Prevalence of Mitral Annulus Calcification in African Americans: Comparison with non-Hispanic Whites and Hispanics

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Background: The association of ethnic ancestry with coronary artery calcifications suggests that mitral annulus calcification may also vary with ethnicity. We sought to compare prevalence and clinical correlates of mitral annulus calcification in non-Hispanic Whites, Hispanics, and African Americans.

Design: This was a retrospective study of 857 patients age 40–75 years that included 217 (25%) African Americans, 349 (41%) Hispanics, and 291 (34%) non-Hispanic Whites referred for echocardiography. Multiple logistic regression was used to determine the interrelationships between mitral annulus calcification, risk factors, and ethnicity.

Results: Mitral annulus calcification was detected in 181 (21.1%) patients including 35 (16.1%) African Americans, 80 (22.9%) Hispanics, and 66 (22.7%) non-Hispanic whites. In univariate analysis, patients with mitral annulus calcification were older and more likely to have hypertension, diabetes, dyslipidemia, smoking history, and two or more risk factors than were those without calcification. In multivariate analysis, age and smoking history were independent predictors of mitral annulus calcification; dyslipidemia and diabetes were borderline significant predictors; and after adjusting for the remaining variables in the model, ethnicity was not an independent significant predictor of mitral annulus calcification.

Conclusion: In a retrospective study of middle-aged and elderly African Americans, non-Hispanic Whites, and Hispanics referred for echocardiography, mitral annulus calcification is common in all three major ethnic groups but not significantly associated with ethnic ancestry. (*Ethn Dis.* 2008;18:48–52)

Key Words: Mitral Annulus Calcification, Ethnicity, African Americans, Hispanics, Echocardiography

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Introduction

The association of ethnic ancestry with prevalence of coronary artery and aortic calcifications suggests that mitral annulus calcification (MAC) may also vary with ethnicity.[1–5] We have previously reported in a retrospective study of middle-aged and elderly non-Hispanic Whites and Hispanics referred for echocardiography that Hispanic ancestry is not associated with prevalence of MAC.[6] The current study extends these observations to African Americans by exploring the prevalence of MAC in African Americans from the same database and making comparisons with non-Hispanic Whites and Hispanics after adjustment for a large number of coronary risk factors. In addition, this study evaluates the correlates of MAC in a multiethnic sample.

Methods

Selection of Hispanic and non-Hispanic White subjects has previously been described.[6] From the same database and time frame of our university-affiliated echocardiography laboratory, we identified 293 consecutive self-reported African Americans, aged 40–75 years. Of these, nine whose risk factor status could not be determined

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from the medical record were excluded. An additional 67 were excluded because of inadequate images of the mitral annulus, a history of mitral valve surgery, rheumatic heart disease, hypertrophic cardiomyopathy, connective tissue disorder, prior chest irradiation, chronic use of corticosteroids, hypercalcemia, or renal insufficiency (end-stage renal disease requiring dialysis or creatinine ≥2 mg/dL). The final dataset for the present analyses consisted of 857 patients (217 African Americans, 349 Hispanics, and 291 non-Hispanic Whites).

Risk factor data and status were determined as described previously.[6] Coronary risk factors included age (10-year age groups), sex, dyslipidemia, diabetes mellitus, hypertension, and smoking. Diabetes mellitus was defined as fasting blood sugar >126 mg/dL or the use of glucose-lowering medication. Hypertension was defined as systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg during at least two clinic visits or the use of antihypertensive medication. Dyslipidemia was defined as use of lipid lowering agents or low-density lipoprotein cholesterol >160 mg/dL, high-density lipoprotein cholesterol <35 mg/dL in men or <45 mg/dL in women, or triglycerides >200 mg/dL. Smoking was classified as ever (current or former) or never. The total number of classical risk factors (hypertension, diabetes, dyslipidemia, history of any smoking) was calculated, and those with two or more risk factors were classified as patients with multiple risk factors.

Our method of diagnosing MAC has been previously described.[6] Briefly, the digital images of the 217 African Americans were retrospectively reviewed

Table 1. Distribution of demographics, clinical characteristics, and MAC status by ethnic group

Parameter	Total (*n*=857)	Non-Hispanic Whites (*n*=291)	Hispanics (*n*=349)	African Americans (*n*=217)	P value
Age, years	59.1±9.1	60.4±8.8	60.1±9.1	55.7±8.6	<.001
Females	457 (53.4)	128 (44)	165 (47.2)	164 (75.6)	<.001
Hypertension	515 (60.1)	142 (48.8)	211 (60.5)	162 (74.7)	<.001
Diabetes	223 (26.0)	58 (19.9)	103 (29.5)	62 (28.6)	.014
Dyslipidemia	463 (54)	167 (57.4)	212 (60.7)	84 (38.7)	<.001
Smoking	274 (32.0)	98 (33.7)	121 (34.7)	55 (25.3)	.051
≥2 risk factors	491 (57.3)	162 (55.7)	209 (59.9)	120 (55.3)	.444
MAC	181 (21.1)	66 (22.7)	80 (22.9)	35 (16.1)	.114

Values are given as mean±standard deviation or *n* (%). MAC=mitral annulus calcification.

off-line (Echopac 6, GE Vingmed, Milwaukee, Wisc) by a single investigator (HJW) blinded to clinical and laboratory data to avoid inter-reader variability. The two-dimensional echocardiographic criterion for MAC in this study was the presence of highly reflective echodensities in the region of the mitral valve annulus that were clearly separate from the valve leaflets and myocardium in the apical long axis or two- and four-chamber views or the parasternal long- and short-axis views as described previously.[7] The intraobserver agreement was assessed in 25 echocardiograms and was 100%.

Statistical Analysis

Demographic and clinical characteristics are reported as means ± standard deviations for continuous variables and as proportions for categorical variables. The demographic and clinical characteristics of patients were compared according to ethnicity and MAC status using analysis of variance for continuous variables and chi-square tests for categorical variables. Multivariate logistic regression was used to assess predictors of MAC using standard clinical risk factors and ethnicity as independent variables, with non-Hispanic Whites as the reference category. We calculated odds ratios and the corresponding 95% confidence intervals. All *P* values reported are two-sided. All tests with a corresponding *P* value <.05 were considered statistically significant. All analyses were performed with NCSS for Windows (Kayesville, Utah).

RESULTS

Demographic and clinical characteristics and prevalence of MAC are shown in Table 1 for the total sample and for each ethnic group. Patients referred for echocardiography from all three ethnic groups had a high prevalence of all risk factors and MAC. The proportion of men was lower among African Americans who were also younger and less likely to smoke than were Hispanics and non-Hispanic Whites. African Americans also had more hypertension and less dyslipidemia than did non-Hispanic Whites and Hispanics. African Americans and Hispanics both had more diabetes than did non-Hispanic Whites. The number of subjects with multiple risk factors in each ethnic group was similar. Although MAC was less common in African Americans than in the other two ethnic groups, the differences were not statistically significant.

Table 2 shows the distribution of demographic characteristics and risk factors according to MAC status for the total sample. Patients with MAC were older and more likely to have hypertension, diabetes, dyslipidemia, smoking history, and multiple risk factors than those without. Sex was not significantly related to MAC status.

Multivariate predictors of MAC for the total population are displayed in the Table 3. Age and smoking history were independent predictors of mitral annulus calcification; dyslipidemia and diabetes were borderline significant predictors; and after adjusting for the remaining variables in the model, ethnicity was not an independent significant predictor of MAC.

DISCUSSION

This retrospective study extends to African Americans our previously reported comparison of the prevalence of MAC in middle-aged and elderly non-Hispanic Whites and Hispanics referred for echocardiography. In our sample, MAC was common in all three major

Table 2. Distribution of demographics and clinical characteristics according to MAC status for total sample

Parameter	MAC (*n*=181)	No MAC (*n*=676)	P value
Age, years	64.0±8.1	57.8±8.9	<.001
Females (*n*=458)	87 (48)	371 (55)	.121
Hypertension (*n*=515)	128 (71)	387 (57)	.001
Diabetes (*n*=223)	64 (35)	159 (24)	.002
Dyslipidemia (*n*=463)	122 (67)	341 (50)	<.001
Smoking (*n*=274)	77 (43)	197 (29)	<.001
≥2 risk factors (*n*=491)	133 (74)	358 (53)	<0.001

Values are given as mean±standard deviation or *n* (%). MAC= mitral annulus calcification.

Table 3. Predictors of MAC by multivariable logistic regression

Parameter	OR (95% CI)	P value
Age/10 years	2.14 (1.72–2.67)	<.001
Female gender	1.02 (.71–1.47)	.902
Hypertension	1.31 (.89–1.92)	.172
Diabetes	1.42 (.97–2.09)	.074
Dyslipidemia	1.43 (.99–1.43)	.058
Smoking	1.61 (1.12–2.31)	.009
Non-Hispanic Whites	Referent	
Hispanics	.94 (.63–1.40)	.782
African Americans	.90 (.53–1.50)	.673

MAC=mitral annulus calcification; OR=odds ratio; CI=confidence interval.

ethnic groups. Age and history of smoking were independent predictors of MAC, and MAC may have been associated with dyslipidemia and diabetes in this multiethnic population. Ethnic origin was not an independent significant predictor of MAC.

We have previously reported that Hispanic ancestry is not significantly associated with prevalence of MAC.[6] Although the frequency of MAC was lower in African Americans than in non-Hispanic Whites and Hispanics, no ethnic differences in the prevalence of MAC persisted after adjustment for standard coronary risk factors. Thus our data are consistent with the possibility that African American ancestry also is not associated with prevalence of MAC. We are aware of only one other study that evaluated the relationship of ethnicity and valvular or perivalvular calcification. In the Cardiovascular Health Study of community dwelling elderly patients,[8] the unadjusted prevalence of MAC was lower in African Americans than in Whites (35% vs 43%, *P*<.001). However, an adjusted analysis was not reported, and the African American cohort, which was

In our sample, MAC was common in all three major ethnic groups.

recruited later than the White cohort, may have been younger.

In contrast to the paucity of studies on valvular and perivalvular calcifications and ethnicity, several studies have investigated the prevalence and severity of arterial calcifications in different ethnic groups, including Hispanics. Although causal mechanisms remain unknown, these investigations of the coronary arteries and aorta in multiethnic populations show substantial ethnic differences in vascular calcifications.[1–5] In the Multiethnic Study of Atherosclerosis, the prevalence of coronary artery calcifications (CAC) in African Americans and Hispanics was 22% and 15% lower than in non-Hispanic Whites, respectively.[1] Because MAC and CAC are associated[9,10] and may share common pathogenic mechanisms, including atherosclerosis,[11] the observation in this study that ethnicity is not significantly associated with MAC is somewhat unexpected and suggests the possibility that ethnic patterns of cardiovascular calcifications are site-specific. This hypothesis is supported by the previously reported divergence between CAC and MAC by sex. Postmenopausal women with osteoporosis have a high prevalence of MAC compared to the predominance of CAC among men in the same age group.[12]

Atherosclerosis and tissue calcification are partially independent processes that play major roles in the pathogenesis of CAC and MAC.[11,13] The focal nature of atherosclerosis despite uni-

form exposure of the arterial circulation to systemic risk factors is due to differences in local hemodynamics and shear stress, which affect the vulnerability and response of atherosclerosis-prone sites to risk factors.[14] The coronary arteries and mitral annulus are also exposed to different hemodynamics and, therefore, may have different susceptibility to risk factors for atherosclerosis (and other causes of vascular calcification). Because these risk factors vary by sex and ethnicity, sex and ethnic patterns at one site may not hold for the other.

An alternative explanation for our observations is that echocardiography may not be as accurate as computed tomography for diagnosing cardiovascular calcifications, and subtle ethnic differences in mitral annulus calcification may not be detectable in an echocardiographic study. Studies of MAC in ethnically diverse populations with computed tomography would thus be of interest.

Association of Standard Coronary Risk Factors and MAC in an Ethnically Diverse Population

The current study examines the correlates of MAC in a middle-aged and elderly sample composed of three well-defined ethnic groups. In this multiethnic population referred for echocardiography, age and history of smoking were independent predictors of MAC. Dyslipidemia and diabetes had possible associations of borderline significance with MAC. Previous studies of the correlates of MAC have focused on more ethnically homogeneous populations or have not defined ethnic composition. In these investigations a variety of standard coronary risk factors were independently associated with MAC, supporting the hypothesis that MAC is a form of atherosclerosis. However, with the exception of age, the association of individual risk factors with MAC has not been consistent across studies. Age,

female sex, hypertension, diabetes, and hypercholesterolemia were predictors MAC in Europeans.[15] In the original Framingham Heart Study cohort, age in both sexes, female sex, obesity in women, and systolic hypertension in men were independently associated with MAC.[16] Age and hypertension, but not other risk factors, were independently associated with MAC diagnosed by electron beam tomography.[17] In the Jackson Cohort of the Atherosclerotic Risk in Communities Study, with the exception of age and renal insufficiency, no standard risk factors predicted MAC in African Americans despite the association of MAC with incident coronary heart disease.[18] Differences in population, sample size, and criteria for diagnosis of MAC may account for some of the variability observed across studies in the clinical correlates of MAC.

Limitations

This study has several potential limitations intrinsic to retrospective data, and our observations must be considered hypothesis-generating rather than conclusive. The number of African Americans with MAC in our sample was small. The study may thus have lacked sufficient statistical power to detect the observed ethnic differences in MAC prevalence. An additional limitation is that the results can not be generalized to the population at large since data pertain to patients referred for clinically indicated echocardiograms to a university teaching hospital. Such patients might be expected to have more coronary risk factors than subjects from a population-based study. Nonetheless, while their absolute risks are likely to be higher, any observed relationships are less likely to differ. We limited our analysis to prevalence of MAC in the three ethnic groups. Given the retrospective nature of this study, a reliable assessment of MAC severity was not possible. Other limitations include possible misclassification of ethnic origin by self-reporting, especially in

patients of mixed descent.[19] Likewise, risk factors were determined from clinical records rather than prospectively but were recorded without knowledge of the hypothesis. There were ethnic differences in baseline demographics and risk factors. However, these differences were similar to those reported in national studies, with the exception of younger age and less smoking in African Americans.[20–24] Hispanics in south Florida are predominantly of South American and Caribbean descent, including a large percentage of Cubans, while most Hispanics in the United States are of Mexican descent. Our results may not be generalizable to other Hispanic populations. Finally, for purposes of excluding patients with renal dysfunction, we used serum creatinine as our measure of renal function. This may have lead to underestimation of the degree of renal dysfunction in some patients who were included in our sample despite kidney-related abnormalities of mineral metabolism, which may have contributed to MAC independent of other coronary risk factors.

Despite these and other limitations, we believe the most plausible interpretation of this retrospective data to be that the prevalence of MAC is high in middle-aged and elderly African Americans, non-Hispanic Whites, and Hispanics referred for echocardiography. Our data are compatible with the possibility that, unlike other vascular calcifications, ethnic ancestry is not associated with MAC. Prospective studies are necessary to validate this hypothesis and, in view of the association of MAC with cardiovascular events[18,25] and emerging evidence of ethnic differences in CAC, to evaluate whether MAC predicts cardiac risk equally in African Americans, non-Hispanic Whites and Hispanics.

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AUTHOR CONTRIBUTIONS

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