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Nonlinear association between blood urea nitrogen to creatinine ratio and obstructive sleep apnea: a cross-sectional study from NHANES

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Abstract

Background Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder that is closely associated with metabolic conditions. The Blood Urea Nitrogen to Creatinine Ratio(BUCR) is commonly utilized as a tool for evaluating renal function, particularly in cases where there are concerns about pre-renal or renal causes of azotemia. However, the connection between OSA and BUCR is not yet fully understood.

Methods This study examined the link between BUCR and OSA in adults over 20 using National Health and Nutrition Examination Surveys(NHANES) data from 2005–2008. Logistic regression models adjusted for multiple variables were used to analyze the relationship. The non-direct correspondence relationship were explored with a smooth curve and a two-part linear regression model, which revealed a threshold effect. Subgroup analyses were conducted to assess variations among different populations.

Results The survey, encompassing a total of 8826 participants, revealed that the median age of all respondents was 48 years, with a notable OSA prevalence of 51.3%. Upon adjusting for pertinent covariates using Model III(age, sex, marital status, education level, BMI, smoking status, drinking, hypertension, and diabetes), our findings indicated a significant association between OSA and BUCR, as evidenced by an odds ratio (OR) of 1.01 (95% CI: 1.00–1.02, $P=0.005$). Furthermore, the risk association was found to be non-linear, featuring an inflection point for BUNR at 10.86. This non-linear relationship adds complexity to our understanding of the interplay between OSA and BUCR. In addition, a subgroup analysis underscored the influence of diabetes on the association between BUCR and OSA.

Conclusion This study reveals a significant correlation between elevated BUCR levels and the incidence of OSA, particularly in the presence of diabetes. This discovery underscores the necessity for additional research to investigate the underlying mechanisms and ramifications of this connection within the diabetic context.

Keywords Blood Urea Nitrogen, NHANES, Creatinine, Obstructive Sleep Apnea

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Introduction

Obstructive sleep apnea is a prevalent sleep disorder marked by recurrent disruptions in breathing and inadequate ventilation during sleep [1]. Its clinical manifestations commonly include snoring, frequent awakenings due to suffocation sensations, excessive daytime sleepiness, and in severe cases, may result in cognitive decline or behavioral abnormalities, as well as a diminished quality of life [2, 3]. If left untreated, OSA can give rise to serious health complications such as hypertension, cardiovascular diseases, metabolic syndrome, and Chronic Kidney Disease (CKD) [4–6]. The prevalence of moderate to severe sleep-disordered breathing (apnea–hypopnea index, measured as events/hour ≥ 15) is reported as follows: 10% among men aged 30–49, 17% among men aged 50–70, 3% among women aged 30–49, and 9% among women aged 50–70, emphasizing its importance as a widespread health issue [7].

OSA as a cause of CKD is intricately linked to hypoxemia, oxidative stress, sympathetic nerve activation, endothelial dysfunction, and the activation of the renin–angiotensin–aldosterone system(RAAS), among others, including hypertension [8, 9]. Furthermore, OSA may elevate the likelihood of renal injury, while CKD, in turn, can amplify the risk of OSA [10–14]. Nevertheless, observational research findings have been inconsistent. For instance, in patients with coronary artery disease(CAD), the severity of OSA did not exhibit an independent association with CKD [15]. Additionally, a separate study revealed that OSA alone does not constitute a standalone risk factor for CKD development [16].

Crucially, OSA holds a marked relationship with alterations in metabolism, particularly in renal function. A prior investigation revealed a notable correlation between the frequency of obstructive apnoea events per hour and biomarkers such as BUN and CR. Additionally, research conducted by Agrawal et al. [17]. Demonstrated an increase in albumin:creatinine ratio (ACR) among OSA patients, further linking ACR to the sleep apnea hypopnea index (AHI) [18]. Nevertheless, another study disputes this finding [19].

A series of previous meta-analyses have shown that OSA is associated with some potential biomarkers, such as triglyceride and glucose(TyG), brain-derived neurotrophic factor(BDNF), Galectin-3(Gal-3), and endothelial function marker endocan [20–23]. However, we remain unclear about whether BUCR is a potential biomarker for OSA, and therefore, there is an urgent need to identify comprehensive biomarkers for assessing the risk of OSA. BUCR, a biochemical marker of renal function, exhibits an increase in various conditions such as hyperdissimilation, high protein diets, gastrointestinal bleeding, and urea reabsorption. Conversely, a decrease in the ratio may be attributed to inadequate protein intake, liver failure, diabetes, dialysis, and the administration of diuretics [24]. Thus, the primary aim of this study is to investigate the potential correlation between BUCR and OSA, utilizing the NHANES database.

Material and methods

Study design and population

This survey examines the link between BUCR and OSA using NHANES data from 2005–2008. NHANES provides a detailed view of the US population, including health, diet, and demographics. The survey uses a complex sampling method. That is, multi-stage stratified sampling: the first stage divides the United States into multiple primary sampling units (PSU), often based on geographical areas. In the second stage, household households are selected in the selected PSU. Finally, the eligible individuals were selected as the survey object. At the same time, it will be stratified according to age, gender, race and other factors to ensure that each layer has sufficient sample size to make the sample more representative. More info on NHANES is at www.cdc.gov/nchs/Nhanes/. Participants consented and the study was approved by the National Center for Health Statistics Ethics Committee. The initial sample had 20,497 individuals, excluding those under 20(9583 samples), lacking BUCR(BUN and CR, 1139 samples), missing OSA and other covariate datas with incomplete info(949 samples). The selection process is shown in Fig. 1.

Calculation of BUCR index

The BUCR index was computed using the methodology [25]:

$$BUCR = \frac{BUN(mmol/L) \times 2.8 \times 88.4}{CR(mmol/l)}$$

Diagnosis of OSA

OSA Diagnosis: 1) A history of OSA was specified in the self-report. 2) High-risk for OSA was defined by responses to three questions in NHANES: (1) Chronic daytime sleepiness despite ≥ 7 h sleep per night, occurring 16–30 times monthly; (2) Breathing pauses, snorting, or gasping ≥ 3 nights/week; (3) Loud snoring ≥ 3 nights/week [26].

OSA patients by subject BMI values: 1) BMI > 30 kg/m^3 for obesity; 2) normal weight for 18.5 kg/m^3 < BMI < 25 kg/m^3); 3) overweight for 25 kg/m^3 < BMI < 30 kg/m^3; 4) underweight for 0 kg/m^3 < BMI < 18.5 kg/m^3.

OSA patients smoking history 1)Never smoker: not smoking more than 100 cigarettes in a lifetime. 2) Former smoker: smoking over 100 in a lifetime but not smoking

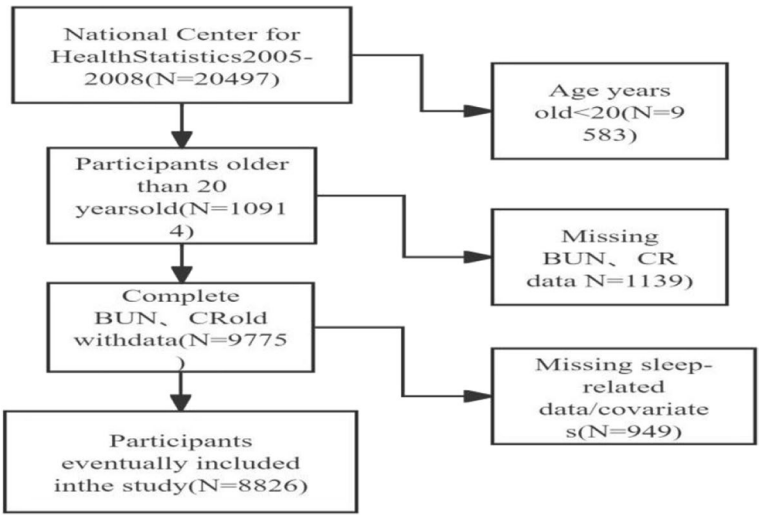

Fig. 1 Flowchart illustrating the process of participant selection. BUN, Blood urea nitrogen; CR, creatinine

now. 3)Current smoker: smoking over 100 in a lifetime and smoking now.

Statistical analysis

Analytical methods using R 4.2.2 and Empowerstats 2.0 software were applied, considering NHANES sampling design with weights. Descriptive statistics included adjusted proportions (%) and weighted averages with dispersion measures. Chi-square tests evaluated qualitative parameters, and ANOVA was used for quantitative data. Multivariable Logit Models (I, II, III) assessed the OR and 95% CI for the BUCR index in relation to OSA. Model I was unadjusted, Model II adjusted for sex and age, and Model III included age, sex, marital status, education level, BMI, smoking status, drinking, hypertension, and diabetes. The study explored differences among populations and investigated nonlinear associations between OSA and the BUCR index using curve fitting and linear regression for threshold analysis. A P value < 0.05 was considered statistically significant.

Results

Participant baseline characteristics

The study presented in this paper involved a total of 8,826 participants, with the youngest being 20 years old and the eldest 85, with a median age of 48. The sample consisted of 51.3% individuals with OSA, 51.2% women, 11.5% with diabetes, and 33.5% with hypertension. The median BUCR index was 13.931. Statistically significant differences ($P < 0.05$) were noted among various factors, such as sex, age, educational attainment, marital status, smoking and alcohol consumption patterns, Body Mass Index (BMI), hypertension, and diabetes status, as shown in Table 1.

Analysis of the Correlation Between BUCR index and OSA

After considering all pertinent variables, each incremental unit of BUCR exhibited a 1% positive correlation with the incidence of OSA (OR = 1.01, 95% CI: 1.00–1.02, $P = 0.005$). This finding underscores a robust and significant positive relationship between BUCR and OSA. Furthermore, upon analyzing the quartiles of BUCR, it was observed that individuals in Quartile 4 had a 17% elevated risk of OSA compared to those in Quartile 1 (OR = 1.17, 95% CI: 1.03–1.33, $P = 0.020$), as detailed in Table 2.

Analysis of RCS curve and threshold effects

The RCS curve depicted in Fig. 2 clearly illustrates that the correlation between OSA and BUCR is nonlinear in nature. A delve into the threshold effect pinpoints a critical turning point at 10.86. Below this threshold, each unit decrease in BUCR index elevates OSA risk by 5% (OR = 1.05, 95% CI: 1.01–1.09, $P = 0.014$). Conversely, upon surpassing 10.86, this association loses statistical significance (OR = 1.01, 95% CI: 0.996–1.02, $P = 0.189$), with the likelihood ratio test yielding a P-value of 0.068 (Table 3), Indicating that BUCR may no longer serve as a reliable marker of OSA risk above a certain threshold. This may be an important reference for clinicians to assess patients' susceptibility to OSA sensitivity.

Table 1 Key Demographic and Baseline Characteristics of Individuals Participating in the NHANES between 2005 and 2008

BUCR index quartile						
Various	**Overall, *N* = 8826**	**Q1, *N* = 2315 (26.22%)**	**Q2, *N* = 2010 (22.77%)**	**Q3, *N* = 2165 (24.52%)**	**Q4, *N* = 2336 (26.47%)**	***P*-value**
Age(years)	48.000 (20.000–85.000)	40.000 (20.000–85.000)	46.000 (20.000–85.000)	50.000 (20.000–85.000)	59.500(20.000–85.000)	< 0.001
BUN(mmol/L)	4.280(0.360–34.990)	2.860 (0.360–22.490)	3.930(1.790–20.350)	4.640(1.790–19.990)	6.070(2.860–34.990)	< 0.001
CR(umol/L)	78.680(27.400–1573.520)	80.440 (28.290–1573.520)	79.560(35.360–450.840)	75.140(29.170–293.490)	70.720(27.400–328.850)	< 0.001
BUCR	13.931(2.016–48.766)	9.087(2.520–11.107)	12.495(11.112–13.755)	15.451(13.774–17.284)	20.000(17.285–48.766)	< 0.001
Sex(%)						< 0.001
Male	4303(48.8%)	1329(57.4%)	1090(54.2%)	1049(48.5%)	835(35.7%)	
Female	4523(51.2%)	986(42.6%)	920(45.8%)	1116(51.5%)	1501(64.3%)	
Age.group(%)						< 0.001
< 60 years	5872(66.5%)	1865(80.6%)	1439(71.6%)	1399 (64.6%)	1168 (50.0%)	
60–69 years	1405(15.9%)	252(10.9%)	295(14.7%)	352(16.3%)	506 (21.7%)	
70–79 years	988(11.2%)	145 (6.3%)	191(9.5%)	275(12.7%)	377(16.1%)	
80 + years	561 (6.4%)	52(2.2%)	85(4.2%)	139 (6.4%)	285(12.2%)	
Drinking(%)						< 0.001
Non-drinker	2658(30.1%)	626 (27.0%)	531(26.4%)	659 (30.4%)	842(36.0%)	
1–5 drinks/month	4266(48.3%)	1133(48.9%)	986(49.1%)	1039(48.0%)	1108(47.4%)	
5–10 drinks/month	695(7.9%)	214 (9.2%)	185(9.2%)	156(7.2%)	140(6.0%)	
10 + drinks/month	1207(13.7%)	342(14.8%)	308(15.3%)	311(14.4%)	246(10.5%)	
Smoking(%)						< 0.001
Never smoker	4600(52.1%)	1070(46.2%)	1020(50.7%)	1152(53.2%)	1358(58.1%)	
Former smoker	2263(25.6%)	479 (20.7%)	514(25.6%)	593(27.4%)	677(29.0%)	
Current smoker	1963(22.2%)	766 (33.1%)	476(23.7%)	420(19.4%)	301(12.9%)	
Education(%)						< 0.001
9-11th Grade	1441(16.3%)	424(18.3%)	297(14.8%)	343(15.8%)	377(16.1%)	
High School Grad/GED	2133(24.2%)	560 (24.2%)	484(24.1%)	518(23.9%)	571(24.4%)	
Less Than 9th Grade	1077(12.2%)	204 (8.8%)	201(10.0%)	282(13.0%)	390(16.7%)	
Some College or AA degree	2411(27.3%)	694(30.0%)	600 (29.9%)	573(26.5%)	544(23.3%)	
College Graduate or above	1764(20.0%)	433(18.7%)	428(21.3%)	449(20.7%)	454(19.4%)	
Hypertension(%)						< 0.001
No	5871(66.5%)	1696(73.3%)	1384(68.9%)	1433(66.2%)	1358(58.1%)	
Yes	2955(33.5%)	619(26.7%)	626(31.1%)	732(33.8%)	978(41.9%)	
Diabetes(%)						< 0.001
No	7815(88.5%)	2158(93.2%)	1819(90.5%)	1922 (88.8%)	1916(82.0%)	
Yes	1011(11.5%)	157(6.8%)	191(9.5%)	243(11.2%)	420(18.0%)	
BMI(%)						0.017
Overweight	3077(34.9%)	786(34.0%)	706(35.1%)	801 (37.0%)	784(33.6%)	
Obesity	3136(35.5%)	811(35.0%)	717(35.7%)	763 (35.2%)	845(36.2%)	
Normal weight	2474(28.0%)	670(28.9%)	549(27.3%)	583(26.9%)	672(28.8%)	
Underweight	139(1.6%)	48(2.1%)	38(1.9%)	18(0.8%)	35(1.5%)	
Martial status(%)						< 0.001
With partner	667(7.6%)	230(9.9%)	165(8.2%)	137(6.3%)	135(5.8%)	
Married	4824(54.7%)	1154(49.8%)	1086(54.0%)	1230(56.8%)	1354(58.0%)	
Single	3335(37.8%)	931(40.2%)	759(37.8%)	798(36.9%)	847(36.3%)	
OSA(%)						0.583
No	4300(48.7%)	1136(49.1%)	954(47.5%)	1054(48.7%)	1156(49.5%)	
Yes	4526(51.3%)	1179(50.9%)	1056(52.5%)	1111(51.3%)	1180(50.5%)	

Categorized according to BUCR quartiles. Median(Min–Max) for continuous variable N(%) for categorical variable

BUCR Blood Urea Nitrogen to Creatinine Ratio, *BMI* Body Mass Index, *BUN* Blood Urea Nitrogen, *CR* Creatinine, *OSA* Obstructive Sleep Apnea

Table 2 Multivariable logistic regression models examining the correlation between BUCR and OSA

Exposure	Model 1 OR (95%CI) *P*-value	Model 2 OR (95%CI) *P*-value	Model 3 OR (95%CI) *P*-value
BUCR index	1.00 (0.93, 1.20) 0.966	1.01 (1.01, 1.02) < 0.001	1.01 (1.00, 1.02) 0.005
BUCR index quartile			
Q1	Reference	Reference	Reference
Q2	1.05 (0.93, 1.18) 0.408	1.08 (0.96, 1.22) 0.192	1.10 (0.97, 1.24) 0.155
Q3	1.01 (0.90, 1.14) 0.823	1.10 (0.98, 1.24) 0.120	1.09 (0.96, 1.24) 0.162
Q4	0.98 (0.87, 1.10) 0.713	1.19 (1.05, 1.34) 0.007	1.17 (1.03, 1.33) 0.020

Model I featured no adjustment for covariates, whereas Model II incorporated adjustments for age and sex. Moving on to Model III, a comprehensive adjustment was made for age, sex, marital status, education level, BMI, smoking status, drinking, hypertension, and diabetes

BUCR Blood Urea Nitrogen to Creatinine Ratio, *OR* Odds Ratio, *CI* Confidence Intervals, *OSA* Obstructive Sleep Apnea

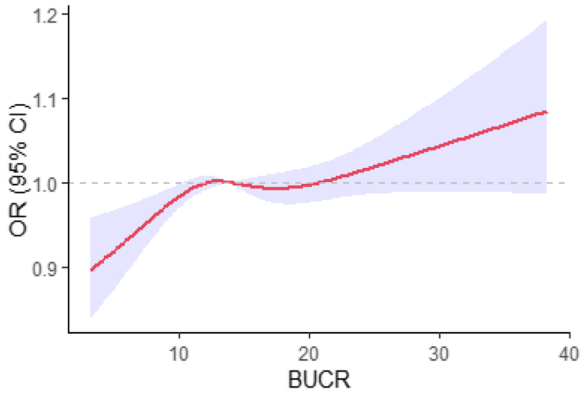

Fig. 2 The RCS curve between OSA and BUCR. BUCR, blood urea nitrogen to creatinine Ratio; OSA, Obstructive Sleep Apnea; OR, odds ratio; CI, confidence intervals

Table 3 The threshold effect analysis of the BUCR on OSA risk

Outcome	the effect size	95%CI	*P* value
Model 1 Fitting model by standard linear regression	1.014	(1.004–1.023)	0.004
Model 2 Fitting model by two-piece wise linear regression			
Inflection point	10.86		
< 10.86	1.05	(1.01–1.09)	0.014
> 10.86	1.01	(0.996–1.02)	0.189
P for likelihood ratio test			0.068

OR Odds Ratio, *CI* Confidence Intervals, *BUCR* Blood Urea Nitrogen to Creatinine Ratio, *OSA* Obstructive Sleep Apnea

Subgroup analysis

Multi-subgroup analyses and interaction tests, incorporating a diverse range of covariates, were conducted to rigorously evaluate the robustness of the BUCR-OSA correlation and to identify potential variations across diverse populations (Table 4). Within the majority of subgroups, a consistent and significant association between BUCR and OSA was observed. However, notable differences emerged among diabetic populations, with a *P*-value for interaction of 0.0221. Specifically, a stronger BUCR-OSA association was observed in non-diabetic individuals (OR = 0.999, 95% CI: 0.990–1.008, *P* = 0.7895) compared to diabetic patients (OR = 0.975, 95% CI: 0.954–0.995, *P* = 0.0165).

Discussion

This cross-sectional study encompassed a comprehensive representative sample of 8,826 American citizens aged 20 and above, sourced from the NHANES dataset. The rigorous analysis unveiled a crucial relationship between BUCR and the probability of OSA. Notably, this strong association persisted even after meticulous adjustments for a range of covariates, highlighting the potential of BUCR as a dependable marker for assessing OSA risk.

Further subgroup analysis illuminated that individuals with diabetes should exercise heightened vigilance in managing their BUCR. Importantly, the findings depicted a nonlinear trend, with a pivotal threshold established at a BUCR of 10.86, above which the association with OSA risk diminished significantly. These findings underscore the clinical significance of maintaining an optimal BUCR level as a potential strategy to mitigate the risk of OSA.

There is a complex interaction between OSA and CKD, as shown in Fig. 3. OSA can lead to renal injury, and the mechanism first involves renal pathological changes triggered by hypoxemia. Untreated OSA can directly cause hypoxemia, posing a persistent hypoxia threat to the kidneys. Within the tubular epithelium, hypoxemia can cause a range of pathological changes, including replacement of fibrotic_healthy tissue by scar tissue and injury of peripheral capillaries that disrupt the fragile vascular network of the kidney [8]. These changes have profound effects on kidney health and may lead to the deterioration of kidney health. Secondly, the vicious cycle of oxidative stress and inflammation is a common phenomenon when OSA patients experience intermittent hypoxia. Oxidative

Table 4 Stratified analysis of the correlation between BUCR and OSA

Various	OR(95%CI) *P*-value	P for interaction
Sex(%)		0.069
Male	0.997(0.983,1.010)0.6191	
Female	1.018(1.007,1.028)0.0009	
Age.group(%)		0.6196
< 60 years	1.005(0.994,1.016)0.3643	
60–69 years	0.995(0.976,1.015)0.6265	
70–79 years	1.007(0.984,1.031)0.5420	
80 + years	1.003(0.973,1.033)0.8515	
Drinking(%)		0.7529
Non-drinker	1.005(0.991,1.019)0.4845	
1–5 drinks/month	1.001(0.990,1.013)0.8448	
5–10 drinks/month	1.003(0.971,1.036)0.8540	
10 + drinks/month	0.990(0.966,1.014)0.4133	
Smoking(%)		0.9619
Never smoker	1.007(0.996,1.018)0.2017	
Former smoker	0.994(0.977,1.010)0.4594	
Current smoker	1.012(0.992,1.032)0.2275	
Education(%)		0.9968
9-11th Grade	0.979(0.960,0.998)0.0342	
High School Grad/GED	0.997(0.981,1.013)0.7368	
Less Than 9th Grade	1.020(0.998,1.042)0.0742	
Some College or AA degree	1.000(0.984,1.017)0.9997	
College Graduate or above	1.003(0.984,1.022)0.7607	
Hypertension(%)		0.4072
No	0.999(0.989,1.010)0.8632	
Yes	0.986(0.973,0.999)0.0331	
Diabetes(%)		0.0221
No	0.999(0.990,1.008)0.7895	
Yes	0.975(0.954,0.995)0.0165	
BMI(%)		0.9529
Overweight	0.992(0.979,1.006)0.2830	
Obesity	1.004(0.990,1.018)0.5886	
Normal weight	1.003(0.987,1.019)0.7059	
Underweight	0.942(0.882,1.007)0.0801	
Martial status(%)		0.8585
With partner	1.008(0.977,1.040)0.6256	
Married	0.995(0.984,1.007)0.4077	
Single	1.001(0.988,1.014)0.8782	

OR Odds Ratio, *CI* Confidence Intervals, *BUCR* Blood Urea Nitrogen to Creatinine Ratio, *OSA* Obstructive Sleep Apnea, *BMI* Body Mass Index

stress is characterized by the overproduction of Reactive Oxygen Species(ROS), the unstable molecules that cause damage to cells and tissues. The resulting exacerbated inflammation not only further worsens oxidative stress but also forms a vicious cycle that negatively affects endothelial function [27]. The endothelium, as a vascular lining, is essential for the maintenance of vascular health. Hypoxemia can cause oxidative stress response, leading to impaired mitochondrial function, the production of ROS beyond the scavenging capacity of the body's antioxidant defense system, and then trigger oxidative stress. Oxidative stress response will aggravate the process of fibrosis, ROS and other products can activate fibroblasts, promote their proliferation and migration, accelerate the synthesis and deposition of extracellular matrix, and eventually lead to fibrosis. Meanwhile, oxidative stress can also regulate a variety of signaling pathways related with fibrosis. The fibrosis process will affect the dispersion of oxygen, and with the increase of fibrous tissue, the thickness of the gas exchange barrier increases, hindering the diffusion of oxygen, which in turn exacerbates hypoxemia. Hyperactivity of the sympathetic nervous system plays an important role in the hypoxic response induced by OSA. This activation triggers a range of physiological responses, among which, include vasoconstriction leading to vascular narrowing and elevated blood pressure. This hypertension may develop into a refractory nature, namely a resistance to treatment, which leads to hypertension that is difficult to control. Furthermore, the sympathetic overdrive can impair renal function because the kidney has difficulty in maintaining homeostasis under systemic fluctuations triggered by OSA [28].

OSA may also lead to CKD progression through the activation of the RAAS. The hypoxic state activates RAAS, and recurrent intermittent hypoxia during sleep in OSA patients stimulates renin secretion by renal parabulb cells and activates RAAS [29]. Renin causes an increase in angiotensin generation, causing renal vasoconstriction, a decrease in renal blood flow, and an increase in internal glomerular pressure. The long-term effect can lead to glomerular injury and promote the development of CKD. RAAS activation triggers oxidative stress and inflammation, and angiotensin produces reactive oxygen species through various ways, inducing the expression of inflammatory factors such as tumor necrosis factor-α, interleukin-6, damages kidney cells and tissues, and aggravates kidney lesions [30]. Angiotensin promotes aldosterone secretion, leading to water and sodium retention, increasing blood volume, and causing peripheral vasocontraction, together with raising blood pressure. Long-term hypertension increases renal pressure load, damages renal blood vessels and glomeruli, and accelerates the progression of CKD.

There is a complex and bidirectional relationship between OSA and CKD [31]. In OSA patients, the upper airway repeatedly collapses and blocks during sleep, triggering apnea and hypopnea events, leading to intermittent hypoxia and hemodynamic changes. This hypoxic state stimulates excessive activation of RAAS, increased

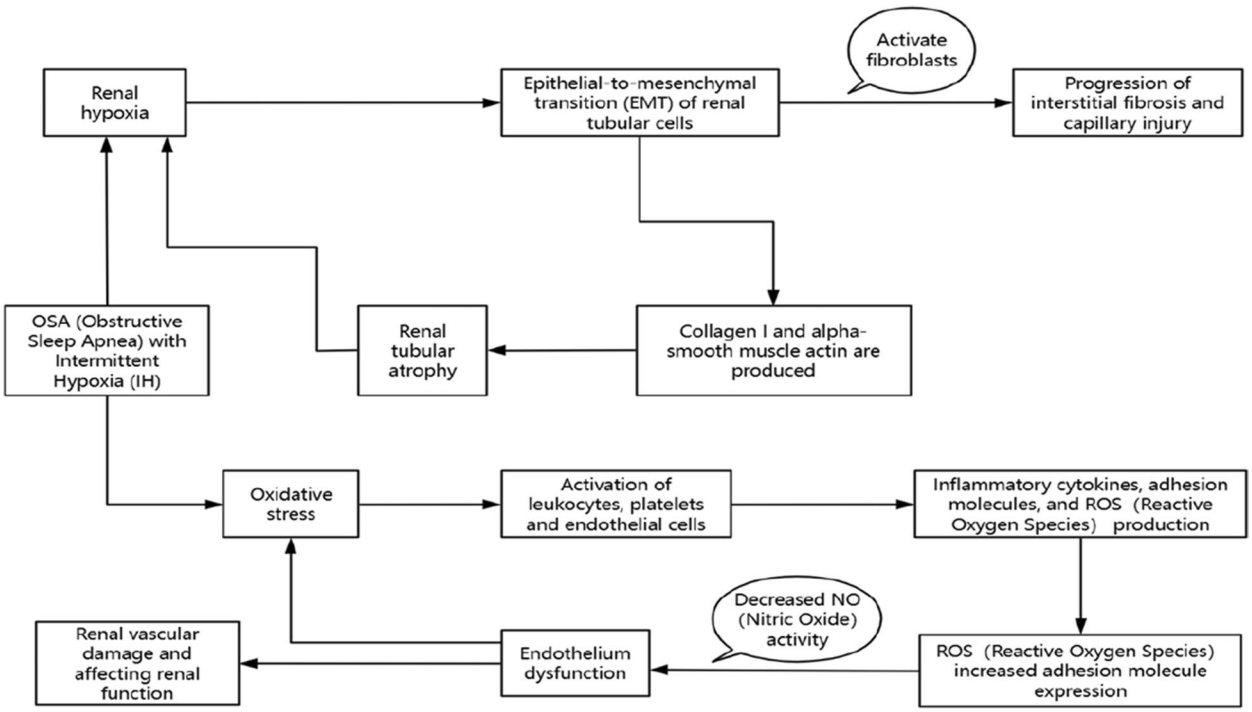

Fig. 3 The partial mechanism of OSA and renal injury

renin secretion, rising angiotensin levels, renal vasoconstriction, reduced renal blood flow, abnormal increase in internal glomerular pressure, impairing glomerular filtration function, appears albuminuria, and gradually causes renal injury [32]. At the same time, continuous intermittent hypoxia triggers the systemic inflammatory response and oxidative stress state, releases a large number of inflammatory factors, generates excessive ROS, attacks kidney cells, destroys the kidney tissue structure and function, and increases the risk of kidney injury. On the other hand, patients with CKD suffer from renal dysfunction and sodium metabolism. Excessive fluid accumulation in the tissue space, resulting in edema of the upper airway mucosa and surrounding tissues, narrowing of the airway lumen, increasing the risk of upper airway obstruction during sleep, and promoting the occurrence or aggravation of the existing disease [33, 34]. In addition, impaired renal function interferes with the regulatory function of the neuroendocrine system, and metabolites and toxins cannot be effectively excreted in vivo, which affects the normal regulation of respiration by the nervous system, reduces the sensitivity and stability of the respiratory center, increases the frequency of apnea and hypopnea events, and amplifies the risk of OSA [35]. Given the bidirectional relationship between OSA and CKD, clinicians need to adopt a comprehensive diagnosis and treatment strategy when facing these two diseases. For patients with OSA, renal function indicators should be closely monitored, and possible renal injury should be detected and intervened in time. For patients with CKD, sleep and respiratory status should be evaluated in detail, and OSA should be actively treated to improve the overall prognosis of patients and improve the quality of life.

The findings contribute to the expanding body of evidence linking Renal metabolism abnormality, specifically BUCR, to the risk of developing OSA. Previous investigations have primarily focused on the roles of BUN and CR concerning OSA. A study has found that CR and BUN levels in OSA patients were significantly increased compared with normal controls, and CR and BUN also increased with the aggravation of the disease [18]. Similarly, a recent study utilizing mendelian randomization has discovered a noteworthy correlation between OSA and BUN [36]. Concurrently, a cohort study conducted by Maliheh Moradzadeh et al. has further validated this observation [37]. Our research revealed a substantial correlation between OSA and BUCR, even after accounting for various confounding factors. Upon conducting additional subgroup analyses, we identified a significant influence of diabetes. Consequently, we hypothesize that diabetes may exacerbate the renal damage induced by OSA. These studies indirectly support this finding, suggesting that there may be a complex interaction between

kidney metabolism and OSA pathogenesis. According to our study, we observed a significant correlation between OSA and BUCR even after considering including age, sex and other possible confounding factors, further indicating that abnormal renal metabolism may exist in OSA patients. By further performing additional subgroup analyses, we successfully identified the significant impact role that diabetes plays in this correlation. Firstly, diabetes itself may cause damage to the kidney, and secondly, based on our results, it is reasonable to speculate that the presence of diabetes may exacerbate the renal damage caused by OSA. Moreover, these findings indirectly support our speculation, suggesting that they may have a complex interactive relationship between the metabolic processes in our kidneys and the pathogenesis of OSA.

However, a multitude of studies have produced varying results, emphasizing the urgent need for additional research and exploration. For instance, a retrospective study conducted in China, which meticulously examined the medical records of a large cohort of patients, found no association between CR and BUN levels and the AHI [38]. This study, which spanned over several years and involved a diverse group of participants, aimed to shed light on the potential biochemical markers of sleep apnea. Similarly, another study, which employed a different methodology and was conducted in a different geographical region, reported no significant correlation between blood urea nitrogen and the AHI [39]. This research, which utilized advanced statistical techniques to analyze its data, sought to understand the complex relationship between renal function and sleep-disordered breathing. These findings, while not definitive, may indicate that there is no clear correlation between BUN and CR levels with OSA. They suggest that other factors may play a more significant role in the pathophysiology of OSA, and that further investigation is warranted to unravel the intricate mechanisms underlying this prevalent sleep disorder. The results of this study reveal that BUCR may serve as a novel biomarker for the early identification of OSA patients. The finding provides a potential adjunct to the diagnosis and treatment of clinical OSA patients.

This study has several significant advantages, first, verifying the correlation between BUCR index and OSA for the first time. Secondly, the underlying mechanism of renal injury in patients with OSA. Finally, the NHANES database ensures the reliability of the research results due to its high-quality data, rigorous data collection procedures, standardized questionnaires, and physical examination procedures.

The conclusion derived from this study is robust, grounded in a vast and geographically diverse sample of US adults from NHANES, with meticulous adjustments for covariates. Nevertheless, it is crucial to acknowledge certain limitations. The inherent nature of this cross-sectional survey design restricts the ability to definitively establish a direct causal relationship between BUCR and OSA, and the possibility of reverse causality remains a consideration that cannot be conclusively dismissed. Furthermore, the study's findings are based on self-reported data, which may introduce a degree of subjectivity and potential bias. Although efforts were made to mitigate this through rigorous data validation and analysis, the potential for recall errors or misinterpretation of survey questions cannot be fully eliminated. Furthermore, it is possible for abnormal BUCR to arise from chronic kidney disease itself, independently of OSA, and the research failed to encompass an examination of BUCR and OSA in pediatric populations. Ultimately, this study did not include some factors such as CKD, which may have caused biased effects of confounding or omitted variables.

In conclusion, this study uncovers a substantial correlation between heightened BUCR levels and the predisposition to OSA, underscoring the significance of these discoveries in facilitating the implementation of timely preventive measures or swift interventions aimed at mitigating OSA.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent to publication
Consent for publication refers to consent for the publication of identifying images or other personal or clinical details of participants that compromise anonymity: not applicable.

Competing interests
The authors declare no competing interests.

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