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Publication Date

2022-05-01

DOI

10.1016/j.amjcard.2022.01.063

Peer reviewed



Published in final edited form as:

Am J Cardiol. 2022 May 15; 171: 165–170. doi:10.1016/j.amjcard.2022.01.063.

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

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Abstract

The menopausal transition is a time of accelerating cardiovascular disease (CVD) risk and promoting cardiovascular health during midlife is an important window 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 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. Women ages 40–84 from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) Study were studied. 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, post-menopausal participants outside the age range of pre-menopausal participants were excluded. In the age-restricted sample, menopause was associated with a higher adjusted odds of hypertension (OR 1.19 [95% CI 1.02–1.41]), and higher systolic blood pressure (β 6.34 [95% CI 0.82–11.87]), and significantly higher subcutaneous fat area (β 42.8 [95% CI 5.8–91.4]). No significant associations between menopause and ectopic fat deposition, CAC or CIMT were observed. In South Asian American women in the MASALA 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.

Keywords

Menopause; South Asian Cardiovascular Health; MASALA

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Declaration of Competing Interest
The authors report no disclosures.

Introduction

Menopause has been associated with a change in cardiovascular risk profile, markers of metabolic health, and subclinical atherosclerosis.¹ Past studies have shown higher carotid intima-media thickness (CIMT), ectopic fat deposition and coronary artery calcium (CAC) progression in post-menopausal compared with pre-menopausal women.²⁻⁴ One challenge in assessing the relationship 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 pre- and peri-menopausal risk factors can impact post-menopausal subclinical vascular disease and lifetime cardiovascular risk.^{5,6} However, the contribution of menopause to cardiovascular risk across race/ethnic groups is less well understood. In particular, individuals 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 among South Asian people 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 pre- and post-menopausal 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 pre- and post-menopausal 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 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 2010–2013 and 136 women were enrolled from 2017–2018, for a total of 556 women included. In a secondary “age-restricted” analysis, post-menopausal women outside the age range of the pre-menopausal participants (40–54 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 pre-menopausal or post-menopausal, 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 detail⁸, and were defined as follows: systolic and diastolic blood pressure were measured using an automated blood pressure monitor, and the average of the last two of three readings was used. Hypertension was defined as a systolic blood pressure of ≥ 140 mmHg

or diastolic blood pressure ≥ 90 mmHg 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 WHO Asian BMI cut-off point of BMI ≥ 27.5 kg/m.¹⁰ Hyperglycemia was based on hemoglobin A1c, and diagnosis of diabetes was defined using the gold standard of a 75g oral glucose tolerance test (OGTT) with a 2-hour post-challenge glucose ≥ 200 mg/dL, or by either fasting serum or plasma glucose ≥ 126 mg/dL or use of diabetes medication among participants. Cholesterol was assessed on 12-hour fasting samples for total cholesterol, triglycerides, high-density lipoprotein (HDL) and LDL cholesterol levels. Hyperlipidemia was defined as a total cholesterol of ≥ 200 mg/dl, triglycerides ≥ 150 mg/dl, LDL-cholesterol ≥ 160 , or using a cholesterol-lowering medication. Alcohol use was self-reported as 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-min/week.

Abdominal visceral, subcutaneous, and intermuscular fat areas were calculated using abdominal computed tomography (CT) scans. Non-contrast gated cardiac CT images were obtained to assess 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 four 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 (standard deviation), median (interquartile range), or frequency (percentage). Multivariable linear or logistic regression were used to evaluate the association of menopause (the primary independent variable) with traditional cardiovascular risk factors (hypertension, systolic blood pressure, obesity, BMI, diabetes, 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, hyperlipidemia, and obesity (e.g., where hypertension was the independent variable of interest, the fully adjusted model adjusted for diabetes, 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, 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 pre-menopausal participants compared with the age-restricted post-menopausal participants. For these models, age adjustment was still performed as in the primary analysis. All statistical

analyses were performed with R version 4.0.3, R Foundation, Vienna, Austria. Two-sided p-values <0.05 indicated statistical significance.

Results

Participant characteristics are summarized in Table 1. There were 154 pre-menopausal women (mean age 46.7 [standard deviation, SD 3.9] years) and 402 post-menopausal women (mean age 59.4 [7.4] years). The age range of pre-menopausal women was 40–54 years, and there were 110 post-menopausal 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 (OR 1.22, 95% CI 1.03–1.44), BMI ($\beta=1.90$; 95% CI 0.31–3.49), and subcutaneous fat area ($\beta=41.5$; 95% CI 1.5–81.5) after adjustment for smoking status, alcohol use, exercise, hypertension, and diabetes. While menopause was associated with higher pericardial fat volume after adjustment for age in the initial model, 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 post-menopausal women to the age range of pre-menopausal women, menopause was associated with significantly higher adjusted odds of hypertension (OR 1.19, 95% CI 1.02–1.41), higher systolic blood pressure ($\beta=6.34$; 95% CI 0.82–11.87) and BMI ($\beta=2.13$; 95% CI 0.03–4.23), after adjustment for both cardiovascular risk behaviors and concurrent metabolic disease. Menopause was also associated with significantly higher subcutaneous fat area ($\beta=42.8$; 95% CI: 5.8–91.4) 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, post-menopausal 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 MT is associated with cardiovascular risk factors in South Asian American women.

Post-menopausal status was associated with a higher BMI in this study. While findings have been mixed previously, 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 relationship 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 ten 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 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 has been limited past study on body fat deposition in menopause, which has been primarily in animal models and small cohorts. In post-menopausal women with an elevated BMI, a higher waist circumference was associated with higher total mortality and incidence of both 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 since South Asian adults have higher average levels of ectopic fat deposits compared to other race/ethnic groups in MESA.²⁰ The significant positive 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 incidence of diabetes; diabetes, 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, CAC, or CIMT. Future directions should explore how dietary patterns may interact with menopausal status in relationship with body fat distribution and CVD risk factors.

Overall, findings regarding CAC and CIMT in menopausal women have been mixed. The multi-ethnic SWAN study showed menopause was independently associated with higher levels of CIMT and carotid adventitial diameter.²³ Another study of Chinese women showed that post-menopausal 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 to the MESA study showed no significant difference in CAC incidence or progression between the two groups.²⁵ Our findings suggest that sub-clinical 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 sex-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 sub-clinical 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 does atherosclerosis. However, it

is still possible that there were no observed associations of menopause with measures of subclinical atherosclerosis due to 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 due to multiple comparisons. These observational findings should be considered hypothesis-generating for future studies. Third, sample size limitations may preclude detection of smaller effect sizes. However, MASALA represents the largest and most comprehensive available assessment of cardiovascular health in South Asian American women. Despite 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.

Funding and Acknowledgements

This project was supported by the National Heart, Lung, and Blood Institute grant numbers R01HL093009 and K23HL157766, and the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through UCSF-CTSI grant numbers UL1RR024131 and UL1TR001872. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, and Blood Institute or the National Institutes of Health. The authors thank the other investigators, the staff, and the participants of the MASALA study for their valuable contributions.

References

- 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* (New York, NY) 2012;19:1081.
- 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. [PubMed: 9626281]
- 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. [PubMed: 16697313]
- 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.
- 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. [PubMed: 17688929]
- Kuller LH, Matthews KA, Edmundowicz D, Chang Y. Incident coronary artery calcium among postmenopausal women. *Atherosclerosis* 2008;200:278–285. [PubMed: 18289547]
- Volgman AS, Palaniappan LS, Aggarwal NT, Gupta M, Khandelwal A, Krishnan AV, Lichtman JH, Mehta LS, Patel HN, Shah KS. 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. [PubMed: 29794080]

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. [PubMed: 24194499]
9. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA* 2003;289:2560–2571. [PubMed: 12748199]
10. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet (London, England)* 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 US South Asians with four racial/ethnic groups: the MASALA and MESA studies. *Atherosclerosis* 2014;234:102–107. [PubMed: 24632509]
12. Shah BM, Shah S, Kandula NR, Gadgil MD, Kanaya AM. Psychosocial factors associated with subclinical atherosclerosis in South Asians: the MASALA study. *Journal of Immigrant and Minority Health* 2016;18:1317–1327. [PubMed: 26897179]
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. [PubMed: 10533334]
14. Hall G, Collins A, Csemiczky G, Landgren B-M. Lipoproteins and BMI: a comparison between women during transition to menopause and regularly menstruating healthy women. *Maturitas* 2002;41:177–185. [PubMed: 11886763]
15. Coylewright M, Reckelhoff JF, Ouyang P. Menopause and hypertension: an age-old debate. *Hypertension* 2008;51:952–959. [PubMed: 18259027]
16. Casiglia 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. [PubMed: 8793695]
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. [PubMed: 32252968]
18. McTigue KM, Chang YF, Eaton C, Garcia L, Johnson KC, Lewis CE, Liu S, Mackey RH, Robinson J, Rosal MC. Severe obesity, heart disease, and death among white, African American, and Hispanic postmenopausal women. *Obesity* 2014;22:801–810. [PubMed: 24493096]
19. Iacobellis G, Gao Y-J, Sharma AM. Do cardiac and perivascular adipose tissue play a role in atherosclerosis? *Curr Diab Rep* 2008;8:20–24. [PubMed: 18366994]
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* 2016;40:639–645.
21. Deshpandey M, Huang C-Y, 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:AP126–AP126.
22. Gujral UP, Narayan KV, 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 Research and 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 (New York, NY)* 2013;20:8.
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;5:1–5.
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. [PubMed: 30630376]

Table 1:

Baseline characteristics of women participants in the MASALA study (2010–2018)

	Pre-menopausal (N = 154)	Post-menopausal (N = 402)	Age-restricted post-menopausal group ^a (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) ^b	1340 ± 1764	1210 ± 1423	1230 ± 1699
Medication use			
Antihyperglycemics	12 (7.8%)	67 (16.7%)	8 (7.3%)
Anti-hypertensives	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 ^c	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 ^d	24.4 (15.6%)	105 (26.1%)	21 (19.1%)
Systolic BP (mmHg)	116 ± 11.4	127 ± 17.9	122 ± 16.4
Diastolic BP (mmHg)	70 ± 8.7	71.2 ± 10.3	72.9 ± 9.34
Hypertension ^e	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 ^f	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

Data is represented as mean ± SD or N (%) unless otherwise indicated

BP: blood pressure, CAC: coronary artery calcium, HDL: high-density lipoprotein, LDL: low-density lipoprotein

^aAge range was 40–54 years old

^bData represented as mean (IQR)

^cObesity = BMI ≥ 27.5 kg/m²

^dDiabetes mellitus = by fasting glucose or glucose tolerance

^eHypertension = SBP ≥ 140 , or DBP ≥ 90 , or anti-HTN medication use

^fHyperlipidemia = TC ≥ 200 or LDL ≥ 160 or Tg ≥ 150 or cholesterol lowering med use

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Table 2.

Association of menopause with cardiovascular risk factors and ectopic fat

Variable	Adjusted for age alone		Model 1 ^a		Model 2 ^b	
	OR (95% CI) ^c	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) ^d	p	Beta (95% CI)	p	Beta (95% CI)	p
Systolic BP (mmHg)	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/m²)	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 (cm²)	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 (cm²)	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 (cm²)	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 (cm³)	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 coefficients, BP: blood pressure, BMI: body mass index, HU: Hounsfield unit, CI: confidence interval, OR: odds ratio

^aModel 1: Adjusted additionally for smoking status, alcohol use, exercise^bModel 2: Additionally adjusted for hypertension, obesity, diabetes, hyperlipidemia^cOR (95% CI) for odds of CV risk factor for post-menopausal (compared with pre-menopausal), in multivariable logistic regression^dBeta (95% CI) for change in ectopic fat measure for post-menopausal (compared with pre-menopausal), in multivariable linear regression

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 ^a		Model 2 ^b	
	OR (95% CI) ^c	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) ^d	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
A1c	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 coefficients, BP: blood pressure, BMI: body mass index, CI: confidence interval, OR: odds ratio

^aModel 1: Adjusted additionally for smoking status, alcohol use, exercise

^bModel 2: Additionally adjusted for hypertension, obesity, diabetes, hyperlipidemia

^cOR (95% CI) for odds of CV risk factor for age-matched post-menopausal (compared with pre-menopausal), in multivariable logistic regression

^dBeta (95% CI) for change in ectopic fat measure for age-matched post-menopausal (compared with pre-menopausal), in multivariable linear regression

Table 4.

Association of menopause with subclinical atherosclerosis

<i>Full Sample</i>						
Variables	Adjusted for age alone		Model 1 ^a		Model 2 ^b	
CAC ^c	OR (95% CI) ^d	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
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 ^e	<i>Beta (95% CI)^f</i>		<i>Beta (95% CI)</i>		<i>Beta (95% CI)</i>	
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
<i>Secondary analysis: Age-restricted sample^c</i>						
	Unadjusted		Model 1		Model 2	
CAC	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
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	<i>Beta (95% CI)</i>		<i>Beta (95% CI)</i>		<i>Beta (95% CI)</i>	
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

^aModel 1: Adjusted additionally for BMI, diabetes, hypertension, smoking status, alcohol use, exercise.

^bModel 2: Additionally adjusted for LDL, HDL, ectopic fat measures, and use of statin medications

^cSecondary analysis includes post-menopausal women only in the age range of pre-menopausal women