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Association of oxidative balance score with all-cause mortality among individuals with chronic kidney disease: a cohort study

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Abstract

Background The Oxidative Balance Score (OBS) is employed for evaluating the body's overall level of oxidative stress. This study aimed to investigate the association between OBS and mortality in individuals with chronic kidney disease (CKD) using a cohort study design.

Methods We used data from adult participants(≥ 20 years old) in the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2018. CKD is diagnosed based on the Kidney Disease Improving Global Outcomes (KDIGO) guidelines. OBS, which consists of 16 dietary factors and 4 lifestyle factors, categorized into pro-oxidants and antioxidants, with a total score range of 0 to 40 .The OBS was divided into four quartiles (Q1 to Q4), with Q1 (5–12), Q2 (13–18), Q3 (19–24), and Q4 (25–36). We excluded patients with missing data on OBS, CKD, and key covariates. Cox regression analysis were used to examine the relationship between OBS and all-cause mortality in CKD patients. Sensitivity analyses included subgroup analysis and multiple imputation.

Results We included a total of 3,984 patients with CKD. During an average follow-up period of 103 months, 1,263 cases (31.7%) of all-cause mortality were recorded. In the fully adjusted model, compared to Q1 the hazard ratios (HRs) and 95% confidence intervals (CIs) for Q4 were as follows: OBS 0.80 (0.68, 0.95) ($p=0.012$), dietary OBS 0.78 (0.66, 0.92) ($p=0.003$), and lifestyle OBS 0.83 (0.70, 0.99) ($p=0.038$). Our sensitivity analyses further confirmed the robustness of these results.

Conclusions Higher OBS was negatively correlated with all-cause mortality risk in American adults with CKD.

Keywords Oxidative balance score, Mortality, Chronic kidney disease, Cohort study NHANES

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Introduction

CKD is a major worldwide health issue, placing a considerable load on public health globally. The Global Burden of Disease study in 2017 estimated that CKD was responsible for 1.2 million fatalities worldwide. Furthermore, a staggering 1.4 million fatalities were ascribed to cardiovascular ailments associated with the deterioration of kidney performance [1]. From 1990 to 2019, the ranking of CKD as a leading cause of death rose from 19th to 11th place [2]. It is predicted that CKD will rank as the fifth primary reason for global mortality by 2040 [3].

The definition of oxidative stress(OS) [4]involves the disruption of the balance between pro-oxidants and antioxidants, serving as a primary mechanism in various chronic diseases, such as CKD and atherosclerosis [5–8]. OS induces inflammation and abnormal signaling pathways, leading to damage to cell membranes, proteins, and nucleic acids, which in turn impairs tissue function and promotes disease progression [9, 10].For example, in CKD, OS-induced damage leads to mitochondrial dysfunction, exacerbating kidney injury and fibrosis [11]. In atherosclerosis, the accumulation of oxidized low-density lipoprotein (LDL) is driven by OS and is closely associated with coronary heart disease and stroke [12]. Diet and lifestyle significantly affect oxidative stress levels.Antioxidants such as vitamin C, carotenoids, magnesium, and selenium can neutralize free radicals and alleviate OS, while excessive iron intake and smoking increase free radical production, thereby worsening OS [13]. Since oxidative balance is influenced by multiple factors, the effect of any single factor often cannot fully reflect the overall balance [14]. Therefore, a comprehensive measurement of various pro-oxidants and antioxidants can provide a more accurate indicator of OS, helping to understand its impact on chronic diseases and mortality and offering effective strategies for disease prevention and management.

OBS [15] is a comprehensive indicator that reflects the overall balance of exposure to pro-oxidants and antioxidants from diet and lifestyle. Zhang et al. [16]reported that the OBS includes 16 dietary factors and 4 lifestyle factors, comprising 15 antioxidants and 5 pro-oxidants, and calculates a comprehensive score. A higher OBS indicates a greater exposure to antioxidants compared to pro-oxidants. Current evidence suggests that OBS is negatively associated with the prevalence and mortality of various diseases, such as cardiovascular disease, diabetes, metabolic syndrome and cancer [17–21].Recent studies have reported a negative correlation between OBS and the incidence of CKD [22–25]. Due to decreased antioxidant defense mechanisms and the stimulation of reactive oxygen species(ROS) release by uremic toxins [26], OS is elevated in CKD patients. These processes accelerate CKD progression and increase the risk of mortality. Therefore, it is crucial to comprehensively assess the association between OS and mortality in CKD patients.

As the association between OBS and mortality risk in adult CKD patients is currently unclear, our study used data from the NHANES in the United States to investigate the relationship between OBS and all-cause mortality risk in CKD patients.

Materials and methods

Study populations

This study was an observational cohort study based on the population, utilizing data from the NHANES. NHANES, conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention, is a recurring population-based survey conducted every two years. It evaluates the nutritional and health status of the U.S. population. The NHANES was conducted with approval from the Ethics Review Board of the National Center for Health Statistics, and written consent was obtained from all participants.

This study analyzed data from ten consecutive cycles of NHANES, spanning from 1999 to 2018. Initially, we included 55,081 adults aged 20 and above, and after excluding pregnant individuals(n=1,547), a total of 53,534 were included in the analysis. Subsequently, we excluded patients with missing OBS calculations(n=24,243) and CKD calculations(n=230). After further excluding non-CKD patients (n=24,654), a total of 4,407 CKD participants with complete OBS scores were included. We excluded participants with missing covariate data (n=421) and those lost to follow-up (n=2), resulting in a final sample of 3,984 adult participants (Fig. 1B).

Definition of OBS

Zhang et al. established the OBS utilized in this research [16], and it had been extensively validated previously. It comprised 16 dietary factors and 4 lifestyle factors(Fig. 1A). Based on their impact on OS, these components were categorized into pro-oxidants and antioxidants. A higher OBS underscored the increasing strength of antioxidant exposure. The components of Dietary OBS comprised fiber, carotenoids, riboflavin, niacin, vitamin B6, total folate, vitamin B12, vitamin C, vitamin E, calcium, magnesium, zinc, copper, selenium, total fat, and iron. Lifestyle OBS comprised body mass index (BMI), physical activity, alcohol consumption, and cotinine. Total fat and iron intake from dietary components, as well as BMI, alcohol consumption, and cotinine from lifestyle factors, were classified as pro-oxidants, while the remaining factors were classified as antioxidants. All OBS components were divided into three groups by gender and assigned scores accordingly. Antioxidant components were scored as 0, 1, or 2, whereas pro-oxidant

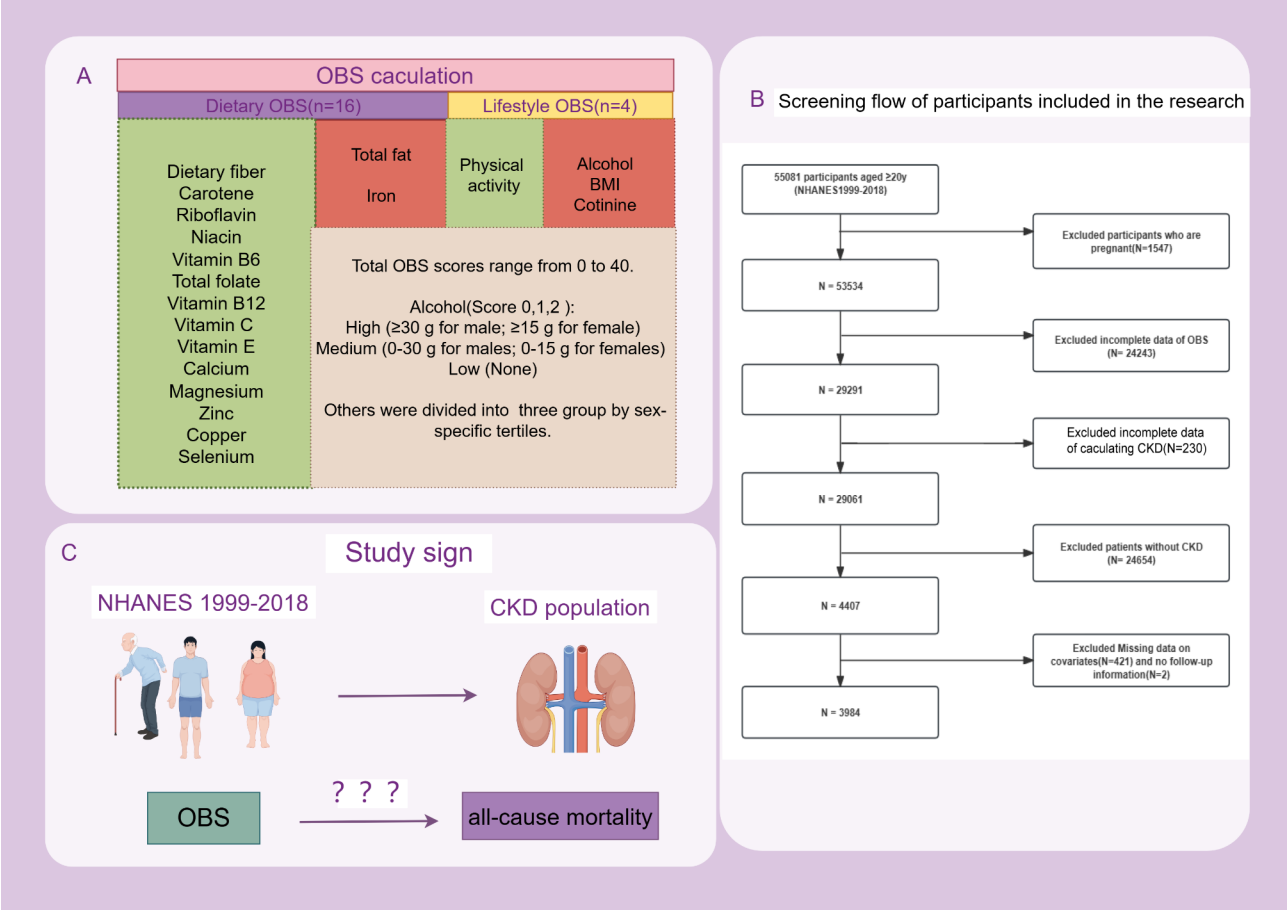

Fig. 1 Overview of the study design. **A**. OBS calculation.The total oxidative balance score(OBS) includes dietary OBS ($n=16$) and lifestyle OBS ($n=4$). Within the OBS components, there are 5 pro-oxidants (represented by red squares) and 15 antioxidants (represented by green squares).Scoring Scheme: Alcohol consumption: Non-drinkers: 2 points; Moderate drinkers (women: 0–15 g/day; men: 0–30 g/day): 1 point; Heavy drinkers (women ≥ 15 g/day; men ≥ 30 g/day): 0 points. Other components: These are divided into tertiles (three groups) based on sex-specific ranges.The total OBS score ranges from 0 to 40 points. B.Screening flow of participants included in the research. C. Study design

components were scored inversely. The total OBS score ranged from 0 to 40. Table S1 displayed the detailed scoring scheme of OBS.In this study, participants were categorized into four quartiles (Q1 to Q4) based on their total OBS scores. The specific ranges for each quartile can be found in Table S2.

Dietary intake data in NHANES from 1999 to 2002 were based on a single 24-hour, face-to-face dietary recall. Since 2003, the survey included two 24-hour dietary recall interviews, with the initial face-to-face interview followed by a telephone interview conducted 3 to 10 days later [27]. In this study, we used data from the initial dietary recall interview to assess daily dietary intake. The evaluation of every nutritional element adhered to the recommendations outlined in the Food and Nutrient Database for Dietary Studies (FNDDS) offered by the USDA [28]. Furthermore, the nutrient calculations did not take into account nutrients acquired from dietary supplements or medications. The alcohol consumption information was obtained from a 24-hour recall. Serum nicotine was utilized as a substitute for smoking since it encompasses levels of both active and passive smoking. The BMI was computed by dividing the weight by the height squared (kg/m^2). METs were computed weekly using information from household interviews about leisure activities performed by individuals in the previous 30 days. For more information on data collection, please refer to previous studies [16].

Definition of CKD and outcome

The KDIGO guidelines [2] utilize estimated glomerular filtration rate (eGFR) and the urine albumin to creatinine ratio (UACR) to establish the diagnosis of CKD. Using the equation [29] from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), the eGFR was computed for every individual. The eGFR was divided into five categories: G1 (≥90 ml/min/1.73 m^2); G2 (60–89 ml/min/1.73m^2); G3a (45–59 ml/min/1.73 m^2); G3b (30–44 ml/min/1.73m^2); G4 (15–29 ml/min/1.73m^2); G5 (<15 ml/min/1.73m^2). The UACR was divided into three

levels: A1 (normal to mildly elevated, UACR < 30 mg/g or < 3 mg/mmol); A2 (moderately elevated, UACR 30–300 mg/g or 3–30 mg/mmol); A3 (severely elevated, UACR > 300 mg/g or > 30 mg/mmol). In this research, CKD was characterized as satisfying the requirements of UACR level A2 and eGFR level G3a or more severe.

All-cause mortality in CKD patients was the main result. Participants in the NHANES were prospectively followed from the date of enrollment until December 31, 2019. By matching various data such as social security numbers, names, birth dates, race/ethnicity, gender, birth status, and residence status, the National Center for Health Statistics (NCHS) connected the mortality records to the National Death Index (NDI).

Assessment of covariates

Based on prior research [30], the covariates in our study included age, gender, race, marital status, education level, poverty-to-income ratio (PIR), cholesterol, triglycerides, diabetes, hypertension, and cardiovascular disease (CVD). Household interviews provided demographic data, with race/ethnicity categorized as non-Hispanic white, non-Hispanic black, Mexican American, and other racial groups. Marital status included married, unmarried, cohabiting with a partner, as well as individuals who were widowed, divorced, or separated. Educational attainment was categorized as less than high school, high school diploma or equivalent, and above high school. PIR was categorized into three groups: ≤1.3, 1.3–3.5, and > 3.5. The diagnosis of hypertension was made using the criteria of having a systolic blood pressure of at least 140 mmHg or a diastolic blood pressure of at least 90 mmHg, or by self-reporting having hypertension. CVD was characterized as a self-reported identification of coronary heart disease, chest pain, stroke, heart attack, or heart failure. Diabetes was diagnosed by a doctor, based on a 2-hour oral glucose tolerance test with blood glucose levels equal to or greater than 11.1 mmol/L, random blood glucose levels equal to or greater than 11.1 mmol/L, fasting glucose levels equal to or greater than 7.0 mmol/L, glycated hemoglobin HbA1c levels above 6.5%, or the administration of diabetes medications or insulin.

Statistical analysis

Means (standard deviations) or medians (interquartile ranges, IQR) were used to present continuous variables, whereas categorical variables were described using numerical values (percentages) in the feature description. ANOVA and chi-square tests were used to analyze the variations in variable characteristics among quartiles of OBS groups. To evaluate the effect of OBS on the overall mortality in the CKD population, we utilized Cox regression analysis.OBS were treated as both continuous variables and categorical variables (quartiles).Linear trend tests were performed by treating the quartiles of OBS as a continuous variable. The analysis was conducted in three progressively adjusted models. Model 1: No adjustment for covariates to assess the basic relationship between OBS and all-cause mortality risk. Model 2: Adjusted for basic demographic variables including age, sex, race/ethnicity, and marital status, to account for their influence on the relationship between OBS and mortality risk. Model 3: Further adjusted for additional factors including PIR, education level, cholesterol, triglycerides, diabetes, hypertension, and CVD, to more comprehensively control for confounding variables and improve the accuracy of the analysis. Additionally, Kaplan-Meier survival curves were used to estimate survival across different OBS levels, and the log-rank test was applied to evaluate survival differences among the groups, providing a visual comparison of the association between OBS and all-cause mortality risk.In our final analysis, we independently investigated the relationship between dietary OBS and lifestyle OBS with all-cause mortality among individuals with CKD.

We performed the following sensitivity analysis. First, to detect potential interactions, we conducted stratified analyses based on age (< 65 years and ≥ 65 years), gender (male and female), marital status (single, non-single), education level (less than high school, high school and above), hypertension (yes and no), diabetes (yes and no), and history of CVD (yes and no). We applied weights according to the NHANES analytic guidelines and used multiple imputation methods to handle missing data, reassessing the robustness of our results.

All analyses were conducted using R, version 4.2.2 (R Project for Statistical Computing), the survey package, version 4.1-1, and Free Statistics software version 1.9.2 (Beijing FreeClinical Medical Technology Co., Ltd.). Significance was attributed to statistics with two-sided P values below 0.05.

Results

Characteristics

Table 1 presents the characteristics of adults grouped by OBS quartiles. The study included 3,984 adult individuals, with an average age of 61.3 ± 17.2 years, of which 50.9% were male. Significant variations were observed in all indicators, including age, gender, race, marital status, education level, PIR, history of CVD, diabetes, and hypertension, across OBS quartiles (all $p < 0.05$). Individuals in the highest OBS quartile exhibited higher PIR, a higher proportion of females, a higher proportion of non-Hispanic white individuals, higher educational attainment, a higher rate of marriage, and lower prevalence of CVD (refer to Table 1). Table S2 displayed the distribution of each OBS component across OBS quartiles, indicating that participants with higher OBS scores

Table 1 Baseline characteristics by oxidative balance score quartile

Characteristics	Total (*N* = 3984)	oxidative balance score				
		Q1 (*N* = 825)	Q2 (*N* = 1066)	Q3 (*N* = 1061)	Q4 (*N* = 1032)	*P*-value
Age, Mean (SE), y	61.3 ± 17.2	61.9 ± 16.7	62.3 ± 17.1	61.2 ± 17.3	59.9 ± 17.6	0.011
Sex, No. (%)						< 0.001
Male	2026 (50.9)	469 (56.8)	561 (52.6)	512 (48.3)	484 (46.9)	
Female	1958 (49.1)	356 (43.2)	505 (47.4)	549 (51.7)	548 (53.1)	
Race/ethnicity, No. (%)						< 0.001
Non-Hispanic White	2157 (54.1)	399 (48.4)	547 (51.3)	590 (55.6)	621 (60.2)	
Non-Hispanic Black	793 (19.9)	215 (26.1)	238 (22.3)	202 (19)	138 (13.4)	
Mexican American	538 (13.5)	113 (13.7)	152 (14.3)	133 (12.5)	140 (13.6)	
Other Hispanic	232 (5.8)	48 (5.8)	67 (6.3)	62 (5.8)	55 (5.3)	
Others	264 (6.6)	50 (6.1)	62 (5.8)	74 (7)	78 (7.6)	
Marital status, No. (%)						0.014
Married	2096 (52.6)	391 (47.4)	575 (53.9)	551 (51.9)	579 (56.1)	
Never married	424 (10.6)	99 (12)	96 (9)	113 (10.7)	116 (11.2)	
Living with partner	201 (5.0)	48 (5.8)	50 (4.7)	53 (5)	50 (4.8)	
Other	1263 (31.7)	287 (34.8)	345 (32.4)	344 (32.4)	287 (27.8)	
Education level, No. (%)						< 0.001
Less than high school	1040(26.1)	282 (34.2)	332 (31.1)	235 (22.1)	191 (18.5)	
High school or equivalent	1008(25.3)	256 (31)	247 (23.2)	268 (25.3)	237 (23)	
Above high school	1936(48.6)	287 (34.8)	487 (45.7)	558 (52.6)	604 (58.5)	
PIR, mean (SE)	2.5 ± 1.6	2.1 ± 1.4	2.4 ± 1.5	2.6 ± 1.5	2.8 ± 1.6	< 0.001
CVD [a]. history, No. (%)						0.003
Yes	931 (23.4)	221 (26.8)	267 (25)	235 (22.1)	208 (20.2)	
No	3053(76.6)	604 (73.2)	799 (75)	826 (77.9)	824 (79.8)	
Hypertension, No. (%)						< 0.001
Yes	2690 (67.5)	591 (71.6)	725 (68)	725 (68.3)	649 (62.9)	
No	1294 (32.5)	234 (28.4)	341 (32)	336 (31.7)	383 (37.1)	
DM history, No. (%)						0.047
Yes	1338 (33.6)	297 (36)	379(35.6)	342 (32.2)	320 (31)	
No	2646 (66.4)	528 (64)	687(64.4)	719 (67.8)	712 (69)	
Cholesterol(mg/dL), median (IQR)	134.0 (91.0, 201.0)	133.0 (92.0, 193.0)	135.0 (96.0, 204.0)	135.0 (91.0, 200.0)	134.0 (86.0, 203.5)	0.546
Triglycerides(mg/dL), median (IQR)	192.0(163.8, 222.0)	189.0 (165.0, 223.0)	193.0 (163.0, 220.0)	193.0 (163.0, 223.0)	192.0 (163.0, 222.0)	0.832

Abbreviations: CVD, Cardiovascular disease; DM, Diabetes mellitus; NHANES, National Health and Nutrition Examination Survey; PIR, Poverty Income Ratio; SE, Standard error

[a]. Includes congestive heart failure, coronary heart disease, angina, heart attack and stroke

had increased dietary antioxidant intake and higher levels of physical activity.

Association between OBS and all-cause mortality

During an average follow-up period of 103 months, a total of 1,263 cases (31.7%) of all-cause mortality were recorded, accounting for 31.7% of the cohort. Kaplan-Meier survival curves indicated a significantly higher survival probability associated with higher OBS levels (P=0.00029; Figure S1). This result suggests that higher OBS levels are linked to a lower risk of all-cause mortality, a finding consistently observed across all models.

Specifically, a significant negative correlation between OBS and overall mortality in CKD patients was observed in all three models (Table 2). When OBS was treated as a categorical variable, all models demonstrated a gradual decrease in CKD all-cause mortality risk with increasing OBS quartiles (P value for trend < 0.05). In the fully adjusted model, compared to the Q1 (reference group), Q4 had a 20% reduction in the risk of overall mortality (HR = 0.80, 95% CI 0.68–0.95, p=0.012). In Model 3, the highest groups (Q4) for dietary OBS and lifestyle OBS were associated with a 22% (HR = 0.78, 95% CI 0.66–0.92, p=0.003) and 17% (HR = 0.83, 95% CI 0.70–0.99, p=0.038) reduction in CKD all-cause mortality, respectively (Table 3).

Sensitivity analyses

In order to examine if the correlation between OBS and the likelihood of CKD all-cause death remained

Table 2 Association of OBS with all-cause mortality in CKD in 1999–2018 NHANES

	Model 1		Model 2		Model 3	
	HR (95%CI)	***P* value**	**HR (95%CI)**	***P* value**	**HR (95%CI)**	***P*-value**
OBS score						
	0.98 (0.98 ~ 0.99)	< 0.001	0.98 (0.97 ~ 0.99)	< 0.001	0.99 (0.98 ~ 1)	0.007
OBS Quartile						
Q1	Ref		Ref		Ref	
Q2	0.96 (0.83 ~ 1.12)	0.635	0.87 (0.74 ~ 1.01)	0.064	0.88 (0.75 ~ 1.03)	0.103
Q3	0.83 (0.71 ~ 0.97)	0.017	0.8 (0.69 ~ 0.94)	0.007	0.88 (0.75 ~ 1.03)	0.117
Q4	0.73 (0.62 ~ 0.86)	< 0.001	0.72 (0.61 ~ 0.85)	< 0.001	0.8 (0.68 ~ 0.95)	0.012
P for trend		< 0.001		< 0.001		0.019

OBS, oxidative balance score; HR, hazard ratio; CI, confidence interval; Q: quartile. CVD, cardiovascular disease

Model 1 was an unadjusted model. Model 2 adjusted for age, sex, race and marital status. Model 3: Model 2 + PIR, education level, Cholesterol, Triglycerides, diabetes, hypertension, and CVD

Table 3 Association of dietary/lifestyle OBS with all-cause mortality in CKD in 1999–2018 NHANES

	Model 1		Model 2		Model 3	
	HR (95%CI)	***P* value**	**HR (95%CI)**	***P* value**	**HR (95%CI)**	***P*-value**
Dietary OBS Quartile						
Q1	Ref		Ref		Ref	
Q2	0.89 (0.76 ~ 1.03)	0.116	0.83 (0.71 ~ 0.96)	0.015	0.84 (0.72 ~ 0.98)	0.026
Q3	0.81 (0.7 ~ 0.94)	0.005	0.83 (0.72 ~ 0.97)	0.016	0.9 (0.77 ~ 1.04)	0.162
Q4	0.63 (0.54 ~ 0.74)	< 0.001	0.7 (0.6 ~ 0.83)	< 0.001	0.78 (0.66 ~ 0.92)	0.003
P for trend		< 0.001		< 0.001		0.011
Lifestyle OBS Quartile						
Q1	Ref		Ref		Ref	
Q2	1.14 (0.94 ~ 1.38)	0.178	0.85 (0.7 ~ 1.03)	0.096	0.87 (0.72 ~ 1.06)	0.162
Q3	1.21 (1.01 ~ 1.45)	0.038	0.75 (0.63 ~ 0.9)	0.002	0.78 (0.65 ~ 0.93)	0.007
Q4	1.38 (1.16 ~ 1.64)	< 0.001	0.77 (0.65 ~ 0.92)	0.004	0.83 (0.7 ~ 0.99)	0.038
P for trend		< 0.001		0.005		0.056

OBS, oxidative balance score; HR, hazard ratio; CI, confidence interval; Q: quartile. CVD, cardiovascular disease

Model 1 was an unadjusted model. Model 2 adjusted for age, sex, race and marital status. Model 3: Model 2 + PIR, education level, Cholesterol, Triglycerides, diabetes, hypertension, and CVD

consistent among different subcategories, we conducted stratified analyses. The P-values of the interaction were greater than 0.05 for all subgroups (age, gender, marital status, education, diabetes, hypertension, and CVD), suggesting that the findings of our study remained consistent across all subgroups (Table 4). Multiple imputation and NHANES weighting indicated that OBS, dietary OBS, and lifestyle OBS remained inversely associated with the risk of all-cause mortality in CKD patients, demonstrating robust results (Tables S3 and S4).

Discussion

To the best of our understanding, this study conducted as a cohort study was the initial evaluation of the correlation between OBS relying on NHANES information and overall mortality in individuals with CKD. This study confirmed that individuals with CKD who exhibited higher OBS levels experienced a reduced risk of mortality from all causes. Furthermore, the risk of all-cause mortality among individuals with CKD was independently linked to dietary and lifestyle OBS. Subgroup analyses and sensitivity analyses further confirmed the robustness of the overall study findings.

An imbalance between the components that prevent and promote oxidation leads to oxidative stress, which is a complex process influenced by multiple factors. Numerous studies have identified oxidative stress as a key factor in the progression of various diseases, such as CKD, Non-Alcoholic Fatty Liver Disease, and CVD [10, 31]. It has been demonstrated that lifestyle factors and dietary choices are associated with levels of oxidative stress and are significantly related to disease progression and mortality risk. Higher dietary fiber intake was associated with a reduced risk of cardiovascular diseases [32]. Dietary components such as vitamins C, D, E, and zinc exhibited anti-inflammatory and antioxidant properties, modulated immunity, and were beneficial for preventing infectious diseases like COVID-19 [33, 34]. Smoking and lack of physical activity were significantly associated with an increased risk of CVD [35]. Notably, dietary factors and lifestyle habits often coexist, with exposures to pro-oxidants or antioxidants potentially counteracting or

Table 4 Subgroup analysis of the associations between OBS and all-cause mortality in CKD in 1999–2018 NHANES

Stratification	Q1	Q2	Q3	Q4	*P* for interaction
Age group					
<65	Ref	0.92 (0.66 ~ 1.28)	0.96 (0.68 ~ 1.35)	0.57(0.38 ~ 0.86)	0.055
≥65	Ref	0.84 (0.71 ~ 1.01)	0.81 (0.68 ~ 0.98)	0.84(0.69 ~ 1.01)	
Gender					
Male	Ref	0.89 (0.73 ~ 1.09)	0.98 (0.79 ~ 1.21)	0.82 (0.66 ~ 1.03)	0.607
Female	Ref	0.89 (0.69 ~ 1.15)	0.81 (0.63 ~ 1.04)	0.82 (0.63 ~ 1.07)	
Education level					
less than high school	Ref	0.84(0.65 ~ 1.07)	0.88 (0.66 ~ 1.15)	0.77 (0.56 ~ 1.05)	0.881
high school or above	Ref	0.90 (0.74 ~ 1.11)	0.88 (0.71 ~ 1.07)	0.81 (0.66 ~ 1.01)	
Marital status					
No-single	Ref	0.77(0.62 ~ 0.96)	0.76 (0.61 ~ 0.95)	0.74 (0.58 ~ 0.95)	0.214
Single	Ref	1.03 (0.83 ~ 1.29)	1.07 (0.84 ~ 1.35)	0.89 (0.71 ~ 1.14)	
Hypertension					
Yes	Ref	0.93 (0.78 ~ 1.1)	0.91 (0.76 ~ 1.09)	0.84 (0.69 ~ 1.01)	0.521
No	Ref	0.7 (0.49 ~ 1.01)	0.79 (0.54 ~ 1.15)	0.71 (0.48 ~ 1.06)	
DM					
Yes	Ref	0.94 (0.73 ~ 1.2)	1.09 (0.83 ~ 1.42)	0.97 (0.73 ~ 1.29)	0.204
No	Ref	0.86 (0.71 ~ 1.05)	0.76 (0.62 ~ 0.93)	0.72 (0.58 ~ 0.89)	
CVD					0.142
Yes	Ref	0.76 (0.59 ~ 0.98)	0.85 (0.65 ~ 1.12)	0.69 (0.52 ~ 0.92)	
No	Ref	0.99 (0.82 ~ 1.22)	0.92 (0.75 ~ 1.13)	0.89 (0.72 ~ 1.1)	

Data are presented as HR (95% CI). Adjusted for age, sex, race, marital status age, gender, education level, PIR, Cholesterol, Triglycerides, diabetes, hypertension, and CVD. CKD, chronic kidney disease; CVD, cardiovascular disease; DM, Diabetes mellitus; OBS, oxidative balance score

cooperating with each other, complicating the determination of individual factors' effects on disease risk [15]. Therefore, a comprehensive measurement of various pro-oxidants and antioxidants can provide a more accurate overall oxidative stress indicator.

OBS is a more comprehensive approach that integrates various dietary and lifestyle factors into a single score to assess overall oxidative balance. Studies have shown that higher OBS levels are significantly associated with a reduced risk of metabolic-associated fatty liver disease (MASLD) [36]and cardiovascular disease (CVD) [37]. Moreover, adopting a healthy diet and lifestyle that increases OBS has been found to help prevent CKD [23]. Therefore, OBS has garnered increasing attention from researchers, not only as a screening tool for predicting chronic disease risk but also as a useful instrument for public health education to promote healthy diets and lifestyle habits in the prevention of chronic diseases. However, there are still relatively few studies examining the association between OBS and the risk of death from specific diseases. Previous studies [18, 38] have reported an association between OBS and all-cause mortality risk, but these studies were limited to specific populations such as elderly women or those at high risk of CVD, and did not comprehensively include all relevant factors. Additionally, some researchers [20, 21]have reported a negative association between OBS and all-cause mortality in populations with diabetes or metabolic syndrome. Given that CKD patients are particularly vulnerable to oxidative stress damage, exploring the association between OBS and mortality risk in this group is of significant clinical and public health importance.

Our study demonstrated that elevated OBS levels were linked to reduced all-cause mortality risk among CKD individuals. Separate analyses of dietary and lifestyle OBS confirmed this association consistently. Previous studies have shown that antioxidant-rich foods and a healthy lifestyle have long been demonstrated to have potential in delaying CKD progression and reducing CKD mortality risk [39–43]. However, the underlying biological mechanisms of this association remain unclear.The kidneys are rich in mitochondria, making them vulnerable to ROS attacks, leading to oxidative stress damage. High levels of oxidative stress may lead to nucleic acid oxidation damage, insulin resistance, impaired endothelial function, and promote vascular calcification, exacerbating CKD progression and cardiovascular complications, thereby increasing mortality risk [44].Additionally, oxidative stress can promote the release of inflammatory mediators, cell apoptosis, and fibrosis, accelerating kidney damage and loss of function. Moreover, CKD patients typically exhibit impaired antioxidant defense systems. On one hand, dietary restrictions on fruits and vegetables lead to reduced levels of vitamins C and E; on the other hand, vitamin C and selenium levels are lost during dialysis, and the function of glutathione (GSH) clearance mechanisms diminishes [45]. Finally, sedentary lifestyles and reduced physical activity are common among CKD

patients and can also impact the clearance of reactive oxygen species [46].Therefore, we hypothesize that the association between OBS and reduced mortality risk in CKD patients may be related to higher antioxidant capacity, which could have a protective effect on kidney health. This finding provides a preliminary theoretical basis for the potential role of enhanced antioxidant capacity in improving CKD prognosis and suggests possible directions for research on lifestyle and dietary interventions. However, further studies are needed to explore the causal relationship of this association and its practical applications in clinical interventions.

Limitation

This study has several limitations. Firstly, the reliance on self-reported dietary data may lead to recall bias, which could affect the accuracy of OBS calculations and subsequent analyses. Additionally, excluding participants with missing OBS or CKD data could lead to selection bias, potentially impacting the generalizability of the findings. However, we used multiple imputation methods to minimize such errors to the greatest extent.Secondly, because NHANES is cross-sectional data, it is not possible to infer causal relationships between OBS levels and CKD mortality risk. Additionally, since the NHANES survey primarily targets the general U.S. population and does not include hospitalized or institutionalized individuals (such as nursing home residents), caution should be exercised when generalizing the results to other populations and clinical settings. Fourth, although we used the widely recognized KDIGO guidelines to define CKD, the generalizability of the findings to populations using different CKD criteria should still be considered. Finally, despite extensive adjustments for known confounding factors, there may still be unmeasured or residual confounders, such as cultural differences in diet and lifestyle, which could influence the relationship between OBS and all-cause mortality. Therefore, the study results should be interpreted with caution.

Conclusion

This study reveals a significant negative correlation between higher OBS levels and all-cause mortality among adult CKD patients in the United States. These findings suggest that better oxidative balance may be associated with a lower risk of mortality, indicating that oxidative balance could have an important role in CKD risk management. Future research should focus on determining causal relationships and exploring potential mechanisms, including broader populations and longitudinal data, to confirm these findings.

Abbreviations

OBS	Oxidative Balance Score
CKD	Chronic kidney disease
OS	Oxidative stress
NHANES	National Health and Nutrition Examination Survey
BMI	Body mass index
FNDDS	Food and Nutrient Database for Dietary Studies
KDIGO	Kidney Disease Improving Global Outcomes
eGFR	Glomerular filtration rate
UACR	Urine albumin to creatinine ratio
PIR	Poverty-to-income ratio
CVD	Cardiovascular disease

Supplementary Information

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Supplementary Material 1

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Author contributions

LC reviewed and approved the final manuscript. HT conducted the analysis. YL drafted the manuscript and conceived the study design. LC contributed to result interpretation. CH critically revised the manuscript for intellectual content.

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Data availability

Publicly available datasets were analyzed in this study. This data can be found here: www.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Research Ethics Review Board of the National Center for Health Statistics (NCHS). The specific dates of ethical approval for each survey cycle can be found in the relevant NHANES protocols or ethical documents. Written informed consent was obtained from all patients/participants prior to their involvement in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Collaboration GBDCKD. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the global burden of Disease Study 2017. Lancet. 2020;395(10225):709–33. https://doi.org/10.1016/S0140-6736(20)30045-3.
2. Kidney Disease: Improving Global Outcomes CKDWG. KDIGO 2024 Clinical Practice Guideline for the evaluation and management of chronic kidney disease. Kidney Int. 2024;105(4S):S117–314. https://doi.org/10.1016/j.kint.2023.10.018.
3. Foreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. Lancet. 2018;392(10159):2052–90. https://doi.org/10.1016/S0140-6736(18)31694-5.

4. Sies H, Berndt C, Jones DP. Oxidative stress. Annu Rev Biochem. 2017;86:715–48. https://doi.org/10.1146/annurev-biochem-061516-045037.
5. Reuter S, Gupta SC, Chaturvedi MM, Aggarwal BB. Oxidative stress, inflammation, and cancer: how are they linked? Free Radic Biol Med. 2010;49(11):1603–16. https://doi.org/10.1016/j.freeradbiomed.2010.09.006.
6. Dounousi E, Papavasiliou E, Makedou A, Ioannou K, Katopodis KP, Tselepis A, et al. Oxidative stress is progressively enhanced with advancing stages of CKD. Am J Kidney Dis. 2006;48(5):752–60. https://doi.org/10.1053/j.ajkd.2006.08.015.
7. Kim BH, Lee ES, Choi R, Nawaboot J, Lee MY, Lee EY, et al. Protective effects of Curcumin on Renal oxidative stress and lipid metabolism in a rat model of type 2 Diabetic Nephropathy. Yonsei Med J. 2016;57(3):664–73. https://doi.org/10.3349/ymj.2016.57.3.664.
8. Kattoor AJ, Pothineni NVK, Palagiri D, Mehta JL. Oxidative stress in atherosclerosis. Curr Atheroscler Rep. 2017;19(11):42. https://doi.org/10.1007/s11883-017-0678-6.
9. Scholze A, Jankowski J, Pedraza-Chaverri J, Evenepoel P. Oxidative stress in chronic kidney disease. Oxid Med Cell Longev. 2016;2016:8375186. https://doi.org/10.1155/2016/8375186.
10. Forman HJ, Zhang H. Targeting oxidative stress in disease: promise and limitations of antioxidant therapy. Nat Rev Drug Discov. 2021;20(9):689–709. https://doi.org/10.1038/s41573-021-00233-1.
11. Ho HJ, Shirakawa H. Oxidative stress and mitochondrial dysfunction in chronic kidney disease. Cells. 2022;12(1). https://doi.org/10.3390/cells12010088.
12. Yang X, Li Y, Li Y, Ren X, Zhang X, Hu D, et al. Oxidative stress-mediated atherosclerosis: mechanisms and therapies. Front Physiol. 2017;8:600. https://doi.org/10.3389/fphys.2017.00600.
13. Halliwell B. Understanding mechanisms of antioxidant action in health and disease. Nat Rev Mol Cell Biol. 2024;25(1):13–33. https://doi.org/10.1038/s41580-023-00645-4.
14. Kong SY, Goodman M, Judd S, Bostick RM, Flanders WD, McClellan W. Oxidative balance score as predictor of all-cause, cancer, and noncancer mortality in a biracial US cohort. Ann Epidemiol. 2015;25(4):256–62. https://doi.org/10.1016/j.annepidem.2015.01.004.
15. Hernandez-Ruiz A, Garcia-Villanova B, Guerra-Hernandez E, Amiano P, Ruiz-Canela M, Molina-Montes E. A review of a Priori defined oxidative balance scores relative to their components and impact on Health outcomes. Nutrients. 2019;11(4). https://doi.org/10.3390/nu11040774.
16. Zhang W, Peng SF, Chen L, Chen HM, Cheng XE, Tang YH. Association between the oxidative balance score and telomere length from the National Health and Nutrition Examination Survey 1999–2002. Oxid Med Cell Longev. 2022;2022:1345071. https://doi.org/10.1155/2022/1345071.
17. Talavera-Rodriguez I, Fernandez-Lazaro CI, Hernandez-Ruiz A, Hershey MS, Galarregui C, Sotos-Prieto M, et al. Association between an oxidative balance score and mortality: a prospective analysis in the SUN cohort. Eur J Nutr. 2023;62(4):1667–80. https://doi.org/10.1007/s00394-023-03099-8.
18. Mao Z, Prizment AE, Lazovich D, Bostick RM. Associations of dietary and lifestyle oxidative balance scores with mortality risk among older women: the Iowa women's Health Study. Eur J Nutr. 2021;60(7):3873–86. https://doi.org/10.1007/s00394-021-02557-5.
19. Ilori TO, Wang X, Huang M, Gutierrez OM, Narayan KM, Goodman M, et al. Oxidative balance score and the risk of end-stage Renal Disease and Cardiovascular Disease. Am J Nephrol. 2017;45(4):338–45. https://doi.org/10.1159/000464257.
20. Xu Z, Liu D, Zhai Y, Tang Y, Jiang L, Li L, et al. Association between the oxidative balance score and all-cause and cardiovascular mortality in patients with diabetes and prediabetes. Redox Biol. 2024;76:103327. https://doi.org/10.1016/j.redox.2024.103327.
21. Xu Z, Lei X, Chu W, Weng L, Chen C, Ye R. Oxidative balance score was negatively associated with the risk of metabolic syndrome, metabolic syndrome severity, and all-cause mortality of patients with metabolic syndrome. Front Endocrinol (Lausanne). 2023;14:1233145. https://doi.org/10.3389/fendo.2023.1233145.
22. Cao Y, Zhou Y, Zhong Y, Liao X, Chen X, Pi Y. Association between oxidative balance score in adults with and without chronic kidney disease: 2011–2028 NHANES. Front Nutr. 2024;11:1374719. https://doi.org/10.3389/fnut.2024.1374719.
23. Son DH, Lee HS, Seol SY, Lee YJ, Lee JH. Association between the oxidative balance score and incident chronic kidney disease in adults. Antioxid (Basel). 2023;12(2). https://doi.org/10.3390/antiox12020335.
24. Yin Y, Zhao C, Niu Y, Qi J, Zhang Y, Lu B. Associations between oxidative balance score and chronic kidney disease events in US adults: a population-based study. Sci Rep. 2024;14(1):13743. https://doi.org/10.1038/s41598-024-64147-9.
25. Wen H, Li X, Chen J, Li Y, Yang N, Tan N. Association of oxidative balance score with chronic kidney disease: NHANES 1999–2018. Front Endocrinol (Lausanne). 2024;15:1396465. https://doi.org/10.3389/fendo.2024.1396465.
26. Pieniazek A, Bernasinska-Slomczewska J, Gwozdzinski L. Uremic toxins and their relation with oxidative stress Induced in patients with CKD. Int J Mol Sci. 2021;22(12). https://doi.org/10.3390/ijms22126196.
27. Shan Z, Rehm CD, Rogers G, Ruan M, Wang DD, Hu FB, et al. Trends in Dietary Carbohydrate, protein, and Fat Intake and Diet Quality among US adults, 1999–2016. JAMA. 2019;322(12):1178–87. https://doi.org/10.1001/jama.2019.13771.
28. Bodner-Montville J, Ahuja JKC, Ingwersen LA, Haggerty ES, Enns CW, Perloff BP. USDA Food and Nutrient Database for Dietary studies: released on the web. J Food Compos Anal. 2006;19:S100–7. https://doi.org/10.1016/j.jfca.2006.02.002.
29. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604–12. https://doi.org/10.7326/0003-4819-150-9-200905050-00006.
30. Chen H, Tang H, Huang J, Luo N, Zhang X, Wang X. Life's essential 8 and mortality in US adults with chronic kidney disease. Am J Nephrol. 2023;54(11–12):516–27. https://doi.org/10.1159/000533257.
31. Steven S, Frenis K, Oelze M, Kalinovic S, Kuntic M, Bayo Jimenez MT, et al. Vascular inflammation and oxidative stress: Major triggers for Cardiovascular Disease. Oxid Med Cell Longev. 2019. https://doi.org/10.1155/2019/7092151.
32. Reynolds AN, Akerman A, Kumar S, Diep Pham HT, Coffey S, Mann J. Dietary fibre in hypertension and cardiovascular disease management: systematic review and meta-analyses. BMC Med. 2022;20(1):139. https://doi.org/10.1186/s12916-022-02328-x.
33. Shakoor H, Feehan J, Al Dhaheri AS, Ali HI, Platat C, Ismail LC, et al. Immune-boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: could they help against COVID-19? Maturitas. 2021;143:1–9. https://doi.org/10.1016/j.maturitas.2020.08.003.
34. Hu W, Mao H, Guan S, Jin J, Xu D. Systematic Review and Meta-analysis of the Association between Malnutrition and Risk of Depression in the Elderly. Alpha Psychiatry. 2024;25(2):183–9. https://doi.org/10.5152/alphapsychiatry.2024.231336.
35. Mallah MA, Soomro T, Ali M, Noreen S, Khatoon N, Kafle A, et al. Cigarette smoking and air pollution exposure and their effects on cardiovascular diseases. Front Public Health. 2023;11:967047. https://doi.org/10.3389/fpubh.2023.967047.
36. Tan Z, Wu Y, Meng Y, Liu C, Deng B, Zhen J, et al. Trends in oxidative balance score and prevalence of Metabolic Dysfunction-Associated Steatotic Liver Disease in the United States: National Health and Nutrition Examination Survey 2001 to 2018. Nutrients. 2023;15(23). https://doi.org/10.3390/nu15234931.
37. Chen X, Wang C, Dong Z, Luo H, Ye C, Li L, et al. Interplay of sleep patterns and oxidative balance score on total cardiovascular disease risk: insights from the National Health and Nutrition Examination Survey 2005–2018. J Glob Health. 2023;13:04170. https://doi.org/10.7189/jogh.14.04170.
38. Talavera-Rodriguez I, Fernandez-Lazaro CI, Hernández-Ruiz Á, Hershey MS, Galarregui C, Sotos-Prieto M, et al. Association between an oxidative balance score and mortality: a prospective analysis in the SUN cohort. Eur J Nutr. 2023;62(4):1667–80. https://doi.org/10.1007/s00394-023-03099-8.
39. Kelly JT, Palmer SC, Wai SN, Ruospo M, Carrero JJ, Campbell KL, et al. Healthy dietary patterns and risk of Mortality and ESRD in CKD: a Meta-analysis of Cohort studies. Clin J Am Soc Nephrol. 2017;12(2):272–9. https://doi.org/10.2215/CJN.06190616.
40. Saglimbene VM, Wong G, Ruospo M, Palmer SC, Garcia-Larsen V, Natale P, et al. Fruit and vegetable intake and mortality in adults undergoing maintenance hemodialysis. Clin J Am Soc Nephrol. 2019;14(2):250–60. https://doi.org/10.2215/CJN.08580718.
41. Hu Y, Cai X, Zhang N, Li Y, Mao Y, Ge S, et al. Relation between Dietary Carotenoid Intake, serum concentration, and Mortality Risk of CKD patients among US adults: National Health and Nutrition Examination Survey 2001–2014. Front Med (Lausanne). 2022. https://doi.org/10.3389/fmed.2022.871767.
42. Nakano T, Tanaka S, Tsuruya K, Kitazono T. Low intake of beta carotene and dietary fiber from vegetables and fruits in patients with chronic kidney disease. Sci Rep. 2022;12(1):19953. https://doi.org/10.1038/s41598-022-24471-4.

43. Kelly JT, Su G, Zhang L, Qin X, Marshall S, Gonzalez-Ortiz A, et al. Modifiable Lifestyle Factors for Primary Prevention of CKD: a systematic review and Meta-analysis. J Am Soc Nephrol. 2021;32(1):239–53. https://doi.org/10.1681/ASN.2020030384.
44. Jomova K, Raptova R, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, et al. Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. Arch Toxicol. 2023;97(10):2499–574. https://doi.org/10.1007/s00204-023-03562-9.
45. Rapa SF, Di Iorio BR, Campiglia P, Heidland A, Marzocco S. Inflammation and oxidative stress in chronic kidney disease-potential therapeutic role of minerals, vitamins and Plant-Derived metabolites. Int J Mol Sci. 2019;21(1). https://doi.org/10.3390/ijms21010263.
46. Hoshino J. Renal Rehabilitation: Exercise intervention and nutritional support in Dialysis patients. Nutrients. 2021;13(5). https://doi.org/10.3390/nu13051444.

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