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Composite dietary antioxidant index is nonlinearly associated with low muscle mass in the general US population: findings from NHANES 2001–2018

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Abstract

Background Oxidative stress is a risk factor for the development of low muscle mass. The Composite Dietary Antioxidant Index (CDAI) is a recently developed tool for comprehensively assessing dietary antioxidant exposure. We aimed to explore the association of the CDAI with low muscle mass in the general U.S. population.

Methods The participants were individuals aged ≥ 20 years who completed the NHANES from 2001 to 2006 and 2011–2018. The CDAI was assessed by 24-h dietary recall, which integrated the dietary intake levels of vitamin A, vitamin C, vitamin E, zinc, selenium, and carotenoids. Low muscle mass was diagnosed by the Foundation for the National Institutes of Health (FNIH) criteria and defined as an appendicular lean mass/body mass index of < 0.789 in men or < 0.521 in women. Multivariate logistic regression analysis was used to explore the associations of the CDAI and its components with low muscle mass.

Results A total of 15,907 participants were included. The prevalence of low muscle mass was 7.985%. After adjusting for all confounders, the CDAI was found to be significantly associated with the odds of low muscle mass (odds ratio [OR] = 0.928, $p < 0.0001$). Compared with Q1, the CDAI values at Q2, Q3, and Q4 were significantly associated with a lower prevalence of low muscle mass (p for trend < 0.0001). Higher intake levels of individual CDAI components were associated with a lower prevalence of low muscle mass. Threshold effect analysis revealed that a CDAI ≤ -2.85 was not associated with the odds of low muscle mass ($p = 0.1564$), while a CDAI > -2.85 was negatively associated with low muscle mass (OR = 0.92, $p < 0.0001$). Physical activity, smoking, and alcohol consumption significantly moderated this association.

Conclusions Adherence to an antioxidant diet is associated with low muscle mass among the general U.S. adult population, especially among individuals who maintain a favourable lifestyle. These findings should be further validated in cohort studies.

Keywords Composite dietary antioxidant index, Oxidative stress, Sarcopenia, Dietary antioxidants, NHANES

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Introduction

Sarcopenia is a progressive systemic skeletal muscle disease that is typically associated with ageing and is primarily characterized by significant loss of skeletal muscle mass and strength as well as diminished physical activity capacity [1, 2]. Additionally, sarcopenia can occur among younger individuals; its onset in this population may be related to other factors, such as medical conditions, physical inactivity, malnutrition, and perinatal factors [3]. Recent large meta-analyses have shown that the global prevalence of sarcopenia ranges from 10 to 27% among people aged ≥ 60 years and from 8 to 36% among people aged < 60 years; the variance in these prevalence rates were due to between-study differences in the definition of sarcopenia [4, 5]. Low muscle mass is a key characteristic of sarcopenia and is associated with a variety of adverse health outcomes, such as osteoporosis, cardiovascular disease (CVD), diabetes, and arthritis [6–8]. Accumulating evidence has suggested that low muscle mass is strongly associated with increased risks of fractures, falls, hospitalization, and all-cause mortality, thereby significantly reducing an individual's quality of life [9].

Oxidative stress is one of the important hallmarks of the pathogenesis and progression of low muscle mass. During the development of low muscle mass, elevated levels of oxidative stress can lead to premature skeletal muscle atrophy [10]. This stress is activated in the early stages of muscle atrophy and can be modulated by various factors. High levels of oxidative stress can cause damage to the mitochondria of myocytes, in turn leading to impaired myocyte function [11]. Scavenging mitochondrial peroxide effectively prevents mitochondrial dysfunction and is associated with the maintenance of muscle mass and strength in mice with sarcopenia [12]. Additionally, excess production of reactive oxygen species (ROS) may inhibit the activity of muscle stem cells, thereby impairing muscle regenerative capacity [13].

Oxidative stress occurs due to the imbalance between pro-oxidant and antioxidant effects in the body, and dietary antioxidant intake has been suggested to regulate oxidative homeostasis. The intake levels of certain dietary antioxidants may play protective roles against the development of sarcopenia [14, 15]. Sparse clinical evidence suggests that the intake levels of some antioxidant vitamins and minerals, such as dietary vitamin C [16], vitamin E [17], and selenium [18], may be associated with a reduced prevalence of low muscle mass; however, the findings have been inconsistent.

A comprehensive assessment of antioxidant intake is important for evaluating dietary antioxidant potential. To address this gap, Wright et al. [19] developed a global dietary antioxidant index, namely, the Composite Dietary Antioxidant Index (CDAI). The CDAI assesses the intake levels of various dietary antioxidant vitamins and minerals, thus reflecting an individual's overall dietary antioxidant exposure. Since the introduction of the CDAI, numerous observational studies have suggested that this index is associated with the development of a range of clinical conditions, such as CVD, metabolic disorders, and osteoporosis [20–22]. However, the association of the CDAI, as an overall indicator of dietary antioxidant intake, with the prevalence of low muscle mass in the general population remains unclear. Several observational studies have shown that the CDAI is associated with ageing and other ageing-related diseases, such as frailty, in the general population [23, 24].

To fill this gap in the current knowledge, we leveraged nationally representative data from the National Health and Nutrition Examination Survey (NHANES) to explore the associations of the CDAI and its components with the occurrence of low muscle mass in the general U.S. population. Uncovering the clinical relationship between the CDAI and low muscle mass may provide an opportunity to reduce the disease burden of low muscle mass in the general U.S. population by optimizing dietary structure and patterns and developing personalized antioxidant-rich dietary regimens.

Methods

Study design and population

The NHANES is a major survey administered by the National Center for Health and Statistics (NCHS) to provide nationally representative data regarding the health and nutritional status of noninstitutionalized populations. Since 1999, the NHANES has been conducted in a two-year survey cycle, with an annual sample of approximately 5,000 cases across the country. The NHANES consists of comprehensive standardized questionnaire interviews and data from a series of medical examinations, including physical examinations, laboratory tests, and other data. The NHANES is a series of ongoing and nationwide population-based cross-sectional surveys, and it is a complex, multistage, probability-sampling cluster design study. The NCHS Ethics Review Board approved all NHANES study protocols, and written informed consent was obtained from all the subjects. Our study used data from nine consecutive cycles of the NHANES from 2001 to 2018. Thus, in terms of study design, our study was a nationally representative, population-based, large cross-sectional study.

The study population selection flowchart is presented in Fig. 1. Briefly, we first included 70,665 participants from the 2001–2006 and 2011–2018 waves of the NHANES. The exclusion criteria were as follows: aged < 20 years (n = 32,617), missing DXA or DXA ineligible data (n = 17,537), missing CDAI data (n = 2662), or missing covariate information (n = 1942). Owing to the small proportion of missing values for each covariate

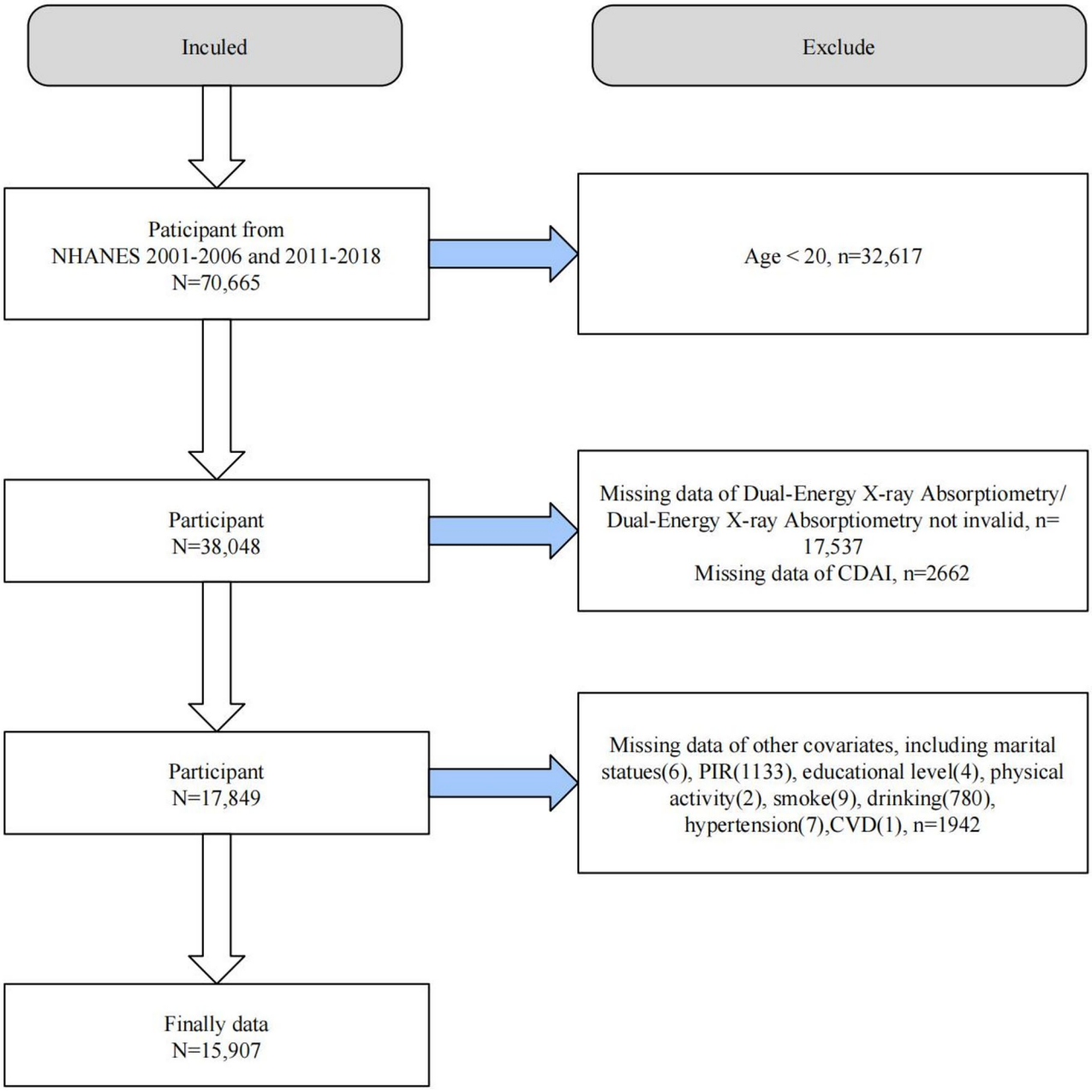

Fig. 1 Flowchart of study population selection, NHANES 2001–2006 and 2011–2018

compared with the total population, we applied complete case analysis to address missing covariates. Ultimately, we included data from 15,907 participants (age range: 20–85 years) for analysis.

Assessment of the CDAI

In the NHANES, the dietary intake data required to obtain the CDAI became available after the 2001–2002 cycle. We used the average intake levels from two 24-h dietary recalls (the first collected in person at a mobile examination centre and the second by telephone 3–10 days later) to reflect an individual's dietary intake. We obtained individual mean intake levels of the six antioxidants in the CDAI, including vitamin A, vitamin C, vitamin E, zinc, selenium, and carotenoids (excluding antioxidants consumed from dietary supplements, medications, or plain drinking water) [25]. The CDAI was calculated based on the validated methodology described in previous studies [25, 26], whereby the intake of each antioxidant was standardized (subtracting the total population mean from the intake of each antioxidant and dividing by the standard deviation), and then, all

the data were summed to obtain an individual's dietary antioxidant profile [22]. Specifically, the calculation of the CDAI consists of the following steps. (1) The intake of each antioxidant (vitamins A, C, and E, zinc, selenium, and carotenoids) was independently standardized. This step ensured that the intake of each antioxidant was converted to a unitless Z value reflecting the location of the distribution of individual intake relative to the total population. (2) The six standardized values were summed to obtain an individual's total CDAI. For example, if the intake of vitamin A in a participant was one standard deviation above the total population mean, its standardized value was + 1.0, and so on for the remaining antioxidants, with the final sum being the CDAI. The formula for calculating the CDAI was as follows:

$$CDAI = \sum_{n=1}^{6} \frac{x - mean}{SD}$$

where x represents an individual's intake of a particular dietary antioxidant, the mean represents the mean intake of that dietary antioxidant in the total population, and SD represents the standard deviation of the mean intake in the total population.

Assessment of sarcopenia

We adopted the diagnostic criteria from the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project to define sarcopenia in the adult population. The ratio of appendicular lean mass (ALM) to body mass index (BMI) was used to determine low muscle mass, which was diagnosed as < 0.789 in men or < 0.521 in women [27]. ALM was detected by dual-energy X-ray absorptiometry (DXA) and was used to assess muscle mass in individuals. Data for DXA to assess body composition were available in 1999–2006 and 2011–2018 waves of the NHANES. Notably, DXA data were only accessible for individuals aged 8–59 years in the 2011–2018 waves of the NHANES, whereas DXA data were accessible for all individual over 8 years of age in the 1999–2006 waves. According to the NHANES documented instructions, individuals who were not eligible for DXA because they were taller than 192.5 centimetres, weighed more than 136.4 kg, or were pregnant were excluded. Additionally, to verify the stability of the results, we conducted sensitivity analysis based on the diagnostic criteria for low muscle mass from the European Working Group on Sarcopenia in Older People. A skeletal muscle mass index (SMI) (defined as ASM/height squared) ≤ 7.26 kg/m^2 in males or ≤ 5.5 kg/m^2 in females was considered to indicate low muscle mass [28].

Covariates

We included multiple potential covariates, including age, sex (male or female), race/ethnicity (non-Hispanic White/Mexican American/non-Hispanic Black/other Hispanic/other race), educational attainment (less than high school/high school/greater than high school diploma), the household income poverty ratio, marital status (single or nonsingle), smoking (never/former/current smoker), drinking (never/former/current light/moderate/heavy drinkers), physical activity (no/moderate/vigorous), daily energy intake (kcal/d), diabetes (yes/no), hypertension (yes/no), and CVD (yes/no).

Smoking status was categorized according to participants' smoking history as follows: never smokers (< 100 lifetime cigarettes), former smokers (≥ 100 lifetime cigarettes but no current cigarettes), and current smokers (≥ 100 lifetime cigarettes and current cigarettes) [29]. Drinking status was categorized as follows: never drinkers (< 12 drinks in a lifetime), former drinkers (≥ 12 drinks in a lifetime or in a given year but no drinks in the last year), current light drinkers (≤ 2 drinks/d for men or ≤ 1 drink/d for women, or 1 day per month of binge drinking), moderate drinkers (≤ 3 drinks/d for men or ≤ 2 drinks/d for women, or 2–5 days per month of binge drinking), and heavy drinkers (≥ 4 drinks/d for men or ≥ 3 drinks/d for women, or ≥ 5 days per month of binge drinking) [30, 31]. Physical activity was categorized as no physical activity, moderate physical activity, or vigorous physical activity participation on the basis of self-reports from the Global Physical Activity Questionnaire [32]. Daily energy intake data were obtained via face-to-face dietary recall questionnaires. Diabetes was diagnosed by self-reported diabetes, biochemical testing, or the use of antidiabetic medications [33]. Hypertension was diagnosed on the basis of history of hypertension, a blood pressure test ≥ 140/90 mmHg, or taking antihypertensive medication [34]. CVD history was obtained through responses to questions on the medical condition questionnaire.

Statistical analysis

We weighed all analyses appropriately (1/7 * wtmec2 year) according to the NHANES Analytic Guidelines to account for the complex study design of NHANES. Data processing and analysis were performed using EmpowerStats (X&Y Solutions, Inc., Boston, MA) and R software (version 4.2.3). A two-sided P value of less than 0.05 was considered statistically significant. In this analysis, we grouped participants according to CDAI quartiles to explore differences in demographic, lifestyle, and other clinical characteristics between groups. Continuous variables are expressed as the means ± standard errors, and differences between groups were examined using weighted analysis of variance. Categorical variables

are expressed as numbers (percentages) and differences between groups were examined using weighted chi-square analysis. Additionally, we grouped the participants according to their muscle status. Weighed multivariate logistic regression models were used to explore the associations of the CDAI and its components with low muscle mass in the general population and to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs). We constructed three models with different levels of adjustment, where the crude model was not adjusted for any covariates; model 1 was adjusted for age, sex, race/ethnicity, education level, PIR, and marital status; and model 2 was further adjusted for smoking, alcohol consumption, physical activity, dietary energy intake, diabetes, hypertension, and CVD. Weighed restricted cubic spline (RCS) analysis was used to explore potential nonlinear or dose–response associations, which was performed using the rms package, and the number of knots was determined on the basis of p for nonlinear values. Weighed subgroup analyses were used to explore whether the association between the CDAI and the prevalence of low muscle mass in the general population remained stable across subgroups, whereas interaction analyses were used to identify potential moderators of this association. Finally, we performed weighted sensitivity analyses using another set of common diagnostic criteria for low muscle mass– SMI (ASM/height squared) to verify the reliability of the results.

Results

Characteristics of the study population

A total of 15,907 participants were included for analysis, with a mean age of 42.214 years and 49.275% male. The prevalence of low muscle mass was 7.985%. As the CDAI quartiles increased, the participants had higher PIRs and daily energy intake levels; were more likely to be male, non-Hispanic white, and nonsingle; were more likely to have an education level greater than a high school diploma; were more likely to engage in involved in rigorous physical activity; were more likely to be never/previous smokers; and were more likely to be light/moderate drinkers. A higher CDAI was associated with lower prevalence rates of diabetes, hypertension, CVD, and low muscle mass. The prevalence rates of low muscle mass from CDAI Q1-Q4 were 11.315%, 9.181%, 7.474%, and 4.516%, respectively (Table 1). Analysis on the basis of low muscle mass status suggested that participants with low muscle mass had significantly lower CDAI values ($p < 0.0001$) (Table S1).

Associations of the CDAI and its components with low muscle mass in the general population

In both the crude model and partially adjusted model 1, the CDAI was found to be associated with the prevalence of low muscle mass among the general adult population, whether treated as a continuous or categorical variable. In model 2, the CDAI remained negatively associated with the prevalence of low muscle mass (OR and 95% CI = 0.928 (0.910, 0.947), $p < 0.0001$). Compared with Q1, the CDAI values in Q2, Q3, and Q4 were significantly associated with lower odds of low muscle mass (Q2: OR = 0.836; Q3: OR = 0.708, and Q4: OR = 0.429; p for trend < 0.0001) (Table 2). The analysis of CDAI components revealed that dietary intake levels of vitamin A (OR = 0.5034, $p < 0.0001$), vitamin C (OR = 0.6640, $p = 0.0021$), vitamin E (OR = 0.4928, $p < 0.0001$), zinc (OR = 0.5638, $p < 0.0001$), selenium (OR = 0.4818, $p < 0.0001$), and carotenoids (OR = 0.6786, $p = 0.0029$) in the highest quartile (compared with that in Q1) were all associated with a lower prevalence of low muscle mass in the general population. (Table S2).

RCS analysis

RCS modelling revealed a nonlinear association between the CDAI and the prevalence of low muscle mass in the general population (p for nonlinearity = 0.0019) (Fig. 2A). Threshold effect analysis revealed that the CDAI was not associated with an odds of low muscle mass at ≤ -2.85 ($p = 0.1564$) and was negatively associated with low muscle mass at > -2.85 (OR = 0.92, $p < 0.0001$) (Table 3). For CDAI components, dietary intake levels of vitamin A (Fig. 2B) and zinc (Fig. 2E) exhibited nonlinear associations with the prevalence of low muscle mass (p for nonlinearity both < 0.0001), whereas dietary vitamin C (p for nonlinearity = 0.0672) (Fig. 2C), vitamin E (p for nonlinearity = 0.2044) (Fig. 2D), selenium (p for nonlinearity = 0.6835) (Fig. 2F), and carotenoid (p for nonlinearity = 0.3956) (Fig. 2G) intake levels were all linearly associated with the prevalence of low muscle mass.

Stratified analysis

On the basis of the RCS results, we performed stratified analyses after the cut-off value that had a significant association (CDAI > -2.85) was reached. Interaction analyses indicated that the three main lifestyle variables– i.e., physical activity (p for interaction = 0.027), smoking (p for interaction = 0.043), and alcohol consumption (p for interaction = 0.031)– were significant association moderators. The association between the CDAI and the prevalence of low muscle mass was significant across all levels of physical activity; however, the association was stronger among individuals who engaged in vigorous physical activity (OR = 0.884). Moreover, the association of the CDAI with low muscle mass was no longer significant among current smokers and heavy drinkers (Fig. 3).

Table 1 Analysis according to the CDAI quartiles

Variables	Total	Q1	Q2	Q3	Q4	*p*-value
Age, year	42.214 ± 0.231	42.639 ± 0.353	42.579 ± 0.306	42.043 ± 0.362	41.676 ± 0.316	0.057
PIR	3.089 ± 0.037	2.683 ± 0.044	3.093 ± 0.039	3.214 ± 0.045	3.307 ± 0.050	< 0.0001
Energy intake, kcal/day	2181.842 ± 9.565	1481.675 ± 10.788	1975.800 ± 12.268	2314.224 ± 12.976	2843.590 ± 21.890	< 0.0001
CDAI	0.931 ± 0.061	-3.685 ± 0.021	-1.039 ± 0.014	1.313 ± 0.015	6.358 ± 0.085	< 0.0001
Vitamin A, mcg	627.447 ± 6.656	271.212 ± 3.363	462.964 ± 5.551	647.624 ± 5.933	1067.239 ± 15.419	< 0.0001
Vitamin C, mg	83.170 ± 1.063	35.144 ± 0.744	59.698 ± 0.858	86.809 ± 1.239	142.778 ± 2.378	< 0.0001
Vitamin E, mg	8.256 ± 0.076	3.973 ± 0.035	6.335 ± 0.050	8.496 ± 0.072	13.492 ± 0.140	< 0.0001
Zinc, mg	11.903 ± 0.092	6.661 ± 0.053	9.998 ± 0.071	12.531 ± 0.094	17.561 ± 0.250	< 0.0001
Selenium, mcg	114.875 ± 0.679	69.004 ± 0.542	99.699 ± 0.656	122.388 ± 0.762	160.964 ± 1.514	< 0.0001
Carotenoid, mcg	10107.225 ± 166.230	3440.550 ± 66.499	6555.005 ± 92.382	9859.925 ± 129.679	19404.627 ± 443.990	< 0.0001
Sex						< 0.0001
male	7945(49.275)	1835(43.469)	1994(49.188)	2018(50.341)	2098(53.263)	
female	7962(50.725)	2143(56.531)	1984(50.812)	1956(49.659)	1879(46.737)	
Race						< 0.0001
Mexican American	2799(8.408)	687(7.823)	750(8.917)	674(8.321)	688(8.514)	
Non-Hispanic Black	3166(10.203)	967(13.668)	781(9.981)	693(8.752)	725(8.890)	
Non-Hispanic White	7250(69.186)	1712(65.859)	1834(69.633)	1833(69.759)	1871(71.037)	
Other Hispanic	1653(6.685)	330(6.144)	373(6.322)	491(7.253)	459(6.927)	
Other Race	1039(5.518)	282(6.506)	240(5.147)	283(5.915)	234(4.631)	
Marital Status						< 0.0001
non-single	9921(65.393)	2327(60.399)	2533(67.495)	2534(66.282)	2527(66.790)	
single	5986(34.607)	1651(39.601)	1445(32.505)	1440(33.718)	1450(33.210)	
Education						< 0.0001
< high school	1329(4.041)	526(6.342)	334(4.123)	254(3.401)	215(2.630)	
high school	5654(32.717)	1653(42.309)	1456(33.664)	1321(29.734)	1224(26.582)	
> high school	8924(63.242)	1799(51.349)	2188(62.212)	2399(66.865)	2538(70.788)	
Physical activity						< 0.0001
no	7210(40.803)	1990(45.006)	1853(41.872)	1697(39.008)	1670(37.981)	
moderate	4156(27.558)	973(26.175)	1041(27.258)	1111(29.274)	1031(27.321)	
vigorous	4541(31.639)	1015(28.818)	1084(30.870)	1166(31.718)	1276(34.698)	
Smoking						< 0.0001
never	8859(54.948)	1987(48.366)	2185(53.960)	2302(56.815)	2385(59.657)	
former	3413(22.071)	783(18.220)	888(22.372)	856(23.089)	886(24.068)	
now	3635(22.980)	1208(33.414)	905(23.667)	816(20.096)	706(16.275)	
Drinking						< 0.0001
never	2062(10.583)	617(13.044)	472(9.648)	500(10.468)	473(9.479)	
former	2288(12.124)	699(14.719)	586(12.395)	488(10.551)	515(11.210)	
mild	5329(35.021)	1124(28.445)	1401(36.682)	1424(36.389)	1380(37.712)	
moderate	2677(18.774)	628(17.985)	643(17.699)	705(19.797)	701(19.450)	
heavy	3551(23.499)	910(25.806)	876(23.577)	857(22.795)	908(22.150)	
Hypertension						0.007
No	10,575(70.332)	2480(67.886)	2625(69.499)	2715(71.209)	2755(72.341)	
Yes	5332(29.668)	1498(32.114)	1353(30.501)	1259(28.791)	1222(27.659)	
Diabetes						0.006
No	14,042(91.387)	3413(90.372)	3490(90.397)	3562(91.868)	3577(92.714)	
Yes	1865(8.613)	565(9.628)	488(9.603)	412(8.132)	400(7.286)	
CVD						< 0.0001
No	14,817(94.974)	3598(92.851)	3691(94.473)	3746(95.762)	3782(96.478)	
Yes	1090(5.026)	380(7.149)	287(5.527)	228(4.238)	195(3.522)	
low muscle mass						< 0.0001
No	14,169(92.015)	3389(88.685)	3494(90.819)	3583(92.526)	3703(95.484)	
Yes	1738(7.985)	589(11.315)	484(9.181)	391(7.474)	274(4.516)	

Continuous variables were expressed as mean ± standard error, and differences between groups were tested using weighted analysis of variance; categorical variables were expressed as number (percentage) and tested using weighted chi-square analysis

Table 2 Association of the CDAI with prevalence of low muscle mass in the general U.S. Population

	Crude model OR (95%CI) *P*-value	Model 1 OR (95%CI) *P*-value	Model 2 OR (95%CI) *P*-value
CDAI	0.914 (0.897, 0.932) < 0.0001	0.927 (0.909, 0.945) < 0.0001	**0.928 (0.910, 0.947) < 0.0001**
CDAI quartile			
Q1	Ref.	Ref.	Ref.
Q2	0.795 (0.684, 0.925) 0.0037	0.843 (0.713, 0.996) 0.0473	**0.836 (0.708, 0.987) 0.0377**
Q3	0.633 (0.531, 0.755) < 0.0001	0.701 (0.576, 0.853) 0.0006	**0.708 (0.576, 0.870) 0.0015**
Q4	0.371 (0.307, 0.449) < 0.0001	0.427 (0.351, 0.519) < 0.0001	**0.429 (0.351, 0.525) < 0.0001**
P for trend	< 0.0001	< 0.0001	**< 0.0001**

The crude model did not adjust for any covariates; model 1 adjusted for age, sex, race/ethnicity, education level, PIR, and marital status; and model 2 added to model 1 adjustments for smoking, alcohol consumption, physical activity, dietary energy intake, diabetes, hypertension, and CVD

Sensitivity analysis

Similar results were obtained the SMI was used to diagnose low muscle mass, thus indicating the stability of our findings. After adjusting for all confounders, the CDAI remained negatively associated with the prevalence of SMI-diagnosed low muscle mass in the general population (OR = 0.987, $p = 0.0078$). Compared with Q1, being CDAI values in Q2, Q3, and Q4 CDAI were all associated with significantly lower odds of low muscle mass (p for trend = 0.0204) (Table S3).

Discussion

In this large, nationally representative cross-sectional study, we found that an emerging dietary antioxidant composite assessment index, i.e., the CDAI, exhibited a nonlinear association with the prevalence of low muscle mass among the general U.S. adult population. Higher intake levels of CDAI components were associated with significantly lower odds of low muscle mass. Threshold effect analyses indicated that a significant negative association with the odds of low muscle mass was observed only when the CDAI was > -2.85. Importantly, interaction analyses of the associations CDAI was > -2.85 indicated that three important lifestyle factors, namely, physical activity, smoking, and alcohol consumption, significantly moderated the association. Overall, our findings suggest that the CDAI may be associated with low muscle mass in the general population by modulating oxidative homeostasis, suggesting that the antioxidant dietary pattern represented by the CDAI may have important public health implications and clinical relevance.

The CDAI is a composite measure of the antioxidant capacity of an individual's dietary sources based on the intake levels of key dietary antioxidant vitamins and minerals. This index was designed to provide a comprehensive assessment of the combined impact of dietary antioxidants on human health. The CDAI provides a more inclusive assessment and more accurately reflects an individual's overall exposure to dietary antioxidants than the assessment of individual antioxidants. Since the introduction of the CDAI, extensive clinical research has explored its association with a range of diseases, such as CVD [35], metabolic disorders [22], and osteoarthritic diseases [20]. Furthermore, research has suggested that the CDAI may have a promising role in disease prevention. However, the association of the CDAI with sarcopenia in the general U.S. adult population remains unclear. There are only a few studies that suggest that the CDAI may be associated with muscle mass in specific diseases or with grip strength in the general population. Similarly, in a recent cross-sectional study using data from the NHANES, Guo et al. reported that the CDAI was negatively associated with low muscle mass in patients with metabolic dysfunction-associated fatty liver disease (OR = 0.88) [36]. Another cross-sectional analysis using the NHANES indicated that the CDAI was positively associated with handgrip strength in the general population, but there were sex differences [25]. Thus, our study provides real-world evidence for the association of the CDAI with low muscle mass in the general population, suggesting that the CDAI may be associated with a lower prevalence of low muscle mass in the general population.

A real-world study provided direct evidence of increased oxidative stress in sarcopenia. Bellanti et al. included 347 elderly participants in a cross-sectional analysis and demonstrated that blood oxidized glutathione/reduced glutathione ratios and plasma malondialdehyde (MDA) and 4-hydroxy-2,3-nonenal (HNE) protein products were significantly increased in individuals with sarcopenia, whereas MDA and HNE were independently associated with sarcopenia [37]. Although there is a lack of research on the association of the CDAI– an emerging dietary antioxidant exposure assessment tool– with sarcopenia in the general population, an association between dietary antioxidant capacity and maintenance of muscle mass has been proposed in several studies. A prospective cohort from the Rotterdam Study demonstrated that increased total dietary antioxidant capacity (DTAC) (as assessed by the ferric reducing capacity of plasma) was associated with increased fat-free muscle mass in the general population but not with handgrip strength or sarcopenia [38]. In a cross-sectional study, Baharirad et al. reported that DTAC was negatively associated with sarcopenia in people with type 2 diabetes mellitus and that DTAC in the top tertile (compared with the bottom tertile) was associated with a significantly lower prevalence of sarcopenia ($p = 0.019$) [39]. In addition to DTAC, several studies have shown that another emerging

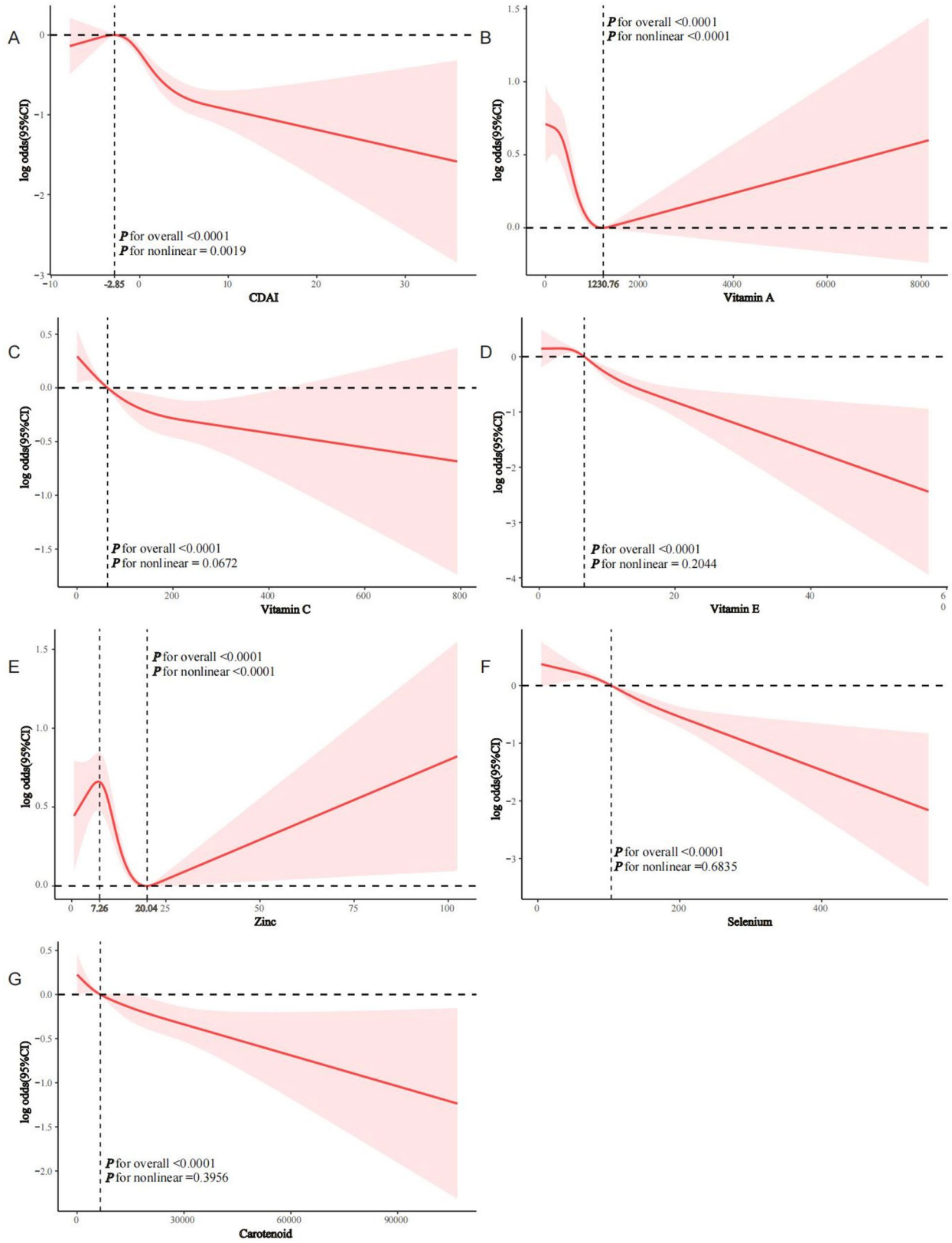

Fig. 2 Association of the CDAI and its components with the prevalence of low muscle mass in the general population. **A**: CDAI; **B**: Vitamin A; **C**: Vitamin C; **D**: Vitamin E; **E**: Zinc; **F**: Selenium; **G**: Carotenoids

Table 3 Threshold effect analysis of the association between the CDAI and the prevalence of low muscle mass

	CDAI ≤ -2.85	CDAI >-2.85	*P*-interaction
	OR (95%CI) P-value	OR (95%CI) P-value	
CDAI	1.107 (0.963, 1.271) 0.1564	**0.920 (0.895, 0.947) < 0.0001**	**0.0138**

Conducted in fully adjusted models (model 2) adjusting for age, sex, race, PIR, education, marital status, smoking, alcohol consumption, physical activity, dietary energy intake, diabetes, hypertension, and CVD

metric for assessing exogenous oxidative balance, namely, the oxidative balance score (OBS), is associated with sarcopenia in the general population. However, the findings have been inconsistent. In a case–control study that included a small sample of 160 older Iranian participants, Mahmoodi et al. reported that the OBS was not associated with the odds of sarcopenia after adjusting for confounders [40]. Two additional cross-sectional analyses using data from the 2011–2018 waves of the NHANES suggested that the OBS, including the dietary OBS, was negatively associated with the prevalence of sarcopenia in nonelderly populations [41, 42]. Additionally, the OBS exhibited a nonlinear association with sarcopenia in the general young and middle-aged population [41], which is comparable to our RCS results. There are several differences between our study and the study by Chen et al. First, the study by Chen et al. focused on young and middle-aged adults aged 20–59 years [41], whereas our study included all adults aged ≥ 20 years, covering a wider age range (including older adults). The OBS integrates dietary and lifestyle antioxidants with pro-oxidant factors, whereas the CDAI assesses only dietary antioxidant components. Consistently, both studies reported a nonlinear association between antioxidant metrics and a reduced prevalence of low muscle mass, with a significant or greater magnitude of association after reaching a certain threshold cumulative level. These findings may indicate that low doses of antioxidants are not sufficient to scavenge ROS, whereas high doses counteract oxidative stress by activating antioxidant-related pathways.

Our study revealed that higher intake levels of individual dietary antioxidants was significantly associated with a lower prevalence of low muscle mass in the general population. Previous clinical evidence has suggested that certain dietary antioxidant vitamin and mineral intake levels may be associated with sarcopenia or its associated parameters. A cross-sectional analysis revealed that dietary intake levels of vitamin C, vitamin E, and carotenoids (especially vitamin C) was associated with skeletal muscle mass-related parameters and/or leg explosiveness in younger and older women [43]. Another cross-sectional analysis using NHANES indicated an association of micronutrient dietary patterns, including antioxidant vitamins, with the prevalence of sarcopenia in people aged 20–59 years, whereas the intake levels of most antioxidant vitamins was negatively associated with the odds of sarcopenia [44]. Accumulating experimental and clinical evidence has also indicated that nutritional vitamin C, vitamin E, selenium, zinc, and carotenoid supplementation may modulate muscle pathophysiology and ameliorate sarcopenia by partially modulating the levels of oxidative stress; however, the results have been inconsistent [45–47].

Sarcopenia is a progressive loss of skeletal muscle mass and function that is commonly observed in the elderly population and is a major component of geriatric syndrome. Some clinical studies have shown that adherence to a CDAI-reflected antioxidant diet can help slow the biological ageing process. A cross-sectional study similar to that of the NHANES indicated that the CDAI was negatively associated with phenotypic age-related ageing (OR = 0.90), and this association was stronger in nonsmokers [23]. Another cross-sectional study using data from the 2001–2018 waves of the NHANES similarly suggested that the CDAI was positively associated with delayed biological ageing [48]. Additionally, a higher CDAI was found to be significantly associated with a reduced prevalence of other geriatric syndrome components, including cognitive decline and frailty [24, 49]. Thus, it is conceivable that the CDAI may serve as an important dietary pattern in the elderly population associated with a reduced prevalence of several geriatric syndromes, including sarcopenia, thus suggesting that adherence to an antioxidant diet may help ameliorate ageing and its associated diseases. Although the mechanism underlying the association of the CDAI with sarcopenia in the general population remains unknown, it may reflect the fact that dietary antioxidants prevent muscle atrophy by modulating intrinsic oxidative homeostasis and other mechanisms, such as ameliorating inflammatory responses. Oxidative stress plays an important role in muscle atrophy and low muscle mass, and excessive ROS production may lead to the inhibition of muscle regeneration, decreased ATP production, and increased protein catabolism/decreased protein synthesis, thus resulting in decreased muscle mass and reduced muscle strength [10].

Importantly, the association of the CDAI with low muscle mass in the general population is moderated by important lifestyle factors, including physical activity, smoking, and alcohol consumption. Vigorous physical activity may amplify the association between the CDAI and a lower prevalence of low muscle mass, whereas current smoking and heavy drinking status significantly attenuated the strength of this association. Physical activity is a recognized modifiable, lifestyle-related risk factor for oxidative stress in the body [50], and a previous study using data from the NHANES similarly revealed that physical activity altered the association of the CDAI with

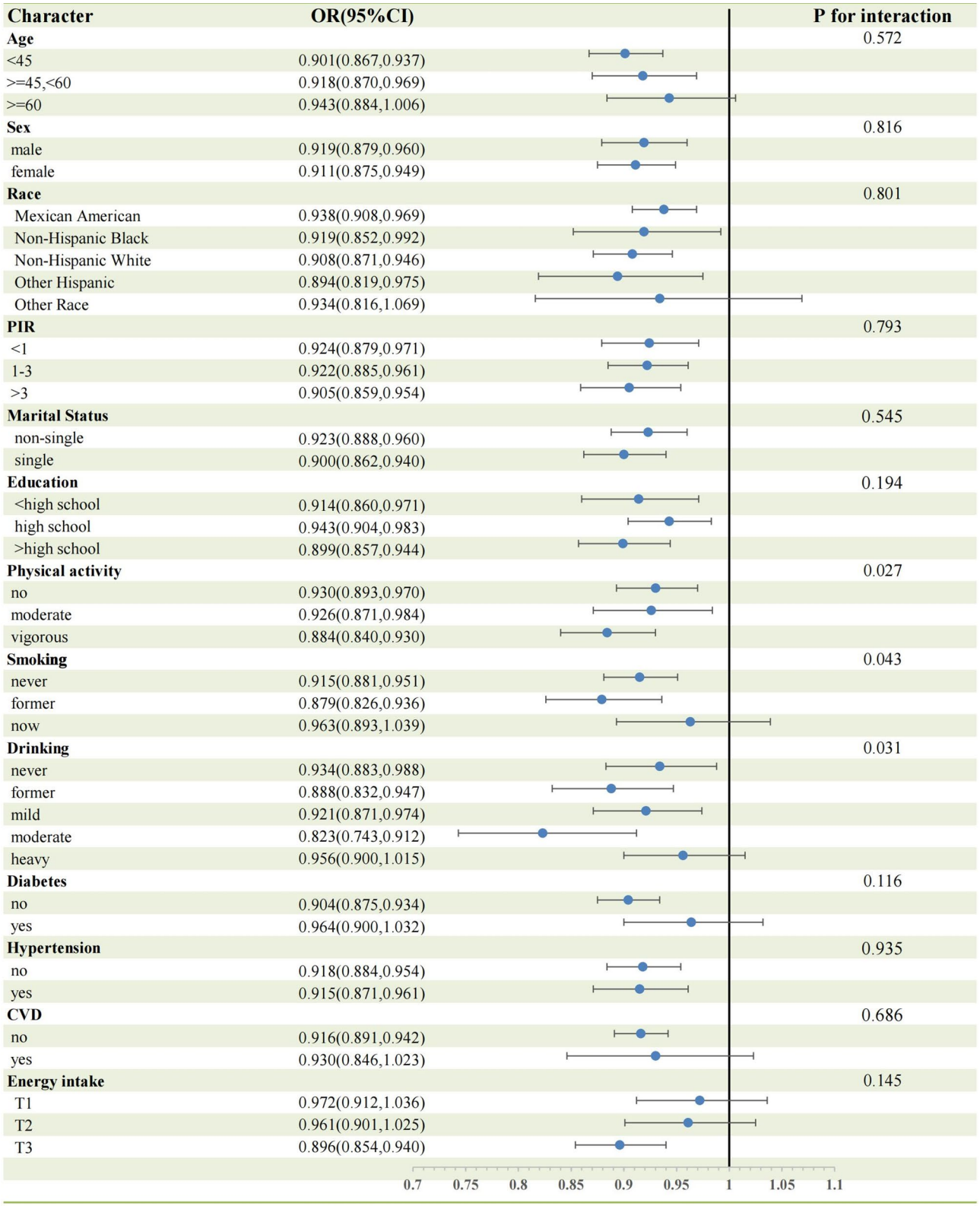

Fig. 3 Stratified analysis of the association between the CDAI and low muscle mass after the inflection point (CDAI > -2.85)

mortality in an osteoarthritis population [51]. However, both smoking and alcohol consumption are well-established risk factors for oxidative stress [52, 53]. Therefore, it can be assumed that the association of the CDAI with sarcopenia exists only in non-current smokers and non-heavy drinkers, emphasizing the importance of adhering to antioxidant dietary patterns while maintaining a good lifestyle.

Our study has several significant advantages. This is the first real-world study to explore the association of the CDAI with low muscle mass in the general population. The findings have important clinical relevance and suggest that antioxidant dietary patterns may be promising for the management of sarcopenia. The NHANES is a large, nationally representative series of cross-sectional surveys, thus ensuring the generalizability of the results. These findings were derived from good robustness and reliability based on well-considered adjustments for confounders and a range of standard statistical analyses. However, our study had several limitations. A major limitation was the use of a cross-sectional design; this design precluded us from drawing causal inferences, and the findings could be influenced by residual confounders. Future cohort studies are needed to confirm our findings. Dietary intake data were obtained on the basis of self-reports of dietary recall and may be subject to recall bias. Although the diagnosis of low muscle mass was assessed by the FNIH criteria, we were unable to consider the associations of the CDAI with muscle strength and physical performance due to the lack of information in the NHANES. These limitations need to be fully considered in future studies.

Conclusions

According to a national cross-sectional analysis, the CDAI was significantly associated with the prevalence of low muscle mass among the general U.S. adult population. There was a nonlinear association between the CDAI and odds of low muscle mass, with a negative association only at >-2.85. According to the stratified analysis of the associations after a CDAI > -2.85, physical activity, smoking, and alcohol consumption significantly interacted with this association, whereas this association was stronger in participants with rigorous physical activity, non-current smokers, and non-heavy drinkers. These findings suggest that the antioxidant dietary pattern assessed by the CDAI contributes to a reduction in muscle mass in the general population, suggesting that adherence to an antioxidant diet, along with the maintenance of a good lifestyle, reduces the burden of low muscle mass.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12937-025-01166-w.

Supplementary Material 1

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None.

Author contributions
Huan Shi planned the study and edited the paper. Miaohong Wang conducted the analysis and wrote the manuscript. All authors have reviewed and endorsed the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics statement
All NHANES research protocols were reviewed and approved by the NCHS Ethics Review Board, and all participants have provided written informed consent.

Competing interests
The authors declare no competing interests.

Conflict of interest
None.

Clinical trial number
Not applicable.

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