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Obesity, composite dietary antioxidant index, and their interactive association with the risk of cardiometabolic multimorbidity in the elderly from a large national survey

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Abstract

Background Dietary antioxidants and obesity are considered significant targets for disease prevention in the elderly. However, a possible cardiometabolic multimorbidity (CMM) correlated to dietary antioxidants and obesity is unknown. This study aimed to examine the relationship between dietary antioxidants and obesity with CMM in the older population.

Methods We used data from the NHANES 2003–2018 cycles, including older adults aged 60 and above. Dietary antioxidant status was assessed using the CDAI, calculated from six micronutrients (vitamins A, C, E, selenium, zinc, and carotenoids), and obesity was classified based on BMI. We applied restricted cubic spline models to explore nonlinear associations and logistic regression to assess the associations between pro-oxidant diet, obesity, and CMM. The joint effects of pro-oxidant diet and obesity on CMM were evaluated using additive interaction indices: RERI, AP, and SI, to determine the synergistic impact of these factors. Subgroup analyses by age, sex, ethnicity, and hypertension status were also conducted to assess the synergistic effect of these factors within different population groups.

Results A total of 13,178 older adults (mean age 69.85 ± 0.10 years; 45.1% male) were included in this study. A pro-oxidant diet and obesity jointly increased CMM risk, with the Pro-oxidant diet & Obese group having the highest risk (adjusted OR 3.11, 95% CI: 2.39–4.04), indicating that their likelihood of CMM was more than three times higher compared to the reference group (Anti-oxidant diet & Non-Obese group). The Anti-oxidant diet & Obese group (adjusted OR 2.03, 95% CI: 1.59–2.59) and the Pro-oxidant diet & Non-Obese group (adjusted OR 1.33, 95% CI: 1.08–1.64) also showed elevated risks, although to a lesser extent. These findings suggest that both dietary factors and obesity independently contribute to CMM risk, but their combined effect is more pronounced. The interaction between a pro-oxidant diet and obesity was synergistic, with the RERI indicating a positive interaction (0.75, 95% CI: 0.21, 1.29), the AP showing 24% of the combined effect due to their interaction, and the SI indicating a synergistic effect greater than additive (SI 1.55, 95% CI: 1.11–2.16). Subgroup analyses showed stronger interactions in females, younger individuals, non-Hispanic Whites, and those with hypertension.

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Conclusions Obesity and a pro-oxidative diet are correlated with the occurrence of CMM; there exists an interaction between obesity and a pro-oxidative diet concerning the initiation and advancement of CMM. Subgroup studies revealed more pronounced interactions among females, younger adults, non-Hispanic Whites, and individuals with hypertension.

Keywords Obesity, CDAI, Cardiometabolic multimorbidity, The elderly, NHANES

Introduction

Increasingly, it is common for adults to have multiple coexisting conditions as the population develops. Following this, cardiometabolic diseases (CMD), which encompass diabetes, cardiovascular disease (CVD), and stroke, present an increasing obstacle in the elderly population [1, 2]. We classified a person as having cardiometabolic multimorbidity (CMM) if they exhibited two or more CMDs [3, 4]. The risk factors for cardiometabolic multimorbidity are not well understood as clinical trials typically exclude patients with comorbidities and observational studies usually concentrate on singular disease outcomes [5, 6]. People with cardiometabolic diseases are living longer and are at a higher risk of developing one or more of these conditions during their lifetime due to improved management of CVD and diabetes and the increasing life expectancy. Increased mortality and adverse health outcomes are significantly associated with cardiometabolic multimorbidity (CMM), which is present in nearly one-third of older individuals [1, 7]. It underscores the substantial public health burden imposed by these conditions and identifies oxidative stress as a pivotal biological mechanism linking them. Oxidative stress, which arises from an imbalance between reactive oxygen species (ROS) and antioxidant defenses, plays a critical role in chronic inflammation, endothelial dysfunction, and insulin resistance—conditions that are further exacerbated by obesity. Adipose tissue, especially visceral fat, not only amplifies ROS production but also increases the secretion of pro-inflammatory cytokines, thereby perpetuating metabolic dysfunction and accelerating the progression of multimorbidity. Although there is established evidence connecting oxidative stress, obesity, and individual cardiometabolic diseases, research exploring their combined effects on multimorbidity remains limited. This study aims to bridge this gap by elucidating the mechanisms through which oxidative stress and obesity contribute to cardiometabolic multimorbidity, with the ultimate goal of identifying targeted interventions and enhancing health outcomes for at-risk populations.

It is widely recognized that obesity is a metabolism and endocrine disorder that is attributed to a variety of chronic conditions, such as diabetes [8], cardiovascular disease, and stroke [9]. CMM was defined as the presence of two or more of the conditions described above. Obesity is on the rise, with an anticipated 60% of the global population being obese or overweight by 2030 [10]. Type 2 diabetes [11] is associated with obesity, notably abdominal fat, as a result of changes in adipose tissue biology. Even in individuals who do not satisfy the BMI criteria, abdominal adiposity is an independent risk factor for elevated fasting glucose. A 26-year follow-up of individuals in the Framingham Heart Study [12] has consistently demonstrated that obesity is an independent risk factor for cardiovascular disease. Moreover, prior research indicates that diabetes and cardiovascular disease are allelic conditions. It also signifies that obesity is intricately linked to diabetes and cardiovascular disease. According to recent fundamental research [13], the degree of insulin resistance mediates the correlation between obesity and cardiovascular disease (CVD), suggesting that effective management of insulin resistance could potentially lessen the impact of obesity on CVD. According to a Mendelian Randomization study [14], abdominal obesity is a contributing factor to cerebrovascular illness, which includes a three-quarters increase in stroke incidence. This association is partially independent of high blood pressure and entirely independent of blood glucose levels. There is a pool of analysis in the USA and Europe [1] showing that the severe BMI can aggravate the risk of CMM by tenfold. A prospective study conducted in China [15] recently discovered that the risk of CMD can be elevated by a history of obesity, even in the absence of current overweight.

Not only that, the aging process is exacerbated by a variety of lifestyle behaviors, including smoking, sedentary lifestyles, and unhealthy diet, which in turn affect CMM. The Composite Dietary Antioxidant Index (CDAI) evaluates an individual's antioxidant capability [16]. The Composite Dietary Antioxidant Index (CDAI) is preferred over other dietary assessment tools, such as the Dietary Inflammatory Index (DII), because it specifically quantifies the antioxidant content of a diet. This makes it particularly relevant to studies focusing on oxidative stress and related health outcomes. The CDAI integrates the intake of various dietary antioxidants, including vitamins A, C, E, selenium, and zinc, thereby providing a comprehensive measure of antioxidant capacity. In contrast, the DII evaluates the inflammatory potential of a diet, which is less pertinent to

research centered on antioxidants. The selection of the CDAI aligns with the study's specific research objectives and questions. It assesses six specific antioxidants: vitamins A, C, and E, carotenoids, selenium, and zinc. Elevated CDAI values signify a diet rich in antioxidants. Recent studies have associated CDAI with chronic conditions such as diabetes [17], coronary heart disease [16], and stroke [18]. Oxidative stress, a physiological condition, arises from an imbalance in the REDOX state, leading to the overproduction of reactive oxygen species (ROS) [19]. Augmented antioxidant consumption may alleviate oxidative stress, indicating that patients' CMM can be reduced with modifications to their diets. The complementary impacts of CDAI and CMM have yet to be investigated.

A recent study [20] identified an adverse impact between CDAI and sarcopenic obesity (SO), presumably considering the strong association between obesity and oxidative stress. This suggests a potential combined effect of obesity and CDAI on the risk of CMM; however, no study has specifically examined this relationship to date. Consequently, our research sought to elucidate the correlation between the presence of obesity and CDAI and the risk of CMM in an aged demographic. Additionally, we aimed to clarify how an antioxidant-rich diet might mitigate the effects of obesity on the risk of CMM in elderly individuals, though its combined effects and interactions. It possesses a specific reference value for diminishing CMM in aged, obese individuals.

Methods

Study population

NHANES is a continuously conducted, multistage, complex sampling survey, and the data are publicly accessible on the CDC website in the United States. This survey was approved by the Research Ethics Review Board of the National Center for Health Statistics. At the beginning of the study, all survey participants gave informed consent. In this analysis, we initially included older adults aged 60 and over from the NHANES cycles between 2003 and 2018 ($n=15,381$). Subsequently, we excluded individuals with missing dietary intake data ($n=1,914$) and those with missing body mass index (BMI) data ($n=1,169$). Finally, after excluding individuals with missing covariate data ($n=13$), a total of 13,178 older adults were included in the final analysis (Fig. 1).

CDAI assessment

CDAI assessment in NHANES was conducted using two 24-h dietary recall interviews. The 24-h dietary recall method was used to capture all foods and beverages consumed by participants over the past 24 h, including detailed information on portion sizes and preparation methods. The initial interview was performed in person at the MEC, while the subsequent interview was carried out via telephone follow-up. The dietary micronutrient

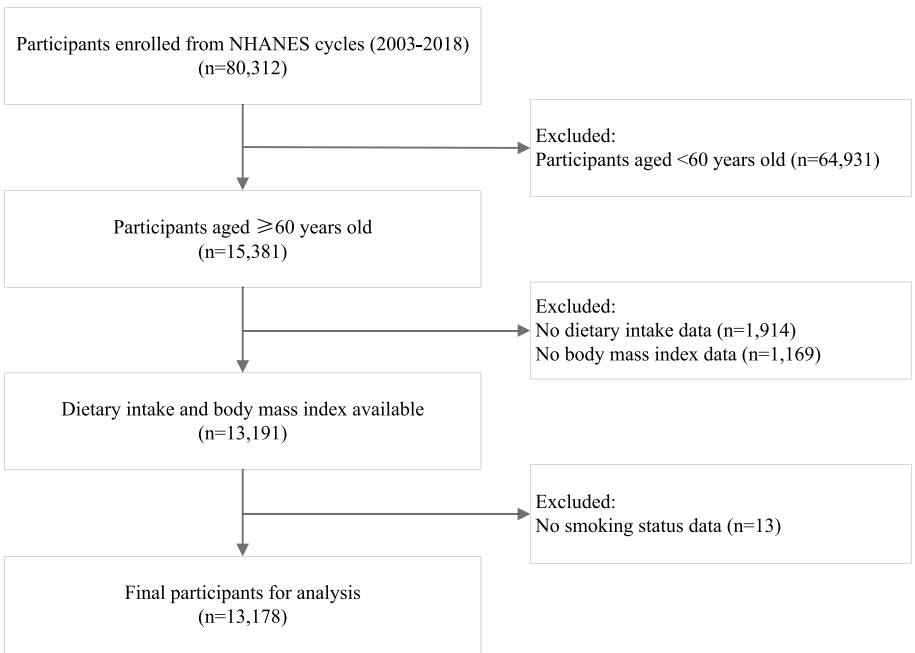

Fig. 1 Flowchart of study sample selection

intake was assessed using the University of Texas Food Intake Analysis System and the United States Department of Agriculture's Survey Nutrient Database. If data from both recalls were available, the average micronutrient intake was utilized; otherwise, the value from the single available recall was adopted. The estimates of dietary micronutrients did not account for any nutrients derived from dietary supplements or medications. The six dietary antioxidant micronutrients used in this study include vitamins A, C, E, selenium, zinc, and total carotenoids. The CDAI was calculated by standardizing each micronutrient by subtracting the mean and dividing by the standard deviation, then summing the six standardized scores as previous described [21, 22]. In this study, a CDAI score at or below the median was defined as a pro-oxidant diet, whereas a score above the median is defined as an antioxidant diet.

BMI measurement

Anthropometric measurements, including height (m) and weight (kg), were conducted by trained examiners at the Mobile Examination Center (MEC). BMI was calculated by dividing weight by the square of height (kg/m^2). According to the WHO Global Obesity Prevention Guidelines, a BMI at or above 30 kg/m^2 was defined as obesity.

Potential covariates

Based on prior knowledge, our study considered socio-demographic and health-related factors. Socio-demographic characteristics included age, sex, ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American/Hispanic, and other), educational attainment (below high school, high school and above), and marital status (married/with a partner, widowed/divorced/separated, single). Health-related factors included smoking status (never, ever, now), physical activity (inactive, defined as <150 METs per week; active, defined as ≥ 150 METs per week), and hypertension.

Statistical analysis

Given the complex sampling methodology of NHANES, all statistical analyses in this study accounted for survey weights. To evaluate the influence of various CDAI/obesity categories on CMM, participants were categorized into four distinct groups: Anti-oxidant diet & Non-Obese, Pro-oxidant diet & Non-Obese, Anti-oxidant diet & Obese, and Pro-oxidant diet & Obese. We employed one-way ANOVA and Rao-Scott chi-square tests to examine variations in socio-demographic and health-related characteristics among these groups. Quantitative data were reported as weighted means along with standard errors, whereas categorical variables were described using counts and weighted percentages. Initially, restricted cubic spline models were applied to investigate the nonlinear relationships between CDAI scores, obesity metrics, and CMM. Subsequently, logistic regression models were used to analyze the separate associations of a pro-oxidant diet and obesity with CMM, presenting results as odds ratios (ORs) and 95% confidence intervals (CIs). Additionally, to account for the potential influence of total energy intake on the relationship between a pro-oxidant diet and CMM, we used the residual method to adjust for total energy intake in the sensitivity analysis, allowing for a reliable adjustment while minimizing the risk of over-adjustment. Furthermore, we explored the combined effects of a pro-oxidant diet and obesity on CMM and evaluated the additive interaction between these two factors. We evaluated three indices of additive interaction: relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (SI). Additive interaction was considered significant if the 95% CI for RERI or AP did not include 0, or if the 95% CI for SI did not encompass 1. Additionally, we further assessed the impact of the interaction between a Pro-oxidant diet and obesity on CMM within different subgroups defined by age, sex, ethnicity, and hypertension status. Finally, we conducted a sensitivity analysis by defining obesity based on waist circumference measurements and explored its interaction with a Pro-oxidant diet on CMM to ensure the stability and reliability of our findings. In all analyses, adjustments were made for age, sex, ethnicity, marital status, education, smoking habits, physical activity, and hypertension in the fully adjusted model. All statistical analyses were conducted using R version 4.0.3, with a significance level set at 0.05.

Results

A total of 13,178 participants (mean age 69.85 ± 0.10 years; 45.1% male) were included in this study. Participant characteristics based on CDAI/obesity categories are presented in Table 1. The Pro-oxidant diet/Non-Obese group had the highest age, the lowest proportion of high school and above education, the lowest proportion of married/with a partner, and the highest proportion of current smokers. The Pro-oxidant diet/Obese group had the lowest proportion of males, the highest proportion of non-Hispanic Black participants, the lowest level of physical activity, and the highest prevalence of hypertension. The prevalence of diabetes, CVD, stroke, and CMM across groups is shown in Fig. 2. Among all groups, the Pro-oxidant diet/Obese group had the highest prevalence rates of diabetes, CVD, stroke, and CMM.

The restricted cubic spline analysis, adjusted for all potential confounders, revealed the associations of BMI

Table 1 Study population baseline characteristics (NHANES 2003–2018, $n = 13,178$)

Characteristics	Anti-oxidant diet /Non-Obese ($n = 4,190$)	Pro-oxidant diet /Non-Obese ($n = 4,028$)	Anti-oxidant diet / Obese ($n = 2,400$)	Pro-oxidant diet / Obese ($n = 2,560$)	*P* value
Weighted number	17,607,867	13,713,927	10,213,257	8,725,218	
Age (years)	69.93 ± 0.17	71.21 ± 0.18	68.38 ± 0.18	69.24 ± 0.21	< 0.001
Sex, n (%)					< 0.001
Female	1666 (45.7)	2213 (64.6)	1086 (46.3)	1669 (68.2)	
Male	2524 (54.3)	1815 (35.4)	1314 (53.7)	891 (31.8)	
Ethnicity, n (%)					< 0.001
Non-Hispanic White	2447 (82.8)	1931 (75.5)	1298 (83.2)	1092 (73.2)	
Non-Hispanic Black	623 (5.4)	827 (9.5)	517 (7.9)	704 (13.8)	
Mexican American/Hispanic	290 (2.5)	373 (4.1)	182 (2.7)	258 (4.0)	
Other	830 (9.3)	897 (10.9)	403 (6.2)	506 (9.0)	
Education, n (%)					< 0.001
Less than high school	966 (13.7)	1585 (26.7)	587 (14.7)	1013 (25.0)	
High school and above	3224 (86.3)	2443 (73.3)	1813 (85.3)	1547 (75.0)	
Marital status, n (%)					< 0.001
Married/with a partner	2668 (69.7)	2163 (57.2)	1462 (65.6)	1336 (58.3)	
Widowed/divorced/separated	1339 (27.2)	1667 (39.1)	826 (30.8)	1069 (37.0)	
Single	183 (3.1)	198 (3.7)	112 (3.6)	155 (4.7)	
Smoking status, n (%)					< 0.001
Never	1993 (48.7)	1925 (49.7)	1091 (44.7)	1340 (51.0)	
Ever	1691 (41.0)	1401 (34.4)	1118 (48.2)	952 (38.5)	
Now	506 (10.3)	702 (15.9)	191 (7.1)	268 (10.5)	
Physical activity, n (%)					< 0.001
Inactive	2439 (53.0)	2766 (64.5)	1507 (59.5)	1791 (67.8)	
Active	1751 (47.0)	1262 (35.5)	893 (40.5)	769 (32.2)	
Hypertension, n (%)					< 0.001
Absence	2019 (51.8)	1724 (45.2)	720 (32.3)	726 (28.3)	
Presence	2171 (48.2)	2304 (54.8)	1680 (67.7)	1834 (71.7)	

All continuous variables were presented as weighted mean and SE, All categorical variables were expressed as non-weighted numbers and weighted percentages

and CDAI with CMM (Fig. 3). For BMI, the overall positive association with CMM was statistically significant (P for overall < 0.001), while no evidence of nonlinearity was observed (P for nonlinear = 0.118). Similarly, for CDAI, the overall negative association with CMM was significant (P for overall < 0.001), and the relationship was predominantly linear (P for nonlinear = 0.082). Adjusted for confounding factors, participants with a pro-oxidant diet had a 1.44 times higher risk of CMM compared to those with an anti-oxidant diet (95% CI 1.23–1.68) (Table 2). Sensitivity analysis results indicate that, after using the residual method adjusting total energy intake, the pro-oxidant diet still had a 1.33 times higher risk of CMM (95% CI 1.13–1.57) (Supplement Table 1). Obese participants had a 2.19 times higher risk of CMM compared to non-obese participants (95% CI 1.81–2.64) (Table 2).

We further evaluated the combined effects of pro-oxidant diet and obesity on the risk of CMM (Table 3). Compared with the Anti-oxidant diet & Non-Obese group (reference), the Pro-oxidant diet & Obese group had the highest risk of CMM (adjusted OR 3.11, 95% CI 2.39–4.04). This was followed by the Anti-oxidant diet & Obese group (adjusted OR 2.03, 95% CI 1.59–2.59) and the Pro-oxidant diet & Non-Obese group (adjusted OR 1.33, 95% CI 1.08–1.64). The additive interaction between a pro-oxidant diet and obesity on CMM risk was evaluated using three metrics (Table 3 and Fig. 4). The RERI was 0.75 (95% CI: 0.21, 1.29), indicating a synergistic interaction between the two factors. The AP was 0.24 (95% CI: 0.09, 0.39), indicating that 24% of the combined impact of a pro-oxidant diet and obesity on CMM risk was due to their interaction. Additionally, the SI was 1.55 (95% CI: 1.11, 2.16), indicating a synergistic effect greater than additive between the two factors.

Sex-specific subgroup analysis (Table 4) demonstrates that the interaction between obesity and dietary antioxidant status had a stronger effect on CMM risk in females, with all three interaction measures statistically significant

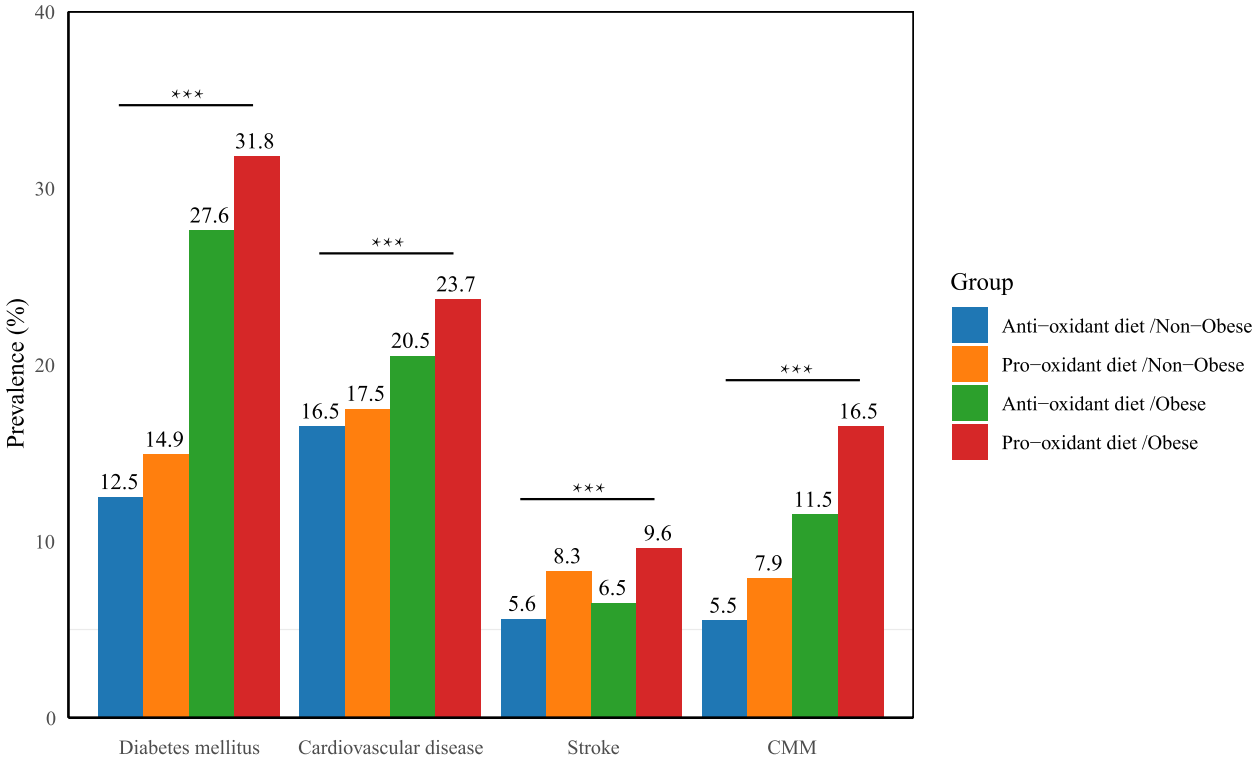

Fig. 2 Comparison of CMM and its component across obesity/CDAI categories

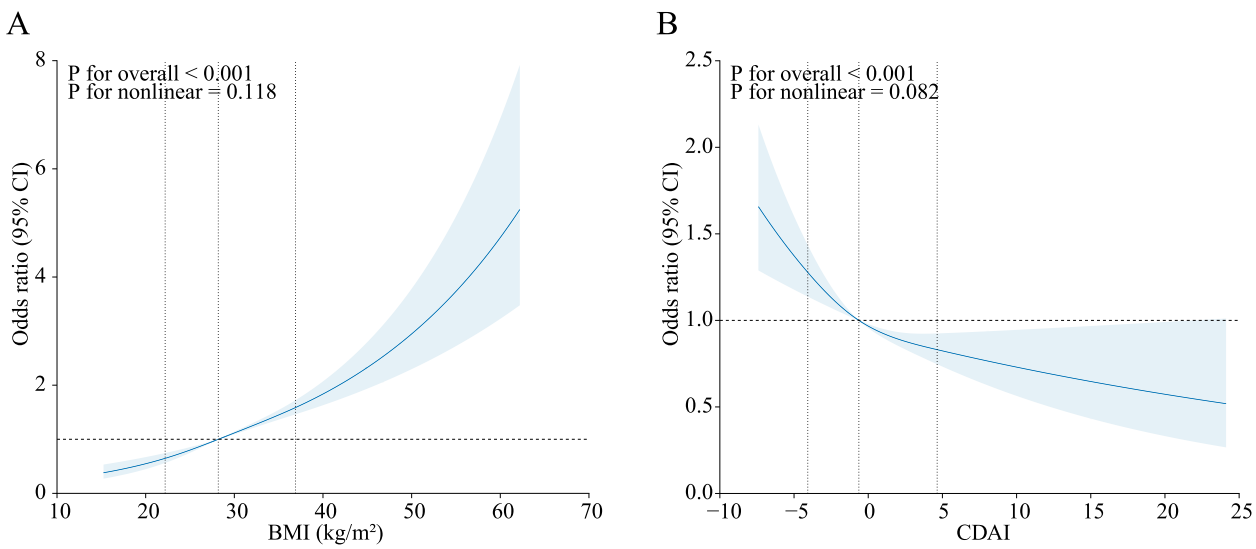

Fig. 3 Associations of obesity and CDAI with CMM risk using restricted cubic splines

(RERI (95% CI): 1.14 (0.10, 2.18); AP (95% CI): 0.26 (0.06, 0.46); SI (95% CI): 1.50 (1.02, 2.22)). In males, the effect was less robust, with only SI significant (SI (95% CI): 1.55 (0.82, 2.92)).

Age-specific subgroup analysis (Table 5) reveals that the interaction between obesity and dietary antioxidant status had a stronger effect on CMM risk in the younger group (Age < 75), with all three interaction measures statistically significant (RERI (95% CI): 1.15 (0.40, 1.90); AP (95% CI): 0.34 (0.16, 0.52); SI (95% CI): 1.93 (1.16, 3.20)). In the older group (Age ≥ 75), the effect was less

Table 2 Separate associations of obesity and CDAI with CMM risk

CDAI	Anti-oxidant diet	Pro-oxidant diet	*P* Value
Unadjusted OR (95%CI)	Ref	1.51(1.29, 1.76)	< 0.001
Adjusted OR (95%CI)			
Model 1[a]	Ref	1.60(1.37, 1.87)	< 0.001
Model 2[b]	Ref	1.44(1.23, 1.68)	< 0.001
Obesity	Non-obese	Obese	*P* Value
Unadjusted OR (95%CI)	Ref	2.28(1.92, 2.70)	< 0.001
Adjusted OR (95%CI)			
Model 1[a]	Ref	2.55(2.15, 3.03)	< 0.001
Model 2[b]	Ref	2.19(1.81, 2.64)	< 0.001

Obesity was defined as BMI ≥ 30 kg/m^2. Pro-oxidant diet was defined as below the median of CDAI score

CI confidence interval, *OR* odds ratio, *CDAI* Composite Dietary Antioxidant Index

[a] *p* vaule after adjustment for age and sex

[b] *p* vaule after adjustment for age, sex, ethnicity, marital status, education, smoking, physical activity, hypertension

pronounced, with only SI significant (SI (95% CI): 0.93 (0.56, 1.52)).

Ethnic-specific subgroup analysis (Supplement Table 2) indicates that the interaction between obesity and dietary antioxidant status had the strongest effect in the non-Hispanic White group, with all three interaction measures statistically significant (RERI (95% CI): 1.08 (0.37, 1.79); AP (95% CI): 0.31 (0.16, 0.47); SI (95% CI): 1.80 (1.22, 2.65)). In the non-Hispanic Black group, the effect was less robust, with only SI significant (SI (95% CI): 1.10 (0.55, 2.20)). In the others group, the interaction was weakest, with neither RERI nor AP significant, and SI had a weaker association (SI (95% CI): 1.06 (0.39, 2.86)).

Hypertension-specific subgroup analysis (Supplement Table 3) shows that the interaction between obesity and dietary antioxidant status had a more pronounced effect in the hypertension group, with all three interaction measures statistically significant (RERI (95% CI): 0.74 (0.11, 1.38); AP (95% CI): 0.23 (0.06, 0.40); SI (95% CI): 1.51 (1.04, 2.17)). In the non-hypertension group ($n = 5,189$), the interaction was weaker, with only SI significant (SI (95% CI): 1.72 (0.59, 5.01)).

We performed a sensitivity analysis using waist circumference as the metric for defining obesity and investigated its interaction with a pro-oxidant diet on CMM (Supplement Table 4). When compared to the Anti-oxidant diet and Non-Obese group (used as a reference), the Pro-oxidant diet & Obese group exhibited the highest risk for CMM, with an adjusted OR of 3.18 (95% CI: 2.39–4.23). Next in line were the Anti-oxidant diet & Obese group, showing an adjusted OR of 1.99 (95% CI: 1.54–2.59), followed by the Pro-oxidant diet & Non-Obese group, which had an adjusted OR of 1.34 (95% CI: 1.08–1.67). The interaction effect remained consistent with the initial analysis, as all three interaction metrics achieved statistical significance. Specifically, the relative excess risk due to interaction (RERI) was 0.84 (95% CI: 0.27, 1.42), the attributable proportion due to interaction (AP) was 0.26 (95% CI: 0.12, 0.41), and the synergy index (SI) was 1.63 (95% CI: 1.16, 2.29).

Discussion

Our research involved 13,178 elderly individuals to investigate the combined impacts of a pro-oxidant diet and obesity on the risk of CMM. Both the pro-oxidant diet and the obese group had the highest risk by more than three times, followed by the obese-only group and the pro-oxidant diet-only group. The RERI indicated a positive interaction (0.75, 95% CI: 0.21, 1.29), the AP showed 24% of the combined impact due to their interaction, and the SI attributed a collaborative effect higher than additive (SI 1.55, 95% CI: 1.11–2.16). The interaction between a pro-oxidant diet and obesity was synergistic. Subgroup analyses revealed that the interaction effect was still significant among women, younger elderly individuals,

Table 3 Joint and interactive effects of obesity and CDAI on the risk of CMM

Group	Unadjusted OR (95%CI)	*P* Value	Model 1[a] OR (95%CI)	*P* Value	Model 2[b] OR (95%CI)	*P* Value
Anti-oxidant diet & Non-Obese	Ref		Ref		Ref	
Pro-oxidant diet & Non-Obese	1.47(1.21, 1.78)	< 0.001	1.53(1.25, 1.87)	< 0.001	1.33(1.08, 1.64)	0.008
Anti-oxidant diet & Obese	2.23(1.78, 2.80)	< 0.001	2.45(1.95, 3.09)	< 0.001	2.03(1.59, 2.59)	< 0.001
Pro-oxidant diet & Obese	3.36(2.64, 4.29)	< 0.001	4.01(3.12, 5.14)	< 0.001	3.11(2.39, 4.04)	< 0.001
Addictive interaction						
RERI (95% CI)	0.67(0.08, 1.26)		1.02(0.32, 1.73)		0.75(0.21, 1.29)	
AP (95% CI)	0.20(0.04, 0.35)		0.26(0.11, 0.40)		0.24(0.09, 0.39)	
SI (95% CI)	1.40(1.04, 1.88)		1.51(1.15, 2.00)		1.55(1.11, 2.16)	

Obesity was defined as BMI ≥ 30 kg/m^2. Pro-oxidant diet was defined as below the median of CDAI score

CI confidence interval, *OR* odds ratio, *CDAI* Composite Dietary Antioxidant Index

[a] *p* vaule after adjustment for age and sex

[b] *p* vaule after adjustment for age, sex, ethnicity, marital status, education, smoking, physical activity, hypertension

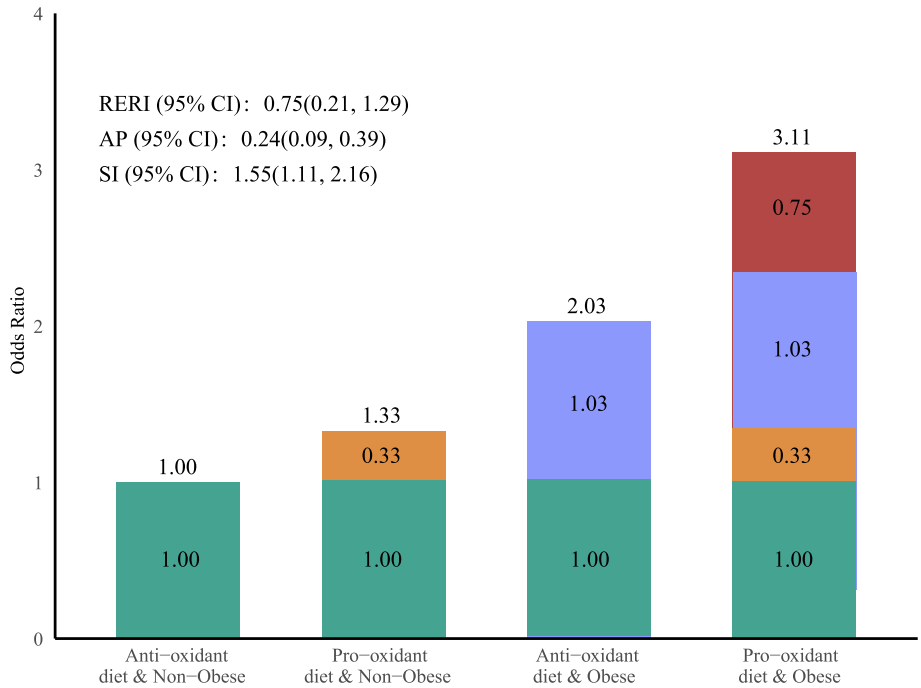

Fig. 4 Visualization of the interactive effects of obesity and CDAI on CMM risk

Table 4 Sex-specific associations of obesity and CDAI with CMM risk

Group	Female (*n* = 6,634)		Male (*n* = 6,544)	
	OR (95%CI)	*P* Value	OR (95%CI)	*P* Value
Anti-oxidant diet & Non-Obese	Ref		Ref	
Pro-oxidant diet & Non-Obese	1.94(1.36, 2.76)	< 0.001	1.00(0.74, 1.35)	0.988
Anti-oxidant diet & Obese	2.32(1.51, 3.56)	< 0.001	1.93(1.46, 2.56)	< 0.001
Pro-oxidant diet & Obese	4.40(2.89, 6.70)	< 0.001	2.45(1.74, 3.46)	< 0.001
Addictive interaction				
RERI (95% CI)	1.14(0.10, 2.18)		0.51(−0.21, 1.24)	
AP (95% CI)	0.26(0.06, 0.46)		0.21(−0.05, 0.47)	
SI (95% CI)	1.50(1.02, 2.22)		1.55(0.82, 2.92)	

Adjusted for age, ethnicity, marital status, education, smoking, physical activity, hypertension. Obesity was defined as BMI ≥ 30 kg/m^2. Pro-oxidant diet was defined as below the median of CDAI score

CI confidence interval, *OR* odds ratio, *CDAI* Composite Dietary Antioxidant Index

non-Hispanic White participants, and those with hypertension. This study confirmed that obesity elevates the risk of CMM and that a low CDAI score, indicative of a pro-oxidant diet, is positively correlated with the risk of CMM. The study identified that the coexistence of obesity and a poor CDAI score may be associated with an increased risk of CMM and a synergistic impact.

Recent studies [15] underscore the significance of obesity, revealing that a history of obesity correlates with an elevated risk of cardiometabolic diseases (CMD), even in the absence of present abnormal BMI. "Epigenetic memory," which sustains the proinflammatory phenotype in adipose tissue macrophages after weight loss, could potentially trigger the onset of CMD by promoting systemic inflammation [23]. Moreover, prior research [24] indicates that moderate weight reduction effectively enhances insulin sensitivity and correlates with a decreased risk of cardiometabolic disorders in overweight or obese individuals. Additionally, a review [25] determined that the treatment of obesity may mitigate the risk of cardiovascular disease by decreasing chronic inflammation. In other words, chronic inflammation in

Table 5 Age-specific associations of obesity and CDAI with CMM risk

Group	Age < 75 (*n* = 8,938)		Age ≥ 75 (*n* = 4,240)	
	OR (95%CI)	*P* Value	OR (95%CI)	*P* Value
Anti-oxidant diet & Non-Obese	Ref		Ref	
Pro-oxidant diet & Non-Obese	1.41(1.03, 1.93)	0.033	1.23(0.94, 1.62)	0.137
Anti-oxidant diet & Obese	1.82(1.31, 2.53)	< 0.001	2.27(1.62, 3.19)	< 0.001
Pro-oxidant diet & Obese	3.39(2.41, 4.76)	< 0.001	2.39(1.69, 3.39)	< 0.001
Addictive interaction				
RERI (95% CI)	1.15(0.40, 1.90)		−0.11(−0.84, 0.62)	
AP (95% CI)	0.34(0.16, 0.52)		−0.05(−0.36, 0.26)	
SI (95% CI)	1.93(1.16, 3.20)		0.93(0.56, 1.52)	

Adjusted for sex, ethnicity, marital status, education, smoking, physical activity, hypertension. Obesity was defined as BMI ≥ 30 kg/m^2. Pro-oxidant diet was defined as below the median of CDAI score

CI confidence interval, *OR* odds ratio, *CDAI* Composite Dietary Antioxidant Index

obesity significantly correlates with the risk of cardiovascular disease. Both diabetes mellitus (DM) and cardiovascular disease (CVD) are components of CMM, thereby indicating a strong correlation between obesity and CMM. Our research indicated that obesity alone could more than double the incidence of CMM in older individuals. Furthermore, current research [26] indicates that older individuals in rural China exhibit diverse food patterns and that healthy dietary practices can markedly diminish the risk of CMM. This also demonstrates that dietary variables are significantly associated with the risk of CMM in the older population.

Moreover, recent studies [27] indicate that an antioxidant-rich diet can mitigate the risk of cardiovascular disease under oxidative stress. A prospective study [28] indicates that the nutritional status of food is strongly correlated with the risk of CMM in older men in the United Kingdom. The aforementioned data indicate a strong correlation between nutrition and the risk of CMM in the older population. A study conducted in Rotterdam [29] confirmed that a diet high in antioxidants could reduce oxidative stress-induced type 2 diabetes, thereby lowering plasma glucose levels and insulin resistance. Research [30] has demonstrated that oxidative stress is a factor in the development of cancer, cardiovascular disease, diabetes, and even ageing. The term "oxidative stress" refers to the physiological levels of oxygen/nitrogen free radicals and non-free radical reactive substances, which are collectively referred to as ROS/RNS. However, the same disease pathway, oxidative stress, is shared by numerous chronic diseases, which can be the result of overreacting. The elderly are able to combat these chronic diseases and even ageing by attenuating oxidative stress through the consumption of dietary antioxidants. The consumption of antioxidants may be beneficial in the reduction of abdominal obesity in patients with diabetes, as previous research [31] has demonstrated that oxidative stress contributes to the pathological mechanism of obesity. This implies that it is logical to conclude that the elderly's CMM is influenced by adiposity and consumption of antioxidants.

Nevertheless, there is a limited number of studies examining the combined impact of obesity and a pro-oxidative diet on the incidence of CMM. The current study indicated that obesity and a pro-oxidative diet were linked to an increased risk of CMM. Additionally, a synergistic effect exists between obesity and a pro-oxidative diet. In addition, our study showed that the risk of CMM was significantly affected by both additive and multiplicative interactions between being overweight and eating a diet high in antioxidants. In this study of subgroups by gender, it was discovered that the risk of CMM was more significantly influenced by the interaction between the quantity of antioxidants in diets and obese status in women. The interaction was statistically significant in all three measures (RERI (95% CI): 1.14 (0.10–2.218), AP (95% CI): 0.26 (0.06–0.46), and SI (95% CI): 1.50 (1.02–2.22). It may be due to the estrogen levels in females, which are associated with insulin resistance that has a more significant effect on obesity. It may elucidate the reason why this female subgroup is at a higher risk of CMM than males, although the molecular mechanism necessitates further investigation. In the age group under 75 years old, our research revealed a more robust interaction between obesity and dietary pro-oxidants in terms of the risk of CMM. It may be attributed to the elderly population, which is over 75 years old and may experience a higher incidence of CMDs due to aging genetic factors or other factors rather than dietary antioxidants and obesity. This indicated that it may be advantageous to conduct a screening of elderly individuals for obesity and dietary pro-oxidants prior to the age of 75. We also

found that there was a stronger interaction of dietary pro-oxidants and obesity with CMM risk in the non-Hispanic White group. It's interesting to note that the collaborative influence of dietary pro-oxidants and adiposity significantly increased the risk of CMM in the hypertension-specific subgroup compared to the non-hypertension group. This could potentially be attributed to the potential for hypertension to cause vascular damage, thereby increasing the risk of CMDs and ultimately CMMs. Hormonal factors, such as decreased estrogen levels, and higher rates of comorbidities, particularly autoimmune diseases, may explain the more pronounced interaction effects observed in women. Younger older adults may exhibit more pronounced effects due to their greater physiological resilience or because they are at a critical juncture in the aging process, which aligns with frameworks such as "compression of morbidity" and "resilience of aging". Socioeconomic advantages among non-Hispanic whites, including better access to healthcare and potential genetic factors, likely contribute to the observed patterns. According to the Vascular Hypothesis of Cognitive Aging and Multifactorial Models of Aging, hypertension exacerbates interactions via vascular mechanisms, such as reduced cerebral blood flow. To enhance understanding, it is important to explore how mechanisms (e.g., hormonal changes, socioeconomic factors) interact across subgroups and propose a biopsychosocial model of aging to integrate biological, psychological, and social factors. Future research should include longitudinal and mechanistic studies to clarify underlying pathways and intersectional impacts, thereby advancing the field's understanding of these complex interactions.

Additionally, potential mechanisms exist that could facilitate an interaction between obesity and a pro-oxidative diet in the development of CMM. The occurrence of CMM may be influenced by shared pathways between obesity and a pro-oxidative diet. Oxidative stress is supposed to be the underlying mechanism that leads to diabetes [17]. Nevertheless, research has demonstrated that the consumption of antioxidant nutrients, including selenium, magnesium, and zinc [32–34], can modulate inflammatory and oxidative cascades. Additionally, the combination of multiple antioxidants may have a synergistic effect, reducing oxidative stress and exerting antioxidant effects. Consequently, the risk of diabetes that is induced by oxidative stress may be mitigated by antioxidant nutrients. Our research indicates that the risk of CMM in elderly patients is significantly elevated by a pro-oxidative diet, whereas no study has examined the impact of an antioxidant diet on this risk. Moreover, researchers have consistently identified obesity as a significant pathogenic contributor to the onset of metabolic syndrome [35]. Animal experiments revealed higher levels of NADPH oxidase in adipose tissue, leading to the production of reactive oxygen species (ROS). Oxidative stress results in the aberrant proliferation of adipocytokines, including inflammatory markers such as adiponectin, plasma fibrinogen activator-1, IL-6, and monocyte chemoattractant protein-1. This indicates that obesity enhances oxidative stress and elevates inflammatory markers. These findings suggest that the risk of CMM in the elderly can be elevated by the combination of obesity and a pro-oxidative diet, and there is a certain theoretical foundation for this. Based on our findings, we highlight that programs incorporating dietary modifications, exercise regimens, and behavioral interventions, particularly those promoting an antioxidant-rich diet and structured weight loss, can benefit older adults. Notably, our findings suggest that these interventions may be especially beneficial among females, younger adults, non-Hispanic Whites, and individuals with hypertension.

This study is the first to employ an interaction analysis with the NHANES database and adhere to the development of CDAI as a direction for cardiometabolic comorbidities. We propose that the risk of developing CMM in obese patients may be mitigated by comprehending the interaction between obesity and elevated CDAI scores. Nevertheless, it is necessary to acknowledge certain constraints. Initially, more prospective clinical trials are required to further validate our findings and investigate the potential processes. However, a number of studies have employed self-reported knowledge of factors that are associated with the risk of CMM [36]. Secondly, this was a cross-sectional study, and it was unable to verify causal inference between obesity and CDAI scores and the risk of cardiometabolic comorbidities in the elderly. In addition, the inherent limitations of using a 24-h dietary recall method, where 2-day dietary datasets may not adequately represent habitual dietary patterns, could compromise the reliability of the CDAI score. Furthermore, it is crucial to recognize that the six micronutrient variables derived from these recalls serve as the foundation for calculating individual CDAI scores, which introduces additional limitations. Finally, due to data limitations, there are potential confounders that were not included in this study, which may have influenced the results and could lead to residual confounding. Future research should prioritize evaluating the effectiveness of both primary and secondary prevention strategies through long-term studies to identify optimal intervention methods. Additionally, more randomized controlled trials are essential. An individualized approach that incorporates genetic, metabolic, and lifestyle

factors could substantially enhance the efficacy of these interventions.

Conclusion

Obesity and a pro-oxidative diet are associated with the incidence of CMM; there is an interaction between obesity and a pro-oxidative diet regarding the onset and progression of CMM. We posit that comprehending the interplay between obesity and a pro-oxidative diet may influence the incidence of CMM in obese older individuals. The elevated risk of CMM associated with obesity may be mitigated by the future implementation of antioxidant dietary interventions for older individuals in community services.

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

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Authors' contributions
Conceptualization, Zhang H, Chen X, and Sun X; Data curation, Zhang H, Chen X, and Sun X; Formal Analysis, Zhang H; Investigation, Zhang H, Chen X, and Sun X; Methodology, Zhang H, Chen X, and Sun X; Project Administration, Resources & Software, Zhang H; Supervision, Zhang H, Dou B, Chen X, and Sun X; Validation, Zhang H, Dou B, Chen X, and Sun X; Visualization, Zhang H; Writing-Original Draft Preparation, Zhang H, Chen X, and Sun X; Writing-Review & Editing, Zhang H, Dou B, Chen X, and Sun X.

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Data availability
The analytical data presented in this manuscript are publicly accessible via the NHANES website (https://www.cdc.gov/nchs/nhanes/index.htm). Additionally, specific datasets utilized in this study can be obtained upon request from the corresponding author.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Ethics Review Board of the National Center for Health Statistics (https://www.cdc.gov/nchs/nhanes/irba98.htm). Written informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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