



Obstructive sleep apnea is associated with postoperative dialysis in patients who underwent coronary artery bypass grafting

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Background: The incidence of obstructive sleep apnea (OSA) is significantly higher in patients who undergo coronary artery bypass grafting (CABG). OSA is correlated with a higher incidence of postoperative complications in patients undergoing CABG. However, whether OSA is associated with a decrease in renal function and a higher incidence of dialysis after CABG remains unclear.

Methods: Data from 178 consecutive patients who underwent isolated CABG at Anzhen Hospital between June 2019 and June 2020 were analyzed. Polysomnography was performed in all the patients.

Results: A total of 142 (79.8%) patients were diagnosed with OSA, 78 with mild OSA, and 64 with moderate-to-severe OSA. Compared to patients without OSA, the level of creatinine was significantly increased, and the level of estimated glomerular filtration rate (eGFR) was decreased in patients with OSA. In addition, the percentage of patients undergoing dialysis during the perioperative period increased with the severity of OSA (0.0% vs. 2.6% vs. 18.8%, $P=0.02$). Multiple linear regression analysis showed that age ($\beta=-0.29$, $P<0.001$), male sex ($\beta=-0.17$, $P=0.02$), apnea-hypopnea index (AHI) ($\beta=-0.35$, $P<0.001$), and creatinine ($\beta=-0.78$, $P<0.001$) were independently associated with a decrease in eGFR (adjusted $R^2=0.376$, $P<0.001$). However, in the multivariate logistic regression model, we found that the level of eGFR (OR =0.94, 95% CI: 0.89–0.99, $P=0.02$) and AHI (OR =1.07, 95% CI: 1.01–1.13, $P=0.02$) were independently associated with dialysis after CABG.

Conclusions: OSA is associated with a decrease in renal function and is an independent risk factor for postoperative dialysis in patients who undergo CABG.

Keywords: Obstructive sleep apnea (OSA); coronary artery bypass grafting (CABG); estimated glomerular filtration rate (eGFR); dialysis

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Introduction

Obstructive sleep apnea (OSA) is the most common type of sleep disordered breathing, with a prevalence of 4–32.9% in the general population (1). The incidence of OSA is significantly high in patients diagnosed with cardiovascular disease, and it has been recognized as one of the risk factors, including hypertension, heart failure, and coronary artery

disease (CAD) (2,3). In addition, the incidence of OSA among patients with CAD is >50%, according to different studies (4). OSA may increase the risk of perioperative complications in patients undergoing noncardiac surgery (5). Many studies have shown that OSA is associated with a higher prevalence of complications after cardiac surgery, mainly including valve procedures (6,7). Recently, few studies have reported that OSA is associated with a higher

incidence of complications after coronary artery bypass grafting (CABG), including atrial fibrillation, prolonged hospital stay, and higher incidence of acute kidney injury (8-11). However, studies on the relationship among OSA, renal function, and dialysis during the perioperative period are not fully understood for those who underwent CABG. Therefore, we mainly studied the effect of OSA on baseline renal function and the use of dialysis after CABG.

We present the current study in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/apm-21-180>).

Methods

Study population

This prospective epidemiologic study included consecutive patients diagnosed with CAD who were referred to Beijing Anzhen Hospital from June 2019 to June 2020. The inclusion criteria included patients whose age >18 years and diagnosis of CAD who underwent CABG. All study procedures were conducted in accordance with institutional guidelines. In addition, we excluded patients who had previously been diagnosed with OSA, those with severe disability, and those with chronic kidney disease who required dialysis before surgery. All patients underwent polysomnography (PSG) before surgery. In addition, all patients provided informed consent prior to enrollment. Approval from the Ethics Committee of Capital Medical University Affiliated Anzhen Hospital (No. 2020034X) was obtained before the start of the study, and each participant signed a written consent form. All studies were conducted in accordance with the ethical principles stated in the Declaration of Helsinki (as revised in 2013) in the present study.

Measurements of renal function and other parameters

Fasting blood samples were collected from all patients on the second day of admission. We calculate the glomerular filtration rate using the following equation: $a \times (\text{serum creatinine}/b)^c \times (0.993)^{\text{age}}$; $a=144$ for women or 141 for men; $b=0.7$ for women or 0.9 for men; $c=-0.329$ if the creatinine is less than 0.7 mg/dL or -1.209 if the creatinine is larger than 0.7 mg/dL for women; $c=-0.411$ if the creatinine is less than 0.7 mg/dL or -1.209 if the creatinine is larger than 0.7 mg/dL for men.

Assessment of postoperative outcomes

In the present study, postoperative outcomes during the perioperative period included acute kidney injury, worsening of heart failure, myocardial infarction, and hemodynamic instability. A previous study defined postoperative acute kidney injury as an increase in serum creatinine ≥ 0.3 mg/dL or ≥ 1.5 -fold the baseline requiring renal replacement therapy (12). Cardiac complications included worsening of heart failure and myocardial infarction, which was indicated by troponin I or by new ST segment elevations (>0.1 mV) (13). The need of vasopressor or inotropes 48 h after CABG was indicative of hemodynamic instability caused by any reasons of (13).

Polysomnography (PSG)

PSG was performed in all patients in our study using standard techniques (Embletta; Embla, UK). OSA is defined as at least 10 s of air flow through the mouth and nose in response to unsynchronized chest and abdominal effort. Hypopnea was defined as a 50% reduction in oral-nasal airflow for 10 s and a 4% reduction in oxygen saturation. Apnea (whether central, obstructive, or mixed) was defined as airflow cessation for ≥ 10 s. The classification of OSA is based on the presence of thoracic movements. The apnea-hypopnea index (AHI) was calculated using the total sleep time as the denominator. AHI was calculated as the average number of apnea and hypopnea per hour of sleep (14). In our study, mild and moderate to severe OSA was defined as $\text{AHI} \geq 5$ events/h and 15 events/h, respectively (15).

Statistical analysis

The results in the present study are shown as mean \pm SD, median (IQR), or percentage, when appropriate. Nominal variables were compared using χ^2 or Fisher's exact tests. One-way analysis of variance was used to compare the differences among the three groups. Multivariate linear regression models were used to determine the estimated glomerular filtration rate (eGFR). In addition, univariate and multivariate logistic regression analyses were used to determine the risk factors associated with dialysis after CABG. Variables with $P < 0.10$ on univariate analysis, age, sex, and body mass index were entered into a multivariate analysis. All reported probability values in the present study were two-tailed, and a P value < 0.05 was considered

statistically significant. The SPSS version 24.0 software (IBM) and Prism GraphPad 7.0 (GraphPad Software Inc., La Jolla, CA, USA) were used for calculation and illustration, respectively.

Results

Baseline characteristics of the study population

The baseline characteristics of the patients in our study are shown in *Table 1*, according to the severity of OSA. OSA was present in 142 (79.8%) patients, including 78 with mild OSA and 64 with moderate-to-severe OSA. There was no difference in age, body mass index, or male sex among the different groups. Compared with none and mild OSA patients, patients with moderate-to-severe OSA have a high prevalence of NYHA III or IV OSA. In addition, compared to patients without OSA, the prevalence of atrial fibrillation (AF) (0.0% vs. 12.8% vs. 21.9%, $P=0.03$) and stent implantation (0.0% vs. 7.7% vs. 21.9%, $P=0.01$) were higher in patients with OSA. Importantly, the level of creatinine was significantly increased with the severity of OSA, and the level of eGFR significantly decreased with OSA severity. Pearson correlation analysis revealed that the levels of eGFR ($r=-0.32$, $P=0.0026$) and creatinine ($r=0.34$, $P=0.0011$) were significantly affected by the severity of OSA, as reflected by AHI (*Figure 1*). Moreover, compared with patients without OSA, PSG parameters, including AHI, oxygen desaturation index, and time ratio of $SpO_2 < 90\%$, were significantly higher in patients with OSA. However, no difference was found in the total sleep time among the different groups.

Baseline characteristics associated with eGFR

As shown in *Table 2*, in the multiple linear regression analysis, after adjustment for age, sex, body mass index, and other relevant variables from spearman analysis, only age ($\beta=-0.29$, $P<0.001$), male sex ($\beta=0.17$, $P=0.02$), creatinine level ($\beta=-0.78$, $P<0.001$), and AHI ($\beta=-0.35$, $P<0.001$) were associated with a decrease in eGFR (adjusted $R^2=0.376$, $P<0.001$).

Perioperative data

As shown in *Table 3*, the number of CABG with cardiopulmonary bypass and concomitant procedures did not differ among the groups. However, the number of

dialysis (0.0% vs. 2.6% vs. 18.8%, $P=0.02$) and intra-aortic balloon pump (0.0% vs. 0.0% vs. 12.5%, $P=0.02$) were higher in patients with OSA. In addition, patients with OSA seemed to have the longer postoperative ventilation time [15.5 (12.5–21.0) vs. 16.8 (12.0–22.3) vs. 18.0 (34.0–15.0), $P=0.05$]. In addition, AHI was significantly higher in patients who underwent dialysis after CABG (*Figure 2*).

Predictor of postoperative dialysis after CABG

Finally, we further studied the factors that might be associated with a higher incidence of dialysis during the perioperative period. As shown in *Table 4*, the multivariate logistic regression model showed that a lower level of eGFR (OR =0.94, 95% CI, 0.89–0.99, $P=0.02$) and AHI (OR =1.07, 95% CI, 1.01–1.13, $P=0.02$) were independently associated with postoperative dialysis when adjusted for age, sex, body mass index, and other parameters.

Discussion

In our study, we studied the impact of OSA on renal function and postoperative dialysis in patients who underwent CABG. The main findings of the present study are as follows: First, the prevalence of OSA was significantly higher in those who underwent CABG, accounting for 79.8% of patients. Second, the multiple linear regression model revealed that age, male sex, AHI, and creatinine were independently associated with a decrease in eGFR. Third, the levels of creatinine, eGFR, and AHI were independently associated with a higher rate of postoperative dialysis after CABG when adjusted for age, sex, and body mass index.

In the present study, the prevalence of OSA was approximately 79.8% in patients who underwent CABG, which is consistent with a previous study (10). OSA may affect the progression of arteriosclerosis and coronary plaque formation in CAD patients in several ways, including activation of the sympathetic nervous system, heart rate, blood pressure, and impaired vascular endothelial function (16). We found that the prevalence of hypertension, which is a risk factor for CAD patients, increased with the severity of OSA in our study, which is consistent with a previous study (17). Many studies have revealed that OSA is an independent risk factor for AF (18). Combined with our results, we believe that by increasing the risk of atrial fibrillation, OSA may contribute to the high NYHA class before surgery, which may represent a more severe disease state. Previous studies revealed that

Table 1 Baseline characteristics of the study population

Variable	Whole cohort (n=178)	No OSA (n=36)	Mild OSA (n=78)	Moderate-severe OSA (n=64)	P value
Age, years	57.3±9.8	55.6±13.2	58.0±7.9	57.4±9.8	0.68
Male sex	128 (71.9%)	20 (55.6%)	60 (76.9%)	48 (75.0%)	0.22
Body mass index, kg/m ²	24.6±3.5	23.4±3.1	24.3±3.6	25.6±3.2	0.07
Heart rate, beats/min	73.2±9.6	72.6±7.7	75.5±11.9	70.6±6.3	0.09
NYHA III or IV	92 (51.7%)	12 (33.3%)	36 (46.2%)	44 (68.8%)	0.04
History of smoking	72 (40.4%)	16 (44.4%)	30 (38.5%)	26 (40.6%)	0.91
Hypertension	92 (51.7%)	14 (38.9%)	34 (43.6%)	44 (68.8%)	0.05
Hyperlipidemia	82 (46.1%)	16 (44.4%)	36 (46.2%)	30 (46.9%)	0.99
Diabetes mellitus	54 (30.3%)	8 (22.2%)	28 (35.9%)	18 (28.1%)	0.55
History of atrial fibrillation	24 (13.5%)	0 (0.0%)	10 (12.8%)	14 (21.9%)	0.03
History of stent implantation	20 (11.2%)	0 (0.0%)	6 (7.7%)	14 (21.9%)	0.01
Echocardiographic indices					
Left atrium, mm	38.2±7.5	36.3±6.6	38.0±6.9	39.6±8.5	0.31
LVEDD, mm	50.5±7.9	50.3±10.0	50.6±7.5	50.5±7.5	0.99
LVEF, %	56.3±8.9	60.2±8.6	58.6±7.2	49.3±8.8	<0.001
Ventricular aneurysm	7 (3.9%)	4 (11.1%)	2 (2.6%)	8 (12.5%)	0.26
E/A	0.98±0.51	0.92±0.45	1.06±0.49	0.92±0.58	0.49
Medical therapy					
Beta-blockers	100 (55.9%)	14 (38.9%)	42 (53.8%)	44 (68.8%)	0.04
Calcium-channel blockers	108 (60.7%)	24 (66.7%)	42 (53.8%)	42 (65.6%)	0.51
Creatinine, μmol/L	75.3±17.4	65.0±13.3	74.5±17.1*	82.2±17.1* [#]	0.003
eGFR, mL/min	91.5±15.8	103.4±7.8	92.6±14.7*	83.5±16.1* [#]	<0.001
Apnea hypoxia index, 1/h	15.4±13.3	2.5±1.3	9.9±3.1*	28.4±13.1* [#]	<0.001
ODI, 1/h	15.3±14.6	3.0±2.1	10.1±3.4*	28.5±17.0* [#]	<0.001
Time ratio of SpO ₂ <90%, %	1.9 (0.2–10.2)	0.1 (0.0–0.6)	1.5 (0.4–5.2)	9.3 (5.0–25.9)* [#]	<0.001
Total sleep time, min	463.5±70.3	462.8±65.3	453.8±84.6	475.7±51.5	0.43

Values are presented as percentage, mean ± SD, or median (interquartile range) when appropriate. *P<0.05, mild OSA or moderate-severe OSA vs. no OSA; [#]P<0.05, mild OSA vs. moderate-severe OSA. NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastole diameter; ODI, oxygen desaturation index; OSA, obstructive sleep apnea.

timely diagnosis and treatment of OSA in patients with CAD undergoing PCI can be regarded as a clinically relevant method of secondary prevention to decrease the risk of repeat revascularization (19). In our study, we also found that the proportion of patients with a history of stent implantation was significantly higher in patients with OSA, especially those with moderate-to-severe OSA. The mechanism by which OSA accelerates the development of

CAD and requires further surgical treatment is unclear. Endothelial dysfunction triggered by oxidative stress and systemic inflammation, which are the results of intermittent hypoxemia occurring in OSA, may be the most important reason for the aggravation of CAD (20).

Previous studies revealed that pneumonia was the most frequent respiratory and infectious complication in patients who underwent CABG. Moreover, studies have shown that

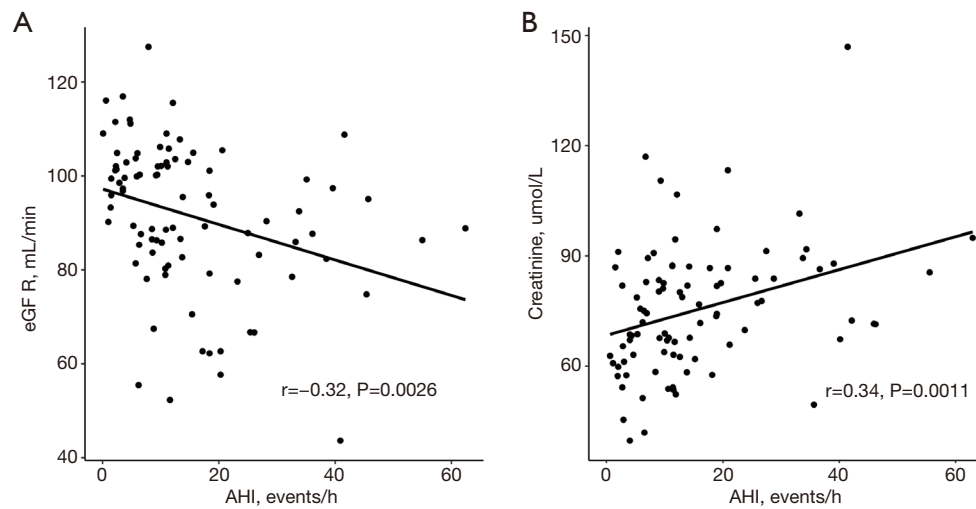


Figure 1 Correlation among AHI, creatinine, and eGFR using Spearman coefficients. (A) Spearman correlation between AHI and eGFR; (B) Spearman correlation between AHI and creatinine. AHI, apnea hypopnea index; eGFR, estimated glomerular filtration rate.

Table 2 Multiple linear regression between eGFR with significant variables from Spearman analysis

Variable	Univariable		Multivariable adjusted R ² =0.376	
	rs	P	β	P
Age	-0.32	0.002	-0.29	<0.001
Sex	0.008	0.94	0.17	0.02
Body mass index	-0.05	0.62		
History of smoking	0.25	0.02		
Hypertension	-0.24	0.02		
LVEF	0.25	0.02		
Creatinine,	-0.69	<0.001	-0.78	<0.001
Apnea hypoxia index	-0.40	<0.001	-0.35	<0.001
ODI, 1/h	-0.36	<0.001		
Time ratio of SpO ₂ <90%, %	-0.33	0.001		

eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; ODI, oxygen desaturation index.

the incidence of AF is high, and OSA is an independent risk factor for postoperative AF after CABG (21,22). However, in the present study, we only found that the postoperative ventilation time was significantly longer than that in patients without OSA, and there was no difference in the prevalence of postoperative atrial fibrillation. The reason for this might be that the patients in our study were relatively young (10). Acute renal failure and hemodynamic instability were the most common complications in our study, reflected by a higher rate of postoperative intra-

aortic balloon pump and dialysis. The elevated incidence of postoperative hemodynamic instability is probably due to the activation of the systemic nervous system, increased heart rate, and increased probability of cardiac arrhythmia due to OSA (23). These adverse factors lead to a decrease in blood pressure and require a large dose of vasoactive drugs to maintain hemodynamic stability.

Importantly, the strength of our study is that both the presence and severity of OSA were associated with a decrease in renal function and a higher rate of postoperative

Table 3 Perioperative data

Variable	Whole cohort (n=178)	No OSA (n=36)	Mild OSA (n=78)	Moderate-severe OSA (n=64)	P value
CABG with CPB	22 (11.7%)	4 (11.1%)	8 (10.3%)	10 (15.6%)	0.78
Grafts per patient	2.9±0.9	2.9±0.9	2.8±1.0	3.0±0.8	0.71
Postoperative dialysis	14 (7.9%)	0 (0.0%)	2 (2.6%)	12 (18.8%)	0.02
Intra-aortic balloon pump	8 (4.5%)	0 (0.0%)	0 (0.0%)	8 (12.5%)	0.02
Cerebral infarction	8 (4.5%)	2 (5.6%)	2 (2.6%)	4 (6.5%)	0.72
Myocardial infarction	2 (1.1%)	0 (0.0%)	0 (0.0%)	2 (3.2%)	0.40
Reoperation for bleeding	4 (2.2%)	0 (0.0%)	2 (2.6%)	2 (3.1%)	0.76
Postoperative atrial fibrillation	50 (28.1%)	10 (27.8%)	18 (23.1%)	22 (34.4%)	0.57
ICU stay, h	18.0 (15.0–24.0)	17.5 (13.8–24.0)	19.0 (14.0–22.0)	18.5 (15.3–25.5)	0.61
Postoperative ventilation time, h	17.0 (13.0–22.0)	15.5 (12.5–21.0)	16.8 (12.0–22.3)	18.0 (14.0–25.0)	0.05
Postoperative hospital stays, d	7.0±2.9	6.8±2.1	6.9±2.8	7.4±3.3	0.72
30-day mortality	4 (2.2%)	0 (0.0%)	2 (2.6%)	2 (3.1%)	0.76

Values are presented as percentage, mean ± SD, or median (interquartile range) when appropriate. CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; AVR, aortic valve replacement; OSA, obstructive sleep apnea.

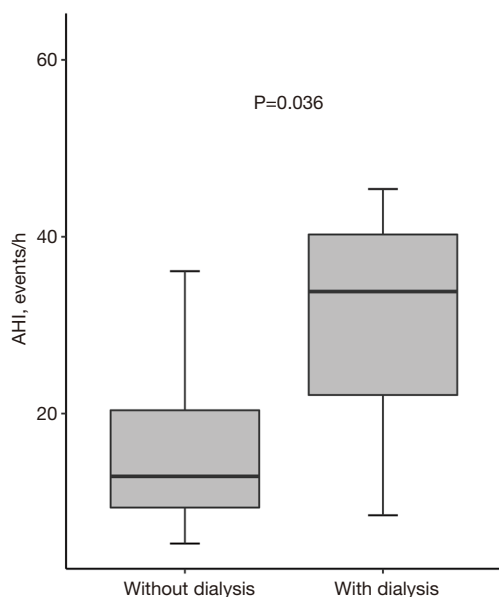


Figure 2 The value of apnea-hypopnea index according to the presence of dialysis between the obstructive sleep apnea (OSA) groups.

dialysis for patients undergoing CABG. Previous studies have reported that OSA might represent a novel risk factor and should be considered in the management of chronic kidney disease (24). In addition, another study revealed that sleep apnea is prevalent and associated with acute kidney injury after CABG (9). However, they did not study the relationship between dialysis, renal function, and OSA in these patients. Studies have shown that oxidative stress, chronic inflammation, activation of the renin-angiotensin system, and direct effects of hypoxia caused by OSA on the kidney might contribute to the impairment of renal function. In our study, there was no clinical manifestation of renal insufficiency in all patients before surgery, and the levels of creatinine and eGFR were within the normal range in most patients. However, compared to patients without OSA, both creatinine and eGFR were significantly changed in patients with OSA. Moreover, after adjustment for age, sex, and body mass index, OSA was also an independent risk factor for postoperative dialysis after CABG. All of these results indicate that we should pay

Table 4 Logistic regression between dialysis and significant variables from univariate analysis

Variable	Univariable		Multivariable	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.07 (0.97–1.19)	0.19		
Sex	2.50 (0.28–21.7)	0.41		
Body mass index	0.91 (0.72–1.15)	0.43		
History of stent implantation	8.03 (1.49–43.35)	0.02		
LVEF	0.92 (0.85–0.99)	0.04		
eGFR	0.94 (0.90–0.99)	0.01	0.94 (0.89–0.99)	0.02
Apnea hypoxia index	1.04 (1.003–1.09)	0.02	1.07 (1.01–1.13)	0.02

LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; OR, odds ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate.

more attention to these patients during the perioperative period, and OSA may need to be evaluated for patients who undergo CABG.

Previous studies have revealed that in a large prospective cohort study, OSA is an independent risk factor for adverse cardiovascular events in the general population, including sudden cardiac death (25). In addition, the severity of OSA is associated with cardiovascular risk, and effective treatment with continuous positive airway pressure can significantly reduce adverse cardiovascular outcomes in these patients (26). In addition, CPAP therapy can significantly decrease the risk of repeat revascularization after percutaneous coronary intervention (19). Importantly, recent studies have also shown that compliance with CPAP therapy is associated with a slower rate of progression of chronic kidney disease complicated by OSA (27). Therefore, we believe that timely treatment of these patients with CPAP may reduce perioperative complications, including postoperative hemodynamic instability and acute renal failure. It may also have a positive effect on long-term clinical results after CABG.

Limitations

As in other studies, the present study has some limitations. First, the sample size was relatively small, and this was a single-center study. Therefore, our results need to be confirmed by further large population studies, as well as multi-center combined clinical registry studies to confirm the effect of CPAP. Second, in our study, patients did not undergo Holter electrocardiographic monitoring, which is an important tool for determining any type of

arrhythmia. Third, we only studied patients with OSA and did not analyze the impact of central sleep apnea on perioperative complications after CABG. Lastly, the clinical and prognostic significance of CPAP on renal function and perioperative complications after CABG remains unclear, and further studies are needed.

Conclusions

In conclusion, we found that OSA was associated with a decrease in renal function, and it was also an independent risk factor for postoperative dialysis in patients who underwent CABG. As the high incidence and negative prognostic implications of OSA are suggestive, screening for OSA in patients who undergo CABG is desirable and might provide a significant clinical benefit. Moreover, further studies are needed to evaluate the safety and clinical efficacy of OSA treatment in these patients, as well as their impact on long-term postoperative outcomes.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/apm-21-180>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Approval from the Ethics Committee of Capital Medical University Affiliated Anzhen Hospital (No. 2020034X) was obtained before the start of the study, and each participant signed a written consent form. All studies were conducted in accordance with the ethical principles stated in the Declaration of Helsinki (as revised in 2013) in the present study.

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