Family History of Premature Coronary Heart Disease and Coronary Artery Calcification
Multi-Ethnic Study of Atherosclerosis (MESA)

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Background—A family history of premature coronary heart disease (CHD) is a known risk factor for CHD events. The purpose of this study was to assess the strength of the association between a family history of premature CHD and coronary artery calcification (CAC) in a multiethnic cohort of asymptomatic individuals. We also sought to determine whether individuals with a reported family history of premature CHD have an increased atherosclerotic burden among those classified as being at low to intermediate risk on the basis of the conventional Framingham risk score.

Methods and Results—The association of family history of premature CHD with CAC was assessed in 5347 asymptomatic individuals (47% men; mean age 62.10 years) in the Multi-Ethnic Study of Atherosclerosis (MESA). The demographics (age, gender, and race)–adjusted OR for CAC >0 with versus without a family history of premature CHD was 1.94 (95% CI, 1.64 to 2.29). On adjustment for CHD risk factors, the association was slightly attenuated to an OR of 1.84 (95% CI, 1.55 to 2.19). Family history of premature CHD was significantly associated with CAC in all ethnic groups. The age-, gender-, and race-adjusted prevalence of CAC >0 was significantly higher with presence of any family history of premature CHD than for those with no family history of premature CHD among individuals classified as low risk (35% versus 23%, P<0.0001) and among those at intermediate risk (70% versus 60%, P=0.01). Similarly, the prevalence of age-gender-race–based CAC ≥75th percentile in low-risk (24% versus 14%, P=0.0003) and intermediate-risk (34% versus 20%, P<0.001) individuals was also higher among those with a family history of premature CHD. Compared with those without a family history of premature CHD, the association with the presence of CAC was strongest in participants reporting such history in both a parent and a sibling (odds ratio, 2.74; 95% CI, 1.64 to 4.59), followed by those reporting a family history in a sibling only (odds ratio, 2.06; 95% CI, 1.64 to 2.58) and those reporting a family history of premature CHD only in a parent (odds ratio, 1.52; 95% CI, 1.19 to 1.93).

Conclusions—An association between family history of premature CHD and the presence of any CAC, as well as advanced CAC, was observed in the present population-based multiethnic study. The relationship was independent of other risk factors and Framingham risk score, which supports the utility of including information on family history of premature CHD in current methods of global risk assessment and practice guidelines. (Circulation. 2007;116:619-626.)

Key Words: epidemiology ■ atherosclerosis ■ risk factors

Coronary artery calcium (CAC) testing is receiving increasing attention as a technique to improve coronary heart disease (CHD) risk prediction in selected adults.1–3 The quantity of CAC strongly correlates with the magnitude of coronary atherosclerotic plaque burden and with the development of subsequent coronary events.4–9

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A family history (FamHx) of premature CHD is a known risk factor for CHD events10,11 and may indicate an increased susceptibility to atherosclerosis development and progression.12,13 Traditional risk factors account for as much as one...
fourth of the variance in CAC quantity among individuals with FamHx of premature CHD.14 Elucidating the association of FamHx of premature CHD with subclinical atherosclerosis may have clinical implications, because those individuals with a FamHx of premature CHD may be considered for subclinical disease screening. CAC scores and percentiles can potentially be incorporated into global CHD risk assessment to identify the need for intensive risk factor reduction.15

Current clinical practice guidelines for the primary prevention of CHD recommend initial assessment and risk stratification based on the Framingham risk score (FRS)16; however, a FamHx of premature CHD is absent from this predictive model, which is based on 5 traditional risk factors. The purpose of the present study was to assess the strength of the association between a FamHx of premature CHD and CAC in a multiethnic cohort of asymptomatic individuals. We also sought to determine whether FamHx of premature CHD is associated with a higher atherosclerotic burden among individuals classified as being at low to intermediate risk by global CHD risk assessment methods such as the FRS.

Methods

The Multi-Ethnic Study of Atherosclerosis (MESA) was initiated in July 2000 to investigate the prevalence, correlates, and progression of subclinical cardiovascular disease (CVD) in individuals without known CVD.17 This prospective cohort study includes 6814 women and men aged 45 to 84 years old recruited from 6 US communities (Baltimore, Md; Chicago, Ill; Forsyth County, North Carolina; Los Angeles County, California; northern Manhattan, New York; and St. Paul, Minn). Cohort participants were 38% white (n=2624), 28% black (n=1895), 22% Hispanic (n=1492), and 12% Chinese (n=803). Medical history, anthropometric measurements, and laboratory data for the present study were taken from the first examination of the MESA cohort (July 2000 to August 2002). Information about age, gender, ethnicity, and medical history were obtained by questionnaires. Current smoking was defined as having smoked a cigarette in the last 30 days. Diabetes mellitus was defined as a fasting glucose ≥126 mg/dL or use of hypoglycemic medications. Use of antihypertensive and other medications was based on clinical staff entry of prescribed medications verified by the staff.

Resting blood pressure was measured 3 times in the seated position, and the average of the second and third readings was recorded. Hypertension was defined as a systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or use of medication prescribed for hypertension. Body mass index was calculated from the equation weight (kg)/ height (m²). Total and high-density lipoprotein cholesterol were measured from blood samples obtained after a 12-hour fast. Low-density lipoprotein cholesterol was estimated by the Friedewald equation.18

In examination 1 of MESA, participants reported only the presence and absence of a FamHx of CHD. Detailed information on FamHx of CHD was obtained in examination 2 of MESA, and information was available for 6201 individuals. The FamHx of CHD was obtained by asking participants whether any member in their immediate family (first-degree relatives) experienced a fatal or nonfatal myocardial infarction and/or coronary angioplasty/coronary artery bypass surgery. The event was considered premature if it occurred before the age of 55 years in male relatives and before 65 years of age in female relatives, whereas events reported after these age cutoffs were considered late onset in nature. We excluded 854 participants (13%) who did not know about the presence/absence of the CHD event in their parents or siblings.

Computed tomography scanning of the chest was performed either with an ECG-triggered (at 80% of the RR interval) electron-beam computed tomography scanner (Chicago, Los Angeles, and New York field centers; Imatron C-150, Imatron, San Francisco, Calif) or with prospectively ECG-triggered scan acquisition at 50% of the RR interval with a multidetector computed tomography system that acquired 4 simultaneous 2.5-mm slices for each cardiac cycle in a sequential or axial scan mode (Baltimore, Forsyth County, and St. Paul field centers; Lightspeed, General Electric, Piscataway, NJ, or Volume Zoom, Siemens, New York, NY).19 Each participant was scanned twice. Scans were read centrally at the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center to identify and quantify coronary calcification. The CAC measurements among scanning centers and between participants were adjusted with a standard calcium phantom scanned simultaneously with each participant. The mean Agatston score was used in all analyses. Agreement with regard to presence of CAC was high (κ-statistic 0.90 to 0.93 between and within readers), and the intraclass correlation coefficient for the Agatston score between readers was 0.99. Concordance for presence of CAC between duplicate scans was high and was similar for both electron-beam and multidetector row computed tomography (96%, κ=0.92).19

Statistical Analysis

The association between FamHx of premature CHD and presence of subclinical CAC (CAC >0) and CAC ≥75th percentile was examined with logistic regression. In the present study, we determined whether an individual in the MESA study had CAC ≥75th percentile (yes/no) based on the normal distribution according to age and gender in each racial/ethnic group as reported in a recent study by McClelland et al.20 The logistic regression analyses were adjusted for age, gender, race, MESA site, systolic blood pressure, hypertension, pack-years of cigarette smoking, diabetes mellitus, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and body mass index (model 1) and separately adjusted for FRS, age, gender, and race (model 2); however, in ethnic-specific analyses, race was not adjusted in either model.

We also examined the prevalence of CAC ≥75th percentile among individuals classified as being at low or intermediate risk by the FRS. FRS for men and women were calculated on the basis of age, total cholesterol, high-density lipoprotein cholesterol, current smoking status, systolic blood pressure, and the use of antihypertensive medication.16 Individuals with an estimated 10-year hard CHD risk (myocardial infarction or CHD death) of 10% to 20% were classified as being at intermediate risk. Those with diabetes mellitus were classified as high risk (FRS ≥20%). The FRS for individuals undergoing therapy with a statin and for subjects >80 years old was not calculated. The association of CHD risk factors with CAC was also assessed across FamHx of premature CHD categories to assess a possible interaction. Statistical differences between groups for association with CAC and with CAC ≥75th percentile were determined by means of an adjusted Wald test. All statistical analyses were performed with Stata version 8.0 (Stata Corp, Austin, Tex; http://www.stata.com). The level of significance was set at P<0.05 (2-tailed).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

The final study population consisted of 5347 asymptomatic individuals (47% men; mean age 62±10 years). The majority of study participants were white (n=2255, 42%), followed by blacks (n=1356, 25%), Hispanics (n=1178, 22%), and Chinese (n=558, 10%). Overall, 2761 participants (42%; 1237 women) reported a FamHx of CHD. For 1044 (619 women), the familial CHD event was premature. Among individuals with a FamHx of premature CHD, 468 (45%) reported it in a parent only, 495 (47%) in a sibling only, and 81 (8%) in parents and siblings.
Table 1 demonstrates the baseline characteristics of study participants with a reported FamHx of premature CHD compared with those without FamHx of CHD. Participants with a reported FamHx of premature CHD were more likely to be younger, female, hypertensive, obese, and/or cigarette smokers. Among all racial groups, Chinese Americans were the least likely to report a FamHx of premature CHD. No differences in lipid levels or in the prevalence of diabetes mellitus were observed between the groups (Table 1).

Overall, 2587 (48%) of the study population had any CAC, whereas age-gender-race–specific CAC ≥75th percentile was observed in 1289 (24%) of the study population. The median (interquartile range) CAC in this population was 0 (0–84). The age-gender-race–adjusted odds ratio (OR) for CAC >0 comparing FamHx of premature CHD versus no FamHx of CHD was 1.94 (95% CI, 1.64 to 2.29). Further adjustment for CHD risk factors (model 1) slightly attenuated the association compared with FamHx of premature CHD versus no FamHx of CHD. As shown in the Figure, among all ethnic groups, the presence of FamHx of premature CHD was associated with a higher prevalence of CAC ≥75th percentile than for those without any FamHx of CHD in both the low and intermediate FRS categories.

**FamHx of Premature CHD and CAC According to Ethnicity**

Table 2 describes the ethnic-specific ORs for presence of any CAC and for CAC ≥75th percentile associated with a FamHx of premature CHD. The estimated ORs were similar across all ethnic groups in either CHD risk factor– or FRS-adjusted models. Overall, the strongest association was observed among Chinese Americans compared with other ethnic groups; however, there was no evidence of a differential relationship of FamHx of premature CHD and CAC by ethnicity in the multivariable models (P for interaction term race×FamHx of premature CHD in all adjusted models ranged from 0.16 to 0.67).

**FamHx of Premature CHD and CAC Among Subjects With Low and Intermediate FRS**

In the present study, 56% and 24% of all individuals were classified as low risk (FRS <10%) and intermediate risk (FRS, 10% to 20%), respectively. The age-gender-race–adjusted prevalence of CAC >0 was significantly higher with the presence of any FamHx of premature CHD than for those with no FamHx of CHD among individuals classified as low risk (35% versus 23%, P<0.0001) or intermediate risk (70% versus 60%, P=0.01). Similarly, the prevalence of age-gender-race–based CAC ≥75th percentile in low-risk (24% versus 14%, P=0.0003) and intermediate-risk (34% versus 20%, P<0.001) individuals was also higher among those with FamHx of premature CHD. As shown in the Figure, among all ethnic groups, the presence of FamHx of premature CHD was associated with a higher prevalence of CAC ≥75th percentile than for those without any FamHx of CHD in both the low and intermediate FRS categories.

**Parental Versus Sibling FamHx of Premature CHD and CAC**

The prevalence of CAC >0 (adjusted for age, gender, and race) was significantly higher (P<0.001) in individuals with a FamHx of premature CHD in both parents and siblings (64%), followed by FamHx of premature CHD in only a sibling (58%) and in only a parent (51%), with the lowest prevalence among those with no FamHx of CHD (40%). The respective prevalences of CAC ≥75th percentile were 38%,
32%, 27%, and 18% \((P<0.001)\). The results persisted in multivariable analysis that assessed the association of presence and magnitude of CAC according to parental and sibling FamHx of premature CHD (Table 3). No differences in the association with CAC were observed between a paternal versus maternal FamHx of premature CHD. The association with CAC of a FamHx of premature CHD in a sister was similar to that of a FamHx of premature CHD in a brother (data not shown).

### CHD Risk Factors and CAC According to FamHx of Premature CHD

We also assessed the association of CHD risk factors with the presence of CAC according to a FamHx of premature CHD (Table 4). The ORs for CAC with known major CHD risk factors among participants with a reported FamHx of premature CHD were similar to those for individuals with no FamHx of CHD. No significant first-order interactions were observed, which indicates similar effects of CHD risk factors among individuals with and without a FamHx of CHD.

### Secondary Analyses

In secondary analyses, the association of FamHx of premature CHD with CAC as a continuous variable \((\log \text{CAC} + 1)\) by linear regression was similar to one observed with CAC as a binary component (Data Supplement, Tables I and II). Also, when individuals with FamHx of late onset of CHD were combined with those without any FamHx of CHD as a reference group, the association of FamHx of premature CHD with CAC remained significant, although it was attenuated (Data Supplement, Tables III and IV).

### Discussion

In a population-based multiethnic cohort of asymptomatic, mostly low- and intermediate-risk men and women, we observed that a FamHx of premature CHD was associated with a higher prevalence and magnitude of coronary calcification. This association was independent of other risk factors and the FRS. Across all ethnic groups, a FamHx of premature CHD was independently associated with CAC, and the effect was similar in all groups. Consistent with prior published studies using subclinical and clinical end points, the present...
The manifestation of CHD is due to an interaction of several unfavorable genetic and environmental factors. Individuals with the greatest number of risk factors (genetic and environmental) likely face the highest risk at an earlier age. Many cross-sectional and some longitudinal studies have found familial clustering of CHD. In the Framingham Heart Study, a FamHx of premature heart disease was associated with an excess risk for an adverse cardiovascular outcome (OR, 1.7 to 2.0). In the present study, a FamHx of premature CHD was associated with an OR in the range of 1.74 to 1.84 for the presence of CAC and for CAC ≥75th percentile in multivariable-adjusted models. Interestingly, the strength of association of this risk factor with CAC is quite similar to those of clinical end points reported in the literature.

These data support the search for new genes that predispose individuals to coronary atherosclerosis beyond the influence of the standard risk factors. In recent years, there has been tremendous progress in sequencing the human genome, along with advances in molecular and population genetics that will pave the way for identification of genes and their potential role in expression of underlying atherosclerosis. Further studies are also needed to identify and determine the functional role of candidate and marker genes for CHD and cardiovascular risk factors, as well as to better understand the interactions between genetic susceptibility and environmental factors.

### TABLE 3. Presence of Any CAC and CAC ≥75th Percentile According to Parental and Sibling FamHx of Premature CHD

<table>
<thead>
<tr>
<th></th>
<th>CAC &gt;0</th>
<th>CAC ≥75th Percentile</th>
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<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No FamHx of CHD</td>
<td>1 (Reference)</td>
<td>1 (Reference)</td>
</tr>
<tr>
<td>FamHx of premature CHD in a parent only</td>
<td>1.52 (1.19 to 1.93)</td>
<td>1.60 (1.25 to 2.04)</td>
</tr>
<tr>
<td>FamHx of premature CHD in a sibling</td>
<td>2.06 (1.64 to 2.58)</td>
<td>2.12 (1.70 to 2.66)</td>
</tr>
<tr>
<td>FamHx of premature CHD in both a parent and a sibling</td>
<td>2.74 (1.64 to 4.59)</td>
<td>2.83 (1.74 to 4.59)</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No FamHx of CHD</td>
<td>1 (Reference)</td>
<td>1 (Reference)</td>
</tr>
<tr>
<td>FamHx of premature CHD in a parent only</td>
<td>1.48 (1.15 to 1.91)</td>
<td>1.68 (1.29 to 2.18)</td>
</tr>
<tr>
<td>FamHx of premature CHD in a sibling</td>
<td>1.90 (1.49 to 2.40)</td>
<td>2.13 (1.67 to 2.71)</td>
</tr>
<tr>
<td>FamHx of premature CHD in both a parent and a sibling</td>
<td>3.23 (1.85 to 5.63)</td>
<td>3.18 (1.88 to 5.35)</td>
</tr>
</tbody>
</table>

Values are expressed as OR (95% CI). Model 1: adjusted for age, gender, race, MESA site, hypertension, systolic blood pressure, smoking status, cigarette pack-years, diabetes mellitus, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and body mass index. Model 2: adjusted for age, gender, race, and FRS.

P value determined by Wald test for difference in association with CAC >0 and CAC ≥75th percentile with sibling versus parental FamHx of premature CHD was <0.05 in model 1, whereas in model 2, it ranged from 0.11 to 0.13.

*Individuals with history of late onset of FamHx of CHD were not included in the analysis.

### TABLE 4. Association of Presence of CAC With Major CHD Risk Factors Among Individuals With and Without FamHx of Premature CHD

<table>
<thead>
<tr>
<th></th>
<th>No FamHx of CHD</th>
<th>FamHx of Premature CHD</th>
<th>P for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 y)</td>
<td>2.54 (2.30 to 2.80)</td>
<td>2.91 (2.48 to 3.68)</td>
<td>0.10</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>3.21 (2.68 to 3.85)</td>
<td>2.76 (2.07 to 3.68)</td>
<td>0.26</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.55 (1.18 to 2.03)</td>
<td>1.53 (1.12 to 2.08)</td>
<td>0.65</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.55 (1.18 to 104)</td>
<td>1.89 (1.20 to 2.97)</td>
<td>0.77</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>1.54 (1.10 to 2.16)</td>
<td>1.51 (0.92 to 2.48)</td>
<td>0.95</td>
</tr>
<tr>
<td>Elevated LDL-C (&gt;160 mg/dL)</td>
<td>1.65 (1.21 to 2.24)</td>
<td>1.69 (0.99 to 2.57)</td>
<td>0.74</td>
</tr>
<tr>
<td>Low HDL-C (&lt;40 mg/dL)</td>
<td>1.45 (1.22 to 1.80)</td>
<td>1.76 (1.20 to 2.59)</td>
<td>0.92</td>
</tr>
<tr>
<td>Elevated TG (&gt;150 mg/dL)</td>
<td>1.41 (1.18 to 1.68)</td>
<td>1.36 (1.00 to 1.86)</td>
<td>0.45</td>
</tr>
<tr>
<td>Obesity (body mass index ≥30 kg/m²)</td>
<td>1.57 (1.28 to 1.93)</td>
<td>1.16 (0.90 to 1.56)</td>
<td>0.09</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>1.68 (1.38 to 2.03)</td>
<td>2.04 (1.52 to 2.74)</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Values are expressed as OR (95% CI). LDL-C indicates LDL cholesterol; HDL-C, HDL cholesterol; and TG, triglycerides.

*Individuals with history of late onset of FamHx of CHD were not included in the analyses.
Most studies demonstrating an association of a FamHx of premature CHD with CVD end points have been performed in primarily white populations, and data on the role of FamHx in other ethnic groups are scarce. Bensen et al demonstrated that the family risk score for CHD was significantly associated with mean carotid artery intima-media wall thickness in white and black participants of the Atherosclerosis Risk In Communities (ARIC) study. Similarly, Li et al reported that the family risk score of CHD in the ARIC study independently predicted incident CHD in both blacks and whites.

The present report adds to the literature by demonstrating that a FamHx of premature CHD is strongly associated with coronary calcification not only in whites and blacks but also in Hispanics and Chinese. In the present study, the association of a FamHx of premature CHD with CAC appeared stronger among Chinese Americans than other ethnic groups. Although the interaction between FamHx and racial groups was not statistically significant, this may be explained by the underlying smaller sample size in this ethnic group. Continuation of the MESA study will allow investigators to assess whether a FamHx of premature CHD is more strongly associated with progression of CAC and future cardiovascular events in Chinese Americans.

Although a FamHx of premature CHD is recognized as a risk factor for CHD events, the future incorporation of sibling and parental FamHx of premature CHD into existing risk prediction and prevention algorithms still needs to be assessed. In the past, it has been considered to reflect an underlying clustering of CHD risk. In the present study, however, the risk of subclinical atherosclerosis with a FamHx of premature CHD persisted even after traditional risk factors and global CHD risk determined by the FRS were taken into account. In the present study, information on the presence of a FamHx of premature CHD was associated with a higher atherosclerotic burden in those classified as being at low risk and particularly those at intermediate risk. These findings argue against the notion that a FamHx of premature CHD is merely a reflection of traditional risk factors.

The observation of increased prevalence of CAC across FRS categories is consistent with recent findings that a FamHx of premature CHD adds prognostic information in terms of clinical end points, especially among intermediate-risk individuals. Recently, Ridker et al showed that the addition of FamHx of premature CHD to global CHD risk models improved prediction for future cardiovascular events. The purpose of risk assessment with the FRS is to predict CHD, not coronary atherosclerosis; however, recent studies have provided strong support for the relationship between CAC (ie, atherosclerosis) and risk of future CHD events. It is important to formally assess whether the presence of a FamHx of premature CHD adds incremental value to the FRS in identifying high-risk asymptomatic individuals, as determined by future cardiovascular events.

In addition, a limitation of the current FRS global risk prediction model is that it was developed in a largely white population; thus, it may have limited capacity for extrapolation to different patient populations. Although the FRS has been noted to work well in blacks, little evidence exists regarding its utility in other ethnic minorities. As a result, there is a need for further adjustments in the FRS to better characterize the absolute population baseline risk of other subgroups of the US population.

Our findings add to the growing evidence that a sibling history of premature CHD is a risk factor for CVD. In a physician-referred, primarily white population, Nasir et al recently demonstrated a stronger association between the presence of moderate CAC and sibling history of premature CHD than between moderate CAC and a parental history of premature CHD. Using clinical end points, Murabito et al from the Framingham Heart Study also found stronger associations for a sibling history than for a parental history of premature CVD. The ORs for incident CVD associated with a sibling history of premature CVD and parental premature CVD in that study were 1.99 and 1.45, respectively. In comparison, ORs for the presence of CAC associated with a sibling FamHx (OR = 1.96) and a parental FamHx of premature CHD (OR = 1.45) in the present study were nearly identical to the risk described in the Framingham Heart Study.

The Third Report of the National Cholesterol Education Program Expert Panel stated that a positive FamHx of premature CHD is an additional risk factor that physicians should use to determine underlying CHD risk. Although the cost/benefit ratio of targeting high-risk families for screening and aggressive therapy remains unknown, on the basis of prior studies and the present findings, such screening would likely identify a very-high-risk group with advanced CAC, as well as a lower-risk group with considerably less than expected coronary calcification based on their age, gender, and ethnicity. We believe that middle-aged adults with a FamHx of premature CHD should be considered for quantification of subclinical atherosclerosis by noninvasive measures. The additional information obtained by subclinical disease testing may change the posttest probability of disease enough to consider altering the treatment of the patient. It is also important to educate the public, healthcare providers, and public health professionals about the importance of family history as a strong CHD risk factor.

It is important to consider, aside from genetic research considerations, why family history has not been part of standard coronary risk prediction. A family history in most cases is ascertained by a report by the offspring or first-degree relative rather than by strict validation of familial events. Before one considers the implications of the above findings, it is inappropriate to consider the validity of the indexes of FamHx, which were based on data obtained from a self-reported questionnaire in the present study.

Studies have demonstrated for reported FamHx of premature CHD a sensitivity of 68% to 86% and specificities ranging from 86% to 98%, and most likely, the bias in recall of FamHx of CHD is toward the null. Because of high specificity and comparatively lower sensitivity, some subjects with a positive FamHx are falsely classified with the group of subjects without FamHx of premature CHD. This might result in underestimation of the risk associated with a positive FamHx of premature CHD. A limitation of the present study is that detailed FamHx of CHD was evaluated in MESA examination 2, whereas computed tomography findings were outside of the study.
based on examination 1. The number of persons who had a negative history at examination 1 but a positive history at examination 2 was minimal. After the exclusion of these individuals from the analyses, the results remained the same.

In summary, the present study findings demonstrate an association between FamHx of premature CHD and the presence of any CAC or advanced coronary atherosclerosis for one’s age and gender. The effect of a reported FamHx of premature CHD was similar across all ethnic groups. The relationship existed with both a sibling history and a parental history of premature CHD. Identification of certain genetic or environmental factors may provide a tool for the understanding and prevention of subclinical atherosclerosis progression, as well as for the development of future clinical events. These data add to the growing body of evidence that a FamHx may be another useful means to more clearly identify those subjects with significant coronary atherosclerosis. More research is warranted to determine whether use of FamHx of CHD in conjunction with the FRS will better identify those subjects who will benefit most from aggressive primary prevention, including intensified exercise and weight loss, as well as pharmacotherapy, including lipid-lowering medication, aspirin, and possibly antihypertensive therapy.

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Disclosures

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References

A family history of premature coronary heart disease (CHD) is a known risk factor for CHD events and may indicate an increased susceptibility to atherosclerosis development and progression. This study evaluated the relationship of family history of premature CHD with coronary artery calcification (CAC), a known marker of subclinical atherosclerosis, in a multiethnic prospective cohort of 5347 women and men aged 45 to 84 years. We also sought to determine whether individuals with a reported family history of premature CHD have an increased atherosclerotic burden among those classified as being at low to intermediate risk on the basis of the conventional Framingham risk score. Family history of premature CHD was strongly associated with the presence of any CAC and with advanced CAC. A higher prevalence of advanced CAC was observed with family history of premature CHD in both individuals classified as low risk and those classified as intermediate risk by global CHD risk assessment algorithms. In the present study, both parental and sibling family history of premature CHD was related to CAC. The study finding supports the utility of including information on family history of premature CHD in current methods of global risk assessment and practice guidelines.
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