The effects of obstructive sleep apnea and high-sensitivity C-reactive protein on clinical outcome in off-pump coronary artery bypass grafting

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Abstract

Purpose

This study aimed to investigate the relationship between obstructive sleep apnea (OSA) and high-sensitivity C-reactive protein (hs-CRP) to determine their effects on postoperative complications and clinical outcomes during hospitalization in patients undergoing off-pump cardiac artery bypass grafting (OPCABG).

Methods

This prospective, single-center study enrolled patients who underwent OPCABG. OSA was evaluated using a portable sleep monitor before OPCABG. Spearman correlation was performed to investigate the relationship between hs-CRP and polygraphy test indicators; regression analysis was performed to determine whether hs-CRP is an independent influencing factor for postoperative atrial fibrillation, duration of hospitalization, and hospital cost.

Results

Partial pressure of carbon dioxide (P = 0.033), high-sensitivity C-reactive protein (hs-CRP) (P = 0.001), apnea hypopnea index (AHI) (P = 0.000), mean apnea time (P = 0.000), maximum apnea time (P = 0.000), and ODI ≥ 3% (P = 0.000) were significantly higher in the moderate–severe OSA group than in the absent–mild OSA group. LVEF (P = 0.034), lowest arterial oxygen saturation (SaO_2) (P = 0.000), and mean SaO_2 (P = 0.000) were significantly lower in the moderate–severe OSA group. Hs-CRP levels correlated with AHI (rs = 0.235, P = 0.009), ODI ≥ 3% (rs = 0.228, P = 0.011), lowest SaO_2 (rs = 0.186, P = 0.040), and mean SaO_2 (rs = 0.331, P = 0.000). AHI independently correlated with hs-CRP levels (P = 0.01); hs-CRP was an independent risk factor for post-CABG atrial fibrillation (POAF) (OR = 1.17, P = 0.006); and hs-CRP level independently correlated with duration of hospitalization (P = 0.002) and hospital cost (P = 0.040).

Conclusion

Hs-CRP levels are closely related to the degree of OSA and have potential utility in predicting POAF, duration of hospitalization, and hospital costs in patients undergoing OPCABG.

Introduction

Obstructive sleep apnea (OSA) is characterized by repeated or partial obstruction of the respiratory tract during sleep, with an incidence of 9–38% in adults [1]. Intermittent hypoxia induced by OSA could trigger oxidative stress and could damage the vascular endothelium; for these reasons, it is an independent risk factor for coronary heart disease (CHD) and affects its prognosis [2]. Currently, off-pump cardiac artery bypass grafting (OPCABG) is one of the primary treatments of CHD [3]. However, there are few reports on

whether OSA is associated with post-OPCABG complications [4]. Traditional OSA severity markers, such as apnea hypopnea index (AHI) have limitations in predicting the prognosis of CABG. Inflammatory processes are central to the pathogenesis of vascular diseases in the context of OSA. High-sensitivity C-reactive protein (hs-CRP) is a marker of acute inflammation and has strong sensitivity; a slight increase in hs-CRP level could indicate coronary plaque inflammation or coronary artery wall injury, which is closely related to CHD and its associated negative events [5].

In this study, we aimed to investigate the relationship between OSA and hs-CRP levels and to determine their effects on postoperative complications and clinical outcomes during postoperative hospitalization in patients who underwent OPCABG.

Methods

Study design

This prospective, single-center study enrolled patients who underwent OPCABG from January 2019 to December 2019 at Beijing An Zhen Hospital. This study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional review board of Beijing An Zhen Hospital of Capital Medical University (approval no.: 2013025). All study participants gave informed written consent prior to participation.

Patients

The inclusion criteria were as follows: age, 40–75 years; with consent to undergo sleep monitoring tests (polygraphy; PG) using a portable sleep monitor; and provision of written informed consent for study participation. We excluded patients with valvular disease combined with other heart diseases, central sleep apnea, severe respiratory diseases (e.g., chronic obstructive pulmonary disease), severe diseases of other organs (e.g., renal failure), body temperature > 37.5℃, and preoperative use of morphine and its analogs, sedative drugs, and/or theophylline. We recorded baseline clinical data, including age, sex, body mass index (BMI), body temperature, pre-existing medical conditions (hypertension, diabetes, stroke), history of smoking, blood biochemistry findings, and left ventricular ejection fraction (LVEF) bases on echocardiography, and PG test data.

PG tests and diagnostic criteria for OSA

Eligible patients were enrolled and admitted to the hospital. PG was performed before OPCABG. Each patient in the sleep monitoring center at Beijing An Zhen Hospital wore a portable sleep monitor (ApneaLink, ResMed, Australia). We used type III PG to detect airflow by nasal catheter, respiratory movement by chest belt, heart rate by electrocardiograph, and arterial oxygen saturation (SaO_2) by pulse oximetry. All PG test data were analyzed by two physicians at the Sleep Center of Beijing An Zhen Hospital. In case of disagreement between the two, a third physician participated in the data analysis. Sleep apnea was defined as the cessation of airflow through the nose and mouth for > 10 s during sleep; hypopnea, a reduction of > 50% in the airflow intensity and ≥ 4% in SaO_2 level during sleep. AHI was defined as the total number of

apnea or hypopnea episodes per hour during sleep (i.e., AHI = total number of apnea or hypopnea episodes/total sleep duration (min) × 60). Moderate–severe OSA was defined as an AHI ≥ 15/h during a 7-h sleep. Oxygen desaturation index (ODI) ≥ 3% is the number of times that oxygen saturation decreases by > 3% per hour [6]. All moderate–severe patients were recommended for continuous positive airway pressure (CPAP) after discharge.

OPCABG

All patients underwent OPCABG after the PG test. The same cardiac surgeon performed all surgeries. The number of grafts and surgical duration were recorded. The quality of graft anastomosis met the criteria recommended by the Operation Quality Committee of Beijing An Zhen Hospital. Two ultrasound specialists performed echocardiography in all patients, and a single nurse measured the blood pressure and collected blood samples from the patients. After surgery, the patients were monitored in the intensive care unit (ICU) until ventilator removal was feasible and vital signs were stable; they were discharged from the hospital once they could move freely. The physician in the ICU and the cardiac surgeon determined the ICU stay and hospitalization duration. We recorded the following postoperative data: incidence of major adverse cardiac and cerebrovascular event (MACCE), lung infection, post-CABG atrial fibrillation (POAF); duration of postoperative tracheal intubation; ICU stay; duration of hospitalization, and hospital cost. POAF was defined as the occurrence of AF within 72 h after surgery. Pulmonary infection was defined as a postoperative increase in white blood cell count, obvious inflammation based on postoperative chest radiography and computed tomography, and meeting one of the following conditions: sputum examination reveals new characteristic changes and pathogenic bacterium could be cultivated from blood or respiratory secretions.

Blinding

The cardiac surgeon, other participating investigators, and research staff were blinded to the findings of the PG tests. After the final enrolled patient was discharged from the hospital in January 2020, all data were revealed to the participating investigators.

Statistical analysis

All statistical analyses were performed using SPSS, version 24.0 (SPSS Inc., Chicago, IL, USA). Continuous variables with a normal distribution were presented as means ± standard deviations and were compared using independent samples *t*-tests. Continuous variables without a normal distribution were presented as medians (interquartile ranges) and were compared using rank-sum tests. Categorical variables are presented as percentages and were compared using $\chi 2$ tests. If the missing quantity of measurement data was < 5%, the average value was used to replace the missing value. No missing values in the counting data were noted. Spearman correlation analysis was employed to determine the relationship between PG test data and hs-CRP; multiple linear regression was used to analyze the relationship between AHI and hs-CRP. Univariate binary logistic regression was used to analyze the relationship between preoperative relevant indicators and POAF occurrence. Indicators with $P < 0.1$ on univariate analysis were included in the multivariate binary logistic regression model to determine whether hs-CRP was an independent risk factor

for POAF. Using a simple linear regression, we analyzed the relationship between relevant preoperative indicators and the duration of hospitalization and hospital cost. Indicators with $P < 0.1$ on univariate analysis were included in the multiple linear regression model to determine whether hs-CRP was an independent influencing factor for the duration of hospitalization and hospital cost. Two-sided P-values < 0.05 were considered statistically significant.

Results

OSA prevalence and hs-CRP

The study flow chart is shown in Fig. 1. One hundred seventy-five patients underwent PG and OPCABG from January 2019 to December 2019. A total of 123 patients were included in the final analysis. Based on the PG findings, 71 patients had an AHI < 15 and were assigned to the absent–mild OSA group, while the remaining 52 had an AHI ≥ 15 and were assigned to the moderate–severe OSA group. We set the threshold hs-CRP level at 2 mg/L, which is according to the results of previous large clinical trials. Seventy-eight patients had an hs-CRP level of < 2 mg/L and were assigned to the normal hs-CRP group; 45 had an hs-CRP level of ≥ 2 mg/L and were assigned to the elevated hs-CRP group.

Preoperative clinical data of the absent–mild OSA and moderate–severe OSA groups were compared (Table 1): PCO_2 (P = 0.033), hs-CRP (P = 0.001; Fig. 2), AHI, mean apnea time, maximum apnea time, and ODI ≥ 3% (all P = 0.000) were significantly higher in the moderate–severe OSA group than in the absent–mild OSA group. LVEF (P = 0.034) and lowest and mean SaO_2 (both P = 0.000) were significantly lower in the moderate–severe OSA group than in the absent–mild OSA group. No significant difference in other preoperative indexes was found. In addition, the number of grafting performed, duration of surgery, MACCEs, lung infection, POAF, duration of ventilator use, ICU stay, duration of hospitalization, and hospital cost were not significantly different between the two OSA groups (Table 2).

Table 1
Baseline clinical data for patients with obstructive sleep apnea (OSA) undergoing off-pump coronary artery bypass grafting (OPCABG)

	Absent–mild OSA (n = 71)	Moderate–severe OSA (n = 52)	P value	Total (n = 123)
Sex (male/female)	55/16	39/13	0.750	94/29
Age (years)	61.3 ± 9.3	62.9 ± 8.2	0.334	62.0 ± 8.88
BMI (kg/m^2)	25.5 ± 3.2	25.2 ± 3.7	0.602	25.4 ± 3.4
Body temperature (˚C)	36.4 ± 0.4	36.3 ± 0.4	0.236	36.3 ± 0.4
Hypertension, n (%)	49 (69)	40 (77)	0.333	89 (72)
Diabetes, n (%)	27 (38)	24 (46)	0.366	51 (42)
Stroke, n (%)	9 (13)	2 (4)	0.090	11 (9)
Smoking history n (%)	33 (47)	28 (54)	0.419	61 (50)
Blood test data				
PO_2 (mmHg)	94.2 ± 18.2	88.9 ± 25.5	0.183	92.0 ± 21.7
PCO_2 (mmHg)	35.5 ± 3.2	37.1 ± 4.4	**0.033***	36.2 ± 3.8
HDL (mmol/L)	1.1 ± 0.3	1.0 ± 0.3	0.273	1.0 ± 0.3
LDL (mmol/L)	2.4 ± 1.0	2.5 ± 1.1	0.677	2.4 ± 1.0
Triglyceride (mmol/L)	1.3 (1.1,1.9)	1.3 (1.0,1.8)	0.916	1.3 (1.1,1.8)
Creatinine (μmol/l)	73.3 ± 17.8	76.8 ± 21.4	0.319	74.8 ± 19.4
hs-CRP (mg/L)	1.1 (0.3,2.2)	2.0 (0.7,6.8)	**0.001***	1.4 (0.5,3.5)
Echocardiography data				
LVEF (%)	59.5 ± 8.5	55.9 ± 9.8	**0.034***	58.0 ± 9.2
LVDD (mm)	48.9 ± 6.7	50.0 ± 5.9	0.326	49.4 ± 6.4
LAD (mm)	36.7 ± 3.8	37.0 ± 4.2	0.645	36.9 ± 4.0
PG test data				

Values are mean (± SD), median (interquartile range), or no. (%).

BMI: body mass index, PO_2: partial pressure of oxygen, PCO_2: partial pressure of carbon dioxide, HDL: high-density lipoprotein, LDL: low-density lipoprotein, hs-CRP: high-sensitivity C-reactive protein, LVEF: left ventricular ejection fraction, LVDD: left ventricular end diastolic diameter, LAD: left atrium diameter, AHI: apnea hypopnea index, SaO_2: arterial oxygen saturation, ODI: oxygen desaturation index.

*P < 0.05

	Absent–mild OSA (n = 71)	Moderate–severe OSA (n = 52)	P value	Total (n = 123)
AHI (events/hour)	7.1 ± 4.1	28.5 ± 11.5	**0.000***	16.1 ± 13.4
Mean apnea time (s)	17(14,24)	24(19,30)	**0.000***	20(16,27)
Maximum apnea time (s)	27(19.35)	40(31,61)	**0.000***	31(22,47)
Lowest SaO_2 (%)	87.0 ± 3.7	81.6 ± 5.8	**0.000***	84.7 ± 5.4
Mean SaO_2 (%)	95.4 ± 2.1	93.0 ± 2.4	**0.000***	94.4 ± 2.5
ODI ≥ 3%	7.4 ± 8.4	25.8 ± 11.9	**0.000***	15.2 ± 13.5
Values are mean (± SD), median (interquartile range), or no. (%).				
BMI: body mass index, PO_2: partial pressure of oxygen, PCO_2: partial pressure of carbon dioxide, HDL: high-density lipoprotein, LDL: low-density lipoprotein, hs-CRP: high-sensitivity C-reactive protein, LVEF: left ventricular ejection fraction, LVDD: left ventricular end diastolic diameter, LAD: left atrium diameter, AHI: apnea hypopnea index, SaO_2: arterial oxygen saturation, ODI: oxygen desaturation index.				
*P < 0.05				

Table 2
Comparison of intraoperative and postoperative clinical data between patients with absent–mild obstructive sleep apnea (OSA) and those with moderate–severe OSA who underwent off-pump coronary artery bypass grafting (OPCABG)

	Absent–mild OSA (n = 71)	Moderate–severe OSA (n = 52)	P value	Total (n = 123)
No. of performed grafting	4.2 ± 0.6	4.2 ± 0.5	0.849	4.2 ± 0.5
Duration of surgery (min)	233.6 ± 35.7	229.4 ± 34.7	0.525	231.8 ± 35.2
MACCEs, n (%)	21 (30)	11 (21)	0.293	32 (26)
Lung infection, n (%)	2 (3)	2 (4)	0.751	4 (3)
POAF, n (%)	16 (23)	16 (31)	0.304	32 (26)
Duration of ventilator use (hour)	21.1 ± 19.6	20.3 ± 13.3	0.799	20.8 ± 17.2
ICU stay (hour)	34.0 ± 31.3	30.4 ± 22.8	0.478	32.5 ± 28.0
Duration of hospitalization (day)	17.2 ± 5.7	18.8 ± 6.7	0.176	17.9 ± 6.2
Hospital cost (×1000 RMB)	128.4 ± 25.6	134.0 ± 28.7	0.260	130.8 ± 27.0
Values are mean (± SD), median (interquartile range), or no. (%).				
MACCEs: major adverse cardiac or cerebrovascular events, POAF: postoperative atrial fibrillation.				

A comparison of postoperative clinical data between the normal hs-CRP and elevated hs-CRP groups (Fig. 3) showed that the proportion of patients with moderate–severe OSA and that of patients with POAF were significantly higher in the elevated hs-CRP group than in the normal hs-CRP group (56% vs. 35%, P = 0.024; 38% vs. 19%, P = 0.024). The duration of hospitalization (P = 0.000) and hospital cost (P = 0.000) in the elevated hs-CRP group were significantly higher than those in the normal hs-CRP group. Mean SaO_2 (P = 0.012) in the elevated hs-CRP group was significantly lower than that in the normal hs-CRP group.

Relationship between hs-CRP level and PG test indexes

Spearman correlation analysis showed positive correlations between hs-CRP levels and AHI (rs = 0.235, P = 0.009) and ODI ≥ 3% (rs = 0.228, P = 0.011). hs-CRP levels negative correlated with the lowest SaO_2 (rs = 0.186, P = 0.040) and mean SaO_2 (rs = 0.331, P = 0.000). Multiple linear regression showed that AHI and hs-CRP levels were significantly correlated (P = 0.01) after correcting for sex, age, and BMI.

Correlation of hs-CRP level with POAF, duration of hospitalization, and hospital cost.

POAF, duration of hospitalization, and hospital costs were significantly different between the normal hs-CRP and elevated hs-CRP groups. To determine whether hs-CRP level was an independent influencing factor for these three indicators, logistic regression analyses (for POAF) and linear regression analysis (for

duration of hospitalization and hospital cost) were performed. Table 3 shows that hs-CRP level was an independent risk factor for POAF (OR = 1.17, P = 0.006). Table 4 shows that hs-CRP level (P = 0.002) and LVEF (P = 0.002) independently correlated with the duration of hospitalization; hypertension (P = 0.014), hs-CRP level (P = 0.040), and LVEF(P = 0.000) independently correlated with hospital costs.

Table 3
Univariate logistic regression and multivariate logistic regression analyses for the correlation between various preoperative clinical indicators and postoperative atrial fibrillation

	Univariate		**Multivariate**	
Covariate	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Sex	0.720 (0.288–1.800)	0.482		
Age	1.028 (0.980–1.078)	0.260		
BMI	1.043 (0.925–1.176)	0.491		
Hypertension	1.507 (0.582–3.900)	0.398		
Diabetes	0.668 (0.289–1.545)	0.346		
Stroke	1.073 (0.267–4.320)	0.921		
Smoking history	0.430 (0.186–0.993)	**0.048***	0.360 (0.142–0.912)	**0.031***
PCO_2	0.924 (0.829–1.030)	0.156		
Hs-crp	1.166 (1.050–1.294)	**0.004***	1.170 (1.045–1.310)	**0.007***
LVEF	0.949 (0.909–0.991)	**0.017***	0.961 (0.914–1.011)	0.122
LAD	1.095 (0.988–1.214)	**0.083**	1.084 (0.964–1.220)	0.151
AHI	1.014 (0.985–1.044)	0.342		

BMI: body mass index, PCO_2: partial pressure of carbon dioxide, hs-CRP: high-sensitivity C-reactive protein, LVEF: left ventricular ejection fraction, LAD: left atrium diameter, AHI: apnea hypopnea index.

*P < 0.05

Table 4
Single logistic regression analysis and multivariate logistic regression analysis for the correlation between various preoperative clinical indicators and postoperative atrial fibrillation, duration of hospitalization, and hospital cost

	Dependent variable: duration of hospitalization				**Dependent variable: hospital cost**			
	Univariate		Multivariate		Univariate		Multivariate	
Covariate	B (95% CI)	P value	B (95% CI)	P value	B (95% CI)	P value	B (95% CI)	P value
Sex	0.868 (-1.730–3.465)	0.510			-0.327 (-11.717–11.063)	0.955		
Age	-0.026 (-0.151–0.099)	0.678			0.270 (-0.274–0.815)	0.328		
BMI	-0.025 (-0.348–0.299)	0.880			-0.954 (-2.360–0.452)	0.182		
Hypertension	-2.131 (-4.570–0.309)	**0.086**	-2.085 (-4.317–0.147)	0.067	-13.934 (-24.450–3.418)	**0.010***	-12.191 (-21.633–2.749)	**0.012***
Diabetes	0.457 (-1.784–2.697)	0.687			1.819 (-7.990–11.627)	0.714		
Stroke	0.442 (-3.427–4.312)	0.821			-9.151 (-26.013–7.712)	0.285		
Smoking history	1.331 (-0.865–3.527)	0.232			4.810 (-4.821–14.441)	0.325		
PCO_2	0.063 (-0.227–0.354)	0.666			-0.360 (-1.633–0.913)	0.577		

BMI: body mass index, PCO_2: partial pressure of carbon dioxide, hs-CRP: high-sensitivity C-reactive protein, LVEF: left ventricular ejection fraction, AHI: apnea hypopnea index.

*P < 0.05

	Dependent variable: duration of hospitalization				Dependent variable: hospital cost			
Creatinine	0.003	0.905			0.051	0.688		
	(-0.054–0.061)				(-0.199–0.301)			
Hs-crp	0.501	**0.000***	0.398	**0.002***	1.080	**0.005***	1.081	**0.041***
	(0.251–0.751)		(0.154–0.642)		(0.500–2.750)		(0.047–2.113)	
LVEF	-0.235	**0.000***	-0.168	**0.003***	-1.346	**0.000***	-1.099	**0.000***
	(-0.347–0.122)		(-0.280–0.056)		(-1.814–0.877)		(-1.571–0.627)	
AHI	0.112	**0.007***	0.067	0.090	0.441	**0.015***	0.251	0.131
	(0.031–0.192)		(-0.011–0.144)		(0.087–0.795)		(-0.076–0.578)	

BMI: body mass index, PCO_2: partial pressure of carbon dioxide, hs-CRP: high-sensitivity C-reactive protein, LVEF: left ventricular ejection fraction, AHI: apnea hypopnea index.

*P < 0.05

Discussion

OSA is closely related to CHD. A study showed that the prevalence of CHD in patients with OSA was 16.2% and that of patients without OSA was 5.4% [7]; in a population with suspected CHD, the proportion of patients with moderate–severe OSA was 24%, four times higher than the prevalence in the normal population [8]. In the present study, we found that the proportion of patients with moderate–severe OSA was 42.3%, significantly higher than that of the aforementioned study. This finding could be because the patients with OSA in our study needed to undergo OPCABG. Moreover, the patients had severe coronary atherosclerotic lesions, which indicates that OSA is a substantial risk factor for CHD.

In addition, we found that the preoperative LVEF of patients with moderate–severe OSA was significantly lower than that of patients with absent–mild OSA. Previous studies also found that LVEF was independently related to moderate–severe OSA. The main mechanisms by which OSA affects cardiac function may be as follows [9, 10]: first, each respiratory obstruction event could result in an intrathoracic negative pressure of 60–70 cm H_2O, and hypoxia could cause pulmonary vasoconstriction, resulting in

preload and afterload imbalance between the left and right ventricles; subsequently, myocardial oxygen consumption increases and myocardial ischemia occurs, which in turn alters cardiac function; second, the long-term repeated fluctuation of intrathoracic pressure could increase intraglomerular pressure variability, leading to impaired cardiac function; and finally, sympathetic hyperactivity affects all-day cardiopulmonary hemodynamics. In addition, hypopharyngeal edema due to decreased cardiac function could also promote the development of OSA.

CABG is one of the primary treatments of CHD. Few studies showed that OSA may affect the prognosis of patients with CABG; Uchôa et al. found that moderate–severe OSA significantly increased the long-term incidence of MACCEs (follow-up time of 4.5 years), revascularization rate, the proportion of angina attacks, and AF incidence in patients with CABG; there was no significant effect on the 30-day prognosis after CABG [11]. Another study found that AHI was an independent risk factor for increased duration of hospitalization and postoperative circulatory fluctuation in patients with CABG [12]. In contrast, we found no significant difference in postoperative indicators, including the duration of hospitalization, between the moderate–severe OSA and absent–mild OSA groups. The possible reason for the discrepancy is that all patients included in our study underwent OPCABG, which in turn avoided the effects of extracorporeal circulation, shortening the postoperative recovery cycle, and reducing the short-term effect of OSA.

Evidence to identify the effect of OSA on the prognosis of OPCABG only using OSA classification is insufficient. OSA may affect the clinical outcome of CABG by influencing other indicators. For example, our previous study found that OSA may further affect the perioperative indicators such as the cardiac function [4]. In addition, biomarkers related to OSA and CHD may also be examined to predict more accurately the effect of OSA on CABG.

CRP is an acute phase reaction protein. Repeated hypoxia and inadequate ventilation in OSA could trigger oxidative stress and systemic inflammatory response, which could in turn enhance the synthesis and release of CRP [13]. Shamsuzzaman et al. showed that CRP has a significant linear correlation with AHI and is an independent influencing factor for OSA severity [14]. Moreover, inflammatory responses play key roles in the development of atherosclerosis. CRP, which is the product and mediator of inflammatory responses in atherosclerosis, is an important marker of endothelial dysfunction. Elevated CRP levels have been shown to be an independent risk factor for diseases such as myocardial infarction, peripheral vascular disease, and stroke [15]. Han et al. found that high CRP levels influence acute renal function injury, all-cause death, duration of hospitalization, and ICU stay after CABG [16].

Compared with the CRP, hs-CRP extends the detection linear range from 3–200 mg/L to 0.005–0.10 mg/L, thereby making the determination of low-concentration CRP more accurate. hs-CRP has a long half-life, with no diurnal difference and no sex- or age-dependence and has a higher value in predicting the prognosis of cardiovascular and cerebrovascular diseases [17]. Previous studies have shown a relationship between hs-CRP levels and OSA, nevertheless, these results are controversial because of obesity and various confounding factors in previous studies [18]. In our study, we found that the hs-CRP level was significantly increased in the moderate–severe OSA group, and there were significant correlations between hs-CRP level

and several indicators of PG (AHI, ODI ≥ 3%, lowest SaO_2, mean SaO_2). Multiple linear regression showed that AHI was an factor affecting hs-CRP level, independent of obesity.

Hs-CRP plays an important role in predicting the prognosis of cardiovascular disease; nevertheless, only one report on the early effect of hs-CRP on OPCABG has been conducted [19]. In the present study, we found that elevated hs-CRP levels were significantly associated with increased AF incidence and duration of hospitalization. Our results also demonstrated that AF incidence, duration of hospitalization, and hospital costs were significantly higher in the elevated hs-CRP group than in the normal group after OPCABG. Further regression analysis showed that hs-CRP level was an independent risk factor for POAF and was independently correlated with the duration of hospitalization and hospital cost.

As previously mentioned, OSA could affect hs-CRP levels, and preoperative hs-CRP level predicts postoperative indicators of OPCABG. CPAP, which could reduce the CRP level, is an important treatment for OSA [20]. For these reasons, the results of our study may suggest the utility of CPAP in patients with OSA who undergo CABG.

Stability of respiratory regulation is an important factor in determining OSA severity [21]. Compared with the normal population, patients with OSA had significantly reduced respiratory center responses to low PaO_2 and high PaO_2 during sleep, and the respiratory center response of some patients was also suppressed during wakefulness. Moreover, patients with OSA have long durations of apnea at night with short intervals. While hyperventilation occurs at the end of an apneic event, it is insufficient to clear the accumulated CO_2, thereby resulting in hypercapnia or even type II respiratory failure. In this study, we found that the periods of apnea were significantly longer and the $PaCO_2$ level was significantly higher in the moderate–severe OSA group than in the absent–mild OSA group when awake. Further study involving the change in $PaCO_2$ and internal environment is needed.

Our study has the following limitations: first, it is a single-center study with a limited sample size; the results need to be validated using multi-center, large-sample studies. Second, we were unable to use polysomnography (PSG), which appears to offer a more accurate evaluation of OSA than does PG. Also, PG may underestimate the OSA severity. PSG requires patients to sleep at the sleep center for more than 8 h. The sleep center in our hospital has not been provided with urgent response equipment and medical teams for patients with heart disease. All of our patients had severe coronary artery disease and were consequently at a high risk of emergent cardiac events. Therefore, we decided to use a portable PG monitor so that we could keep our patients in the cardiac surgery department for the assessment of OSA. Finally, we only analyzed hs-CRP levels at one time point; thus, it remains unclear as to whether hs-CRP level has the same predictive value at other time points.

Conclusions

Moderate–severe OSA has a higher incidence in patients who undergo OPCABG. Compared with patients with absent–mild OSA, those with moderate–severe OSA have poorer cardiac function and higher PCO_2 and hs-CRP levels. The hs-CRP level is closely related to the severity of OSA and has an important predictive

value for POAF, duration of hospitalization, and hospital cost among patients with OPCABG. The effect of OSA on the short-term prognosis of OPCABG may be predicted using preoperative hs-CRP levels.

Declarations

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Conflicts of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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Ethical approval

This study was approved by the Institutional Review Board of Beijing An Zhen Hospital of Capital Medical University (Approval No: 2013025).

Consent to participate

All study participants gave informed written consent prior to participation.

Consent for publication

All study participants gave informed written consent prior to participation.

Availability of data and material

All data generated or analysed during this study are included in this published article (and its supplementary information files).

Code availability

Not applicable

Authors' contributions

Dr Gao and Fan contributed equally to this article.

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Figures

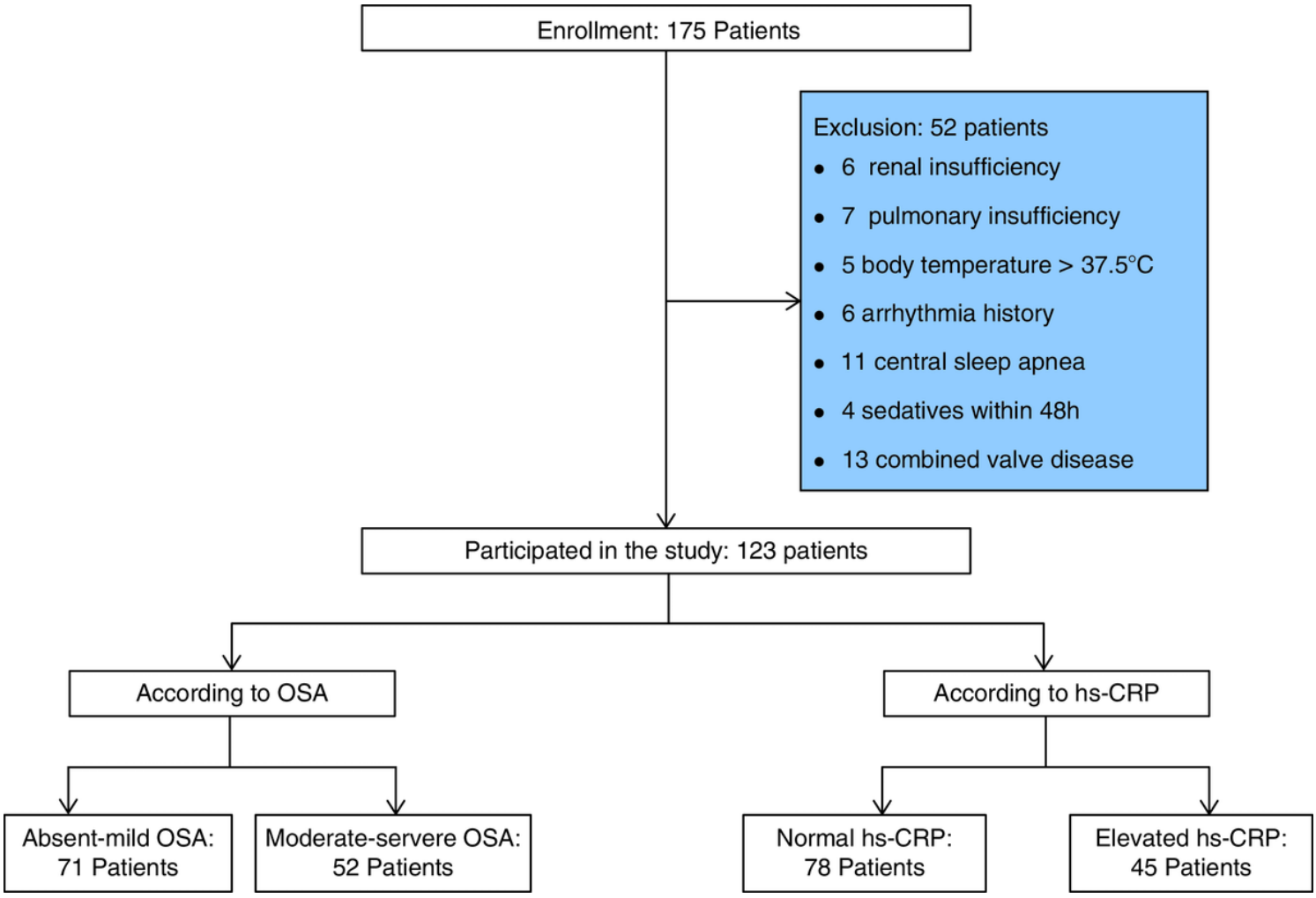

Figure 1

Flow chart showing the inclusion of patients in this study.

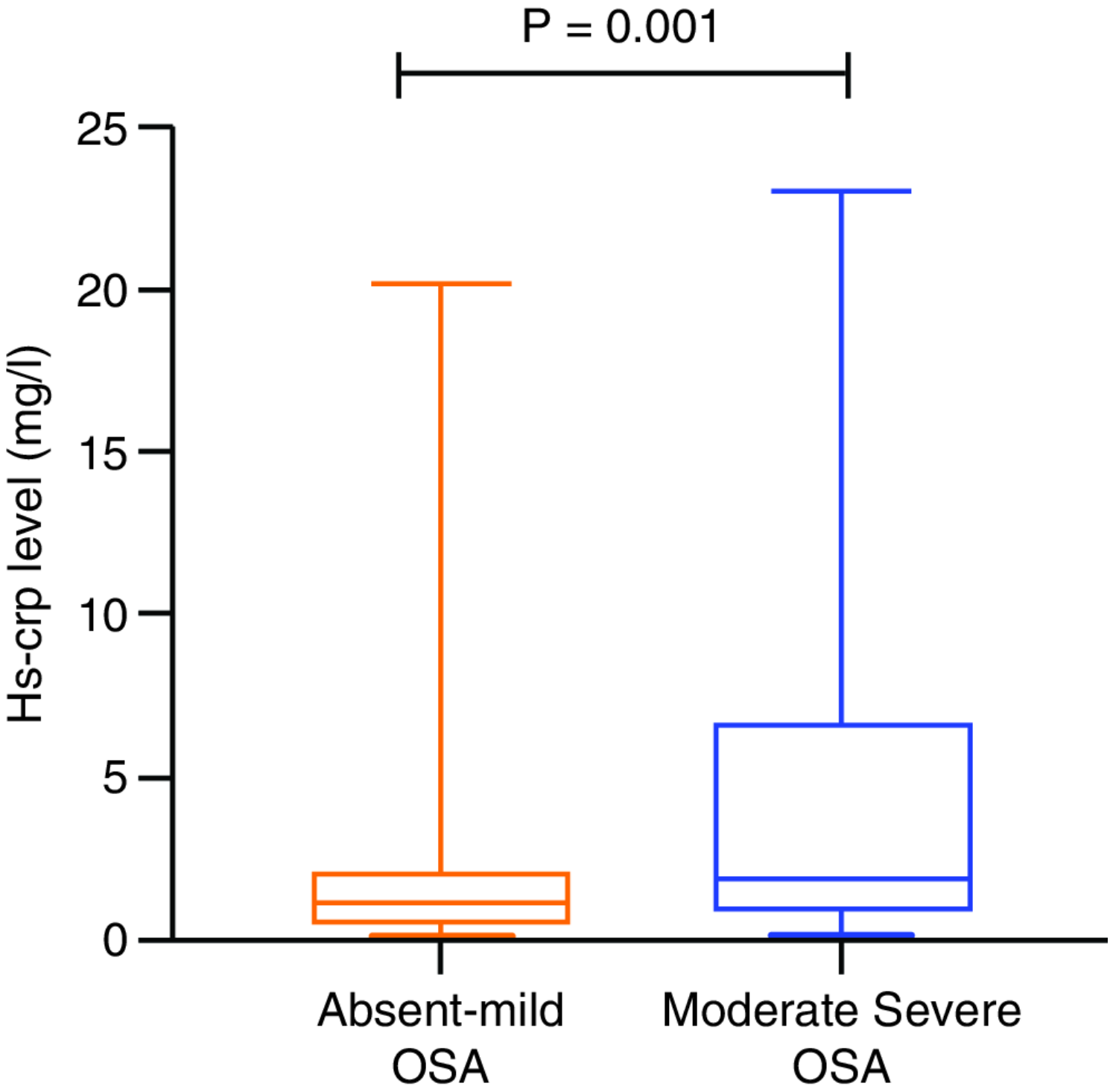

Figure 2

The hs-CRP level in the moderate–severe OSA group was significantly higher than that in the no–mild OSA group.

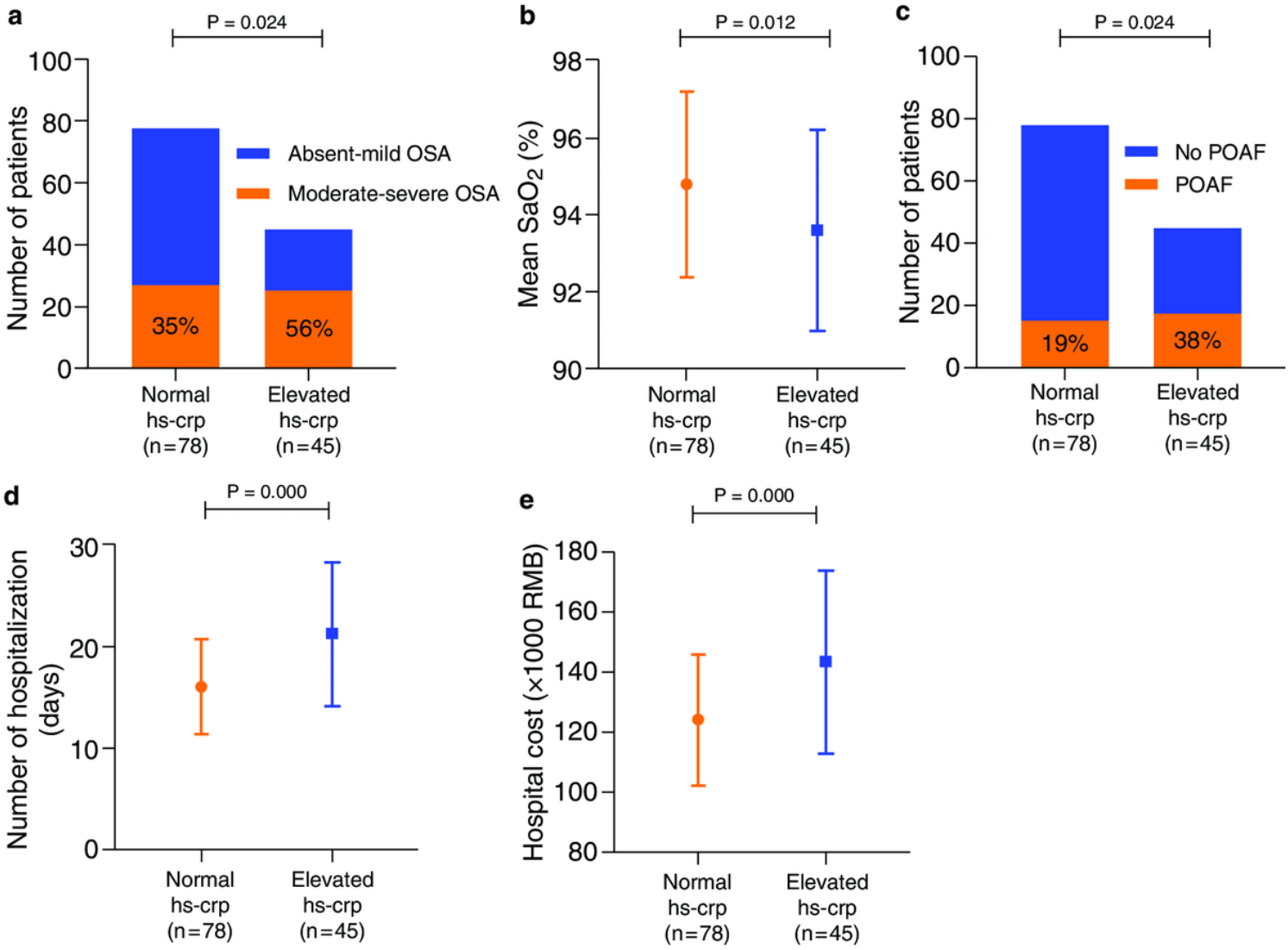

Figure 3

A The proportion of patients with moderate–severe OSA in the elevated hs-CRP group was significantly higher than that in the normal hs-CRP group. B The mean SaO2 in the elevated hs-CRP group was significantly lower than that in the normal hs-CRP group. C The proportion of patients with POAF in the elevated hs-CRP group was significantly higher than that in the normal hs-CRP group. D The duration of hospitalization in the elevated hs-CRP group was significantly longer than that in normal group. E The hospital cost in the elevated hs-CRP group was significantly greater than that in the normal hs-CRP group.