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Association between the composite dietary antioxidant index and metabolic syndrome: evidence from NHANES 2003-2018

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Abstract. – OBJECTIVE: A healthy and nutritional diet has been considered a promising approach to improve many adverse clinical outcomes. However, current evidence of the association of the intake of composite dietary antioxidants with metabolic syndrome (MetS) is limited. The current study was performed to explore the effect of the composite dietary antioxidant index (CDAI) on MetS and its components based on the National Health and Nutrition Examination Survey (NHANES) from 2003 to 2018.

MATERIALS AND METHODS: The dietary consumption was evaluated using the 24-hour diet recall method, and a previously validated approach that included six antioxidants was used to calculate CDAI. The National Cholesterol Education Program-Adult Treatment Panel III (NCEP ATP III) was applied to evaluate MetS. ORs and 95%CIs were computed by logistic regression. The association between CDAI and MetS was determined by subgroup analyses and restricted cubic spline (RCS) regressions.

RESULTS: This study included 24,705 individuals; approximately 18,378 (74.39%) participants were determined to be without MetS and 6,327 (25.61%) with MetS. After considering all confounders, compared to individuals of the lowest quartile of CDAI, those of the highest quartile showed a 31% lower risk of MetS (OR, 0.69, 95% CI: 0.57-0.82). RCS revealed a non-linear relationship between CDAI and MetS risk.

CONCLUSIONS: A non-linear association was found between CDAI and decreased MetS risk, which indicated that selective combined intake of antioxidants could be a promising and effective approach to preventing MetS for the public.

Key Words:
Composite dietary antioxidant index, Metabolic syndrome, Evidence.

Introduction

As a cluster of multiple risk factors, MetS is mainly caused by obesity and insulin resistance gathering in one individual, including central obesity, hypertension, hyperglycemia, and dyslipidemia[1], which subsequently results in higher risks of diabetes, cardiovascular disease (CVD), cerebrovascular accident (CVA), non-alcoholic fatty liver disease (NAFLD), malignant tumors, sarcopenia, etc., and ultimately leads to an increase in mortality[1-4]. The medical profession refers to the combination of diabetes with insulin resistance, hypertension, hyperlipidemia, CVD, and CVA as the "death quintet", which is a leading cause of death in the 21st century. More than a quarter of people worldwide suffer from MetS, and its prevalence will rise further in the future because of the popularity of excessive calorie intake, reduced physical activity, and obesity[5]. It is reported that the total prevalence of MetS among American adults has increased from 37.6% in 2011-2012 to 41.8% in 2017-2018[6]. Therefore, dealing with MetS has become an important challenging issue.

Although the basic components and clinical significance of MetS have been basically clarified, the underlying pathophysiological mechanisms are complex and multifactorial, such as genetic, environmental, and immune factors[7]. Therefore, interventions for MetS are also comprehensive and specific. Although drug treatment for risk factors such as hyperglycemia, dyslipidemia, or hypertension is necessary, dietary intervention and exercise, as two controllable environmental factors, are still important first-line treatments for

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MetS. Obesity is not only the most common clinical manifestation but also an important pathogenic factor of MetS. It is generally accepted that unreasonable intake of nutrients (such as excessive fat and carbohydrate) contributes hugely to the initiation and development of MetS, especially in fat. Additionally, it has been shown that asprosin, visfatin, and subfatin in fat metabolism are new markers of the metabolic syndrome[8]. The reasonable, regular, and selective intake of nutrients can effectively improve the progress and prognosis of MetS[9]. In addition to total calories and fat intake, natural antioxidants from food sources, such as various fat-soluble vitamins and trace elements, have received widespread attention due to their antioxidant, anti-inflammatory, and glycolipid metabolism regulation effects.

Epidemiologic and experimental studies have demonstrated a close relationship between diet total antioxidant capacity (TAC) and MetS risk[10-12]. However, because TAC is determined basically by the reductase activity of ferric ions in plasma, it is limited to focusing on a single aspect of antioxidant ability in the body. The CDAI is a summary evaluation of the dietary antioxidant intake (vitamins A, C, E, and selenium, etc.), reflecting individual antioxidant characteristics[13,14]. There is a lack of studies exploring the link between CDAI and MetS risk. Thus, the public research data from the NHANES 2003-2018 was used to investigate the association of CDAI with MetS risk as well as its components to further ascertain the beneficial effect of CDAI on MetS.

Materials and Methods

Study Design

The NHANES is a biennial program that is nationally replicated by the NCHS. It is used to investigate the prevalence and risk factors of common diseases. The program includes dietary, demographic, socioeconomic, and health-related data in their datasets. All participants must provide informed consent forms upon enrollment; therefore, additional local informed consent is not required.

The database used in this study was extracted from eight-year cycles of NHANES from 2003 to 2018. Specifically, of the 40,570 participants in the NHANES 2003-2018, they were progressively excluded if meeting the following conditions: 1) subjects without available CDAI data (n=7,348), 2) subjects without demographic data (n=5,517), smoke (n=1,739), alcohol (n=2,006), physical activity (n=7,069) and other covariates (n=864), 3) subjects with excessive daily energy intake (<800 or >4,200 kcal/day for male, n=681 and <600 or >3,500 kal/day for female). Finally, 19,846 subjects were grouped into 5,060 with MetS and 14,786 without MetS (**Supplementary Figure 1**).

MetS Definition

The National Cholesterol Education Program-Adult Treatment Panel III (NCEP ATP III) was selected as the criteria of MetS diagnosis[15]. The individuals were determined to be with MetS if fitting 3 or more following conditions. (1) Hypertriglyceridemia: serum TG ≥150mg/dL; (2) central obesity: waist circumference ≥102 cm in men or ≥88 cm in women; (3) decreased HDL: serum HDL <40 mg/dL in men and <40 mg/dL in women; (4) hypertension: SBP ≥130 mmHg or DBP ≥85 mmHg or drug treatment for hypertension; (5) hyperglycemia: fasting glucose ≥100 mg/dL or drug treatment for increased blood glucose. In order to determine the maximum inflation level, all participants for blood pressure measurement should rest quietly for 5 minutes. The arithmetic mean of blood pressure was calculated for the final recording.

Calculation of Composite Dietary Antioxidant Index

All examinees were eligible to attend two 24-hour dietary recall surveys to obtain data on dietary intake. The first survey was face-to-face, and the second was performed over the phone 3-10 days later. Dietary intake data with missing values were excluded directly. Thus, in order to reduce bias, the average antioxidant intake of more than 2 days was used.

The modified version of CDAI developed by Wright et al[13], and validated in other studies[14,16] was used to assess the potential interaction between different antioxidants. Specifically, vitamins A, E, C, selenium, zinc, and carotenoids from food sources, not dietary supplements, for each subject were only considered. Subtracting the total mean and dividing the total standard deviation were used to standardize each antioxidant. Then, the standardized intake of individual nutrients was summed to compute the CDAI according to the equation reported in the previous study[14].

Assessment of Covariates

A series of standardized questionnaires were used to collect the demographic features and

dietary and lifestyle behaviors by information collectors. The covariates associated with MetS included age, gender, ethnicity, education, energy intake, poverty ratio income (PIR), marital status, coffee, estimated glomerular filtration rate (eGFR), alanine aminotransferase (ALT), aspartate aminotransferase (AST), smoke, CVD, physical activity, alcohol status, and NHANES years cycle. The activity of serum ALT and AST was evaluated using the enzymatic rate method. More details about laboratory methodology were publicly provided on the NHANES website. Ethnicity included 4 classes: non-Hispanic black, non-Hispanic white, Mexican American, and other ethnicities. PIR included <1.30, 1.30-3.49, and ≥3.50. Marital status included married, unmarried, and others. Education included <9th grade, 9th-11th grade, high school, some college, and college or above. Alcohol status had four levels: never drinker (<12 drinks in a lifetime), former drinker (≥12 drinks in 1 year and did not drink last year), mild/moderate drinker (≤2 drinks/day for men or ≤1 drink/day for women), and heavy drinker (≥3 drinks/day for men or ≥2 drinks/day for women)[17]. Metabolic equivalent (MET)-minutes/week was used to present physical activity and included <600, 600-1,200, and ≥1,200 MET-min/week[18]. eGFR was obtained by the CKD-EPI equation[19].

Statistical Analysis

The present study utilized R software version 4.1.3 (Auckland, New Zealand). According to NHANES analysis tutorial, a complex survey design was fully considered and appropriate sampling weights were adopted to ensure unbiased estimation. The continuous variable was shown by mean and standard error (SE), as well as the category variable by frequency with percentage. The Chi-square test and Student's *t*-test were taken to assess the baseline characteristics on the basis of MetS status. A series of logistic regressions were used to estimate ORs and 95% CIs between CDAI and MetS after confounding factors were adjusted. Variables were not adjusted in model 1. In Model 2, age, gender, ethnicity, and NHANES years cycle were adjusted. All covariates in Model 2 plus marital status, education level, PIR, smoke, alcohol status, physical activity, ALT, AST, eGFR, CVD, coffee, and daily intake of energy were adjusted in Model 3. The ORs (95% CIs) per 1-SD increase in these different models were computed. Moreover, CDAI was treated as continuous exposure in these logistic models to further verify the association of CDAI with MetS risk. The MetS risk and the daily intake of individual antioxidants were evaluated by dividing individual antioxidants into quartiles. The linear trend was conducted by assigning CDAI or individual antioxidant quartiles as an ordinal variable. To visualize the relationship of CDAI and its components with MetS, RCS was carried out. Next, the correlation between CDAI and MetS in different populations was determined by subgroup analyses. The interactions among these subgroups were calculated by likelihood ratio tests. Finally, the association between CDAI and MetS components was examined to explore the influence of CDAI on individual MetS components in model 3. All tests were bilateral, with the significance level set as α=0.05. While $p<\alpha$ indicates a statistical significance of the data.

Results

Characteristics of Study Participants

Overall, this study enrolled 24,705 individuals from NHANES 2003-2018. The average age was 46.14 years (SE: 0.26), including 9,568 (48.21%) females and 10,278 (51.79%) males (Table I). Of them, 18,378 (74.39%) participants were determined to be without MetS, and 6,327 (25.61%) were with MetS. The mean CDAI was (0.10±0.05) for the overall population. The mean CDAI (0.20±0.06) for subjects without MetS was significantly higher than the mean CDAI (-0.21±0.08) for subjects with MetS. Specifically, compared with participants without MetS, those with MetS tended to be older, non-Hispanic white, married, former/never drinkers, physically inactive and were at a lower education and PIR level, poor renal function, a higher level of ALT, AST, and CVD prevalence (all $p<0.05$). There was not a significant difference in gender, daily intake of energy, coffee, and smoke status between the two groups (all $p>0.05$).

Association of CDAI with MetS and its Components

Table II shows the logistic regression results between CDAI and MetS. In model 1 for non-covariates adjustment, comparing the highest quartile (Q4) to the lowest one (Q1) of CDAI, the OR was (0.75, 95% CI: 0.65-0.86). The corresponding OR per SD was 0.89 (95% CI: 0.84-0.94, *p* for trend <0.001). After controlling all confounding factors in model 3, CDAI was noticeably associated with decreased MetS risk. Compared to Q1 of

Table I. Characteristics of study participants by MetS status, weighted (n=24,705)[a].

Characteristic	Overall	Non-MetS	MetS	*p*
Sample	24,705	18,378 (74.39%)	6,327 (25.61%)	
Age, years	46.14±0.26	44.70±0.30	50.72±0.30	<0.001
Gender, n (%)				0.720
Female	9,568 (48.21)	6,986 (49.29)	2,582 (48.80)	
Male	10,278 (51.79)	7,800 (50.71)	2,478 (51.20)	
Ethnicity, n (%)				<0.001
Mexican American	2,854 (14.38)	1,986 (7.04)	868 (8.83)	
Non-Hispanic Black	3,811 (19.20)	2,990 (9.79)	821 (7.93)	
Non-Hispanic White	9,749 (49.12)	7,192 (71.93)	2,557 (72.44)	
Other ethnicities	3,432 (17.29)	2,618 (11.23)	814 (10.79)	
Education, n (%)				<0.001
Less than 9th grade	1,436 (7.24)	998 (3.17)	438 (4.13)	
9th-11th grade	2,300 (11.59)	1,613 (7.82)	687 (9.84)	
High school	4,488 (22.61)	3,147 (20.48)	1,341 (27.91)	
Some college	6,241 (31.45)	4,597 (32.08)	1,644 (34.90)	
College or above	5,381 (27.11)	4,431 (36.45)	950 (23.22)	
PIR, n (%)				<0.001
<1.30	5,287 (26.64)	3,770 (17.64)	1,517 (19.79)	
1.30-3.49	7,451 (37.54)	5,477 (33.20)	1,974 (37.29)	
≥3.50	7,108 (35.82)	5,539 (49.16)	1,569 (42.93)	
Marital status, n (%)				<0.001
Unmarried	3,635 (18.32)	3,070 (20.93)	5,65 (11.72)	
Married	10,746 (54.15)	7,806 (55.91)	2,940 (61.11)	
Others	5,465 (27.54)	3,910 (23.16)	1,555 (27.17)	
Energy, kcal/day	2,103.33±7.50	2,108.33±7.78	2,087.43±17.84	0.274
Coffee, g/day	320.70±6.30	317.41±6.75	331.13±8.93	0.123
eGFR, (ml/min/1.73 m^2)	94.58±0.35	95.91±0.38	90.34±0.45	<0.001
ALT, U/L	25.69±0.18	24.24±0.20	30.30±0.40	<0.001
AST, U/L	25.48±0.15	25.01±0.16	26.99±0.34	<0.001
Smoke, n (%)	3,908 (19.69)	2,907 (19.27)	1,001 (19.11)	0.864
CVD, n (%)	1,755 (8.84)	1,062 (5.18)	693 (12.06)	
Physical activity (MET-minute/week), n (%)			<0.001	
<600	5,807 (29.26)	4,262 (27.79)	1,545 (30.35)	
600-1,200	2,963 (14.93)	2,142 (13.79)	821 (15.80)	
≥1,200	11,076 (55.81)	8,382 (58.42)	2,694 (53.86)	
Alcohol status, n (%)				<0.001
Never	2,308 (11.63)	1,605 (8.93)	703 (11.26)	
Former	3,031 (15.27)	2,026 (10.57)	1,005 (17.17)	
Mild	7,280 (36.68)	5,611 (39.30)	1,669 (36.28)	
Heavy	7,227 (36.42)	5,544 (41.20)	1,683 (35.30)	
CDAI[b]	0.10±0.05	0.20±0.06	-0.21±0.08	<0.001
Q1	4,963 (25.01)	3,556 (21.14)	1,407 (24.67)	
Q2	4,960 (24.99)	3,687 (24.13)	1,273 (24.94)	
Q3	4,961 (25.00)	3,740 (26.49)	1,221 (25.74)	
Q4	4,962 (25.00)	3,803 (28.24)	1,159 (24.65)	
NHANES cycles (n, %)				0.014
2003-2004	2,332 (11.75)	1,822 (12.37)	510 (10.52)	
2005-2006	2,426 (12.22)	1,865 (12.55)	561 (12.40)	
2007-2008	2,610 (13.15)	1,880 (11.78)	730 (12.62)	
2009-2010	2,825 (14.23)	2,112 (12.14)	713 (11.25)	
2011-2012	2,527 (12.73)	1,920 (13.31)	607 (11.25)	
2013-2014	2,727 (13.74)	2,027 (13.04)	700 (13.66)	
2015-2016	2,437 (12.28)	1,735 (13.06)	702 (15.99)	
2017-2018	1,962 (9.89)	1,425 (11.75)	537 (12.31)	

Continuous variables were presented as mean±SE, categorical variables were presented as frequency (percentage). [a]All estimates accounted for complex survey designs, and all percentages were weighted. [b]Q1: CDAI ≤ -2.64; -2.64 < CDAI ≤ -0.69; -0.69< CDAI ≤ 1.72; CDAI>1.72. MetS, metabolic syndrome; PIR, poverty income ratio; eGFR, estimated glomerular filtration rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CVD, cardiovascular disease; MET, metabolic equivalent; CDAI, composite dietary antioxidant index; SE, standard error.

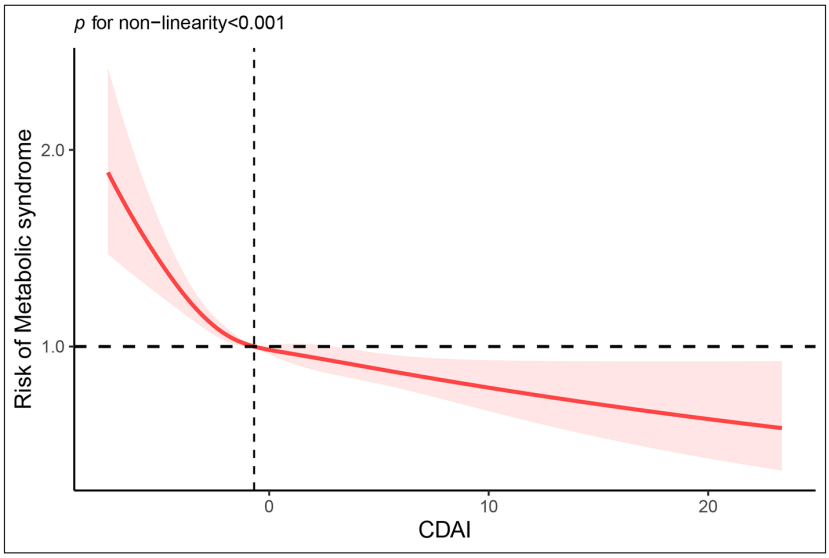

Figure 1. Restricted cubic spline (RCS) analysis with multivariate-adjusted association between CDAI and MetS.

CDAI, those in Q4 had a 31% lower risk of having MetS (OR, 0.69, 95% CI: 0.57-0.82). At the same time, the OR per SD was 0.87 (95% CI: 0.81-0.93, *p* for trend <0.001) in model 3. Moreover, a similar association was observed (model 1: β=0.97, 95% CI: 0.95-0.98; model 2: β=0.97, 95% CI: 0.95-0.98; model 3: β=0.96, 95% CI: 0.94-0.98). Additionally, multivariate-adjusted RCS regression displayed a non-linear relationship between CDAI and MetS risk (*p* for non-linearity <0.001) (Figure 1), suggesting that associations plateaued in the higher CDAI exposure range.

The associations between CDAI and each MetS component are summarized in Table III. After considering all covariates, the OR for comparing participants in Q4 with Q1 of CDAI was 0.69 (95% CI: 0.58-0.81) for reduced HDL, 0.68 (0.58-0.81) for hypertriglyceridemia, and 0.65 (0.55-0.77) for central obesity. However, these inverse associations of CDAI with hyperglycemia and hypertension were not observed.

Individual Antioxidant Components and MetS

A correlation between individual antioxidant constituents and MetS was assessed by dividing the value of individual antioxidants into quartiles, and the first quartile (Q1) was set as the reference (Table IV). In model 3, comparing Q4 with Q1, the OR were 0.81(95% CI: 0.70-0.95, *p* for trend <0.001) for vitamin A, 0.59 (95% CI: 0.50-0.70, *p* for trend <0.001) for vitamin E, 0.64 (95% CI: 0.55-0.74, *p* for trend <0.001) for vitamin C and 0.83 (95% CI: 0.72-0.96, *p* for trend =0.034) for carotenoids. By contrast, the intake of dietary zinc and selenium was not associated with MetS. Furthermore, RCS showed that vitamins A, E, and C were non-linearly associated with MetS risk (Figure 2).

Subgroup Analyses

In order to test whether the correlation between CDAI and MetS risk was robust in different populations when stratified by age, gender, smoke, PIR, marital status, and ethnicity, subgroup analyses were further carried out (**Supplementary Figure 2**). No differential associations among these subgroups were found (all *p* for interaction >0.05).

Discussion

In the current large-scale NHANES study, the results showed that a higher level of CDAI was related to decreased MetS risk among US adults aged 40 and older. Specifically, CDAI was non-linearly associated with decreased risk of MetS. Moreover, CDAI was closely related to the occurrence of MetS components, including elevated TG, low HDL, and central obesity. These findings highlight the advantages of combined intake of antioxidants in MetS patients.

Oxidative stress refers to a reactive oxygen species (ROS) overload state induced by excessive generation and/or elimination of reduction

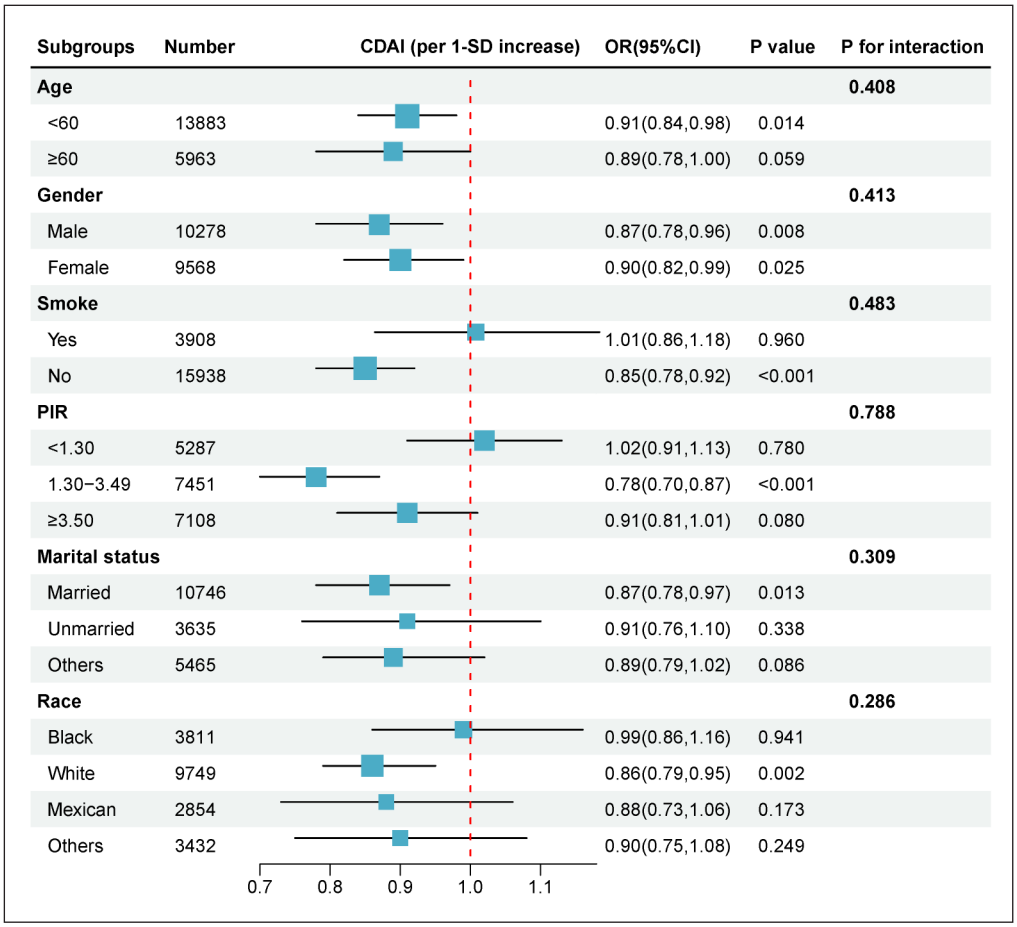

Figure 2. Subgroup analysis of the association between CDAI and MetS.

of ROS in the body under various harmful internal and external stimulation[20]. Under physiological conditions, endogenous antioxidant systems maintain intracellular redox homeostasis by reducing ROS production or scavenging free radicals. Under a series of MetS pathological conditions (obesity, hypertension, hyperglycemia, and dyslipidemia), ROS production is excessive, and antioxidant system expression is insufficient[21-23]. Excessive ROS can directly or indirectly oxidize and damage cellular DNA, proteins, and lipids, induce gene mutations, protein denaturation, lipid peroxidation, and inflammatory processes, mediate cell apoptosis and tissue damage, and ultimately exacerbate the occurrence of MetS and its complications, forming a vicious cycle[21-23].

Most prior studies[24,25] put emphasis on the correlation of individual dietary antioxidants with MetS. The results of two meta-analyses concluded an inverse correlation between the dietary intake of vitamin E as well as vitamin C and MetS risk. Liu and Park[26] established the causal association of the insufficient dietary vitamin C intake with higher MetS risk in Asian adults. Yakut et al[27] found that nucleotide analogue therapy affected MetS parameters when used to treat patients with chronic hepatitis B with drugs. Thus, there is a correlation between antioxidants and the risk of MetS initiation.

There are a few reports regarding the influence of total dietary carotenoid intake on MetS risk. Animal studies[28] find that dietary supplementation with astaxanthin reduces animal blood sugar and systolic pressure levels. A randomized clinical trial[29] involving 44 MetS subjects shows that crocin administration (30 mg/d, 8 weeks improves cholesterol uptake capacity by HDL in MetS patients. The findings above are basically consistent with the results of the present study. A meta-analysis[30] also shows a negative correlation between the level of serum carotenoid, particularly β-carotene, and the risk of MetS.

β-carotene is hydrolyzed into two vitamin A molecules after absorption. It is worth noting that

Table II. Association between CDAI and MetS risk.

	Model 1		Model 2		Model 3	
Variables	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Continuous	0.97 (0.95,0.98)	<0.001	0.97 (0.95,0.98)	<0.001	0.96 (0.94,0.98)	<0.001
Categories						
Q1	Reference		Reference		Reference	
Q2	0.89 (0.78,1.01)	0.073	0.86 (0.75,0.99)	0.035	0.82 (0.70,0.96)	0.014
Q3	0.83 (0.72,0.97)	0.016	0.82 (0.71,0.96)	0.012	0.77 (0.66,0.91)	0.002
Q4	0.75 (0.65,0.86)	<0.001	0.74 (0.64,0.85)	<0.001	0.69 (0.57,0.82)	<0.001
p for trend	<0.001		<0.001		<0.001	
Per 1-SD increase	0.89 (0.84,0.94)	<0.001	0.89 (0.84,0.94)	<0.001	0.87 (0.81,0.93)	<0.001

Model 1: Adjusted for none variables. Model 2: Adjusted for age, gender, ethnicity, and NHANES years cycle. Model 3: Adjusted for age, gender, ethnicity, NHANES years cycle, marital status, education level, PIR, smoke, alcohol status, physical activity, ALT, AST, eGFR, CVD, energy, and coffee intake.

Table III. Association between CDAI and individual MetS components*.

	Q1	Q2		Q3		Q4	
		OR (95% CI)	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Hyperglycemia	Ref	1.01 (0.87,1.16)	0.910	0.95 (0.81,1.12)	0.543	0.97 (0.80,1.17)	0.761
Reduced HDL	Ref	0.90 (0.78,1.04)	0.162	0.84 (0.72,0.98)	0.023	0.69 (0.58,0.81)	<0.001
Hypertriglyceridemia	Ref	0.85 (0.72,1.01)	0.059	0.80 (0.69,0.92)	0.003	0.68 (0.58,0.81)	<0.001
Central obesity	Ref	0.85 (0.74,0.97)	0.021	0.78 (0.67,0.90)	0.001	0.65 (0.55,0.77)	<0.001
Hypertension	Ref	0.95 (0.81,1.12)	0.533	0.92 (0.76,1.11)	0.379	0.91 (0.76,1.10)	0.345

Model 1: Adjusted for none variables. Model 2: Adjusted for age, gender, ethnicity, and NHANES years cycle. Model 3: Adjusted for age, gender, ethnicity, NHANES years cycle, marital status, education level, PIR, smoke, alcohol status, physical activity, ALT, AST, eGFR, CVD, energy, and coffee intake.

vitamin A cannot be confused with β-carotene because the latter has a stronger antioxidant capacity. There are mixed observations on the relationship between vitamin A and MetS risk; for example, dietary vitamin A intake from food or supplements has been found to have some beneficial effects on MetS in Korean adults[31,32]; however, a cross-sectional study (n=54,269) of children and adolescents has found that circulating vitamin A has an adverse impact on MetS risk in a dose reliant pattern[33]. This difference may be related to the phase dependence of the effect of vitamin A on fat synthesis, as the findings have shown that long-term oral β-carotene administration improves body weight as well as the storage of subcutaneous fat in infant ferrets in animal studies[34], while short-term oral β-carotene supplementation reduces the tendency to obesity in adult ferrets[35].

Zinc, selenium, and other trace elements are also essential components of antioxidants. Several documents indicate that zinc and selenium have dual antioxidant/prooxidant effects: lower concentrations of zinc and selenium mainly exhibit antioxidant capacity, while high levels of zinc and selenium play a prooxidant role[36]. This may partly interpret the association of Zinc intake or serum concentration with MetS[37], as well as the various types of correlation found between MetS and circulating selenium levels, including positive, negative, non-correlation[38], and a U-type association found recently[39]. A correlation was not observed between the dietary selenium intake and MetS in one meta-analysis[40]. One meta-analysis[41] concluded that although selenium administration improved insulin sensitivity to some extent, no beneficial effects on lipid profiles or glucose homeostasis were observed. This minimal biological function may be due to the lower bioavailability of selenium in MetS patients, as the concentration of Selenoprotein P (SeP) in individuals with MetS was lower than in those without MetS[42]. Sep participates in the liver's transport of selenium to target tissues.

For decades, people have recognized the interaction between antioxidants; for example, selenium prevents the formation of lipid hydroperoxides

Table IV. Multivariable-adjusted logistic regression for MetS according to the daily intake of individual antioxidant components.

	Model 1		Model 2		Model 3	
Variables	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Vitamin A, mcg/day						
Q1	Ref		Ref		Ref	
Q2	1.06 (0.92,1.21)	0.448	0.99 (0.86,1.15)	0.935	1.02 (0.87,1.19)	0.825
Q3	0.85 (0.74,0.98)	0.024	0.77 (0.67,0.89)	<0.001	0.81 (0.69,0.94)	0.007
Q4	0.85 (0.74,0.97)	0.020	0.77 (0.67,0.89)	<0.001	0.81 (0.70,0.95)	0.008
p for trend	0.002		<0.001		<0.001	
Vitamin E, mg/day						
Q1	Ref		Ref		Ref	
Q2	0.81 (0.70,0.94)	0.005	0.78 (0.67,0.90)	0.001	0.75 (0.64,0.88)	<0.001
Q3	0.82 (0.71,0.94)	0.004	0.78 (0.67,0.89)	<0.001	0.74 (0.64,0.86)	<0.001
Q4	0.69 (0.60,0.79)	<0.001	0.64 (0.55,0.74)	<0.001	0.59 (0.50,0.70)	<0.001
p for trend	<0.001		<0.001		<0.001	
Vitamin C, mg/day						
Q1	Ref		Ref		Ref	
Q2	0.89 (0.79,1.00)	0.053	0.81 (0.72,0.91)	<0.001	0.83 (0.73,0.94)	0.004
Q3	0.84 (0.72,0.98)	0.024	0.75 (0.64,0.88)	<0.001	0.79 (0.67,0.92)	0.003
Q4	0.67 (0.58,0.76)	<0.001	0.60 (0.52,0.69)	<0.001	0.64 (0.55,0.74)	<0.001
p for trend	<0.001		<0.001		<0.001	
Zinc, mg/day						
Q1	Ref		Ref		Ref	
Q2	0.98 (0.85,1.13)	0.809	0.99 (0.86,1.14)	0.902	1.01 (0.87,1.18)	0.882
Q3	0.95 (0.82,1.10)	0.507	0.97 (0.84,1.13)	0.710	0.96 (0.82,1.13)	0.649
Q4	1.03 (0.91,1.17)	0.600	1.10 (0.96,1.26)	0.167	1.12 (0.97,1.30)	0.112
p for trend	0.684		0.227		0.208	
Selenium, mcg/day						
Q1	Ref		Ref		Ref	
Q2	1.03 (0.88,1.21)	0.697	1.07 (0.91,1.25)	0.427	1.08 (0.91,1.28)	0.356
Q3	0.99 (0.84,1.17)	0.894	1.05 (0.89,1.24)	0.540	1.06 (0.88,1.27)	0.539
Q4	1.03 (0.90,1.18)	0.666	1.16 (0.99,1.35)	0.066	1.19 (0.98,1.45)	0.077
p for trend	0.828		0.090		0.121	
Carotenoids, mcg/day						
Q1	Ref		Ref		Ref	
Q2	0.86 (0.76,0.98)	0.027	0.84 (0.73,0.96)	0.010	0.88 (0.77,1.02)	0.084
Q3	0.89 (0.79,1.00)	0.059	0.86 (0.76,0.97)	0.014	0.94 (0.81,1.07)	0.338
Q4	0.78 (0.68,0.89)	<0.001	0.76 (0.66,0.86)	<0.001	0.83 (0.72,0.96)	0.026
p for trend	0.001		<0.001		0.034	

*Adjusted for age, gender, ethnicity, NHANES years cycle, marital status, education level, PIR, smoke, alcohol status, physical activity, ALT, AST, eGFR, CVD, energy, and coffee intake.

with vitamin E through glutathione peroxidase[43], and zinc deficiency affects the mobilization of vitamin A in the liver[44]. Thus, although individual dietary antioxidants may help fight the development and progression of MetS, it would be more meaningful to assess their combined effects on MetS risk.

There were several noteworthy advantages in this study. First, this study has a large sample size. Second, CDAI is more applicable than TAC, as it is a summary score of various dietary antioxidants and represents the antioxidant characteristics of individuals. Moreover, the study only considers antioxidants from food sources, not dietary supplements. Therefore, it enables us to focus on people with relatively low dietary antioxidant intake (it is reported that more than 50% of United States adults use dietary antioxidant supplements, including antioxidant vitamins and trace elements)[45].

Limitations

This study has several limitations. As mentioned above, causality between CDAI and MetS was not established due to the nature of the cross-sectional study, so basic and prospective research is still necessary to explore the mixed effect of CDAI on MetS and its biological mechanism further. The impact of any subsequent changes in the dietary habits could not be taken

into consideration because the diet was only collected by a two 24-hour dietary recall. Although several common variables were fully adjusted in this study, there were still several unmeasured confounders that were not considered.

Conclusions

In summary, the present study suggested that CDAI was non-linearly associated with decreased MetS risk. For this reason, high adherence to combined intake of antioxidants could be a promising and effective approach to prevent MetS for public.

Authors' Contributions

Guarantor of integrity of the entire study: Qiang She. Study concepts: Zhiyin Liao, Minghan Xiao.
Study design: Zhiyin Liao, Minghan Xiao. Definition of intellectual content: Zhiyin Liao, Minghan Xiao.
Literature research: Zhiyin Liao, Minghan Xiao. Data acquisition: Bingquan Xiong. Data analysis: Bingquan Xiong. Statistical analysis: Bingquan Xiong. Manuscript preparation: Zhiyin Liao, Minghan Xiao. Manuscript editing: Zhiyin Liao, Minghan Xiao. Manuscript review: Zhiyin Liao, Qiang She.

Data Availability

The original contributions presented in this study are included in the article/supplementary materials; further inquiries can be directed to the corresponding author/s..

Ethics Approval

The study was reviewed and approved by the National Center for Health Statistics Research Ethics Review Board (Protocol#2021-05).

Informed Consent

As all participants' data are from a public database, informed consent was not applicable. The participants' information was non-identifiable.

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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