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Psychosocial Factors Associated with Subclinical Atherosclerosis in South Asians: The MASALA Study

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Abstract South Asians have the highest rates of premature atherosclerotic cardiovascular disease amongst all ethnic groups in the world; however this risk cannot be fully explained by traditional risk factors. Participants from the Mediators of Atherosclerosis in South Asians Living in America Study were included in this cross-sectional analysis. The purpose of this study was to investigate the association of psychosocial factors (including anger, anxiety, depressive symptoms, current and chronic stress, and everyday hassles) with carotid intima-media thickness (CIMT). Three multivariate models were examined to evaluate the association between the psychosocial factors and CIMT. Findings suggest that the impact of psychosocial factors on subclinical atherosclerosis is differential for South Asian men and women. For men, anxiety and depression were associated; while for women, stress was associated with common carotid intima media thickness, independent of traditional CVD risk factors, diet and physical activity.

Keywords Risk factors · Atherosclerosis · South Asians · MASALA Study

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Background

A number of studies have demonstrated that South Asians (SAs) have an increased risk for diabetes, cardiovascular disease and the metabolic syndrome [1–4]. SAs have the highest rates of premature atherosclerotic cardiovascular disease (ASCVD) amongst all ethnic groups in the world [2, 5]. In addition, ASCVD occurs about 10 years earlier among SAs than among other populations worldwide [3, 5]. Myocardial infarction (MI), the major complication of ASCVD presents among SAs with a median age of 52 years compared to 62 years in Europeans and 63 years among the Chinese [6]. In North America, SAs have the highest prevalence of ASCVD with age-adjusted mortality rates two to three times higher than those of Caucasians [5, 7].

This increased risk of ASCVD and related mortality cannot be fully explained by the traditional risk factors for ASCVD [7]. SAs have a lower body mass index (BMI) and lower body weight than Caucasians. In addition, SAs immigrants to the United States tend to have high educational attainment and a high socioeconomic status—both of which traditionally protect against ASCVD mortality. This calls for an investigation into other modifiable risk factors which may contribute to ASCVD among this population.

Several studies have shown a link between psychosocial factors and clinical ASCVD, however few studies have reported associations with subclinical ASCVD [8, 9].

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Findings from the Multi-Ethnic study of Atherosclerosis (MESA) have shown that psychosocial factors such as anger, anxiety and depression may be associated with the development of cardiovascular disease as measured by intima media thickness and coronary artery calcium [10, 11]. In a study by Ohira and colleagues, anger scores were associated with the presence of higher carotid intima media thickness even after adjustment for age, sex and ethnicity. These associations were stronger in men compared to women and also varied by ethnicity [10]. In another study, life stress was found to be associated with the development of subclinical atherosclerosis through unhealthy coping behaviors such as smoking, sedentary lifestyle and caloric intake [12]. However, there is currently no information available regarding the relationship of these factors with early indicators of subclinical cardiovascular disease in the high risk SA population.

In this analysis, we investigated the relationship between psychosocial factors and subclinical cardiovascular disease as measured by carotid intima media thickness (IMT). Since prior literature indicates that the effect of psychosocial factors on ASCVD varies by sex, we conducted separate analyses for men and women [8, 10, 11, 13–15].

Methods

Study Design and Population

The MASALA prospective cohort study includes 906 South Asian men and women recruited from two clinical sites—the University of California, San Francisco (UCSF) and Northwestern University [16]. To be included in MASALA, participants had to have South Asian ancestry, be between the ages of 40–84 years old, and be able to speak and/or read English, Hindi, or Urdu. The baseline clinical examination was done between 2010 and 2013 and study enrollment was stratified by age and sex at both sites [16]. Those with physician diagnosed MI, stroke, transient ischemic attack, heart failure, angina, use of nitroglycerin, active treatment for cancer or history of cardiovascular procedures (such as coronary artery bypass, graft surgery, angioplasty, valve replacement, pacemaker or defibrillator implantation, or any surgery on heart or arteries) were excluded. Additionally, participants who have atrial fibrillation, have impaired cognitive ability, have life expectancy less than 5 years due to serious medical illness, plan to move out of the study region within the next 5 years, or live in a nursing home/on waiting list for one were also excluded. Additional details pertaining to study design have been published elsewhere [16]. The study was approved by the IRB at UCSF and Northwestern University.

Psychosocial Measurements

Symptoms of anger, anxiety, depression, stress, chronic stress, and hassle were studied for their potential role as CVD risk factors. The psychosocial status of each participant was self-reported by a coordinator-administered questionnaire. Each measurement instrument used below has been widely used and validated [11, 16–20].

Anger/Anxiety

Anger and anxiety symptoms were measured using the 10-item Spielberger trait anger and anxiety scales (STAXI). These scales measure patients' anger and anxiety using items such as "I am quick tempered" and "I have a fiery temper" and response options include: almost never (1); sometimes (2); often (3); almost always (4). The scores range from 10 to 40 and are categorized as followed: low (10–14), moderate (15–21), and high (22–40) for anger and anxiety [18, 20].

Depression

Depressive symptoms were measured using the 15-item Center for Epidemiologic Studies—Depression Scale (CES-D). This scale measures a subject's depressive symptoms through questions such as "I felt fearful" and "I felt depressed". Response options include: rarely or none of the time (1); some or a little of the time (2); a moderate amount of the time (3); most of the time (4). The scale's scores range from 0 to 60, with a score of 16 or greater indicating depressive symptoms [11].

Current/Chronic Stress

Feelings of current stress and chronic stress were measured using the five-item chronic stress burden scale, which measures current life stress and life stress over the past 6 months. Burden is assessed using questions such as, "Are you having serious ongoing health problems?" For each question with an affirmative response, subjects must then answer how stressful the experience is on a scale from "not very stressful (0); moderately stressful (1); to very stressful (2)." Subjects must also indicate if the experience has been a problem for 6 months or more. Subjects who answer yes for two or more questions are considered to have "high stress level" [11, 18].

Everyday Hassles

The everyday hassles score was measured using the nine-item scale from the everyday discrimination scale, adapted from The Detroit Area Study. This scale captures the daily minor incidents of unfair treatment through questions such as, “People act as if they think you are not smart” and “You are called names or insults.” The range of responses include: almost every day (1); at least once a week (2); a few times a month (3); a few times a year (4); less than once a year (5); never (6). Score ranges continuously from 9-54, and higher scores are indicative of more everyday hassles [19].

Outcome Variables

Subclinical atherosclerosis was determined through measurements of the internal and common CIMT. High resolution B-mode ultrasonography was used to capture images of the right and left internal CIMT (ICA) and common CIMT (CCA). To perform carotid ultrasound recordings, the GE Vivid 7 ultrasound system with an 8-MHz linear array transducer (General Electric Healthcare) and the Acuson Sequoia C256 system (Siemens Healthcare, Mountain View, CA) were used at NWU and UCSF, respectively. All wall thickness measurements were calculated at the Reading Center in Wake Forest University. The measurement of CIMT consisted of 12 predefined segments (6 per side), including 1 transverse scan sequence of the common carotid through the bulb and 5 longitudinal images taken from both the right and left carotid arteries for each subject [16]. We studied both common CIMT and internal CIMT because prior literature indicated that the two measurements are related to different CVD risk factors [16].

Covariates

Participants’ systolic blood pressure (SBP), hypertension medication use (yes/no), current smoking behavior (yes/no), body-mass index (in kg/m^2), diabetes mellitus (yes/no), cholesterol ratio, education level, and physical activity were included as covariates in the multivariable analyses. Physical activity was measured in metabolic equivalent of tasks (MET) in minutes per week using the Typical Week’s Physical Activity Questionnaire [21]. SBP was measured using the automated blood pressure monitor (V100 Vital Signs Monitor; GE Healthcare, Fairfield, CT) with the average of the last 2 readings being used for analysis. BMI was measured using a standard balance beam scale or digital weighing scale and stadiometer. Cholesterol ratio was calculated as a participant’s total cholesterol/HDL cholesterol [16].

Participants’ level of social support was measured using the six-item scale from the Enhancing Recovery in Coronary Heart Disease Patients Study Social Support Instrument. This scale measures the range of emotional social support a subject has. Questions in this scale include: “Is there someone available to you who shows you love and affection?” and “Is there someone available to help you with daily chores?” The range of responses include: none of the time (1); a little of the time (2); some of the time (3); most of the time (4); all of the time (5). The overall score ranges from 6-30, with a score less than or equal to 18 indicative of the highest risk category for lack of social support (low vs. high) [17, 18].

The covariates were selected because of their role as potential confounders in the association between psychosocial factors and subclinical atherosclerosis and CIMT [10]. In addition, these same covariates were used in the study by Ohira et al. [10] which studied the association between anger, anxiety, and depression on subclinical atherosclerosis in non-Hispanic Whites, African American, Hispanic, and Chinese populations in the MESA Study.

Dietary Data

Dietary data was collected using a validated Food Frequency Questionnaire (FFQ) from the Study of Health Assessment and Risk in Ethnic (SHARE) groups South Asian FFQ [22]. This FFQ (163 total items) contains 61 items that are unique to the South Asian diet and assesses usual eating habits, frequency and portion sizes over the last 12 months.

Analysis of the dietary data among MASALA participants showed that three major dietary patterns were prevalent among SA–Western/animal protein; fried snacks, sweets and high-fat dairy; and fruits, vegetables, nuts and legumes [23]. Of these, the animal protein and fried snacks, sweets and high-fat dairy patterns were associated with adverse metabolic outcomes whereas the fruits, vegetables, nuts and legumes pattern was associated with a decreased prevalence of hypertension and metabolic syndrome [23]. Therefore, we included dietary pattern and total caloric intake as additional covariates in our multivariate model.

Statistical Analysis

Descriptive statistics (Chi square, *t* test) were used to compare baseline demographic data, and to compare differences between men and women for all psychosocial measures, outcome variables, and covariates. A Mann–Whitney *U* test was used for variables with a skewed data distribution. Linear regression models estimating mean differences in CCA and ICA per-standard deviation increase in psychosocial factors were performed to determine the relationship between psychosocial variables and the continuous CCA and ICA variables. We developed three models to assess the relationship between psychosocial factors and CIMT—(1) an age-adjusted model; (2) a multivariate model adjusting for age and for the traditional CVD risk factors (SBP, hypertension medication use, current smoking, BMI, diabetes, cholesterol ratio and education level); (3) a multivariate model adjusting for factors above and further adjusting for total caloric intake, dietary pattern and physical activity. Regression diagnostics were checked on the regression models, specifically looking at studentized residuals, leverage, cook's D, and *df* beta to determine influence and outliers. All statistical tests were two-sided with a 5 % significance level.

Prior research has shown that central obesity (measured as waist circumference in cm) is predictive of diabetes and CVD in the South Asian population and may be a better marker than BMI [24]. Therefore, we ran variations of models 2 and 3 for all psychosocial variables including waist circumference instead of BMI as a covariate. We also explored the possibility that social support may serve as a mediator or moderator between the psychosocial factors and CCA/ICA.

Prior studies have reported that the effect of psychosocial variables on subclinical cardiovascular disease markers varies by sex [8, 10, 11, 13–15, 25]. Furthermore, it has been shown that the sex difference in atherosclerosis in the coronary vessels is large, particularly for younger patients and that these differences persist at older ages [26]. In our study, interactions of sex with psychosocial measures were significant for anxiety and depression ($p < 0.05$) but not for other psychosocial variables. However, our data showed that there were significant sex differences in the common and internal CIMT scores, demographic and clinical characteristics and psychosocial variable scores. Therefore, we present results based on sex stratified age-adjusted and multivariable-adjusted models.

When taking into consideration that all psychosocial variables were measured using different questionnaires, we standardized them prior to the regression analyses. By doing this, our psychosocial variables were rescaled to have a mean of zero and a standard deviation of one, thus analyzing all psychosocial variables on one scale. All analyses were conducted using Stata (version 13.1, 2014, StataCorp, College Station, TX).

Results

Of the 906 participants in the MASALA study, 4 participants were excluded due to intervening CHD events, two participants had missing CIMT measurements and six participants (three men and three women) were deemed to be outliers resulting in a final analytic sample of 894 participants. Three men and two women were outliers for depression and one woman was an outlier for the stress outcome. Participants were deemed to be outliers based on univariate and bivariate plots, were >4 SD's away from the mean, and were influential based on regression diagnostics. Outliers that were not influential were retained in the analysis.

We analyzed data from 894 South Asian men and women (477 men, 417 women) free of any ASCVD at the baseline MASALA Study examination. Baseline variables are presented in Table 1. Significant differences were observed between men and women on most demographic, clinical and psychosocial characteristics. Overall, men were slightly older than women in this study (56.0 ± 9.9 vs. 54.4 ± 8.7, $p < 0.01$). Men had a greater average CCA (0.91 vs. 0.84 mm, $p < 0.001$) and greater ICA (1.26 vs. 1.14 mm, $p < 0.001$) compared to women. Women had greater average mean scores of anxiety ($p = 0.04$), depression ($p = 0.05$), current stress ($p = 0.03$), and chronic stress ($p = 0.02$) compared to men (Table 1). A higher percentage of men were currently smoking ($p < 0.001$), had type 2 diabetes and hypertension and were taking hypertension medications ($p = 0.001$ for all). A greater proportion of men followed the Western diet while a greater proportion of women followed the fruits/vegetables/nuts/legumes diet ($p < 0.001$). Overall, women had a healthier profile with lower rates of smoking, diabetes and hypertension while having higher HDL cholesterol, greater physical activity and a healthier diet. Table 2 shows correlations between the psychosocial measures used in the study.

Table 3 presents sex stratified mean differences in CCA per 1-SD increase in psychosocial factors for the 3 models—(1) age-adjusted, (2) multivariable-adjusted (for traditional CVD risk factors) and (3) multivariate, diet, and physical activity adjusted. In all 3 models for women, current life stress and life stress over the past 6 months remained positively associated with CCA [mean difference per-SD increase (CI) was 0.018 (0.002–0.035; $p = 0.03$) and 0.017 (0.001–0.034; $p = 0.04$), respectively] in the final model adjusted for traditional CVD risk factors, diet and physical activity. There was no relationship between stress and CCA for males.

We found that among men, anxiety was positively associated with CCA [mean difference per 1-SD increase (CI) was 0.023 (0.004–0.041; $p = 0.02$)] in the final model adjusted for traditional CVD risk factors, diet and physical activity. Depressive symptoms were also positively associated with CCA among men, [mean difference per 1-SD increase (CI) was 0.022 (0.003–0.042; $p = 0.03$)] in the model adjusting for traditional CVD risk factors. However, once the model was adjusted for diet and physical activity, these results were no longer significant (Table 2). None of the other psychosocial factors were significantly associated with CCA in the age adjusted, or multivariable adjusted models. ICA was not associated with any psychosocial factor in age-adjusted or multivariable adjusted models (data not shown).

Given that waist circumference is a well-known risk factor for South Asians we ran additional analysis for all

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

Variable	Overall (n = 894)	Men (n = 477)	Women (n = 417)	*P* value
Age	55.3 ± 9.4	56.0 ± 9.9	54.4 ± 8.7	**0.01**
Marital status (%)				
Married	91.4	96.4	85.7	
Divorced	2.8	1.7	4.1	
Widowed	4.0	1.1	7.4	
Single	1.8	0.8	2.9	**<0.001**
Education (%)				
< Bachelor's degree	12.3	10.1	14.9	
≥ Bachelor's degree	87.7	89.9	85.1	**0.03**
Family Income (%)				
<$75,000	26.4	27.1	25.6	
≥$75,000	73.6	72.9	74.4	0.61
Current Smoking (%)	3.2	5.2	0.96	**<0.001**
Physical Activity (MET-min/week)	9409 (7335–11,970)	9150 (7343–11,393)	9690 (7335–12,720)	**0.01**
Total alcoholic drinks/wk	2.5 ± 4.3	3.4 ± 5.0	1.0 ± 1.8	**<0.001**
BMI (kg/m^2)	26.0 ± 4.3	25.9 ± 4.4	26.1 ± 4.2	0.50
Total cholesterol, mg/dL	188 ± 37	183 ± 37	193 ± 35	**<0.001**
HDL cholesterol, mg/dL	50 ± 13	45 ± 11	56 ± 14	**<0.001**
SBP (mm Hg)	125 ± 16	126 ± 15	123 ± 17	**<0.001**
Antihypertensive med use (%)	30.9	35.4	25.6	**0.001**
Diabetes prevalence (%)	25.4	28.7	21.6	**0.001**
Hypertension prevalence (%)	40.5	44.9	35.5	**0.001**
Total caloric intake	1669.3 ± 520.7	1758.2 ± 570.5	1567.6 ± 436.2	**<0.001**
Dietary pattern (%)				
Western	33.6	39.4	27.1	
Sweets/refined grains	34.0	35.6	32.1	
Fruits/vegetables	32.5	25.0	40.8	**<0.001**
Common carotid IMT (mm)	0.87 ± 0.22	0.91 ± 0.23	0.84 ± 0.20	**<0.001**
Internal carotid IMT (mm)	1.20 ± 0.44	1.26 ± 0.48	1.14 ± 0.39	**<0.001**
Anger[a]	16.0 ± 3.9	15.9 ± 3.8	16 .2 ± 4.0	0.32
Anxiety[b]	16 .1 ± 4.4	15.8 ± 4.5	16.4 ± 4.2	**0.04**
Depression[c]	7.6 ± 6.9	7.2 ± 6.7	8.1 ± 7.1	**0.05**
Current stress[d]	0.81 ± 1.0	0.74 ± 1.0	0.89 ± 1.1	**0.03**
Chronic stress[d]	0.72 ± 0.96	0.65 ± 0.9	0.80 ± 1.0	**0.03**
Social support[e]	24.9 ± 4.9	25.2 ± 4.9	24.7 ± 4.8	0.12
Hassle[f]	15.0 ± 6.0	15.2 ± 5.5	14.8 ± 6.5	0.26

Results in bold are statistically significant

* n (%) or mean ± SD is displayed; median (interquartile range) is shown for skewed variables

[a] Spielberger trait—Anger Scale

[b] Spielberger trait—Anxiety Scale

[c] Center for Epidemiologic Studies Depression Scale (CES-D): ≥16 (depressive symptoms)

[d] Chronic Stresss Scale: 0 (low), 1 (moderate), ≥2 (high)

[e] Social Support Score as measured by ENRICHD (enhanced recovery in coronary heart disease) instrument: low emotional support (≤18), high (>18)

[f] Everyday Discrimination Scale: range from 9 to 54, measured continuously with higher score indicating more everyday hassles

psychosocial variables including waist circumference instead of BMI as a covariate for models 2 and 3. The results were essentially unchanged (data not shown).

Table 4 shows associations between tertiles of anxiety and depressive symptoms and demographic/clinical characteristics. We found that among men, exercise time

Table 2 Correlations between the psychosocial measures (n = 894)

	Anger	Anxiety	Depression	Current stress	6-month stress	Hassle
Anger	1.00					
Anxiety	0.36***	1.00				
Depression	0.35***	0.67***	1.00			
Current Stress	0.14***	0.25***	0.30***	1.00		
6-month stress	0.13***	0.25***	0.29***	0.94***	1.00	
Hassle	0.25***	0.34***	0.38***	0.20***	0.18***	1.00

*** $p < 0.001$

Table 3 Sex-stratified association between psychosocial factors and CCA (n = 894)

Psychosocial Measures	CCA Age adjusted model		CCA Multivariable[a] adjusted model		CCA [b]MV + diet/exercise adjusted	
	Men	Women	Men	Women	Men	Women
Anger						
Mean difference in 1-SD increase (95 % CI)	0.013 (−0.006 to 0.032)	0.009 (−0.008 to 0.025)	0.013 (−0.005 to 0.032)	0.004 (−0.012 to 0.021)	0.009 (−0.010 to 0.029)	0.004 (−0.013 to 0.020)
p value	0.19	0.30	0.16	0.60	0.33	0.65
Anxiety						
Mean difference in 1-SD increase (95 % CI)	**0.023 (0.005–0.041)**	−0.013 (−0.031 to 0.005)	**0.022 (0.004–0.040)**	−0.014 (−0.032 to 0.004)	**0.023 (0.004–0.041)**	−0.011 (−0.029 to 0.006)
p value	**0.01**	0.15	**0.02**	0.12	**0.02**	0.19
Depression						
Mean difference in 1-SD increase (95 % CI)	**0.024 (0.004 to 0.043)**	−0.009 (−0.026 to 0.008)	**0.022 (0.003–0.042)**	−0.011 (−0.028 to 0.006)	0.019 (−0.001 to 0.039)	−0.011 (−0.028 to 0.006)
p value	**0.02**	0.31	**0.03**	0.21	0.063	0.21
Current stress						
Mean difference in 1-SD increase (95 % CI)	0.007 (−0.012 to 0.026)	**0.024 (0.007–0.040)**	0.005 (−0.014 to 0.024)	**0.018 (0.002–0.035)**	0.003 (−0.016 to 0.022)	**0.018 (0.002–0.035)**
p value	0.48	**0.01**	0.62	**0.03**	0.73	**0.03**
6-Month stress						
Mean difference in 1-SD increase (95 % CI)	0.010 (−0.010 to 0.029)	**0.021 (0.005–0.038)**	0.007 (−0.012 to 0.026)	**0.018 (0.002–0.034)**	0.006 (−0.013 to 0.025)	**0.017 (0.001–0.034)**
p value	0.33	**0.01**	0.47	**0.03**	0.53	**0.04**
Hassle						
Mean difference in 1-SD increase (95 % CI)	0.010 (−0.010 to 0.030)	−0.005 (−0.021 to 0.010)	0.012 (−0.008 to 0.032)	−0.009 (−0.024 to 0.007)	0.012 (−0.007 to 0.033)	−0.010 (−0.025 to 0.006)
p value	0.33	0.50	0.24	0.27	0.23	0.20

Results in bold are statistically significant

[a] Model adjusted for the traditional CVD risk factors—SBP, hypertension medication use, current smoking, BMI, diabetes, cholesterol ratio and education level

[b] Model adjusted for factors above + dietary pattern and physical activity

(MET-mins/week) decreased (p-trend = 0.01) and TV watching (in mins) (p-trend = 0.03) increased as anxiety scores increased. We also found that time spent watching TV increased significantly as depressive symptom scores increased (p-trend = 0.01) and exercise time (MET-mins/week) decreased, although not significantly (p-trend = 0.10). Additionally, we found that social support scores were inversely correlated with anxiety and depressive symptom scores among men (p-trend < 0.001 for both). We also found an increased prevalence of hypertension and unhealthy diet as anxiety levels increased (p-trend = 0.04 for both).

Table 5 shows associations between high stress and 6 month stress symptoms and demographic/clinical characteristics among women. Once again we found that exercise time decreased as stress (p-trend = 0.04) and

Table 4 Means or prevalence of cardiovascular risk factors by tertiles of anxiety and depression for males

Male characteristics	Anxiety				Depressive symptoms			
	Tertile 1 (n = 178)	Tertile 2 (n = 155)	Tertile 3 (n = 144)	P-trend	Tertile 1 (n = 172)	Tertile 2 (n = 159)	Tertile 3 (n = 164)	P-trend
Age	55.7 ± 10.3	56.3 ± 9.7	56.1 ± 9.8	0.65	55.1 ± 9.8	55.8 ± 9.7	57.4 ± 10.3	**<0.05**
Exercise (MET-mins/week)	1491.3 ± 1332.4	1376.9 ± 1456.3	1113.3 ± 1108.0	**0.01**	1393.9 ± 1320.1	1371.3 ± 1223.6	1242.5 ± 1417.8	0.10
TV watching (mins)	458.2 ± 399.0	528.6 ± 461.4	570.2 ± 466.1	**0.03**	437.5 ± 345.3	516.4 ± 475.5	604.5 ± 489.6	**0.01**
Alcohol consumption/week	3.0 ± 3.6	3.7 ± 5.6	3.5 ± 5.9	0.88	2.8 ± 3.5	3.7 ± 5.7	3.7 ± 5.8	0.58
Total calories	1790.9 ± 604.3	1729.8 ± 504.1	1748.4 ± 596.2	0.64	1710.4 ± 557.4	1815.7 ± 520.3	1752.0 ± 633.0	0.60
Social support	27.1 ± 3.4	25.3 ± 4.9	22.7 ± 5.5	**<0.001**	27.2 ± 3.4	26.2 ± 3.8	21.7 ± 5.6	**<0.001**
Total cholesterol	181.0 ± 38.9	182.0 ± 35.2	185.3 ± 36.0	0.16	180.7 ± 39.8	180.0 ± 31.2	187.9 ± 38.6	0.08
HDL	45.1 ± 11.4	46.2 ± 11.6	44.3 ± 8.5	0.96	45.2 ± 11.6	45.5 ± 11.2	44.9 ± 8.9	0.87
SBP	125.4 ± 14.9	126.9 ± 14.5	126.7 ± 14.6	0.23	126.0 ± 14.2	125.1 ± 13.7	127.9 ± 16.3	0.35
BMI	25.8 ± 3.7	25.9 ± 5.5	26.1 ± 3.8	0.48	26.1 ± 4.0	25.8 ± 5.3	25.8 ± 3.6	0.73
Waist circumference	95.7 ± 9.6	94.9 ± 9.4	97.1 ± 9.5	0.18	95.8 ± 9.6	95.2 ± 9.7	96.7 ± 9.1	0.33
Hypertension (%)	40.5	43.2	52.1	**0.04**	44.2	39.0	52.1	0.19
Metabolic syndrome (%)	33.2	31.0	39.6	0.25	35.5	33.3	34.3	0.81
Diabetes (%)	29.4	26.6	30.1	0.93	25.2	30.4	31.0	0.24
Smoking (%)	3.9	6.5	5.6	0.49	4.7	4.4	6.9	0.40
Total calories	1790 ± 604	1730 ± 504	1748 ± 596	0.64	1710 ± 557	1815 ± 520	1752 ± 633	0.60
Dietary pattern (%)								
Western	36.6	40.4	42.0		37.5	36.9	44.6	
Snacks/sweets	32.0	35.1	40.6		35.7	35.0	36.0	
Fruits/vegetables	31.4	24.5	17.4	0.04	26.8	28.0	19.4	0.13
Anger	14.5 ± 3.2	16.0 ± 3.3	17.5 ± 4.3	**<0.001**	14.6 ± 3.1	15.6 ± 3.4	17.9 ± 4.2	**<0.001**
Stress	0.5 ± 0.8	0.7 ± 0.9	1.1 ± 1.2	**<0.001**	0.5 ± 0.8	0.6 ± 0.9	1.1 ± 1.2	**<0.001**
Chronic stress	0.4 ± 0.7	0.6 ± 0.8	1.0 ± 1.1	**<0.001**	0.5 ± 0.7	0.5 ± 0.8	1.0 ± 1.1	**<0.001**
Everyday Hassles	13.6 ± 4.5	15.0 ± 5.2	17.6 ± 6.1	**<0.001**	13.7 ± 4.2	14.6 ± 5.0	17.8 ± 6.5	**<0.001**
Common CIMT	0.9 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	0.08	0.9 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	**<0.05**
Internal CIMT	1.2 ± 0.5	1.2 ± 0.5	1.3 ± 0.5	0.18	1.2 ± 0.4	1.2 ± 0.4	1.3 ± 0.5	0.24

Results in bold are statistically significant

Table 5 Means or prevalence of cardiovascular risk factors for females with stress/chronic stress

Female characteristics	Stress			6 month stress		
	Low (n = 191)	High (n = 226)	P-trend	Low (n = 207)	High (n = 210)	P-trend
Age	55.0 ± 8.4	53.8 ± 8.8	0.14	54.9 ± 8.5	53.8 ± 8.8	0.18
Exercise (MET-mins/week)	1419.9 ± 1407.0	1148.0 ± 1282.6	**0.04**	1446.2 ± 1440.6	1101.4 ± 1225.7	**0.02**
TV watching (mins)	557.7 ± 449.5	613.3 ± 529.3	0.48	565.4 ± 448.5	609.9 ± 536.2	0.71
Alcohol consumption/week	0.9 ± 1.5	1.1 ± 1.9	0.42	0.8 ± 1.4	1.1 ± 2.0	0.19
Total calories	1543.1 ± 451.9	1588.3 ± 422.3	0.21	1541.9 ± 447.8	1592.9 ± 424.0	0.18
Social support	25.4 ± 4.3	24.1 ± 5.0	**0.01**	25.5 ± 4.2	23.9 ± 5.1	**<0.05**
Total cholesterol	193.6 ± 36.8	192.7 ± 34.3	0.86	193.9 ± 37.3	192.4 ± 33.6	0.75
HDL	56.1 ± 12.6	55.1 ± 14.8	0.11	55.7 ± 12.5	55.5 ± 15.0	0.30
SBP	123.2 ± 17.3	122.1 ± 16.0	0.35	123.0 ± 17.2	122.2 ± 16.0	0.47
BMI	25.6 ± 3.8	26.5 ± 4.5	**0.02**	25.6 ± 3.8	26.6 ± 4.6	**0.04**
Waist circumference	88.3 ± 9.6	89.9 ± 10.4	0.11	88.6 ± 9.7	89.7 ± 10.4	0.28
Hypertension (%)	33.1	38.3	0.87	33.8	37.1	0.48
Metabolic syndrome (%)	30.1	40.5	0.08	30.9	37.5	0.16
Diabetes (%)	18.6	23.5	0.68	20.5	22.6	0.60
Smoking (%)	0.0	2.0	0.40	0.5	1.4	0.32
Total calories	1543 ± 451	1588 ± 422	0.21	1541 ± 447	1593 ± 423	0.18
Dietary pattern (%)						
Western	24.2	26.6		24.2	30.0	
Snacks/sweets	30.6	37.0		30.4	33.8	
Fruits/vegetables	45.2	36.4	0.08	45.4	36.2	0.06
Anger	15.9 ± 4.3	16.5 ± 3.8	**0.01**	15.9 ± 4.2	16.4 ± 3.8	0.07
Anxiety	15.7 ± 4.0	17.0 ± 4.2	**<0.05**	15.9 ± 4.1	16.9 ± 4.2	**0.01**
Depression	6.7 ± 6.5	9.3 ± 7.4	**<0.001**	6.8 ± 6.5	9.4 ± 7.5	**<0.001**
Hassle	13.5 ± 6.0	15.8 ± 6.8	**<0.001**	13.8 ± 6.5	15.7 ± 6.4	**<0.001**
Common CIMT	0.8 ± 0.2	0.9 ± 0.2	0.50	0.8 ± 0.2	0.9 ± 0.2	0.59
Internal CIMT	1.1 ± 0.3	1.2 ± 0.4	0.25	1.1 ± 0.3	1.1 ± 0.4	0.07

Results in bold are statistically significant

chronic stress increased (p-trend = 0.02). Additionally, we found that social support scores were inversely correlated with stress (p-trend = 0.01) and 6-month stress scores among women (p-trend < 0.05). We also found that BMI increased as stress (p-trend = 0.02) and chronic stress increased (p-trend = 0.04).

We explored the possibility that social support may serve as a mediator or moderator between the psychosocial factors and CCA/ICA. However, we did not find any evidence to support this in the overall population or after sex stratification.

Discussion

Although a number of studies have investigated psychosocial factors for their role in predicting CVD and subclinical atherosclerosis, these data are limited to certain ethnic groups. The present study sought to examine the relationship of psychosocial factors with carotid intima media thickness in the high risk South Asian population. Our study shows that the impact of psychosocial factors on subclinical atherosclerosis differs between men and women. Anxiety and depressive symptoms were related to increased common carotid intima media thickness among men while stress and chronic stress were associated with increased CCA IMT thickness in women. The magnitude of these effects was comparable to that of a 2 year increase in age for the South Asian participants in our study.

The results of our study can be directly compared to those from the MESA study which examined the associations of anger, anxiety and depressive symptoms with subclinical atherosclerosis in non-Hispanic Whites, African American, Hispanic, and Chinese populations [10]. The MESA Study results found trait anger was positively associated with higher carotid artery IMT. When stratified by sex, associations of anger with CIMT were seen in men but not in women. Further, these associations were only significant among non-Hispanic Whites. No associations were seen among African American, Hispanic and Chinese participants. In our study we found that among South Asians anger was not significantly associated with CCA, or ICA. Prior work on the relationship of anger to CIMT has also showed mixed results with another study showing that trait anger was associated with carotid IMT in black men not among black women or Whites [27]. These results show that the effects of trait anger on subclinical atherosclerosis are inconsistent among racial/ethnic groups and even among men and women.

Because prior literature has suggested that psychosocial factors may differentially impact men and women, we examined the associations of psycholocigal factors in sex-stratified models. We found that anxiety and depressive symptoms were significantly associated with CCA in South Asian men but not among women. In contrast, the MESA Study did not find any association of anxiety or depressive symptoms with subclinical atherosclerosis in any race/ethnic group. In a cross-sectional analysis of the Brazilian longitudinal study of adult health, the authors found that both anxiety and depressive symptoms were associated with carotid intima media thickness in a sample of middle aged adults (the authors did not stratify results based on race/ethnicity or sex) [28]. Further, longitudinal studies have shown that depressive symptoms are associated with accelerated progression of subclinical atherosclerosis over a 3–5 year follow-up [29, 30].

The mechanisms by which anxiety and depressive symptoms may impact carotid wall thickness are not entirely clear. Bonnet et al. [31] proposed that anxiety and depressive symptoms are associated with an unhealthy lifestyle—physical inactivity, unhealthy diet, and smoking in individuals at risk of cardiovascular disease. They found that both anxiety and depressive symptoms were significantly associated with physical inactivity and smoking in both sexes. In their study, unhealthy diets were seen among men with anxiety and depressive symptoms but not in women. In our study, South Asian men with high anxiety and depressive symptoms had significantly less physical activity and spent more time watching TV. Men with increased anxiety and depressive symptoms also reported significantly lower levels of social support. We also found higher rates of hypertension and unhealthier diets in men with higher levels of anxiety. It is possible that unhealthy behaviors tend to cluster in individuals at high risk of cardiovascular disease and modify the impact of psychosocial factors on subclinical atherosclerosis, and we were unable to fully adjust for these behavioral differences. In the study by Mainous et al. they found that although chronic stress did not directly impact subclinical atherosclerosis, it had an indirect effect through unhealthy coping behaviors such as smoking, physical inactivity and a high caloric intake. The results from these studies indicate the importance of modifying lifestyle behaviors and coping mechanisms in individuals with poor psychosocial well-being, due to an increased risk of developing CVD.

South Asian women with higher stress/chronic stress had increased atherosclerosis in our study. These results can be compared to those from another MESA Study where the relationship between stress/chronic stress and atherosclerosis (as measured by coronary artery calcium) was examined. Their results showed that there was no relationship between chronic stress and atherosclerosis, when adjusted for unhealthy life behaviors such as smoking, excessive alcohol use, high caloric intake, sedentary lifestyle and obesity [12]. The authors did not stratify the results based on sex or ethnicity. However, they did find significant indirect pathways between chronic stress and atherosclerosis through smoking, sedentary lifestyle and high caloric intake. In our analysis, we found that women with high stress/chronic stress reported less exercise time, high BMI and low social support. In the literature, work-related stress has been studied in relation to the risk for CVD for men and women [8]. However, for women, it has been hypothesized that stress due to multiple roles, family responsibilities and lack of supportive relationships may be more important. More studies are needed to understand the complex relationships between stress and atherosclerosis for women and elucidate the pathways through which it acts.

Others have found an association between low social support and an increased risk for future cardiac events in participants with low social support [32–35]. In this study of South Asian adults, we did not find an independent association between social support and CIMT; further, social support did not appear to mediate or moderate the association of psychological variables and CIMT. Overall, participants in our study reported fairly high levels of social support [mean for men and women was 25 (range 6–30); with >18 indicating high social support], possibly obscuring the effect of social support on subclinical atherosclerosis. In addition, the social support measure used in the MASALA Study focused on general forms of support (feeling listened to, getting help when needed) and perhaps more specific types of support are needed. Therefore, to detect mediation/moderation effects in future studies, measurements that evaluate specific types and quality of support may be needed.

This study had several strengths. First, this study included a large cohort of South Asian participants recruited from two major geographic locations in the US Second, high resolution ultrasonography was used to precisely capture images of the CIMT, allowing for accurate measurements. Third, all psychosocial scales were standardized prior to analyses, thus increasing the internal validity of the study. Limitations to the study include that it was cross-sectional, and all psychosocial factors were potentially subject to recall or social bias, and these scales were not created or validated in South Asians. However, the scales used in this study are reliable and valid in other race/ethnic populations [10–12, 16, 18]. Psychosocial measures in this study were studied as individual entities, however these factors tend to cluster together, thereby increasing the detrimental effect on a person's health. Future studies should consider studying how a combination of these factors may affect subclinical atherosclerosis.

In summary, our results show that the effects of psychosocial factors are differential for men and women. Anxiety and depressive symptoms are potentially modifiable risk factors that contribute to subclinical atherosclerosis among South Asian men. For women, stress is an independent contributor to subclinical atherosclerosis. Further research is needed to find the mechanisms through which these psychosocial factors affect atherosclerosis, as early detection may allow for risk-reduction interventions, such as lifestyle changes and/or pharmacotherapy, to limit the progression of atherosclerosis to cardiovascular disease.

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