

Educational Attainment and Coronary and Aortic Calcification in Postmenopausal Women

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Objective: Low socioeconomic status is a risk factor for clinical coronary heart disease, a relatively crude outcome associated with important biases. By avoiding these biases, subclinical assessments could facilitate efforts to understand the association between socioeconomic status and coronary disease. The current study 1) evaluated the nature of the associations between educational attainment and subclinical atherosclerosis and 2) examined if biologic, behavioral, and psychosocial factors mediated these associations. **Methods:** Participants were 308 women from the Healthy Women Study who underwent a clinic examination of risk factors either 5 ($N = 32$) or 8 ($N = 276$) years after the menopausal transition. Aortic and coronary calcification were measured using electron beam tomography. **Results:** Logistic regression analysis with orthogonal polynomials revealed a marginally significant linear trend for coronary calcification, with the more educated groups showing lower calcification than the less educated groups. A significant linear trend was also observed for aortic calcification. In addition, a marginally significant quadratic trend was observed for aortic calcification so that the effect began to reverse at the highest level of education. Measured risk factors were associated with education and with the calcification outcomes, but they explained little of the associations between educational attainment and coronary or aortic calcification. None of the factors tested met the minimum criterion for mediation. **Conclusions:** The findings show that lower education is associated with greater early stage atherosclerosis. Subclinical assessments, such as electron beam tomography, represent useful alternatives for studies of socioeconomic status and coronary artery disease. **Key words:** atherosclerosis, calcium, educational level, risk factors, psychosocial, socioeconomic factors.

ANOVA = analysis of variance; DBP = diastolic blood pressure; EBT = electron beam tomography; HDL-C = high-density lipoprotein cholesterol; HRT = hormone replacement therapy; HWS = Healthy Women Study; LDL-C = low-density lipoprotein cholesterol; SBP = systolic blood pressure; SES = socioeconomic status.

INTRODUCTION

Considerable research shows that socioeconomic status (SES) is an important predictor of cardiovascular morbidity and mortality in men and in women (1–4; for review see Ref. 5). However, the reasons for this association are not fully understood (5). A limitation of most prior research concerning SES and coronary disease is a focus on clinical events, that is, angina, myocardial infarction, and cardiac death, outcomes that may be associated with specific biases.

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Specifically, many asymptomatic individuals have significant underlying atherosclerosis (6), and studies that quantify clinical events may therefore underestimate the number of "cases." Similarly, some individuals with clinically debilitating angina have no underlying occlusion in the coronary arteries. This is especially true of women, in whom only about 50% who present with chest pain have coronary atherosclerosis (7). Physician expectations can also bias the diagnosis of clinical coronary disease. Women who present with angina are less likely to be referred for advanced diagnostic testing than are men (8, 9). In the past, objective assessments of atherosclerosis were invasive and therefore did not represent viable research alternatives. Newly available noninvasive techniques for assessing subclinical (ie, presymptomatic) atherosclerotic burden, such as electron beam tomography (EBT), have the potential to advance research concerning risk factors for coronary disease by circumventing these research difficulties.

Subclinical assessment techniques may be especially useful for efforts to study the role of SES in coronary disease. Because subclinical measurements quantify atherosclerosis before the appearance of symptoms, they can reduce the possible confound of reverse causation (ie, the effects of poor health on socioeconomic position) in studies of SES and coronary disease. Subclinical measurements can also facilitate efforts to identify the biopsychosocial mechanisms through which SES affects coronary risk, by allowing an examination of mediational paths at early disease stages. As a result, they may help identify which subgroups of individuals with low SES are at

highest risk for later cardiovascular morbidity and mortality, facilitating early prevention and intervention efforts.

Several recent studies have used subclinical measurement techniques to study the association between SES and atherosclerosis. Lynch et al. (10) found that indicators of SES were inversely associated with the extent of atherosclerosis quantified by ultrasound measures of carotid intima-media thickness in a population of Finnish men. Low SES was also associated with faster progression of atherosclerosis measured at follow-up (11). Adjustment for risk factors attenuated some of the cross-sectional associations but did not affect the inverse associations of income and education with atherosclerotic progression. Another study showed that income, education, and occupation were inversely associated with carotid intima-media thickness in men and women (12). In this study, statistical control for coronary risk factors substantially attenuated the associations. Finally, van Rossum et al. (13) measured aortic calcification by radiography and found that low occupation and education were associated with only marginally increased aortic calcification in Dutch women but not men.

EBT is another noninvasive method for evaluating subclinical atherosclerosis, which to our knowledge has not been studied in conjunction with measures of SES. EBT quantifies the extent of calcification present in the targeted region. Calcification is a process comparable to bone formation, which occurs as calcium is deposited in atherosclerotic plaques (14–16). Research has shown that EBT measures of calcification in the large coronary arteries are closely related to the amount of coronary atherosclerosis observed on pathologic study (17, 18) and angiography (18–20). In addition, the extent of coronary calcification predicts coronary morbidity and mortality in both symptomatic and asymptomatic individuals (21–23). Although useful, measures of intima-media thickness in the carotid arteries are considered a surrogate marker of diffuse atherosclerosis because they are not measured in the heart, and some consider them a marker of structural changes in the carotid wall due to long-term exposure to high blood pressure. Radiographic calcification measures are relatively crude because their image requires little movement, whereas EBT calcification measures can be taken when there is substantial movement, as occurs in the beating heart. The EBT procedure, therefore, shows considerable promise as an alternative outcome for studies of SES and coronary artery disease.

The Current Study

The first goal of the current study was to use EBT measures of coronary and aortic calcification to evaluate the association between education and subclinical atherosclerosis in a group of postmenopausal women. The second goal was to examine whether biological, behavioral, and psychosocial factors could account for associations between education and calcification scores. We examined aortic as well as coronary calcification because atherosclerotic changes emerge much earlier in the aorta (24, 25) and because the pronounced gender differences observed in the coronary arteries (with men showing more disease than women) do not occur in this region (24). In fact, some research suggests that women show more prevalent aortic atherosclerosis when compared with men (26, 27). Measures of aortic calcification predict cardiovascular morbidity and mortality in both men and women (27–29).

We examined education rather than other markers of SES because research has shown that education strongly predicts generalized cardiovascular risk (5) and cardiovascular mortality (30, 31). A recent study comparing the predictive utility of education, income, and occupation found that education was the strongest predictor of cardiovascular risk factors; education was a particularly strong predictor for women (32). In addition, occupational prestige might underestimate SES for individuals who are not in the labor force, whereas income is prone to missing or distorted responses (33) and in this population could be unduly affected by retirement or the recent loss of a spouse.

In previous research, known risk factors for coronary artery disease, such as systolic (SBP) or diastolic blood pressure (DBP), smoking, body size and fat distribution, and lipid profiles, predicted levels of coronary and aortic calcification (26, 34–38). Known cardiovascular risk factors have also been associated with education (32, 39–41). We therefore examined biologic and behavioral cardiovascular risk factors as possible mediators in the current research. In addition, we examined a number of psychosocial variables thought to predict cardiovascular morbidity and mortality, including depression, social support, job satisfaction, hostility, and anxiety (see Ref. 42 for review). Many of these variables have been associated with SES in previous research (for reviews see Refs. 43 and 44). Furthermore, at least some evidence suggests that psychosocial factors may contribute to the association between SES and health (45–47), although other research has not supported this conclusion (48, 49).

METHODS

Participants

Three hundred eight women from the University of Pittsburgh's Healthy Women Study (HWS) participated in the study. The HWS is a prospective study of the biological and behavioral risk factor changes associated with the menopause. The University of Pittsburgh's Institutional Review Board has approved all aspects of the HWS. The total HWS sample consists of 541 women who were recruited into the study between 1983 and 1985. As detailed elsewhere (39, 50), a recruitment letter was sent to randomly selected women within selected area codes in Allegheny County, Pennsylvania. Follow-up phone calls were placed, and of the 2405 women contacted, approximately 60% agreed to participate. The final sample represents the proportion of these women who were eligible according to the following criteria: age between 42 and 50 years, DBP less than 100 mm Hg, no dependence on medications that would affect biological risk factors (eg, lipid-lowering drugs, insulin, antihypertensive agents), no use of hormone replacement therapy (HRT), and menstruation within 3 months of the first visit.

Clinic Visits

All participants attended a baseline clinic visit and then began reporting their menstrual status through monthly postcards. Women were considered postmenopausal when they had stopped menstruating for 12 months and/or had used HRT for 12 months. At that point, participants attended a follow-up clinic visit, and they were also seen approximately 2, 5, and 8 years after menopause. In the current study, we report risk factor data from the visit closest in time to the EBT scan, either the eighth postmenopausal year visit ($N = 276$) or the fifth postmenopausal year visit ($N = 32$). In addition, if data points were missing for the 8-year visit (ie, the participant did not undergo a blood draw or did not complete a questionnaire) but were available from the 5-year evaluation, these values were substituted.

Clinic visits occurred after a 12-hour fast. Measurements included height, weight, waist and hip circumference, SBP and DBP, and a fasting blood draw. Laboratory assays were performed at a central laboratory that conforms to the quality-control standards of the Centers for Disease Control and Prevention and the National Heart, Lung, and Blood Institute. Measurements of total serum cholesterol (51), total high-density lipoprotein cholesterol (HDL-C) (52), and triglycerides (53) were obtained. The Friedewald equation (54) was used to estimate low-density lipoprotein cholesterol (LDL-C). An enzymatic assay was used to measure plasma glucose (Yellow Springs glucose analyzer, Yellow Springs Instruments, Yellow Springs, OH). Blood pressure was measured with the random zero-muddler method by technicians certified according to the Multiple Risk Factor Intervention Trial protocol (55). Technicians measured blood pressure two times, and the results were averaged.

Participants provided information concerning their health behaviors at each visit. For this report, we examined smoking (current smoking status) and exercise habits (estimated kilocalories expended in leisure during the week before the clinic visit, measured with the Physical Activity Index, Ref. 56). Participants also completed questionnaires assessing demographic characteristics and personality and social characteristics. In the current study, we used the following measures: the Cook-Medley Hostility Inventory (57), Spielberger Trait Anger (58) and Anxiety (59) Scales, Beck Depression Inventory (60), job dissatisfaction (61), perceived appraisal support (ie, emotional support) from the Interpersonal Support Evaluation List (62), and the Cohen Perceived Stress Scale (63). Administration of the Spielberger Anger and Anxiety scales and the Cook-

Medley inventory was discontinued after 1997. Thus, for these scales, a greater proportion of data were from the fifth- rather than the eighth-postmenopausal-year visit ($N = 80$ for the anger and anxiety scales and $N = 95$ for the Cook-Medley inventory). The test-retest correlations for a subset of women who completed these measures at both the fifth- and eighth-postmenopausal-year visits were quite high ($r = 0.81$ for hostility, $r = 0.75$ for Spielberger Anger, and $r = 0.74$ for Spielberger Anxiety).

Electron Beam Tomography

Beginning in 1997 women who had already attended or were scheduled to attend the clinic for their 8- ($N = 276$) or 5-year ($N = 32$) postmenopausal visits were invited to undergo an EBT of their heart and aorta. Of the women offered the procedure to date, 40 have refused. These women did not differ significantly from the participants in terms of educational attainment ($\chi^2(3) = 2.49, p = .48$). None of the women who have obtained an EBT scan were symptomatic for coronary heart disease at the time of the scan.

A trained technician performed the EBT study using an Imatron C150 scanner (Imatron, South San Francisco, CA). The first pass focused on the coronary arteries from the level of the aortic root to the apex of the heart. The scan recorded between 30 and 40 contiguous 3-mm-thick transverse images during maximal breath holding. The second pass imaged 6-mm contiguous segments of the aorta from the aortic arch to the iliac bifurcation. Electrocardiograph triggering was used so that each 100-ms exposure derived from the same phase of the cardiac cycle (60% of the RR interval). A trained technician used the method reported by Agatston et al. (64), with a densitometric program from the Imatron C150 scanner, to derive calcium scores for both the heart and the aorta. Examination of scores from 40 subjects with varied calcification values indicated high reproducibility with interclass correlations of 0.99 and 0.98 for the coronary and aortic scores, respectively (65). Complete coronary artery scans were available for 308 women, and aortic scans were available for 298 women. Aortic and coronary calcium were significantly correlated ($r = 0.40, p < .001$).

Calcification and Education Groups

The distributions of scores for both the aorta and coronary arteries were extremely positively skewed. For coronary calcium, 54.5% of the participants had a score of 0, and the 60th, 80th, and 90th, percentile scores were 2.0, 56.4, and 144.2, respectively; this distribution is similar to the distribution of coronary calcium observed in similar populations (eg, Ref. 66). For aortic calcification, 25.5% of participants had an aortic calcium score of 0, and the 40th, 60th, 80th, and 90th percentile scores were 24.2, 159.6, 544.8, and 1226.3, respectively. Because of the shapes of these distributions, it was not feasible to analyze the full continuum of calcification scores, and these data were instead dichotomized. No clinical cutoff score currently exists, but in a recent presentation of guidelines for use of EBT in asymptomatic individuals, Rumberger et al. (67) suggested that individuals with high coronary calcification relative to a sex- and age-matched comparison group are likely to be at greater disease risk. Thus, we created a high coronary subclinical disease group consisting of individuals with scores in the top quintile for the sample. Sixty-one women had coronary calcification scores above the 80th percentile score of 56.4. To our knowledge, aortic calcification scores have not been used previously to describe clinical risk. For consistency, we also used the 80th percentile cutoff to indicate "high" aortic subclinical disease. Fifty-nine women had aortic calcification scores above this cutoff point of 544.8. Education consisted of four groups: participants with a high school education or

less ($N = 92$), of which 89 had a high school degree, 2 had 10 to 11 years, and 1 had 7 to 9 years of education; participants with some college ($N = 65$); those with a 4-year college degree ($N = 77$); and those with a graduate degree ($N = 74$).

Analytic Strategy

The association between education and calcification was examined through logistic regression with polynomial contrasts to test for a linear trend. Thus, we tested the hypothesis that increasing levels of education would be associated with decreasing levels of calcification.

We used the procedure suggested by Baron and Kenny (68) to examine mediators of the association between education and calcification. A variable can be considered a mediator if it accounts statistically for a relationship between a predictor (ie, education) and an outcome (ie, aortic or coronary calcification). Only variables that exhibit an association with the predictor variable can be considered possible mediators. Thus, we first examined education group differences on the biological, behavioral, and psychosocial variables using analyses of variance (ANOVAs) with tests for linear trend for continuous variables and cross-tabs analyses with the Cochran-Armitage test for linear trend for categorical variables. To minimize the number of analyses, we tested as mediators only those variables associated with the outcome variables (ie, coronary and aortic calcification; see Ref. 69 for discussion of this approach to mediation analysis). We considered a possible mediator as any variable that discriminated the education and calcification groups at $p < .1$. Univariate outliers (ie, at least 3 SDs from the mean; Ref. 70) were excluded on an analysis-specific basis, and variables with substantially skewed distributions (triglycerides, exercise, depression, and emotional support) were analyzed using a logarithmic transformation. To facilitate interpretation, transformations were reversed before presentation of means and standard deviations in the tables.

The association between education and calcification was then examined in a series of multiple logistic regression analyses, which included each possible mediating risk factor along with age. Importantly, change in significance level for an effect is not an adequate indicator of mediation because it does not directly address the degree of attenuation. For example, a small effect may become nonsignificant after accounting for a potential mediator, even if a relatively minor change occurs in the variance accounted for by the original predictor. Likewise, a large effect may remain statistically significant even if inclusion of a mediator attenuates the initial effect substantially. Thus, the level of mediation was assessed by comparing the unstandardized regression coefficient for education in the model that controlled only for age with the unstandardized regression coefficient in the model that included age and the potential mediator. Mediation was indicated by a reduction in the regression coefficient for the linear trend of at least 1.65 of its standard error, the criterion recommended for smaller samples (eg, Refs. 71 and 72). We adopted the mediation approach because our purpose was to identify variables that might help explain the association of education with coronary or aortic calcification. Other recent work has focused explicitly on identifying risk factors for coronary and aortic calcification (34, 35) irrespective of SES.

RESULTS

Participant Characteristics

On average, participants were 61.76 years old ($SD = 1.61$) and 9.00 years postmenopausal ($SD = 2.08$) at the

time of the EBT scans. The education groups did not differ in age ($F(3,304) = 1.16$) or years after menopause ($F(3,304) = 0.66$) at the time of EBT scan. The high aortic calcification group was marginally older (mean = 62.15 years, $SD = 1.59$) than the low aortic calcification group (mean = 61.71 years, $SD = 1.60$) ($F(1,296) = 3.49$, $p < .1$), but there was no difference between these groups according to years after menopause ($F(1,296) = 0.001$). The high (mean = 62.01 years, $SD = 1.68$) and low (mean = 61.70 years, $SD = 1.59$) coronary calcification groups did not differ in age ($F(1,306) = 1.80$) or years past menopause ($F(1,306) = 0.11$).

Education and EBT Measured Calcification

Coronary calcification. Figure 1 depicts the proportion of each education group that had coronary calcification scores in the upper quintile of the distribution of scores (ie, scores at or above 56.4). The logistic regression analysis that tested the association between education and coronary calcification revealed a marginally significant linear trend ($\chi^2 = 3.77$, $p = .05$), suggesting that individuals with greater education show lower levels of coronary calcification. As shown in Figure 1, similar proportions of individuals in the two less educated groups had upper quintile scores for coronary calcification, as did individuals in the two more educated groups.

Aortic calcification. The logistic regression analysis that examined the association between education and aortic calcification revealed a significant linear trend ($\beta = -0.49$, $SE = 0.15$; $\chi^2 = 10.51$, $p < .01$). In addition, a marginally significant quadratic trend was observed ($\beta = 0.33$, $SE = 0.17$; $\chi^2 = 3.79$, $p = .05$). As shown in Figure 2, the associations between education

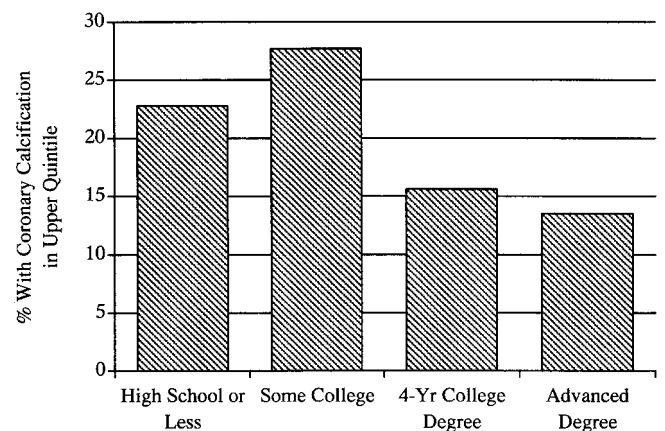


Fig. 1. Percentage of each education group with coronary calcification scores in the top quintile of the sample distribution ($N = 308$).

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and aortic calcification was generally linear until the advanced degree point, when the effect reversed.

Identification of Possible Mediators

Table 1 summarizes the results from the analyses of the association between education and the biologic and behavioral variables considered possible mediators. A significant linear trend was observed for measures of LDL-C, HDL-C, waist-to-hip ratio, fasting glucose, exercise expended in leisure activity, current smoking status, and a marginally significant linear trend was observed for use of HRT. As shown in Table 2, a significant linear trend was also observed for hostility, anxiety, and perceived support, and a marginally significant trend was observed for depression.

Although the association between education and coronary calcification was only marginally significant, we examined possible mediators because the effect was in the expected direction and because we wanted to see the extent to which risk factors explained the linear trend. The coronary calcification groups differed significantly on measures of HDL-C ($F(1,305) = 6.68, p < .01$), smoking ($\chi^2(1) = 7.28, p < .01$), and marginally on waist-to-hip ratio ($F(1,303) = 2.58, p = .1$). The higher coronary calcification group showed the more atherogenic risk factor profile. The coronary calcification group did not differ according to LDL-C, fasting glucose, or on any of the psychosocial measures related to the education grouping (all p values $> .1$). Thus, HDL-C, smoking, and waist-to-hip ratio were tested as possible mediators of the association between education and coronary calcification.

ANOVAs and χ^2 tests showed that the aortic calcification groups differed significantly on measures of LDL-C ($F(1,289) = 4.56, p < .05$), HDL-C ($F(1,294) =$

$5.41, p < .05$), waist-to-hip ratio ($F(1,293) = 4.66, p < .05$), smoking status ($\chi^2 = 13.28, p < .0001$), HRT ($\chi^2 = 10.81, p < .001$), depression ($F(1,290) = 7.01, p < .01$), and marginally on trait anxiety ($F(1,276) = 3.09, p < .1$). The higher aortic calcification group showed the more atherogenic risk factor profile in all analyses. The aortic calcification groups did not differ according to fasting glucose, exercise, hostility, or perceived support (all p values $> .10$). Thus, LDL-C, HDL-C, waist-to-hip ratio, smoking status, HRT, depression, and anxiety were related both to education and to aortic calcification and were tested as possible mediators.

Mediational Analyses

A series of logistic regression analyses examined the association between education and coronary or aortic calcification, adjusting for age and for each of the identified possible mediators. The final models adjusted for all possible mediators simultaneously. As noted above, these analyses involve a comparison of parameters across analyses that include different variables. For these comparisons to be accurate, the analyses should include identical samples. Thus, to accommodate variations in sample size (ie, due to missing data or excluded outliers), the initial analyses regressing calcification on education and age were first repeated using only participants with data for the targeted potential mediator(s). The unstandardized regression coefficients from these analyses were then compared with the coefficients from the analyses that also included the hypothesized mediator(s).

Coronary calcification. The results from the mediation tests for coronary calcification are summarized in Table 3. To qualify as a significant mediator, the variable had to account for at least a reduction of 0.25 in the weight of the unstandardized regression coefficient associated with linear contrast for education (ie, 1.65×0.15). As shown, smoking status and HDL-C were the only variables tested for mediation that predicted coronary calcification in these analyses and therefore that could represent mediators. However, inclusion of these variables did not attenuate the effect for education to a level suggesting mediation. In the logistic regression analysis that included all mediators in a single regression model, education did not significantly predict coronary calcification. However, the regression coefficient for the linear trend was not attenuated to a level suggesting mediation. Smoking ($\beta = -0.93, p < .05$) was a significant predictor in this model, and HDL-C ($\beta = -0.36, p = .06$) was a marginally significant predictor.

Aortic calcification. The results from the mediation tests for aortic calcification are summarized in Table 4.

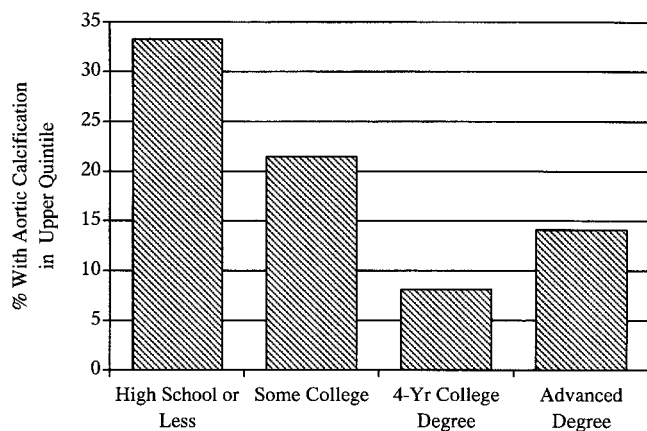


Fig. 2. Percentage of each education group with aortic calcification scores in the top quintile of the sample distribution ($N = 298$).

TABLE 1. Analyses of Differences Among Education Groups on the Biological/Behavioral Variables Considered Possible Mediators

Variable	Education				Test for Linear Trend ^a
	High School or Less (N = 92)	Some College (N = 65)	4-y College Degree (N = 77)	Advanced Degree (N = 74)	
DBP, mm Hg, mean (SD)	72.91 (8.71)	70.97 (8.81)	71.12 (8.70)	71.54 (8.11)	$F(1,303) = 0.86$
SBP, mm Hg, mean (SD)	122.91 (17.71)	122.05 (17.52)	121.86 (18.18)	120.40 (17.78)	$F(1,303) = 0.76$
LDL-C, mg/dl, mean (SD)	130.79 (33.70)	129.33 (32.13)	124.79 (27.38)	120.88 (32.63)	$F(1,297) = 4.67^{**}$
HDL-C, mg/dl, mean (SD)	58.04 (14.96)	63.09 (16.82)	62.04 (18.26)	65.33 (19.06)	$F(1,302) = 5.86^{**}$
Triglycerides, ^b mg/dl, mean (SD)	128.01 (70.52)	123.13 (65.37)	113.61 (59.52)	115.24 (55.26)	$F(1,301) = 1.38$
Fasting glucose, mg/dl, mean (SD)	92.58 (12.80)	90.84 (9.40)	89.20 (7.69)	89.32 (9.40)	$F(1,298) = 5.02^{**}$
Waist-to-hip ratio, mean (SD)	0.82 (0.07)	0.78 (0.07)	0.78 (0.07)	0.78 (0.07)	$F(1,301) = 10.44^{***}$
Exercise, ^b kcal in past week, mean (SD)	1647.82 (1162.99)	2490.27 (2412.50)	1961.94 (1603.02)	2055.35 (1366.09)	$F(1,300) = 3.17^*$
Current smoker, % (N)	22.8 (21)	9.2 (6)	11.7 (9)	4.1 (3)	$\chi^2(1) = -3.40^{***d}$
Using HRT, % (N)	39.6 (36)	53.1 (34)	50.6 (39)	58.1 (43)	$\chi^2(1) = -2.23^{**d}$
Taking medication that might affect biological risk factors, ^c % (N)	26.1 (24)	24.6 (16)	20.8 (16)	17.6 (13)	$\chi^2(1) = 1.40^d$

^a Degrees of freedom vary as a result of pairwise treatment of missing data.

^b Analysis based on log-transformed data. Means and SDs reflect nontransformed data.

^c Includes antihypertensive, lipid-lowering, digitalis, other heart, and diabetic medications.

^d Cochran-Armitage test for linear trend.

* $p < .1$; ** $p < .05$; *** $p < .01$.

TABLE 2. Analyses of Differences Among Education Groups on the Psychosocial Variables Considered Possible Mediators

Variable	Education				Test for Linear Trend ^a
	High School or Less (N = 92)	Some College (N = 65)	4-y College Degree (N = 77)	Advanced Degree (N = 74)	
Cook-Medley hostility, mean (SD)	15.01 (7.11)	11.87 (5.45)	12.33 (6.70)	11.42 (5.73)	$F(1,259) = 9.00^{***}$
Spielberger trait anger, mean (SD)	17.17 (3.94)	16.55 (3.84)	16.58 (3.46)	16.17 (3.41)	$F(1,284) = 2.50$
Spielberger trait anxiety, mean (SD)	17.05 (4.65)	16.02 (3.97)	15.27 (3.48)	16.36 (4.13)	$F(1,284) = 4.16^{**}$
Beck Depression Inventory, ^b mean (SD)	5.83 (5.46)	5.02 (3.85)	3.99 (3.68)	4.44 (3.70)	$F(1,298) = 3.25^*$
Job dissatisfaction, mean (SD)	7.98 (2.67)	7.66 (1.93)	8.21 (2.21)	7.46 (2.40)	$F(1,164) = 0.43$
ISEL ^c appraisal support, ^b mean (SD)	7.54 (2.39)	8.21 (1.92)	8.42 (1.89)	8.44 (1.83)	$F(1,298) = 7.79^{***}$
Cohen perceived stress, mean (SD)	11.33 (4.01)	10.62 (3.48)	10.55 (3.66)	11.12 (3.56)	$F(1,297) = 0.13$

^a Degrees of freedom vary as a result of pairwise treatment of missing data.

^b Analysis based on log-transformed data. Means and SDs reflect nontransformed data.

^c ISEL = Interpersonal Support Evaluation List.

* $p < .1$; ** $p < .05$; *** $p < .01$.

Again, to qualify as a significant mediator, the variable had to account for a reduction of at least 0.25 in the weight of the coefficient associated with the linear trend for education. LDL-C, HDL-C, smoking, and HRT predicted aortic calcification in models with education. However, as shown, no analysis met the minimal criteria for evidence of mediation. In the final model, the magnitude of the education coefficient was not sufficiently reduced to suggest mediation, although the linear trend was no longer statistically significant. Smoking was a statistically significant predictor in this model ($\beta = -1.23$, $p < .05$), and HRT was a marginally significant predictor ($\beta = -0.69$, $p = .06$).

DISCUSSION

Education and EBT Measures of Calcification

In this group of postmenopausal women, increasing levels of educational attainment were associated with decreasing levels of coronary and aortic calcification as quantified by EBT. All participants were asymptomatic for coronary disease, and these findings therefore add to a growing number of studies suggesting that the effects of SES emerge very early in the atherosclerotic process (10–13). To our knowledge, this study is the first to demonstrate a relationship between education and subclinical coronary artery and aortic disease as-

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TABLE 3. Unstandardized Coefficients From the Regression of Coronary Calcification on Education With and Without the Proposed Mediators^a

Variable	β (SE)	
	Model Without Mediator	Model With Mediator
HDL-C, ^b mg/dl (N = 306)		-0.44** (0.17)
Linear polynomial contrast for education	-0.29** (0.15)	-0.26* (0.15)
Smoking (N = 308)		-0.95** (0.39)
Linear polynomial contrast for education	-0.29** (0.15)	-0.23 (0.15)
Waist-to-hip ratio ^b (N = 305)		0.23 (0.16)
Linear polynomial contrast for education	-0.29** (0.15)	-0.24 (0.15)
All mediators (N = 304)		
Linear polynomial contrast for education	0.30** (0.15)	0.17 (0.16)

^a All models are adjusted for age.

^b Scores were standardized before entry into the logistic regression model so that effect is for a 1-SD increase in the variable.

* $p < .1$; ** $p \leq .05$.

essed by EBT. This study also builds on previous research by focusing on two disease locations (ie, the coronary arteries and the aorta) within the same sample.

The overall range of aortic calcification scores was considerably wider, scores tended to be higher, and fewer participants had aortic calcification scores of 0 when compared with the coronary calcification scores. These findings are consistent with prior research suggesting that disease may develop earlier in the aorta (24, 25) and that women especially are likely to display a prevalence of disease in this location (26, 27). The wider range of disease in the aorta, and the fact that individuals with high aortic subclinical disease had more calcification relative to those with high coronary subclinical disease, may have contributed to the differential education effects. In other words, the effect of education on coronary calcification could be weaker simply because there is less variance to predict in coronary calcification. Additional research evaluating individuals with more varied stages of disease is needed to further explore this hypothesis.

In addition to the difference in the strength of the effect of education across the targeted sites, the shapes of the distributions showed differences. A significant linear trend was observed for both sites so that the less educated groups tended to show lower levels of high calcification when compared with the more educated groups. However, for the coronary measurements, the high school or less and some college groups had very similar proportions of high calcification, as did the

TABLE 4. Unstandardized Coefficients From the Regression of Aortic Calcification on Education With and Without the Proposed Mediators^a

Variable	β (SE)	
	Model Without Mediator	Model With Mediator
LDL-C, ^b mg/dl (N = 296)		0.30* (0.17)
Linear polynomial contrast for education	-0.47*** (0.15)	-0.44*** (0.15)
HDL-C, ^b mg/dl (N = 296)		-0.39** (0.18)
Linear polynomial contrast for education	-0.49*** (0.15)	-0.47*** (0.15)
Waist-to-hip ratio ^b (N = 295)		0.23 (0.16)
Linear polynomial contrast for education	-0.49*** (0.15)	-0.47*** (0.15)
Smoking (N = 298)		-1.22*** (0.41)
Linear polynomial contrast for education	-0.49*** (0.15)	-0.43*** (0.15)
HRT (N = 296)		-0.94*** (0.32)
Linear polynomial contrast for education	-0.49*** (0.15)	-0.46*** (0.15)
Depression ^b (N = 285)		0.09 (0.19)
Linear polynomial contrast for education	-0.43*** (0.15)	-0.41** (0.16)
Trait anxiety ^b (N = 278)		0.17 (0.16)
Linear polynomial contrast for education	-0.49*** (0.15)	-0.41*** (0.15)
All mediators (N = 276)		
Linear polynomial contrast for education	-0.42*** (0.15)	-0.24 (0.17)

^a All models are adjusted for age.

^b Scores were standardized before entry into the logistic regression model so that effect is for a 1-SD increase in the variable.

* $p < .1$; ** $p < .05$; *** $p < .01$.

college educated and advanced degree groups. The association between education and aortic calcification was linear until the most highly educated group, when the effect reversed. In other words, a somewhat higher proportion of women in the advanced degree group had high aortic calcification scores when compared with the 4-year college degree group. Consistently, a marginally significant quadratic trend was observed for this association. Although some prior research suggests a linear association between SES and cardiovascular health outcomes, the identification of a nonlinear effect is not uncommon. For example, previous research suggests that individuals who fail to complete a program of education might have worse health than those who simply do not pursue a higher educational stage (eg, Ref. 73). In addition, two recent studies examining income and health outcomes in US populations showed nonlinear associations (74, 75). In the first, the association between income and mortality was curvilinear (74). In the second, very poor individuals showed more negative health outcomes, whereas

differences among the other groups were less pronounced (75). Further research is needed to explore variability in the association between SES and coronary disease and to identify the mechanisms underlying these differential patterns.

Notably, the use of EBT measures for clinical purposes remains controversial, primarily because of questions about costs of such procedures in asymptomatic populations and the absence of alert values for abnormal levels in such populations. There is also a debate about the criterion for what constitutes an abnormal level of calcification in patient groups (16, 18), in part because of the newness of the technique. Likewise, atherosclerotic plaques that have calcified are not necessarily the same plaques that will lead to the clinical manifestations of coronary heart disease. In fact, some researchers believe that calcification is the body's mechanism for stabilizing plaques that might otherwise be prone to rupture (16). Despite the remaining questions about the calcification process, research does show that the level of calcification is a valid indicator of atherosclerotic burden (17–20), which predicts cardiovascular morbidity and mortality (21–23). Thus, the women who have scores in the upper quintile of either the aortic or coronary distributions will be more likely to show the clinical manifestations of coronary disease later in time.

Do Measured Risk Factors Explain the Association Between Education and Calcification?

The education groups differed significantly on a number of the measured biological, behavioral, and psychosocial cardiovascular risk factors. Consistent with previous research (32, 39–41), the general pattern was that educational attainment was inversely associated with level of cardiovascular risk. Nevertheless, statistical control for the factors related to education did not attenuate the excess risk for high aortic or coronary calcification to a level suggesting mediation. Thus, consistent with many prior studies using clinical (76–81) and subclinical outcomes (10–12), we were unable to account fully for the association between SES and coronary artery disease. Overall, the results from previous research and from the current study suggest that established risk factors may contribute to the association between SES and coronary disease, but they do not completely explain it. Further research is needed to continue to elucidate the processes that leave lower SES individuals disproportionately vulnerable to coronary disease, and subclinical assessments may facilitate this goal.

Limitations

Several limitations of the current research warrant discussion. The generalizability of the findings may be limited by the fact that women in the HWS were initially healthier and better educated than the general population because of the study entrance criteria (39). In addition, the sample consisted almost exclusively of white women, and the mechanisms contributing to the association between educational attainment and coronary artery disease might differ depending on ethnic status. Ethnic minority and white groups display differential prevalence rates for cardiovascular risk factors (82–84). Some research also suggests that the pattern of relationships between SES and specific risk factors varies according to ethnicity. For example, SES and lipid levels show disparate patterns of association within African American and white groups (85). Other research has shown that hostility is more closely associated with education in black than in white individuals (86).

Additional limitations relate to the cross-sectional study design. Because we assessed calcification and cardiovascular risk factors at roughly the same point in time, we are unable to ascertain the direction of these associations. Longitudinal research, preferably examining children from an early age, should focus on the associations among indicators of SES, biologic, behavioral, and psychological risk patterns as they develop across the lifespan. Some research suggests that even in childhood, biologic and behavioral cardiovascular risk factors distribute according to SES (87, 88). Another study found that among African Americans, lower SES was associated with higher hostility as early as childhood and adolescence (89). Lower SES was also associated with greater cardiovascular responses to laboratory stressors in both white and African American children (89). Other research shows that childhood SES predicts behavioral, biological, and psychosocial cardiovascular risk factors measured in adulthood (90, 91). Thus, the link between SES and cardiovascular risk seems to emerge at an early age. By implementing longitudinal research that incorporates measures of subclinical cardiovascular pathophysiology, we could therefore gain a more comprehensive understanding of the early trajectories that place lower SES individuals at risk for the etiology and progression of coronary disease.

SUMMARY AND CONCLUSIONS

The current study shows that subclinical measures of coronary artery disease have the potential to contribute to our understanding of SES and coronary

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health outcomes. As noted above, EBT and other sub-clinical assessments can eliminate the potential biases associated with clinical coronary outcomes. Moreover, in this study the participants were asymptomatic, indicating that EBT identified a link between educational attainment and atherosclerosis very early in the disease process. The results indicate the potential importance, from health and financial standpoints, of early cardiovascular prevention efforts targeted toward lower SES women. In addition, they point to the need for further research designed to better explicate the paths linking SES with cardiovascular health.

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