Abuse and Subclinical Cardiovascular Disease Among Midlife Women
The Study of Women’s Health Across the Nation

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Background and Purpose—Some evidence suggests that abuse may be related to cardiovascular disease (CVD) risk among women. However, this relation has largely been addressed using self-reported measures of CVD. We tested whether a history of abuse was related to subclinical CVD among midlife women without clinical CVD.

Methods—The Study of Women’s Health Across the Nation (SWAN) is a longitudinal cohort study of women transitioning through the menopause. One thousand four hundred two white, black, Hispanic, and Chinese SWAN participants completed measures of childhood and adult physical and sexual abuse, underwent a blood draw, completed physical measures, and underwent a carotid artery ultrasound at SWAN study visit 12. Associations between abuse and intima media thickness and plaque were tested in linear and multinomial logistic regression models controlling for age, site, race/ethnicity, financial strain, education, body mass index, lipids, blood pressure, measures of insulin resistance, smoking, alcohol use, physical activity, and medication use.

Results—Findings indicated that a history of childhood sexual abuse was associated with higher intima media thickness controlling for standard CVD risk factors and other confounders ($\beta=0.022$; SE=0.010; $P<0.05$; adjusted mean childhood sexual abuse: 0.800 mm versus no childhood sexual abuse: 0.782 mm).

Conclusions—Childhood sexual abuse was associated with higher intima media thickness controlling for CVD risk factors and other confounders. These findings indicate the importance of considering the potential impact of early-life stressors on women’s later cardiovascular health. (Stroke. 2014;45:2246-2251.)

Key Words: atherosclerosis ■ carotid intima media thickness ■ child abuse ■ menopause ■ women

Cardiovascular disease (CVD) is the leading cause of death among women. More than a third of women in the United States are living with CVD, and more than half die from CVD.1 Psychosocial factors are increasingly understood to be important to the development of CVD.2 One of the more potent psychosocial adversities is abuse or victimization. Estimates indicate a lifetime incidence of rape and assault of 17.6% and 51.1%, respectively, among US women, with exposures often occurring before age 18.3 Exposure to abuse, particularly childhood sexual abuse, has been linked to later CVD risk.4,5 However, most of these studies relied on self-reported CVD events, and additional investigation with rigorous quantification of cardiovascular health is required.

No studies to date have investigated the relation between abuse and CVD risk using subclinical CVD indices. One of the most well-validated measures of subclinical CVD is carotid intima media thickness (IMT) in which the thickness of the lumen–intima and the media–adventitia interface of the carotid artery and carotid plaque is quantified via ultrasound. This measure is highly reproducible and significantly associated with later CVD events7 and can be useful in mitigating biases in CVD event presentation, detection, and reporting and in quantifying CVD risk in relatively low-risk samples (eg, midlife women).7,8

We tested whether midlife women with a history of physical or sexual abuse had greater carotid IMT compared with women without this history. We hypothesized that these associations would persist controlling for traditional CVD risk factors. Given racial/ethnic differences in the prevalence of abuse9 and CVD risk,8 we also explored whether associations varied by race/ethnicity. We tested these hypotheses in the cohort study, the Study of Women’s Health Across the Nation (SWAN).
Methods
SWAN is a community-based study of midlife women. Briefly, SWAN is conducted at 7 sites: Boston; Chicago; the Detroit area; Los Angeles; Newark, New Jersey; Pittsburgh, Pennsylvania; and Oakland, California. Each site recruited white women plus 1 additional racial/ethnic group. The 6 sites participating in carotid measurements recruited white women plus black (Pittsburgh, Chicago, Michigan, Boston), Chinese (Oakland), or Hispanic (Newark) women. Women were recruited from lists of names or household addresses; select sites supplemented primary sampling frames to obtain adequate numbers of racial/ethnic minority women. Seventy-three percent of these women were contacted and provided informed information to determine eligibility. Baseline eligibility criteria included age 42 to 52 years, having a uterus and 1 ovary, not being pregnant or lactating, not using oral contraceptives or hormone therapy, and ≥1 menstrual cycle in the prior 3 months. Fifty-one percent (n=3302) of eligible women enrolled. Annual clinic assessments began in 1996 to 1997, and ultrasound data were collected at visit 12. SWAN protocols were approved by the institutional review board at each site. Each participant provided written informed consent. This investigation was an analysis of associations between child and adult abuse and carotid ultrasound indices assessed at SWAN visit 12.

Of the 1552 women who underwent carotid measurements at visit 12, 149 women were excluded because of stroke, angina, or myocardial infarction before their carotid scan and 1 woman for an invalid scan. Women excluded because of prevalent CVD more often reported being physically abused as a child (included 17.7% versus excluded 31.2%; P<0.001), sexually abused as a child (included 15.9% versus excluded 26.1%; P<0.002), physically abused as an adult (included 18.0% versus excluded 37.0%; P<0.0001), and sexually abused as an adult (included 11.4% versus excluded 22.7%; P<0.0001) compared with women in the analytical sample. Excluded women were also more likely to be black, smokers, using antihypertensive, glucose-lowering, or lipid-lowering medications, and to have lower education, higher body mass index, higher systolic blood pressure, a poorer lipid profile, higher insulin resistance, and higher IMT compared with women included (all P<0.05), differences expected given the exclusion of women with CVD. One thousand four hundred two and 1369 women were included in models for plaque and IMT, respectively.

Abuse and Trauma
At visit 12, women reported the occurrence of childhood and adult physical and sexual abuse via 4 questions: As a child, were you ever beaten, physically attacked, or physically abused? As a child, were you ever sexually attacked, raped, or sexually abused? As an adult, have you ever been beaten, physically attacked, or physically abused? As an adult, have you ever been sexually attacked, raped, or sexually abused? (yes, no, do not know). Childhood questions were compared with physical/sexual abuse subscales from the validated Child Trauma Questionnaire11 administered on a subsample of participants, with moderate–high correlations between indices (physical abuse: r=0.51; P<0.0001; sexual abuse: r=0.73; P<0.0001 considered continuous variables).

Ultrasound Measures
Ultrasound images were obtained using a Terason t3000 Ultrasound System (Teratech, Burlington, MA) equipped with a variable frequency (5 to 12 MHz) linear array transducer. Digitized images were obtained from the near and far wall of the left and right distal common carotid artery, 1 cm proximal to the carotid bulb. IMT measures were obtained by electronically tracing the lumen–intima interface and the media–adventitia interface across a 1-cm segment for each of these 4 segments; 1 measurement was generated for each pixel over the area, for a total of 140 measures per segment. Averages for these measures were recorded for all 4 locations, with the mean of the average readings used in analyses. Presence and extent of plaque were evaluated in 5 segments of the left and right carotid artery (distal and proximal common carotid artery, carotid bulb, and proximal internal and external carotid arteries).12 Plaque was defined as a protrusion into the vessel lumen ≥50% thicker than the adjacent IMT. For each segment, plaque was graded between 0 (no plaque) to 3 (plaque covering ≥50% of vessel diameter). Grades from all segments of the left and right carotid artery were summed for the plaque index. Sonographers at each study site were trained by the University of Pittsburgh Ultrasound Research Laboratory and monitored for reliability. Images were read centrally at the University of Pittsburgh Ultrasound Reading Center using AMS software. Reproducibility was excellent (IMT intraclass correlation coefficient ≥0.77 between sonographers) and 0.90 (between readers); plaque intraclass correlation coefficients =0.86–0.93.14

Covariates and Other Variables
Race/ethnicity was reported at baseline. Education was assessed at baseline and categorized as less than college (high school, some college, vocational school) versus college or higher. Other covariates were taken from annual visit 12 (concurrent with the carotid measure). Age, smoking status (current versus past/never), depressive symptoms (assessed by the Center for Epidemiological Studies Depression Scale),13 financial strain (how hard it was to pay for basics: very hard, somewhat hard, not hard at all), alcohol use (weekly servings of beer, wine, liquor, mixed drinks), physical activity,16 and menopausal stage were derived from questionnaires and interviews. Menopausal stage was defined from self-reported bleeding patterns over the year, with most women postmenopausal (ie, ≥12 of amenorrhea). Height and weight were measured and body mass index calculated (kg/m²). Blood pressure averaged from 2 seated measurements. Given the high correlation between systolic and diastolic blood pressure, the measure with the strongest association with the outcome was included. Use of medications for diabetes mellitus, blood pressure lowering, lipid lowering, or hormone therapy at any point during the 12 years of the study were considered as covariates.

Phlebotomy was performed after overnight fast <90 days of the annual visit. Blood was separated, frozen (~80°C), and sent on dry ice to the University of Michigan Pathology Laboratory, Clinical Laboratory Improvement Amendments-certified and accredited by the College of American Pathologists. Measurements were performed on a Siemens ADVIA 2400 automated chemistry analyzer using Siemens ADVIA chemistry system reagents. Glucose was measured using a 2-step enzymatic reaction that uses hexokinase and glucose-6-phosphate dehydrogenase enzymes. Serum insulin was measured using radioimmunoassay. Homeostatic model assessment–insulin resistance was calculated as (fasting insulin×fasting glucose)/22.5.17 Lipid fractions were determined from EDTA-treated plasma.18–20 High-sensitivity C-reactive protein (CRP-hs) was measured using an ultrasensitive rate immunonephelometry method (Dade-Behring, Marburg, Germany) that had a sensitivity of 0.03 mg/dL and coefficients of variation at CRP concentrations of 0.05 and 2.2 mg/dL of 10% to 12% and 5% to 7%, respectively.

Data Analyses
IMT, homeostatic model assessment–insulin resistance, and triglyceride values were natural log-transformed for analysis. The plaque index was categorized as none (0), moderate (1–2), or high (>2). Baseline differences between included/excluded participants were tested using Wilcoxon rank-sum and χ² tests. Associations between abuse variables and carotid outcomes were estimated in linear and multinomial logistic regression models. Models were first adjusted for age, race/ethnicity, and site, with additional adjustment for covariates associated with outcomes at P<0.05. Interactions between abuse and race/ethnicity and between childhood and adult abuse were examined as cross-product terms in multivariable models. Residual analysis and diagnostic plots were used to verify model assumptions of normality and R² and likelihood ratio χ² tests to assess model fit. Analyses were performed with SAS v9.2 (SAS Institute, Cary, NC).

Results
Participant characteristics are presented in Table 1. Approximately 26% of women reported either physical or...
black women. Ninety-nine (7%) women reported both childhood physical and sexual abuse, and 86 (6%) women reported both adulthood physical and sexual abuse.

A history of childhood sexual abuse, but not childhood physical abuse, was related to higher IMT (Table 3; Figure). Associations persisted when adjusting for covariates and CVD risk factors. None of the adult exposures were related to IMT in minimally adjusted or fully adjusted models. Adult sexual abuse was associated with an increased risk of plaque (Table 4), although these relations were not monotonic and must be viewed with caution.

We considered whether the relation between childhood or adulthood abuse and carotid outcomes varied by race/ethnicity. No interactions by race/ethnicity were evident (interaction P>0.10). We additionally tested interactions between multiple types of abuse as a child or adult. None of these interactions were significant (interaction P>0.10). We considered several other treatments of covariates, adjusting for covariates averaged during the course of the study, including depressive symptoms (despite its lack of association with study outcomes) and dietary variables (available on a subset of participants) to multivariable models; findings were unchanged (data not shown).

Given prior work demonstrating associations between childhood abuse and CRP, we also considered models adjusting for CRP-hs, and results were largely unchanged (eg, childhood sexual abuse in relation to IMT: β=0.022; SE=0.010; P=0.05; adulthood sexual abuse in relation to plaque score: score 1–2: odds ratio, 0.657; confidence interval, 0.422–1.022; score >2: odds ratio, 1.422; confidence interval, 0.839–2.411; P=0.032).

**Discussion**

This is the first investigation to show that a history of childhood sexual abuse is related to higher IMT. These associations persisted even after adjusting for multiple demographic and CVD risk factors. They were similar across racial/ethnic groups and were observed among women without clinical CVD. Furthermore, findings provided suggestive evidence of adult sexual abuse related to elevated plaque.

Existing research links childhood abuse, particularly sexual abuse, to reported CVD.1–6,22 One meta-analysis found childhood abuse reliably associated with reported CVD events in adulthood.4 In the National Comorbidity Study, child/adolescent rape or sexual molestation was associated with a 5-fold increased reported heart disease among women. In the Nurses Health Study (NHS) 2, severe physical abuse and forced sex in childhood were associated with a 1.5-fold increased risk of reported incident CVD events, although this association was largely accounted for by CVD risk factors.22 Notably, existing studies are based largely on self-reports of CVD. The NHS verified a subset of events via medical record; however, medical record availability was significantly lower among women with an abuse history, and associations were nonsignificant when restricted to verified events.22 Thus, the present study contributes to the literature showing childhood sexual abuse is associated with increased subclinical CVD.

This study is notable in its use of subclinical CVD measures. IMT is a widely used and well-validated subclinical CVD measure significantly associated with later CVD events, even among low-risk populations.7 It is useful for indexing the...
development of atherosclerosis before frank disease is evident. It can represent an advantage compared with self-reported disease, because reports are subject to biases of recall, reporting, and medical care access. This index is also useful in measuring cardiovascular risk among midlife women in whom clinical events are rare.

Women with prevalent heart disease or stroke were excluded from this study. We show that women with prevalent CVD more often reported a history of childhood or adulthood physical or sexual abuse. However, associations between abuse and IMT were still apparent after excluding these high-risk women. Thus, sexual abuse appears to be related to having prevalent CVD in midlife as well as being related to greater IMT among women without prevalent CVD.

In prior investigations, associations between childhood sexual abuse and CVD are often explained by traditional CVD risk factors. Indeed, women with an abuse history have elevated smoking, obesity, insulin resistance, sedentary behavior, hypertension, and the metabolic syndrome.23–27 However, associations between abuse and subclinical CVD were not fully explained by CVD risk factors. Thus, other pathways may be at play. Negative psychological factors (eg, depression, anxiety) are important sequelae of abuse28 and have been associated with elevated CVD risk.2 Although the psychological factors assessed here were largely unrelated to IMT and plaque (data not shown) and did not explain the observed relations, ongoing consideration of psychological factors in the relation between abuse and CVD risk is warranted. A third pathway linking childhood sexual abuse and CVD risk may be a direct physiological one. Some evidence shows altered hypothalamic pituitary adrenal axis function29 among adults having experienced childhood abuse, which in turn has been associated with atherosclerosis.30 Furthermore, childhood adversity may be linked to altered peripheral adrenergic function.31 Finally, childhood adversity may be linked to inflammatory dysfunction,32 and although adjustment for CRP-hs did not explain results, a wider range of inflammatory markers should be considered in future work.

Associations were most clearly observed for childhood sexual abuse. These findings are broadly consistent with other work.4–6,22 The reason for this more pronounced association for sexual abuse may be because childhood sexual abuse is particularly toxic, more precisely recalled than other abuse types, or is a marker for abuse severity.33 Furthermore, there was indication of adult sexual abuse related to increased carotid plaque, although we recommend caution in interpreting these results because associations were not monotonic. However, they do indicate the potential importance in assessing both child and adult exposures in future work.

Table 2. Prevalence of Child and Adult Physical and Sexual Abuse by Race/Ethnicity

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Total Sample (n=1402), n (%)</th>
<th>Black (n=417), n (%)</th>
<th>White (n=711), n (%)</th>
<th>Chinese (n=189), n (%)</th>
<th>Hispanic (n=85), n (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical abuse</td>
<td>223 (17.73)</td>
<td>94 (20.75)</td>
<td>135 (18.6)</td>
<td>29 (15.10)</td>
<td>18 (22.22)</td>
<td>0.33</td>
</tr>
<tr>
<td>Sexual abuse</td>
<td>208 (15.89)</td>
<td>90 (19.82)</td>
<td>130 (18.08)</td>
<td>14 (7.29)</td>
<td>10 (12.20)</td>
<td>0.001</td>
</tr>
<tr>
<td>Any abuse</td>
<td>342 (25.83)</td>
<td>141 (30.79)</td>
<td>199 (27.34)</td>
<td>36 (18.56)</td>
<td>23 (28.05)</td>
<td>0.02</td>
</tr>
<tr>
<td>Adult</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical abuse</td>
<td>237 (17.97)</td>
<td>132 (28.95)</td>
<td>132 (18.16)</td>
<td>9 (4.64)</td>
<td>15 (18.75)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sexual abuse</td>
<td>150 (11.38)</td>
<td>65 (14.25)</td>
<td>103 (14.23)</td>
<td>4 (2.06)</td>
<td>9 (11.11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any abuse</td>
<td>301 (22.79)</td>
<td>150 (32.75)</td>
<td>181 (24.90)</td>
<td>11 (5.67)</td>
<td>17 (20.99)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 3. Child and Adult Abuse in Relation to Carotid IMT

<table>
<thead>
<tr>
<th>IMT</th>
<th>Child Model 1 β (SE)</th>
<th>Model 2 β (SE)</th>
<th>Adult Model 1 β (SE)</th>
<th>Model 2 β (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical abuse</td>
<td>0.016 (0.010)</td>
<td>0.008 (0.010)</td>
<td>0.006 (0.010)</td>
<td>0.004 (0.010)</td>
</tr>
<tr>
<td>Sexual abuse</td>
<td>0.027 (0.010)†</td>
<td>0.022 (0.010)†</td>
<td>0.016 (0.012)</td>
<td>0.009 (0.012)</td>
</tr>
<tr>
<td>Any abuse</td>
<td>0.023 (0.009)†</td>
<td>0.015 (0.009)‡</td>
<td>0.005 (0.009)</td>
<td>0.002 (0.009)</td>
</tr>
</tbody>
</table>

Each abuse variable considered in a separate model; IMT log-transformed for analysis. Model 1: site, age, race/ethnicity; model 2: site, age, race/ethnicity, education, financial strain, body mass index, high-density lipoprotein, triglycerides, systolic blood pressure, homeostatic model assessment, smoking, alcohol use, physical activity, blood pressure-lowering medications, cholesterol-lowering medications, and anti-diabetic medications. IMT indicates intima media thickness.

*P<0.01; †P<0.05; ‡P<0.10.

Figure. Adjusted mean intima media thickness (IMT) by history of childhood sexual abuse (adjusted for site, age, race/ethnicity, education, financial strain, body mass index, high-density lipoprotein, triglycerides, systolic blood pressure, homeostatic model assessment, smoking, alcohol use, physical activity, blood pressure-lowering medications, cholesterol-lowering medications, and anti-diabetic medications).
Several limitations deserve mention. Abuse was measured via a brief assessment rather than a validated scale. However, the child abuse question here correlated highly with a validated measure, particularly in the case of childhood sexual abuse, the focus here. Additional limitations are that the abuse exposures were retrospectively reported, they were assessed once during the study, and not all types of childhood adversities were assessed (eg, neglect). Future work should examine these associations with a full multidimensional scale. Moreover, our findings may not generalize to all women, because high-risk women (women with prevalent CVD, women who dropped out before visit 12) were not included in primary analysis. It is notable that associations were observed even among these comparably lower-risk women. Finally, men were not included in this investigation.

The study had several strengths. It included a large, well-characterized sample of midlife women spanning 4 racial/ethnic groups. Several types of abuse in childhood and adulthood were assessed. The outcome considered here was subclinical CVD. Several potential demographic, biological, and behavioral CVD risk factors were considered as confounders or pathways, allowing for a rigorous test of these relations.

A history of childhood sexual abuse was associated with greater carotid IMT among midlife women free of overt clinical disease. These associations persisted after controlling for CVD risk factors and were observed across racial/ethnic groups. These findings add to the growing literature showing the potentially deleterious effect of child abuse, and childhood sexual abuse in particular, to women’s cardiovascular health. They underscore the importance of considering psychosocial factors in relation to cardiovascular health, of assessing abuse history in clinical practice, and of ongoing efforts to prevent child abuse to improve population health.

**Acknowledgments**

The content of this article is solely the responsibility of the authors and does not necessarily represent the views of the National Institute on Aging, National Institute of Nursing Research, Office of Research on Women’s Health, or the National Institutes of Health (NIH). Clinical Centers: University of Michigan, Ann Arbor—Siobán Harlow, Principal Investigator (PI) 2011 to present; MaryFran Sowers, PI 1994 to 2011; Massachusetts General Hospital, Boston, MA—Joel Finkelstein, PI 1999 to present; Robert Neer, PI 1994 to 1999; Rush University Medical Center, Chicago, IL—Howard Kravitz, PI 2009 to present; Lynda Powell, PI 1994 to 2009; University of California, Davis—Kaiser-Ellyn Gold, PI; University of California, Los Angeles—Gail Greendale, PI; Albert Einstein College of Medicine, Bronx, NY—Carol Derby, PI 2011 to present; Rachel Wildman, PI 2010 to 2011; Nanette Santoro, PI 2004 to 2010; University of Medicine and Dentistry, New Jersey Medical School, Newark—Gerson Weiss, PI 1994 to 2004; University of Pittsburgh, PA—Karen Matthews, PI. NIH Program Office: NIA, Bethesda, MD—Winifred Rossi, 2012 to present; Sherry Sherman, 1994 to 2012; Marcia Ory, 1994 to 2001; NINR, Bethesda, MD—program officers. Central Laboratory: University of Michigan, Ann Arbor—Daniel McConnell (Central Ligand Assay Satellite Services). Coordinating Center: University of Pittsburgh, PA—Maria Mori Brooks, PI 2012 to present; Kim Sutton-Tyrrell, PI 2001 to 2012; New England Research Institutes, Watertown, MA—Sonja McKinlay, PI 1995 to 2001. Steering Committee: Susan Johnson, Current Chair; Chris Gallagher, Former Chair.

**Sources of Funding**

Study of Women’s Health Across the Nation has grant support from the National Institutes of Health (NIH), Department of Health and Human Services (DHHS), through the National Institute on Aging, the National Institute of Nursing Research, and the NIH Office of Research on Women’s Health (U01NR004061, U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495).

**Disclosures**

None.

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Stroke. 2014;45:2246-2251; originally published online July 17, 2014;
doi: 10.1161/STROKEAHA.114.005928
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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