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SCIENTIFIC INVESTIGATIONS

Nocturnal blood pressure and nocturnal blood pressure fluctuations: the effect of short-term CPAP therapy and their association with the severity of obstructive sleep apnea

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Study Objectives: We determined the relationship of cardiovascular risk factors, cardiovascular diseases, nocturnal blood pressure (NBP), and NBP fluctuations (NBPFs) with the severity of obstructive sleep apnea (OSA). We also investigated the effect of short-term continuous positive airway pressure therapy on NBP parameters.

Methods: This retrospective study included 548 patients from our cardiac clinic with suspected OSA. Patients underwent polysomnography and continuous NBP measurement using the pulse transit time. According to their apnea-hypopnea index (AHI), patients were subclassified as controls (AHI < 5 events/h), mild (AHI 5 to < 15 events/h), moderate (AHI 15 to < 30 events/h), and severe OSA (AHI ≥ 30 events/h); 294 patients received continuous positive airway pressure therapy.

Results: Analysis of covariance showed that NBP and the frequency of NBPFs were the highest in severe followed by moderate and mild OSA (all $P < .001$). Multivariable regression analysis revealed a significant association of NBPFs with AHI, body mass index, systolic NBP, and lowest SpO_2. The severity of OSA is also associated with the frequency of obesity, hypertension, diabetes mellitus, atrial fibrillation, heart failure (all $P < .001$), and coronary artery disease ($P = .035$). Short-term continuous positive airway pressure decreased the frequency of NBPFs in all OSA groups and the systolic NBP in severe and moderate but not in mild OSA.

Conclusions: The severity of OSA is associated with an increase in NBP and NBPFs. Continuous positive airway pressure reduces NBP parameters already after the first night. In addition to BP, the diagnosis and therapy of NBPFs should be considered in patients with OSA.

Clinical Trial Registration: Registry: German Clinical Trials Register; Name: Nocturnal blood pressure and nocturnal blood pressure fluctuations associated with the severity of obstructive sleep apnea; URL: https://www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00024087; Identifier: DRKS00024087.

Keywords: obstructive sleep apnea, cardiovascular risk factors, cardiovascular disease, nocturnal blood pressure, nocturnal blood pressure fluctuations, continuous positive airway pressure

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Previous studies investigating the effect of obstructive sleep apnea (OSA) on nocturnal blood pressure (NBP) and blood pressure fluctuations (NBPFs) have mainly focused on moderate-to-severe OSA. No previous studies have assessed the effect of continuous positive airway pressure on NBPFs in different OSA severities. This study evaluated NBP, NBPFs, and cardiovascular risk factors in relation to OSA severity and assessed the effect of short-term continuous positive airway pressure on NBP and NBPFs.

Study Impact: NBP, and in particular NBPFs, were associated with OSA severity. Continuous positive airway pressure reduces NBPFs in mild, moderate, and severe OSA. In addition to blood pressure, the diagnosis and therapy of NBPFs should be considered in patients with OSA.

INTRODUCTION

Obstructive sleep apnea (OSA) is common in patients with cardiovascular disease (CVD) and may causally contribute to hypertension, coronary artery disease, heart failure, and atrial fibrillation.[1,2] The association between OSA and CVD is not entirely understood, but endothelial damage, increased blood pressure (BP), frequent BP variations, and obesity seem to play an important role.[1,3–5]

Apneas and hypopneas lead to arousal from sleep and induce hypoxemia, associated with activation of the sympathetic nervous system. It is widely known that severe OSA induces hypertension but the association of mild-to-moderate OSA with hypertension remains unclear.[4–6] In the last years, several reports on the underlying mechanism by which OSA increases BP have been published. Recent studies suggest that the activation of the sympathetic nervous system leads to nocturnal BP (NBP) variations and, as a result, the mean value of NBP increases.[3,7,8] On the other hand, NBP but also NBP fluctuations (NBPFs) have been reported to increase cardiovascular risk independently of each other.[9,10]

Previous studies have shown that OSA is associated with cardiovascular risk factors and that CVD increased in patients with

severe OSA. In patients with mild-to-moderate OSA there are limited data published and the correlation remains unclear.[11–13]

Continuous positive airway pressure (CPAP) treatment is the most effective therapy for OSA. Numerous studies have shown that CPAP opens the airways and prevents airflow collapse during sleep.[14–16] The therapy is highly effective in reducing the episodes of hypoxemia, improving the quality of sleep and reducing daytime sleepiness. In contrast, there are different findings about the effect of CPAP on BP and limited data on the relationship between NBPFs and OSA.[17–19] It can be postulated that short-term CPAP therapy shows an immediate effect on NBPFs already in the first night with the consequence of reduced episodes of hypoxemia.

The aim of the current study was to evaluate the relationship between cardiovascular risk factors, CVDs, NBPFs, and NBP in patients with different severities of OSA compared to patients without OSA. Additionally, we investigated the effect of short-term CPAP therapy on NBPFs and NBP in mild, moderate, and severe OSA. To the best of our knowledge, the effect of CPAP therapy on NBPFs in different OSA groups has not yet been examined.

METHODS

Study population

The following research represents a retrospective monocentric study and was approved by the local ethics committee of the Medical Association of Witten/Herdecke. Between January 2014 and January 2019, 548 consecutive patients from our cardiac clinic with suspected sleep-disordered breathing (self-reported daytime sleepiness, heavy snoring, history of witnessed apneas, obesity) were enrolled in the study. Patients presented due to hypertension, CVD, or screening for heart diseases. We excluded patients previously diagnosed with OSA or central sleep apnea or who were unwilling to participate in the study. The trial included an evaluation of cardiovascular risk factors and CVDs, and all participants underwent overnight full polysomnography (PSG), continuous NBP measurement, echocardiography, and an evaluation via the Epworth Sleepiness Scale. According to their apnea-hypopnea index (AHI), patients were divided into four subgroups: AHI < 5 events/h were controls, AHI ≥ 5 events/h and < 15 events/h were grouped as mild sleep apnea, AHI ≥ 15 events/h and < 30 events/h as moderate sleep apnea, and AHI ≥ 30 events/h as severe sleep apnea.[20]

PSG

All patients underwent overnight PSG using the SOMNOscreen plus system (SOMNOmedics, Randersacker, Germany). The data were scored manually according to the guidelines of the American Academy of Sleep Medicine.[21] Apnea was defined as a decrease in airflow by ≥ 90% of the baseline for ≥ 10 s. Hypopnea was defined as a decrease in airflow by ≥ 30% of baseline for > 10 s associated with an oxygen desaturation of ≥ 3%.[21] We calculated the following variables during the sleep period: AHI, mean apnea duration, mean hypopnea duration, oxygen desaturation index, mean oxygen saturation (SpO_2), minimum SpO_2, duration SpO_2 < 90%, arousal index, sleep efficacy, and rapid eye movement sleep variables.

PSG was conducted at baseline for diagnosis and at the next consecutive day to titrate CPAP therapy in case of diagnosed sleep apnea. Daytime sleepiness was estimated using the Epworth Sleepiness Scale.[22]

NBP and NBPFs

We determined the NBP beat-to-beat continuously and synchronized with PSG by measuring the pulse transit time (SOMNOscreen Plus System, SOMNOmedics, Randersacker, Germany). This recently established method allows the detection of NBPFs and shows a clinical acceptable accuracy under physiological and pathological conditions.[7,23] Several studies have shown that pulse transit time has a linear correlation with BP and the SOMNOscreen Plus System has passed the requirements of the European Society of Hypertension international protocol revision 2010.[23,24] Calibration of pulse transit time was implemented by cuff measurement of each patient after a supine resting period of 10 minutes. All systolic and diastolic BP values were synchronized with PSG and analyzed using DOMINO software (version 2.7) (SOMNOmedics, Randersacker, Germany).

We defined BP parameters as follows: NBP as the average of BP during the period from 10 PM to 6 AM; maximum systolic BP (SBP) as the highest nocturnal SBP value; NBPFs as an increase in SBP > 12 mmHg within 30 seconds per hour of sleep time; and respiratory-related NBPFs as an increase of SBP > 12 mmHg within 30 seconds associated with a respiratory event such as hypoxemia, hypopnea, or apnea per hour of sleep time.

Echocardiographic evaluation

Echocardiographic evaluation was performed on patients by an experienced physician using a Philips iE 33 ultrasound system (Philips Healthcare, Hamburg, Germany). The following parameters of the left ventricle were measured: left ventricular end-diastolic diameter, left ventricular posterior wall thickness in end-diastole, interventricular septum thickness during diastole, and left ventricular ejection fraction. The measurements were determined by following the recommendations of the American Society of Echocardiography.[25]

Statistical analysis

Statistical analysis was performed using SPSS 26.0 for Windows. Continuous data were either expressed as mean ± standard deviation or as adjusted means with the 95% confidence interval and tested for normal distribution with the Shapiro-Wilk test. Categorical variables were presented as frequencies and percentages. The Pearson's chi-square test was used to assess the overall effect of the OSA group on categorical variables like risk factors, CVDs and sex. Pairwise comparisons between the OSA groups were performed by z-test for proportions.

Analysis of covariance was used to compare differences between the OSA groups in continuous data like BP, NBPFs, and polysomnographic parameters. To address differences between OSA groups we analyzed the following covariates: age, male, obesity (body mass index [BMI] ≥ 30 kg/m^2), nicotine use, hypertension, diabetes mellitus, hypercholesterolemia, coronary artery disease, previous myocardial infarction,

nonischemic cardiomyopathy, atrial fibrillation, heart failure, and intake of ≥ 3 antihypertensive drugs.

To determine the associations between NBPFs, or rather respiratory-related NBPFs with other variables like age, male, BMI, polysomnographic data, and BP data, we performed a multivariable linear regression analysis.

Comparisons of data collected before and after the first night of CPAP therapy were evaluated with Student's *t* test. Results with a *P* value below .05 were considered statistically significant.

RESULTS

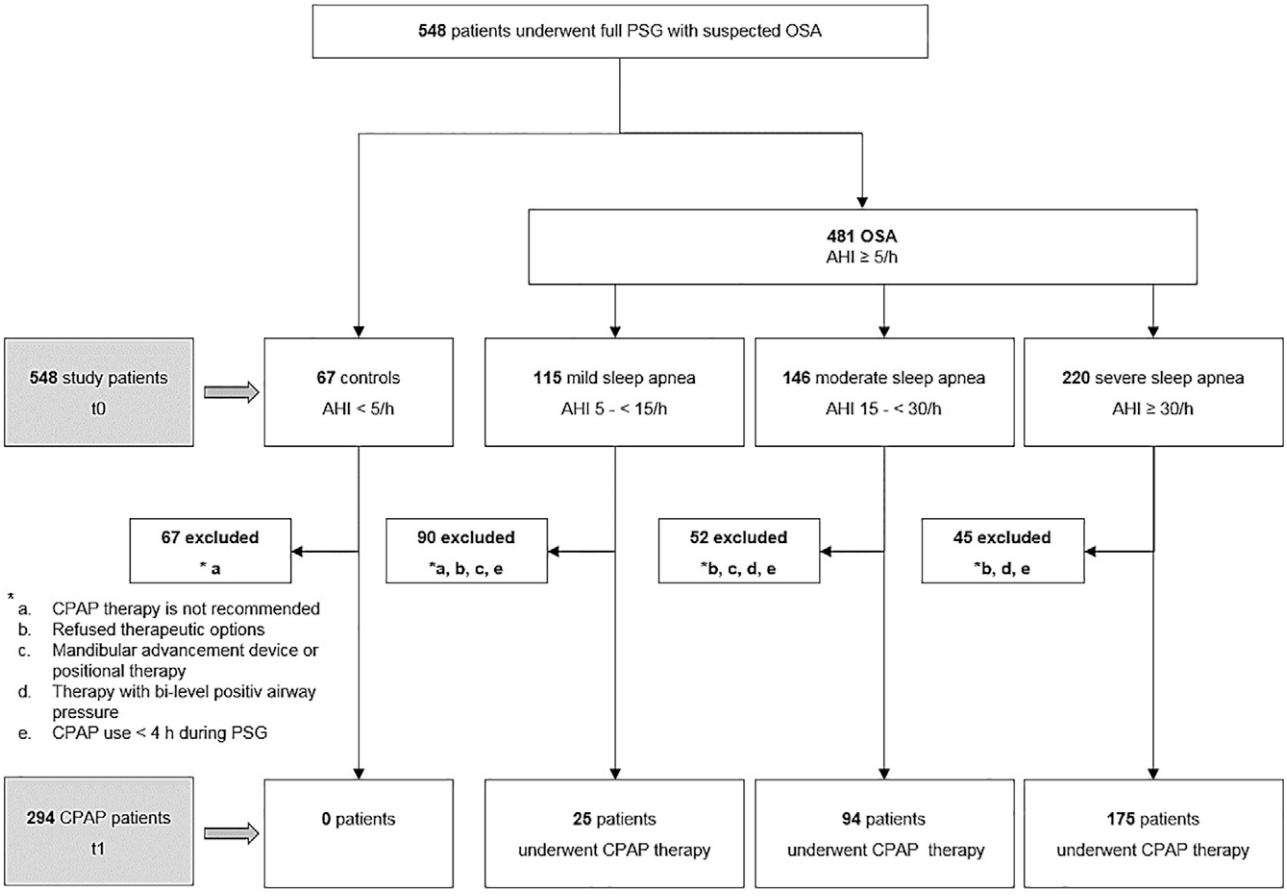
Patient characteristics and cardiovascular risk factors

Figure 1 outlines the study flowchart and **Table 1** lists the clinical baseline characteristics. Of the 548 patients with CVD with suspected sleep-disordered breathing (364 men, 184 women; 35 to 89 years) included in the study 481 of these were additionally diagnosed with OSA (AHI ≥ 5 events/h). In patients with OSA, there were 156 (32.4%) females and 325 (67.6%) males compared with 32 (47.8%) females and 35 (52.2%) males in controls ($P = .013$). The age range in the OSA group was 35–89 years and the average age was 68.1 years ± 11.1; in controls the age range was 39–87 years (average age: 64.3 ± 12.7 years); $P = .014$. The mean BMI range was 18.8–49.5 kg/m^2 (mean: 30.8 ± 5.6 kg/m^2) in the OSA group and 17.4–35.3 kg/m^2 (mean: 26.9 ± 3.8 kg/m^2) in the non-OSA group ($P < .001$). The patients were divided into four groups according to their AHI: controls (AHI < 5 events/h) consisted of 67 patients, mild OSA (AHI 5 to < 15 events/h) consisted of 115 patients, moderate OSA (AHI 15 to < 30 events/h) consisted of 146 patients, and severe OSA (AHI > 30 events/h) consisted of 220 patients. According to statistics, the frequency of obesity ($P < .001$), hypertension ($P < .001$), therapy-resistant hypertension (≥ 3 antihypertensive drugs) ($P < .001$), diabetes mellitus ($P < .001$), and male sex ($P = .002$) increases with severity of OSA. The prevalence of obesity (BMI > 30 kg/m^2) in the severe OSA group was four times higher compared to controls and two times higher compared to those with mild OSA. In patients with severe OSA the prevalence of diabetes mellitus was five times higher and in the mild OSA group 2.5 times higher compared with controls. **Figure 2A** shows the frequency of cardiovascular risk factors in relation to OSA severity.

CVDs

According to statistics we observed significant differences between the OSA groups concerning the frequency of coronary

Figure 1—Flowchart of study patients.



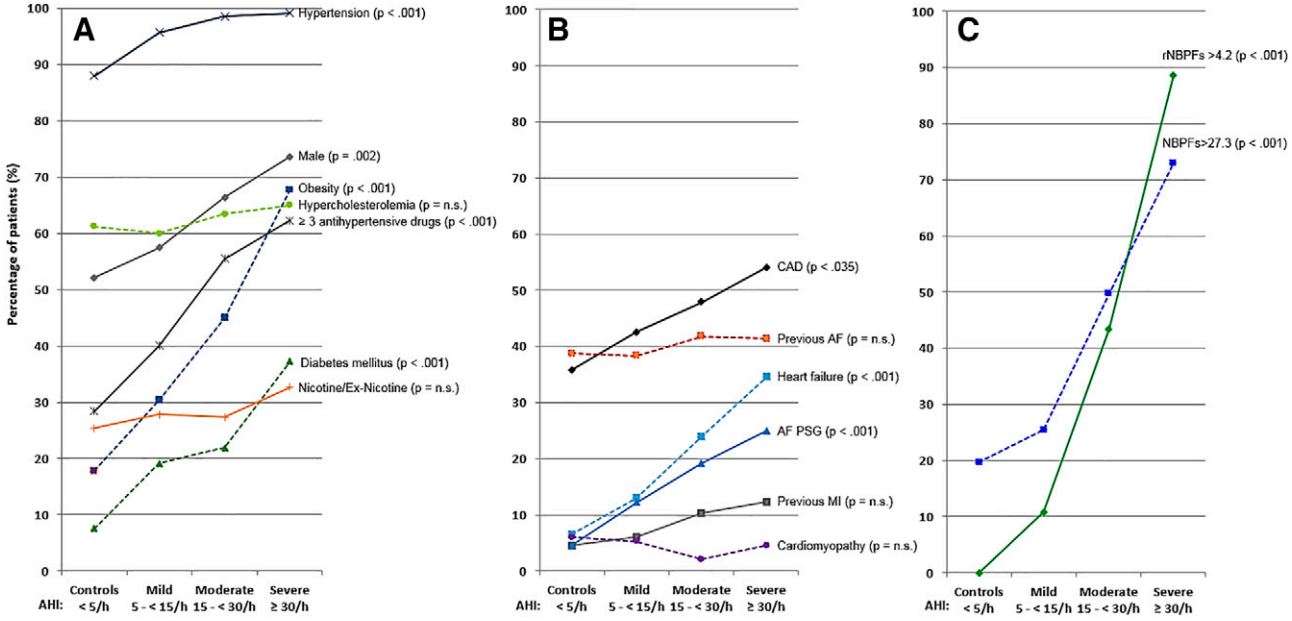
The 548 patients underwent full PSG and were separated into four subgroups according to their AHI; 294 of 548 study patients were treated with CPAP therapy. AHI = apnea-hypopnea index, CPAP = continuous positive airway pressure, OSA = obstructive sleep apnea, PSG = polysomnography, t0 = data at baseline, t1 = data obtained at the next consecutive day after titrate CPAP therapy.

Table 1—Baseline characteristics of the study population.

	Controls, AHI < 5 Events/h (n = 67)	Mild OSA, AHI 5 to < 15 Events/h (n = 115)	Moderate OSA, AHI 15 to < 30 Events/h (n = 146)	Severe OSA, AHI ≥ 30 Events/h (n = 220)	*P* Across All
Risk factors					
Age, y	64.3 ± 12.7	68.0 ± 11.5	69.0 ± 10.6	67.6 ± 11.3	.14
Male	35/67 (52.2)	66/115 (57.4)	97/146 (66.4)	162/220 (73.6)	.002
Body mass index, kg/m^2	26.8 ± 3.9	28.7 ± 5.2	30.1 ± 5.1	32.3 ± 5.6	<.001
Obesity (≥ 30 kg/m^2)	12/67 (17.9)	35/115 (30.4)	64/146 (45.0)	149/220 (67.7)	<.001
Obesity grade 1 (30–34.9 kg/m^2)	11/67 (16.4)	23/115 (20.0)	47/146 (32.2)	85/220 (38.6)	<.001
Obesity grade 2 (35–39.9 kg/m^2)	1/67 (1.5)	7/115 (6.1)	10/146 (6.8)	41/220 (18.6)	<.001
Obesity grade 3 (≥ 40 kg/m^2)	0/67 (0)	6/115 (5.2)	8/146 (5.5)	22/220 (10.0)	.023
Nicotine/ex-nicotine	17/67 (25.4)	32/115 (27.8)	40/146 (27.4)	72/220 (32.7)	.548
Hypercholesterolemia[a]	41/67 (61.2)	69/115 (60.0)	91/146 (63.4)	139/220 (63.2)	.950
Hypertension[b]	59/67 (88.1)	110/115 (95.7)	144/146 (98.6)	218/220 (99.1)	<.001
Heart disease					
CAD	24/67 (35.8)	49/115 (42.6)	70/146 (47.9)	119/220 (54.1)	.035
Previous MI	3/67 (4.5)	7/115 (6.1)	15/146 (10.3)	27/220 (12.3)	.133
Atrial fibrillation	3/67 (4.5)	14/115 (12.2)	28/146 (19.2)	55/220 (25)	<.001
Previous diagnosed atrial fibrillation	26/67 (38.8)	44/115 (38.3)	61/146 (41.8)	91/220 (41.4)	.922
CIED	6/67 (9.0)	6/115 (5.2)	14/146 (9.6)	29/220 (13.2)	.139
Nonischemic cardiomyopathy	4/67 (6.0)	6/115 (5.2)	3/146 (2.1)	10/220 (4.5)	.466
Echocardiographic data					
Heart failure[c]	4/67 (6.0)	15/115 (13)	35/146 (24)	76/219 (34.5)	<.001
Mild	3/67 (4.5)	7/115 (6.1)	19/146 (13)	32/219 (14.5)	.027
Moderate	1/67 (1.5)	6/115 (5.2)	10/146 (6.8)	26/219 (11.8)	.019
Severe	0/67 (0)	2/115 (1.7)	6/146 (4.1)	19/219 (8.6)	.005
LVEDD[d] increased	0/55 (0)	4/100 (4)	11/122 (9)	22/191 (11.5)	.015
IVSD[e] increased	29/52 (55.8)	61/99 (61.6)	75/115 (65.2)	135/180 (75)	.022
LVPWD[f] increased	21/51 (41.2)	48/96 (50)	56/112 (50.5)	101/177 (57.1)	.209
Further disease					
Diabetes mellitus	5/67 (7.5)	22/115 (19.1)	32/146 (21.9)	82/220 (37.3)	<.001
Renal insufficiency	9/67(13.4)	13/115 (11.3)	29/146 (19.9)	50/220 (22.7)	.048
COPD	2/67 (3.0)	9/115 (7.8)	14/146 (9.6)	15/220 (6.8)	.321
Antihypertensive drugs					
ACEI	24/67 (35.8)	35/115 (30.4)	63/146 (66.4)	93/220 (42.3)	.119
AT1 receptor antagonists	27/67 (40.3)	52/115 (45.2)	60/146 (41.1)	97/220 (44.1)	.861
β-Blocker	43/67 (64.2)	80/115 (69.6)	112/146 (76.7)	176/220 (80.0)	.027
Calcium channel blocker	19/67(28.4)	36/115 (31.3)	61/146 (41.8)	100/220 (45.5)	.027
Diuretics	17/67 (25.4)	47/115 (40.9)	72/146 (49.3)	125/220 (56.8)	<.001
Mean value antihypertensive drugs	1.9 ± 1.1	2.2 ± 1.1	2.5 ± 1.0	2.8 ± 1.0	<.001
≥ 3 Antihypertensive drugs	19/67 (28.4)	46/115 (40.0)	81/146 (55.5)	137/220 (62.3)	<.001

Continuous variables are presented as mean ± SD. Categorical variables are presented as frequencies with percentages. [a]Hypercholesterolemia was defined as previous diagnosis of hypercholesterolemia, intake of lipid-lowering medications, low-density lipoprotein cholesterol levels > 160 mg/dL, high-density lipoprotein cholesterol < 40 mg/dL, or cholesterol levels > 200 mg/dL. [b]Hypertension was defined as previous diagnosis of hypertension and intake of antihypertensive medications. [c]Heart failure was defined in men as LVEF < 52%, in women as LVEF < 54% (mild: men: LVEF 41–51%, women: LVEF 41–53%; moderate: LVEF 30–40%; severe: LVEF < 30%). [d]LVEDD was defined as increased in men > 58 mm, in women > 52 mm. [e]IVSD was defined as increased in men > 10 mm, in women > 9 mm. [f]LVPWD was defined as increased in men > 10 mm, in women > 9 mm. ACEI = angiotensin-converting-enzyme inhibitor, AHI = apnea-hypopnea index, AT1 = angiotensin 1-receptor antagonist, CAD = coronary artery disease, CIED = cardiac implantable electronic device, COPD = chronic obstructive pulmonary disease, IVSD = interventricular septum thickness, LVEDD = left ventricular end diastolic diameter, LVEF = left ventricular ejection fraction; LVPWD = left ventricular posterior wall thickness, MI = myocardial infarction, OSA = obstructive sleep apnea.

Figure 2—Cardiovascular risk factors, cardiovascular disease, and NBPFs in relation to OSA severity.



(A) There were significant differences between the OSA groups concerning the frequency of hypertension, resistant hypertension, obesity, male sex, and diabetes mellitus. **(B)** There were significant differences between the OSA groups concerning the frequency of CAD, atrial fibrillation during PSG measurement, and heart failure. **(C)** NBPFs and rNBPFs increase in relation to OSA severity. We used the median for NBPFs (27.3/h) and for rNBPFs (4.2/h) of the entire study population to define cut-off values. AF = atrial fibrillation, AF PSG = atrial fibrillation during PSG measurement, AHI = apnea-hypopnea index, CAD = coronary artery disease, MI = myocardial infarction, NBPF = nocturnal blood pressure fluctuation, OSA = obstructive sleep apnea, PSG = polysomnography, rNBPF = respiratory-related nocturnal blood pressure fluctuation.

artery disease ($P = .035$), atrial fibrillation ($P < .001$), and heart failure ($P < .001$). In patients with severe OSA the prevalence of heart failure with reduced ejection fraction was six times higher, in moderate OSA four times higher, and in mild OSA 2.1 times higher compared to controls. There were no significant differences between the study groups concerning previous myocardial infarction, previous diagnosed atrial fibrillation, cardiac implantable electronic device, and nonischemic cardiomyopathy (**Table 1** shows heart diseases, further diseases, and echocardiographic data in the different OSA groups and **Figure 2B** shows the frequency of CVDs in relation to OSA severity).

PSG-derived parameters

Compared to controls, patients with OSA had a significantly higher AHI value (32.1 ± 19.2 events/h vs 3.2 ± 1.4 events/h, $P < .001$), a significantly longer apnea duration (24.0 ± 7.5 seconds vs 21.0 ± 10.0 seconds, $P = .010$), a significantly higher oxygen desaturation index (32.2 ± 18.8/h vs 3.4 ± 2.4/h, $P < .001$), a significantly lower SpO_2 value in mean (92.5 ± 3.0% vs 95.1 vs 1.7%, $P < .001$), and a significantly lower minimum SpO_2 value (80.1 ± 7.0% vs 89.1 vs 2.9%, $P < .001$).

According to their AHI, patients were grouped into controls and mild, moderate, and severe OSA. After adjusting for covariates (age, male, obesity [BMI ≥ 30 kg/m^2], nicotine, hypertension, diabetes mellitus, hypercholesterolemia, coronary artery disease, previous myocardial infarction, nonischemic cardiomyopathy, atrial fibrillation, heart failure, and intake of antihypertensive drugs) analysis of covariance showed significant differences between the OSA groups concerning AHI, mean apnea duration, oxygen desaturation index, mean SpO_2, lowest SpO_2, arousal index (all $P < .001$), and mean hypopnea duration ($P = .022$). **Table 2** shows the adjusted mean values and the 95% confidence intervals.

As shown in **Table 3**, CPAP therapy improved all PSG-derived parameters immediately after the first night in patients with severe OSA (all $P < .001$); in patients with mild-to-moderate sleep apnea CPAP therapy improved all PSG-derived parameters apart from arousal index and mean SpO_2 (all P between < .001 and .002).

NBP parameters

The mean values of nocturnal systolic, but not of diastolic, BP were significantly higher in patients with OSA than in controls (SBP: 130.1 ± 18 mmHg vs121.1 ± 14 mmHg, $P = .044$; diastolic BP: 78.4 ± 12.5 mmHg vs 74.5 ± 12.4 mmHg, $P = .201$). Overall and respiratory-related NBPFs were significantly more frequent in the whole OSA group (P in each case < .001). NBPFs and respiratory-related NBPFs increased also in relation to OSA severity. We used the median for NBPFs (27.3/h) and for respiratory-related NBPFs (4.2/h) of the entire study population to define cut-off values (**Figure 2C**).

After adjusting for covariates analysis of covariance showed significant differences between the OSA groups concerning the BP parameters (shown in **Table 2**). The highest nocturnal systolic and diastolic BP was found in patients with severe OSA followed

Table 2—Polysomnographic and blood pressure data in relation to OSA severity.

	Controls, AHI < 5 Events/h (n = 67)	Mild OSA AHI 5 to < 15 Events/h, t0 (n = 115)	Moderate OSA, AHI 15 to < 30 Events/h, t0 (n = 146)	Severe OSA, AHI ≥ 30 Events/h, t0 (n = 220)	Test Statistic	*P*
Polysomnographic data						
AHI, per h	4.40 [1.97–6.83]	11.88 [10.10–13.65]	22.68 [21.15–24.22]	48.36 [47.03–49.70]	$F(3, 529) = 463.54$	<.001
Mean apnea duration, s	21.48 [19.54–23.42]	21.35 [19.94–22.77]	22.85 [21.63–24.08]	25.65 [24.59–26.71]	$F(3, 523) = 8.66$	<.001
Mean hypopnea duration, s	30.64 [28.50–32.78]	34.30 [32.74–35.86]	33.79 [32.45–35.14]	32.67 [31.50–33.84]	$F(3, 524) = 3.23$	.022
ODI, per h	5.24 [2.58–7.90]	12.27 [10.33–14.22]	23.18 [21.49–24.86]	45.64 [44.18–47.11]	$F(3, 529) = 319.66$	<.001
Mean SpO_2, %	94.48 [93.74–95.22]	92.94 [92.40–93.48]	92.78 [92.31–93.25]	92.15 [91.75–92.56]	$F(3, 529) = 8.84$	<.001
Lowest SpO_2, %	87.64 [86.04–89.23]	84.27 [83.10–85.43]	82.56 [81.54–83.57]	78.56 [77.69–79.44]	$F(3, 528) = 34.80$	<.001
Arousal index, per h	9.42 [6.94–11.90]	10.24 [8.70–11.78]	10.60 [9.27–11.93]	17.27 [16.12–18.42]	$F(3, 499) = 25.54$	<.001
Blood pressure data						
Mean SBP, mmHg	123.3 [118.7–127.7]	126.5 [123.3–129.7]	127.3 [124.5–130.1]	133.4 [130.9–135.9]	$F(3, 512) = 6.33$	<.001
Mean DBP, mmHg	73.9 [70.9–77.6]	76.8 [74.6–78.9]	77.1 [75.2–79.0]	81.1 [79.4–82.8]	$F(3, 511) = 6.29$	<.001
Maximum SBP, mmHg	149.8 [143.2–156.5]	155.9 [151.4–160.7]	158.7 [154.8–163.0]	174.2 [170.6–178.9]	$F(3, 514) = 18.34$	<.001
Overall NBPFs, per h	17.18 [10.64–23.72]	21.16 [16.42–25.89]	32.24 [28.09–36.39]	50.93 [47.29–54.57]	$F(3, 515) = 38.89$	<.001
Respiratory-related NBPFs, per h	0.76 [−1.66 to 3.18]	2.02 [−1.66 to 3.18]	4.83 [3.36–6.30]	16.15 [14.85–17.44]	$F(3, 515) = 73.60$	<.001

The table shows adjusted means and [95% confidence intervals]. Means were adjusted for age, male, obesity (body mass index ≥ 30 kg/m^2), nicotine, hypertension, diabetes mellitus, hypercholesterolemia, coronary artery disease, previous mitral infarction, nonischemic cardiomyopathy, atrial fibrillation, heart failure, and intake of antihypertensive drugs. AHI = apnea-hypopnea index, DBP = diastolic blood pressure, NBPF = nocturnal blood pressure fluctuation, ODI = oxygen desaturation index, OSA = obstructive sleep apnea, SBP = systolic blood pressure, SpO_2, oxygen saturation, t0 = data at baseline.

by patients with moderate and mild OSA. The differences between the severe OSA group and all other groups were significant (all $P < .001$). Between moderate and mild OSA as well as between mild OSA and controls we observed no significant difference regarding the SBP and diastolic PB. The frequency of overall and respiratory-related NBPFs increased with the severity of OSA and was significantly different between all OSA subgroups. CPAP therapy decreased the frequency of both, overall NBPFs and respiratory-related NBPFs, in all OSA groups. In severe OSA we also observed decrease of the SBP ($P < .001$) and diastolic BP ($P = .034$) and in moderate OSA a decrease of SPB ($P = .003$) after CPAP therapy. The differences of those parameters in mild sleep apnea were not significant. **Table 3** shows NBP data at baseline and after CPAP therapy and **Figure 3** illustrates the NBPFs of the OSA subgroups (**Figure S1** in the supplemental material shows the other BP parameters).

We performed multivariable regression analysis to determine the potential predictors of NBPFs. In order to reduce the risk of overadjustment we used the variables most likely to be important clinically. The results revealed a significant association of NBPFs with mean SBP ($P = .003$), AHI ($P < .001$), and male sex ($P < .001$). Respiratory-related NBPFs were significantly associated with AHI ($P < .001$), lowest SpO_2 ($P = .040$), BMI ($P = .033$), and male sex ($P = .030$). **Table 4** shows the results of multivariable linear regression analysis.

DISCUSSION

In this study we included patients with mild-to-severe OSA and found that the amount of NBPFs and the average NBP were associated with OSA severity. We also investigated the effect of short-term CPAP therapy on NBP parameters. To the best of our knowledge, the effect of CPAP therapy on NBPFs in different OSA groups has not yet been examined. Moreover, we evaluated the association between cardiovascular risk factors and CVD with differing OSA severities.

BP was analyzed beat-to-beat continuously with the pulse transit time measurement synchronized with PSG. The beat-to-beat measurement enables the detection of acute BP changes such as

Table 3—Polysomnographic data and blood pressure data at baseline and after short-term CPAP therapy.

	Mild OSA, AHI 5 to < 15 Events/h, t0*/t1 (n = 25)	Moderate OSA, AHI 15 to < 30 Events/h, t0*/t1 (n = 94)	Severe OSA, AHI ≥ 30 Events/h, t0*/t1 (n = 175)
Apnea-hypopnea index, per h			
t0*	12.7 ± 2.1	22.9 ± 4.4	48.8 ± 14.8
t1	2.70 ± 1.46	6.5 ± 5.2	10.1 ± 8.6
P, t0* vs t1	<.001	<.001	<.001
Mean apnea duration, s			
t0*	21.6 ± 6.6	23.8 ± 6.6	25.6 ± 8.4
t1	16.6 ± 9.7	17.6 ± 5.6	17.6 ± 7.7
P, t0* vs t1	.017	<.001	<.001
Mean hypopnea duration, s			
t0*	35.6 ± 10.7	33.8 ± 7.2	32.1 ± 7.2
t1	26.5 ± 10.8	24.6 ± 11.5	23.8 ± 10.1
P, t0* vs t1	.001	<.001	<.001
ODI, per h			
t0*	11.7 ± 3.2	23.2 ± 7.3	46.3 ± 14.6
t1	3.6 ± 2.8	9.4 ± 6.9	14.7 ± 11.5
P, t0* vs t1	<.001	<.001	<.001
Mean SpO_2, %			
t0*	93.2 ± 2.3	92.7 ± 2.3	91.9 ± 4.0
t1	95.0 ± 1.9	93.4 ± 9.9	93.4 ± 3.5
P, t0* vs t1	<.001	.515	<.001
Lowest SpO_2, %			
t0*	85.2 ± 4.1	81.5 ± 6.5	78.1 ± 7.6
t1	89.3 ± 3.5	86.6 ± 4.4	85.2 ± 6.0
P, t0* vs t1	<.001	<.001	<.001
Arousal index, per h			
t0*	9.9 ± 5.0	10.2 ± 5.6	17.9 ± 11.2
t1	9.0 ± 5.4	11.7 ± 7.8	11.1 ± 6.4
P, t0* vs t1	.279	.090	<.001
Mean SBP, mmHg			
t0*	122.4 ± 15.8	128.0 ± 14.7	134.0 ± 17.5
t1	120.7 ± 12.8	123.4 ± 14.6	127.6 ± 17.8
P, t0* vs t1	.586	.003	<.001
Mean DBP, mmHg			
t0*	74.1 ± 11.3	76.5 ± 11.7	82.2 ± 13.7
t1	75.8 ± 8.6	76.9 ± 12.4	79.7 ± 13.3
P, t0* vs t1	.457	.728	.034
Maximum SBP, mmHg			
t0*	149.9 ± 18.3	159.1 ± 24.4	175.2 ± 31.4
t1	143.6 ± 17.6	150.2 ± 19.5	159.8 ± 27.9
P, t0* vs t1	.121	<.001	<.001
Overall NBPFs, per h			
t0*	23.4 ± 15.0	30.1 ± 22.5	49.8 ± 32.7
t1	13.6 ± 11.7	20.5 ± 17.6	31.2 ± 30.5
P, t0* vs t1	<.001	<.001	<.001
Respiratory NBPFs, per h			
t0*	2.4 ± 1.6	4.7 ± 3.9	16.1 ± 11.0

(continued on following page)

Table 3—Polysomnographic data and blood pressure data at baseline and after short-term CPAP therapy. (*Continued*)

	Mild OSA, AHI 5 to < 15 Events/h, t0*/t1 (n = 25)	Moderate OSA, AHI 15 to < 30 Events/h, t0*/t1 (n = 94)	Severe OSA, AHI ≥ 30 Events/h, t0*/t1 (n = 175)
t1	0.4 ± 0.47	0.9 ± 1.1	2.2 ± 3.1
P, t0* vs t1	<.001	<.001	<.001

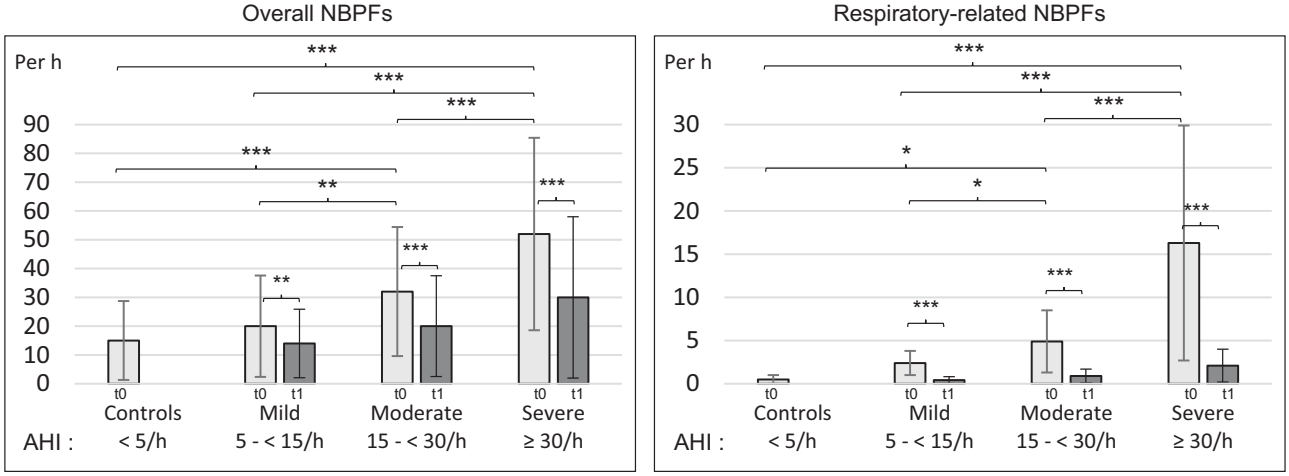
Variables are presented as mean ± standard deviation. AHI = apnea-hypopnea index, CPAP = continuous positive airway pressure, DBP = diastolic blood pressure, NBPF = nocturnal blood pressure fluctuation, ODI = oxygen desaturation index, OSA = obstructive sleep apnea, SBP = systolic blood pressure, t0* = polysomnographic data at baseline in patients who decided to use CPAP therapy at the next consecutive day, t1 = polysomnographic data during titrate CPAP therapy.

NBPFs.[23,24] NBPFs, which are defined as an increase of SBP > 12 mmHg within 30 seconds, are presumably caused by hypoxemia or arousals. In the present study, we demonstrated that the frequency of NBPFs increases with the severity of OSA and is significantly different between all OSA subgroups. In the past years there were only few data published about the relationship between NBPFs and OSA.[3,7,26] A recently published study indicated a high frequency of NBPFs in patients with severe OSA, but there are limited data about mild OSA available.[13] The data of the current study showed that the highest frequency of NBPFs is found in severe OSA followed by moderate and mild OSA. Furthermore, this also suggests that frequent NBPFs increase the maximum of SBP and as a result the average NBP. Our findings confirm this hypothesis: NBPFs were associated with a higher maximum and average of nocturnal SBP. This effect is most significant in severe OSA but also demonstrable in moderate OSA. It is well known that a hypertensive BP should be controlled < 140/90 mmHg to avoid future cardiovascular events, but recent studies suggest that even BP variations lead to more frequent cardiovascular outcomes, independently of the average BP.[3,9,26] A study by Webb et al analyzed different kinds of BP variations and showed that beat-to-beat BP variations predict cardiovascular events and recurrent stroke.[27] In contrast, the visit-to-visit office BP variability seems not to be a predictor of cardiovascular events.[28]

It is reasonable to assume that also mild OSA in the long term leads to hypertension, and therefore the early diagnosis and treatment of mild OSA is of far-reaching importance.[6] Moreover, mild OSA may progress to a more severe OSA, so an effective treatment is of even greater relevance.

In view of the above, it is particularly important to reduce the average BP as well as NBPFs. In the present study we investigated the effect of CPAP therapy on NBP parameters in different OSA groups. To the best of our knowledge there are hardly any data available regarding the effect of CPAP therapy on NBPFs. In our recently published study we demonstrated that CPAP therapy decreased the frequency of NBPFs in patients with severe OSA.[8] Our findings of the current study suggest that CPAP therapy immediately reduces the frequency of NBPFs in mild (−9.8/h; $P < .001$), moderate (−9.6/h; $P < .001$), and severe (−18.6/h; $P < .001$) OSA from the first night forward. It can be assumed that this effect leads to an improvement of the average BP. Our data confirm this assumption: After short-term CPAP therapy we observed a decrease of the average NBP in moderate and severe OSA. We did not find a decrease of average BP in mild OSA, but presumably this effect will be demonstrable after long-term CPAP therapy. On the other hand, there are controversial findings presented about the effectiveness of CPAP on BP.[14,18,29] A recently published meta-analysis identified

Figure 3—Nocturnal blood pressure fluctuations at baseline and after titrate CPAP therapy.



AHI = apnea-hypopnea index, CPAP = continuous positive airway pressure, NBPF = nocturnal blood pressure fluctuation, t0 = data at baseline, t1 = data obtained at the next consecutive day after titrate CPAP therapy. * $P < .05$; ** $P < .01$; *** $P < .001$.

Table 4—Results of multivariable linear regression analysis of potential predictors on nocturnal blood pressure fluctuations.

Variable	NBPFs			rNBPFs		
	β	95% CI	P	β	95% CI	P
Age, y	−.02	−0.10, 0.07	.689	.00	−0.07, 0.07	.996
Male	.24	0.16, 0.32	<.001	.07	0.01, 0.14	.030
BMI, kg/m^2	−.05	−0.14, 0.05	.329	−.08	−0.15, 0.00	.040
AHI, per h	.43	0.33, 0.54	<.001	.65	0.57, 0.74	<.001
Mean apnea duration, s	−.03	−0.12, 0.06	.495	−.02	−0.09, 0.05	.658
Lowest SpO_2, %	−.03	−0.13, 0.07	.560	−.08	−0.16, 0.00	.040
Arousal index, per h	−.07	−0.16, 0.02	.108	.04	−0.03, 0.11	.285
Mean SBP, mmHg	−.12	0.04, 0.20	.003	.03	−0.03, 0.10	.344
Model summary	R^2 = .27, P < .001			R^2 = .51, P < .001		

AHI = apnea-hypopnea index, BMI = body mass index, CI = confidence interval, NBPF = nocturnal blood pressure fluctuation, rNBPF = respiratory-related nocturnal blood pressure fluctuation, SBP = systolic blood pressure, SpO_2 = oxygen saturation, β = standardized regression coefficient.

subgroups of patients who respond best to the treatment. Patients younger than 60 years with uncontrolled BP and with severe hypoxemia showed a greater reduction of BP after CPAP therapy.[30] Most of our study patients have hypertension (mild OSA: 95.7%, moderate OSA: 98.6%, severe OSA: 99.1%) and a large part of them need to take ≥ 3 antihypertensive drugs (mild OSA: 40.0%, moderate OSA: 55.5%, severe OSA: 62.3%). The authors of another recently published study postulate that the antihypertensive effect of CPAP therapy depends on the cause of hypertension. CPAP reduces the BP in patients whose hypertension is strongly associated with respiratory events.[3] It can be speculated that one reason for hypertension in our study population is based on respiratory events and following NBPFs. Further studies to clarify the cause of NBP variations are necessary to treat hypertensive patients with OSA efficiently. Besides an optimal BP adjustment, the control of other cardiovascular risk factors is of importance to avoid further cardiovascular events.

In our study we evaluated the cardiovascular risk factors associated with OSA severity. We found that the frequency of male sex, obesity, and diabetes mellitus increase with the severity of OSA. The prevalence of obesity defined as BMI > 30 kg/m^2 in the severe OSA group was four times higher (67.7%), in moderate OSA 2.5 times higher (45.0%), and in mild OSA patients 1.7 times higher (30.4%) compared to controls (17.9%) (P < .001). The average BMI for patients with severe OSA was 32.3 kg/m^2, for moderate OSA 30.1 kg/m^2, for mild OSA 28.7 kg/m^2, and for the non-OSA group 26.8 kg/m^2 (P < .001). Our study suggests that BMI was a clinical predictor for AHI; we demonstrated a correlation between BMI and AHI (r = .363, P < .001). There are divergent findings published about the relationship between BMI and AHI; this suggests that the correlation between BMI and AHI is complex.[11,31,32] Most of the published literature demonstrated that an increase in BMI is related to an increase in AHI, but there are also studies published that did not find a significant relationship between AHI und BMI.[11,31,32]

However, obesity is a strong independent risk factor for OSA due to increased pharyngeal collapsibility and lung volume reduction in the recumbent position.[1] Apart from that, OSA can also enhance the risk of obesity due to physical inactivity and hormonal dysregulation.[33] Both OSA and obesity increase the risk of developing hypertension and CVD due to an activation of the sympathetic nervous system, increase of endothelial dysfunction, and metabolic dysregulation.[32] Consistent with these findings, we demonstrated in our study group a strong association between diabetes mellitus and OSA severity. In patients with mild OSA the prevalence of diabetes was 2.5 times higher and in severe OSA about five times higher compared to controls (P < .001). OSA, obesity, and metabolic syndrome are well known to be risk factors for the development of CVD. Our study demonstrated a higher frequency of atrial fibrillation, coronary artery disease, and heart failure in patients with OSA and a correlation with the severity of OSA. In light of the above, for an effective therapy of OSA it is also important for obese patients to address a weight reduction, in addition to the consequent use of CPAP treatment.

It must be addressed that this study has certain limitations. First, patients were enrolled from our cardiological department and it can be questioned whether our findings can be generalized to other populations. In particular, the large proportion of hypertensive patients (> 95% in all OSA groups) and the average age around 67 years in our study population may have influenced the results.

Second, the number of patients in the various OSA groups was different; especially the mild OSA group with 115 participants was comparatively small. Therefore, conclusions must be treated with some caution. Third, we investigated the effect of CPAP on NBPFs after the first night. More data about long-term CPAP therapy are needed before drawing final conclusions about the effectiveness of CPAP therapy.

In conclusion, our results suggest that NBP and NBPFs are associated with the severity of OSA. In all OSA groups, CPAP decreased the frequency of NBPFs after the first night of

treatment. The severity of OSA is also associated with the frequency of male sex, obesity, hypertension, diabetes mellitus, atrial fibrillation, heart failure, and coronary artery disease.

ABBREVIATIONS

AHI, apnea-hypopnea index
BMI, body mass index
BP, blood pressure
CPAP, continuous positive airway pressure
CVD, cardiovascular disease
NBP, nocturnal blood pressure
NBPF, nocturnal blood pressure fluctuation
OSA, obstructive sleep apnea
PSG, polysomnography
SBP, systolic blood pressure
SpO_2, oxygen saturation

REFERENCES

1. Bauters F, Rietzschel ER, Hertegonne KBC, Chirinos JA. The link between obstructive sleep apnea and cardiovascular disease. *Curr Atheroscler Rep.* 2016;18(1):1.
2. Oldenburg O, Arzt M, Bitter T, et al. Positionspapier "Schlafmedizin in der Kardiologie" update 2014. *Kardiologe.* 2015;9(2):140–158.
3. Xu J, Ding N, Zhang X, et al. Nocturnal blood pressure fluctuation and associated influential factors in severe obstructive sleep apnea patients with hypertension. *Sleep Breath.* 2018;22(4):1045–1052.
4. Sánchez-de-la-Torre M, Campos-Rodriguez F, Barbé F. Obstructive sleep apnoea and cardiovascular disease. *Lancet Respir Med.* 2013;1(1):61–72.
5. Collen J, Lettieri C, Wickwire E, Holley A. Obstructive sleep apnea and cardiovascular disease, a story of confounders! *Sleep Breath.* 2020;24(4):1299–1313.
6. Bouloukaki I, Grote L, McNicholas WT, et al.; European Sleep Apnoea Database Network. Mild obstructive sleep apnea increases hypertension risk, challenging traditional severity classification. *J Clin Sleep Med.* 2020;16(6):889–898.
7. Gehring J, Gesche H, Drewniok G, Küchler G, Patzak A. Nocturnal blood pressure fluctuations measured by using pulse transit time in patients with severe obstructive sleep apnea syndrome. *Sleep Breath.* 2018;22(2):337–343.
8. Picard F, Panagiotidou P, Weinig L, Steffen M, Tammen A, Klein RM. Effect of CPAP therapy on nocturnal blood pressure fluctuations, nocturnal blood pressure, and arterial stiffness in patients with coexisting cardiovascular diseases and obstructive sleep apnea. *Sleep Breath.* 2020;25(1):151–161.
9. Kuwabara M, Tomitani N, Shiga T, Kario K. Polysomnography-derived sleep parameters as a determinant of nocturnal blood pressure profile in patients with obstructive sleep apnea. *J Clin Hypertens (Greenwich).* 2018;20(6):1039–1048.
10. Cuspidi C, Tadic M, Sala C, Gherbesi E, Grassi G, Mancia G. Blood pressure non-dipping and obstructive sleep apnea syndrome: a meta-analysis. *J Clin Med.* 2019;8(9):1367.
11. Zhou X, Lu Q, Li S, Pu Z, Gao F, Zhou B. Risk factors associated with the severity of obstructive sleep apnea syndrome among adults. *Sci Rep.* 2020;10(1):13508.
12. Nozato S, Yamamoto K, Nozato Y, et al. Severity of obstructive sleep apnea is associated with the nocturnal fluctuation of pulse rate, but not with that of blood pressure, in older hypertensive patients receiving calcium channel blockers. *Geriatr Gerontol Int.* 2019;19(7):604–610.
13. Xu J, Ding N, Chen L, et al. Inducers of post-apneic blood pressure fluctuation monitored by pulse transfer time measurement in obstructive sleep apnea varied with syndrome severity. *Sleep Breath.* 2019;23(3):769–776.
14. Joyeux-Faure M, Baguet JP, Barone-Rochette G, et al. Continuous positive airway pressure reduces night-time blood pressure and heart rate in patients with obstructive sleep apnea and resistant hypertension: the RHOOSAS randomized controlled trial. *Front Neurol.* 2018;9:318.
15. Tserenpil G, Gebre M, Zergham AS, Sekhon AK, Malik BH. Managements for obstructive sleep apnea in adults: review. *Cureus.* 2020;12(8):e9905.
16. Tarraubella N, Sánchez-de-la-Torre M, Nadal N, et al. Management of obstructive sleep apnoea in a primary care vs sleep unit setting: a randomised controlled trial. *Thorax.* 2018;73(12):1152–1160.
17. Pak VM, Maislin DG, Keenan BT, et al. Changes in sleepiness and 24-h blood pressure following 4 months of CPAP treatment are not mediated by ICAM-1. *Sleep Breath.* 2021.
18. Martínez-García MA, Capote F, Campos-Rodríguez F, et al.; Spanish Sleep Network. Effect of CPAP on blood pressure in patients with obstructive sleep apnea and resistant hypertension: the HIPARCO randomized clinical trial. *JAMA.* 2013;310(22):2407–2415.
19. Liu L, Cao Q, Guo Z, Dai Q. Continuous positive airway pressure in patients with obstructive sleep apnea and resistant hypertension: a meta-analysis of randomized controlled trials. *J Clin Hypertens (Greenwich).* 2016;18(2):153–158.
20. Epstein LJ, Kristo D, Strollo PJ Jr, et al.; Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med.* 2009;5(3):263–276.
21. Berry RB, Budhiraja R, Gottlieb DJ, et al; Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. *J Clin Sleep Med.* 2012;8(5):597–619.
22. Johns MW. Sleepiness in different situations measured by the Epworth Sleepiness Scale. *Sleep.* 1994;17(8):703–710.
23. Bilo G, Zorzi C, Ochoa Munera JE, Torlasco C, Giuli V, Parati G. Validation of the Somnotouch-NIBP noninvasive continuous blood pressure monitor according to the European Society of Hypertension International Protocol revision 2010. *Blood Press Monit.* 2015;20(5):291–294.
24. Patzak A, Mendoza Y, Gesche H, Konermann M. Continuous blood pressure measurement using the pulse transit time: Comparison to intra-arterial measurement. *Blood Press.* 2015;24(4):217–221.
25. Lang RM, Bierig M, Devereux RB, et al.; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European society of Cardiology. *J Am Soc Echocardiogr.* 2005;18(12):1440–1463.
26. Martynowicz H, Porębska I, Poręba R, Mazur G, Brzecka A. Nocturnal blood pressure variability in patients with obstructive sleep apnea syndrome. *Adv Exp Med Biol.* 2016;952:9–15.
27. Webb AJS, Mazzucco S, Li L, Rothwell PM. Prognostic significance of blood pressure variability on beat-to-beat monitoring after transient ischemic attack and stroke. *Stroke.* 2018;49(1):62–67.
28. Chang TI, Reboussin DM, Chertow GM, et al.; SPRINT Research Group. Visit-to-visit office blood pressure variability and cardiovascular outcomes in SPRINT (Systolic Blood Pressure Intervention Trial). *Hypertension.* 2017;70(4):751–758.
29. Lozano L, Tovar JL, Sampol G, et al. Continuous positive airway pressure treatment in sleep apnea patients with resistant hypertension: a randomized, controlled trial. *J Hypertens.* 2010;28(10):2161–2168.
30. Pengo MF, Soranna D, Giontella A, et al. Obstructive sleep apnoea treatment and blood pressure: which phenotypes predict a response? A systematic review and meta-analysis. *Eur Respir J.* 2020;55(5):1901945.
31. Ernst G, Bosio M, Salvado A, Dibur E, Nigro C, Borsini E. Difference between apnea-hypopnea index (AHI) and oxygen desaturation index (ODI): proportional increase associated with degree of obesity. *Sleep Breath.* 2016;20(4):1175–1183.
32. Ciavarella D, Tepedino M, Chimenti C, et al. Correlation between body mass index and obstructive sleep apnea severity indexes—a retrospective study. *Am J Otolaryngol.* 2018;39(4):388–391.
33. Salman LA, Shulman R, Cohen JB. Obstructive sleep apnea, hypertension, and cardiovascular risk: epidemiology, pathophysiology, and management. *Curr Cardiol Rep.* 2020;22(2):6.

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DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. Work for this study was performed at the Department of Cardiology, Augusta Hospital Düsseldorf, Academic Teaching Hospital of the University Faculty of Health, Düsseldorf, Germany. The authors report no conflicts of interest.