Relation of Menopause With Cardiovascular Risk Factors in South Asian American Women (from the MASALA Study)

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The menopausal transition is a time of accelerating risk of cardiovascular disease (CVD), and promoting cardiovascular health during midlife is an important period of time to prevent CVD in women. The association of menopause with cardiovascular risk factors or subclinical atherosclerosis has not previously been evaluated in South Asian American women, a population with a disproportionately higher CVD burden compared with other race/ethnic groups. The objective of this study was to evaluate the association of menopause with CVD risk factors and subclinical cardiometabolic disease markers. We studied women aged 40 to 84 years from the Mediators of Atherosclerosis in South Asians Living in America study. The association of self-reported menopausal status with multiple demographic and clinical variables was assessed with linear and logistic regression adjusted for age and cardiovascular health behaviors. In a secondary ("age-restricted") analysis, postmenopausal participants outside the age range of premenopausal participants were excluded. In the age-restricted sample, menopause was associated with a higher adjusted odds of hypertension (odds ratio = 1.19, 95% confidence interval [CI] 1.02 to 1.41), and higher systolic blood pressure (β = 6.34, 95% CI 0.82 to 11.87), and significantly higher subcutaneous fat area (β = 42.8, 95% CI 5.8 to 91.4). No significant associations between menopause and ectopic fat deposition, coronary artery calcium, or carotid intima-media thickness were observed. In South Asian American women in the Mediators of Atherosclerosis in South Asians Living in America study, menopause was associated with cardiovascular risk factors and higher subcutaneous fat deposition. Menopausal status is an important factor to examine and address CVD risk factors. **(Am J Cardiol 2022;00:1−6)**

Introduction

Menopause has been associated with a change in cardiovascular risk profile, markers of metabolic health, and subclinical atherosclerosis.[1] Previous studies have shown higher carotid intima-media thickness (CIMT), ectopic fat deposition and coronary artery calcium (CAC) progression in postmenopausal compared with premenopausal women.[2−4] One challenge in assessing the relation between menopause and cardiovascular risk is that observational associations may be influenced by the role of chronologic age on cardiovascular risk factors. Previous longitudinal studies have demonstrated that premenopausal and perimenopausal risk factors can impact postmenopausal subclinical vascular disease and lifetime cardiovascular risk.[5,6] However, the contribution of menopause to cardiovascular risk across race/ethnic groups is less understood. In particular, subjects of South Asian ethnicity have disproportionately more cardiovascular disease (CVD) compared with White and other Asian populations.[7] The influence of menopause on clinical cardiovascular risk factors, and consequently, assessments of CVD risk in South Asian subjects remains unknown. To address this evidence gap, we evaluated the association of menopause with traditional CVD risk factors, as well as measures of subcutaneous and ectopic fat, CAC, and CIMT in premenopausal and postmenopausal women from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study, to inform clinical cardiovascular risk assessment and stratification for South Asian American women.

Methods

We conducted a cross-sectional analysis examining data from both premenopausal and postmenopausal women enrolled in the MASALA study, who were predominantly (98%) born outside the United States. The MASALA study is a community-based cohort of South Asian adults recruited from the San Francisco and Chicago metropolitan areas. The study design and detailed methods have been

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published previously.[8] Briefly, eligible participants were aged 40 to 84 years, self-identified as South Asian (having ≥3 grandparents born in India, Pakistan, Nepal, Bangladesh, or Sri Lanka), without known CVD at enrollment. Study visits were conducted in English, Hindi, or Urdu. For this analysis, 420 women were enrolled from 2010 to 2013 and 136 women were enrolled from 2017 to 2018, for a total of 556 women included. In a secondary "age-restricted" analysis, postmenopausal women outside the age range of the premenopausal participants (40 to 54 years) were excluded (n = 292 excluded), to minimize the influence of age in comparisons across menopausal status. The institutional review boards at the University of California, San Francisco and Northwestern University approved the MASALA study protocol. All study participants provided written informed consent.

Participants were categorized as premenopausal or postmenopausal, defined by self-report in response to questions asking if the participant had already or was currently going through menopause. Measurement of traditional CVD risk factors have previously been described in detail,[8] and were defined as follows: systolic and diastolic blood pressure were measured using an automated blood pressure monitor, and the average of the last 2 of 3 readings was used. Hypertension was defined as a systolic blood pressure of ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or use of a blood pressure lowering medication.[9] Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Obesity was defined according to the World Health Organization Asian BMI cut-off point of BMI ≥ 27.5 kg/m^2.[10] Hyperglycemia was based on hemoglobin A1c, and diagnosis of diabetes mellitus was defined using the gold standard of a 75 g oral glucose tolerance test with a 2-hour postchallenge glucose ≥200 mg/100 ml, or by either fasting serum or plasma glucose ≥126 mg/100 ml or use of diabetes mellitus medication in participants. Cholesterol was assessed on 12-hour fasting samples for total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol levels. Hyperlipidemia was defined as total cholesterol of ≥200 mg/100 ml, triglycerides ≥ 150 mg/100 ml, LDL-cholesterol ≥160, or using a cholesterol-lowering medication. Alcohol use was self-reported as the number of drinks per week. Tobacco use was self-reported as pack-years. Physical activity was assessed using a detailed, semi-qualitative questionnaire adapted from the Cross-Cultural Activity Participation Study and reported as MET-minutes/week.

Abdominal visceral, subcutaneous, and intermuscular fat areas were calculated using abdominal computed tomography (CT) scans. Noncontrast gated cardiac CT images were obtained to assess the pericardial fat volume and hepatic fat content (measured as hepatic fat attenuation). The gated cardiac CT was also used to calculate CAC Agatston scores for each of the 4 major coronary arteries to obtain a summed score. In this study, CAC was evaluated as present (score > 0) versus absent (score = 0). Further details on CT image acquisition have previously been published.[11] CIMT was measured via high-resolution B-mode ultrasonography of the right and left internal and common arteries. Further details on image acquisition and CIMT calculation have previously been detailed.[12]

Participant characteristics were evaluated overall and by menopausal status as mean (SD), median (interquartile range), or frequency (percentage). Multivariable linear or logistic regression was used to evaluate the association of menopause (the primary independent variable) with traditional cardiovascular risk factors (hypertension, systolic blood pressure, obesity, BMI, diabetes mellitus, hemoglobin A1c, hyperlipidemia, and total cholesterol), subcutaneous fat, ectopic fat measures (visceral fat area, intramuscular fat area, pericardial fat volume, and liver fat attenuation), and measures of subclinical atherosclerosis (CAC, common and internal CIMT). For analysis of traditional cardiovascular risk factors and fat measures, models were initially adjusted for age alone. A second model additionally adjusted for smoking status, alcohol use, and physical activity. The fully adjusted model additionally adjusted for hypertension, diabetes mellitus, hyperlipidemia, and obesity (e.g., where hypertension was the independent variable of interest, the fully adjusted model adjusted for diabetes mellitus, hyperlipidemia, and obesity). For evaluation of the association of menopause with CAC and CIMT, the base model adjusted for age alone. A second model additionally adjusted for BMI, diabetes mellitus, hypertension, smoking status, alcohol use, and physical activity. A final model additionally adjusted for LDL, HDL, ectopic fat measures, and use of statin medication.

For all regression analyses, secondary analyses were performed using the premenopausal participants compared with the age-restricted postmenopausal participants. For these models, age adjustment was still performed as in the primary analysis. All statistical analyses were performed with R Software Version 4.0.3, (R Foundation for Statistical Computing, Vienna, Austria). Two-sided p values <0.05 indicated statistical significance.

Results

Participant characteristics are listed in Table 1. There were 154 premenopausal women (mean age 46.7 [SD 3.9] years) and 402 postmenopausal women (mean age 59.4 [7.4] years). The age range of premenopausal women was 40 to 54 years, and there were 110 postmenopausal women in this age range included in the secondary "age-restricted" analysis (mean age 50.8 [3.0] years).

In the primary analysis (Table 2), menopause was associated with significantly higher adjusted odds of hyperlipidemia (odds ratio 1.22, 95% CI 1.03 to 1.44), BMI (β = 1.90, 95% CI 0.31 to 3.49), and subcutaneous fat area (β = 41.5, 95% CI 1.5 to 81.5) after adjustment for smoking status, alcohol use, exercise, hypertension, and diabetes mellitus. Diabetes mellitus in menopause was associated with higher pericardial fat volume after adjustment for age in the initial model, but the association was not statistically significant in the fully adjusted model. There was no association observed between menopause and other cardiovascular risk factors in the adjusted analysis.

In secondary analysis (Table 3) restricting the age of postmenopausal women to the age range of premenopausal women, menopause was associated with significantly higher adjusted odds of hypertension (OR 1.19, 95% CI 1.02 to 1.41), higher systolic blood pressure (β = 6.34, 95%

Table 1
Baseline characteristics of female participants in the MASALA study (2010 to 2018)

	Premenopausal (n = 154)	Postmenopausal (n = 402)	Age-restricted post-menopausal Group* (n = 110)
Age (years)	46.7±3.9	59.4±7.4	50.8±3.0
Alcohol use (drinks/week)	1.23±2.13	0.96±1.74	0.88±1.52
Smoking (pack-years)	0.13±0.82	0.25±2.29	0.04±0.39
Exercise (MET-min/week)†	1,340±1,764	1,210±1,423	1,230±1,699
Medication use			
Antihyperglycemics	12 (7.8%)	67 (16.7%)	8 (7.3%)
Antihypertensives	18 (11.7%)	137 (34.1%)	21 (19.1%)
Statin	18 (11.7%)	124 (30.8%)	18 (16.4%)
BMI (kg/m^2)	25.7±3.81	26.6±4.46	27.0±5.4
Obesity‡	50 (32.5%)	142 (35.3%)	34 (30.9%)
Hemoglobin A1c	5.73±0.43	6.07±0.92	5.87±0.71
Diabetes mellitus§	24.4 (15.6%)	105 (26.1%)	21 (19.1%)
Systolic BP (mm Hg)	116±11.4	127±17.9	122±16.4
Diastolic BP (mm Hg)	70±8.7	71.2±10.3	72.9±9.34
Hypertension¶	26 (16.9%)	183 (45.5%)	30 (27.3%)
Total cholesterol (mg/dL)	190±34.8	195±36.5	200±33.8
LDL (mg/dL)	114±28.8	114±32.5	118±29.1
HDL (mg/dL)	53.1±13.5	57.1±14.0	57.0±14.6
Triglycerides (mg/dL)	117±62	123±59	124±54
Hyperlipidemia‖	67 (43.5%)	295 (73.4%)	73 (66.4%)
Presence of CAC (score>0)	14 (9.1%)	149 (37.1%)	11 (10.0%)
Carotid-intimal thickness, mm			
Common carotid	0.75±0.14	0.88±0.21	0.79±0.13
Internal carotid	0.98±0.21	1.23±0.44	1.07±0.30
Ectopic fat			
Subcutaneous fat area (cm^2)	250±90.2	265±101.0	277±127.0
Visceral fat area (cm^2)	103±38.8	120±46.4	117±48.4
Intramuscular fat area (cm^2)	18.4±6.8	23.1±7.8	21.1±7.6
Pericardial fat volume (cm^3)	38.1±16.1	53.0±23.2	47.1±22.4
Liver fat attenuation (HU)	58.6±10.2	58.0±11.2	56.0±13.2

BMI = body mass index; BP = blood pressure; CAC = coronary artery calcium; HDL = high-density lipoprotein; HU = Hounsfield unit; LDL = low-density lipoprotein.

Data are represented as mean±SD or n (%) unless otherwise indicated.

* Age range was 40 to 54 years.

† Data represented as mean (IQR).

‡ Obesity = BMI ≥ 27.5 kg/m^2.

§ Diabetes mellitus = by fasting glucose or glucose tolerance.

¶ Hypertension = SBP ≥140 mm Hg, or DBP ≥90 mm Hg, or anti-HTN medication use.

‖ Hyperlipidemia = TC ≥200 or LDL ≥160 or Tg ≥150 or cholesterol-lowering medicine use.

CI 0.82 to 11.87) and BMI (β = 2.13, 95% CI 0.03 to 4.23), after adjustment for both cardiovascular risk behaviors and concurrent metabolic disease. Menopause was also associated with a significantly higher subcutaneous fat area (β = 42.8, 95% CI 5.8 to 91.4) in the fully adjusted model. No associations between menopause and any ectopic fat measures were observed.

There were no associations observed between menopause and prevalent CAC, common CIMT, or internal CIMT, after adjustment for age, cardiovascular risk factors and behaviors, and statin medication use, in both the unrestricted and age-restricted cohorts (Table 4).

Discussion

In South Asian American women in the MASALA study, postmenopausal status was significantly associated with hyperlipidemia, higher BMI, and greater subcutaneous fat area. In a secondary age-restricted analysis, menopause was also associated with higher systolic blood pressure and hypertension. These data indicate that menopause is associated with cardiovascular risk factors in South Asian American women.

Postmenopausal status was associated with a higher BMI in this study. Although previous findings have been varied, some studies show that independent of age, BMI was significantly higher in postmenopausal women than in premenopausal women.[13] BMI has also been shown to play a significant role in circulating lipoprotein levels during transition to menopause.[14] This study also implicates menopause as related to hypertension, independent of other comorbidities. Previously, the relation between blood pressure and menopause was thought to be explained by chronologic age rather than by menopause independently.[15,16] However, a recent meta-analysis of 10 studies involving women with early menopause (defined as menopause at <45 years) demonstrated that women with early menopause were at higher risk of arterial hypertension compared with

Table 2
Association of menopause with cardiovascular risk factors and ectopic fat

Variable	Adjusted for age alone		Model 1*		Model 2†	
	OR (95% CI)‡	*p*	*OR (95% CI)*	*p*	*OR (95% CI)*	*p*
Hypertension	1.05 (0.94, 1.17)	0.57	1.07 (0.91, 1.26)	0.59	1.09 (0.93, 1.27)	0.58
Obesity	1.02 (0.90, 1.14)	0.38	1.08 (0.92, 1.27)	0.38	1.08 (0.92, 1.27)	0.38
Diabetes mellitus	0.98 (0.89, 1.09)	0.69	0.91 (0.79, 1.04)	0.52	0.91 (0.79, 1.04)	0.52
Hyperlipidemia	**1.20 (1.07, 1.34)**	**0.03**	**1.21 (1.02, 1.44)**	**0.04**	**1.22 (1.03, 1.44)**	**0.03**
	Beta (95% CI)§	*p*	*Beta (95% CI)*	*p*	*Beta (95% CI)*	*p*
Systolic BP (mm Hg)	2.38 (−1.49, 6.25)	0.23	5.30 (−0.16, 10.76)	0.06	5.36 (−0.19, 10.91)	0.06
BMI (kg/m^2)	**1.31 (0.26, 2.37)**	**0.02**	**2.15 (0.50, 3.81)**	**0.01**	**1.90 (0.31, 3.49)**	**0.02**
HbA1c (%)	0.15 (−0.05, 0.35)	0.15	0.08 (−0.20, 0.36)	0.56	−0.01 (−0.29, 0.26)	0.92
Total cholesterol (mg/dl)	**10.46 (1.60, 19.31)**	**0.02**	9.83 (−2.88, 22.53)	0.13	9.86 (−2.94, 22.66)	0.13
Subcutaneous fat area (cm^2)	19.6 (−8.3, 47.4)	0.17	**48.4 (2.8, 93.9)**	**0.04**	**41.5 (1.5, 81.5)**	**0.04**
Visceral fat area (cm^2)	9.1 (−2.9, 21.1)	0.14	6.2 (−11.4, 23.9)	0.49	0.6 (−14.3, 15.5)	0.94
Intramuscular fat area (cm^2)	1.3 (−0.7, 3.4)	0.19	2.8 (−0.3, 6.0)	0.08	2.2 (−0.8, 5.3)	0.15
Pericardial fat volume (cm^3)	**6.3 (0.7, 11.9)**	**0.03**	4.3 (−3.9, 12.4)	0.30	2.3 (−5.3, 9.9)	0.56
Liver fat attenuation (HU)	−2.2 (−5.2, 0.8)	0.14	−1.4 (−6.1, 3.4)	0.58	−0.3 (−4.5, 3.9)	0.89

Beta = beta coefficient; BMI = body mass index; BP = blood pressure; CI = confidence interval; HbA1c = glycated hemoglobin; HU = Hounsfield unit; OR = odds ratio.

* Model 1: Adjusted additionally for smoking status, alcohol use, and exercise.

† Model 2: Additionally adjusted for hypertension, obesity, diabetes, and hyperlipidemia.

‡ OR (95% CI) for odds of cardiovascular risk factor for postmenopausal (compared with premenopausal), in multivariable logistic regression.

§ Beta (95% CI) for change in ectopic fat measure for postmenopausal (compared with premenopausal), in multivariable linear regression.

those of normal age at menopause.[17] Ultimately, BMI and blood pressure screening may be particularly important to characterize cardiovascular risk in South Asian women after menopause.

There was an association between menopause and greater subcutaneous fat deposition in this study. There have been limited previous studies on body fat deposition in menopause, which have been primarily in animal models and small cohorts. In postmenopausal women with an elevated BMI, a higher waist circumference was associated with higher total mortality and incidence of coronary artery disease and heart failure.[18] Pericardial fat deposition has been an area of particular interest, given its close proximity to the myocardium and role in secreting inflammatory cytokines.[19] Our study did not find any association between any ectopic fat stores (including pericardial fat) and menopausal status. This finding is important because South Asian adults have higher average levels of ectopic fat deposits compared with other race/ethnic groups in the Multi-Ethnic Study of Atherosclerosis (MESA).[20] The significant positive

Table 3
Secondary analysis of the association of menopause with cardiovascular risk factors and ectopic fat in the age-restricted sample

Variables	Adjusted for age alone		Model 1*		Model 2†	
	OR (95% CI)‡	*p*	*OR (95% CI)*	*p*	*OR (95% CI)*	*p*
Hypertension	1.10 (0.98, 1.23)	0.24	1.15 (0.97, 1.36)	0.19	**1.19 (1.02, 1.41)**	**0.02**
Obesity	0.98 (0.86, 1.12)	0.36	1.09 (0.90, 1.32)	0.47	1.10 (0.91, 1.34)	0.45
Diabetes mellitus	1.00 (0.90, 1.12)	0.28	0.92 (0.79, 1.08)	0.63	0.87 (0.74, 1.01)	0.60
Hyperlipidemia	**1.15 (1.00, 1.32)**	**0.03**	1.17 (0.96, 1.43)	0.08	1.20 (0.99, 1.48)	0.07
	Beta (95% CI)§	*p*	*Beta (95% CI)*	*p*	*Beta (95% CI)*	*p*
Systolic BP	2.6 (−1.3, 6.4)	0.19	**6.4 (1.0, 11.7)**	**0.02**	**6.34 (0.82, 11.87)**	**0.03**
BMI	**1.4 (0.1, 2.7)**	**0.03**	**2.5 (0.4, 4.6)**	**0.02**	**2.13 (0.03, 4.23)**	**0.04**
HbA1c	0.10 (−0.06, 0.26)	0.23	0.03 (−0.23, 0.29)	0.83	−0.04 (−0.31, 0.22)	0.74
Total cholesterol	8.0 (−1.8, 17.7)	0.11	7.04 (−6.46, 20.53)	0.30	7.12 (−6.80, 21.05)	0.31
Subcutaneous fat area	22.7 (−10.8, 56.1)	0.18	48.9 (−6.9, 104.7)	0.09	42.8 (−5.8, 91.4)	0.08
Visceral fat area	6.5 (−6.4, 19.4)	0.32	6.4 (−12.9, 25.7)	0.51	0.3 (−16.0, 16.5)	0.98
Intramuscular fat area	1.1 (−1.1, 3.3)	0.32	2.7 (−0.7, 6.1)	0.12	2.1 (−1.2, 5.4)	0.21
Pericardial fat volume	**5.7 (0.1, 11.3)**	**0.04**	5.7 (−3.1, 14.5)	0.20	4.2 (−3.7, 0.3)	0.29
Liver fat attenuation	−2.5 (−6.0, 1.0)	0.16	−1.0 (−6.8, 4.8)	0.72	−0.1 (−5.2, 5.1)	0.98

Beta = beta coefficient; BMI = body mass index; BP = blood pressure; CI = confidence interval; HbA1c = glycated hemoglobin; OR = odds ratio.

* Model 1: Adjusted additionally for smoking status, alcohol use, and exercise.

† Model 2: Additionally adjusted for hypertension, obesity, diabetes, hyperlipidemia.

‡ OR (95% CI) for odds of cardiovascular risk factor for age-matched postmenopausal (compared with premenopausal), in multivariable logistic regression.

§ Beta (95% CI) for change in ectopic fat measure for age-matched postmenopausal (compared with premenopausal), in multivariable linear regression.

Table 4
Association of menopause with subclinical atherosclerosis

Full Sample						
Variables	Adjusted for age alone		Model 1*		Model 2†	
CAC‡	*OR (95% CI)*	p	*OR (95% CI)*	p	*OR (95% CI)*	p
Prevalent CAC	0.95 (0.86, 1.05)	0.36	0.95 (0.82, 1.09)	0.44	0.92 (0.79, 1.08)	0.32
CIMT	*Beta (95% CI)*		*Beta (95% CI)*		*Beta (95% CI)*	
Common carotid IMT	0.02 (−0.03, 0.07)	0.43	0.00 (−0.07, 0.08)	0.92	−0.03 (−0.11, 0.06	0.53
Internal carotid IMT	0.03 (−0.07, 0.12)	0.59	0.04 (−0.08, 0.16)	0.53	0.00 (−0.13, 0.13)	0.99
Secondary analysis: age-restricted sample‡						
	unadjusted		Model 1		Model 2	
CAC	*OR (95% CI)*	*p*	*OR (95% CI)*	*p*	*OR (95% CI)*	*p*
Prevalent CAC	0.95 (0.88, 1.03)	0.25	0.93 (0.83, 1.04)	0.19	0.92 (0.82, 1.05)	0.22
CIMT	*Beta (95% CI)*	*p*	*Beta (95% CI)*	*p*	*Beta (95% CI)*	*p*
Common carotid IMT	0.00 (−0.04, 0.04)	0.87	−0.01 (−0.07, 0.05)	0.81	−0.05 (−0.12, 0.01)	0.10
Internal carotid IMT	0.02 (−0.05, 0.09)	0.63	0.05 (−0.07, 0.16)	0.44	0.00 (−0.12, 0.12)	0.96

Beta = beta coefficient; CAC = coronary artery calcium; CI = confidence interval; CIMT = carotid intima-media thickness; IMT = intima-media thickness; OR = odds ratio.

* Model 1: Adjusted additionally for body mass index, diabetes, hypertension, smoking status, alcohol use, and exercise.

† Model 2: additionally adjusted for low-density lipoprotein, high-density lipoprotein, ectopic fat measures, and use of statin medications.

‡ Secondary analysis includes postmenopausal women only in the age range of premenopausal women.

association we observed of menopause with subcutaneous fat, but no association of menopause with ectopic fat, may provide important context to how cardiovascular risk changes in South Asian American women during the menopausal transition and after menopause. Previous studies in MASALA have shown that ectopic fat deposition was strongly associated with the incidence of diabetes mellitus. Diabetes mellitus, in turn, is one of the strongest predictors for incident CAC and CAC progression.[21,22] Thus, the association of menopausal status with subcutaneous fat but not ectopic fat may explain why no association was seen between menopause and diabetes mellitus, CAC, or CIMT. Future directions should explore how dietary patterns may interact with menopausal status in relation to body fat distribution and CVD risk factors.

Overall, findings regarding CAC and CIMT in menopausal women have been varied. The multi-ethnic Study of Women's Health Across the Nation study showed menopause was independently associated with higher levels of CIMT and carotid adventitial diameter.[23] Another study of Chinese women showed that postmenopausal status was associated with higher CIMT and higher rates of unstable carotid plaque.[24] Notably, neither of these studies included South Asian participants. Previous studies examining female participants in MASALA compared with the MESA study showed no significant difference in CAC incidence or progression between the 2 groups.[25] Our findings suggest that subclinical markers of atherosclerosis, such as CAC or greater CIMT, may not be directly related to menopausal status in this population.

These data provide important insight into the role of gender-specific factors in CVD risk across the lifespan in South Asian American women. Our findings suggest that traditional risk factors such as hypertension and BMI are important in evaluating CVD risk in menopausal South Asian women. In contrast to other studies, including those of multi-ethnic populations, our study showed that subclinical markers of atherosclerosis, such as CAC, greater CIMT, or ectopic fat, may not be directly related to menopausal status in this population. Such associations may have been observed because menopause occurs more proximal to CVD risk factors in causal pathways than atherosclerosis. However, it is still possible that there were no observed associations of menopause with measures of subclinical atherosclerosis because of the sample size.

This study has several limitations. First, only menopausal status was examined. Information about the duration of menopausal transition, menopausal symptoms, previous treatment with hormonal therapy, or estrogen/progesterone levels was not available. Further, few participants had surgical oophorectomy or premature menopause. Future directions for research in this population may focus on the potential contributions of these factors. Second, there was a possibility of identifying significant associations because of multiple comparisons. These observational findings should be considered hypothesis-generating for future studies. Third, sample size limitations may preclude the detection of smaller effect sizes. However, MASALA represents the largest and most comprehensive available assessment of cardiovascular health in South Asian American women. Regardless of these limitations, these findings support understanding of how menopause may contribute to CVD risk in women of South Asian ethnicity. In conclusion, menopause was associated with traditional cardiovascular risk factors, particularly measures of cholesterol and higher BMI, in South Asian American women in the MASALA study.

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Disclosures

The authors have no conflicts of interest to declare.

1. Wellons M, Ouyang P, Schreiner PJ, Herrington DM, Vaidya D. Early menopause predicts future coronary heart disease and stroke: the Multi-Ethnic Study of Atherosclerosis (MESA). *Menopause* 2012;19:1081–1087.
2. Sutton-Tyrrell K, Lassila HC, Meilahn E, Bunker C, Matthews KA, Kuller LH. Carotid atherosclerosis in premenopausal and postmenopausal women and its association with risk factors measured after menopause. *Stroke* 1998;29:1116–1121.
3. Kok HS, van Asselt KM, van der Schouw YT, van der Tweel I, Peeters PH, Wilson PW, Pearson PL, Grobbee DE. Heart disease risk determines menopausal age rather than the reverse. *J Am Coll Cardiol* 2006;47:1976–1983.
4. Subramanya V, Zhao D, Ouyang P, Ying W, Vaidya D, Ndumele CE, Heckbert SR, Budoff MJ, Post WS, Michos ED. Association of endogenous sex hormone levels with coronary artery calcium progression among post-menopausal women in the Multi-Ethnic Study of Atherosclerosis (MESA). *J Cardiovasc Comput Tomogr* 2019;13:41–47.
5. Matthews KA, Kuller LH, Chang Y, Edmundowicz D. Premenopausal risk factors for coronary and aortic calcification: a 20-year follow-up in the healthy women study. *Prev Med* 2007;45:302–308.
6. Kuller LH, Matthews KA, Edmundowicz D, Chang Y. Incident coronary artery calcium among postmenopausal women. *Atherosclerosis* 2008;200:278–285.
7. Volgman AS, Palaniappan LS, Aggarwal NT, Gupta M, Khandelwal A, Krishnan AV, Lichtman JH, Mehta LS, Patel HN, Shah KS, Shah SH, Watson KE, American Heart Association Council on Epidemiology and Prevention; Cardiovascular Disease and Stroke in Women and Special Populations Committee of the Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Stroke Council. Atherosclerotic cardiovascular disease in South Asians in the United States: epidemiology, risk factors, and treatments: a scientific statement from the American Heart Association. *Circulation* 2018;138:e1–e34.
8. Kanaya AM, Kandula N, Herrington D, Budoff MJ, Hulley S, Vittinghoff E, Liu K. Mediators of Atherosclerosis in South Asians Living in America (MASALA) study: objectives, methods, and cohort description. *Clin Cardiol* 2013;36:713–720.
9. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ, National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA* 2003;289:2560–2572.
10. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363:157–163.
11. Kanaya AM, Kandula NR, Ewing SK, Herrington D, Liu K, Blaha MJ, Srivastava S, Dave SS, Budoff MJ. Comparing coronary artery calcium among U.S. South Asians with four racial/ethnic groups: the MASALA and MESA studies. *Atherosclerosis* 2014;234:102–107. Published correction appears in *Lancet* 2004;363:902.
12. Shah BM, Shah S, Kandula NR, Gadgil MD, Kanaya AM. Psychosocial factors associated with subclinical atherosclerosis in South Asians: the MASALA study. *J Immigr Minor Health* 2016;18:1317–1327.
13. Ijuin H, Douchi T, Oki T, Maruta K, Nagata Y. The contribution of menopause to changes in body-fat distribution. *J Obstet Gynaecol Res* 1999;25:367–372.
14. Hall G, Collins A, Csemiczky G, Landgren BM. Lipoproteins and BMI: a comparison between women during transition to menopause and regularly menstruating healthy women. *Maturitas* 2002;41:177–185.
15. Coylewright M, Reckelhoff JF, Ouyang P. Menopause and hypertension: an age-old debate. *Hypertension* 2008;51:952–959.
16. Casíglia E, d'Este D, Ginocchio G, Colangeli G, Onesto C, Tramontin P, Ambrosio GB, Pessina AC. Lack of influence of menopause on blood pressure and cardiovascular risk profile: a 16-year longitudinal study concerning a cohort of 568 women. *J Hypertens* 1996;14:729–736.
17. Anagnostis P, Theocharis P, Lallas K, Konstantis G, Mastrogiannis K, Bosdou JK, Lambrinoudaki I, Stevenson JC, Goulis DG. Early menopause is associated with increased risk of arterial hypertension: a systematic review and meta-analysis. *Maturitas* 2020;135:74–79.
18. McTigue KM, Chang YF, Eaton C, Garcia L, Johnson KC, Lewis CE, Liu S, Mackey RH, Robinson J, Rosal MC, Snetselaar L, Valoski A, Kuller LH. Severe obesity, heart disease, and death among White, African American, and Hispanic postmenopausal women. *Obesity (Silver Spring)* 2014;22:801–810.
19. Iacobellis G, Gao YJ, Sharma AM. Do cardiac and perivascular adipose tissue play a role in atherosclerosis? *Curr Diab Rep* 2008;8:20–24.
20. Shah AD, Kandula NR, Lin F, Allison MA, Carr J, Herrington D, Liu K, Kanaya AM. Less favorable body composition and adipokines in South Asians compared with other US ethnic groups: results from the MASALA and MESA studies. *Int J Obes (Lond)* 2016;40:639–645.
21. Deshpandey M, Huang CY, Kandula N, Kanaya AM. Abstract P126: Comparing cardiovascular risk factor progression between South Asian men and women with diabetes: a longitudinal analysis from the MASALA study. *Circulation* 2020;141(Suppl_1). AP126.
22. Gujral UP, Narayan KMV, Kandula NR, Liu K, Kanaya AM. Incidence of diabetes and prediabetes and predictors of glycemic change among South Asians in the USA: the MASALA study. *BMJ Open Diabetes Res Care* 2020;8:e001063.
23. El Khoudary SR, Wildman RP, Matthews K, Thurston RC, Bromberger JT, Sutton-Tyrrell K. Progression rates of carotid intima-media thickness and adventitial diameter during the menopausal transition. *Menopause* 2013;20:8–14.
24. Zhou Y, Wang D, Yang X, Wang A, Gao X, Guo Y, Wu S, Zhao X. Effect of menopausal status on carotid intima-media thickness and presence of carotid plaque in Chinese women generation population. *Sci Rep* 2015;5:8076.
25. Kanaya AM, Vittinghoff E, Lin F, Kandula NR, Herrington D, Liu K, Blaha M, Budoff MJ. Incidence and progression of coronary artery calcium in South Asians compared with 4 race/ethnic groups. *J Am Heart Assoc* 2019;8:e011053.