Journal of the American Heart Association

ORIGINAL RESEARCH

Sexual Assault and Carotid Plaque Among Midlife Women

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BACKGROUND: Sexual assault is a risk factor for poor mental health, yet its relationship to cardiovascular disease risk is not understood. We tested whether women with a sexual assault history had greater carotid atherosclerosis levels and progression over midlife.

METHODS AND RESULTS: A total of 169 non-smoking, cardiovascular disease-free women aged 40 to 60 years were assessed twice over 5 years. At each point, women completed questionnaires, physical measures, phlebotomy, and carotid ultrasounds. Associations between sexual assault and carotid plaque level (score 0, 1, ≥2) and progression (score change) were assessed in multinomial logistic and linear regression models, adjusted for age, race/ethnicity, education, body mass index, blood pressure, lipids, insulin resistance, and additionally depression/post-traumatic stress symptoms; 28% of the women reported a sexual assault history. Relative to non-exposed women, women with a sexual assault history had an over 4-fold odds of a plaque score of ≥2 at baseline (≥2, odds ratio [OR] [95% CI]=4.35 [1.48–12.79], *P*=0.008; 1, OR [95% CI]=0.49 [0.12–1.97], *P*=0.32, versus no plaque; multivariable); and an over 3-fold odds of plaque ≥2 at follow-up (≥2, OR [95% CI]=3.65 [1.40–9.51], *P*=0.008; 1, OR [95% CI]=1.52 [0.46–4.99], *P*=0.49, versus no plaque; multivariable). Women with a sexual assault history also had an over 3-folds greater odds of a plaque score progression of ≥2 (OR [95% CI]=3.48[1.11–10.93], *P*=0.033, multivariable). Neither depression nor post-traumatic symptoms were related to plaque.

CONCLUSIONS: Sexual assault is associated with greater carotid atherosclerosis level and progression over midlife. Associations were not explained by standard cardiovascular disease risk factors. Future work should consider whether sexual assault prevention reduces women's cardiovascular disease risk.

Key Words: carotid atherosclerosis ■ psychological trauma ■ sexual violence ■ women's health

Cardiovascular disease (CVD) is the leading cause of death among women.[1] A burgeoning body of evidence points to the importance of psychosocial factors to the development of CVD. However, much of this work focused on psychological factors, such as depression. Relatively little work considers the role of interpersonal violence on chronic disease outcomes such as CVD. Notably, sexual violence is highly prevalent among women living in the United States. A recent nationally-representative survey (National Intimate Partner and Sexual Violence Survey) indicates that 21% of US women have experienced rape, and 44% of women have experienced sexual assault (rape, being made to penetrate someone else, sexual coercion, and/or unwanted sexual contact) in their lifetime.[2]

There has been growing interest in the impact of sexual assault on women's cardiovascular health. For example, 2 surveys indicated that a history of sexual assault was associated with increased risk of self-reported heart disease and stroke[3] and that intimate partner violence was associated with reported coronary heart disease.[4] Military sexual assault was related to self-reported treatment for a heart attack[5] and medical record-documented congestive heart failure and cerebrovascular disease.[6] A history of sexual assault

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Supplementary material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.017629

For Sources of Funding and Disclosures, see page 8.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Sexual assault is a prevalent experience among women.
- In this longitudinal study of midlife women, this study is the first to show that a sexual assault history is associated with greater level and progression of carotid plaque over time.
- Associations are not explained by standard cardiovascular disease risk factors, by depression, or by post-traumatic stress symptoms.

What Are the Clinical Implications?

- Clinicians should consider women's sexual assault history when considering their future cardiovascular disease risk.
- Future work should investigate whether preventing or treating the sequelae of sexual assault can reduce women's cardiovascular disease risk.

or intimate partner violence has also been linked to poorer self-reported CVD-related risk factor profiles (obesity, smoking, adverse lipid profiles) in adulthood,[3,7–10] even for assaults that occurred years earlier in adolescence.[11] However, findings are not uniformly consistent, with other studies finding no associations of sexual violence to CVD risk factors[12,13] or to self-reported CVD.[6,9] Limitations of this literature include a reliance on cross-sectional designs and generally self-reported CVD outcomes. Notably, self-reported CVD is subject to a number of biases, including contact with the healthcare system and health literacy, which can systematically vary by key social and demographic factors which are also associated with risk of sexual assault.[14–17]

To investigate the relationship of sexual violence to women's CVD risk, use of objective measurements is warranted. As women typically develop clinical CVD later than men, in their sixth decade of life, use of subclinical CVD measurements are important for understanding the development of CVD among women earlier in the lifespan. One such subclinical CVD measure is carotid atherosclerosis assessed via ultrasound, which yields the indices carotid intima-media thickness (IMT) and carotid plaque[18] that are predictive of later CVD events, even among low-risk populations.[18,19] Further, multiple assessments of subclinical CVD over time provide estimates of changes in vascular health over time, important to understanding disease progression. Only 1 study, conducted among Mexican women, investigated sexual assault as part of a broader examination of the relationship between violence and subclinical CVD. This study found that exposure to physical violence was related to higher carotid IMT, but found no association between sexual assault and IMT or plaque.[20] However, this study had a number of characteristics that limit understanding about the relationship of sexual assault to cardiovascular health, including use of a sexual assault definition that included both contact and non-contact (eg, sexual harassment) sexual violence, and had a low prevalence of sexual assault (7%) that likely limited power to detect associations. More targeted investigation of sexual assault in relationship to CVD health is needed, ideally with direct assessments of the vasculature measured at multiple time points.

In the present investigation, we examined the relationship between sexual assault and carotid atherosclerosis among a well-characterized sample of CVD-free midlife women. Participants underwent assessments of sexual assault and subclinical CVD (carotid atherosclerosis) at 2 time points over 5 years of midlife. We tested the hypothesis that a history of sexual assault would be associated with greater subclinical CVD as well as greater progression of subclinical CVD over time. We considered a wide range of potential confounders and mechanisms in these relationships. Finally, we additionally considered whether non-contact sexual violence (eg, sexual harassment), was associated with CVD outcomes.

METHODS

The data and associated materials that support the findings of this study are available from the corresponding author upon reasonable request.

Sample

Participants were recruited from a cohort of non-smoking late perimenopausal and postmenopausal midlife women who had participated in a study on menopausal symptoms and cardiovascular health (MsHeart) between 2012 and 2015. MsHeart exclusion criteria included: current smoking; reported history of CVD/stroke/cerebrovascular accident; insulin-dependent diabetes mellitus; Parkinson's disease; hysterectomy and/or bilateral oophorectomy; current pregnancy; and use of hormone therapy (oral or transdermal estrogen and/or progesterone), select cardiovascular medications (beta-blockers, calcium channel blockers, alpha-2 adrenergic agonists), selective estrogen receptor modulators, aromatase inhibitors, selective serotonin reuptake inhibitors or serotonin norepinephrine reuptake inhibitors. One hundred and sixty-nine of the MsHeart participants returned for a follow-up visit between 2017 and 2020 for a study focused on menopause and brain aging (MsBrain). Women underwent carotid ultrasound at both visits. Exclusion criteria for this follow-up visit included: a reported history of stroke/cerebrovascular

accident; dementia; seizure disorder; brain tumor; Parkinson's Disease; a history of head trauma with loss of consciousness; current chemotherapy; active substance abuse; pregnancy; and current use of medications including hormone therapy (oral or transdermal estrogen and/or progesterone), selective estrogen receptor modulators, aromatase inhibitors, selective serotonin reuptake inhibitors, or serotonin norepinephrine reuptake inhibitors.

Of the 169 women with carotid ultrasound data at both visits, 1 was excluded from baseline analyses because of missing blood data, 4 from follow-up analyses because of missing data on sexual assault (n=2) or blood biomarkers (n=2), and 4 who initiated smoking (smoking was a baseline exclusion criterion) from follow-up models to support model convergence; these 9 women were excluded from longitudinal models incorporated from both time points. Thus, samples sizes for analyses were n=168 (baseline models), n=160 (follow-up models), and n=160 (longitudinal models).

Design and Procedures

At both baseline and follow-up, participants underwent telephone and in-person screening procedures, physical measurements, completion of questionnaires, and carotid ultrasound measurements. Procedures were approved by the University of Pittsburgh Institutional Review Board. Participants provided written informed consent.

Measures

Sexual Violence

Sexual assault was assessed from select items of the Brief Trauma Questionnaire items developed for the Nurses' Health Study II[21] adapted from the Brief Trauma Interview.[22,23] This measure has high inter-rater reliability relative to the *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition) for presence of Criterion A1 trauma exposure [k=0.70].[21] Two questions were considered. Sexual assault was assessed as: "Have you ever been made or pressured into having some type of unwanted sexual contact? By sexual contact we mean any contact between someone else and your private parts or between you and someone else's private parts." In additional analyses, we considered workplace sexual harassment, assessed as "Have you ever experienced sexual harassment at work that was either physical or verbal?" Response options for each item were yes/no.

Carotid Atherosclerosis

At both baseline and follow-up visits, trained and certified sonographers at the University of Pittsburgh's Ultrasound Research Laboratory obtained bilateral carotid images via B-mode ultrasound using a Sonoline Antares (Siemens, Malvern, Pennsylvania) high resolution duplex scanner equipped with a VF10-5 transducer according to a standardized protocol.[24] Digitized images were obtained at end-diastole from 8 locations (4 locations each from the left and right carotid arteries): the near and far walls of the distal common carotid artery, the far walls of the carotid bulb, and the internal carotid artery. Images were read using semi-automated reading software.[25] Values were obtained by electronically tracing the lumen-intima interface and the media-adventitia interface across a 1-cm segment for each of these 8 segments. Average values were recorded for each of the 8 locations; the mean of these readings comprised mean IMT. Reproducibility of IMT measures was excellent [intraclass correlation coefficient between sonographers ≥0.87, between readers =0.92]. IMT at baseline and at follow-up and change in IMT over the 2 visits (follow-up IMT–baseline IMT) was considered for analysis.

Carotid plaque was defined as a distinct focal area protruding into the vessel lumen ≥50% thicker than the adjacent IMT.[26] Sonographers assessed plaque in 5 carotid artery segments in the left and right side: proximal common, distal common (1-cm proximal to the carotid bulb), carotid bulb (the point in which the near and far walls of the common carotid are no longer parallel, extending to the flow divider), and internal and external carotid (beginning at the flow divider). For each segment, the degree of plaque was graded using the following criteria: Grade 0=no observable plaque; grade 1=1 small plaque (<30% of the vessel diameter); grade 2=1 medium plaque (30%–50% of the vessel diameter) or multiple small plaques; grade 3=1 large plaque (>50% of the vessel diameter) or multiple plaques with at least 1 medium plaque. The grades were summed across segments to create a plaque index, a measure of extent of plaque.[27] Reliability of plaque index scoring between sonographers was κ=0.78, demonstrating high reliability. For cross-sectional analyses, the plaque index was categorized as 0, 1, or ≥2 for analysis. Change in plaque between visits was calculated as plaque index (follow-up)–plaque index (baseline) and considered as both a continuous variable and categorized as a plaque index change of ≤0, 1, or ≥2.

Covariates

At baseline and follow-up visits, height was measured via fixed stadiometer and weight via balance beam scale, and body mass index was calculated (weight (kg)/height^2 (m)). Systolic blood pressure and diastolic blood pressure was the average of 3 seated measurements taken via a Dinamap v100. Demographics, medical history, medication use, and

health behaviors were assessed by questionnaires and interview. Medications were documented at both visits via interview and classified according to their indication for analysis (for blood pressure-lowering, lipid-lowering, diabetes mellitus). Race/ethnicity was self-reported. Educational attainment was assessed as years of completed education (classified as high school/vocational, college graduate, >college for analysis). Depressive symptoms were assessed via the Center for Epidemiologic Studies Depression Survey.[28] Post-traumatic stress disorder (PTSD) symptoms were assessed (at follow-up only) with the PTSD civilian symptom checklist.[29] Physical activity was assessed via the International Physical Activity Questionnaire.[30] Participants provided a morning fasting blood sample for assessment of glucose, insulin, and lipids. Glucose, total cholesterol, high-density lipoprotein cholesterol, and triglycerides were determined using an enzymatic assay; insulin was determined by immunoturbidimetric assay in serum. Low-density lipoprotein cholesterol was calculated using the Friedewald equation.[31] Homeostatic model assessment, an index reflecting insulin resistance, was calculated ([fasting insulin×fasting glucose]/22.5).[32]

Statistical Analysis

Variables were examined for distributions, outliers, and cell sizes. Body mass index, homeostatic model assessment, and triglycerides were log-transformed to conform to model assumptions of normality. Bivariate relationships between study variables and carotid indices were examined via Pearson and Spearman correlation coefficients. We tested 3 models: the relationship between sexual assault and carotid outcomes (1) cross-sectionally at baseline, (2) at follow-up, and (3) in relationship to change in carotid indices over the 2 visits. Cross-sectional associations of whether women with a sexual assault history (yes/no) had increased odds of plaque (scores 1 or ≥2 relative to no plaque) were tested via multinomial logistic regression. Associations between sexual assault and plaque change over time as well as associations between sexual assault and IMT were tested via linear regression. For baseline models, baseline sexual assault was examined in relationship to baseline subclinical CVD, with covariates derived from baseline. For follow-up models, sexual assault reported at either time point was examined in relationship to subclinical CVD at follow-up, with covariates derived from both visits and averaged over the 2 visits. For change over time models, sexual assault reported at either time point was considered in relationship to change in subclinical CVD, with covariate values incorporating both visits (eg, averaged for continuous variables, any exposure/use over the visits for categorical variables such as medication use). Select covariates were a priori selected for inclusion in models: age, race, and education in all models and the time difference between measurements in longitudinal models. All other covariates were included based upon their relationship with the outcome at $P<0.10$. We alternatively considered addressing potential confounding with the use of propensity scores or adjusting for a composite atherosclerotic cardiovascular disease risk score[33] in lieu of individual risk factors; since findings from these models were comparable, models adjusting for individual risk factors are presented. Smoking was a study exclusion criterion at baseline, yet 4 women initiated smoking between baseline and follow-up; the smokers were excluded from follow-up and change models to support model convergence (small cell sizes). In additional analyses, we considered depressive symptoms or PTSD symptoms (continuous scale scores). All tests were 2-tailed with an alpha set to 0.05. Analyses were conducted using SAS v9.4 (SAS Institute, Cary, North Carolina).

RESULTS

At baseline, participants were on average 54 years old, overweight, and normotensive (Table 1). At baseline, 19% (n=32) of women reported a history of sexual assault, 23% (n=38) at follow-up, and 28% (n=47) at either visit. At baseline, women with a history of sexual assault did not differ from women without a history of sexual assault with the exception of the women with a sexual assault history being somewhat younger (yes sexual assault, mean age=52.69; no sexual assault, mean age=54.25; $P=0.049$) and less likely to be taking anti-hypertensive medications (yes sexual assault, 3%; no sexual assault, 27%; $P=0.02$) at baseline.

At baseline, 75 (44%) women had carotid plaque and 41 (24%) women had a plaque score ≥2. At follow-up, 101 (60%) of women showed any carotid plaque and 64 (38%) women had a plaque score ≥2. The average IMT at baseline was 0.69 mm (SD=0.11) and at follow-up 0.72 mm (SD=0.13). The average duration between visits was 4.92 (SD=0.67) years. Over this time, the average change in the plaque score was 0.51 (SD=0.92) and in IMT was .04 mm (SD=0.06); 25 (15%) women had a plaque score progression of ≥2.

At both baseline and follow-up, a history of sexual assault was associated with a 3- to 4-fold increased odds of a carotid plaque score ≥2 in multivariable models (Table 2; Figure 1). Further, women who reported sexual assault at either time point had greater progression of carotid plaque over the 2 visits than women who had not (Table 3, Figure 2). In fact, women with a sexual assault history had an over 3-fold odds

Table 1. Sample Characteristics by Sexual Assault at Baseline

Sexual Assault	Yes (n=32)	No (n=137)
Age, y, M (SD)*	52.69 (4.67)	54.25 (3.83)
Race/ethnicity, n (%)		
White	25 (75.00)	96 (70.07)
Black/ other†	8 (25.00)	41 (29.93)
Education, n (%)		
High school/some college/vocational	9 (28.13)	59 (43.07)
College graduate or higher	23 (71.88)	78 (56.93)
BMI, median (IQR)	27.91 (22.74, 32.96)	28.41 (24.76, 32.94)
SBP, mm Hg, M (SD)	115.92 (12.78)	119.33 (14.34)
DBP, mm Hg, M (SD)	69.03 (8.03)	69.72 (8.97)
LDL, mg/dL, M (SD)	132.56 (33.76)	131.87 (32.78)
HDL, mg/dL, M (SD)	69.03 (8.03)	69.72 (8.97)
Triglycerides, mg/dL, median (IQR)	101.00 (73.50, 136.50)	94.00 (70.00, 126.00)
HOMA, median (IQR)	2.16 (1.40, 2.73)	2.42 (1.77, 3.25)
Medications, n (%)		
Anti-hypertensive*	1 (3.13)	27 (19.71)
Anti-diabetic	0 (0)	7 (5.11)
Lipid-lowering	1 (3.13)	21 (15.33)

BMI indicates body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein cholesterol; HOMA, homeostatic model assessment; IQR, interquartile range; LDL, low-density lipoprotein cholesterol; M, mean; SBP, systolic blood pressure; and SD, standard deviation.

*Varies by sexual assault, $P<0.05$.

†Other race/ethnicity includes Asian/Pacific Islander and Mixed race.

of carotid plaque change of ≥2. Associations persisted with adjustment for demographic factors and standard CVD risk factors. Sexual assault was not significantly associated with IMT level at either visit or change over time (data not shown).

We conducted several additional analyses. We considered depressive symptoms and PTSD symptoms; neither of these psychological factors were related to IMT or plaque at either time point or change in IMT or plaque and thus were not considered in models. We additionally considered workplace sexual harassment (reported by 48 (29%) women at ≥1 time points), but it was not associated with level or change in either subclinical CVD measure (Tables S1 and S2).

DISCUSSION

In the present study of midlife women free of clinical CVD assessed at 2 time points over midlife, we found that a history of sexual assault was associated with greater carotid plaque level cross-sectionally, as well as greater progression of carotid plaque over 5 years. At each time point, women with a history of sexual assault had 3- to 4-fold odds of having a carotid plaque score of ≥2, as well as having over 3-folds odds of showing significant plaque progression (plaque score change ≥2). Associations were not accounted for by potentially confounding or explanatory factors, including demographic factors, standard CVD risk factors, nor depressive or PTSD symptoms. These findings point to the potential cardiovascular sequelae of sexual assault.

These findings add importantly to the existing literature on sexual violence and cardiovascular health. The existing literature is largely based on self-reported outcomes and cross-sectional analyses. Existing work adjusted for sociodemographic variables but typically not standard CVD risk factors or mental health symptoms. Further, many studies combine physical and sexual violence, making it difficult to understand the unique contribution of sexual violence to cardiovascular health. Sexual violence is particularly germane to women's health, as unlike physical violence, sexual violence is over twice as likely among women relative to men.[34] Our study represents a substantial advancement of this literature with its use of direct measures of the vasculature at several time points over midlife and comprehensive consideration of potential mechanisms and confounders. Notably, only 1 other study examined the relationship between sexual assault and subclinical CVD in women and found no relationship between sexual violence and carotid IMT or plaque in their sample of Mexican women.[20] However, their

Table 2. Sexual Assault in Relationship to Carotid Plaque at Baseline and Follow-Up

	Plaque Index (Baseline)*		Plaque Index (Follow-Up)*	
	1	≥2	1	≥2
	Odds Ratio (CI)	Odds Ratio (CI)	Odds Ratio (CI)	Odds Ratio (CI)
Sexual assault (yes)†	0.49 (0.12–1.97)	4.35 (1.48–12.79)‡	1.52 (0.46–4.99)	3.65 (1.40–9.51)‡

Adjusted for age, race, education, body mass index, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, homeostatic model assessment, blood pressure-lowering medication, diabetes mellitus medication, lipid-lowering medication (covariates derived from baseline for baseline plaque models and averaged over the visits for follow-up plaque models);

n=168 for baseline models, n=160 for follow-up models.

*Referent: no plaque.

†Baseline sexual assault history for baseline plaque models; sexual assault reported at either time point for follow-up plaque models; relative to no sexual assault.

‡$P<0.01$.

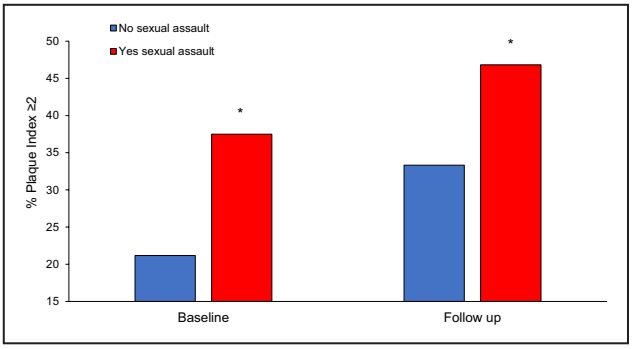

Figure 1. Associations of sexual assault and plaque at baseline and follow-up.
Raw percentages are presented in figures. Adjusted odds ratios for plaque ≥2 vs. no plaque at baseline: odds ratio (OR) (95% CI)=2.20 (0.75–6.48); at follow-up: OR (95% CI)=3.65 (1.40–9.51), adjusted for age, race, education, body mass index, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, homeostatic model assessment, use of blood pressure-lowering medication, diabetes mellitus medication, lipid-lowering medication. *P<0.01.

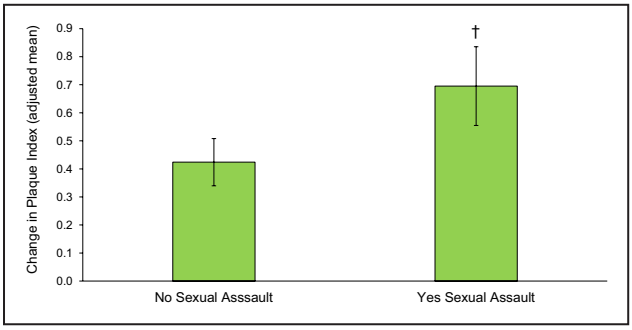

Figure 2. Sexual assault and plaque progression (adjusted mean) across visits.
Means adjusted for race, education, time difference between visits, and averaged across visits: age, body mass index, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, homeostatic model assessment, and at either visit: use of blood pressure-lowering medication, diabetes mellitus medication, lipid-lowering medication. †P<0.05.

study differed from ours in multiple ways, including their use of a composite variable of sexual harassment and/or assault, which may have weakened associations, particularly in light of the lack of associations for workplace sexual harassment here; a different population; and a low prevalence of sexual violence that may have limited their ability to detect associations.[20] Our study represents the most conclusive study to date documenting the association between sexual assault and subclinical CVD as well as subclinical CVD progression.

We found that 28% of the sample reported sexual assault at some point during the study. This rate is lower than the National Intimate Partner and Sexual Violence Survey's findings of 44% of women reporting experiencing some form of unwanted sexual contact in their lifetime.[2] Several factors may explain our lower rate. First, when establishing the cohort, we excluded women who were smokers, had undergone hysterectomy or bilateral oophorectomy, or were using common antidepressants and certain cardiovascular medications. Women taking antidepressants or with a history of head injury with loss of consciousness were further excluded from follow-up. Thus, more depressed women, women at high risk of CVD, and women losing consciousness secondary to assault would have been excluded, yielding a lower-risk sample on psychological, behavioral, and physical characteristics than the general population. The highest risk women were thereby excluded. It is possible that the associations of sexual assault with carotid plaque might have been stronger if study participants were more representative of the population. Importantly, the National Intimate Partner and Sexual Violence Survey used multiple items measuring sexual contact that was broader than that used in the present study (including items such as forced kissing[2]); our study focused solely on contact with "private parts," which likely yielded lower numbers.

Associations were observed for carotid plaque but not IMT. The reasons for the stronger associations of sexual assault to plaque relative to IMT is not immediately clear. However, it is notable that IMT may reflect adaptation of the vasculature to persistent hemodynamic changes (eg, high blood pressure).[18] Notably, in contrast to findings for other CVD risk factors (eg, adiposity, lipids, smoking),[3,7–10] studies typically do

Table 3. Sexual Assault in Relationship to Change in Carotid Plaque Over Time

	Plaque Index (Continuous Change)	Plaque Index (Categorical Change)*	
		1	≥2
	B (SE)	Odds Ratio (CI)	Odds Ratio (CI)
Sexual assault (yes)†	0.34 (0.17)‡	1.55 (0.59–4.08)	3.48 (1.11–10.93)‡

Adjusted for race, education, time difference between visits, and averaged across visits: age, body mass index, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, homeostatic model assessment, and at either visit: use of blood pressure-lowering medication, diabetes mellitus medication, lipid-lowering medication; n=160.

*Referent: plaque change ≤0.

†Reported at either time point; relative to no sexual assault.

‡P<0.05.

not find associations of sexual assault or intimate partner violence with hypertension (eg,[3,4,6,7,12,35,36]), a major determinant of vascular remodeling.[37] In contrast, plaque is a more direct measure of the development of atherosclerotic lesions. Carotid plaque may be a particularly strong predictor of future CVD events relative to IMT among women.[38] Given that the thrombotic potential of plaque may depend on its characteristics,[39] future work should investigate whether sexual assault relates to plaque characteristics and stability.

The mechanisms underlying these relationships require further investigation. We considered standard CVD risk factors assessed both at baseline and follow-up, including obesity, blood pressure, lipids, insulin resistance, and use of key medications, but these factors did not explain observed associations. We also considered behavioral mechanisms. By design, no women were smokers. Notably, physical activity, assessed by a validated instrument at both baseline and follow-up visits, was not associated with subclinical CVD, did not meet criteria for covariate inclusion, and thus did not explain associations. However, the measurement of physical activity via self-report, while standard practice, may have limited our ability to detect these associations. Moreover, neither depressive symptoms nor PTSD symptoms were associated with either subclinical CVD outcome and thus could not explain associations observed here. Notably, the rates of depression and PTSD symptoms were relatively low, and women taking major classes of antidepressants were excluded, limiting our ability to examine the relationships of psychological symptoms to carotid plaque. It is notable that associations between sexual assault and plaque were observed even in this relatively high functioning population. We measured these psychological indicators at 2 time points over midlife, and we cannot comment on the role of psychological health earlier in life when many sexual assaults occur.[40] However, our findings are broadly consistent with prior work that show trauma exposure even in the absence of PTSD symptoms is associated with incident CVD risk.[41] Future work should investigate additional mechanisms such as the autonomic nervous system, the hypothalamic pituitary adrenal axis, inflammatory pathways, or epigenetic changes.

This work has limitations. First, sexual assault was assessed via a single item administered at each time point, rather than a full multidimensional scale. However, the experiences defined as sexual assault for this study were defined behaviorally, which supports internal validity and comparability between respondents. However, other details about the experience were not assessed. For example, we do not have information on when the assault occurred, who the perpetrator was, and the number or chronicity of assaults; these factors may be important to understanding the implications of assault for women's health. Critical next steps of this work include more deeply assessing the sexual assault experiences and considering their relationship to women's cardiovascular health. Whereas we did consider workplace sexual harassment, future work should consider a range of forms of non-contact sexual violence as described by the Centers for Disease Control and Prevention,[42] including the threat of physical force to gain compliance with a sexual act, unwanted exposure to sexual situations (eg, pornography), and unwanted recording or dissemination of video/photographs of a sexual nature of another person. Men were not assessed here; future work should consider whether sexual assault relates to men's cardiovascular health.

This study has notable strengths. Considering sexual assault in relationship to cardiovascular health, as opposed to psychiatric health or acute injuries, is a novel line of inquiry. In contrast to much existing work that investigates self-reported outcomes, direct measurements of the vasculature were used, thereby avoiding biases of self-report. Both sexual assault and subclinical CVD were assessed at 2 time points, a significant advancement over studies that use an exclusively cross-sectional design. Our design allowed for not only consideration of sexual assault in relationship to level of subclinical CVD, but also to progression over time.

In this study, women with the common experience of sexual assault had a greater burden of subclinical carotid atherosclerosis as evidenced by a higher prevalence as well as a greater progression of carotid plaque over midlife. These associations were not explained by standard CVD risk factors nor by depressive or post- traumatic stress disorder symptoms. Clinicians should consider women's sexual assault experiences when considering their future CVD risk. Future work should investigate whether preventing or treating the sequelae of sexual assault can reduce women's CVD risk. Addressing this prevalent and potent exposure may be critical to preventing CVD in women.

ARTICLE INFORMATION

Received July 17, 2020; accepted November 2, 2020.

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Sources of Funding

This research was supported by the National Institutes of Health, National Institute on Aging (RF1AG053504 to Thurston and Maki) and the National Institutes of Health Heart Lung and Blood Institute (R01HL105647 and 2K24HL123565 to Thurston) and the National Institute on Mental Health (R01MH101269 to Koenen). This work was also supported by the University of Pittsburgh Clinical and Translational Science Institute (National Institutes of Health Grant UL1TR000005) and the University of Pittsburgh Small Molecule Biomarker Core (National Institutes of Health Grant S10RR023461).

Disclosures

Dr. Thurston reports personal fees from Astellas, Pfizer, Procter & Gamble, and Virtue Health, that are unrelated to the submitted work. Dr. Maki reports personal fees from Abbvie, Pfizer, and Balchem, that are unrelated to the submitted work. The remaining authors have no disclosures to report.

Supplementary Material

Tables S1–S2

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SUPPLEMENTAL MATERIAL

Table S1. Workplace sexual harassment in relation to carotid plaque at baseline and follow up.

	Plaque Index (baseline)#		Plaque index (follow up)#	
	1	≥2	1	≥2
	Odds ratio (confidence interval)	Odds ratio (confidence interval)	Odds ratio (confidence interval)	Odds ratio (confidence interval)
Sexual harassment (yes)§	1.59 (0.49-5.11)	2.20 (0.75-6.48)	0.60 (0.21-1.68)	1.55 (0.69-3.52)

N=168 for baseline models, N=160 for follow up models

§Baseline sexual harassment history for baseline plaque models; sexual harassment reported at either time point for follow-up plaque models; relative to no sexual harassment

#Referent: no plaque

Adjusted for age, race, education, body mass index, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, homeostatic model assessment, blood pressure-lowering medication, diabetes medication, lipid-lowering medication (covariates derived from baseline for baseline plaque models and averaged over visits for follow up plaque models)

Table S2. Workplace sexual harassment in relation to change in carotid plaque over time.

	Plaque Index (continuous change)	Plaque index (categorical change)#	
		1	≥2
	B (SE)	Odds ratio (confidence interval)	Odds ratio (confidence interval)
Sexual harassment (yes)§	-0.06 (0.16)	0.55 (0.22-1.39)	0.74 (0.25-2.16)

N=160

§Reported at either time point; relative to no sexual harassment

#Referent: plaque change ≤0

Adjusted for race, education, time difference between visits, and averaged across visits: age, body mass index, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, homeostatic model assessment, and at either visit: use of blood pressure-lowering medication, diabetes medication, lipid-lowering medication