Published in final edited form as:

J Hypertens. 2014 February ; 32(2): 267–275. doi:10.1097/HJH.000000000000011.

Obstructive sleep apnea and diurnal nondipping hemodynamic indices in patients at increased cardiovascular risk

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Abstract

Rationale—We hypothesized increasing obstructive sleep apnea (OSA) severity would be associated with nondipping blood pressure (BP) in increased cardiovascular disease (CVD) risk.

Methods—Baseline data from 298 cardiology patients recruited for a multicenter randomized controlled trial were examined. Dipping was defined as a sleep-related BP or heart rate (HR) reduction of at least 10%. Logistic regression models were fit, adjusting for age, sex, race, BMI, CVD risk factors, CVD, and study site.

Results—There was a statistically significant 4% increase in the odds of nondipping SBP per 1-unit increase in both Apnea Hypopnea Index (AHI) and Oxygen Desaturation Index (ODI). There was no significant relationship between AHI and nondipping mean arterial pressure (MAP); however, a 3% increase in the odds of nondipping MAP per 1-unit increase in ODI was observed (odds ratio, OR =1.03; 95% confidence interval, CI 1.00–1.05). At severe OSA levels, a 10 and 4% increase in odds of nondipping DBP per 1-unit increase in AHI and ODI were observed,

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Conflicts of interest

The present study is supported by NIH National Heart Lung Blood Institute RC2 HL101417 and K23 HL079114, NIH M01 RR00080, NIH UL1 RR024989 from the National Center for Research Resources (NCRR). D.J.G. is a consultant for ResMed Corporation and principal investigator or co-investigator on multiple VA-funded sleep apnea research studies. R.M. was supported by NIH NHLBI 1R01HL109493 and R21HL108226. R.M. serves on the Medical Advisory Board for Care Core National, has received funding from the National Institutes of Health for research, and her institution has received positive airway devices from Philips Respironics for research for which she is the Principal Investigator. S.R.P. received funding from the Resmed Foundation and equipment from Philips Respironics for research activities. S.R.P. has served as a consultant for Apnex Medical, Apnicure, and Vertex Pharmaceuticals. D.L.B. has received NIH funding RC2HL101417. S.R. is a principal investigator for NIH-funded research of sleep apnea and cardiac disease, principal investigator of grant from ResMed, and has received equipment from Philips Respironics and ResMed for research. N.M.P. has received Resmed research grant. S.F.Q. has received funding from Jazz Pharmaceuticals and Saatchi and Saatchi. E.F.L. has received funding from the NIH and has served as a consultant to ResMed. R.B. has received funding from the NIH. H.W. and M.R. report no conflicts of interest.

respectively. A 6% [OR =1.06; 95% CI (1.01–1.10)] increase in nondipping HR odds was observed with each increase in ODI until the upper quartile of ODI.

Conclusion—In patients at cardiovascular risk and moderate-to-severe OSA, increasing AHI and/or ODI were associated with increased odds of nondipping SBP and nondipping MAP. More severe levels of AHI and ODI also were associated with nondipping DBP. These results support progressive BP burden associated with increased OSA severity even in patients managed by cardiology specialty care.

Keywords

cardiovascular disease; hypertension; hypoxia; sleep apnea

INTRODUCTION

Recurrent episodes of hypoxia, arousals, and swings in intrathoracic pressure that occur in obstructive sleep apnea (OSA) may alter blood pressure (BP) via interacting pathophysiologic mechanisms including chronically elevated sympathetic tone, alterations in baroreceptor function, and cardiovascular remodeling [1–4]. Apneic episodes during sleep are recognized to result in acute BP perturbations [5–7]. Animal models of intermittent hypoxia have been shown to cause BP elevations that persist even after the removal of the hypoxic exposure [8,9] and these findings have been corroborated in human studies [10].

Increasingly, diurnal BP profiles have been identified to contain predictive information of future cardiovascular events and mortality [11–16]. Under normal circumstances, the BP value drops during sleep by at least 10% of the wake value. However, a nondipping pattern defined as nocturnal reduction in BP less than 10% occurs in a subset of individuals [17] and those with OSA may be at increased risk [18]. Although relationships of OSA and nondipping BP patterns have been reported, there are some important knowledge gaps. In particular, it is unclear whether OSA is associated with nondipping BP in patients with cardiovascular disease (CVD) risk who are under the care of cardiology specialists who are trained to use guideline-based interventions, including aggressive treatment of BP and heart rate (HR) [19]. Similar to nondipping BP, nocturnal nondipping of HR also predicts cardiovascular events in hypertensive patients, but its relationship to OSA has yet to be examined [20]. Moreover, the existing literature is unclear on which nondipping BP index types [i.e., SBP, DBP, mean arterial pressure (MAP)] are associated with OSA [21,22]. Furthermore, many studies are also limited by small sample sizes [21,23], single center geographic distributions [21,24,25], and lack of data from 24-h BP monitoring [6,26,27], and have not sought to identify the relationships among OSA severity metrics with nondipping patterns.

Given limitations of existing data, we elected to examine the association between OSA and nondipping BP indices and HR in a group of individuals with high background cardiovascular risk or established CVD recruited from cardiology specialty clinics. We postulated that despite specialty cardiology care, OSA severity would be associated with a progressive increase in nondipping SBP (defined as a wake-sleep reduction of less than 10%), a clinically relevant marker for increased rates of adverse cardiovascular outcomes

and mortality [28,29]. We examined the relationship of several common metrics of OSA severity with nondipping BP and HR by considering both linear and nonlinear relationships. Secondarily, we hypothesized that OSA severity would be associated with progressive increases in other indices of nondipping BP and HR.

METHODS

Study sample

The current study includes individuals participating in the baseline examination conducted for the Heart Biomarker Evaluation in Apnea (Heart BEAT), a randomized controlled trial aimed at comparing conservative medical therapy, supplemental nocturnal oxygen therapy, and positive airway pressure therapy on cardiovascular biomarkers in OSA (clinicaltrials.gov Trial Registration Number: NCT01086800). Patients with moderate-to-severe OSA were recruited from outpatient cardiology clinics at four sites (Brigham and Women's Hospital, Case Medical Center, Johns Hopkins Medical Institutions, and Veterans Affairs Boston Healthcare System). All of which follow standard American Heart Association/American College of Cardiology guideline-based approaches for primary and secondary CVD risk reduction. Participants were recruited using questionnaire screening and medical chart review, followed by overnight Type III sleep testing (Embletta-Gold; Embla, Broomfield, Colorado, USA). Inclusion criteria included an Apnea Hypopnea Index (AHI) of 15–50 events/hour; age 45–75 years; and established stable coronary artery disease (CAD; documented prior myocardial infarction or coronary revascularization >3 months prior to entry or angiographically documented 50% stenosis in a major coronary artery) or at least three cardiovascular risk factors [physician treated hypertension (HTN) or antihypertensive medication use; diabetes mellitus; BMI ≥ 30 kg/m²; or dyslipidemia]. Exclusion criteria included a central apnea index more than 5 events/hour, nocturnal oxygen saturation less than 85% for more than 10% of the sleep monitoring record, heart failure with an ejection fraction less than 30% or New York Heart Association (NYHA) classification more than 2, poorly controlled HTN (>170 mmHg/>110 mmHg) or diabetes (HbA1c > 9.0%), prior stroke with functional impairment, severe uncontrolled medical problems, severe chronic insomnia or circadian rhythm, resting oxygen saturation less than 90%, current smoking, and use of either supplemental oxygen or positive airway pressure.

Institutional Review Board approval was obtained from all sites and full written informed consent was obtained.

Sleep apnea assessment

Sleep apnea severity was derived from the results of an in-home sleep study that was scored by a single registered polysomnologist following the 2007 American Academy of Sleep Medicine guidelines [30]. Apnea was defined as a complete cessation of air flow, measured using nasal pressure, for at least 10 s. Hypopnea was defined as 50% reduction in breathing amplitude lasting at least 10s associated with at least 3% oxygen desaturation. The following parameters were obtained: AHI (the number of apneas and hypopneas per hour of estimated sleep time); oxygen desaturation index (ODI; the number of oxygen desaturations >3% per

hour of estimated sleep time); and percentage of estimated sleep time below 90% oxygen saturation (TST<90).

Twenty four-hour ambulatory blood pressure monitoring

In conjunction with a baseline study visit, which included measurement of resting BP in triplicate, participants were instructed in the use of the Spacelabs 90217 Ambulatory Blood Pressure monitor (SpaceLabs Medical Inc., Issaquah, Washington, USA). The device was programmed to measure SBP, DBP, and HR every 20 min from 6 a.m. to 10 p.m. and every 30 min between 10 p.m. and 6 a.m. for a 24-h period of time. MAP was calculated using the following formula: $[1/3 \times \text{SBP}] + [2/3 \times \text{DBP}]$. Participants were instructed to engage in usual activities and continue usual medication regimens including antihypertensive therapy. Participants completed a sleep diary indicating bed and wake times; these time periods were used to identify periods of wake and sleep for BP analysis.

Statistical methods

Given the strong existing data demonstrating high cardiovascular risk related to systolic HTN, the primary outcome considered was nondipping SBP [28]. The secondary outcomes were nondipping DBP, MAP, and HR. Nondipping hemodynamic parameters were defined by a ratio of mean sleep BP (or HR) to mean wake BP (or HR) greater than 0.90. The OSA exposure metrics were AHI, ODI, and TST less than 90.

To identify linear and possible nonlinear associations between each OSA metric and the log-odds of nondipping BP or HR, logistic models assuming linear and piecewise linear (defined using one knot at the first, second, and third quartile for each OSA metric) associations between each OSA metric and the log-odds of nondipping BP or HR were compared using a 0.632 bias-corrected prediction error that was obtained from a leave-one-out bootstrap cross-validation procedure based on 5000 bootstrap samples. Prediction error was calculated using a Brier score [31], a measure of the squared difference between the model-based predicted probability of nondipping BP or HR and the observed value of nondipping BP or HR averaged across all participants. Because lower Brier scores represent models with higher accuracy, the model that had the lowest Brier score was selected as the final model. This cross-validation procedure was used because this is a standard approach when selecting the best fitting model among competing models [32].

To examine the effect of potential confounders on these associations, three logistic regression models were considered: Model 1 (adjusted for the OSA exposure and site only), Model 2 (adjusted for Model 1 covariates as well as age, sex, race, and BMI), and Model 3 [adjusted for Model 2 covariates as well as HTN, diabetes mellitus (diagnosed or taking oral hypoglycemic medications or insulin), dyslipidemia (diagnosed or on statin medication), smoking (pack years) and established CVD]. Established CVD was defined as the presence of CAD (outlined under inclusion criteria) or more than 3 months since stroke occurred without functional impairment.

We also explored whether CVD or diabetes mellitus were effect modifiers of the association between each OSA metric and nondipping hemodynamic indices by including an interaction term between each possible effect modifier and each OSA metric in each model.

All tests were performed assuming a significance level of 0.05 and using SAS v 9.2 (SAS Institute Inc., Cary, North Carolina, USA) for analyses and R 2.15.2 for graphs.

RESULTS

Participant characteristics

Of a total of 318 participants who completed the baseline examination of the randomized trial, 15 were excluded due to invalid or missing BP data and five were excluded due to missing covariate data, yielding an analytical sample of 298 participants. There was no statistically significant difference in participant characteristics between this sample and those who were excluded (age 63.0 ± 7.2 versus 62.3 ± 9.2 years, male sex 74 versus 70%, and median BMI 33.3 versus 35.0 kg/m², respectively). The majority of the sample included older, obese, male participants with nearly all participants carrying a diagnosis of HTN (97.3%) and over half with documented CAD (Table 1). The vast majority of participants were prescribed antihypertensive medications (95.6%) and the most common medications were angiotensin converting enzyme (ACE) inhibitors/angiotensin receptor blockers (69.8%) and β -blockers (67.5%).

Overall, resting BP measurements reflected well controlled indices: SBP, 126.9 ± 15.2 mmHg and DBP, 73.8 ± 10.0 mmHg; 81.9% of the participants had a SBP less than 140 mmHg and DBP of less than 90 mmHg. The 24-h BP profiles showed that on average, BP and HR were higher while awake than while sleep; however, there was a high prevalence of nondipping BP, ranging from 42.6 to 54.0% for the different hemodynamic indices (Table 1). The average number of valid readings obtained from the 24-h BP monitoring was 49.4 ± 11.5 and ranging between 11 and 69 (wake: 34.6 ± 10.1 ; sleep: 15.1 ± 4.4).

Nondipping SBP and sleep apnea indices

Evaluation of the association between AHI and ODI with nondipping SBP demonstrated that the logistic model based on a linear association minimized prediction error (linear and nonlinear Brier's score of 0.245 versus 0.246–0.247 for AHI and 0.244 versus 0.245–0.246 for ODI). Under this model, there was a 4% increase in the adjusted odds of nondipping SBP per 1-unit increase in AHI [odds ratio, OR =1.04; 95% confidence interval, CI (1.01–1.07), P value =0.012] and a 4% increase in the adjusted odds of nondipping SBP per 1-unit increase in ODI (OR =1.04; 95% CI 1.01–1.06; P value =0.009; Table 2 and Fig. 1)

Nondipping mean arterial pressure and sleep apnea indices

When evaluating the association between AHI and ODI with nondipping MAP, the logistic model based on a linear association minimized prediction error (linear and nonlinear Brier's score of 0.248 versus 0.250 for AHI and 0.246 versus 0.248 for ODI). There was a 3% increase in the adjusted odds of nondipping MAP per 1-unit increase in ODI [OR =1.03; 95% CI (1.00–1.05); P value =0.043; Table 2 and Fig. 2]. In contrast, a significant relationship was not detected between AHI and nondipping MAP under the fully adjusted model.

Nondipping DBP and sleep apnea indices

In the assessment of the association between AHI and nondipping DBP, the logistic model based on a piecewise linear association defined by a knot at the 3rd quartile of AHI, 30.0, minimized prediction error (Brier's score of 0.248 versus 0.249–0.251). The fitted relationship is reflected in Fig. 3a and shows a decreasing but not statistically significant relationship between AHI and the probability of non-dipping DBP when AHI less than 30.0 and a statistically significant increasing relationship when AHI at least 30.0, such that for every 1-unit increase in AHI beyond 30, there was a 10% increase in the odds of nondipping DBP (OR =1.10; 95% CI 1.02–1.19; *P* value =0.012; Table 3).

Alternatively, when evaluating the association between ODI and nondipping DBP, the logistic model based on a piecewise linear association defined by a knot at the 1st quartile of ODI, 24.8, minimized prediction error (Brier's score =0.247 versus 0.249 in other models). Consistent with the findings for AHI, a decreasing but not statistically significant relationship between ODI and nondipping DBP was observed when ODI less than 24.8 and a statistically significant increasing relationship was noted when ODI at least 24.8, such that for every 1-unit increase in ODI, there was a 4% increase in the odds of nondipping DBP (OR =1.04; 95% CI (1.01–1.07), *P* value =0.007; Table 4; Fig. 3b).

Nondipping heart rate and sleep apnea indices

For the association between ODI and nondipping HR, the logistic model based on a piecewise linear association defined by a knot at the 3rd quartile of ODI, 38.9, minimized prediction error (Brier's score of 0.2452 versus 0.2454–0.2469). In this case, for every 1-unit increase in ODI when ODI less than 38.9, there was a 6% increase in the odds of nondipping HR (OR =1.06; 95% CI 1.01–1.10; *P* value =0.01), although this relationship did not persist when ODI at least 38.9 (Fig. 4). A significant association between AHI and nondipping HR was not observed.

Nondipping hemodynamic indices and total sleep time less than 90% oxygen saturation

No significant associations between TST less than 90 and nondipping hemodynamic indices were observed.

Effect modification via coronary vascular disease, diabetes mellitus

No statistically significant interactions between each OSA index and CVD or diabetes mellitus were detected in any of the models considered. Consequently, there was no evidence that the effect of each OSA index on each non-dipping hemodynamic index differed by CVD, diabetes mellitus status. There were insufficient numbers of individuals not using BP medications to explore potential effect modification by medication.

DISCUSSION

The primary finding was evidence that the prevalence of nondipping SBP progressively increased with increasing levels of AHI and ODI in participants with moderate-to-severe untreated OSA and with cardiovascular risk factors or established CVD recruited from cardiology practices who had well controlled resting BP profiles. Specifically, after

adjusting for a number of potential confounders, we observed that the odds of nondipping SBP increased by approximately 3–4% for each 1-unit increase in AHI or ODI. Linear relationships were also observed between ODI (but not AHI) and the log-odds of nondipping MAP. In contrast, the odds of nondipping DBP increased with increasing OSA severity only after threshold levels of severity; that is, an AHI more than 30 and ODI more than 25 were associated with a 10 and 4% increase in the odds of nondipping DBP, respectively. A piecewise linear association was also noted between ODI and the log-odds of nondipping HR at the lower levels of ODI in this sample.

It is important to note that these findings were observed in individuals with a restricted range of AHI (15–50) and high cardiovascular risk or burden. Also, this trial excluded those patients with BP more than 170/110 – the patients most likely to be nondippers – and, therefore, our results are likely an underestimate of the true impact of OSA on nondipping hemodynamic profiles. Despite expert medical management of cardiology subspecialists adhering to national treatment guidelines and well controlled resting BP indices, the relationship of increasing OSA severity and nondipping SBP was evident in the current work, thereby emphasizing the importance of OSA pathophysiologic influences on nondipping hemodynamic profiles.

Nondipping BP patterns were noted in up to 50% of participants in the current study, which is higher than in the general population, but consistent with the high prevalence (50–80%) of nondipping in OSA noted in prior work [21,33]. The current results extend prior research by explicitly addressing dose–response associations between metrics of OSA severity and several indices of 24-h hemodynamic parameters. The dose–response association between increasing AHI or ODI levels with nondipping SBP provides an explanation for the increased cardiovascular morbidity observed in patients with moderate-to-severe OSA [34]. This is supported by observations that individuals with nondipping BP have more evidence of HTN-induced target organ damage including left ventricular hypertrophy, microalbuminuria, and reduced arterial compliance as well as suffer from increased rates of CVD [35]. The linear relationship between OSA and the log-odds of nondipping SBP observed in the current study, therefore, highlights nocturnal SBP as an important therapeutic target to improve cardiovascular outcomes in patients with OSA.

The data published thus far examining nondipping BP parameters and OSA metrics have been inconsistent, particularly regarding the role of nocturnal hypoxia and levels of OSA-related physiological perturbations associated with nondipping BP abnormalities. We sought to overcome these limitations by examining both linear and nonlinear relationships in the context of various definitions of OSA physiologic and hypoxic exposures. Our results are consistent with longitudinal data from the Wisconsin Sleep Cohort Study, a community-based cohort with predominantly mild OSA, which demonstrated a dose–response increase in the development of nondipping SBP (and not nondipping DBP) with increasing category of OSA severity defined by the AHI (hypopnea based upon a >4% oxygen desaturation) [36]. Our study differs from the Wisconsin study as we used the current American Academy of Sleep Medicine recommendations that require a 3% or greater oxygen desaturation with hypopneas, examined other OSA metrics such as ODI and percentage of time less than 90% oxygen saturation, and considered a cohort with increased cardiovascular risk.

It is now accepted by many that data from ambulatory BP monitoring, as utilized in the current study, have superior prognostic value [37–39] and better cardiovascular risk prediction [29,40] than office BP measurements, and may assist with improving HTN diagnosis [39,41]. In the recently published guidelines for the management of HTN, more strict BP control during a 24-h period is identified for management of high-risk hypertensive patients [42,43]. Given the high prevalence of nondipping BP in OSA, ambulatory BP monitoring may also be useful for this patient population of increased cardiovascular risk [7,13,29].

Strengths of this study include careful consideration of various OSA definitions and linear and threshold associations and use of a rigorous statistical cross-validation procedure to guard against spurious findings. Other strengths include the multicenter design and the use of 24-h ambulatory BP monitoring. Standardized methods were also used for the collection of sleep and BP measures, which were scored by certified technicians using centralized reading and subject to quality control procedures. We considered various confounding factors, such as cardiovascular risk factors and CVD status. Furthermore, we considered nondipping HR, which is novel in the OSA literature and potentially important, given increased cardiovascular risk associated with nondipping HR [20]. Different nondipping BP parameters were considered due to their potential differential underlying physiology and cardiovascular risk associations. The study also had several limitations, in particular, inclusion of individuals with only moderate-to-severe OSA. Despite the limited spectrum of OSA severity, we were able to detect significant relationships between OSA and nondipping SBP as well as identify thresholds of potential risk for nondipping DBP and HR. This observational study examined multiple comparisons; thus, the results should be viewed as exploratory. The current study is also limited by its cross-sectional nature precluding the inference of temporal relationships. Although biologic plausibility supports the notion of OSA physiology contributing to nondipping hemodynamic profiles, we cannot exclude the possibility of reverse or bi-directionality.

Perspectives

Our data highlight in potential utility of 24-h ambulatory BP monitoring to identify nondipping patterns in patients with OSA as part of strategies to improve cardiovascular outcomes. Future investigations should focus on better understanding of the mechanisms underlying the influences of OSA contributing to nondipping hemodynamic patterns including the role of baroreflex or autonomic dysfunction, relative nocturnal volume overload, and abnormal sodium handling. Future research is also needed to rigorously consider the role of OSA treatment, including continuous positive airway pressure and supplemental oxygen, in 24-h BP profiles.

Acknowledgments

The study investigators acknowledge the invaluable help of the study staff: Anna Maria Kibler, Joan Aylor, Amanda Barbeau, Denise P. Clarke, Daniel Cooper, Kelly Devine, Melissa Minotti, Rawan Nawabit, Ashley Wagner, and Cynthia Williams.

D.L.B.: Advisory Board: Elsevier Practice Update Cardiology, Medscape Cardiology, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care; Chair: American Heart Association Get With The Guidelines Steering Committee; Honoraria: American College of Cardiology (Editor,

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Abbreviations

AHI	Apnea Hypopnea Index
BP	blood pressure
CAD	coronary artery disease
CVD	cardiovascular disease
HR	heart rate
MAP	mean arterial pressure
ODI	Oxygen Desaturation Index
OSA	obstructive sleep apnea

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FIGURE 1.

Apnea Hypopnea Index and Oxygen Desaturation Index versus model-based probability of nondipping SBP. Solid line represents the model-based probability of nondipping SBP for white men at Case Medical Center with an Apnea Hypopnea Index between 14.6 and 49.3 (a) or an Oxygen Desaturation Index between 13.9 and 69.7 (b) who are 63.2 years old with a BMI of 33.3 kg/m², 6.4 smoking pack years with hypertension, dyslipidemia and cardiovascular disease and without diabetes mellitus. Dotted lines represent the associated 95% confidence intervals (CIs).

FIGURE 2.

Apnea Hypopnea Index and Oxygen Desaturation Index versus model-based probability of nondipping mean arterial blood pressure. Solid line represents the model-based probability of nondipping mean arterial blood pressure with attributes and index ranges as outlined in Figure 1 demonstrating Apnea Hypopnea Index in (a) and Oxygen Desaturation Index in (b). Dotted lines represent the associated 95% confidence intervals (CIs).

FIGURE 3.

Apnea Hypopnea Index and Oxygen Desaturation Index versus model-based probability of nondipping DBP. Solid line represents the model-based probability of nondipping DBP with attributes and index ranges as outlined in Figure 1 demonstrating Apnea Hypopnea Index in (a) and Oxygen Desaturation Index in (b). Dotted lines represent the associated 95% confidence intervals (CIs).

FIGURE 4.

Oxygen Desaturation Index versus model-based probability of nondipping heart rate. Solid line represents the model-based probability of nondipping heart rate with attributes and oxygen desaturation index range as outlined in Figure 1. Dotted lines represent the associated 95% confidence intervals (CIs).

TABLE 1

Participant characteristics

Demographics	
Age (years)	63.0 ± 7.2
Men	73.8%
Whites	79.2%
BMI (kg/m ²)	34.0 ± 5.6
Hypertension	97.3%
Diabetes mellitus	45.0%
Dyslipidemia	96.3%
History of smoking	61.1%
Smoking (pack years)	19.8 ± 27.8
Coronary artery disease	53.4%
Stroke	5.4%
Cardiovascular disease	54.7%
Site	CMC: 30.2%; BWH: 14.4%; JHU: 28.9%; BVA: 26.5%
Measures of OSA severity	
Apnea Hypopnea Index	25.1 ± 8.5
Oxygen Desaturation Index	32.5 ± 10.3
Minimum oxygen saturation	79.1 ± 6.0
Percentage sleep time less than 90% oxygen saturation	9.7 ± 13.0
Number of antihypertensive medications (%)	
None	4.4
One	25.8
Two	36.9
Three	21.2
Four	11.7
Any antihypertensive medications	95.6%
ACE inhibitor or ARB	69.8%
β-Adrenergic blocker	67.5%
α-Adrenergic blocker	2.7%
Calcium channel blocker	31.5%

Demographics	
Diuretics	38.6%
Responses measured while asleep	
Mean SBP (mmHg)	116.1 ± 16.4
Mean DBP (mmHg)	64.6 ± 8.6
Mean arterial pressure (mmHg)	81.8 ± 10.2
Mean heart rate (bpm)	64.9 ± 9.7
Responses measured while awake	
Mean SBP (mmHg)	127.6 ± 15.1
Mean DBP (mmHg)	73.2 ± 8.7
Mean arterial pressure (mmHg)	91.3 ± 9.7
Mean heart rate (bpm)	71.2 ± 10.7
Nondipping status	
SBP	54.0%
DBP	42.6%
Mean arterial pressure	47.0%
Heart rate	59.1%

Categorical variables are presented as percentages and continuous variables are presented as means ± standard deviations. ACE, angiotensin converting enzyme; BVA, Boston Veterans Affairs Hospital; BWH, Brigham and Women's Hospital; CMC, Case Medical Center; JHU, Johns Hopkins University.

TABLE 2

Odds ratio of nondipping systolic and mean arterial blood pressure per 1-unit increase in Apnea Hypopnea Index and Oxygen Desaturation Index

Nondipping blood pressure	Model	Odds ratio of nondipping blood pressure per 1-unit increase in AHI (95% CI); <i>P</i> value	Odds ratio of nondipping blood pressure per 1-unit increase in ODI (95% CI); <i>P</i> value
Nondipping SBP	Model 1	1.04 (1.01–1.07); <i>P</i> = 0.005	1.04 (1.01–1.06); <i>P</i> = 0.003
	Model 2	1.04 (1.01–1.07); <i>P</i> = 0.009	1.04 (1.01–1.06); <i>P</i> = 0.005
	Model 3	1.04 (1.01–1.07); <i>P</i> = 0.012	1.04 (1.01–1.06); <i>P</i> = 0.009
Nondipping MAP	Model 1	1.02 (0.99–1.05); <i>P</i> = 0.15	1.03 (1.01–1.05); <i>P</i> = 0.019
	Model 2	1.02 (0.99–1.05); <i>P</i> = 0.25	1.03 (1.00–1.05); <i>P</i> = 0.028
	Model 3	1.02 (0.99–1.04); <i>P</i> = 0.32	1.03 (1.00–1.05); <i>P</i> = 0.043

Model 1, adjusted for site; model 2, adjusted for site, age, sex, race, and BMI; model 3, adjusted for site, age, sex, race, BMI, hypertension, diabetes, dyslipidemia, smoking pack per years, and cardiovascular disease. AHI, Apnea Hypopnea Index; CI, confidence interval; MAP, mean arterial pressure.

TABLE 3

Odds ratio of nondipping DBP per 1-unit increase in Apnea Hypopnea Index

Model	Odds ratio of nondipping DBP per 1-unit increase in AHI (95% CI); <i>P</i> value		<i>P</i> value for test if the odds ratio of nondipping DBP per 1-unit increase in AHI differs above and below 30.0
	AHI <30.0	AHI ≥30.0	
Model 1	0.96 (0.91–1.01); <i>P</i> = 0.097	1.11 (1.03–1.19); <i>P</i> = 0.005	<i>P</i> = 0.009
Model 2	0.96 (0.91–1.01); <i>P</i> = 0.11	1.10 (1.02–1.18); <i>P</i> = 0.011	<i>P</i> = 0.016
Model 3	0.96 (0.91–1.01); <i>P</i> = 0.13	1.10 (1.02–1.19); <i>P</i> = 0.012	<i>P</i> = 0.019

Model 1, adjusted for site; model 2, adjusted for site, age, sex, race, and BMI; model 3, adjusted for site, age, sex, race, BMI, hypertension, diabetes, dyslipidemia, smoking pack per years, and cardiovascular disease. AHI, Apnea Hypopnea Index; CI, confidence interval.

TABLE 4

Odds ratio of nondipping DBP per 1-unit increase in Oxygen Desaturation Index

Model	Odds ratio of nondipping DBP per 1-unit increase in ODI (95% CI); <i>P</i> value		<i>P</i> value for test if the odds ratio of nondipping DBP per 1-unit increase in ODI differs before and after 24.8
	ODI <24.8	ODI ≥24.8	
Model 1	0.90 (0.79–1.02); <i>P</i> = 0.093	1.4 (1.01–1.07); <i>P</i> = 0.005	<i>P</i> = 0.04
Model 2	0.91 (0.8–1.04); <i>P</i> = 0.16	1.04 (1.01–1.07); <i>P</i> = 0.01	<i>P</i> = 0.07
Model 3	0.90 (0.79–1.03); <i>P</i> = 0.12	1.04 (1.01–1.07); <i>P</i> = 0.01	<i>P</i> = 0.055

Model 1, adjusted for site; model 2, adjusted for site, age, sex, race, and BMI; model 3, adjusted for site, age, sex, race, BMI, hypertension, diabetes, dyslipidemia, smoking pack per years, and cardiovascular disease. CI, confidence interval; ODI, Oxygen Desaturation Index.