Research Article

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The association between hypoxic burden and blood pressure in patients with obstructive sleep apnea

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Abstract

Objectives: Obstructive sleep apnea (OSA) is an independent risk factor for hypertension. Hypoxic burden (HB) is a more comprehensive indicator of OSA severity than apnea-hypopnea index (AHI), and this study aims to evaluate the association between HB and blood pressure in patients with OSA.
Methods: A total of 129 subjects diagnosed with OSA by polysomnography and completed 24-h ambulate blood pressure monitoring (ABPM) were prospectively recruited. According to the median HB, the patients were divided into high and low groups. Linear regression analyses were performed to investigate the association between 24-h mean systolic blood pressure (SBP) and other ABPM parameters with HB or AHI.
Results: In univariate linear regression analysis, high HB was identified as a significant risk factor for daytime SBP elevation (B=4.96, 95 % CI=2.57–7.35 mmHg, p=0.04). After adjustment, high HB was still significantly associated with daytime SBP elevation (B=6.04, 95 % CI=0.02–12.06 mmHg, p=0.049). Subgroup analyses further revealed that this association was more pronounced in female, aged ≥45 years, and overweight populations. However, there was no significant differences between AHI and all ABPM parameters.
Conclusions: Higher HB is as an independent risk factor for daytime SBP elevation in patients with OSA.

Keywords: obstructive sleep apnea; blood pressure; hypoxic burden; apnea-hypopnea index

Introduction

Obstructive Sleep Apnea (OSA) is a systemic chronic disease associated with multi-system organ damage, particularly affecting the respiratory, cardiovascular, and nervous systems, and is closely linked to various comorbidities such as hypertension, coronary heart disease, and diabetes [1]. Among these, hypertension is the most prevalent chronic disease worldwide, often leading to the development and mortality of cardiovascular diseases [2, 3]. Emerging evidence demonstrates that individuals with systolic blood pressure (SBP) of 130–139 mmHg and/or diastolic blood pressure (DBP) of 80–89 mmHg exhibit a 30–90 % higher risk of cardiovascular events and mortality compared to normal individuals, while antihypertensive therapy has been shown to significantly reduce cardiovascular risk [4, 5].

OSA and hypertension share numerous common risk factors, including advanced age, male gender, smoking, obesity, and diabetes [6]. Furthermore, OSA is identified as an independent risk factor for hypertension and a major cause of secondary hypertension [7]. Compared to the general population, individuals with OSA exhibit a higher prevalence of hypertension, and conversely, approximately 30–50 % of

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hypertensive patients are diagnosed with comorbid OSA [8]. Hypertension associated with OSA is characterized by its propensity for underdiagnosis and treatment resistance. Notably, studies have shown that continuous positive airway pressure (CPAP) therapy leads to a significant reduction in blood pressure among OSA patients with hypertension, underscoring the therapeutic importance of CPAP in improving blood pressure control [9–11].

The intermittent hypoxia associated with OSA exerts multiple mechanisms influencing blood pressure regulation. First, recurrent episodes of hypoxia trigger oxidative stress, generating excessive free radicals that impair endothelial function, leading to a reduction in endothelium-dependent vasodilation and subsequent increases in peripheral vascular resistance and blood pressure [12]. Second, intermittent hypoxia activates the sympathetic nervous system, resulting in tachycardia and increased epinephrine secretion, which further contributes to elevated blood pressure [13]. Additionally, hypoxia may impact the function of blood pressure regulatory centers, disrupting homeostatic mechanisms [14]. The cumulative effect of these mechanisms renders individuals with OSA particularly susceptible to dysregulation of blood pressure.

Traditional assessment of OSA severity using the Apnea-Hypopnea Index (AHI) has limitations in evaluating its relationship with hypertension, as it solely considers the number of respiratory events without accounting for event duration, oxygen desaturation severity, or clinical symptoms [15]. In contrast, hypoxic burden (HB), defined as the ratio of total time spent with reduced oxygen saturation to total sleep time, expressed in units of (%min)/h, provides a more comprehensive evaluation [16]. Unlike AHI, HB is derived directly from polysomnographic (PSG) signals, thereby more accurately reflecting both the duration and the severity of respiratory events and oxygen desaturation [17]. Accumulating evidence highlights the strong correlation between HB and cardiovascular disease mortality, as well as its significant predictive value for cardiovascular events such as heart failure [18, 19].

Despite the growing body of research on OSA, studies investigating the patterns of blood pressure changes in OSA patients are limited, with most focusing on the impact of sleep stage alterations on blood pressure. Therefore, this study aims to comprehensively evaluate the association between HB and 24-h ambulatory blood pressure monitoring (ABPM) in patients with OSA.

Although previous studies have demonstrated the prognostic role of HB in cardiovascular outcomes, few have examined its relationship with ambulatory blood pressure parameters. Our study extends previous work by integrating HB and ABPM data in a prospectively recruited OSA cohort, aiming to determine whether HB provides incremental value beyond the AHI in assessing hypertension risk. Understanding this association may help refine cardiovascular risk stratification and guide individualized management strategies for OSA-related hypertension.

Methods

Participants

All study subjects were prospectively enrolled from Jan 2020 to Oct 2023, at the Sleep Medicine Center of the First Affiliated Hospital of Guangzhou Medical University. They were referred by their physician to complete PSG and 24-h ABPM for further confirmation of OSA and hypertension. The primary inclusion criteria were adults who agreed to complete PSG and 24-h ABPM, and had completely independent behavioral and cognitive functioning, and the exclusion criteria were (1) previous diagnosis of or treatment for OSA and hypertension; (2) respiratory events dominated by central or mixed sleep apnea; (3) total sleep time less than 6 h; (4) The valid data from 24-h ABPM accounted for <90 %; and (5) patients with secondary hypertension-related diseases. One hundred twenty-seven subjects finally met the inclusion and exclusion criteria, and the flow chart of this study is shown in Figure 1.

Ethics approval and consent to participate

Approval was granted by the Ethics Committee of The Affiliated Hospital of Guangzhou Medical University (No.05, 2017). Informed consent was obtained from all individual participants included in the study.

Data collection

Extracting baseline data for all participants from the medical electronic system, including demographic characteristics such as age, gender, body mass index (BMI), and smoking condition. Self-reported comorbidities: diabetes, atrial fibrillation, heart failure and hyperlipidemia. Additionally, we collected the Epworth sleep scale (ESS) score as well as PSG parameters including AHI, minimum arterial oxygen saturation (SaO_2), and HB. The definition and calculation of HB are as follows: Raw pulse oximetry data were extracted from the Philips Sleepware G3 software, and the desaturation area for each event was automatically computed using a customized Python script. The algorithm was adapted from the method proposed by Azarbarzin et al. (Eur Heart J 2019),

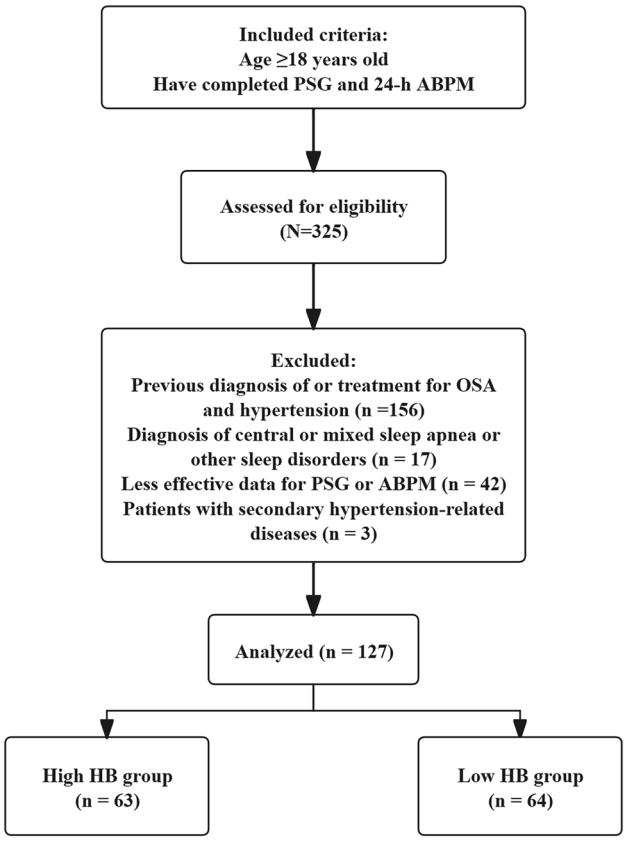

Figure 1: Study flowchart. OSA, obstructive sleep apnea; PSG, polysomnography; ABPM, ambulatory blood pressure monitoring; HB, hypoxic burden.

which integrates the total area under all oxygen desaturation events relative to baseline per hour of sleep [18, 20]. The total desaturation area was divided by the total sleep time to generate HB values, expressed as (%·min)/h, regardless of scored events. To ensure accuracy and reproducibility, 10 % of recordings were visually inspected by two independent raters, yielding an inter-rater reliability >0.9.

Polysmnography and OSA

Sleep monitoring was conducted in a sleep center using the Alice 6 PSG (Philips Wellcome, USA) for at least 7 h. The monitoring parameters included electroencephalogram, electromyography, blood oxygen saturation, electrooculogram, electrocardiogram, snoring, oral airflow, nasal airflow, chest wall movement, and body position [21]. Two experienced sleep professionals manually analyzed the data separately, following the 2017 American Academy of Sleep Medicine manual for sleep scoring and associated events [22]. Respiratory events were defined as having a minimum duration of 10 s. Specifically, obstructive apneas were identified as a complete cessation of airflow lasting for 10 s, while hypopneas were defined as a reduction in airflow signal amplitude of ≥30 % associated with a ≥3 % oxygen desaturation. The AHI was calculated as the total number of apneas and hypopneas divided by the total recording duration in hours. OSA was defined as an AHI ≥5 events/h, and high AHI was an AHI ≥15 events/h.

24-h Ambulatory blood pressure monitoring and hypertension

ABPM was conducted for continuous long-term monitoring, with an cuff attached to the left upper arm of the participant. The measurement was performed using a device compliant with international standards. The monitoring period was defined as daytime (08:00–23:00) and nighttime (23:00–08:00). Normal daily activities were allowed during the monitoring period, with valid readings recorded every hour without gaps, meeting the following valid blood pressure reading standards: systolic blood pressure 70–260 mmHg, diastolic blood pressure 40–150 mmHg, and pulse pressure 20–150 mmHg. Valid blood pressure measurements must exceed 90 %. Furthermore, we collected the parameters including 24-h mean systolic blood pressure (SBP), 24-h mean diastolic blood pressure (DBP), daytime mean SBP, daytime mean DBP, nighttime mean SBP, and nighttime mean DBP. The definition of hypertension based on ABPM was SBP ≥130/80 mmHg (mean) or SBP ≥135/85 mmHg (daytime) and ≥120/70 mmHg (nighttime).

Statistical analysis

The sample size was estimated using G*Power 3.1, assuming an effect size of 0.3, α=0.05, and 80 % power to detect group differences in daytime SBP, resulting in a required minimum of 110 participants. To account for potential data loss, 127 subjects were enrolled. Patients were categorized according to the baseline HB level as the “low-HB group” or “high HB-group” when the HB was below or above the median value of the population (<17.6 %min/h or ≥17.6 %min/h, respectively). Additionally, patients with AHI <15 events/h and AHI ≥15 events/h were assigned to “low-AHI group” and “high-AHI group”, respectively. Statistical analysis was performed using SPSS 26.0 software. Continuous data were presented as mean ± standard deviation or median (interquartile range, IQR: P25-P75). Independent sample t-tests were used for normally distributed data, while the Mann-Whitney U test was employed for non-normally distributed data. Non-normally distributed data were log-transformed. Categorical variables were expressed as counts (%) and compared between groups

using the chi-square test. Pearson correlation analysis or Spearman correlation analysis was utilized to assess the relationships between variables. Multiple linear regression analysis was applied to adjust for confounding factors in correlation analysis, using the enter method.

Ethics approval and consent to participate

Approval was granted by the Ethics Committee of The Affiliated Hospital of Guangzhou Medical University (No.05, 2017). Informed consent was obtained from all individual participants included in the study.

Results

Participants

The characteristics of participants categorized by the median HB are presented in Table 1. A total of 127 participants were recruited, with 63 classified in the high-HB group and 64 in the low-HB group. Compared with patients with low-HB, the high-HB patients were heavier (BMI 29.0 vs. 26.0 kg/m^2). No significant differences were observed in age, gender, smoking condition and ESS score, as well as various comorbidities including hypertension, diabetes atrial fibrillation, heart failure, coronary heart disease and hyperlipidemia.

As for PSG parameters, statistically significant differences ($p<0.001$) were found in AHI (47.4 vs. 18.3 events/h), minimum SaO2 (76.0 vs. 84.0 %), and HB (42.2 vs. 8.0 %min/h). Compared with patients in low-HB group, the analyses results of 24-h ABPM showed that patients with high-HB had higher blood pressure, while only 24-h mean DBP (81.3 vs. 77.6 mmHg, $p=0.042$) and daytime mean SBP (131.1 vs. 126.4 mmHg, $p=0.040$) showed statistically significant differences.

The association of HB and AHI with different 24-h ABPM parameters

Three models were performed through the following sequential strategies: Model 1 was unadjusted univariate analysis. Model 2 was adjusted for age, gender, BMI and

Table 1: Baseline characteristics for the total, high-HB group and low-HB group.

	Total (n=127)	High-HB group (n=63)	Low-HB group (n=64)	p-Value
Demographic characteristics				
Age, years	53.8 ± 12.2	53.5 ± 12.5	54.1 ± 12.0	0.734
BMI, kg/m^2	27.0 (24.9, 30.8)	29.0 (26.0, 32.1)	26.0 (24.1, 28.1)	<0.001
Male, n, %	90 (70.9)	47 (74.6)	43 (67.2)	0.358
Smoking, n, %	45 (35.4)	23 (36.5)	22 (34.4)	0.802
ESS score, points	8.0 (5.0, 13.0)	9.0 (5.0, 13.0)	8.0 (3.3, 12.0)	0.796
PSG parameters				
AHI, events/h	25.1 (15.0, 48.2)	47.4 (21.1, 62.3)	18.3 (11.8, 26.9)	<0.001
Minimum SaO_2, %	82.0 (75.0, 85.0)	76.0 (65.0, 82.0)	84.0 (82.0, 88.0)	<0.001
HB, %min/h	17.6 (7.71, 42.2)	42.2 (25.0, 80.8)	8.0 (4.4, 13.0)	<0.001
Comorbidities				
Hypertension, n, %	75 (59.1)	41 (65.1)	34 (53.1)	0.171
Diabetes, n, %	26 (20.5)	15 (23.8)	11 (17.2)	0.355
Atrial fibrillation, n, %	7 (5.5)	4 (6.3)	3 (4.7)	0.682
Heart failure, n, %	4 (3.2)	2 (3.2)	2 (3.1)	0.987
Coronary heart disease,n, %	34 (26.8)	18 (28.6)	16 (25.0)	0.649
Hyperlipidemia, n, %	72 (56.7)	36 (57.1)	36 (56.3)	0.919
ABPM parameters				
24-h Mean SBP, mmHg	127.6 ± 13.8	130.0 ± 12.1	125.3 ± 15.0	0.053
24-h Mean DBP, mmHg	79.4 ± 10.3	81.3 ± 9.5	77.6 ± 10.7	0.042
Daytime mean SBP, mmHg	128.8 ± 13.6	131.3 ± 12.3	126.4 ± 14.5	0.040
Daytime mean DBP, mmHg	80.6 ± 10.3	82.4 ± 9.5	78.9 ± 10.9	0.059
Nighttime mean SBP, mmHg	123.6 ± 16.0	125.1 ± 14.0	122.1 ± 17.9	0.302
Nighttime mean DBP, mmHg	75.6 ± 11.4	77.1 ± 10.9	74.1 ± 11.7	0.133

Non-normally distributed variables are expressed as the median (inter quartile range). All other values are expressed as mean ± SD, or n, %. HB, hypoxic burden; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; ESS, epworth sleepiness scale; PSG, polysomnography; AHI, apnea-hypopnea index; SaO_2, oxygen saturation; APBM, ambulatory blood pressure monitoring.

smoking condition. Model 3 included covariates in Model 2 and further adjusted for AHI values and minimum SaO_2. In linear regression analyses with Model 1, the 24-h mean DBP as well as the daytime mean SBP in the high-HB group was 3.71 mmHg (95 % CI=0.14–7.28, p=0.042) and 4.96 mmHg (95 % CI=0.23–9.69, p=0.040) higher than that in the low-HB group, respectively. While there were no statistical significance found in analyses with Model 2, the patients with high-HB still showed a higher daytime mean SBP for 6.04 mmHg (95 % CI=0.02–12.06, p=0.049) with Model 3. For another, no statistically significant differences were observed in various blood pressure parameters with three models when comparing the high and low AHI groups. The results are shown in Table 2. The scatter plots of the association between HB and 24-h ABPM parameters are shown in Figure 2.

The subgroup analyses for the association between HB and daytime mean SBP

Based on above findings, the subgroup analyses according to age, gender, and BMI, were conducted to further determine the association between HB and daytime mean SBP (Table 3). Age and BMI were grouped by 45 years and BMI=25 kg/m^2, respectively. The results suggested that compared with low-HB group, high-HB exhibited higher risk for elevated daytime mean SBP in patients whom were female, age ≥45 years and BMI ≥25 kg/m^2,both in Model 2 and Model 3. After adjusted for all selected confounding factors, the patients with high-HB presented a higher daytime mean SBP for 13.47 mmHg (95 % CI=1.20–25.92, p=0.035), 7.72 mmHg (95 % CI=1.46–13.99, p=0.016), and

Table 2: The comparison of linear regression analysis results between HB and AHI groups with different ABPM parameters.

	24-h mean SBP		24-h mean DBP		Daytime mean SBP		Daytime mean DBP		Nighttime mean SBP		Nighttime mean DBP	
	HB	AHI	HB	AHI	HB	AHI	HB	AHI	HB	AHI	HB	AHI
Model 1												
B-BP	4.72	3.32	3.71	3.57	4.96	3.23	3.46	3.29	2.95	2.30	3.03	3.50
95 % CIL	−0.06	−1.52	0.14	−0.02	0.23	−1.57	−1.14	−0.33	−2.69	−3.38	−0.94	−0.48
95 % CIU	9.50	8.17	7.28	7.16	9.69	8.03	7.05	6.91	8.60	7.98	7.01	7.48
Beta (β)	0.17	0.12	0.18	0.17	0.18	0.12	0.17	0.16	0.09	0.07	0.13	0.15
t-value	1.95	1.36	2.06	1.97	2.08	1.33	1.91	1.80	1.04	0.80	1.51	1.74
p-value	0.053	0.177	**0.042**[a]	0.051	**0.040**[a]	0.186	0.059	0.074	0.302	0.425	0.133	0.085
Model 2												
B-BP	4.27	2.59	3.67	3.44	4.38	2.36	3.44	3.17	2.43	1.56	2.75	3.26
95 % CIL	−0.94	−2.60	−0.25	−0.44	−0.76	−2.78	−0.50	−0.73	−3.71	−4.53	−1.62	−1.05
95 % CIU	9.47	7.77	7.58	7.31	9.53	7.49	7.38	7.08	8.52	7.64	7.12	7.57
Beta (β)	0.16	0.09	0.18	0.17	0.16	0.09	0.17	0.15	0.08	0.05	0.12	0.14
t-value	1.62	0.99	1.86	1.75	1.69	0.91	1.73	1.61	0.78	0.51	1.25	1.50
p-value	0.107	0.325	0.066	0.082	0.094	0.366	0.086	0.110	0.435	0.613	0.215	0.137
Model 3												
B-BP	5.60	351	3.86	3.95	6.04	3.45	3.90	3.89	2.92	1.64	2.13	3.05
95 % CIL	−0.50	−2.47	−0.73	−0.52	0.02	−2.46	−0.72	−0.61	−4.30	−5.37	−3.00	−1.92
95 % CIU	11.70	9.49	8.45	8.43	12.06	9.37	8.52	8.39	10.15	8.65	7.27	8.02
Beta (β)	0.20	0.13	0.19	0.19	0.22	0.13	0.19	0.19	0.09	0.05	0.09	0.13
t-value	1.82	1.16	1.67	1.75	1.99	1.16	1.67	1.71	0.80	0.46	0.82	1.22
p-value	0.072	0.247	0.098	0.083	**0.049**[a]	0.250	0.097	0.090	0.425	0.644	0.413	0.227

Low-HB and low-AHI group were considered as the reference. Model 1, univariate linear regression; Model 2 was adjusted for age, gender, BMI and smoking condition; Model 3 for HB was adjusted for age, gender, BMI and smoking condition, AHI values and minimum oxygen saturation; Model 3 for AHI was adjusted for age, gender, BMI, smoking condition, HB values and minimum oxygen saturation; HB, hypoxic burden; AHI, apnea-hypopnea index; ABPM, ambulate blood pressure monitoring; BP, blood pressure; 95 % CIL, 95 % confidence lower bound; 95 % CIU, 95 % confidence upper bound; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; [a] indicated p-value<0.05.

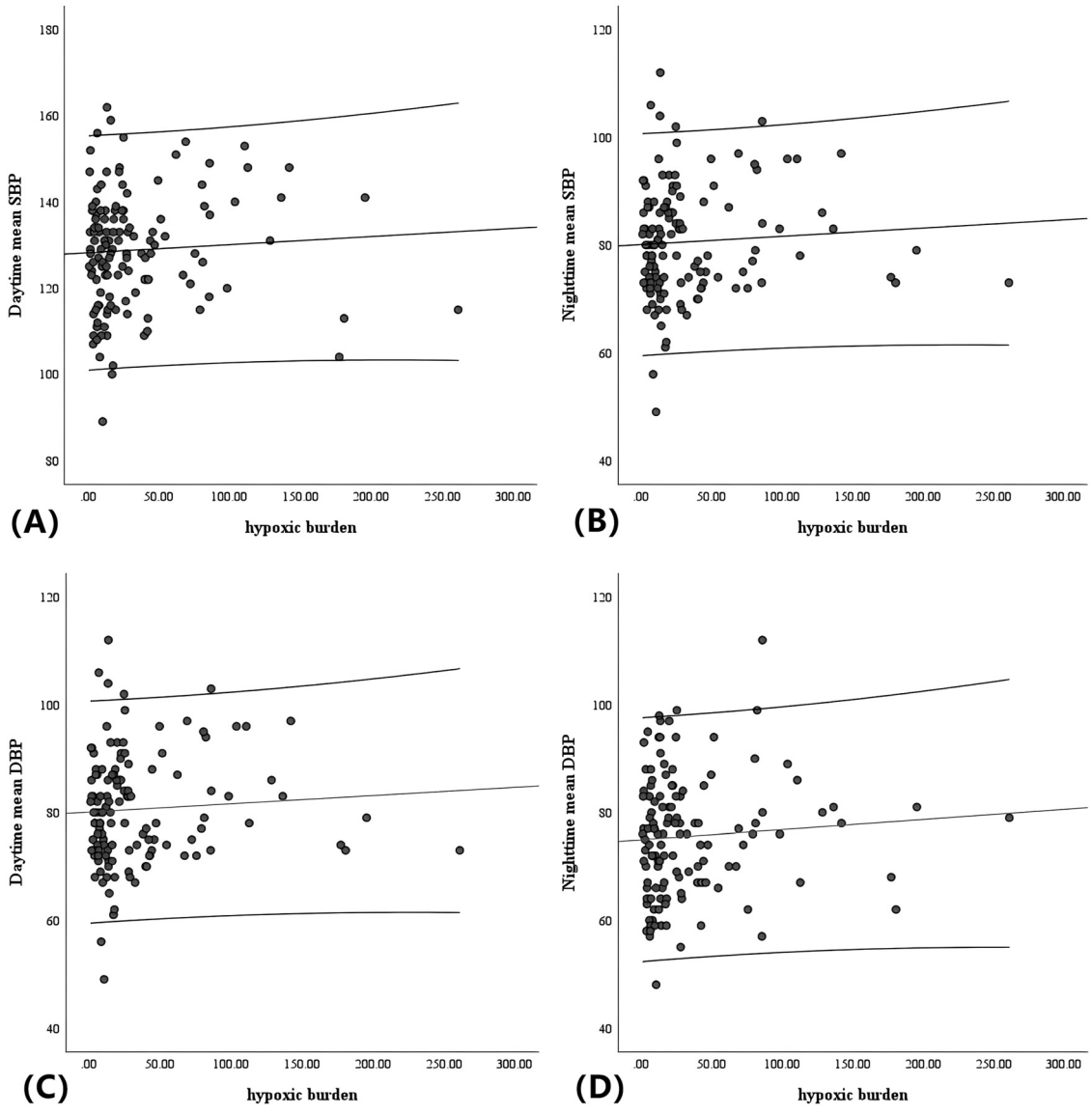

Figure 2: Scatter plots of the association between hypoxic burden and 24-h ambulatory blood pressure parameters. (A) Daytime mean SBP, (B) nighttime mean SBP, (C) daytime mean DBP, (D) nighttime mean DBP. The central solid line in each panel represents the linear regression fit. The upper and lower solid lines indicate the 95 % confidence interval for the regression line. The linear correlation between HB (as a continuous variable) and all blood pressure parameters was not statistically significant (all p>0.05). For significant associations between HB grouping and blood pressure, please refer to the primary analysis presented in the main text. HB, hypoxic burden; SBP, systolic blood pressure; DBP, diastolic blood pressure.

7.52 mmHg (95 % CI=0.54–13.52, p=0.035), in subgroup of female, age≥45 years and BMI≥25 kg/m^2, respectively.

Discussion

Main findings and interpretation

To our knowledge, this is the first prospective study to investigate the association between HB and ABPM in patients with OSA. We compared HB with the AHI, the standard measure of OSA severity, and found that higher HB, but not AHI, was independently associated with elevated daytime SBP. This association was particularly evident among women, older adults, and individuals with higher BMI. These findings add new insights into the mechanisms linking nocturnal hypoxia and blood pressure regulation and suggest that HB provides a more comprehensive physiological assessment than AHI.

Previous studies have shown that the prevalence of hypertension among OSA patients is substantially higher than in the general population, with reported rates of 59 %, 62 %, and

Table 3: The subgroup analyses of linear regression between HB with daytime mean SBP based on age, gender and BMI.

	Daytime mean SBP					
	Male n=90	**Female n=37**	**Age <45 n=33**	**Age ≥45 n=94**	**BMI <25 n=34**	**BMI ≥25 n=93**
Model 1						
B-BP	2.90	9.82	−0.22	6.99	3.93	5.62
95 % CIL	−2.55	−0.02	−10.45	1.85	−5.89	−0.01
95 % CIU	8.34	19.66	10.00	12.13	13.75	11.24
Beta (β)	0.11	0.32	−0.01	0.27	0.11	0.20
t-value	1.06	2.03	−0.05	2.70	2.08	1.98
p-value	0.294	0.051	0.965	**0.008**[a]	0.421	0.050
Model 2						
B-BP	2.15	10.72	−1.70	6.61	5.85	5.61
95 % CIL	−3.87	0.03	−13.65	1.26	−5.13	0.03
95 % CIU	8.16	21.41	10.25	11.95	16.83	11.24
Beta (β)	0.08	0.35	−0.06	0.26	0.21	0.20
t-value	0.71	2.04	−0.29	2.45	1.09	2.02
p-value	0.480	**0.049**[a]	0.773	**0.016**[a]	0.285	**0.049**[a]
Model 3						
B-BP	2.79	13.47	0.28	7.72	5.10	7.52
95 % CIL	−4.43	1.02	−15.52	1.46	−8.72	0.54
95 % CIU	10.01	25.92	16.08	13.99	18.92	14.51
Beta (β)	0.11	0.44	0.01	0.30	0.19	0.27
t-value	0.77	2.21	0.04	2.45	0.76	2.14
p-value	0.444	**0.035**[a]	0.971	**0.016**[a]	0.456	**0.035**[a]

Low-HB group were considered as the reference. Model 1, univariate linear regression; Model 2 for gender subgroup was adjusted for age, BMI and smoking condition; Model 2 for age subgroup was adjusted for gender, BMI and smoking condition; Model 2 for BMI subgroup was adjusted for age, gender and smoking condition; Model 3 was Model 2 plus AHI values and minimum oxygen saturation; HB, hypoxic burden; AHI, apnea-hypopnea index; ABPM, ambulate blood pressure monitoring; BP, blood pressure; 95 % CIL, 95 % confidence lower bound; 95 % CIU, 95 % confidence upper bound; BMI, body mass index; SBP, systolic blood pressure; [a]indicated p-value <0.05.

67 % for mild, moderate, and severe OSA, respectively [23]. The exact mechanisms underlying this association remain unclear, but multiple physiological pathways have been proposed. Our study supports the growing evidence that nocturnal hypoxic burden, rather than event frequency alone, plays a crucial role in blood pressure dysregulation in OSA.

Potential mechanisms linking HB and blood pressure

Intermittent hypoxia, the hallmark feature of OSA, induces oxidative stress and inflammatory activation, both of which can impair vascular function and increase peripheral resistance. Repeated cycles of hypoxia and reoxygenation lead to excessive production of reactive oxygen species (ROS), which damage the endothelium, reduce nitric oxide bioavailability, and promote vasoconstriction [24, 25]. In addition, sympathetic nervous system activation contributes to the elevation of blood pressure. Chronic intermittent hypoxia triggers enhanced catecholamine release and renin-angiotensi-aldosterone system activation, resulting in tachycardia, vasoconstriction, and persistent hypertension [26–29].

At the molecular level, OSA-related hypoxia involves dysregulation of hypoxia-inducible factors (HIF-1 and HIF-2) [30, 31]. HIF-1 activation increases ROS generation through oxidase gene upregulation, while HIF-2 inhibition suppresses antioxidant gene transcription. The imbalance between oxidant and antioxidant systems aggravates vascular injury, activates the sympathetic nervous system, and leads to sustained blood pressure elevation. These mechanisms together explain why a higher cumulative hypoxic load – quantified by HB – is more strongly associated with blood pressure alterations than the number of apnea and hypopnea events captured by AHI.

Comparison with previous evidence

Our findings are consistent with prior studies demonstrating the prognostic and clinical relevance of HB. Wojciech et al. reported that HB independently predicts cardiovascular events and mortality in patients with OSA [32], while Margaux et al. found that both HB and heart rate variability from polysomnography were significant predictors of stroke risk [33]. In line with these studies, we observed that elevated HB, but not AHI, was associated with increased daytime SBP. Similarly, John et al. reported that higher HB levels were related to diastolic and uncontrolled systolic blood pressure in untreated OSA patients [34]. However, their study relied on office blood pressure measurements, which may not accurately reflect circadian blood pressure variation. By contrast, our use of 24-h ABPM allowed a more precise evaluation of blood pressure patterns, particularly daytime changes.

Emerging evidence indicates that OSA contributes to arterial stiffness and endothelial dysfunction, both key mechanisms in hypertension and atherosclerosis [35, 36]. Chronic intermittent hypoxia accelerates vascular remodeling, reduces arterial elasticity, and promotes early vascular aging. These vascular alterations provide a plausible explanation for the observed association between HB and daytime SBP elevation in our study. Furthermore, hypoxia-induced sympathetic activation increases catecholamine levels and inflammatory mediators such as ROS and cytokines, further aggravating blood pressure dysregulation [37, 38]. Altogether, these mechanisms underscore the pathophysiological importance of hypoxic burden in mediating OSA-related hypertension.

Subgroup analyses

Subgroup analyses revealed that the association between higher HB and elevated daytime SBP appeared stronger in women, older adults (≥45 years), and overweight patients (BMI ≥25 kg/m^2). These trends may be explained by population-specific physiological differences. For example, the decline in estrogen levels during the perimenopausal period weakens vascular protection and increases vascular reactivity to hypoxia, thereby enhancing peripheral resistance and sympathetic responsiveness [39]. In older individuals, age-related arterial stiffness and diminished baroreflex sensitivity may amplify the hypertensive effects of nocturnal hypoxia. Similarly, in overweight patients, chronic inflammation, oxidative stress, and elevated sympathetic tone contribute to vascular dysfunction and blood pressure elevation.

Nevertheless, these subgroup findings should be interpreted cautiously. The current study was not powered to detect small subgroup differences, and the analyses were exploratory in nature. Although effect estimates were adjusted for potential confounders, residual confounding cannot be excluded. Future multicenter studies with larger, well-balanced cohorts are required to validate these subgroup-specific associations and clarify their underlying mechanisms.

Clinical implications and limitations

The present study highlights the potential clinical value of incorporating HB into cardiovascular risk assessment for OSA. Unlike AHI, HB captures both the duration and depth of oxygen desaturation, reflecting the true hypoxic load imposed on the cardiovascular system. Measuring HB may improve identification of OSA patients at higher risk for blood pressure dysregulation and guide individualized management, such as prioritizing blood pressure monitoring or initiating early therapeutic interventions.

However, several limitations must be acknowledged. First, as a cross-sectional study, causal inference between HB and hypertension cannot be established. Second, the relatively small sample size limits the statistical power, especially in subgroup analyses. Third, other relevant parameters such as lipid profiles, hormone levels, or vascular imaging data were not included, preventing a more comprehensive mechanistic evaluation. Finally, the study population consisted mainly of newly diagnosed OSA patients with borderline blood pressure, which may not represent patients with established hypertension. Future longitudinal studies with larger sample sizes and mechanistic measures such as heart rate variability and arterial stiffness indices are warranted to confirm these associations and further elucidate the pathophysiological role of HB.

Conclusions

In summary, this prospective study demonstrates that higher hypoxic burden, but not AHI, is independently associated with elevated daytime SBP in patients with OSA. HB reflects both the severity and duration of hypoxia and may serve as a more comprehensive indicator for evaluating OSA-related cardiovascular risk. These findings emphasize the clinical relevance of HB and support its integration into future risk stratification models for OSA-related hypertension.

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Conflicts of interest: All authors have seen and approved the manuscript. The authors have no conflicts of interest.

Data availability statement: The data used to support the findings of this study are available from the corresponding author upon request.

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