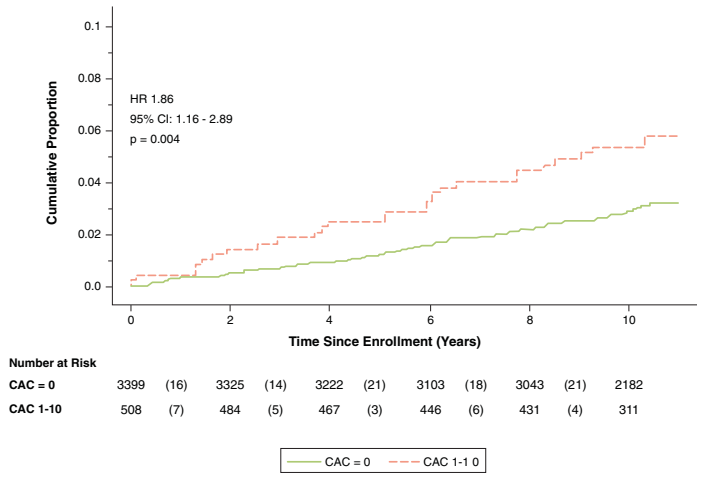
FIGURE 1 Cumulative Proportion With ASCVD Events by CAC Group



Kaplan-Meier curves demonstrate low overall event rates (note truncated y-axis) with approximately 86% increased risk for atherosclerotic cardiovascular disease (ASCVD) among patients with coronary artery calcium (CAC) 1 to 10 compared with those with zero coronary artery calcium. CI = confidence interval; HR = hazard ratio.

reduction beyond 10 years, although balanced with the risk of side effects (i.e., myalgia, hyperglycemia).

The absence of CAC identifies those persons at low absolute 10-year ASCVD risk. This aspect of CAC scanning should be factored into the clinician-patient discussion.

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REFERENCES

1. Paixao AR, Ayers CR, El Sabbagh A, et al. Coronary artery calcium improves risk classification in younger populations. J Am Coll Cardiol Img 2015;8:1285–93.

2. Blaha MJ, Cainzos-Achirica M, Greenland P, et al. Role of coronary artery calcium score of zero and other negative risk markers for cardiovascular disease: the Multi-Ethnic Study of Atherosclerosis (MESA). Circulation 2016;133:849–58.

3. Shaw LJ, Giambrone AE, Blaha MJ, et al. Long-Term prognosis after coronary artery calcification testing in asymptomatic patients: a cohort study. Ann Intern Med 2015;163:14–21.

4. Bild DE, Bluemke DA, Burke GL, et al. Multi-Ethnic Study of Atherosclerosis: objectives and design. Am J Epidemiol 2002;156:871–81.

5. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2889–934.

Family History of CHD Is Associated With Severe CAC in South Asians

Comparing the MASALA and MESA Studies

South Asians (SA) have higher rates of atherosclerotic cardiovascular disease (ASCVD) than most ethnic groups (1). Modifiable risk factors only partially explain this disparity, suggesting a familial or genetic influence on ASCVD pathogenesis. The association of a family history of coronary heart disease (FH) with coronary artery calcium (CAC) in SA is unknown and may inform preventive approaches in this high-risk population. We analyzed the association between FH and CAC in SA compared with other racial or ethnic groups in the United States.

We included participants 45 to 84 years of age from 2 community-based studies: MASALA (Mediators of Atherosclerosis in South Asians Living in America) and MESA (Multi-Ethnic Study of Atherosclerosis). MASALA was designed with methods similar to those used in MESA to allow for cross-ethnic comparisons. Methods of both studies have been described (2,3). After excluding MASALA participants younger than 44 years of age and those missing FH information, the study population included 7,197 participants with mean age of 61 ± 10 years and 47% men (802 SA, 2,470 Non-Hispanic whites [NHW], 1,782 African Americans [AA], 1,405 Hispanics [HP], and 738 Chinese Americans [CA]).

CAC was measured at baseline as previously described (2,3). FH consisted of a self-reported

TABLE 1 Demographic Characteristics and Prevalence of CAC Score of 0 and >300 by FH Status Across Each Group: The MASALA and MESA Studies Compared

	MASALA South Asian		MESA								p Value*
			Non-Hispanic White		African American		Hispanic		Chinese American		
FH status	+	−	+	−	+	−	+	−	+	−	
n (%)	373 (47)	429 (54)	1,274 (52)	1,196 (48)	747 (42)	1,035 (58)	566 (40)	839 (60)	147 (20)	591 (80)	–
CAC = 0	198 (53)	242 (56)	483 (38)	587 (49)	382 (51)	633 (61)	270 (48)	505 (60)	68 (46)	305 (52)	<0.001
p value†	0.35		<0.001		<0.001		<0.001		0.25		
CAC >300	50 (13)	30 (7)	255 (20)	157 (13)	85 (11)	88 (9)	81 (14)	54 (6)	17 (12)	48 (8)	<0.001
p value†	0.003		<0.001		0.04		<0.001		0.19		

Values are n (%) unless otherwise indicated. *p value comparing only those with a positive family history of any CHD by race or ethnicity. †p value comparing those with and without a family history of any CHD within each racial or ethnic group.

CAC = coronary artery calcium; CHD = coronary heart disease; FH = family history of any coronary heart disease; MASALA = Mediators of Atherosclerosis in South Asians Living in America; MESA = Multi-Ethnic Study of Atherosclerosis; − = negative; + = positive.

history of CHD in a first-degree relative at any age. We assessed the association of FH with CAC (>0 and >300) by using multivariable models adjusted for age, sex, tobacco use, diabetes mellitus, systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, use of lipid-lowering medications, and use of medication for hypertension. We assessed FH when added to the American College of Cardiology/American Heart Association pooled cohort equation (PCE) to discriminate and reclassify among CAC categories by using C-statistic and continuous net reclassification improvement (NRI); SA and CA were categorized as "other" in the PCE.

Family history of CHD was present in 3,107 (43%) of the total participants and in 377 (47%) of SA. The prevalence of FH was highest in NHW, followed by SA (Table 1). Additionally, 3,524 (49%) participants had prevalent CAC >0, including 865 (25%) participants with severe CAC >300 with a median CAC score of 0 (interquartile range: 0 to 82). The presence of an FH carried a risk factor adjusted odds ratio for the presence of any CAC of 1.58 (95% confidence interval: 1.47 to 1.76). The association between FH and prevalent CAC (CAC >0) was significant in NHW, AA, and HP (Table 1).

Although FH was not independently associated with prevalent CAC >0 in SA after adjustment, it was significantly and independently associated with CAC >300 in SAs (Table 2). FH added modestly to the PCE for the discrimination of CAC >300 in SA (C-statistic increased from 0.853 to 0.863; p = 0.001), NHW, AA, and HP. The presence of an FH significantly improved the NRI for CAC >300 in SA (38.9% [95% confidence interval: 14.6% to 62.6%]), NHW, and HP. There was no significant interaction of FH with ethnicity. The associations between FH with CAC were similarly significant in models excluding statin users and individuals with diabetes across all groups. In sensitivity analyses, there was no association between FH and CAC >10 and CAC >100 after risk factor adjustment in SA.

The presence of an FH in SA was associated with a high burden of CAC, independent of conventional risk factors. Additionally, FH provided significant information for the prediction and reclassification of severe CAC in SA. These findings may help clarify the

TABLE 2 Ethnic-Specific Associations Between a Positive FH and the Presence and Burden of CAC (>0 and >300): The MASALA and MESA Studies Compared

	Odds Ratios for the Presence of Calcification by Race or Ethnicity With a Positive FH (95% Confidence Interval)						
	MASALA South Asian	MESA				p Value*	p Value†
		Non-Hispanic White	African American	Hispanic	Chinese American		
CAC >0 vs. 0							
Unadjusted	1.14 (0.87–1.51)	1.58 (1.34–1.85)	1.50 (1.24–1.82)	1.66 (1.34–2.06)	1.24 (0.86–1.78)	0.21	0.94
Model 1‡	1.02 (0.71–1.45)	1.62 (1.34–1.97)	1.59 (1.28–1.97)	1.59 (1.23–2.05)	1.33 (0.89–1.98)	0.25	0.64
CAC >300 vs. ≤300							
Unadjusted	2.06 (1.28–3.31)	1.66 (1.33–2.06)	1.38 (1.01–1.89)	2.43 (1.69–3.49)	1.47 (0.82–2.66)	0.18	0.35
Model 1‡	2.81 (1.60–4.93)	1.82 (1.42–2.33)	1.45 (1.03–2.05)	2.47 (1.65–3.69)	1.63 (0.86–3.10)	0.25	0.52

Values are odds ratios, 95% confidence intervals, and p values. *p value for interaction by ethnicity. †p value for interaction by age. ‡Adjusted for age, sex, tobacco use, diabetes mellitus, systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, use of lipid-lowering medications, and use of medication for hypertension.

Abbreviations as in Table 1.

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value of including FH data *after* quantitative risk estimation in SA, particularly when the decision to initiate statin therapy remains less clear (4). Future data on incident ASCVD events in MASALA will allow further validation of the association between FH and CAC. In other ethnic groups, CAC is a robust maker of absolute and relative risk of future ASCVD among those with an FH (5). The absence of an association in CA was likely related to the low prevalence of FH in this group. Notable limitations include the potential for reporting errors and recall bias when assessing FH status, as well as possible ascertainment bias.

An FH was associated with a severe CAC burden in an SA population living in the United States, similar to other racial or ethnic groups, and represents a meaningful and inexpensive tool to assess ASCVD risk.

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REFERENCES

1. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. JAMA 2007;297:286–9.

2. Kanaya AM, Kandula N, Herrington D, et al. Mediators of Atherosclerosis in South Asians Living in America (MASALA) study: objectives, methods, and cohort description. Clin Cardiol 2013;36:713–20.

3. Bild DE, Bluemke DA, Burke GL, et al. Multi-Ethnic Study of Atherosclerosis: objectives and design. Am J Epidemiol 2002;156:871–81.

4. Goff DC Jr., Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2935–59.

5. Patel J, Al Rifai M, Blaha MJ, et al. Coronary artery calcium improves risk assessment in adults with a family history of premature coronary heart disease: results from Multiethnic Study of Atherosclerosis. Circ Cardiovasc Imaging 2015;8:e003186.