence of degenerative calcific aortic stenosis compared with Western populations. However, this situation is rapidly changing because of increasing life expectancy, urbanization, dietary changes, and the epidemiological transition from infectious diseases toward chronic cardiovascular disorders. Countries such as Japan, South Korea, and China are experiencing a substantial increase in the number of elderly individuals, resulting in a growing burden of calcific aortic valve disease (12).

Japan provides an important example of this demographic transition. Historically, rheumatic valve disease represented an important cause of valvular pathology; however, contemporary studies demonstrate that degenerative calcific aortic stenosis is now the dominant form among elderly Japanese patients (12). The prevalence of severe AS increases markedly after 75 years of age, paralleling trends observed in Western countries.

Several population-based studies have suggested that Asian individuals may have a lower degree of aortic valve calcification compared with Caucasian populations at similar ages. In the Multi-Ethnic Study of Atherosclerosis (MESA), Asian participants demonstrated lower prevalence and severity of aortic valve calcium compared with White participants after adjustment for conventional cardiovascular risk factors (5). These observations suggest that ethnic differences in valve mineralization may involve biological mechanisms beyond aging and cardiovascular risk factors.

Genetic factors may contribute to these differences. Variations in genes regulating lipid metabolism, inflammatory pathways, and extracellular matrix remodeling appear to influence susceptibility to calcific aortic valve disease. For example, the frequency and impact of LPA gene variants, which strongly influence lipoprotein(a) concentrations, differ among ethnic groups and may partially explain variation in AS risk worldwide (10).

However, important differences exist within Asian populations. Japanese patients often demonstrate lower body mass index and lower rates of obesity compared with Western cohorts, whereas rapidly developing Asian economies are experiencing increasing prevalence of obesity, diabetes mellitus, and metabolic syndrome. These changes may accelerate the future burden of calcific AS.

Another important aspect is the clinical phenotype of AS in Asian populations. Several studies have reported that Asian patients undergoing aortic valve replacement are frequently older and have a higher prevalence of small aortic annulus anatomy compared with Western populations. This anatomical characteristic has implications for prosthesis selection, risk of patient–prosthesis mismatch, and surgical planning (13).

The development of transcatheter aortic valve implantation (TAVI) has significantly improved treatment access for elderly Asian patients, particularly those considered high surgical risk. Nevertheless, differences in body size, coronary anatomy, and annular dimensions require careful adaptation of device selection and procedural strategies.

3.4 South Asian Populations

South Asian populations, including individuals originating from India, Pakistan, Bangladesh, Sri Lanka, and Nepal, represent one of the fastest-growing cardiovascular disease populations worldwide. Although epidemiological data specifically addressing aortic stenosis remain limited, several factors suggest a potentially increasing future burden of AS in these populations.

South Asians exhibit a high prevalence of premature coronary artery disease, diabetes mellitus, insulin resistance, and metabolic syndrome. These metabolic abnormalities are associated with chronic inflammation, endothelial dysfunction, and accelerated atherosclerotic processes, which may contribute to the initiation and progression of calcific aortic valve disease (14).

Unlike coronary artery disease, where South Asians have clearly demonstrated increased susceptibility, the relationship between South Asian ethnicity and AS remains incompletely defined. Current evidence suggests that lower reported prevalence may reflect demographic differences, younger population structure, limited access to diagnostic echocardiography, and under-recognition of valvular disease rather than true biological protection.

Genetic studies have demonstrated substantial diversity among South Asian populations. Differences in lipid-related genes, inflammatory pathways, and calcium metabolism genes may influence susceptibility to valve calcification. However, large-scale genomic studies focusing specifically on AS in South Asians remain insufficient.

Healthcare disparities represent a major determinant of outcomes. Many patients in South Asia present with advanced symptomatic valve disease because of delayed diagnosis and limited access to specialized cardiac services. Consequently, surgical mortality may be influenced more by late presentation and comorbidity burden than by ethnicity itself.

Expansion of echocardiographic screening programs and improved access to valve intervention are essential to accurately define and address the future burden of AS in South Asian populations.

3.5 Hispanic and Latino Populations

Hispanic and Latino populations represent one of the most rapidly expanding ethnic groups in North America and include individuals with diverse genetic backgrounds originating from Europe, Africa, and Indigenous American populations.

Epidemiological studies suggest that Hispanic individuals generally have a lower prevalence of calcific aortic valve disease compared with non-Hispanic White populations; however, the available evidence remains limited and heterogeneous (5).

Several explanations have been proposed:

● younger average population age;
● different genetic ancestry;
● dietary and lifestyle factors;
● variable access to cardiovascular healthcare;
● differences in cardiovascular risk factor distribution.

Interestingly, Hispanic populations have high prevalence rates of obesity, diabetes mellitus, and hypertension, factors traditionally associated with cardiovascular calcification. However, these risk factors do not appear to translate proportionally into higher rates of AS, suggesting that genetic background and biological mechanisms may modify disease expression.

The Hispanic population is genetically heterogeneous, and admixture between European, African, and Native American ancestry creates substantial variation in susceptibility genes. Future genomic studies are required to determine whether specific ancestry-related variants influence calcific valve disease progression.

From a clinical perspective, disparities in diagnosis and treatment remain important concerns. Hispanic patients may experience delayed referral for valve intervention and lower utilization rates of advanced cardiovascular procedures, including TAVI. Improving access to echocardiographic evaluation and specialized valve centers represents a major public health priority.

4. Genetic and Biological Mechanisms Explaining Ethnic Differences in Aortic Stenosis

Ethnic differences in AS prevalence are likely the consequence of complex interactions between genetic susceptibility, environmental factors, and healthcare systems. Unlike monogenic disorders such as Marfan syndrome, calcific aortic stenosis represents a polygenic disease influenced by multiple biological pathways.

4.1 Lipoprotein(a) and Lipid Metabolism

Among genetic determinants, lipoprotein(a) [Lp(a)] represents one of the strongest established risk factors for calcific AS. Elevated Lp(a) promotes valve calcification through pro-inflammatory and pro-osteogenic mechanisms, including deposition of oxidized phospholipids within valve tissue (10).

The concentration of Lp(a) is predominantly genetically determined by variants in the LPA gene. Significant differences exist among ethnic groups, with some African populations demonstrating higher average Lp(a) levels but paradoxically lower rates of calcific AS. This observation highlights that a single genetic factor cannot fully explain ethnic variation.

4.2 Inflammatory and Calcification Pathways

Calcific AS shares several biological characteristics with atherosclerotic disease, including:
● endothelial injury;
● inflammatory cell infiltration;
● oxidative stress;
● lipid accumulation;
● osteogenic transformation of valvular interstitial cells.

Genetic variation affecting inflammatory mediators, bone morphogenetic proteins, and extracellular matrix remodeling may modify individual susceptibility (15).

The NOTCH1 pathway, initially identified through familial bicuspid valve studies, also participates in calcific degeneration by regulating osteogenic differentiation of valve cells. Reduced NOTCH1 activity promotes expression of bone-related transcription factors such as RUNX2, accelerating mineralization (11).

5. CLINICAL IMPLICATIONS FOR CARDIAC SURGERY AND TRANSCATHETER THERAPY

Understanding ethnic differences in AS distribution has direct implications for cardiac surgical practice. Population-specific characteristics influence:
● age at presentation;
● severity of valve calcification;
● associated pathologies of aorta
● surgical risk;
● prosthesis selection;
● ong-term outcomes.

Patients of European ancestry frequently present with severe calcific AS at advanced age, whereas Asian patients may have additional challenges related to smaller annular dimensions and body size. African and Hispanic populations may experience worse outcomes because of delayed diagnosis and limited access to specialized treatment rather than intrinsic biological differences.

For surgeons, recognition of genetic and ethnic factors is particularly important in patients with:
● bicuspid aortic valve;
● early-onset AS;
● family history of valve disease;
● associated ascending aortic aneurysm.

In these patients, assessment should extend beyond valve replacement to include evaluation of the aortic root and ascending aorta.

6. FUTURE PERSPECTIVES

Future research should focus on large multinational studies integrating:

- genomic sequencing;
- ethnic ancestry analysis;
- advanced imaging biomarkers;
- environmental exposures;
- socioeconomic determinants.

The development of personalized medicine may allow identification of individuals at high risk before severe stenosis develops. Potential therapeutic targets include Lp(a) reduction, anti-inflammatory strategies, and inhibitors of osteogenic signaling pathways.

Increasing diversity in cardiovascular clinical trials is essential because current evidence is predominantly derived from European and North American populations. Better representation of Asian, African, and Hispanic populations will improve global understanding and treatment of aortic stenosis.

CONCLUSION

Aortic valve stenosis demonstrates significant geographical and ethnic variation worldwide. The highest documented prevalence of calcific AS occurs among elderly Caucasian populations, whereas lower rates have historically been reported among African, Asian, and Hispanic populations. However, these differences reflect complex interactions between genetics, demographic structure, environmental exposure, and healthcare accessibility.

As global populations age, the burden of AS will increase across all ethnic groups. Improved epidemiological surveillance, genetic investigation, equitable access to diagnostic tools, and individualized therapeutic strategies will be essential to address this growing cardiovascular challenge.

Table 1. Ethnic Differences in Aortic Valve Stenosis

Population	Epidemiological pattern	Main contributing factors
Caucasian/European	Highest prevalence of calcific AS	Aging, BAV, Lp(a), genetic susceptibility
African/African-American	Lower valve calcium burden	Genetic factors, underdiagnosis, healthcare disparities
East Asian	Increasing rapidly	Aging population, lifestyle transition
South Asian	Limited data, expected increase	Diabetes, metabolic syndrome, healthcare access
Hispanic/Latino	Lower reported prevalence	Younger demographics, genetic admixture, disparities

REFERENCES

1. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary Circulation. 2021;143(5):e35-e71.
2. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al.2021 ESC/EACTS Guidelines for th e management of valvular heart disease. Eur Heart J. 2022;43(7):561-632.
3. Lindman BR, Clavel MA, Mathieu P, Iung B, Lancellotti P, Otto CM. Calcific aortic stenosis. Nat Rev Dis Primers. 2016;2:16006.
4. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. Lancet. 2006;368(9540):1005-1011.
5. Budoff MJ, Nasir K, Katz R, Takasu J, Carr JJ, Wong ND, et al. Ethnic differences in the presence and extent of coronary calcium and thoracic aortic calcification: the Multi-Ethnic Study of Atherosclerosis. Circulation. 2006;113(3):348-355.
6. Owens DS, Budoff MJ, Katz R, Takasu J, Shavelle DM, Carr JJ, et al.Aortic valve calcium independently predicts coronary and cardiovascular events in a multi-ethnic population. J Am Coll Cardiol. 2010;56(20):1674-1683.
7. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al.Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. J Am Coll Cardiol. 2020;76(25):2982-3021.
8. Coffey S, Cox B, Williams MJ.The prevalence, incidence, progression, and risks of aortic valve sclerosis: a systematic review and meta-analysis. J Am Coll Cardiol. 2014;63(25 Pt A):2852-2861.
9. Thanassoulis G, Campbell CY, Owens DS, Smith JG, Smith AV, Peloso GM, et al.Genetic associations with valvular calcification and aortic stenosis. New Engl J Med. 2013;368(6):503-512.
10. Kamstrup PR, Tybjærg-Hansen A, Nordestgaard BG.Elevated lipoprotein(a) and risk of aortic valve stenosis in the general population. J Am Coll Cardiol. 2014;63(5):470-477.
11. Garg V, Muth AN, Ransom JF, Schluterman MK, Barnes R, King IN, et al. Mutations in NOTCH1 cause aortic valve disease. Nature. 2005;437(7056):270-274.
12. Mathieu P, Boulanger MC. Basic mechanisms of calcific aortic valve disease. Can J Cardiol. 2014;30(9):982-993.

13. Otto CM, Prendergast B. Aortic-valve stenosis — from patients at risk to severe valve obstruction. N Engl J Med. 2014;371(8):744-756.
14. Siontis GCM, Overtchouk P, Cahill TJ, Modine T, Prendergast B, Praz F, et al Transcatheter aortic valve implantation vs surgical replacement: a systematic review and meta-analysis. Lancet. 2019;393(10185):119-127.
15. Michelena HI, Della Corte A, Evangelista A, Maleszewski JJ, Enriquez-Sarano M, Bissell MM, et al.International consensus statement on nomenclature and classification of the congenital bicuspid aortic valve and its aortopathy. J Am Coll Cardiol. 2021;77(15):1967-1987.