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Relation of Depressive Symptoms with Coronary Artery Calcium Determined by Electron-Beam Computed Tomography (From the Rancho Bernardo Study)

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Abstract

Studies linking depressive symptoms and coronary artery calcium (CAC), a measure of subclinical atherosclerosis, have yielded mixed results. No longitudinal studies of depressive symptoms and CAC have included older adults of both sexes. This study examined the association of depressive symptoms with CAC and CAC progression in older men and women. Participants were 417 community-dwelling older adults (mean age=67±7) with no history of heart disease who attended a 1997–99 research clinic visit when depressive symptoms were assessed using the Beck Depression Inventory (BDI). CAC was measured using electron beam computed tomography in 2000–02 and again in 2005–2007. Median BDI was 3, range=0–37; 39% of men and 10% of women had severe CAC (Agatston score ≥400) in 2000–02. Ordinal logistic regression analyses examining the odds of greater compared to lesser CAC severity by BDI quartiles showed an unexpected negative association whereby women with the lowest depressive symptoms had 2.4 times the odds of increasing CAC severity compared to women in the second BDI quartile (95% CI: 1.1–5.4). A nonlinear, u-shaped association was observed among men with those in the first and fourth BDI quartiles having 2.6 and 3.0 times higher odds of increasing CAC severity than persons in the second quartile (95% CI: 1.2–5.6 and 1.3–6.9, respectively) after adjustment for CHD risk factors. No significant associations were observed for CAC progression although similar nonlinear patterns were observed among men. In conclusion, our results suggest that depressive

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symptoms have a gender-specific, cross-sectional association with CAC, but no statistically significant associations with CAC progression.

Keywords

Coronary artery calcium; depressive symptoms; atherosclerosis; sex differences

Introduction

Coronary artery calcium (CAC) is a marker of subclinical atherosclerosis that independently predicts coronary heart disease (CHD) risk, future coronary events,^{1,2} and stroke.³ While the evidence establishing depression as an independent risk factor for CHD is not conclusive, a recent meta-analysis found depression increased the risk by 80%.⁴ Depressive symptoms, not always severe enough to meet thresholds indicative of clinical depression, have been identified as an independent risk factor for CHD among older adults (>65 years).⁵ A body of research has emerged testing the hypothesis that depressive symptoms increase the risk of CHD through an association with CAC. Results from cross-sectional analyses are mixed with three studies reporting null associations,^{6–8} two reporting negative associations,^{8,9} and two reporting positive associations.^{10,11} Longitudinal studies of CAC progression among middle aged adults have shown that higher depressive symptoms are associated with greater CAC progression.^{12,13} The only study of depressive symptoms and CAC progression in older adults included only women and did not find statistically significant associations.¹⁴ To our knowledge, no study has examined the association of CAC progression and depressive symptoms in a community based population of older women *and* men. Therefore, we examined the associations of depressive symptoms, CAC, and CAC progression in older men and women with repeat CAC assessments 4.5±0.5 years apart. We hypothesized that higher levels of depressive symptoms would be cross-sectionally associated with greater CAC severity and that persons with higher baseline levels of depressive symptoms would experience greater CAC progression.

Methods

Data used in analyses were from participants of the Rancho Bernardo Study, a prospective population-based cohort study of heart disease risk factors that began in 1972–1974 when 6,629 Caucasian middle class adults from a Southern California community were enrolled. Between 1997 and 1999, 1,096 adults, representing 77% of surviving participants, attended a research clinic visit when depressive symptoms were assessed. Between 2000 and 2001, 525 of these attendees were contacted to have chest electron beam computed tomography (EBCT) screening for coronary artery calcium. Eligible participants were: (1) evaluated by our research team between 1997 and 1999; (2) postmenopausal (more than 1 year without menses) if female; and (3) free of clinically manifest CHD (no physician-diagnosed angina, myocardial infarction, or coronary artery revascularization). Of the 525 contacted, 2 were deceased, 15 were ineligible due to clinically manifest CHD, 38 declined to participate, and 48 were not seen due to scheduling problems. The 86 men and women who were eligible but did not participate were similar in age, sex and depression symptom scores to the 422 men

and women who participated. Five participants were excluded from analyses for missing BDI measures. Between 2005 and 2007, 323 (176 women and 147 men) of the originally screened participants still without clinically manifest CHD returned for a follow-up CAC scan. Reasons for not returning included refusal (n=43), death (n=21), and unknown (n=35). The study protocol was approved by the Human Research Protections Program at the University of California, San Diego. Written consent was obtained prior to participation at all three visits.

Depressive symptoms were assessed during the 1997–1999 research clinic visit using the self-administered BDI. The BDI consists of 21 items, each assessing symptoms and attitudes related to depression. Respondents rated each item from 0 (lowest intensity) to 3 (highest intensity)¹⁵ and scores were summed to quantify depressive symptomology. The BDI has high internal consistency among non-psychiatric patients¹⁵ and adequate reliability in older adults.¹⁶

Anthropometric measurements made during the 1997–1999 clinic visit included height, weight, and waist and hip circumference. Body mass index (BMI) was used as an estimate of overall obesity while waist-to-hip ratio was used as an estimate of central adiposity. Blood pressure was measured twice in seated participants after 5 minutes of rest using the Hypertension Detection and Follow-up Program protocol;¹⁷ the average measures were used. Hypertension was defined as systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or reported use of antihypertensive medication.

Plasma glucose, triglycerides, total cholesterol, and high density and low density lipoprotein (LDL) were assessed using standard methods¹⁸ after a requested 12–16 hour overnight fast. Age, alcohol use (drinks per day), cigarette smoking (never, past, or present), and exercise (3 times per week, no/yes) were obtained by standardized questionnaire. Medication use, including anti-depressant, statin and estrogen use, was queried and validated by trained nurses who reviewed prescriptions and pill containers brought to the clinic for that purpose.

CAC was measured using chest EBCT scans at two clinic visits, EBCT1 (2000–2002) and EBCT2 (2005–2007). An Imatron C-150 scanner took 40 contiguous images while participants held a single breath. CAC was defined as a plaque of ≥ 2 pixels (area 0.67 mm^2) with a density ≥ 130 Hounsfield units. Calcium scores used to classify adults by CAC severity were calculated using the method of Agatston et al.¹⁹ Total volume scores (mm^3) were calculated as the sum of volume scores for each lesion.¹⁹ Data on visceral and subcutaneous fat (assessed by EBCT) as well as statin use were obtained at each EBCT visit.

Substantial gender differences in CAC severity suggested stratified analyses of men and women were appropriate; subsequent tests of effect modification confirmed this ($p=0.08$). Participants were grouped into gender-specific quartiles based on BDI scores. The methods of Rumberger et al. were used to group participants by CAC severity: Agatston scores of 0–10=minimal; 11–100=mild; 101–399=moderate; and ≥ 400 =severe.²⁰ A binary indicator of CAC progression was computed using the method proposed by Hokanson et al., in which the difference in the square root transformed total calcium volume scores are computed and

differences 2.5 mm^3 are considered progression.²¹ The Hokanson method is considered the best measure of CAC progression.²²

Depressive symptoms, CAC, and potential covariates were described using age-adjusted means (for continuous variables) or percentages (for categorical variables). Comparisons of CAC and potential covariates across BDI quartiles were assessed using a Wald test. Covariates were selected for inclusion based on known risk factors for CAC.

Multivariable ordinal logistic regression models were fit using the OLOGIT command to assess the odds of increasing CAC severity (an ordinal indicator of CAC) by BDI quartile. While assessing the functional form of BDI, we observed non-linear patterns among men. Non-linear relations were then tested by regressing CAC severity on the continuous and quadratic form of BDI and testing the null hypothesis that coefficients of the squared term were equal to zero. To satisfy the proportional odds assumption to complete tests for non-linearity, one man and one woman with BDI scores more than 5 standard deviations from the overall mean were removed after which the assumption was met at the standard alpha of 0.10. Data for both older adults were included in all subsequent analyses using BDI quartiles. To evaluate non-linear patterns, men and women in the second quartile were selected as the referent category. For all models, proportional odds assumptions were tested using the Brant test and were met at an alpha level of 0.10. Longitudinal analyses of CAC progression followed the same approach described above using multivariable logistic regression models fit using the LOGISTIC command.

Associations of BDI with CAC severity and progression were examined using four sequential models: Model 1 adjusted for age and follow-up time; Model 2 added LDL and fasting plasma glucose; Model 3 added visceral fat and statin use to Model 2; Model 4 added a measure of the number of alcohol drinks per week to Model 3. CAC severity models used age, statin use, and visceral fat assessed at EBCT1 and time from baseline to EBCT1. CAC progression models used age, statin use, and visceral fat measured at EBCT2 and time between the first and second EBCT measurements. Estimates were unchanged when total cholesterol was included in models instead of LDL; therefore, LDL was retained for analyses. Full models were tested for multicollinearity and all variance inflation factors were < 5 . All data were analyzed using Stata Version 11.2.²³ Alpha levels were set to 0.05 unless otherwise stated.

Results

Average baseline age of participants was 67 ± 7.2 years. A total of 417 participants underwent CAC screening (EBCT1) 2.3 ± 1.0 years after the baseline visit and 326 returned for EBCT2 4.5 ± 0.5 years later. Age and age-adjusted characteristics are shown in Table 1.

Figure 1 shows the distribution of CAC severity for men and women separately. Nearly 50% of women had minimal CAC compared to 17% for men. Conversely, the largest proportion of men had severe CAC (39%) whereas only 10% of women had severe CAC.

Demographic, behavioral, clinical, and anthropometric characteristics across BDI quartiles were compared separately for men and women. Notable significant differences among men

were LDL and total cholesterol which followed a u-shaped pattern with the highest mean values observed among men in the first and fourth BDI quartiles (Table 2). Among women, age varied significantly by BDI quartile at baseline and EBCT1 ($p's < 0.05$; Table 3). Antidepressant use also differed ($p = 0.01$) with 25% of women in the fourth BDI quartile using depression medication compared to 7%, 5% and 9% in the first, second and third quartiles, respectively.

Visual inspection of Figure 2 suggests a higher proportion of men and women in the first and fourth BDI quartiles (compared to those in the second and third quartiles) had severe CAC. A similar u-shaped trend was also apparent for moderate to severe CAC (Agatston scores > 100) in men (but not women) with rates of 64% for those in BDI quartile one, and 53%, 69%, 81% for persons in BDI quartiles two, three and four, respectively.

Results from multivariable ordinal logistic regression models corroborate the observed non-linear associations among men. As shown in Table 4, the fully adjusted odds for increasing CAC severity were 2.60 and 3.00 times higher for men in BDI quartiles one and four (compared to BDI quartile two), respectively. Unexpected results were also observed among women which indicated that those in the first BDI quartile had 2.39 times higher adjusted odds of increasing CAC severity compared to women in the second BDI quartile, with odds ratios (OR) near unity for quartiles three and four. Results using BDI quartiles were corroborated using models that included the quadratic form of total BDI score (p -values for the squared term are reported in Table 4), suggesting a significant u-shaped relation between BDI and the fully adjusted odds of increasing CAC severity for men ($p = 0.01$), but not for women ($p = 0.20$).

The association of BDI with CAC progression is shown in Table 5. Analyses using BDI quartiles and BDI in quadratic form yielded non-significant associations. Nonetheless, the fully adjusted odds ratios for men showed a u-shaped pattern similar to that seen for CAC severity.

To examine whether observed associations between CAC severity and BDI could be explained by chronic health conditions, we included a variable measuring 10-year prevalence of *any* of the following self-reported chronic conditions: emphysema; non-skin cancer; thyroid problems; arthritis; hip fracture. We also included variables that measured the (a) total number of chronic conditions, (b) self-reported chest pain, and (c) pressure or heaviness in the chest; all measured at the baseline visit. There were no appreciable changes to the results in minimally and fully adjusted models (data not shown). The potential influence of antidepressant use on depressive symptoms was tested by including depression medication use in the final models for CAC severity and CAC progression. There were no measurable changes to the reported results (data not shown).

To examine survival and nonresponse bias, we examined differences between participants who attended both EBCT1 and EBCT2 compared to participants who attended only EBCT1. Baseline ages of participants who attended only EBCT1 were greater (mean age 71.2 years vs. 66.2 years, $p < 0.01$), but there were no differences by gender, regular exercise, BMI, alcohol consumption, BDI, or CAC severity ($p's > 0.05$).

Discussion

Results of this study suggest that depressive symptoms have a gender-specific, non-linear association with CAC. Contrary to our hypothesis, men with the lowest *and* highest depressive symptoms and women with the lowest depressive symptoms had the most severe CAC scores. Over 4.5 ± 0.5 years of follow-up, we observed similar nonlinear patterns (not statistically significant) among men but no clear patterns among women. Observed cross-sectional associations were not explained by several other comorbidities or CHD risk factors common with depression.

These gender-specific results are in accord with two previous studies in which clinical depression¹¹ and depressive symptoms (assessed using the BDI)¹⁰ were positively associated with CAC in men only. To our knowledge, this study is the first to report a non-linear u-shaped association between depressive symptoms and CAC, although other studies have reported monotonically increasing nonlinear associations in men using Spearman's correlation,¹⁰ and positive linear associations among men and women combined.^{13,24} Negative associations among women were also observed in a sample of CHD-free active duty Army personnel⁸ and among a subsample of younger adults (mean age 57) with suspected coronary artery disease.⁹

Social desirability bias as well as self- and public-stigma surrounding depression may contribute to these unexpected findings. Evidence suggests that both men and women underreport depressive symptoms when completing a depression assessment,^{25,26} and that adults with neurotic disorders such as depression rarely present their symptoms to health professionals.²⁷ Furthermore, those with the most severe depressive symptoms may be the least likely to report them.²⁷ Taken together, it is plausible that men and women with higher depressive symptoms might be more inclined to purposely report little or no depressive symptoms on the BDI.

Our findings with respect to CAC progression were similar to those of Low et al. who found no significant associations between depressive symptoms and CAC progression in a small sample of 149 women aged 64 ± 2 years.¹⁴ However, our findings disagree with two other studies of depressive symptoms and CAC progression.^{12,13} Stewart et al. used data from 2,352 middle-aged adults and found depressive symptoms were positively related to CAC progression after 5 years of follow-up. Their study sample (average age 40 ± 3.6) differed from ours in many ways, the most striking of which was a baseline CAC prevalence of only 18%¹³ compared to 76% in our study, likely reflecting the younger age of their study participants. A positive association was also reported in a study of 346 women aged 51 ± 3 years with a baseline CAC prevalence of 45%.¹² Both studies reported a baseline CAC prevalence lower than that found in our study and baseline CAC prevalence is thought to be the most important factor in CAC progression^{28,29} which could explain our differing results. Additionally, both of these studies had larger gender-specific sample sizes than ours, giving more power to detect significant associations. However, it is also plausible that associations between depressive symptoms and CAC vary over the lifecourse. These other studies suggest that CAC progression in younger persons may be related to depressive symptoms while our study suggests this association may not exist in older adults.

Several methodological limitations and strengths warrant discussion. The Rancho Bernardo cohort is composed of white, middle to upper-middle class Southern California residents thereby limiting the external validity of our findings. However, the ethnic and socioeconomic homogeneity implies that results are not likely due to differences in access to healthcare, diet, or other depression- and CHD-related factors associated with income. Additionally, BDI measured at one time point might not represent the entire prospective burden of depressive symptoms, thus one bad (or good) day could lead to misclassification. The observed nonsignificant associations of BDI with odds of CAC progression in men were likely due to low statistical power from the smaller sample size because of participants not returning to EBCT2. Furthermore, participants not returning for EBCT2 included an unknown number individuals diagnosed with CHD after EBCT1, which could remove persons most likely to progress further limiting progression results.

Our study had several strengths. Our sample consisted of participants from a population-based cohort who were followed for 43 years. The study sample was composed of men and women who, although older, had no history of CHD. Furthermore, depression was measured an average 2.3 years before CAC measures, indicating that depressive symptoms are likely not related to knowledge of heart disease.

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Figure 1.

Distribution of coronary artery calcium (CAC) by gender. Shading of bars indicates CAC severity with the darkest blue bars indicating severe CAC (Agatston scores ≥ 400) followed by moderate CAC (Agatston scores between 101–399), mild CAC (Agatston scores between 11–100) and the lightest bars indicate minimal CAC (Agatston scores between 0–10).

Figure 2.

Distribution of coronary artery calcium (CAC) severity across BDI quartiles, by gender. Shading of bars indicates CAC severity with the darkest blue bars indicating severe CAC (Agatston scores ≥ 400) followed by moderate CAC (Agatston scores between 101–399), mild CAC (Agatston scores between 11–100) and the lightest blue bars indicate minimal CAC (Agatston scores between 0–10).

Table 1

Age and age adjusted characteristics of men and women who underwent coronary artery calcium testing during 2000–02: the Rancho Bernardo Cohort

	Men	Women	
	(n = 199)	(n = 218)	p-value
<u>Baseline visit (1997–1999)</u>			
Age (years) ^a	70 (0.6)	66 (0.4)	< 0.01
Ever smoker	60%	51%	0.46
Exercise >3 days per week	79%	76%	0.41
Alcoholic drinks per week	7.5 (0.46)	4.4 (0.44)	< 0.01
Body mass index (kg/m ²)	27 (0.3)	26 (0.3)	< 0.01
Waist to hip ratio	0.9 (0.01)	0.8 (0.00)	< 0.01
Low density lipoprotein (mg/dl)	122 (2.1)	123 (2.0)	0.58
High density lipoprotein (mg/dl)	50 (1.0)	67 (1.0)	< 0.01
Total cholesterol (mg/dl)	197 (2.3)	216 (2.2)	< 0.01
Triglycerides (mg/dl)	126 (4.8)	130 (4.6)	0.71
Fasting plasma glucose (mg/dl)	107 (1.4)	99 (1.3)	< 0.01
Systolic blood pressure (mm Hg)	131 (1.3)	130 (1.2)	0.93
Diastolic blood pressure (mm Hg)	78 (0.6)	75 (0.6)	< 0.01
Hypertension	48%	47%	0.84
Antidepressant use	7.1%	11.3%	0.15
Beck Depression Index	3.7 (0.29)	4.4 (0.28)	0.10
Depressed (% with BDI > 12)	2.7 (1.20)	3.9 (1.30)	0.47
<u>EBCT1 visit (2000–2002)</u>	(n = 199)	(n = 218)	
Age (years) ^a	71 (0.6)	68 (0.5)	< 0.01
Time from baseline to EBCT1 (years)	2.2 (0.04)	2.4 (0.03)	< 0.01
Statin use	22%	14%	0.05
Visceral fat (cm ³)	94 (4)	61 (4)	< 0.01
Subcutaneous fat (cm ³)	128 (5.4)	151 (5.2)	< 0.01
<u>EBCT2 visit (2005–2007)</u>	(n = 147)	(n = 176)	
Age (years) ^a	74 (0.7)	72 (0.5)	0.01
Time from EBCT1 to EBCT2 (years)	4.5 (0.03)	4.4 (0.03)	0.03
Statin use	40%	28%	0.02
Visceral fat (cm ³)	108 (4)	72 (3)	< 0.01
Subcutaneous fat (cm ³)	135 (5)	141 (5)	0.33
Coronary Artery Calcium progression	55%	39%	< 0.01

Abbreviations: Electron beam computed tomography (EBCT)

Continuous variables are presented as mean and SE and compared with two-sample t-tests; Categorical variables are presented as % and compared with Pearson's chi-squared tests

^aValues are not adjusted for age

Bolded values are significant at an alpha < 0.05

Age adjusted characteristics of men who underwent coronary artery calcium testing during 2000–02, by Beck Depression Inventory quartile: the Rancho Bernardo Cohort

Table 2

	Quartile, Beck Depression Inventory Range				p-value ^b
	I, 0–1	II, 2–3	III, 4–5	IV, 6–7	
Baseline visit (1997–1999)	(n = 64)	(n = 53)	(n = 51)	(n = 31)	
Age (years) ^a	68 (1.0)	69 (1.0)	69 (1.1)	70 (1.4)	0.48
Ever smoker	43%	60%	51%	81%	0.01
Exercise >3 days per week	85%	79%	83%	67%	0.21
Alcoholic drinks per week	7.1 (0.9)	7.3 (1.0)	7.7 (1.1)	8.6 (1.4)	0.81
Body mass index (kg/m ²)	27 (0.4)	27 (0.5)	27 (0.5)	27 (0.6)	0.93
Waist to hip ratio	0.9 (0.01)	0.9 (0.01)	0.9 (0.01)	0.9 (0.01)	0.73
Low density lipoprotein (mg/dl)	126 (3.7)	113 (4.0)	120 (4.1)	129 (5.2)	0.04
High density lipoprotein (mg/dl)	50 (1.5)	50 (1.7)	51 (1.7)	51 (2.2)	0.96
Total cholesterol (mg/dl)	201 (3.9)	187 (4.3)	196 (4.4)	206 (5.6)	0.03
Triglycerides (mg/dl)	128 (8.7)	122 (9.6)	126 (9.8)	130 (12.5)	0.96
Fasting plasma glucose (mg/dl)	106 (2.1)	110 (2.3)	105 (2.4)	106 (3.1)	0.32
Systolic blood pressure (mm Hg)	129 (2.2)	132 (2.5)	136 (2.5)	130 (3.2)	0.20
Diastolic blood pressure (mm Hg)	77 (1)	79 (1.1)	80 (1.1)	80 (1.4)	0.17
Hypertension	43%	49%	55%	61%	0.32
Antidepressant use	0%	8%	10%	16%	0.47
Beck Depression Inventory	0.4 (0.3)	2.5 (0.3)	4.9 (0.3)	10.8 (0.4)	<0.01
EBCT1 visit (2000–2002)	(n = 64)	(n = 53)	(n = 51)	(n = 31)	
Age (years) ^a	70 (1.0)	71 (1.1)	72 (1.3)	73 (1.5)	0.43
Time from baseline to EBCT1 (years)	2.3 (0)	2.4 (0.1)	2.4 (0.1)	2.5 (0.1)	0.13
Statin use	23%	18%	20%	29%	0.07
Visceral fat (cm ³)	100 (8.3)	86 (9.1)	94 (9.5)	91 (11.8)	0.73
Subcutaneous fat (cm ³)	135 (10.0)	116 (11.0)	118 (11.4)	131 (14.2)	0.53
EBCT2 visit (2005–2007)	(n = 46)	(n = 41)	(n = 39)	(n = 21)	
Age (years) ^a	73 (1.1)	75 (1.2)	75 (1.3)	74 (1.8)	0.50

	Quartile, Beck Depression Inventory Range				
	I, 0–1	II, 2–3	III, 4–5	IV, 6–37	
Time from EBCT1 to EBCT2 (years)	4.4 (0)	4.5 (0)	4.6 (0)	4.5 (0.1)	0.23
Statin use	35%	32%	32%	36%	0.27
Visceral fat (cm ³)	104 (6.8)	111 (7.0)	109 (7.3)	115 (9.8)	0.82
Subcutaneous fat (cm ³)	140 (8.5)	119 (8.7)	139 (9.1)	136 (12.2)	0.29

Abbreviations: Electron beam computed tomography (EBCT)

Continuous variables are presented as mean (SE) and compared using ANCOVA models adjusted for age and follow-up time; Categorical variables are presented as % and compared with Pearson's chi-squared tests

^aValues are not adjusted for age

Bolded values are significant at an alpha < 0.05

^bp-values from Wald tests following linear (continuous variables) or logistic (binary variables) regression

Age adjusted characteristics of women who underwent Coronary Artery Calcium testing during 2000–02, by Beck Depression Inventory quartile: the Rancho Bernardo Cohort

Table 3

	Quartile, Beck Depression Inventory Range				p-value ^b
	I, 0–1	II, 2–3	III, 4–6	IV, 7–27	
Baseline visit (1997–1999)	(n = 67)	(n = 42)	(n = 57)	(n = 52)	
Age (years) ^a	65 (0.8)	65 (0.9)	67 (0.7)	67 (0.9)	0.03
Ever smoker	51%	45%	48%	60%	0.50
Exercise >3 days per week	78%	82%	77%	60%	0.07
Alcoholic drinks per week	4.0 (0.7)	4.4 (0.8)	4.7 (0.7)	4.7 (0.7)	0.89
Body mass index (kg/m ²)	25 (0.6)	26 (0.7)	26 (0.6)	26 (0.6)	0.44
Waist to hip ratio	0.8 (0.01)	0.8 (0.01)	0.8 (0.01)	0.8 (0.01)	0.28
Low density lipoprotein (mg/dl)	121 (3.7)	129 (4.6)	122 (4.0)	123 (4.2)	0.57
High density lipoprotein (mg/dl)	65 (2.1)	63 (2.6)	67 (2.2)	71 (2.3)	0.12
Total cholesterol (mg/dl)	212 (4.0)	219 (5.0)	215 (4.3)	220 (4.5)	0.47
Triglycerides (mg/dl)	126 (8.1)	133 (10.2)	136 (8.8)	131 (9.2)	0.87
Fasting plasma glucose (mg/dl)	98 (2.7)	104 (3.4)	96 (3.0)	100 (3.1)	0.44
Systolic blood pressure (mm Hg)	129 (2.3)	128 (2.9)	131 (2.5)	129 (2.6)	0.89
Diastolic blood pressure (mm Hg)	74 (1.0)	77 (1.2)	76 (1.1)	75 (1.1)	0.29
Hypertension	38%	47%	43%	50%	0.57
Antidepressant use	7%	5%	9%	25%	0.01
Beck Depression Inventory	0.3 (0.2)	2.5 (0.3)	5.1 (0.2)	10 (0.3)	<0.01
EBCT1 visit (2000–2002)	(n = 67)	(n = 42)	(n = 57)	(n = 52)	
Age (years) ^a	67 (0.9)	67 (0.9)	70 (0.8)	69 (1.1)	0.03
Time from baseline to EBCT1 (years)	2.3 (0.1)	2.2 (0.1)	2.2 (0.1)	2.4 (0.1)	0.18
Statin use	15%	19%	19%	21%	0.88
Visceral fat (cm ³)	55 (4.2)	62 (5.2)	68 (4.6)	64 (4.7)	0.22
Subcutaneous fat (cm ³)	136 (8.8)	159 (10.8)	159 (9.6)	165 (9.9)	0.12
EBCT2 visit (2005–2007)	(n = 50)	(n = 35)	(n = 47)	(n = 44)	
Age (years)	70 (0.9)	71 (1.0)	73 (0.8)	73 (1.1)	0.06

	Quartile, Beck Depression Inventory Range				
	I, 0–1	II, 2–3	III, 4–6	IV, 7–27	
Time from EBCT1 to EBCT2 (years)	4.5 (0.1)	4.5 (0.1)	4.6 (0.1)	4.4 (0.1)	0.08
Statin use	30%	29%	26%	28%	0.75
Visceral fat (cm ³)	67 (5.7)	78 (6.8)	71 (5.9)	70 (6.1)	0.67
Subcutaneous fat (cm ³)	127 (9.3)	152 (11.1)	146 (9.7)	150 (10.0)	0.28

Abbreviations: Electron beam computed tomography (EBCT)

Continuous variables are presented as mean (SE) and compared using ANCOVA models adjusted for age and follow-up time; Categorical variables are presented as % and compared with Pearson's chi-squared tests

^aValues are not adjusted for age

Bolded values are significant at an alpha < 0.05

^bp-values from Wald tests following linear (continuous variables) or logistic (binary variables) regression

Adjusted odds ratios for increasing coronary artery calcium severity and depressive symptoms; results from multivariable ordinal logistic regression models

Table 4

	Men			Women		
	OR	95% CI	p-value [‡]	OR	95% CI	p-value [‡]
Model 1	(n=199)			(n=217)		
Beck Depression Inventory			0.016			0.393
Quartile 1	2.28	(1.15–4.52)		2.19	(0.99–4.83)	
Quartile 2	1.00	referent		1.00	referent	
Quartile 3	2.28	(1.06–4.89)		1.01	(0.45–2.27)	
Quartile 4	2.88	(1.33–6.26)		1.13	(0.49–2.62)	
Model 2	(n=199)			(n=216)		
Beck Depression Inventory			0.020			0.312
Quartile 1	2.20	(1.09–4.43)		2.38	(1.06–5.32)	
Quartile 2	1.00	referent		1.00	referent	
Quartile 3	2.27	(1.05–4.90)		1.08	(0.48–2.44)	
Quartile 4	2.84	(1.29–6.27)		1.11	(0.47–2.59)	
Model 3	(n=192)			(n=209)		
Beck Depression Inventory			0.010			0.189
Quartile 1	2.29	(1.10–4.80)		2.39	(1.05–5.41)	
Quartile 2	1.00	referent		1.00	referent	
Quartile 3	2.00	(0.90–4.43)		1.05	(0.46–2.39)	
Quartile 4	2.65	(1.17–6.03)		1.03	(0.44–2.44)	
Model 4	(n=192)			(n=209)		
Beck Depression Inventory			0.013			0.202
Quartile 1	2.53	(1.24–5.6)		2.39	(1.05–5.41)	
Quartile 2	1.00	referent		1.00	referent	
Quartile 3	2.16	(0.89–4.5)		1.04	(0.46–2.39)	
Quartile 4	3.18	(1.3–6.82)		1.03	(0.44–2.44)	

Model 1: adjusted for age at EBCT1 and baseline to EBCT1 time interval

Model 2: model 1 covariates + low density lipoprotein and fasting plasma glucose

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Model 3: model 2 covariates + visceral fat and statin use.
Model 4: model 3 covariates + number of alcohol drinks per week
† all models adjusted for current estrogen use
‡ p-value from the squared term when Beck Depression Inventory scores were modeled as a quadratic to test for nonlinearity
* significant at an alpha < 0.05

Table 5

Adjusted odds ratios for coronary artery calcium progression and depressive symptoms; results from multivariable logistic regression models

	Men				Women			
	OR	95% CI	p-value [‡]		OR	95% CI	p-value [‡]	
Model 1	(n=147)				(n=174)			
Beck Depression Inventory			0.867				0.442	
Quartile 1	1.88	(0.79–4.47)			0.83	(0.32–2.20)		
Quartile 2	1.00	referent			1.00	referent		
Quartile 3	1.12	(0.43–2.89)			1.47	(0.56–3.83)		
Quartile 4	2.25	(0.84–6.06)			1.26	(0.48–3.34)		
Model 2	(n=147)				(n=173)			
Beck Depression Inventory			0.839				0.414	
Quartile 1	1.91	(0.79–4.61)			0.94	(0.35–2.54)		
Quartile 2	1.00	referent			1.00	referent		
Quartile 3	1.17	(0.44–3.07)			1.69	(0.63–4.51)		
Quartile 4	2.46	(0.89–6.79)			1.39	(0.52–3.76)		
Model 3	(n=141)				(n=166)			
Beck Depression Inventory			0.804				0.467	
Quartile 1	2.17	(0.86–5.47)			0.96	(0.35–2.64)		
Quartile 2	1.00	referent			1.00	referent		
Quartile 3	1.33	(0.48–3.61)			1.66	(0.61–4.54)		
Quartile 4	2.73	(0.94–7.92)			1.37	(0.50–3.78)		
Model 4	(n=141)				(n=166)			
Beck Depression Inventory			0.799				0.448	
Quartile 1	2.30	(0.89–5.76)			0.94	(0.34–2.60)		
Quartile 2	1.00	referent			1.00	referent		
Quartile 3	1.30	(0.46–3.51)			1.64	(0.60–4.50)		
Quartile 4	2.80	(0.94–8.11)			1.38	(0.50–3.79)		

Model 1: adjusted for age at ebct1 and baseline to EBCT1 time interval

Model 2: model 1 covariates + low density lipoprotein and fasting plasma glucose

Model 3: model 2 covariates + visceral fat and statin use.

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Model 4: model 3 covariates + number of alcohol drinks per week

[†] all models adjusted for current estrogen use

[‡] p-value from the squared term when Beck Depression Inventory scores were modeled as a quadratic to test for nonlinearity

* significant at an alpha < 0.05