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Inflammation and coronary artery calcification in South Asians: The Mediators of Atherosclerosis in South Asians Living in America (MASALA) study

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ABSTRACT

Background and aims: Inflammatory biomarkers and adipocytokines (IBA) may contribute to atherosclerosis by promoting vascular inflammation. The association between IBA and coronary artery calcium (CAC), a marker of subclinical atherosclerosis, is not well defined in South Asians (SA). We hypothesized that IBA (high sensitivity C-reactive protein [hsCRP], tumor necrosis factor alpha [TNF-α], adiponectin, and leptin) were independently associated with and improved discrimination of CAC among SA.

Methods: We analyzed IBA and CAC among participants in the prospective Mediators of Atherosclerosis in South Asians Living in America (MASALA) study. We used logistic regression models to examine cross-sectional associations of IBA with CAC presence (CAC >0) and severity (CAC >100), and C-statistics to assess the incremental contribution of each IBA to traditional risk factors (TRF) from the AHA/ACC Pooled Cohort Equations (PCE) for discrimination of CAC.

Results: Among 906 participants in the MASALA study, women (n = 420) had significantly higher levels of hsCRP, adiponectin, and leptin but lower levels of TNF-α than men ($p < .01$ for all). There was no significant association between any of the four IBA and either CAC category in multivariable-adjusted models, respectively. Lastly, none of the four IBA improved discrimination of CAC presence or severity when added to elements of the PCE.

Conclusions: IBA were not associated with CAC presence or severity in the MASALA population. IBA did not help identify SA at risk of subclinical atherosclerosis, although associations with ASCVD events remain unclear. In SA, CAC may have a distinct pathophysiology independent of inflammation as measured by IBA.

1. Introduction

Inflammation plays a pivotal role in the development of atherosclerosis and is a marker of increased cardiovascular risk [1]. Multiple epidemiological and clinical studies have shown an independent association between various inflammatory biomarkers

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and adipocytokines (IBA) and incident atherosclerotic cardiovascular disease (ASCVD) [2–8]. Asymptomatic individuals with elevated inflammatory markers may be predisposed to advanced subclinical atherosclerosis [9]. Coronary artery calcium (CAC), a surrogate marker of subclinical atherosclerosis, is a robust predictor of ASCVD among asymptomatic individuals [10–12]. However, previous studies investigating the association between IBA and CAC have been inconclusive [13–17].

South Asians (SA) have a high rate of ASCVD mortality at younger ages, which is not fully explained by traditional risk factors (TRF) [18–21]. Current ASCVD risk prediction models may underestimate risk in SA [22]. Determining the association between IBA and CAC in SA may help identify those who are at higher risk and could potentially benefit from more aggressive preventive therapy.

Therefore, we sought to determine the association of two inflammatory biomarkers, high sensitivity C-reactive protein (hsCRP) and tumor necrosis factor-alpha (TNF-α), and two adipocytokines, adiponectin and leptin, with CAC presence and severity among immigrant SA. We hypothesized that an independent association exists between IBA and CAC among participants of the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study.

2. Materials and methods

2.1. Study population

The MASALA study protocol and details of the study methods have been previously published [23]. Briefly, MASALA is a prospective, community-based cohort of 906 asymptomatic immigrant SA men and women, aged 40–84 years old, recruited from two clinical field centers (University of California, San Francisco [UCSF] and Northwestern University [NWU], Chicago) between October 2010 and March 2013 (baseline examination). The study protocol conforms to the ethical guidelines of the 1975 declaration of Helsinki, institutional review boards at each site approved the study, and all participants provided written informed consent.

2.2. Study measurements and definitions

All participants completed a detailed questionnaire to ascertain medical history, socio-demographic information, family history of coronary heart disease in first degree relatives, smoking status, and medication use. Seated resting blood pressure was measured three times using an automated blood pressure monitor (V100 Vital sign monitor, GE Medical Systems, Fairfield, CT) and the average of the last two readings used. Hypertension was defined as medication use for hypertension, or a systolic blood pressure above 140 mm Hg or a diastolic blood pressure above 90 mm Hg [23]. Weight and height measurements were used to calculate body mass index (BMI) as kg/m^2.

Blood samples were obtained after a 12-h fast. Fasting plasma glucose was measured by the glucose oxidase method. Diabetes was diagnosed if a participant was using an anti-diabetic medication, had fasting plasma glucose greater than 126 mg/dl, or plasma glucose greater than 200 mg/dl on two-hour glucose tolerance testing [23]. Total cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol were measured by enzymatic methods (Quest, San Jose, CA) and low-density lipoprotein (LDL) cholesterol was calculated by the Friedewald equation [24]. Visceral abdominal tissue (VAT) area was calculated using computed tomography (CT) scans of the abdomen as previously described [25].

2.3. Inflammatory markers and adipocytokines

High sensitivity C-reactive protein levels were measured using the BNII nephelometer (N High Sensitivity CRP; Siemens Healthcare Diagnostics, Deerfield, IL) from samples that were processed and stored at −80 °C for batched assays serum; the intra-assay coefficient of variation was 3.5%. TNF-α and leptin levels were measured using the Millipore Adipokine panel B (EMD Millipore, Billerica, MA) and the intra-assay coefficient of variation was 18.6% for TNF-α and 6.0% for leptin. Serum total adiponectin was measured using Millipore Luminex adipokine panel A (EMD Millipore, Billerica, MA) with an inter-assay coefficient of variation was 2.3–4.1%.

2.4. Coronary artery calcium measurement

Detailed methods of CAC score ascertainment in the MASALA study have been described [26]. Briefly, non-contrast cardiac CT scans were performed using a cardiac gated electron-beam computed tomography scanner (UCSF: Phillips 16D scanner or a Toshiba MSD Aquilion 64; and NWU: Siemens Sensation Cardiac 64 Scanner). A four-sample calibration phantom was placed under the thorax for attenuation correction. All scans were interpreted at the CT reading center at Harbor-UCLA using the Rephot Imaging Software. Phantom-adjusted CAC Agatston scores were reported for each of the four major coronary arteries and the summed score was used.

2.5. Statistical analysis

Baseline characteristics were summarized as counts with proportions for categorical variables and means and standard deviation (SD) or medians and interquartile range [25th-75th percentile] for continuous variables, as appropriate. The Chi-square test was used for comparing categorical variables and the *t*-test or Kruskal Wallis test was used for continuous variables to test for differences by sex. Univariable and multivariable-adjusted logistic regression models (model 1 - adjusted for age, sex, and education; and model 2 – additionally adjusted for diabetes, cigarette smoking status, hypertension, total cholesterol, HDL cholesterol, lipid-lowering medication use, and family history of CHD) were used for studying the association of each of the four IBA with coronary artery calcium presence (CAC >0) and severity (CAC >100).

IBA levels were grouped into tertiles, with lower two tertiles serving as reference group for analyses involving hsCRP, TNF- α, and leptin; and upper two tertiles serving as reference for adiponectin. We formally tested for the presence of interaction with sex in the association of each IBA and CAC category using multiplicative interaction terms. Results were also reported using CAC as a continuous variable, Ln (CAC+1) using multivariable linear regression models sequentially adjusted as listed above. In sensitivity analyses, we excluded statin users (n = 243), further adjusted for BMI and VAT, utilized the four IBA as log-transformed variables in our models, and used a 'dyslipidemia' variable (defined as HDL <40 mg/dl for men or <50 mg/dl for women, LDL ≥130 mg/dl, TG ≥150 mg/dl or lipid-lowering medication use) in model 2 instead of incorporating total cholesterol, HDL cholesterol, and lipid-lowering medication use separately, respectively.

We examined the utility of IBA tertiles to discriminate CAC when added to risk factors from the 2013 ACC/AHA Pooled Cohort Equation (PCE) for ASCVD risk estimation (age, sex, total cholesterol, HDL-cholesterol, systolic blood pressure, anti-hypertensive therapy use, diabetes and smoking status) [27]. Discrimination was evaluated using the area under the receiver operating characteristic curves (AUC) for CAC prevalence and severity. As sensitivity analysis, we utilized IBA as log-transformed variables in our discrimination analysis. All analyses were conducted using Stata version 13.1 (Stata Corporation, College Station, TX). A two-sided *p*-value of <.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

The baseline characteristics of the study population are shown in Table 1. Men comprised 54% of the MASALA study population and were older, had a higher prevalence of hypertension, diabetes, smoking, and education status of bachelor's degree and above. Additionally, men had higher statin use with lower total-, HDL-, and LDL-cholesterol levels. Overall, women had lower TNF-α levels and higher hsCRP, adiponectin, and leptin, but a lower prevalence of CAC presence and severity, compared to men. IBA levels across CAC categories are described in Figs. 1 and 2. Participants with no CAC had higher hsCRP and leptin levels, but lower TNF-α levels as compared to those with CAC >0 (Fig. 1). Similarly, participants with CAC <100 had higher leptin and lower TNF-α levels as compared to those with CAC ≥100 (Fig. 2).

3.2. Association between IBA and presence of coronary artery calcium

The four IBA analyzed in our study were differentially associated with the presence of CAC (Table 2A). In unadjusted models, significant inverse associations between high levels of hsCRP and leptin, and a direct association with TNF-α and CAC presence were observed in the overall population. In both demographic- and multivariable-adjusted models these associations were lost. Interaction testing by sex was significant for adiponectin ($p = .01$) and leptin ($p = .046$). In analyses stratified by sex, low adiponectin levels were inversely associated with CAC presence in women in both unadjusted and multivariable-adjusted models.

3.3. Association between IBA and coronary artery calcium severity

The association between IBA and CAC severity (>100) is described in Table 2B. High levels of TNF-α were directly associated and high levels of leptin were inversely associated with CAC severity in unadjusted models. However, these associations were lost after demographic and risk-factor adjustment. Unlike CAC prevalence, interaction testing revealed no significant interaction between sex and the four IBA for CAC severity.

3.4. Improvement of CAC discrimination by using IBA in addition to PCE

The addition of each individual IBA to elements of the ACC/AHA PCE did not improve discrimination of CAC presence or severity (Supplementary Table 1).

Table 1
Baseline characteristics of the MASALA study population, 2010–2013.

Characteristics	Overall (N = 906)	Men (N = 486)	Women (N = 420)	*p* value
Age, years (SD)	55 (9)	56 (10)	54 (9)	.004
Educational status (%)				.020
Less than high school	61 (6.7)	22 (4.5)	39 (9.3)	
Less than bachelor's degree	49 (5.4)	26 (5.4)	23 (5.5)	
Bachelor's degree or above	796 (87.9)	438 (90.1)	358 (85.2)	
Family history of CHD (%)	412 (46)	207 (43)	205 (49)	.070
Smoking status (%)				<.001
Never	751 (83)	345 (71)	406 (97)	
Former	124 (14)	115 (24)	9 (2)	
Current	31 (3)	26 (5)	5 (1)	
Body mass index, kg/m^2 (SD)	26.0 (4.3)	25.9 (4.4)	26.1 (4.2)	.55
SBP, mmHg (SD)	125 (16)	126 (15)	123 (17)	<.001
DBP, mmHg (SD)	73 (10)	77 (9)	70 (10)	<.001
Hypertension (%)	367 (41)	218 (45)	149 (35)	.004
Total cholesterol, mg/dL (SD)	188 (37)	182 (37)	194 (36)	<.001
HDL cholesterol, mg/dL (SD)	50 (13)	45 (11)	56 (14)	<.001
Triglycerides, mg/dL (SD)	119 (69)	127 (81)	112 (59)	<.001
LDL cholesterol, mg/dL (SD)	111 (32)	109 (32)	114 (32)	.010
Fasting plasma glucose, mg/dL (SD)	102 (27)	105 (28)	98 (25)	<.001
Diabetes (%)	189 (21)	122 (25)	67 (16)	.001
Visceral fat area, cm^2 (SD)	134 (56)	152 (59)	114 (44)	<.001
IBAs				
hsCRP, μg/mL [25th-75th percentile]	1.23 [0.65–2.77]	0.96 [0.54–1.98]	1.69 [0.81–3.65]	<.001
TNF-α, pg/mL [25th-75th percentile]	2.60 [1.86–3.63]	2.75 [1.95–3.67]	2.43 [1.74–3.57]	.007
Adiponectin, ng/mL [25th-75th percentile]	10,622 [6959–15,309]	8618 [5713–12,029]	13,814 [9950–17,896]	<.001
Leptin, pg/mL [25th-75th percentile]	12,594 [7187–21,391]	8457 [5016–12,922]	19,902 [13,472–28,090]	<.001
Anti-hypertensive use (%)	279 (31)	172 (35)	107 (25)	.001
Statin use (%)	243 (27)	152 (31)	91 (22)	.001
Coronary artery calcium				
CAC score [25th-75th percentile]	0 [0–49]	13 [0–139]	0 [0-0]	<.001
CAC >0 (%)	381 (42)	282 (59)	99 (24)	<.001
CAC >100 (%)	175 (19)	139 (29)	36 (9)	<.001

Continuous data presented as means (SD) or medians [25th-75th percentile] and categorical data as number (%).
SBP: systolic blood pressure, DBP: diastolic blood pressure, LDL: low-density lipoprotein, HDL: high-density lipoprotein, CHD: coronary heart disease, IBAs: inflammatory biomarkers and adipocytokines, hsCRP: high sensitivity C-reactive protein, TNF-α: tumor necrosis factor-alpha, CAC: coronary artery calcium, CHD: coronary heart disease.

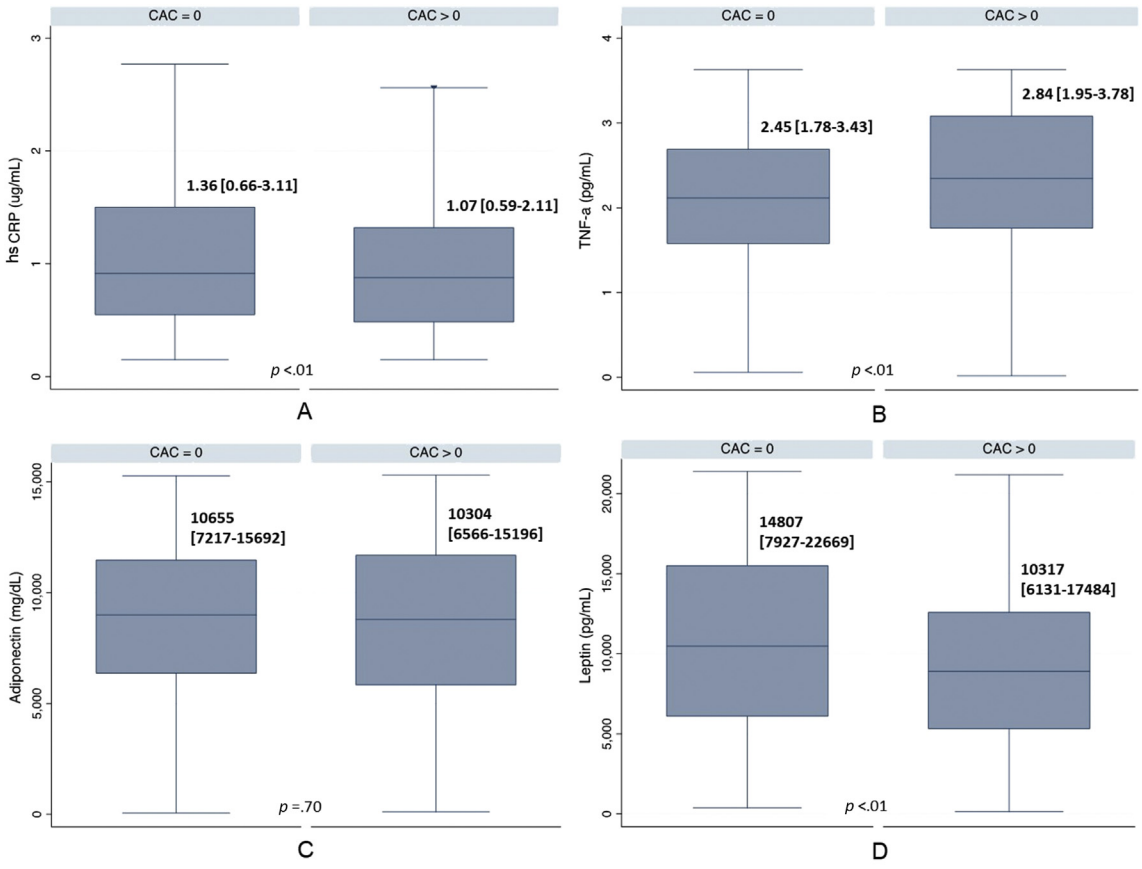

Fig. 1. Comparison of inflammatory biomarker and adipocytokine levels among participants with absent CAC and CAC >0. IBA levels presented as median [25th-75th percentile] along with *p*-value for comparison.

3.5. Sensitivity analyses

The mean differences in continuous CAC scores [ln (CAC+1)] across IBA tertiles are shown in Supplementary Table 2. Overall, results were quantitatively similar to CAC presence and severity for each of the four IBA, yielding non-significant associations after multivariable adjustment. In analyses excluding 243 statin users, high leptin levels were inversely associated with CAC >100 among men: adjusted OR (95% CI), 0.24 (0.07–0.83) (Supplementary Tables 3A and B). Interaction testing by sex was significant only with adiponectin in multivariable-adjusted models for CAC presence ($p = .046$). Low adiponectin levels were inversely associated with CAC presence in women, after further adjustment for BMI and VAT after full adjustment (Supplementary Tables 4A and B). Additionally, elevated hsCRP levels was inversely associated with CAC presence. In the multivariable-adjusted model utilizing the four IBA as log-transformed variables there was no significant association between any of the IBA and CAC presence or severity (Supplementary Tables 5A and B). In the multivariable-adjusted model utilizing the dyslipidemia variable, the inverse association of low adiponectin with CAC presence in women persisted (Supplementary Tables 6A and B). Lastly, the addition of each individual IBA as a log-transformed variable to elements of the AHA/ACC PCE failed to improve discrimination of CAC presence or severity (Supplementary Table 7).

4. Discussion

In this prospective, contemporary, community-based cohort of South Asians living in the US and free of ASCVD at baseline, hsCRP, TNF-α, adiponectin, and leptin levels were not associated with, and did not improve discrimination of CAC presence or severity. Overall, SA women had higher levels of hsCRP and adipocytokines, but lower CAC prevalence and severity compared to men. Lastly, the lowest tertile of adiponectin was associated with lower odds of any CAC in SA women.

Our study is the first to prospectively evaluate the association between markers of inflammation and adipocytokines with CAC in South Asians. Similar to a recent study, we observed significant sex-based differences in IBA levels [28]. Previous studies in white and black populations have reported conflicting results regarding the association between IBA and CAC [9,13–17,29–34]. The demographic profile of participants included in these studies is described in Supplementary Table 8. Nevertheless, our results largely parallel those reported in previous studies of individuals free from known CVD [9,14,29].

Specific to markers of inflammation, the Study of Inherited Risk of Coronary Atherosclerosis (SIRCA), the Dallas Heart Study, and the Multi-Ethnic Study of Atherosclerosis (MESA), reported that hsCRP levels were not associated with CAC after adjustment for TRF. Blaha et al. reported that hsCRP was not associated with CAC in the absence of obesity among MESA participants [30]. In the predominantly Caucasian Framingham Offspring Study, hsCRP levels significantly correlated with continuous CAC scores in risk factor-adjusted models for men only [13]. Among Japanese patients with diabetes, high TNF-α levels were independently associated with CAC [31]. With respect to adipocytokines, leptin but not adiponectin, was a significant predictor of CAC presence in both men

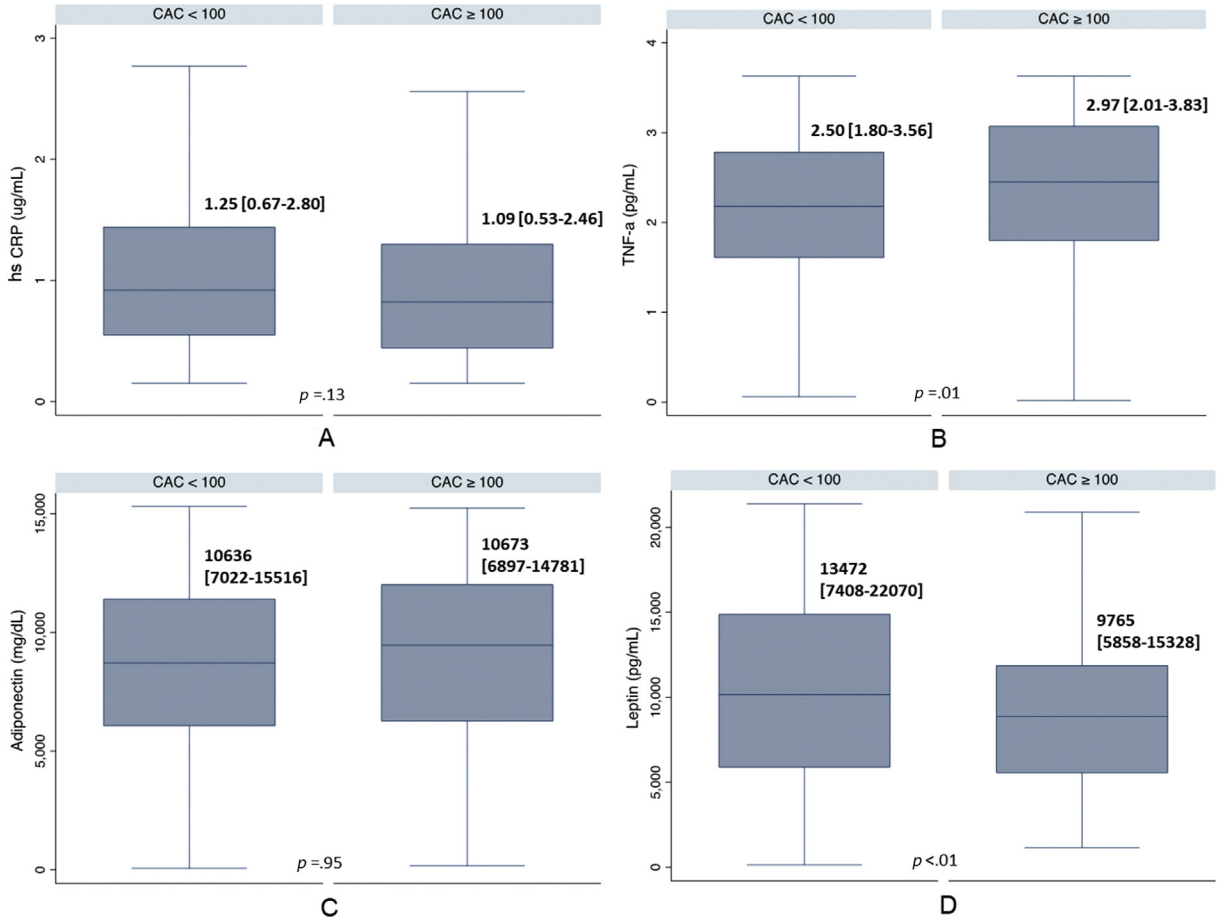

Fig. 2. Comparison of inflammatory biomarker and adipocytokine levels among participants with CAC <100 and CAC ≥100.
IBA levels presented as median [25th-75th percentile] along with *p*-value for comparison.

and women [17]. High leptin levels were independently associated with CAC in the presence of high hsCRP among asymptomatic overweight and obese participants of the SIRCA and Penn Diabetes Heart Study studies [34]. In patients with diabetes, high levels of leptin have been shown to be independently associated with CAC [16]. Our findings are consistent with a systematic review showing weak associations between various inflammatory markers and CAC, which disappeared after traditional risk factor adjustment [35].

The gender differences in IBA levels observed in our study are consistent with previous reports of asymptomatic men and women belonging to different ethnicities [36–40]. For example, in the Dallas Heart Study, hsCRP levels were higher among white and black women as compared to men, respectively [36]. Cartier et al. reported higher hsCRP and lower TNF-α levels among women as compared to men in a healthy Canadian cohort [37]. Similar to our study, Hellstrom et al. observed that asymptomatic Swedish women have higher serum leptin levels than men [38]. Lastly, women are known to have higher circulating levels of adiponectin than men [39,40]. It is plausible that sex-related differences in IBA levels in our cohort may be driven by visceral obesity, adipose tissue proportion and distribution, testosterone levels, and states of insulin resistance [37–40].

The inverse association between low adiponectin levels and CAC presence among female participants in this study merits attention. Prospective data from the Health Professionals Follow-up Study suggested cardio-protective effects of high adiponectin serum concentrations; low levels have been linked to the presence of atherosclerosis and risk of future ASCVD events [41]. Adiponectin is inversely correlated with mixed and non-calcified coronary atherosclerotic plaque burden among individuals undergoing CT-angiography (lesions otherwise not fully captured by CAC testing), and CAC progression independent of other TRFs [15,42]. Conversely, in a community-based cohort of African Americans, high adiponectin levels were not associated with incident CHD events in men and women [43]. Additionally, a Mendelian randomization study using data from the ADIPOGen consortium failed to show an independent association of adiponectin with CHD [44]. Given that CAC is a surrogate marker for future ASCVD events, our findings of an association between lower adiponectin levels and CAC prevalence in females should be interpreted with caution in the context of these heterogeneous historical findings. Future data on incident ASCVD events in MASALA will help clarify the association of adiponectin in SA females with ASCVD risk.

The four IBA evaluated in our study did not improve the discrimination of CAC presence or severity when added to TRF, respectively. In contrast, Qasim et al. reported that leptin significantly improved prediction of CAC beyond TRF, while hsCRP and adiponectin did not [17]. Differing results from our study may be due to the differing racial/ethnic groups studied and the risk equation used (PCE vs. Framingham). This report extends the current literature to SA, demonstrating that the presence of IBA does not correlate with a higher risk of subclinical atherosclerosis presence or severity.

Atherosclerotic calcification is a complex and regulated process

Table 2
Association of inflammatory biomarkers and adipocytokines with presence (CAC >0) and severity (CAC >100) of coronary artery calcium.

	Unadjusted	Model 1[a]	Model 2[b]	*p* interaction by sex[c]
	Odds ratio (95% confidence interval)			
CAC presence (CAC >0)				
hsCRP	0.62 (0.47–0.83)	0.89 (0.63–1.26)	0.74 (0.51–1.07)	.68
Tertile 3 *vs.* Tertiles 1–2				
Male	0.81 (0.53–1.24)	0.88 (0.55–1.41)	0.83 (0.50–1.37)	
Female	0.87 (0.55–1.38)	0.88 (0.53–1.49)	0.66 (0.37–1.19)	
TNF-α	**1.46 (1.10–1.94)**	1.05 (0.75–1.47)	0.88 (0.61–1.25)	.44
Tertile 3 *vs.* Tertiles 1–2				
Male	1.05 (0.72–1.53)	0.87 (0.57–1.33)	0.75 (0.48–1.19)	
Female	**2.04 (1.26–3.28)**	1.33 (0.77–2.28)	1.01 (0.55–1.86)	
Adiponectin	1.15 (0.87–1.53)	1.06 (0.74–1.51)	0.94 (0.64–1.38)	**.01**
Tertile 1 *vs.* Tertiles 2–3				
Male	0.72 (0.50–1.03)	1.33 (0.87–2.04)	1.18 (0.74–1.89)	
Female	**0.44 (0.21–0.92)**	0.45 (0.20–1.01)	**0.32 (0.13–0.81)**	
Leptin	**0.49 (0.36–0.66)**	1.15 (0.77–1.73)	1.00 (0.65–1.55)	**.046**
Tertile 3 *vs.* Tertiles 1–2				
Male	1.65 (0.89–3.08)	1.93 (0.96–3.87)	1.94 (0.94–4.03)	
Female	0.91 (0.58–1.45)	0.88 (0.52–1.48)	0.65 (0.36–1.17)	
CAC severity (CAC >100)				
hsCRP	0.81 (0.56–1.16)	1.28 (0.84–1.96)	1.17 (0.74–1.85)	.69
Tertile 3 *vs.* Tertiles 1–2				
Male	1.05 (0.66–1.67)	1.21 (0.72–2.04)	1.22 (0.70–2.13)	
Female	1.23 (0.61–2.46)	1.43 (0.68–3.01)	1.03 (0.44–2.42)	
TNF-α	**1.65 (1.17–2.32)**	1.25 (0.85–1.85)	0.99 (0.65–1.51)	.37
Tertile 3 *vs.* Tertiles 1–2				
Male	1.24 (0.83–1.87)	1.05 (0.66–1.66)	0.84 (0.52–1.38)	
Female	**2.82 (1.40–5.69)**	1.79 (0.84–3.80)	1.28 (0.55–2.97)	
Adiponectin	0.90 (0.62–1.28)	0.99 (0.64–1.51)	0.78 (0.48–1.24)	.57
Tertile 1 *vs.* Tertiles 2–3				
Male	**0.53 (0.35–0.79)**	1.03 (0.64–1.65)	0.80 (0.47–1.34)	
Female	0.63 (0.21–1.83)	0.78 (0.25–2.40)	0.54 (0.14–2.03)	
Leptin	**0.43 (0.29–0.64)**	0.89 (0.53–1.49)	0.80 (0.46–1.38)	.52
Tertile 3 *vs.* Tertiles 1–2				
Male	0.73 (0.37–1.45)	0.67 (0.32–1.43)	0.62 (0.28–1.38)	
Female	1.17 (0.57–2.40)	1.23 (0.57–2.64)	1.14 (0.48–2.71)	

hsCRP: high sensitivity C-reactive protein, TNF-α: tumor necrosis factor-alpha, CAC: coronary artery calcium, CHD: coronary heart disease.
Bold items are significant.
[a] Model 1 adjusted for age, sex, and education.
[b] Model 2 adjusted for age, sex, education, diabetes mellitus, cigarette smoking status, hypertension, total cholesterol, HDL cholesterol, lipid-lowering medication use, and family history of CHD.
[c] Interaction testing done in model 2.

widely believed to be triggered by underlying inflammation, resulting in a cascade of mineralization regulating proteins and ultimately, calcification [45]. Plaque morphology changes over time and markers such as hsCRP and adiponectin, for example, may be more strongly associated plaque vulnerability, rupture, and thrombosis [46,47]. Consistent with our study, observation such as these argue that IBA and CAC likely reflect different pathophysiologic processes, and hence provide distinct information towards ASCVD risk prediction [35].

The results of this study should be interpreted in the context of several limitations. First, we describe the cross-sectional association between IBA and CAC among South Asians; as such, we cannot establish a causal association or temporality and our results are not generalizable without longitudinal data. However, available evidence suggests that CAC and IBA predict incident cardiovascular events [10,48–50]. Second, our sample size is small and limits the generalizability of this study and under-powers subgroup analyses. Third, we have studied only four IBA in our cohort and these cannot map every inflammatory mechanism that may be associated with subclinical atherosclerosis measured using CAC [51]. Fourth, participants of the MASALA study are relatively young and may have had non-calcified coronary artery plaque which subsequently was not captured on CAC scanning [52]. This would explain the low prevalence of CAC >0 in our study population (42%), which in turn might have attenuated the association between IBA and CAC. Lastly, the MASALA sample was limited to SA populations from two specific geographic regions in the US, which may not represent other SA in the United States or at a global level. However, the similarity of MASALA population to the Census 2010 South Asian data has been previously reported [23].

4.1. Conclusions

In the MASALA study, inflammatory biomarkers and adipocytokines were not independently associated with CAC presence and severity. The indirect association of adiponectin levels with CAC presence in SA women should be cautiously interpreted given an overall small sample size. As the MASALA cohort continues to mature, incident ASCVD data will clarify the utility of integrating circulating biomarker information into risk prediction models as it applies to those of SA descent. Similar to other non-Asian populations, CAC may have a distinct pathophysiology independent of inflammation, likely contributing complementary information towards ASCVD risk.

Conflict of interest

The authors declared they do not have anything to disclose

regarding conflict of interest with respect to this manuscript.

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Author contributions

A.M. interpreted the data and wrote the manuscript; J.P. and P.H.J. designed the study, acquired the data, reviewed and wrote the manuscript; M.A.R. analyzed the data and critically reviewed the manuscript; C.R.A. analyzed the data and reviewed the manuscript; A.M.K. and N.K. interpreted the data, revised the manuscript, and are principal investigators for the MASALA study; I.J.N., M.J.B., K.N., R.S.B. interpreted the data and revised the manuscript.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.atherosclerosis.2018.01.033.

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