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Atherosclerotic Biomarkers and Aortic Atherosclerosis by Cardiovascular Magnetic Resonance Imaging in the Framingham Heart Study

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***Background*—**The relations between subclinical atherosclerosis and inflammatory biomarkers have generated intense interest but their significance remains unclear. We sought to determine the association between a panel of biomarkers and subclinical aortic atherosclerosis in a community-based cohort.

***Methods and Results*—**We evaluated 1547 participants of the Framingham Heart Study Offspring cohort who attended the 7th examination cycle and underwent both cardiovascular magnetic resonance imaging (CMR) and assays for 10 biomarkers associated with atherosclerosis: high-sensitivity C-reactive protein, fibrinogen, intercellular adhesion molecule-1, interleukin-6, interleukin-18, lipoprotein-associated phospholipase-A2 activity and mass, monocyte chemoattractant protein-1, P-selectin, and tumor necrosis factor receptor-2. In logistic regression analysis, we found no significant association between the biomarker panel and the presence of aortic plaque (global P=0.53). Using Tobit regression with aortic plaque as a continuous variable, we noted a modest association between biomarker panel and aortic plaque volume in age- and sex-adjusted analyses (P=0.003). However, this association was attenuated after further adjustment for clinical covariates (P=0.09).

***Conclusions*—**In our community-based cohort, we found no significant association between our multibiomarker panel and aortic plaque. Our results underscore the strengths and limitations of the use of biomarkers for the identification of subclinical atherosclerosis and the importance of traditional risk factors. **(*J Am Heart Assoc*. 2013;2:e000307 doi: 10.1161/JAHA.113.000307)**

Key Words: aorta • atherosclerosis • biomarkers • cardiovascular magnetic resonance imaging

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Cardiovascular disease (CVD) due to atherosclerosis is the leading cause of morbidity and mortality in the industrialized world.[1,2] As a result, there is significant interest in early identification of individuals at risk for atherosclerosis in order to optimally target primary prevention.[3] Aortic atheroma is a manifestation of systemic atherosclerosis[4–7] and calcified atheroma in the abdominal and thoracic aorta strongly predict increased risk for CVD outcomes adjusting for traditional risk factors.[8–12] Inflammation plays a central role in atherosclerosis and several individual inflammatory biomarkers have been associated with atherosclerosis, including high-sensitivity C-reactive protein, fibrinogen, and tumor necrosis factor receptor-2.[3,13–16]

Inflammatory biomarkers have been correlated with subclinical atherosclerosis by 2-dimensional noninvasive imaging techniques including high-resolution B-mode carotid ultrasound[13,17] and epicardial coronary calcification by electron beam computed tomography.[18–20] However, there are limited data regarding associations between these biomarkers and aortic plaque, as defined by a contemporary, advanced noninvasive imaging modality such as cardiovascular magnetic

resonance imaging (CMR). CMR has the ability to measure the entire aorta (ascending and descending) in 3 dimensions, thereby increasing the detection of subclinical aortic atheroma. CMR offers unique advantages as a noninvasive technique for the identification of aortic atheroma, including highly reproducible measurements of aortic anatomy, quantification of atherosclerosis, and lack of ionizing radiation.[21] We sought to determine the association between a panel of 10 biomarkers associated with atherosclerosis and aortic plaque, as determined by CMR, and performed an exploratory analysis to assess for effect modification of the associations between inflammatory biomarkers and aortic plaque by sex, in a longitudinally followed community-based cohort.

Methods

Study Population and Sample Selection

The Framingham Offspring Study was initiated in 1971 when 5124 adult children (and offspring spouses) of the Original Framingham Heart Study (FHS) Cohort were enrolled. Offspring participants have been examined approximately every 4 to 7 years since the study's inception. Offspring participants who attended the 7th examination cycle (1998-2001) were eligible for the present study (n=3799), of whom 1794 were in sinus rhythm, lived in Massachusetts or a contiguous state, and had no contraindications to CMR. Assays for several biomarkers were also measured during this cycle visit, as previously described.[22] Only participants who had both a CMR and the panel of biomarkers were included in this study. The study was approved by the Institutional Review Boards of the Boston University Medical Center and the Beth Israel Deaconess Medical Center. Written informed consent was obtained from all participants.

Cardiovascular Magnetic Resonance (CMR)

Participants underwent thoracoabdominal aortic CMR using a 1.5-T whole-body CMR system (Gyroscan ACS-NT; Philips Medical Systems) as previously reported.[23] Thirty-six transverse slices encompassing the aorta from the arch to the aortoiliac bifurcation were obtained using a free-breathing, ECG-gated, fat-suppressed, black blood 2D T2-weighted turbo spin-echo sequence with in-plane spatial resolution of 1.03×0.64 mm^2 and 5 mm slice thickness. Twelve slices with a 10 mm slice gap was used for the thoracic aorta and a denser sampling of 24 slices with a 5 mm gap was used for the abdominal aorta.

Aortic and Atherosclerotic Plaque Analysis

A single expert reviewer (N.O.) blinded to all clinical data analyzed CMR images using commercial software (QMASS v 6.1; QT-MEDIS).[23] Atherosclerotic plaque was defined as characteristic luminal protrusions of ≥1 mm in radial thickness that could be visually distinguished from the minimal residual blood signal of each plaque. For each participant, plaque cross-sectional areas were measured at each slice (descending thoracic and abdominal) and total plaque volume was calculated. Individual plaque volume was also normalized for calculated body surface area (BSA) based on 7th examination cycle. Intra- and inter-reader reproducibility or aortic plaque volume was good with intraclass correlation coefficients of 0.99 and 0.94, respectively.[23]

Biomarker Selection and Measurement

We selected a panel of 10 biomarkers available at Cycle 7 that were associated with vascular inflammation and atherosclerosis; criteria for selection were previously described.[22,24,25] These included high-sensitivity C-reactive protein (hs-CRP, a marker of inflammation); fibrinogen (a marker of thrombosis and inflammation); intercellular adhesion molecule-1 (a marker associated with progressive atherosclerotic plaque); interleukin-6 (a pro-inflammatory marker); interleukin-18 (a pro-inflammatory marker); lipoprotein-associated phospholipase A2 activity and mass (a low-density lipoprotein particle thought to promote atherosclerosis); monocyte chemoattractant protein-1, (a chemokine associated with damaged endothelium and atherosclerotic plaque); P-selectin (a marker associated with inflammatory cell adhesion and atherosclerosis); and tumor necrosis factor receptor-2 (a marker of inflammation associated with atherosclerotic plaque).

Blood samples were collected from fasting participants and stored at −80°C until analysis. Details for biomarker measurements have been described elsewhere.[22] The intra-assay coefficients of variation for the biomarkers were <8%.

Clinical Covariate Assessment

We obtained clinical covariates at the time of the Cycle 7 examination. Medication use (including lipid-lowering treatment and aspirin) and current smoking within the year preceding the exam were self reported. Hypertension was defined as systolic blood pressure of ≥140 mm Hg, diastolic ≥90 mm Hg, or use of any antihypertensive medication. Body mass index was calculated as weight in kilograms divided by the height in meters squared. Diabetes was defined as fasting blood glucose of ≥126 mg/dL or use of insulin or oral hypoglycemic agents. An endpoint adjudication panel consisting of 3 investigators determined prevalent CVD (angina pectoris, coronary insufficiency, myocardial infarction, stroke, transient ischemic attack, or heart failure), using standardized criteria.[26]

Statistical Analysis

We summarized data on demographics and clinical covariates using mean±1 standard deviation (SD) or median (25th, 75th percentile) for continuous variables and percentages for categorical variables. We natural log-transformed biomarkers and plaque volumes (cm^3) and standardized them to mean=0 and SD=1 to normalize the skewed distribution. Linear correlations between pairs of biomarkers have been previously described and are described in Table 1.[27] We used logistic regression models to examine the association between inflammatory biomarkers and presence/absence of aortic plaque. Further, because approximately half the participants did not have evidence of aortic plaque on CMR, we used Tobit regression to evaluate the association between inflammatory biomarkers and aortic plaque volume as a continuous variable. Tobit models are censored regression models that are applicable when a seemingly normally distributed dependent variable has floor or ceiling effects.[28] In multivariable models, we adjusted for age at CMR scan and the following covariates collected at Cycle 7 examination: sex, body mass index, cigarette smoking, hypertension, diabetes mellitus, total/HDL cholesterol, lipid-lowering treatment, and prevalent CVD.

To reduce inflation of Type I error due to multiple testing, we determined a "global" *P* value for the biomarker panel as a whole using a likelihood ratio test, which, in our case, was a χ^2 test with 10 degrees of freedom calculated as—2 log-likelihood for the model with clinical covariates and 10 biomarkers minus 2 log-likelihood for the model with clinical covariates only. If the global *P*-value reached statistical significance (2-sided $P<0.05$), we planned to use backward elimination to select a parsimonious set of informative biomarkers with $P<0.05$ for retention in the final model.

Lastly, to assess for effect modification of the associations between inflammatory biomarkers and aortic plaque by sex, we included interaction terms in age-adjusted regression models for each biomarker. In these analyses, we accounted for multiple testing by applying Bonferroni adjustment; a $P\leq0.005$ was used to indicate statistical significance for each interaction term.

We used the SAS procedures PROC LOGISTIC, PROC REG, and PROC LIFEREG with normal distribution option to fit logistic, linear, and Tobit regression models, respectively. We conducted all analyses using SAS Version 9.3 (SAS Institute).

Results

Participant Characteristics

Of the 1794 Offspring participants who underwent aortic CMR imaging, 31 (1.7%) were incomplete, 28 (1.6%) did not have plaque data, 37 (2.1%) had poor image quality precluding measurement of aortic plaques, 34 (1.8%) did not have biomarker data, and 148 (8.2%) had at least 1 missing covariate, leaving 1547 participants (86%) eligible for analysis.

Table 1. Age- and Sex-adjusted Correlations Among Biomarkers*

Other Biomarker	CRP	Fibrinogen	ICAM-1	IL-6	IL-18	LpPLA2a	LpPLA2m	MCP-1	P-selectin	TNFR-2
CRP	1.000									
Fibrinogen	0.45442 <0.0001	1.000								
ICAM-1	0.19187 <0.0001	0.17618 <0.0001	1.000							
IL-6	0.45274 <0.0001	0.35347 <0.0001	0.23445 <0.0001	1.000						
IL-18	0.16938 <0.0001	0.10856 <0.0001	0.30983 <0.0001	0.20336 <0.0001	1.000					
LpPLA2a	−0.02645 0.2985	0.03074 0.2268	0.19527 <0.0001	0.06418 0.0116	0.20820 <0.0001	1.000				
LpPLA2m	0.00340 0.8938	0.02667 0.2946	0.10704 <0.0001	0.06697 0.0084	0.11828 <0.0001	0.49874 <0.0001	1.000			
MCP-1	0.09032 0.0004	0.04237 0.0958	0.07876 0.0019	0.15891 <0.0001	0.05286 0.0376	0.01397 0.5830	0.03045 0.2313	1.000		
P-selectin	0.14125 <0.0001	0.12454 <0.0001	0.17588 <0.0001	0.15488 <0.0001	0.10669 <0.0001	0.07319 0.0040	0.06826 0.0072	0.09192 0.0003	1.000	
TNFR-2	0.21070 <0.0001	0.18052 <0.0001	0.35456 <0.0001	0.29168 <0.0001	0.32732 <0.0001	0.18794 <0.0001	0.16364 <0.0001	0.10588 <0.0001	0.14134 <0.0001	1.000

CRP indicates C-reactive protein; ICAM-1, intracellular adhesion molecule-1; IL-6, interleukin-6; IL-18, interleukin-18; LpPLA2a, lipoprotein-associated phospholipase A2 activity; LpPLA2m, lipoprotein-associated phospholipase A2 mass; MCP-1, monocyte chemoattractant protein-1; TNFR-2, tumor necrosis factor receptor 2.
*Values are age- and sex-adjusted Spearman's rank correlation coefficients (n=1547).

Overall, participants who underwent CMR, represented a healthier cohort (3 years younger, less obese, lower systolic blood pressure, smoked less, less hypertensive, less likely to be diabetic, less likely to be on lipid lowering medication or antihypertensive medications, and less likely to have prevalent CVD) (Table 2). These differences are likely due to the fact that the population who underwent CMR had to be free of prevalent CVD, not be claustrophobic, and not be above a certain weight in order to fit in the CMR scanner.

Median time between Cycle 7 examination and acquisition of CMR scans was 4.4 years (1.8, 6.8 years). Our cohort comprised of middle-aged to older adults, slightly more than half were women, and 428 (28%) were obese. More detailed clinical characteristics are listed in Table 3. As previously reported, 738 of 1547 participants (48%) had evidence of aortic plaque, predominantly located in the abdomen (plaque prevalence ratio of abdomen to thorax, 7:1).[23] All those with thoracic plaque also had abdominal plaque. Among those with aortic plaque, the median (25th and 75th percentile) plaque volumes were the following: total plaque burden was 0.4 cm^3 (0.2, 5.5) in men and 0.5 cm^3 (0.2, 3.8) in women; abdominal plaque burden was 0.5 cm^3 (0.29, 3.8) in men and 0.4 cm^3 (0.26, 3.8) in women; thoracic plaque burden was 0.4 cm^3 (0.2, 4.3) in men and 0.4 cm^3 (0.2, 3.4) in women.

Aortic Atherosclerosis and Biomarkers

Median (25th to 75th percentile) levels of biomarkers by aortic plaque status are shown in Table 4. After adjusting for age, sex, and clinical covariates, the presence of aortic plaque was not associated with the multibiomarker panel (Global P=0.53) (Table 5). In age- and sex-adjusted analyses, a modest statistically significant association was noted between continuous aortic plaque volume and multibiomarker panel (Global P=0.03). However, this association was attenuated after further adjustment for clinical covariates (Global P=0.09). Backward elimination was not performed because the global P values for both logistic regression and Tobit regression models after adjustment for all covariates were greater than 0.05.

Aortic Atherosclerosis, Biomarkers, and Sex

In logistic regression models evaluating aortic plaque as a dichotomous variable (present/absent), we did not observe

Table 2. Clinical Characteristics at Examination Cycle 7 Among Participants With and Without CMR

Characteristics	CMR (n=1547)	No CMR (n=2137)	P Value
Age, y	60±9	63±10	<0.0001
Sex, n (%)			
Men	725 (47)	901 (45)	
Women	822 (53)	1092 (55)	0.3266
Body mass index, kg/m^2	28±5	28±6	0.0009
Obesity, n (%)	420±27	569±32	0.0030
Total cholesterol, mg/dL	201±36	200±38	0.3410
Total HDL:total cholesterol	0.27±0.1	0.27±0.1	0.5625
Systolic blood pressure, mm Hg	125±18	129±20	<0.0001
Diastolic blood pressure, mm Hg	74±10	74±10	0.2605
HDL cholesterol, mg/dL	54±17	54±17	0.9674
Alcohol (number of drinks per week)	3±3	3±4	0.1121
Triglycerides, mg/dL	134±95	140±83	0.1121
Current smoker, n (%)	328 (10)	155 (17)	<0.0001
Hypertension, n (%)	629 (41)	1006 (51)	<0.0001
Diabetes mellitus, n (%)	262 (9)	133 (15)	<0.0001
Use of statin medications, n (%)	281 (18)	461 (23)	0.0003
Use of antihypertensive therapy, n (%)	451 (29)	768 (39)	<0.0001
Use of hormone replacement therapy, n (%)	276 (18)	276 (16)	0.0717
Daily use of aspirin, n (%)	467 (30)	588 (33)	0.0741
Prevalent cardiovascular disease, n (%)	136 (9)	344 (17)	<0.0001

Values are mean±standard deviation or percentages as appropriate. Obesity defined as a body mass index of greater than 30 kg/m^2. CMR indicates cardiovascular magnetic resonance imaging; HDL, high-density lipoprotein.

Table 3. Clinical Characteristics at Examination Cycle 7

Characteristics	All (n=1547)	No Plaque (n=810)	Plaque (n=737)
Age, y	60±9	58±9	62±9
Sex, n (%)			
Men	726 (47)	386 (48)	340 (46)
Women	821 (53)	424 (52)	397 (54)
Body mass index, kg/m^2	28±5	28±55	28±5
Obesity, n (%)	428 (28)	234 (55)	194 (45)
Total cholesterol, mg/dL	201±36	200±36	202±36
LDL-c	121±32	120±32	122±32
Total HDL:total cholesterol	4±1	4±1	4±1
Systolic blood pressure, mm Hg	125±18	124±17	127±18
Diastolic blood pressure, mm Hg	74±10	75±9	73±10
HDL cholesterol, mg/dL	54±17	54±17	53±17
Alcohol (number of drinks per week)	3±3	2±3	3±4
Triglycerides, mg/dL	134±95	130±91	139±99
Current smoker, n (%)	155 (10)	66 (8)	89 (12)
Hypertension, n (%)	634 (41)	295 (36)	339 (46)
Diabetes mellitus, n (%)	158 (10)	66 (8)	92 (12)
Use of statin medications, n (%)	281 (18)	116 (14)	165 (22)
Use of antihypertensive therapy, n (%)	451 (29)	210 (26)	241 (33)
Use of hormone replacement therapy, n (%)	276 (18)	145 (18)	131 (18)
Daily use of aspirin, n (%)	467 (30)	220 (27)	247 (34)
Prevalent cardiovascular disease, n (%)	52 (3)	13 (2)	39 (5)

Values are mean±standard deviation or percentages as appropriate. Obesity defined as a body mass index >30 kg/m^2. HDL indicates high-density lipoprotein; LDL-c, calculated low-density lipoprotein.

effect modification by sex of the association between any biomarker and presence/absence of aortic atherosclerosis (Table 6, all *P*-values >0.09). Similarly, in Tobit regression analyses restricted to participants with quantified aortic plaque volume, we did not note significant sex interactions with any individual biomarker after adjusting for age and

Table 4. Biomarkers According to Aortic Plaque Status Determined by Cardiovascular Magnetic Resonance Imaging

	No Plaque (n=810)		Plaque (n=737)	
Biomarker Panel	Median	25th, 75th Percentile	Median	25th, 75th Percentile
High-sensitivity C-reactive protein, mg/L	1.8	0.9, 4.1	2.0	0.9, 4.9
Fibrinogen, mg/dL	365	323, 405	369	330, 415
Intracellular adhesion molecule-1, ng/mL	234	205, 265	241	209, 280
Interleukin-6, pg/mL	2.3	1.6, 3.7	2.7	1.8, 4.2
Interleukin-18, pg/mL	225	163, 300	238	178, 307
LpPLA2 activity, ng/mL	139	118, 165	140	119, 166
LpPLA2 mass, nmol/(mL min)	285	228, 358	283	228, 353
Monocyte chemoattractant protein-1, pg/mL	300	242, 370	310	251, 387
P-selectin, pg/mL	35	28, 43	36	28, 45
Tumor necrosis factor receptor-2, pg/mL	1896	1606, 2292	1971	1677, 2367

LpPLA2 indicates lipoprotein-associated phospholipase A2.

Table 5. Results of Regression Models Examining the Association Between Circulating Biomarker Levels and Aortic Plaque

Description of Model	χ^2 Statistic (10 degrees of freedom)	Global *P* Value
Logistic Regression Models (Aortic plaque as a dichotomous variable, yes/no)		
Adjusted for age and sex	15.9	0.10
Adjusted for age, sex, and other covariates*	9.0	0.53
Tobit Regression Models (Aortic plaque as a continuous variable, per cm^3 increase)		
Adjusted for age and sex	26.4	0.003
Adjusted for age, sex, and other covariates*	16.5	0.09

*Adjusted for the following covariates at exam cycle 7: age at CMR scan, body mass index, hypertension, total cholesterol/high density lipoprotein, sex, lipid lower treatment, smoking, diabetes, and prevalent cardiovascular disease.

clinical covariates (all $P \geq 0.01$). For each of the biomarkers in the panel of 10, we conducted post-hoc statistical power calculations and determined that at most we had 52% statistical power to detect the odds ratio associated with a 1 standard deviation unit of the logarithm of the biomarker value. Therefore, we did not have sufficient power to detect a clinically significant effect of the biomarkers studied.

Discussion

In our community-based study, we found no statistically significant associations between a panel of inflammatory and atherosclerotic biomarkers and aortic plaque (presence or volume) after adjustment for age, sex, and clinical covariates. While our secondary analyses also found no interaction between any biomarker and sex among participants with aortic plaque after multivariable adjustment, we did not have sufficient power to detect a clinically significant effect of the biomarkers studied.

Our results differ from that of prior studies, which found associations between similar biomarkers and other noninvasive measures of atherosclerosis among a comparable cohort.[13,17,20] This disparity may be due to several factors. First, previous studies predominantly used carotid ultrasound and x-ray techniques (coronary calcium) for noninvasive measures of atherosclerosis. CMR is a specialized, advanced imaging modality and its ability to detect and measure aortic plaque among asymptomatic individuals may be more sensitive due to its greater anatomical coverage (abdominal and thoracic aorta versus carotid/coronary arteries). As mentioned earlier, nearly half of our cohort (48%, n=738) had evidence of subclinical atheroma by CMR. Consequently, CMR may identify subclinical atherosclerosis in participants with normal or marginally elevated biomarkers, thus attenuating any significant associations and biasing our results toward the null. Also, whereas our biomarker panel and CMR scans were conducted within the same examination cycle (Cycle 7), they

Table 6. *P* Values for Effect Modification Between Sex and Individual Biomarkers in Logistic and Tobit Regression Models Predicting Aortic Plaque (Binary and Continuous Aortic Plaque)

	P Values*			
	Logistic Regression Models†		Tobit Regression Models‡	
Biomarker	Age-Adjusted	Multivariable-Adjusted§	Age-Adjusted	Multivariable-Adjusted§
High-sensitivity C-reactive protein, mg/L	0.86	0.64	0.01	0.04
Fibrinogen, mg/dL	0.83	0.99	0.15	0.17
Intracellular adhesion molecule-1, ng/mL	0.16	0.09	0.02	0.03
Interleukin-6, pg/mL	0.29	0.24	0.09	0.06
Interleukin-18, pg/mL	0.87	0.99	0.42	0.43
LpPLA2 activity, ng/mL	0.53	0.99	0.82	0.47
LpPLA2 mass, nmol/(mL min)	0.61	0.90	0.31	0.17
Monocyte chemoattractant protein-1, pg/mL	0.28	0.29	0.35	0.38
P-selectin, pg/mL	0.20	0.32	0.04	0.06
Tumor necrosis factor receptor-2, pg/mL	0.10	0.13	0.04	0.05

LpPLA2 indicates lipoprotein-associated phospholipase A2.
*Bonferroni adjusted $P<0.005$ was used to indicate statistical significance.
†Aortic plaque was modeled as a dichotomous variable, yes/no.
‡Aortic plaque was modeled as a continuous variable, per cm^3 increase.
§Adjusted for age, body mass index, cigarette smoking, hypertension, diabetes mellitus, total/HDL cholesterol ratio, lipid lower treatment, and prevalent cardiovascular disease.

were not obtained concomitantly. However, prior Framingham Heart Study investigations with even greater time delays (eg, Cycle 5 biomarkers, Cycle 6 imaging, median time between biomarker acquisition and imaging >6 years) were still able to find relationships between a similar panel of biomarkers and noninvasive imaging.[17,20] Additionally, aortic atherosclerosis measured by CMR may represent a very early form of plaque burden, which initiates in the abdomen and is only seen in the thorax, coronaries, and carotid arteries much later in its progression. It may be that this early form of atherosclerosis may not be strongly associated with our biomarker panel, which has been associated with atheroma in the coronaries and carotid arteries. Furthermore, these biomarkers also may be closely associated with clinical states leading to the development of atherosclerosis (eg, obesity, elevated cholesterol, diabetes), which may explain the attenuation of statistical significance after further adjustment for clinical covariates. Our findings are consistent with a systematic review of 12 studies assessing the relationship of similar biomarkers (hs-CRP, MCP-1, LpPLA2, IL-6) with coronary calcium that found weak relationships that were no longer significant when corrected for traditional risk factors.[19]

Our results underscore the strengths and limitations of the use of biomarkers for the identification of subclinical atherosclerosis and the importance of traditional risk factors. Whereas multiple biomarkers have been associated with subclinical CVD, by themselves, they each provide minimal incremental value to predict subclinical atherosclerosis for an individual person after a noninvasive assessment. Moreover, despite the considerable interest in identifying participants with subclinical atherosclerosis and CVD risk through biomarkers, studies using specific biomarkers have generally shown only modest effects over and above traditional risk factors.[29–31]

Strengths and Limitations

The strengths of this study include the community-based cohort design, the rigorous biomarker quality control, a single-expert CMR reader for aortic plaque measurements blinded to clinical data, and standardized measures of clinical variables. However, there were several limitations to our analysis that merit comment. Our study is observational and not designed to characterize atherosclerotic plaque components or address clinical outcomes outside of noninvasive imaging. Additionally, our CMR scanning was performed during the 7th examination cycle (1998-2001) using a 1.5 MRI system, which was current and up to date for its time. Significant advancements in MRI have occurred since then, including 3T MRI scanners (approved by the FDA in 2002), which may have increased the sensitivity of detecting smaller aortic plaques. We selected inflammatory and atherosclerotic biomarkers based on biological plausibility, prior data, and availability in our cohort at exam Cycle 7. Although our biomarker panel and CMR scans were conducted within the same exam cycle, they were not obtained concomitantly. Medication usage (aspirin, antihypertensives, and statins) may have affected biomarker concentrations, particularly among those with evidence of aortic atheroma. Given the observational study design and nonrandomized medication usage, our investigation was not well suited to inform the relations between medications and subclinical or clinical CVD. Finally the FHS Offspring cohort is predominantly of European ancestry, which may limit generalizability to individuals to other races/ethnicities.

Conclusion

In our community-based CMR cohort, we found no significant associations between the multibiomarker panel with the presence or volume of aortic plaque as measured by CMR. Our findings highlight the strengths and limitations of biomarkers for the identification of subclinical atherosclerosis and the importance of traditional risk factors.

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Disclosures

None.

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