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Association of Depressive Symptoms and Anti-Depressants with Body Mass Index and Waist Circumference in Elderly Men and Women: The ARIC Carotid MRI Study

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Abstract: *Background:* Depressive symptoms are associated with obesity, a precursor to type 2 diabetes and cardiovascular disease, and might in part explain the association of depressive symptoms with adverse metabolic outcomes. We determined the cross-sectional association between depressive symptoms and body mass index (BMI) and waist circumference (WC) in 1,314 elderly men and women age 60 to 83 years in the Atherosclerosis Risk in Communities (ARIC) Carotid MRI Study.

Methods: Depressive symptoms were assessed using the Center for Epidemiological Studies Depression (CES-D) Scale. Elevated depressive symptoms were defined as CES-D score ≥16 and/or anti-depressant medication use. CES-D score was also modeled continuously.

Results: In unadjusted analyses, each 5-point higher CES-D score was associated with a 0.48 kg/m^2 higher BMI (95% CI: 0.24 to 0.69) and a 1.23 cm higher WC (95% CI: 0.67 to 1.82). Adjustment for potential confounders, including physical activity, attenuated the associations with BMI (0.16 kg/m^2; 95% CI: -0.07 to 0.39) and WC (0.45 cm; 95% CI: -0.11 to 1.01). Compared to individuals without elevated depressive symptoms, those with elevated symptoms had significantly greater BMI (0.99 kg/m^2; 95% CI: 0.07 to 1.90) and WC (3.22 cm; 95% CI: 1.04 to 5.40), even after multivariable adjustment. In a subsidiary analysis, compared to individuals not taking anti-depressants, those taking anti-depressants had significantly higher waist circumference (1.54 cm; 95% CI: 0.18 to 2.90) and BMI (4.23 kg/m^2; 95% CI: 0.90 to 7.55) following multivariable adjustment. All results were similar when individuals with diabetes and coronary heart disease were excluded and when waist to height ratio was used an alternative measure of body fat.

Conclusions: We found a significant cross-sectional association between depressive symptoms and BMI and WC in elderly individuals that was partially explained by health behaviors, particularly physical activity.

Keywords: Depressive symptoms, Waist circumference, Body mass index, Elderly.

INTRODUCTION

Major depression and depressive symptoms are risk factors for the development of both type 2 diabetes [1] and cardiovascular disease [2]. Longitudinal and cross-sectional studies have demonstrated an association between major depression and depressive symptoms and obesity, although the literature has been mixed [3-5]. Because obesity is a metabolic precursor to type 2 diabetes and cardiovascular disease, it might explain, in part, the association of depression with these two metabolic clinical outcomes.

A recent meta-analysis showed that elevated depressive symptoms might lead to development of overweight and/or obesity [4]. In an earlier study of middle aged women, depressive symptoms at baseline were associated with a greater likelihood of weight gain over 6 years [6]. Another study, however, failed to show that major depression in middle and later adulthood predicted obesity [7]. Two studies in older adults that have measured abdominal visceral fat directly have demonstrated that depressive symptoms predict longitudinal accumulation of visceral fat [8, 9], despite similar weight gain in one study [9]. Even though clinical depression may cause anorexia and overeating, most population-based studies have shown that individuals with elevated depressive symptoms are more likely to engage in obesity-promoting behaviors, including consumption of a higher calorie diet and physical inactivity [10]. Depression is also associated with enhanced neuroendocrine activity and elevated inflammatory markers [11] that may alter eating behavior and/or promote weight gain.

That same meta-analysis also showed that overweight and obesity lead to an increased risk of developing depression [4]. Cross-sectional studies examining the

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association between depressive symptoms and obesity have also been mixed [12]. It is hypothesized that the positive association between depression and obesity seen in some studies may be related to body image dissatisfaction and repeated diet failures [3]. While two prior studies have examined the association between clinical depression and BMI continuously [13, 14] and one recent study examined the association between depressive symptoms and visceral adiposity continuously [15], most prior studies have not examined the linear association between subclinical depressive symptoms and BMI and waist circumference. In addition, several prior studies used self-report as opposed to measured weight and height to determine BMI [12, 16, 17], which may contribute to disparate findings. Finally, only a few studies have focused on the elderly [8, 9].

Using data from the Atherosclerosis Risk in Communities Study (ARIC) Carotid MRI Study, we examined the cross-sectional association between depressive symptoms and BMI and waist circumference in older community-dwelling men and women to determine the magnitude and direction of these associations. Our study had two primary objectives. First, we sought to determine whether there was an association between depressive symptoms and BMI and waist circumference independent of its association with diabetes and coronary heart disease. Second, we sought to determine what behavioral and biological factors might explain this association.

METHODS

Study Population

Study participants were selected from participants in the Atherosclerosis Risk in Communities (ARIC) Study [18]. The ARIC Study is a prospective observational cohort of 15,792 Caucasian and African-American individuals who were between the ages of 45 and 64 at baseline enrollment in 1987-1989. They were recruited from a probability sample of four U.S. communities (Forsyth County, NC; Jackson, MS; suburban Minneapolis, MN; and Washington County, MD). Participants took part in clinic examinations, starting with a baseline visit during 1987-9, and including three follow-up examinations at approximately three year intervals.

Participants for the ARIC Carotid MRI Study, now aged 60 to 84 years, were selected from the surviving ARIC Study participants under a stratified sampling plan designed to oversample for the presence of carotid artery plaque based on carotid thickness measurements from a prior ultrasound exam [19]. A total of 4,307 persons were contacted and invited to participate in the exam. Of these, 1,404 refused, 837 were ineligible, and 2,066 participated. We received approval to collect data on depressive symptoms from 1,478 consecutive participants 6 months after the initiation of the ARIC Carotid MRI exam. The analyses presented are cross-sectional data from the ARIC Carotid MRI exam. Written informed consent was obtained from participants and the study was approved by the Institutional Review Boards of each institution.

Assessment of Depressive Symptoms

Depressive symptoms were assessed using the Centers for Epidemiological Studies Depression (CES-D) Scale, a 20-item questionnaire aimed at measuring depressive symptoms in community populations [20]. The items represent the major components of depression and include depressed mood, feelings of worthlessness, feelings of hopelessness, loss of appetite, poor concentration, and sleep disturbance. The scale does not include items for increased appetite or sleep, anhedonia, psychomotor agitation or retardation, guilt, or suicidal thoughts. Cronbach's alpha for reliability of the instrument has been reported to range between 0.84 and 0.93 [21]. Participants are asked to rate each item on a scale from 0 to 3 based on "how often you have felt this way during the past week." Scores range from 0 to 60, with higher scores indicating more severe depressive symptoms. For our analyses, elevated depressive symptoms were defined as a CES-D score $\geq$16, consistent with mild-to-moderate depression or dysthymia at the population level [22] and/or self-reported use of anti-depressant medications (selective serotonin reuptake inhibitors, tricyclics, and monoamine oxidase inhibitors), as defined in previous studies [10].

Assessment of BMI and Waist Circumference

Anthropometry was performed in the fasting state with the urinary bladder empty. Participants wore lightweight, non-constricting underwear and scrub suits. Height (without shoes) was measured using a wall-mounted ruler. Weight was measured using a balance scale (Detecto, model #437), which was zeroed daily. BMI was calculated as weight (kg) divided by height squared (m^2). Waist circumference was measured in centimeters at the level of the umbilicus. Prior work has suggested waist to height ratio as another predictor of abdominal fat distribution [23]. We therefore calculated waist to height ratio as waist circumference in cm divided by height in cm.

Covariates

Sex, age, race/ethnicity, years of educational attainment, and cigarette smoking history were self-reported. Educational attainment was categorized as basic ($\leq$ 11 years), intermediate (12-16 years), and advanced (17-21 years). Physical activity was ascertained from a self-administered questionnaire developed [24] and was summarized as the number of leisure hours/week spent in sports and other physical activities. C-reactive protein (CRP) was measured using an immunoturbidimetric assay. Medication usage in the 2 weeks preceding the examination was determined by having participants bring their medications to the field center to be recorded and coded. Individuals were classified as having prevalent diabetes mellitus if they met any of the following criteria: fasting serum glucose levels $\geq$7.0 mmol/L, non-fasting serum glucose $\geq$11.0 mmol/L, current self-reported use of medications prescribed to treat diabetes (e.g. insulin or sulfonylureas), or a positive response to the question "Has a doctor ever told you that you had diabetes?" Prevalent coronary heart disease (CHD) was determined by contacting ARIC participants annually to determine recent hospitalizations for cardiac events and/or procedures and by reviewing records of all hospitalizations for acute myocardial infarction and CHD deaths in the study communities. A CHD event was defined as a definite or probably myocardial infarction, definite CHD death, or

Table 1. Demographic, Socioeconomic, Behavioral and Metabolic Characteristics of 1,314 Elderly Adults in the ARIC Carotid MRI Study by Depressive Symptoms Status

Variable	CES-D<16 N=1010	CES-D≥16 or Use of Anti-Depressants N=304	p-value
Age, mean (SD)†	70.94 (5.61)	71.43 (5.77)	0.1091
Sex %			
Female	47.82	64.80	<.0001
Male	52.18	35.20	
Ethnicity, %			
Caucasian African- American	72.67 27.33	61.84 38.16	0.0019
BMI (kg/m^2), mean (SD)†	28.92 (5.11)	29.85 (5.79)	0.0003
Waist circumference (cm), mean (SD)†	101.79 (13.80)	104.40 (14.55)	<0.0001
Waist to Height Ratio, mean (SD)†	0.6074 (0.084)	0.6335 (0.093)	<0.001
C-reactive protein, median (IQR)*	1.93 (3.02)	2.35 (5.05)	<.0001
Current smokers, %	7.62	10.53	0.1719
Prevalent diabetes, %	23.86	36.51	0.0002
Prevalent coronary heart disease, %	12.28	10.20	0.3491
Educational Attainment, %			
Basic (≤ 11 years)	14.65	25.33	<.0001
Intermediate (12-16 years)	41.09	43.42	
Advanced (17-21 years)	44.26	31.25	
Physical activity (leisure time), mean (SD)†			
Sports (hrs)	2.88 (0.86)	2.60 (0.82)	<.0001
Other physical activities (hrs)	2.44 (0.59)	2.28 (0.61)	0.0002

*Summary statistic represents median and interquartile range.
†SD=standard deviation; SSRIs=selective serotonin reuptake inhibitors; TCAs=tricyclic anti-depressants

coronary revascularization procedure as adjudicated by the ARIC Morbidity and Mortality Classification Committee.

Analysis

All analyses were weighted to account for the ARIC Carotid MRI Study sampling scheme. Of the 1,478 individuals administered the CES-D, participants were excluded if they were missing in any covariates of interest (n=164), leaving 1,314 individuals for this cross-sectional analysis.

Baseline characteristics were compared between individuals with and without elevated depressive symptoms. The comparisons were tested using weighted simple linear regression analysis. Weighted linear regression analysis was used to determine the mean difference in BMI, waist circumference, and waist to height ratio for each 5-point difference in CES-D score, adjusting for age, sex, and race-ARIC center. A combined race-center variable was created to avoid co-linearity since the Jackson field center only recruited African-Americans. Similar analyses were performed in which depressive symptoms were dichotomized as elevated (CES-D≥16 and/or anti-depressant medication use) or non-elevated (CES-D<16). In these analyses, weighted linear regression was used to determine the mean difference in BMI, waist circumference, and waist to height ratio for individuals with and without elevated depressive symptoms. In multivariable analyses, adjustment was made for age, sex, race-center, diabetes status, CHD status, CRP, smoking status, educational attainment, and physical activity to determine if these covariates reduced the association between depressive symptoms and BMI/waist circumference/waist to height ratio to a p-value>0.05. A two-sided p-value<0.05 was used to determine statistical significance. Statistical analyses were performed using SAS version 9.2 (Cary, NC).

RESULTS

Baseline Characteristics

Table **1** summarizes the baseline characteristics of individuals with and without elevated depressive symptoms. Compared to those without elevated depressive symptoms, those with elevated depressive symptoms were more likely to be female, African-American, current smokers, and less educated, to have prevalent diabetes, and to have higher

Table 2. Mean Difference in Body-Mass Index (BMI), Waist Circumference, and Waist to Height Ratio for each 5-Point Higher CES-D Score in 1,314 Elderly Adults

	Beta-Coefficient* (95% CI) p-value	**Beta-Coefficient* (95% CI) p-value**	**Beta-coefficient* (95% CI) p-value**
	BMI (kg/m^2)	Waist circumference (cm)	Waist to Height Ratio
Model 1	0.47 (0.24, 0.69) <0.0001	1.23 (0.67, 1.82) <0.0001	0.0105 (0.0068, 0.0141) <0.0001
Model 2	0.27 (0.04, 0.49) 0.019	0.78 (0.21, 1.34) 0.007	0.0056 (0.002, 0.0093) 0.002
Model 3	0.16 (-0.07, 0.39) 0.16	0.45 (-0.11, 1.01) 0.11	0.0035 (0, 0.0071) 0.05
Subsidiary analyses excluding individuals with diabetes and coronary heart disease (CHD) [models adjusted for same covariates as above except diabetes and CHD]			
Model 1	0.42 (0.12, 0.71) 0.006	0.97 (0.21, 1.74) 0.013	0.0092 (0.0044, 0.014) 0.0002
Model 2	0.30 (0.02, 0.58) 0.04	0.72 (-0.0006, 1.44) 0.05	0.006 (0.0014, 0.0106) 0.01
Model 3	0.22 (-0.07, 0.51) 0.13	0.44 (-0.27, 1.16) 0.22	0.0042 (-0.0003, 0.0087) 0.07

*Interpreted as the mean difference in BMI, waist circumference, or waist to height ratio for each 5-point higher CES-D score
Model 1: Unadjusted
Model 2: Adjusted for age, race-center, sex, CRP, smoking status, education, diabetes and coronary heart disease (CHD).
Model 3: Adjusted for age, race-center, sex, CRP, smoking status, education, diabetes, CHD, and physical activity (sport time and physical activity at leisure time)

BMI, waist circumference, waist to height ratio, and CRP. Individuals with elevated depressive symptoms also engaged in fewer hours of weekly physical activity than those without depressive symptoms.

Univariate and Multivariable Cross-Sectional Analyses

In unadjusted analyses, there was significant graded association between CES-D score and BMI and waist circumference. Each 5-point higher CES-D score was associated with a 0.47 kg/m^2 higher BMI (95% CI: 0.24 to 0.69) and a 1.23 cm higher waist circumference (95% CI: 0.67 to 1.82)(Table **2**, Model 1). The associations were attenuated but remained statistically significant following adjustment for age, race-center, sex, CRP, educational attainment, smoking, diabetes and CHD (Table **2**, Model 2); however, the associations became non-significant following additional adjustment for physical activity (Table **2**, Model 3). We found similar results when individuals with diabetes or CHD were excluded (n= 449) and when waist to height ratio was substituted for BMI and waist circumference (Table **2**).

We observed similar and somewhat stronger associations when participants were categorized by depressive symptom status (Table **3**). Compared to individuals without elevated depressive symptoms, those with elevated depressive symptoms had significantly higher BMI (1.78 kg/m^2; 95% CI: 0.82 to 2.73) and waist circumference (4.82 cm; 95% CI: 2.47 to 7.17); however, while attenuated, these associations remained statistically significant following multivariable adjustment (BMI: 0.99 kg/m^2; 95% CI: 0.07 to 1.90; waist circumference: 3.22 cm; 95% CI: 1.04 to 5.40). When individuals with diabetes and CHD were excluded, results were similar--compared to those without elevated depressive symptoms, those with elevated depressive symptoms had significantly higher BMI (1.40 kg/m^2; 95% CI: 0.26 to 2.55) and waist circumference (3.80 cm; 95% CI: 1.12 to 6.48), following multivariable adjustment (Table **3**). Results were also similar when waist to height ratio was substituted for BMI and waist circumference (Table **3**).

In sensitivity analyses in which elevated depressive symptoms were defined only as a CES-D≥16 (excluding anti-depressant medication use from the definition), results were similar but attenuated. In the fully-adjusted model, compared to individuals with a CES-D<16, those with a CES-D≥16 had higher BMI (0.42 kg/m^2; 95% CI: -0.54 to 1.41) and waist circumference (1.90 cm; 95% CI: -0.44 to 4.23); however, these results were not statistically significant. We also performed a subsidiary analyses comparing body fat measures among users and non-users of anti-depressants. Compared to individuals not taking anti-depressants, those taking anti-depressants had significantly higher waist circumference (1.54 cm; 95% CI: 0.18 to 2.90) and BMI (4.23 kg/m^2; 95% CI: 0.90 to 7.55) following multivariable adjustment (Table **4**). These associations were even stronger after excluding individuals with diabetes and CHD and when substituting waist to height ratio for BMI and waist circumference (Table **4**).

DISCUSSION

Among elderly community dwelling adults in the ARIC Carotid MRI Study, there was a significant graded cross-sectional association between depressive symptoms and BMI

Table 3. Mean Difference in Body-Mass Index (BMI), Waist Circumference, and Waist to Height Ratio for Individuals with Elevated (CES-D≥16) or Anti-Depressant Usage Versus Non-Elevated Depressive Symptoms in 1,314 Elderly Adults

	Beta-Coefficient* (95% CI) p-value	**Beta-Coefficient* (95% CI) p-value**	**Beta-Coefficient* (95% CI) p-value**
	BMI (kg/m^2)	Waist circumference (cm)	Waist-to-Height Ratio
Model 1	1.78 (0.82, 2.73) 0.0003	4.82 (2.47, 7.17) <0.0001	0.0392 (0.0245, 0.0539) <0.0001
Model 2	1.24 (0.3, 2.18) 0.01	4.00 (1.75, 6.26) 0.0005	0.025 (0.0106, 0.0395) 0.0007
Model 3	0.99 (0.07, 1.9) 0.03	3.22 (1.04, 5.4) 0.004	0.0199 (0.006, 0.0338) 0.005
Subsidiary analyses excluding individuals with diabetes and coronary heart disease (CHD) [models adjusted for same covariates as above except diabetes and CHD]			
Model 1	1.69 (0.47, 2.91) 0.006	4.15 (1.28, 7.03) 0.005	0.0361 (0.0179, 0.0544) 0.0001
Model 2	1.56 (0.38, 2.74) 0.009	4.35 (1.58, 7.12) 0.002	0.0293 (0.0116, 0.047) 0.001
Model 3	1.40 (0.26, 2.55) 0.02	3.80 (1.12, 6.48) 0.006	0.0256 (0.0086, 0.0427) 0.003

*Interpreted as the mean difference in BMI, waist circumference, or weight to height ratio for individuals with elevated versus non-elevated depressive symptoms
Model 1: Unadjusted
Model 2: Adjusted for age, race-center, sex, CRP, smoking status, education, diabetes and coronary heart disease (CHD).
Model 3: Adjusted for age, race-center, sex, CRP, smoking status, education, diabetes, CHD, and physical activity (sport time and physical activity at leisure time)

Table 4. Mean Difference in Body-Mass Index (BMI), Waist Circumference, and Waist to Height Ratio for Individuals with (n=304) Versus without (n=1010) Anti-Depressant Usage in 1,314 elderly Adults

	Beta-Coefficient* (95% CI) p-value	**Beta-Coefficient* (95% CI) p-value**	**Beta-Coefficient* (95% CI) p-value**
	BMI (kg/m^2)	Waist circumference (cm)	Waist to Height Ratio
Model 1	1.72 (0.33, 3.11) 0.02	3.91 (0.25, 7.56) 0.04	0.0324 (0.011, 0.0538) 0.003
Model 2	1.85 (0.40, 3.30) 0.01	5.29 (1.72, 8.86) 0.004	0.0306 (0.0079, 0.0533) 0.008
Model 3	1.54 (0.18, 2.90) 0.03	4.23 (0.90, 7.55) 0.01	0.0237 (0.0026, 0.0448) 0.03
Subsidiary analyses excluding individuals with diabetes and coronary heart disease (CHD) [models adjusted for same covariates as above except diabetes and CHD]			
Model 1	2.39 (0.45, 4.32) 0.0157	4.25 (-0.68, 9.19) 0.09	0.0412 (0.0117, 0.0707) 0.006
Model 2	3.05 (1.26, 4.84) 0.0009	7.31 (3.01, 11.62) 0.009	0.0473 (0.0197, 0.0748) <0.001
Model 3	2.69 (1.01, 4.37) 0.0017	6.05 (2.01, 10.09) 0.003	0.0389 (0.0131, 0.0646) 0.003

*Interpreted as the mean difference in BMI or waist circumference for individuals with versus without anti-depressant usage
Model 1: Unadjusted
Model 2: Adjusted for age, race-center, sex, CRP, smoking status, education, diabetes and coronary heart disease (CHD).
Model 3: Adjusted for age, race-center, sex, CRP, smoking status, education, diabetes, CHD, and physical activity (sport time and physical activity at leisure time)

and waist circumference. The association of depressive symptoms with BMI and waist circumference was attenuated but remained significant following adjustment for demographic factors, educational attainment, diabetes, CHD, and health behaviors, particularly physical activity. Our findings were similar when individuals with diabetes and CHD were excluded and when waist to height ratio, an alternative estimate of abdominal fat distribution, was substituted for BMI and waist circumference. Our findings from the present cross-sectional study are consistent with those from another population-based study of elderly adults (Health ABC Study), which found that elevated depressive symptoms were longitudinally associated with increased abdominal adiposity [8]. We believe that the 2-3 cm difference in waist circumference that we observed in individuals with and without elevated depressive symptoms in our multivariable analysis is clinically meaningful. While this difference appears to be small, prior studies have shown that even a 2 cm, or 1 standard deviation, difference in waist circumference is associated with an increased risk of type 2 diabetes [25, 26]. We observed this magnitude of difference even when excluding individuals with diabetes and CHD. Finally, we also found that anti-depressant medication use was significantly associated with greater BMI, waist circumference, and waist to height ratio.

As recently reviewed [3], there are several mechanisms by which depression and obesity may be associated. Both depression and obesity are associated with low socioeconomic status and in our study elevated depressive symptoms were associated with lower educational attainment. Low socioeconomic status is an important risk factor for both obesity and depressive symptoms and individuals with depressed mood and fewer economic resources may be predisposed to maladaptive obesity-promoting behaviors [27]. However, there are also data suggesting that obese individuals with some college education have a higher risk of developing elevated depressive symptoms [3].

As summarized in a recent meta-analysis, longitudinal studies suggest that elevated depressive symptoms and clinical depression lead to development of overweight and obesity [4]. There are several potential mechanisms through which elevated depressive symptoms might lead to obesity. First, clinical and subclinical depression are associated with subclinical hypercortisolism and enhanced stress reactivity [11]. Subclinical hypercortisolism can lead to accumulation of visceral fat by promoting differentiation and proliferation of adipocytes, redistributing fat from peripheral to central depots, and increasing adipocyte size and number [28]. Elevated depressive symptoms are also associated with elevated inflammatory markers, which can be more pronounced in the setting of obesity [11]. Studies of exogenous cytokine administration suggest that they influence eating behaviors [29]; thus, inflammatory markers may promote obesity by stimulating eating behaviors. In our study, CRP levels were higher in those with compared to those without elevated depressive symptoms. Second, depressive symptoms are associated with obesity-promoting health behaviors, including physical inactivity and increased caloric intake [10]. Individuals with elevated depressive symptoms are less adherent to weight loss and exercise programs [3]. Individuals with elevated depressive symptoms in our study were less physically active than those without elevated depressive symptoms, as shown in prior studies [10, 30-33]. Finally medications used to treat clinical depression may also lead to weight gain [3], which is supported by our data. In our study, anti-depressant medication use was cross-sectionally associated with significantly greater waist circumference, BMI, and waist to height ratio.

Longitudinal studies also suggest that obesity leads to development of depressive disorders [4] through biological and psychological mechanisms. There are several proposed biological pathways. First, obesity is associated with inflammation and cytokinemia and inflammatory markers have been implicated in the development of depression [34-36], particularly late-life depression that occurs in the elderly [35, 36]. In our study, associations persisted following adjustment for CRP. Second, as previously discussed, obesity is associated with subclinical hypercortisolism and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis [11]. HPA axis dysfunction has also been implicated in the etiology of depression [37]. Finally, obesity is associated with insulin resistance and risk of type 2 diabetes, which might cause central nervous system alterations that predispose these individuals to depression [38]. Prior studies have also shown that individuals with type 2 diabetes are at increased risk for depression. In our study, the association between depressive symptoms and BMI and waist circumference was independent of diabetes. There are also proposed psychological mechanisms through which obesity may also lead to development of depressive symptoms. Through the appearance concern pathway, obese individuals experience more body image dissatisfaction, distress regarding repeated diet failures, and actual or perceived stigma related to obesity [3]. This can lead to low self-esteem, contributing to depressive symptoms. In our study, we were unable to examine this latter potential determinant of the depression-obesity relationship.

Our study has several strengths. First, our assessment of depressive symptoms, BMI, and waist circumference were performed using standardized questionnaires and measurement methods, respectively. Second, we are one of the few studies to examine the continuous, graded association between depressive symptoms and BMI and waist circumference. Finally, we were able to adjust for prevalent diabetes and CHD, two chronic diseases known to be associated with depressive symptoms and obesity, resulting in less confounding of our observed association.

Several limitations should be kept in mind in interpreting our data. First, our study is cross-sectional and not longitudinal, which limits our ability to establish a temporal relationship or to infer causality from our analysis. Second, the CES-D measures depressive symptoms but is not designed to measure clinical depression; rather, it is a self-report of symptoms over the past week and cannot be used to make a psychiatric diagnosis of depression. CES-D, however, is an efficient and valid tool for epidemiological studies [39] and is commonly used to assess mild-to-moderate depression and dysthymia in epidemiological studies conducted in the United States [40]. Third, we lacked data on dietary intake and on a reliable measure of

endogenous subclinical hypercortisolism and were thus unable to examine these factors as potential mediators in the depressive symptom-adiposity association. Fourth, the average BMI of our study participants was in the overweight range, which may limit conclusions that can be drawn about the relation between depressive symptoms and obesity. Finally, we did not have a more direct measure of visceral fat, such as an abdominal CT assessment. This is an important limitation because BMI in an elderly population may not adequately reflect body composition or metabolic risk. Aging is associated with an increase in fat mass, particularly visceral adiposity, and a decrease in lean muscle mass [41]. Therefore older individuals will have more visceral fat at the same BMI than younger individuals, leading to an underestimate of weight-related risk [41]. In contrast, height loss associated with aging may lead to an overestimation of BMI and metabolic risk [41]. Overall, however, BMI and waist circumference are still associated with adverse metabolic outcomes in the elderly [41].

In conclusion, future longitudinal studies are needed to further define the temporal relation between depressive symptoms and adiposity, particularly in determining whether depressive symptoms are a risk factor for increased adiposity and weight gain in older men and women. These studies should incorporate measures of cortisol production, inflammatory markers, as well as psychological measures to further elucidate the mechanisms linking depressive symptoms with obesity. Finally, intervention studies are needed to determine whether treatment of depressed mood might be an adjunctive therapy for weight loss in individuals with elevated depressive symptoms given the growing public health burden of obesity and its metabolic consequences in our aging population.

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CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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ABBREVIATIONS

ARIC = Atherosclerosis Risk in Communities Study

BMI = Body mass index

CES-D = Center for Epidemiological Studies Depression scale

CHD = Coronary heart disease

CRP = C-reactive protein

HPA = Hypothalamic-pituitary-adrenal

MRI = Magnetic resonance imaging

WC = Waist circumference

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