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Absence of Relation between Depressive Symptoms and Carotid Intimal Medial Thickness in the Baltimore Longitudinal Study of Aging

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Abstract

Objective—Prior literature has identified inconsistent cross-sectional associations between depressive symptoms and carotid intimal medial thickness (IMT) in healthy persons, and existing longitudinal work has relied on depression assessment at a single time point. The present investigation examined the relation of longitudinal trajectories of depressive symptoms, as well as history of significant symptoms, to subsequent carotid IMT among participants enrolled in the Baltimore Longitudinal Study of Aging. We also assessed longitudinal covariation of depressive symptoms and carotid IMT over two time points.

Methods—Five hundred fifty-six participants (303 women and 253 men), aged 20 to 93 years (*M*=55.8, *SD*=15.9), completed the Center for Epidemiological Studies-Depression (CES-D) scale from one to eight times over one to 15 years. Participants later underwent high-resolution B-mode ultrasonography to assess IMT of the far wall of the common carotid artery. A subset of these participants (*n*=68) underwent reassessment of IMT an average of 3.9 years later. Linear and mixed-effects regression models were adjusted for sex, race, education, systolic blood pressure (SBP), low-density lipoprotein (LDL) cholesterol, body mass index (BMI), diabetes, smoking, and antihypertensive, lipid-lowering, and antidepressant medications.

Results—There was no relation between trajectory of depressive symptoms or history of significant depressive symptoms and future carotid IMT. There was also no evidence for longitudinal covariation of depressive symptoms and IMT over time. Additional analyses similarly revealed a lack of significant associations.

Conclusion—There is no association between depressive symptoms and carotid IMT in the present sample of healthy community-dwelling volunteers.

Keywords

atherosclerosis; carotid intimal medial thickness; depression

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Introduction

Depressive symptoms and clinical depression are related to both concurrent and prospective risk for clinical cardiovascular and cerebrovascular disease, including myocardial infarction and stroke (1–6). Furthermore, depressive symptomatology is a consistent independent predictor of these diseases, above and beyond standard demographic and physiologic risk factors. Numerous pathophysiological and psychosocial mechanisms may account for the link between depressive symptoms and cardiovascular disease, including hypothalamic-pituitary-adrenal axis dysfunction, alterations in heart rate variability, exaggerated platelet reactivity, inflammatory processes, poor treatment adherence, and lifestyle characteristics (7–11).

Recent literature has attempted to extend these findings to an association between depressive symptoms and carotid atherosclerosis, as measured by either intimal medial thickness (IMT) or plaque (12–17). IMT, a measure of arterial wall thickness, has been used as a surrogate measure for generalized atherosclerotic disease (18–20). In cross-sectional studies, both concurrent depressive symptoms and clinically diagnosed depression have been associated with greater carotid IMT in selected healthy samples (12,16). However, other cross-sectional work has noted a lack of association between current depressive symptoms and both carotid IMT and plaque (15). Furthermore, lifetime history of clinical depression has been linked with presence of carotid plaque, but not carotid IMT, among middle-aged women (15). Longitudinal research has identified baseline depressive symptoms (17) and hopelessness (13) as predictors of accelerated progression of carotid IMT over 3-or 4-year follow-up. In addition, elevated depressive symptoms at baseline have been found to predict presence of carotid plaque at 10-year follow-up (14). A particular weakness of the current literature involves a nearly exclusive reliance on measurement of depression or depressive symptoms at a single time point (with the exception of Everson et al. (13), who studied hopelessness only). Because the relation between depressive symptoms and carotid IMT is unlikely to be a static one, additional research examining the relation between change in depressive symptoms and carotid IMT may help elucidate existing inconsistencies in the literature. Accordingly, the present study captured change in depressive symptoms over multiple time points and related these trajectories to future carotid IMT.

In brief, cross-sectional findings to date are inconsistent, and longitudinal research is limited. Only two studies have examined change in carotid IMT over time (13,17). Narrowly-defined sample demographics of several of the studies (e.g., pre-menopausal women (15), the elderly (16), men only (13)) also make generalization of these associations to the population at-large premature. To address these limitations, the present study included both men and women, examined a substantially wider age range (20 to 93 years), tracked depressive symptoms over longer follow-up (up to 15 years), and utilized a standard inventory of depressive symptoms.

The present investigation had two primary aims. First, to our knowledge, this is the first investigation to examine the relation of longitudinal trajectories of depressive symptoms to subsequent carotid IMT among healthy community-dwelling volunteers. We also investigated the relation of clinically significant depressive symptoms to subsequent carotid IMT over the same time period. Second, this is the first examination of longitudinal covariation in depressive symptoms and IMT across two time points. Unlike prior investigations, the present study combined two unique statistical approaches, past trajectory analysis and longitudinal covariation, to examine the relation between depressive symptoms and carotid IMT over time.

Methods

Participants

Participants from the Baltimore Longitudinal Study of Aging (BLSA), a prospective study of community-dwelling volunteers initiated by the National Institute on Aging in 1958, return to the Gerontology Research Center in Baltimore approximately every two years for medical, psychological, and cognitive testing. The BLSA is a sample of convenience, and all testing takes place over the course of a 2.5 day visit. Carotid ultrasonography was performed on a subset of the BLSA population as a function of sonographer availability (presumed to be random) and patient willingness to participate. No exclusion criteria were applied to this subsample. Data collection for the present study took place over 25 years, from 1980 through 2005.

Six hundred thirty-two participants (ages 20–93) were available for potential inclusion. We excluded persons with dementia (n=28 following protocol published previously (21)), cerebrovascular diseases including stroke (n=27), myocardial infarction (n=21), and carotid endarterectomy (n=0) across all assessment visits. Five hundred fifty-six participants (303 women and 253 men) were included in the analyses. Participants completed the Center for Epidemiological Studies-Depression (CES-D) scale an average of three times (*SD*=1.5, range= 1–8) over one to 15 years (*M*=5, *SD*=2.5), prior to initial carotid IMT assessment. The total number of participants by number of visits is listed in Table 1. The average time between first CES-D assessment and initial IMT assessment was 4.2 years (*SD*=3.1, range= 0–17). The average time between last CES-D assessment and initial IMT assessment was 0.3 years (*SD*=0.9, range= 0–8). Variation in frequency of CES-D sampling was due to differential participant entry times in the project.

A subset of 68 participants (34 women and 34 men) with available carotid IMT data at two repeated time points, an average of 3.9 (*SD*=2.28, range= 1–10) years apart, was utilized for covariation analyses. Availability of patients to participate in the repeated carotid IMT assessments was dependent on sonographer availability and patients' willingness to undergo a repeat assessment. Table 2 shows characteristics of study participants in both the primary analysis sample (n=556) and the covariation sample (n=68) at initial carotid IMT measurement. Although we were unable to perform statistical significance tests due to non-mutually exclusive samples, there appeared to be only minor sample characteristic differences between the primary analysis sample and the covariation sample. Demographic characteristics of both samples paralleled those of the current overall BLSA sample. Institutional Review Board approval was obtained from the Johns Hopkins Bayview Medical Center prior to 2002, and the MedStar Research Institute on or after 2002. All participants provided written informed consent. Data analyses were approved by the Institutional Review Board of the University of Maryland, Baltimore County.

Depressive Symptomatology

The CES-D is a 20-item inventory developed by the Center for Epidemiological Studies of the National Institute of Mental Health for use in studies of depressive symptoms in the general population (22). Nested in a standard battery of screening psychosocial questionnaires administered at each BLSA visit, the CES-D asks participants to rate the frequency and severity with which symptoms of depression were experienced during the preceding week. Participants rate each symptom on a 4-point scale, which ranges from *rarely or none of the time* (less than 1 day) to *most or all of the time* (5–7 days). Scores range from 0 to 60, with higher scores indicating greater depressive symptoms. The CES-D has been extensively validated and is strongly correlated with other self-report depression inventories (22–24). It also significantly distinguishes between depressed patients and normal controls, as well as among different

psychiatric populations (23). In this sample, internal consistency reliability of the CES-D was . 74.

Carotid Intimal Medial Thickness (IMT)

High resolution B-mode carotid ultrasonography was performed with a linear-array, 5- to 10-MHz transducer (Ultramark 9 HDI, Advanced Technology Laboratories, In., Seattle, Washington). This method allows quantitative measurement of the thickness of the intimal medial layers of superficial large arteries in a noninvasive manner. Initially, each participant lay in the supine position in a dark, quiet room. The right common carotid artery (CCA) was examined with the head tilted slightly upward in the mid-line position. The transducer was manipulated so that the near and far walls of the CCA were parallel to the transducer footprint, and the lumen diameter was maximized in the longitudinal plane. A region 1.5 cm proximal to the carotid bifurcation was identified, and the IMT of the far wall was evaluated as the distance between the lumen-intima interface and the media-adventitia interface. The IMT was measured on the frozen frame of a suitable longitudinal image, with the image magnified to achieve a higher resolution of detail. The IMT measurement was obtained from five contiguous sites at 1-mm intervals, and the average of the five measurements was used for analyses. Specific care was taken to measure IMT in areas devoid of plaque. All measurements were performed by a single sonographer. The intrarater correlation between repeated IMT measurements from 10 subjects was 0.96 ($p<0.001$), with similar averages for the two sets of readings (0.47 ± 0.13 vs. 0.45 ± 0.12 mm, p=NS) (25).

Covariates

Age and education were assessed in years. Binary covariates included race (white, non-white), smoking (ever/never), diabetes diagnosis (yes/no), use of antihypertensive or lipid-lowering medications (yes/no), and use of antidepressant medications (yes/no). With the exception of diabetes diagnosis, these covariate data were obtained via a self-report interview conducted by a BLSA physician or nurse practitioner. Diabetes diagnosis was determined by criteria based on the 1997 American Diabetes Association recommendations (26). Participants were categorized as diabetic if they a) were already being treated for diabetes or b) had 9- to 12-hour fasting glucose concentrations ≥126 mg/dl and 2-hour oral glucose tolerance test (OGTT) glucose concentrations ≥200 mg/dl. For participants without OGTT data who were not already being treated for diabetes, a fasting glucose concentration ≥126 mg/dl observed on two BLSA visits was sufficient for assignment of a diabetes diagnosis.

Blood pressure measurements were performed in the morning by trained nursing staff following a five minute resting period, at least 90 minutes after a light breakfast. Blood pressure was measured in both arms with a mercury sphygmomanometer using an appropriately sized occluding cuff. The blood pressure values used for data analyses are the average of the second and third measurements on both the right and left arms. Values for systolic (SBP) and diastolic (DBP) blood pressure were defined by Korotkoff phases I and V, respectively.

After an overnight fast, blood for lipid assay was drawn from an antecubital vein between 7:00 and 8:00 a.m. while the participant was supine. Concentrations of total cholesterol were determined by an enzymatic method (ABA-200 ATC Biochromatic Analyzer; Abbott Laboratories, Irving, TX), high-density lipoprotein (HDL) cholesterol concentrations were determined by a dextran sulfate-magnesium precipitation procedure, and low-density lipoprotein (LDL) cholesterol concentrations were estimated by the Friedewald formula.

Body mass index (BMI) was calculated as the ratio of weight (in kilograms) to height (in meters) squared. Height and weight were measured with a clinical calibrated scale during the anthropometric assessment of each BLSA visit.

Statistical Analyses

A priori power analyses were conducted using GPOWER, version 3.0 (27). Power calculations indicated that the study was powered to detect a small effect size (f^2=.03) for the linear regression step of the longitudinal trajectory analyses (n=556) and a medium effect size (f^2=.11) for the mixed-effects regression covariation analyses (n=68) at conventional levels of power (.80) and alpha (.05) using standard regression assumptions.

All statistical analyses were conducted using SAS version 9.1 (Cary, NC). To address our first aim, we conducted a series of analyses to examine the relation of trajectory of depressive symptoms (including clinically significant symptoms) to subsequent carotid IMT. First, longitudinal trajectories of CES-D scores were calculated based on all available CES-D data for participants included in the present study. To calculate these trajectories, preliminary mixed-effects regression analyses were conducted with continuous CES-D score entered as the dependent variable, and age and sex were entered as fixed effects. Time was modeled as a random effect. Sex was included because of the differential male/female patterns of CES-D scores in the BLSA (i.e., women score higher overall). Due to time-dependent missing data and a desire to model fundamental depressive symptom trajectories only, we did not include additional covariates in this initial step of the trajectory analyses. Mixed-effects models are the preferred method of analyzing data with repeated outcome measurements obtained at non-uniform intervals (28,29). These models examine the unique effects of individual predictors adjusted for all other predictors in the model, include both fixed and random effects, account for the correlation among repeated measurements on the same participant, and remain unaffected by randomly missing data. We used this approach to model the most basic trajectory of CES-D scores over time.

Resultant Bayesian slope estimates from these mixed-effects models represented each participant's unique longitudinal CES-D trajectory relative to the group mean. Positive slope estimates represented a rising trajectory of depressive symptomatology over time, whereas negative slope estimates indicated a declining trajectory of symptoms over time. Next, these slope estimates were entered into linear regression analyses as the predictor of interest, with carotid IMT as the dependent variable. Associated intercept values were entered to adjust for baseline CES-D levels. In addition, age, years of education, SBP, BMI, and LDL cholesterol were entered as continuous covariates, and race, sex, diabetes diagnosis, antidepressant use, antihypertensive or lipid-lowering medication use, and smoking were entered as categorical covariates. Covariate data analyzed here were collected during the same study visit as initial IMT assessment. We utilized this two-step approach (i.e., initial mixed-effects trajectory analysis, followed by linear regression analyses) because it provides a method by which all available information from data collected at multiple time points may be used to predict a distal outcome variable. Alternative longitudinal strategies, such as latent growth curve modeling, were inappropriate for the present data set due to the presence of repeated measures obtained at highly non-uniform time intervals across participants.

To examine history of clinically significant depressive symptoms (in place of continuous CES-D score trajectories), we distinguished participants who scored greater than or equal to 16 on the CES-D at any point in their history of BLSA visits (n=107) from those who never scored 16 or greater (n=449). A score of 16 on the CES-D is a well-accepted, standard cutoff for identification of clinically significant depressive symptoms (22,24). History of clinically significant depressive symptoms was then entered as a dichotomous predictor of interest into a multiple regression analysis, along with the aforementioned set of covariates, including age, sex, race, education, SBP, BMI, LDL cholesterol, diabetes, antidepressant use, antihypertensive or lipid-lowering medication use, and smoking. Carotid IMT again acted as the dependent variable.

To address the second aim of our study, we used mixed-effects regression analyses to model change in carotid IMT as a function of change in depressive symptoms (and all relevant covariates) in the subset of participants with repeat carotid IMT data. Concurrent measures of depressive symptoms and carotid IMT were available at two time points for this analysis. Other than sex and race, all covariates were modeled as time-dependent.

Lastly, in an effort to replicate and extend prior literature, we performed multiple variations of the primary analyses. All analyses were repeated with the exclusion of antidepressant use, separation of men and women, removal of non-demographic covariates (hereafter referred to as "partial" covariate elimination), and removal of all covariates (hereafter referred to as "complete" covariate elimination).

Results

The mean CES-D slope trajectory estimate was −0.003 (*SD*=.048, range= −0.27 – 0.18). Eighty-four participants (15.1%) showed increasing depressive symptoms over time, 65 participants (11.7%) showed decreasing depressive symptoms over time, and 407 participants (73.2%) remained stable over time (within ±1 SD of mean slope). At first CES-D assessment, 52 participants (9.4%) demonstrated clinically significant depressive symptoms, and mean CES-D score was 6.9 (*SD*=6.3, range= 1–42). At last CES-D assessment, 46 participants (8.3%) demonstrated clinically significant depressive symptoms, and mean CES-D score was 6.8 (*SD*=5.8, range= 1–44).

All of the primary analyses revealed no significant relation of depressive symptoms to carotid IMT (see Table 3 and Table 4). The correlation between CES-D score and carotid IMT at initial IMT assessment was non-significant (r=−.04, p=.34). Depressive symptom trajectories did not significantly predict future carotid IMT, t(1)=0.42, p=.68. Significant relations did arise between carotid IMT and select covariates, including age (p<.001), sex (p=.004), SBP (p<.001), and BMI (p=.046). There was also no significant relation of history of clinically significant depressive symptoms to subsequent carotid IMT, t(1)=0.39, p=.69. This analysis showed significant associations between carotid IMT and the covariates age (p<.001), sex (p=.004), race (p=.04), SBP (p<.001), and BMI (p=.048).

Furthermore, in a subset of participants, change in carotid IMT was not significantly associated with change in depressive symptoms across two time points, t(1)=− 0.84, p=.40. Significant covariates included age (p<.001) and race (p=.047). Distributions of CES-D scores at initial carotid IMT measurement (M=5.5, SD=5.0, range 0 to 27) and follow-up measurement (M=6.1, SD=5.1, range 0 to 20) were similar. Average IMT progression was .04 mm (SD=.13, range=−.26 to .52).

All variations of these primary analyses also failed to yield meaningful associations.[1] Following exclusion of antidepressant use, no relation of depressive symptoms to carotid IMT was observed for either past CES-D trajectory [t(1)=0.94 p=.35] or history of clinically significant symptoms [t(1)=0.69, p=.49]. When separate analyses were constructed for men and women, there was no significant relation of CES-D trajectory to carotid IMT in either men [t(1)=0.64, p=.52] or women [t(1)=−0.22, p=.82]. Similarly, there was no significant relation of history of clinically significant symptoms to carotid IMT in either men [t(1)=− 0.32, p=.75] or women [t(1)=1.05, p=0.30]. Lastly, we observed no significant relation of CES-D trajectory to carotid IMT following both partial [t(1)=0.28, p=.78] and complete covariate elimination [t

[1]In addition to those analyses presented, interactions of age and sex with both CES-D trajectory and history of significant depressive symptoms were non-significant. Also, analyses utilizing CES-D log transformations (due to positive skewness) yielded non-significant findings.

(1)=− 1.03, p=.30]. History of clinically significant symptoms was not related to carotid IMT after partial covariate elimination [t(1)=0.25, p=.80] but attained significance with complete covariate elimination [t(1)=−1.99, p=.047]. These alternative analyses were computed in the subset of participants with repeat carotid IMT data and also did not yield significant associations.

Discussion

This study is the first to examine the relation of longitudinal trajectories of depressive symptoms (over as many as 15 years), including clinically significant symptoms, to future carotid IMT among healthy community-dwelling participants. We are also the first to examine longitudinal covariation of depressive symptoms and carotid IMT over two time points. Results from the present study do not provide support for either of these hypothesized relations between depressive symptoms and carotid IMT. Neither CES-D score trajectories nor history of clinically significant symptoms offered any unique predictive power of future levels of carotid intimal medial thickening. In a subset of participants, change in depressive symptomatology did not independently predict concurrent change in carotid IMT over two time points. A number of variations of these analyses (i.e., exclusion of antidepressants, separation of men and women, and covariate removal) failed to identify an adequate explanation for the absence of expected results, given the only significant finding did not withstand adjustment for even basic covariates.

The results of this study contradict certain previous findings in the literature. Two studies found evidence for a concurrent relation between depressive symptoms and carotid IMT (12,16). One of these studies found an association only among men (12), whereas no association among either men or women was found in the present study. The other study applied only to late-life depression (onset at 60 years or older) (16), whereas the present study examined depressive symptomatology across the lifespan. Jones et al. found that the relation between lifetime history of depression and carotid IMT did not withstand adjustment for a standard set of covariates (15). In the present study, there was no relation between depressive symptoms and carotid IMT either before or after statistical adjustment for covariates. There was also no association between history of significant depressive symptoms and carotid IMT in the present sample. This finding suggests that the relation is not dependent on a standard threshold of depressive symptoms in the present study. However, it remains possible that a threshold effect may explain inconsistencies among findings.

Moreover, the results of this study do not replicate previous findings of a longitudinal association between depressive symptoms and carotid IMT or plaque (13,14,17). However, important conceptual differences between the current study and these previous studies are worth noting. Everson and colleagues (13) studied hopelessness, a symptom of depression, rather than the larger construct of depression, Haas and colleagues (14) studied only carotid plaque, and Stewart and colleagues (17) relied on a single assessment of depressive symptoms. It also remains possible that the variable locations from which the samples were drawn (e.g., New York, Pittsburgh, Finland, Netherlands) may contribute to the variability in findings. Data collected from psychosocial measures, such as the CES-D, may vary according to the sociocultural context of different geographic regions and nations.

Methodological differences in both depression and carotid wall measurement are prevalent across studies. For depressive symptoms, measurement has ranged from a two-item hopelessness measure (13) to a screening inventory (12,17) to full-scale diagnostic interviews (15,16). Despite this variability, significant relations have been identified using each of these approaches in select investigations. Regarding measurement of carotid IMT, some studies utilized far wall measurement (12,13,17), whereas others used an average of near and far wall

measurements (15,16). Most studies examined IMT of the common carotid artery (12,13,16), although two studies utilized a mean measure of IMT across the common carotid artery, internal carotid artery, and carotid bulb (15,17). Furthermore, most studies examined mean carotid IMT (12,15–17), but one study explored both mean and maximum carotid IMT (13). Again, significant associations have been identified using each of these methods. So, although the present study represents only a cross-section of the available approaches (i.e., use of a depression screening inventory with mean, far wall measurement of the common carotid artery), these methodological differences do not appear to account for the absence of a significant relation in the present study.

However, another methodological difference in carotid IMT measurement may account for variability of findings across studies. The distinction involves whether plaques were included in the measurement of IMT, compared to a specific avoidance of vessel areas containing plaque. The present study used the latter approach, whereas existing studies failed to specify their approach in this regard. The two methods may yield different findings, given that depressive symptom-plaque relations may differ from depressive symptom-IMT relations. To the extent that previous studies included plaque in their IMT measurements, the present study's findings indicate that no depressive symptom-carotid IMT relation may exist when care is taken to measure IMT in areas devoid of plaque. In addition, individuals with clinical cerebrovascular disease or past myocardial infarction were excluded from our sample, thus potentially excluding persons at greater risk for a measurable impact of depressive symptoms on carotid IMT.

Another explanation for the absence of expected findings involves the present study's power to detect significant effects relative to its sample size. The current study's moderate sample size is comparable to past research, but the observed effects in prior literature have also been generally small. Odds ratios describing the likelihood of an association between depressive symptoms and carotid IMT or plaque typically achieved significance with confidence intervals that narrowly escaped overlap with 1.0. Examples include Tiemeier et al. (OR=1.24; 95% CI, 1.02–1.51), Jones et al. (OR=2.30; 95% CI, 1.10–4.82), and Haas et al. (OR=2.63; 95% CI, 1.10–6.28). However, although the issue of power warrants mention, we failed to identify marginally significant effects in any of our primary analyses. Given that a priori power analyses revealed sufficient power to detect even a small effect size in our primary analyses, these trending patterns would have been expected even if our analyses were not sensitive enough to detect statistically significant effects. Nonetheless, with respect to the covariation analysis, the absence of consistently significant associations between the traditional coronary risk factors and carotid IMT likely reflects the low power to detect effects in this small sub-sample of participants.

Strengths of the present study include its prospective design, length of follow-up, examination of both men and women, and an expanded age range in comparison with previous studies. Several limitations also warrant mention. The study was based on a convenience, non-representative sample of primarily white, generally upper middle-class, well-educated participants. The homogeneity and non-representative nature of the sample may limit the generalizability of the study's findings. However, this is also a benefit because the homogeneous demographics of this sample restrict the influences of income, education, and occupation that might obscure the association between depressive symptomatology and carotid IMT. It should also be noted that participant refusal was not tracked during the study, introducing the possibility of selection bias. However, given that participant refusal would be expected to relate positively to depression, it is likely that any selection bias would have underestimated the relation between depressive symptoms and carotid IMT. In addition, the study examined only depressive symptomatology, rather than diagnosis of clinical depression. It is possible that the relation between depressive symptoms and carotid IMT is unique to

clinically-defined major depression for the present sample, rather than the larger spectrum of depressive symptomatology. Also, infrequent CES-D sampling may have contributed to the null findings, and future research should examine whether the present results replicate to study designs that better capture true chronicity of depressive symptomatology via more frequent assessments., Furthermore, a limited amount of repeat carotid IMT data was available, and our study may not have been sufficiently powered to detect significant longitudinal covariation. Future research with an increased sample size and increased number of repeat visits would allow further investigation into this possibility and permit analysis of non-linear change over time.

Lastly, although carotid IMT is often used as a surrogate marker of atherosclerosis, IMT is not synonymous with “subclinical” atherosclerosis, particularly in the absence of plaques. Instead, increased IMT, which could be related to either intimal or medial hypertrophy or both, could represent non-atherosclerotic age-associated changes in the vessel wall, or an adaptive response to changes in flow, wall tension, or lumen diameter (30,31). Future investigations should continue to evaluate the relation of depressive symptomatology with direct measures of atherosclerotic plaques, given existing discrepancies in the literature (13–16). If such associations are not found consistently, this would suggest that depression is unlikely to be involved in the pathogenesis or progression of atherosclerotic plaques. Instead depression, which is a known risk factor for clinical events (1–6), could exert its effects through enhancing the risk of plaque rupture (e.g., through hemodynamic, thrombotic, inflammatory, neuroendocrine alterations) (32).

In sum, we found no evidence to support the hypothesized relation between depressive symptomatology and carotid IMT in the studied population. Neither depressive symptom trajectories nor history of clinically significant depressive symptoms was associated with future levels of carotid IMT. These findings suggest that the effects of depressive symptomatology on cardiovascular outcomes may be mediated by mechanisms other than intimal medial thickening.

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Acronyms

BLSA, Baltimore Longitudinal Study of Aging; BMI, body mass index; CCA, common carotid artery; CES-D, Center for Epidemiological Studies – Depression scale; DBP, diastolic blood pressure; HDL, high-density lipoprotein; IMT, intimal medial thickness; LDL, low-density lipoprotein; OGTT, oral glucose tolerance test; SBP, systolic blood pressure.

Table 1

Sample Size by Number of Visits

Number of Visits	n (% of Sample)
1	556 (100.0)
2	465 (83.6)
3	335 (60.3)
4	206 (37.1)
5	104 (18.7)
6	36 (6.5)
7	12 (2.2)
8	4 (.7)

Table 2

Characteristics of Study Sample at Initial Carotid IMT Measurement

	Trajectory Analyses (n=556)				Covariation Analyses (n=68)			
Variable	**Mean / % (n)**	***SD***	**Min**	**Max**	**Mean / % (n)**	***SD***	**Min**	**Max**
Age (years)	55.8	15.9	20	93	56.3	15.4	23	90
Sex (% male)	45.5 (253)				50.0 (34)			
Race (% white)	75.4 (419)				75.0 (51)			
Education (years)	16.8	2.5	8	24	16.5	2.6	12	23
SBP (mm Hg)	130.6	22.3	90	210	126.4	20.8	90	190
LDL cholesterol (mg/dL)	110.1	33.3	35	326	117.4	36.6	76	326
Body mass index (kg/m^2)	26.1	4.2	18.2	47.1	25.8	3.8	19.6	36.9
Diabetes (%)	5.2 (29)				7.4 (5)			
Antihypertensive or lipid-lowering medications (%)	22.1 (123)				23.5 (16)			
Antidepressants (%)	9.4 (52)				4.4 (3)			
Smokers (% ever)	47.1 (262)				54.4 (37)			
CES-D (total score)	6.7	6.3	0	44	5.5	5.0	0	27
Mean carotid IMT (mm)	0.52	0.13	0.28	1.00	0.54	0.14	0.30	0.90

Table 3

Multiple Regression Analyses Relating Depressive Symptom Trajectory and History of Significant Depressive Symptoms to Future Carotid IMT

	Depressive Symptom Trajectory				History of Significant Depressive Symptoms			
Variable	**Beta**	**Standard error**	**t**	***p***	**Beta**	**Standard error**	**t**	***p***
Age	0.0048	0.0003	14.42	<.001*	0.0048	0.0003	14.48	<.001*
Sex[1]	0.0258	0.0090	2.88	.004*	0.0258	0.0089	2.89	.004*
Race[2]	−0.0198	0.0101	−1.96	.05	−0.0205	0.0101	−2.03	.04*
Education	0.0014	0.0017	0.81	.42	0.0014	0.0017	0.79	.43
SBP	0.0008	0.0002	3.54	<.001*	0.0008	0.0002	3.54	<.001*
LDL cholesterol	0.0002	0.0001	1.16	.25	0.0002	0.0001	1.14	.25
Body mass index	0.0021	0.0011	1.99	.046*	0.0021	0.0011	1.98	.048*
Diabetes	0.0128	0.0198	0.65	.52	0.0128	0.0198	0.64	.52
Antihypertensive or lipid-lowering medications	0.0067	0.0109	0.61	.54	0.0070	0.0109	0.65	.52
Antidepressants	−0.0041	0.0149	−0.27	.79	−0.0044	0.0150	−0.29	.77
Smoking	−0.0023	0.0086	−0.27	.79	−0.0023	0.0086	−0.27	.79
CES-D intercept	0.0009	0.0021	0.44	.66	--	--	--	--
CES-D (trajectory or significant symptoms)	0.0816	0.1949	0.42	.68	0.0044	0.0111	0.39	.69

*$p<.05$

[1] Sex was coded female (0) vs. male (1).

[2] Race was coded as non-White (0) vs. White (1).

Table 4

Mixed-Effects Regression Analyses Examining the Covariation of Depressive Symptoms with Carotid IMT over Time

Variable	Beta	Standard error	t	*p*
Age	0.0043	0.0012	3.72	<.001*
Sex[1]	−0.0168	0.0309	−0.54	.590
Race[2]	−0.0706	0.0344	−2.05	.047*
Education	−0.0074	0.0062	−1.20	.24
SBP	0.0006	0.0007	0.79	.434
LDL cholesterol	0.0003	0.0003	0.96	.342
Body mass index	−0.0009	0.0035	−0.26	.796
Diabetes	0.0819	0.0708	1.16	.252
Antihypertensive or lipid-lowering medications	0.0502	0.0316	1.59	.115
Antidepressants	0.0726	0.0611	1.19	.237
Smoking	−0.0221	0.0282	−0.78	.438
CES-D	−0.0017	0.0021	−0.84	.401

* $p<.05$

[1] Sex was coded female (0) vs. male (1).

[2] Race was coded as non-White (0) vs. White (1).