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Relationship between chronic stress and carotid intima-media thickness (IMT) in elderly Alzheimer's disease caregivers

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Abstract

The stress associated with providing care for a spouse diagnosed with Alzheimer's disease can have adverse effects on cardiovascular health. One potential explanation is that chronic caregiving stress may contribute to the development of atherosclerosis. The purpose of this study was to determine if the duration that one has provided care is associated with degree of atherosclerotic burden, as measured by carotid artery intima-media thickness (IMT). One hundred and ten Alzheimer caregivers (mean age 74 ± 8 years, 69% female) underwent in-home assessment of carotid artery IMT via B-mode ultrasonography. Data regarding medical history, blood pressure, and multiple indicators of caregiving stress were also collected. Multiple regression indicated that duration of care was positively associated with IMT measured in the internal/bifurcation segments of the carotid artery ($\beta = 0.202$, $p = 0.044$) independent of risk factors such as age, gender, body mass index, smoking history, sleep quality, hypertension status, and caregiving stressors. Duration of care was positively associated with IMT in the common carotid artery, but the relationship was not significant. These findings provide more evidence of the link between chronic caregiving stress and cardiovascular disease and suggest that enduring the experience of caregiving over a period of years might be associated with atherosclerotic burden.

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[1]The "caregiving stressors" variable was an aggregate component score derived from three indicators of caregiving stress (i.e., Clinical Dementia Rating score, Activities of Daily Living/Instrumental Activities of Daily Living dependence, and role overload). The aggregate component score was calculated using principal component analysis. These indicators have been previously characterized by Pearlin and colleagues (1990) as objective and subjective indicators of primary caregiving stressors.

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Declaration of Interest
The funding agency did not participate in the study design, the collection, analysis, or interpretation of the data, in writing the report, or in the decision to submit the manuscript for publication. All authors of this manuscript have no financial or personal conflicts of interest.

Keywords

Alzheimer's disease; Atherosclerosis; Caregiving; Chronic Stress; Coronary Heart Disease; Intima-media thickness

INTRODUCTION

Spousal caregivers to patients diagnosed with Alzheimer's disease represent a chronically stressed population and have been shown to have increased physical and psychiatric morbidity (Mahoney et al. 2005; Schulz et al. 1995), as well as increased risk for overall mortality (Schulz & Beach 1999). Furthermore, previous work has found that caregivers are at increased risk for coronary heart disease (Vitaliano et al. 2002; von Känel et al. 2008). The chain of biologic adaptations due to encountering environmental challenges might be an important mechanism linking chronic caregiving stress to adverse health outcomes. Past research suggests that distressed caregivers exhibit increased sympathetic-adrenal-medullary (SAM) arousal compared to non-caregivers (Aschbacher et al. 2008; Mills et al. 1997), a process that might explain why caregivers have increased risk of hypertension (Shaw et al. 1999). If this system is frequently activated or sustained over time, one's risk for cardiovascular diseases may increase (Ross 1999).

Throughout the atherosclerotic process, changes in the vascular walls occur that can result in wall thickening and narrowing due to plaque formation. If severe, these changes can increase the probability of occlusion, resulting in acute atherothrombotic events such as myocardial infarction and stroke. These changes are mediated by a combination of physiological processes that may be enhanced by stress-related sympathetic arousal (Black & Garbutt 2002).

Mounting evidence suggests that stressed caregivers exhibit dysregulation on several processes associated with atherosclerotic development, including elevated SAM tone (Aschbacher et al. 2008; Mausbach et al. 2005; Mills et al. 1997), blood pressure (Kim & Knight 2008; Shaw et al. 1999; von Känel et al. 2008), and inflammation (von Känel et al. 2006). This evidence, in combination with findings that dysregulation of these physiological processes are associated with each other and with atherosclerotic disease (Clinton & Libby 1992; de Freitas et al. 2008; Flaa et al. 2008; Ross 1986, 1999), suggests that stressed caregivers may potentially experience higher levels of arterial damage over time. Moreover, chronically stressed caregivers also exhibit increased cardiovascular arousal in response to acute psychological stress (Aschbacher et al. 2008; Mausbach et al. 2005), which has been associated with increased carotid intima-media thickness (IMT) (Alevizaki et al. 2007; Steptoe et al. 2006), a marker of subclinical atherosclerosis (Lorenz et al. 2007). Conversely, a study by Heponiemi and colleagues (2007) found that higher heart rate, respiratory sinus arrhythmia, and preejection period reactivity to acute stress were associated with lower IMT. However, quicker heart rate recovery was also associated with lower IMT, suggesting that the pairing of cardiac autonomic reactivity and fast heart rate recovery might be beneficial to arterial health.

Research in other populations has demonstrated that chronic stress may play an important role in the development of carotid IMT and its progression over time (Gallo, Troxel, Kuller et al. 2003; Gallo, Troxel, Matthews et al. 2003; Hintsanen et al. 2007; Hintsanen et al. 2005; Janicki et al. 2005; Kamarck et al. 2007; Rosvall et al. 2002; Troxel et al. 2003). For example, individuals working in professions characterized by high demand and low control have higher carotid IMT (Hintsanen et al. 2005). Similar results have been found in women reporting poor marital satisfaction (Gallo, Troxel, Kuller et al. 2003). Another study by

Troxel and colleagues (2003) found that African American women who reported experiencing racial discrimination had more carotid plaques compared to those who did not report racial discrimination.

Measurement of carotid IMT has been conducted in a variety of ways. Although it is generally recommended that IMT be measured in the common carotid artery (Stein et al. 2008), emerging research suggests that there might be differential associations between cardiovascular disease risk factors and specific segments of IMT (Dietrich et al. 2011; Polak et al. 2010). Differences in hemodynamics, shear stress, and histology of these segments may account for these observations (Gimbrone et al. 2000; Heath et al. 1973; Malek et al. 1999).

Given that Alzheimer caregivers exhibit stress-related dysregulation of the cardiovascular system and that previous research has found links between chronic stress and atherosclerotic burden, it is plausible that the chronic stress associated with caregiving may increase one's vulnerability to atherosclerotic disease. The present study aimed to examine the relationship between length of time providing care to a spouse with Alzheimer's disease and degree of atherosclerotic burden, as measured by carotid IMT at the common, bifurcation, and internal segments. We hypothesized that length of time caregiving would be positively associated with IMT, such that caregivers who have provided care to their demented spouse for longer periods of time would be more likely to have elevated IMT compared to newer caregivers.

MATERIALS AND METHODS

Participants

A total of 110 community-dwelling Alzheimer caregivers participated in this study examining the psychobiologic effects of stress on physical and psychological health. All participants were at least 55 years of age, married, and cohabitating with their spouse diagnosed with Alzheimer's disease. Caregivers were excluded if they were currently diagnosed with or receiving treatment for a serious or terminal medical condition that required rigorous medical attention (e.g., Parkinson's disease) or were currently receiving or had received previous treatment for cancer within the past 5 years. Caregivers were recruited from Alzheimer caregiver support groups, senior health fairs, flyers, and referrals from other participants in the study and the University of California, San Diego (UCSD) Alzheimer's Disease Research Center (ADRC). All participants were enrolled in the UCSD Alzheimer Caregiver Study (approved by the UCSD Institutional Review Board) and provided written informed consent.

Procedure

Assessments were administered in each participant's home by a nurse and two research associates, one trained in sonography. After obtaining informed consent, the research assistant administered a semi-structured interview assessing medical history, health behaviors, caregiver burden, and care-recipient impairment. Within a week, the nurse and sonographer returned to administer the following biological assessments. Blood pressure was measured after 5, 10, and 25 minutes of rest with the participant lying in a supine position. Ultrasound assessment of the carotid artery was then conducted with the participant lying in the same position (see below for details).

The Alzheimer Caregiver Study is a 5-year longitudinal study in which participants were evaluated annually. For the current investigation, all analyses were cross-sectional in nature. At the first exam, ultrasound images of the bilateral carotid arteries were obtained so that IMT could be measured in the common, bifurcation, and internal segments of these arteries. At the second year assessment, IMT was only measured in the common carotid artery. For

individuals who had incomplete common IMT data from their year 1 assessment but complete data at year 2, we substituted year 2 data as the "baseline" for this cross-sectional analysis. This was the case for 11 caregivers.

Demographics and Health Information

During the semi-structured interview, participants were asked to report demographic information such as age, gender, education, ethnicity, and income. Participants were also asked to self-report their height and weight, which was calculated into body mass index by dividing weight in kilograms by the square of height in meters. Participants also reported information regarding their smoking history (i.e., whether or not one is currently or has ever been a smoker). Finally, participants were asked to report if they had any medical diagnoses, including hypertension.

Biological Measures

Blood Pressure—Blood pressure measurements were collected using a Microlife blood pressure monitor, model #3AC1-1PC. Three resting measurements were averaged in order to obtain a more stable assessment. Participants were considered to be hypertensive if they either a) self-reported history of hypertension, b) had systolic blood pressure ≥ 140 mmHg, c) had diastolic blood pressure ≥ 90 mmHg, or d) were taking antihypertensive medication.

Cholesterol—Low-density lipoprotein (LDL) cholesterol was assessed in serum using the Beckman-Coulter LX20 PRO.

Carotid Artery Imaging—Images of the carotid artery were collected using an Acuson Cypress Portable Ultrasound Unit with a 5.4 – 6.6 MHz Acuson 7L3 transducer which produced high quality B-mode ultrasound images from the far walls of the common, bifurcation, and internal carotid artery segments from 2 standardized interrogation angles for each vessel (right: 180° and 120°, left: 180° and 240°). The carotid flow divider was used as a reference point from which segments are defined: (a) the common carotid was defined as the segment 1 to 2 cm proximal to the flow divider, (b) the bifurcation was defined as the segment 0 to 1 cm proximal to the flow divider, and (c) the internal carotid was defined as the segment 0 to 1 cm distal to the flow divider. Imaging was conducted by a single sonographer for all participants.

Images were saved, archived, and read off-line using the computer program Vascular Research Tools (Medical Imaging Applications, Coralville, IA) by a reader blinded to the characteristics of the participants. IMT was defined as the distance between the intimal-luminal and the medial-adventitial interfaces of the carotid artery. Two different IMT outcomes were calculated. First, IMT of the common carotid artery was defined as the highest (maximum) value of IMT measured from the far wall (i.e., the maximum of 4 IMT measurements of the common carotid artery). The maximum IMT value was chosen in accordance with Allan and colleagues (Allan et al. 1997) who argued that examining the maximum IMT is preferable to the mean IMT of all segments because examining the mean might result in underestimated atherosclerotic risk for those with high measurements in one particular segment, but not necessarily in others. Moreover, previous investigations suggest that IMT measured in the common carotid is a strong predictor of cardiovascular events, including myocardial infarction and stroke (Lorenz et al. 2007; O'Leary et al. 1999).

Second, the maximum IMT measured from the far walls of either the internal carotid artery or the bifurcation was also calculated in order to determine IMT from carotid segments that are typically more diseased due to turbulent flow and histological differences (Heath et al. 1973; Touboul et al. 2004). Previous work from the Cardiovascular Health Study used a

similar combination measure of internal and bifurcation IMT in older adults (O'Leary et al. 1996) and found that the presence of prevalent atherosclerotic disease and coronary heart disease was more strongly related to IMT in the internal/bifurcation segment compared to the common in an elderly sample.

Psychosocial Measures

Care-receiver Dementia Severity—The Clinical Dementia Rating (CDR) scale (Morris 1993) was used to obtain a global assessment of the dementia severity of participants' spouses. Caregivers rated their spouse's ability in 6 behavioral and cognitive domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. Dementia severity ratings ranged from 0-3 (0 = no dementia; 3 = severely demented) on each dimension, and the overall dementia severity score represented the average rating across these dimensions. Cronbach's alpha was 0.87 in our total sample.

Patient Daily Dependency—Pearlin's 15-item measure of Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) (Pearlin et al. 1990) was used to determine the extent to which demented spouses required assistance from caregivers for a number of daily activities. Caregivers rated the degree to which spouses depended on them for activities such as feeding, bathing, and medication management on a 4-point scale: 1 = not at all; 2 = somewhat; 3 = quite a bit; 4 = completely. Item rankings were summed to obtain a total ADL/IADL dependence score. Cronbach's alpha was 0.91 in our total sample.

Role Overload—Caregiver overload, or burden, was assessed with the Role Overload scale (Pearlin et al. 1990). Participants were instructed to rate their agreement with four statements on a 4-point scale (0 = "not at all" to 3 = "a great deal"). Items included, "I have more things to do than I can handle" and "I work hard but never seem to make any progress." Scores on all items were summed into a total Role Overload score. Cronbach's alpha was 0.77 in our total sample.

Sleep Quality—Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) (1989). This self-report instrument assessed sleep quality in seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medication, and daytime dysfunction. A "Global" PSQI score is derived by summing the scores on each of the seven components and can range from 0-21, with higher scores indicative of poorer sleep. Past work has found high internal consistency of the PSQI with a Cronbach's alpha of 0.83 (Buysse et al. 1989). In our sample, Cronbach's alpha was 0.67.

Duration of Care—Participants provided the year in which their spouse was diagnosed with Alzheimer's disease (i.e., the year that the participant became a caregiver). The time elapsed between the diagnosis year and the time of the assessment was considered the duration of care.

Statistical Analysis

Given the large association between conceptually similar measures of Alzheimer patient impairment and caregiver perceived stress in our sample ($r = 0.37$-0.66, all p-values < 0.001), an aggregate component score was calculated using principal component analysis (PCA) to reduce the number of covariates in our primary analysis to minimize potential problems of over-fitting our regression analysis. The aggregate component score was derived from three indicators of caregiving stressors (i.e., CDR score, ADL/IADL dependence, and role overload). These indicators have been previously characterized by Pearlin and colleagues (1990) as objective and subjective indicators of primary caregiving

stressors. The resulting component, referred to as "caregiving stressors," was saved as a z-score (i.e., mean = 0, SD = 1). This PCA procedure was conducted twice given that the two analyses conducted in our study examined two different subsets of caregivers. Doing so assured that the caregiving stressor score reflected stress within each subsample, and was not influenced by individuals who were not included in a given analysis.

Hierarchical linear regression analysis was conducted in order to assess the relationship between caregiving duration and measures of IMT. Two regression models were tested: Analysis 1 assessed the association between caregiving duration and common carotid IMT and Analysis 2 assessed the association between caregiving duration and internal/bifurcation IMT. In both analyses, the following covariates were entered in step 1 of the regression model: age, gender (coded 0 = male; 1 = female), body mass index, smoking history (coded 0 = never was a smoker; 1 = was either a past or current smoker), global PSQI score, hypertension status (coded 0 = normotensive; 1 = hypertensive), and caregiving stressors. Duration of caregiving (in years) was entered in step 2 in order to assess its unique contribution to the models. For the model assessing common carotid IMT, we included only those caregivers with all 4 measurements available. In the analysis examining IMT in the internal/bifurcation, we included individuals who had at least one IMT measurement from these segments in order to optimize our sample size, given that measurements taken from these segments tend to be more difficult to image and are typically less likely to produce complete data at each angle measured (i.e., having 8 out of 8 IMT measurements from images for these segments) (Bots et al. 2003).

Covariates were chosen based on their theoretical and empirical association with IMT. Traditional cardiovascular risk factors were included in addition to sleep quality. Sleep quality was included because caregivers experience disturbed sleep, which has been associated with increased risk for coronary heart disease events (Chandola et al. 2010) as well as sympathoadrenal arousal and other markers of atherosclerosis in caregivers (Mausbach et al. 2006). Although the sample size precluded our ability to include all important covariates, exploratory analyses were conducted to include other variables relevant to IMT such as LDL cholesterol (Polak et al. 2010) and socioeconomic status (Steptoe et al. 2006). Thus, Analyses 1 and 2 were rerun and expanded to include LDL cholesterol, years of education, and monthly household income as covariates.

RESULTS

Caregiver demographic and health information is presented in Table 1. The majority of caregivers was female (69%) and Caucasian (93%) with a mean ± standard deviation age of 73.7 ± 8.2. The mean dementia rating score for Alzheimer patients was 1.6 ± 0.6. On average, caregivers had provided 4.2 ± 3.5 years of care to their spouse. The range of duration of caregiving in this sample was 0.5-16.8 years of care.

Analysis 1: Caregiving Duration and Common Carotid IMT

In the PCA to derive an aggregate "caregiving stressors" variable, Kaiser-Meyer-Oklin Measure of Sampling Adequacy was 0.57 and Bartlett's Test of Sphericity was 65.8 ($p < 0.001$), indicating a factorable correlation matrix. As anticipated, PCA analysis of patient dementia rating score, dependence for activities of daily living, and role overload yielded a single component solution representing "caregiving stressors." The caregiving stressor component had an eigenvalue of 1.9 (compared to 0.8 for the next highest component) and explained 63% of the variance; therefore, the single component solution was considered the most parsimonious characterization of these indicators of caregiving stressors. Factor loadings were 0.62-0.89 for each variable, indicating strong associations with the caregiving

stressor component. This component score was significantly associated with duration of care (r = 0.216, $p = 0.036$).

Age was the only significant predictor of common carotid IMT in steps 1 and 2 of the regression model. Caregiving duration (in years) was not a significant predictor of common IMT (β = 0.078, $p = 0.449$). These results are presented in Table 2. Age was unassociated with duration of caregiving (r = −0.06, p= 0.555). The full model accounted for 19% of the variance in IMT.

Analysis 2: Caregiving Duration and Internal/Bifurcation Carotid IMT

In the PCA to derive an aggregate "caregiving stressor" variable for this analysis, results were similar to those in Analysis 1 and indicated a factorable correlation matrix. Kaiser-Meyer-Oklin Measure of Sampling Adequacy was 0.63 and Bartlett's Test of Sphericity was 89.9 ($p < 0.001$). As in Analysis 1, PCA analysis of patient dementia score, dependence for activities of daily living, and role overload yielded a single component solution representing "caregiving stressors." The caregiving stressor component had an eigenvalue of 2.0 (compared to 0.7 for the next highest component) and explained 68% of the variance. Factor loadings were 0.73-0.89 for each variable, indicating strong associations with the caregiving stressor component. This component score was also significantly associated with duration of care (r = 0.256, $p = 0.007$).

Regression indicated that gender was the only significant predictor of internal/bifurcation IMT in steps 1 and 2 of the regression model, with men having higher IMT than women (β = −0.282, $p = 0.006$). Hypertension status was marginally associated with IMT (β = 0.193, p = 0.058), with hypertensives having higher IMT than normotensives. In step 2, caregiving duration (in years) emerged as a significant predictor of internal/bifurcation IMT (β = 0.202, $p = 0.044$). For each year of caregiving, IMT increased by 0.011 mm. These results are presented in Table 3. Age was also unassociated with duration of caregiving in this analysis (r = −0.04, $p = 0.647$). The full model accounted for 14% of the variance in IMT with length of time caregiving uniquely explaining 4% of this variance.

Exploratory Analyses: Inclusion of LDL Cholesterol, Education, and Income

In the expanded Analysis 1, LDL cholesterol (β = −0.014, p = 0.904), education (β = −0.103, p = 0.360), and monthly income (β = 0.017, p = 0.884) were insignificant in the model. Inclusion of these variables did not change the overall pattern of the findings. Duration of care remained unassociated with common IMT (β = 0.109, p = 0.334). This analysis included 85 of the original 95 caregivers in Analysis 1 due to missing data on income.

In the expanded Analysis 2, the addition of these covariates did not change the pattern of significant covariates included in the original model. Duration of care remained significantly associated with IMT (β = 0.242, p = 0.021). LDL cholesterol (β = −0.011, p = 0.916) and monthly income (β = 0.124, p = 0.236) were unassociated with internal/bifurcation IMT. Education was significantly associated with IMT in this model (β = −0.286, p = 0.007). This analysis included 98 of the original 108 caregivers in Analysis 2 due to missing data on income.

Finally, in order to rule out the possibility that the discrepant association between duration of care and common versus internal/bifurcation IMT was driven by the added caregivers in Analysis 2, we reran Analysis 2 (internal/bifurcation IMT as outcome) with only the caregivers who were included in Analysis 1. The overall pattern of results was consistent with the originally reported results in Analysis 2. Gender remained the only significant

covariate in the model (β = −0.268, p = 0.026). The association between duration of care and internal/bifurcation IMT also remained significant (β = 0.223, p = 0.046).

DISCUSSION

The current study examined the relationship between length of time caregiving and carotid IMT in spousal Alzheimer caregivers. The results indicated that the duration that one had provided care to a demented spouse was positively associated with IMT measured in the internal/bifurcation segments of the carotid artery. That is, caregivers who had provided care for longer periods of time had evidence of more severe atherosclerotic burden in those carotid segments. Duration of care was not significantly associated with IMT in the common carotid artery, but the direction of the relationship was still positive.

Our findings provide additional support for other studies suggesting that caregivers may be at increased risk for coronary artery disease (Lee et al. 2003; Vitaliano et al. 2002; von Känel et al. 2008). The presence of atherosclerosis in the carotid arteries is an indicator of generalized atherosclerosis throughout the vasculature, including the coronary arteries (Craven et al. 1990). Previous studies have found that carotid IMT is associated with increased risk for cerebrovascular events (Prati et al. 2008) and myocardial infarction (O'Leary et al. 1999). Therefore, due to their increased IMT, caregivers who have been in the caregiving role for a longer period of time may be at elevated risk for adverse cardiovascular outcomes.

Previous studies have found segment-specific cardiovascular risk factor associations for common, bifurcation, and internal IMT. For example, a study by Polak and colleagues (2010) reported that risk factors such as hypertension, diabetes, and smoking have qualitatively stronger associations with IMT in the bifurcation, compared to the common and internal segments. Low-density lipoprotein cholesterol was more strongly associated with internal IMT compared to other segments. Furthermore, IMT progression over time in the internal segments is higher and more strongly associated with CVD risk factors compared to other segments (Mackinnon et al. 2004). Although past work has found positive associations between IMT (measured at a variety of sites) and age (Ando et al. 2000; Polak et al. 2010), age was only associated with IMT at the common carotid artery in our study. One possible explanation is that age effects might be less apparent in the internal and bifurcation segments compared to the common segment (Polak et al. 2010). Given that our sample was limited to elderly adults, these effects might be more difficult to capture. However the literature examining age and IMT associations at various segments has been inconsistent, with other studies suggesting that age might be more strongly associated with IMT in the internal and bifurcation segments (Howard et al. 1993). There has been relatively little research examining segment-specific associations between IMT and cardiovascular disease risk factors, therefore more work in this area can help establish the specific mechanisms that might explain arterial thickening in these distinct regions.

Importantly, the internal and bifurcation segments of the carotid arteries are more prone to atherosclerotic plaque and lesions compared to the common carotid (Heath et al. 1973; Touboul et al. 2004). Therefore, IMT from the internal carotid and the bifurcation may be a better estimate of true atherosclerosis compared to the common (Mackinnon et al. 2004). Indeed, past work suggests that measuring IMT at the internal carotid rather than the common carotid alone improves prediction of vascular events (O'Leary et al. 1999). Differences in blood flow, shear stress, and histology of these arterial segments might account for these observations. Therefore, the differential association between duration of caregiving and IMT at the internal/bifurcation compared to the common carotid may reflect pathophysiologic changes due to caregiving that are operating via the risk factors that have a

stronger association with internal/bifurcation IMT, rather than common IMT. Alternatively, perhaps the physiologic perturbations due to caregiving are only operative for more advanced disease that is more likely detected in the internal and bifurcation segments.

Our finding that duration of care is associated with increased IMT in the internal/bifurcation is also consistent with previous work finding that chronic stressors may play an important role in the development and/or progression of atherosclerosis (Gallo, Troxel, Kuller et al. 2003; Gallo, Troxel, Matthews et al. 2003; Hintsanen et al. 2007; Hintsanen et al. 2005; Janicki et al. 2005; Kamarck et al. 2007; Rosvall et al. 2002; Troxel et al. 2003). However, it is important to note that in the current study, duration of care was associated with IMT in the absence of an association between self-reported caregiving stressors and IMT. This is particularly interesting given the association between duration of care and self-reported caregiving stressors. One potential explanation may be that the particular caregiving stressor measures used did not reflect pathways that influence IMT. Another potential explanation may be that chronic stressors experienced over time may be of overriding importance as a predictor of IMT as compared to caregiver ratings of stress assessed at a single time point. In support of this theory, a study by Low and colleagues (2009) found that neither self-report measures of chronic stress nor cardiovascular reactivity to an acute stressor were associated with carotid IMT in adolescents. Rather, increasing diastolic blood pressure reactivity over time (an average of 3.3 years after baseline) was significantly associated with increased IMT measured at time 2. Whether or not similar relationships apply in older adults should to be tested directly in future studies. Importantly, although we postulate that duration of care might reflect a level of “accumulated chronic stress,” we cannot be certain if this is truly the case, and therefore, more work needs to be done to investigate the direct relationships between specific caregiving stressors and atherosclerotic burden in dementia caregivers.

Exploratory analyses indicated that caregivers with higher education were more likely to have reduced internal/bifurcation IMT compare to caregivers with lower education. This finding is consistent with previous work demonstrating that socioeconomic status might play an important role in atherosclerotic burden (Nash et al. 2011; Steptoe et al. 2006). Income level, another variable reflective of socioeconomic status, was not associated with IMT in any segment. Notably, the majority of our sample had at least some college education and a relatively high income level. This in combination with the reduced sample sizes available for these exploratory analyses suggest that caution should be taken when interpreting this finding. Future work would benefit from examining the role of socioeconomic status in atherosclerotic burden in a more socioeconomically-diverse group of dementia caregivers.

Our study has several limitations worthy of mention. First, the cross-sectional design does not allow for a causal explanation. The understanding of how chronic stress impacts arterial health over time would benefit from future longitudinal work to determine if caregivers have accelerated IMT progression compared to older adults not providing such care. Accordingly, prospective studies on the association between IMT and caregiving stressors are currently underway to increase the validity of our findings. Further research might also focus on the psychosocial correlates of IMT in caregivers. Finally, as is generally the case, we had less complete data in the internal and bifurcation segments compared to the common carotid artery. These segments are more difficult to image (Bots et al. 2003; O’Leary et al. 1996; O’Leary et al. 1991) and in our case, missing data was often associated with more advanced disease, therefore our data likely represent a conservative estimate.

In sum, the current study found that caregivers who had provided care to spouses diagnosed with Alzheimer’s disease for longer periods of time exhibited elevated carotid IMT in the internal/bifurcation segments. This finding might suggest that chronic caregiving stressors endured over several years may contribute to the development of atherosclerosis.

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Table 1

Caregiver Characteristics (N=110)

Age in years, mean (SD),	73.7 (8.2)
Female Gender, n (%)	76 (69)
Caucasian Ethnicity, n (%)*	102 (93)
Education, n (%)	
Did Not Graduate High School	2 (2)
High school Graduate	21 (19)
Some College	38 (35)
College Graduate	49 (45)
Monthly Household Income in Dollars, median **	4000
Taking Antihypertensive Medication, n (%)	65 (59)
Resting Systolic Blood Pressure in mmHg, mean (SD)	135.1 (15.5)
Resting Diastolic Blood Pressure, mean (SD)	76.1 (8.8)
Resting MAP in mmHg, mean (SD)	95.8 (9.9)
Past or Current Smoker, n (%)	49 (45)
Global PSQI Score, mean (SD)	6.6 (3.5)
BMI, mean (SD)	26.5 (4.7)
AD Patient CDR Score, mean (SD)	1.6 (0.6)
AD Patient ADL/IADL Dependence Score, mean (SD)	9.0 (3.7)
Duration of Caregiving in Years, mean (SD)	4.2 (3.5)
Maximum Common Carotid IMT in Millimeters (Analysis 1 Sample, N=95), mean (SD)	0.81 (0.13)
Maximum Internal/Bifurcation Carotid IMT in Millimeters (Analysis 2 Sample, N=108), mean (SD)	0.87 (0.19)

Note. AD=Alzheimer's disease; ADL=Activities of Daily Living; BMI=Body Mass Index; CDR=Clinical Dementia Rating; IADL=Instrumental Activities of Daily Living; IMT=Intima-media Thickness; MAP=Mean Arterial Pressure; PSQI=Pittsburg Sleep Quality Index.

* 2 caregivers declined to disclose information about ethnicity; therefore these participants were excluded from this value.

** 11 caregivers declined to disclose monthly household income information; therefore these participants were excluded from this value.

Table 2

Analysis 1: Regression Model Predicting Common Carotid IMT

F	df	*p*	R^2	Entered Variables	B	SE	Cohen's d
2.5	8,86	0.017	0.19	Intercept*	0.373	0.158	
				Age**	0.005	0.002	0.79
				Female	−0.028	0.029	−0.20
				BMI	<0.001	0.003	0.12
				Ever Smoked	−0.003	0.027	−0.02
				Global PSQI	0.005	0.004	0.37
				Hypertension	0.045	0.030	0.42
				Caregiving Stressors[1]	−0.021	0.013	−0.33
				Years Caregiving	0.003	0.004	0.25

Note. BMI=Body Mass Index; IMT=Intima-media Thickness; PSQI=Pittsburg Sleep Quality Index.

* Significant at $p < 0.05$

** Significant at $p < 0.01$

Table 3

Analysis 2: Regression Model Predicting Internal/Bifurcation Carotid IMT

F	df	*p*	R^2	Entered Variables	B	SE	Cohen's d
1.9	8,99	0.064	0.14	Intercept**	1.027	0.236	
				Age	−0.002	0.002	−0.20
				Female**	−0.114	0.041	−0.58
				BMI	−0.001	0.004	−0.05
				Ever Smoked	−0.023	0.037	−0.12
				Global PSQI	0.004	0.005	0.27
				Hypertension	0.082	0.043	0.49
				Caregiving Stressors^2	−0.026	0.019	−0.27
				Years Caregiving*	0.011	0.005	0.51

Note. BMI=Body Mass Index; IMT=Intima-media Thickness; PSQI=Pittsburg Sleep Quality Index.

*Significant at $p < 0.05$

**Significant at $p < 0.01$