Prospective Study of Sleep-disordered Breathing and Hypertension

The Sleep Heart Health Study

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Rationale: **Cross-sectional epidemiologic studies show an association between sleep-disordered breathing and hypertension, but only one cohort study has examined sleep-disordered breathing as a risk factor for incident hypertension.**

Objectives: **To examine whether sleep-disordered breathing increases the risk of incident hypertension among persons 40 years of age and older.**

Methods: **In a prospective cohort study, we analyzed data from 2,470 participants who at baseline did not have hypertension, defined as blood pressure of at least 140/90 mm Hg or taking antihypertensive medication. The apnea-hypopnea index (AHI), the number of apneas plus hypopneas per hour of sleep, was measured by overnight in-home polysomnography. We estimated odds ratios for developing hypertension during 5 years of follow-up according to baseline AHI.**

Measurements and Main Results: **The odds ratios for incident hypertension increased with increasing baseline AHI; however, this relationship was attenuated and not statistically significant after adjustment for baseline body-mass index. Although not statistically significant, the observed association between a baseline AHI greater than 30 and future hypertension (odds ratio, 1.51; 95% confidence interval, 0.93–2.47) does not exclude the possibility of a modest association.**

Conclusions: **Among middle-aged and older persons without hypertension, much of the relationship between AHI and risk of incident hypertension was accounted for by obesity. After adjustment for body mass index, the AHI was not a significant predictor of future hypertension, although a modest influence of an AHI greater than 30 on hypertension could not be excluded.**

Keywords: sleep apnea; sleep-disordered breathing; hypertension; cohort study

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Cross-sectional epidemiologic studies reveal an association between sleep-disordered breathing and hypertension, but only one cohort study has examined sleep-disordered breathing as a risk factor for incident hypertension.

What This Study Adds to the Field

Our prospective cohort study shows that sleep-disordered breathing was not a significant independent risk factor for hypertension after adjusting for the effect of body mass index, although a modest effect on hypertension risk of severe sleep-disordered breathing could not be excluded. These findings may influence clinical decision-making regarding the management of adults with mild-to-moderate sleep-disordered breathing.

Sleep-disordered breathing, the recurrent episodic disruption of normal breathing during sleep, is a common condition affecting as much as 17% of US adults (1). Cross-sectional studies have shown an association between sleep-disordered breathing and hypertension that is not explained by potential confounding from age, sex, and obesity (2–6), although the evidence is not uniformly consistent in showing an independent association (7, 8). Additionally, cross-sectional studies cannot characterize the temporal relationship between sleep-disordered breathing and hypertension.

Few prospective studies have directly investigated sleep-disordered breathing as an independent risk factor for the future development of hypertension in the general population. In a cohort study of 709 working, middle-age adults in Wisconsin, Peppard and colleagues (9) observed that the risk of developing hypertension over 4 years increased with the degree of sleep-disordered breathing at baseline. In addition, in the Nurses' Health Study of over 70,000 female nurses, self-reported snoring at baseline, a surrogate for sleep-disordered breathing, predicted incident physician-diagnosed hypertension, even after adjustment for potential confounders (10). Evidence of a link between sleep apnea and hypertension is also provided by clinical trials of nasal continuous positive airway pressure (CPAP), showing that this treatment lowers blood pressure (11, 12).

In this article, we report findings on sleep-disordered breathing and risk of incident hypertension in the Sleep Heart Health Study (SHHS), a multicenter prospective cohort study of sleep-disordered breathing and risk for hypertension and cardiovascular disease. Based on cross-sectional data, we have previously reported that sleep-disordered breathing is associated with increased risk for prevalent hypertension (2).

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METHODS

Study Population

As previously reported (13, 14), participants were recruited during the years 1995 through 1998 from ongoing cohort studies of cardiovascular and pulmonary disease. Participants were eligible if they were 40 years of age or older and denied nasal CPAP treatment, tracheotomy, and home oxygen therapy. Among 11,053 eligible participants in the combined parent cohorts who were screened for potential participation in SHHS, 3,394 (31%) declined participation, and 818 (7%) could not be located or were too ill to participate. The remaining 6,841 persons (62% of total eligible) completed a polysomnogram (PSG), and 6,441 of these (94% of those having a PSG) met PSG acceptability criteria and were included in the SHHS cohort. The 760 participants from the New York center were excluded because the performance of the second examination did not meet quality standards, leaving 5,681 subjects who were potentially eligible for inclusion in this analysis (Figure 1). The institutional review boards of all participating institutions approved the study, and participants signed a consent form.

Baseline Examination

Baseline data included a health interview; assessment of current medication use; and standardized measurement of blood pressure, weight, and neck circumference. Measurements of height and the circumference of waist and hips were obtained from the parent study. Subjects underwent unattended, in-home, overnight PSG, as previously described (13, 14). Sleep data were scored at a central reading center (14). The blood pressure measurement, PSG, and PSG scoring methods are described more fully in the online supplement.

Follow-up Examinations

Approximately 2 years (mean, 2.0 yr; range, 0.4–3.6 yr) after baseline, the first follow-up examination was conducted in the participants' home or at the parent-study clinic. Data collection included measurement of seated blood pressure and weight and recording of current medications. One site was not able to conduct a follow-up examination at this time and instead obtained data by mail questionnaire on medications for hypertension. The second follow-up examination was conducted in the participants' home approximately 5 years (mean, 5.2 yr; range, 4.6–7.2 yr) after baseline. The data collected included blood pressure measurements and current medication use.

Data Analysis

Hypertension at the baseline and follow-up examinations was defined as systolic blood pressure (SBP) $\geq$140 mm Hg, diastolic blood pressure (DBP) $\geq$90 mm Hg, or current treatment with antihypertensive medications. Body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters.

The apnea-hypopnea index (AHI) was analyzed as a categorical variable: 0 to 4.9, 5.0 to 14.9, 15.0 to 29.9, and 30 or more events per hour. The relationship of baseline AHI to subsequent hypertension at the first or second follow-up examination was analyzed using generalized estimating equations (GEE), a multivariate regression method that accounts for the correlation between repeated observations when analyzing longitudinal data. We used GEE models because of the correlated values of the two observations for participants with data at both follow-up examinations. We also used GEE models to analyze the relationship of baseline AHI to subsequent change in SBP and DBP, between the baseline and second follow-up examination, among those participants who denied treatment with blood pressure medications at any examination. Statistical analyses were performed using SAS (SAS, Inc., Carey, NC) and *R* (15).

RESULTS

Among the 5,681 subjects included in the analysis, 2,869 (51%) had hypertension at the baseline examination, whereas 2,812 subjects (49%) did not (Figure 1). Among the 2,812 initially normotensive subjects, 2,470 (88%) participated in at least one follow-up examination and had data on blood pressure and medication use. These 2,470 subjects were middle-aged to older and were overweight on average (Table 1). Among men and women, BMI was higher in those with higher AHI, and BMI increased by an average of 0.8 kg/m^2 during the follow-up interval, an increase that was consistent across strata of AHI (*see* Table E1 in the online supplement).

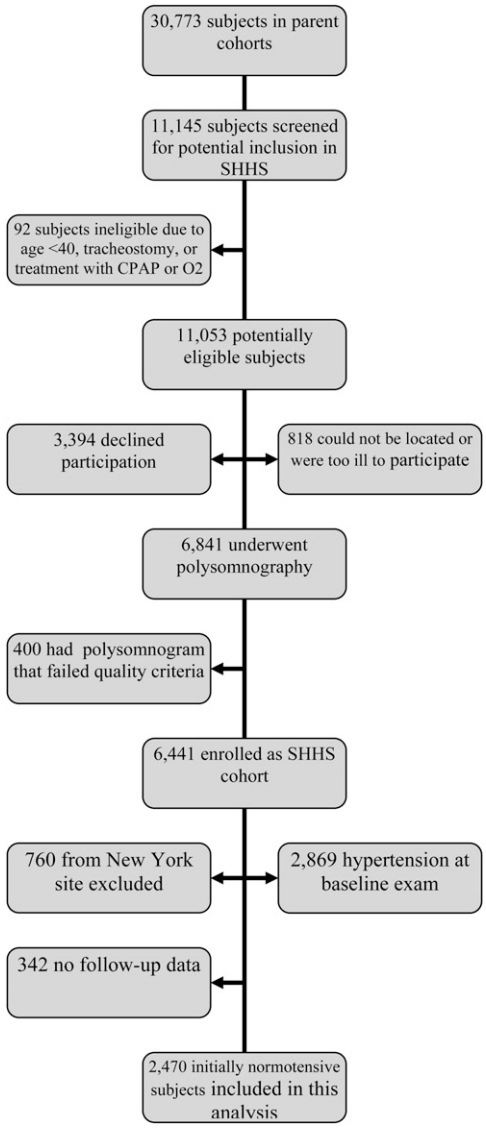

Figure 1. Flow diagram explaining the recruitment of the sleep heart health study (SHHS) cohort and the selection of subjects included in the present analysis.

Of the 2,470 initially nonhypertensive participants, 1,863 attended the first follow-up examination, and 391 (21%) had hypertension at that time (Table E2). The hypertension status of 1,915 participants was ascertained at the second follow-up examination, and 438 (23%) had hypertension (Table E2). An additional 212 persons attended the second follow-up examination but had uncertain hypertension status because they had normal blood pressure and were taking a medication with antihypertensive activity for an uncertain indication; these persons were excluded from the main analyses reported in Tables 2 through 6. We used GEE models to examine the relationship of baseline AHI category to the risk of developing hypertension (Table 2). In model 1, which adjusted only for age, sex, race, and time since baseline PSG, the risk of developing hypertension significantly increased with increasing baseline

TABLE 1. CHARACTERISTICS OF 2,470 SLEEP HEART HEALTH STUDY SUBJECTS WHO WERE NORMOTENSIVE AT BASELINE AND HAD AT LEAST ONE FOLLOW-UP EXAMINATION

Characteristic	Measure at Baseline
Sex, n (%)	
Male	1,103 (44.7)
Female	1,367 (55.3)
Race, n (%)	
White	1,935 (78.3)
Black	102 (4.1)
American Indian	433 (17.5)
Other	0 (0.0)
Smoking, n (%)	
Never	1,097 (44.5)
Former	1,033 (41.9)
Current	333 (13.5)
Age, years, mean (SD)	59.6 (10.3)
BMI, kg/m^2, mean (SD)	27.9 (5.0)
Waist/hip ratio, mean (SD)	0.9 (0.1)
Neck girth, cm, mean (SD)	37.3 (4.1)
Apnea-hypopnea index	
Median (interquartile range)	3.2 (1.0–8.7)
Categories, n (%)	
0–4.9 events/h	1,510 (61.2)
5–14.9 events/h	629 (25.5)
15–29.9 events/h	234 (9.5)
⩾30.0 events/hr	97 (3.9)

AHI. This relationship was attenuated and no longer statistically significant after adjustment for baseline BMI (model 2) (odds ratio [OR] for association of AHI ⩾30 and hypertension, 1.51; 95% confidence interval [CI], 0.93–2.47) and a nonsignificant test for trend for increasing OR with increasing baseline AHI. Further adjustment for waist/hip ratio and neck girth (model 3) did not appreciatively change the results. We repeated these models with inclusion of the 212 participants taking an antihypertensive medication for uncertain indication, classifying them as hypertensive at follow-up, and observed no difference in the results.

We examined the relationship of baseline AHI to incident hypertension within strata of sex, BMI (⩽ the median BMI of 27.3 kg/m^2 vs. >27.3 kg/m^2), age (⩽ the median age of 59 years vs. >59 years), and Epworth Sleepiness Scale score (⩽11; i.e., a clinically determined cut-point indicating excessive sleepiness [16], vs. >11), using a GEE model that adjusted for sex (except in the sex-stratified models), age, BMI, race, and time since baseline. Among women but not men, a baseline AHI 30 or greater was associated with a significantly increased OR for onset of hypertension (Table 3). The number of participants with baseline AHI 30 or greater was relatively small, and in a combined model with both sexes, the AHI × sex interaction term was not statistically significant (P value for interaction = 0.09). Among less obese subjects (BMI ⩽27.3 kg/m^2), but not among more obese subjects, a baseline AHI ⩾30 was associated with a significantly increased risk of hypertension (OR, 2.71; 95% CI, 1.24–5.93) (Table 4). As with sex, the interaction between BMI and AHI was not statistically significant (P value for interaction = 0.36). In analyses stratified by age at the median of 59 years, neither group demonstrated a consistent significant increase in the odds of developing hypertension with higher baseline AHI (Table 5). There was a suggestion that an AHI between 15 and 30 was associated with a greater risk of hypertension among participants with a Epworth Sleepiness Scale score greater than 11, but the risk associated with an AHI of 30 or greater did not vary with Epworth Sleepiness Scale score (Table 6), and the interaction between AHI and the Epworth score was not significant in a combined model (P value for interaction = 0.11).

Among the 2,470 initially nonhypertensive participants, 1,522 denied any treatment with medications that lower blood pressure at both follow-up examinations. In the latter group, the change in SBP and DBP between baseline and the second follow-up examination was not associated with the baseline AHI, with or without adjustment for BMI (Table 7).

As an alternative metric of sleep-disordered breathing, we used the percentage of sleep time with oxygen saturation less than 90% and repeated the above analyses. The results of these analyses were comparable to those for AHI; in the total sample, after adjusting for BMI, the baseline percentage of sleep time with oxygen saturation less than 90% was not a significant predictor of the subsequent development of hypertension.

TABLE 2. ADJUSTED ODDS RATIOS* OF INCIDENT HYPERTENSION AT FOLLOW-UP IN RELATION TO BASELINE APNEA-HYPOPNEA INDEX AMONG 2,470 SLEEP HEART HEALTH STUDY SUBJECTS WITHOUT HYPERTENSION AT BASELINE

Baseline AHI	n	Model 1†	Model 2‡	Model 3§
0–4.9	1,511	—	—	—
5–14.9	629	1.13 (0.90–1.43)	0.92 (0.72–1.17)	0.94 (0.73–1.22)
15–29.9	234	1.54 (1.12–2.11)	1.12 (0.80–1.56)	1.09 (0.77–1.54)
⩾30	97	2.19 (1.39–3.44)	1.51 (0.93–2.47)	1.50 (0.91–2.46)

Definition of abbreviations: AHI = apnea-hypopnea index; BMI = body mass index.

* Estimated by generalized estimating equation models with each subject contributing one or two follow-up intervals.

Values are odds ratio (95% confidence interval) or n.

† Adjusted for age, sex, race, and time since baseline.

‡ Adjusted for factors in model 1 plus BMI.

§ Adjusted for factors in model 2 plus waist/hip ratio and neck girth.

TABLE 3. ADJUSTED ODDS RATIOS FOR INCIDENT HYPERTENSION AMONG SLEEP HEART HEALTH STUDY SUBJECTS WHO WERE NORMOTENSIVE AT BASELINE, ACCORDING TO BASELINE APNEA-HYPOPNEA INDEX, STRATIFIED BY SEX

	Male Subjects		Female Subjects	
Baseline AHI	n	OR (95% CI)	n	OR (95% CI)
0–4.9	505	—	950	—
5–14.9	341	0.96 (0.68–1.36)	261	0.83 (0.59–1.18)
15–29.9	155	0.89 (0.57–1.39)	72	1.59 (0.95–2.64)
⩾30	56	1.10 (0.57–2.10)	31	2.27 (1.07–4.80)

Definition of abbreviations: AHI = apnea-hypopnea index; CI = confidence interval; OR = odds ratio.

TABLE 4. ADJUSTED ODDS RATIOS FOR INCIDENT HYPERTENSION AMONG SLEEP HEART HEALTH STUDY SUBJECTS WHO WERE NORMOTENSIVE AT BASELINE, ACCORDING TO BASELINE APNEA-HYPOPNEA INDEX, STRATIFIED BY BODY MASS INDEX

	BMI ⩽27.3		BMI >27.3	
Baseline AHI	n	OR (95% CI)	n	OR (95% CI)
0–4.9	887	—	541	—
5–14.9	213	0.89 (0.59–1.34)	378	0.92 (0.67–1.27)
15–29.9	58	0.93 (0.46–1.90)	164	1.13 (0.76–1.68)
⩾30	21	2.71 (1.24–5.93)	65	1.18 (0.64–2.19)

Definition of abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; CI = confidence interval; OR = odds ratio.

TABLE 5. ADJUSTED ODDS RATIOS FOR INCIDENT HYPERTENSION AMONG SLEEP HEART HEALTH STUDY SUBJECTS WHO WERE NORMOTENSIVE AT BASELINE, ACCORDING TO BASELINE APNEA-HYPOPNEA INDEX, STRATIFIED BY AGE

	Age ⩽59 yr		Age >59 yr	
Baseline AHI	n	OR (95% CI)	n	OR (95% CI)
0–4.9	879	—	576	—
5–14.9	262	1.02 (0.70–1.50)	340	0.85 (0.62–1.16)
15–29.9	96	1.79 (1.08–2.95)	131	0.82 (0.53–1.26)
⩾30	33	1.47 (0.64–3.37)	54	1.53 (0.84–2.79)

Definition of abbreviations: AHI = apnea-hypopnea index; CI = confidence interval; OR = odds ratio.

DISCUSSION

This prospective cohort study of middle-aged and older adults shows that among participants without hypertension at baseline, sleep-disordered breathing at baseline was positively associated with incidence of hypertension during follow-up; however, this relationship was attenuated and no longer statistically significant after adjustment for BMI. Although not statistically significant, the BMI-adjusted association between a baseline AHI greater than 30 and future hypertension (OR, 1.51; 95% CI, 0.93–2.47) does not exclude the possibility of a modest association of a magnitude consistent with risk estimates from our earlier cross-sectional analysis (2).

The results of the key models need to be interpreted within the context of possible mechanisms by which sleep-disordered breathing might cause hypertension. Without adjustment for BMI, there is a clear dose–response relationship between AHI and risk for hypertension (*see* Table 2). With adjustment for BMI, the dose–response relationship is flattened, and risk estimates are no longer statistically significant. The attenuation of this relationship after adjustment for baseline BMI may indicate that the association between sleep-disordered breathing and hypertension risk is confounded by obesity. Alternatively, this change in the estimated effect with adjustment for BMI is consistent with an underlying causal mechanism in which sleep-disordered breathing raises blood pressure by increasing BMI.

After adjustment for BMI, these results, showing at most a small effect of sleep-disordered breathing on the risk of developing future hypertension, are consistent with previous reports of cross-sectional investigations. Our earlier cross-sectional analysis of SHHS data revealed that participants with an AHI of 30 per hour or greater were more likely to have hypertension than those with an AHI below 1.5 per hour (OR, 1.37; 95% CI, 1.03–1.83; P for trend = 0.005) even after adjustment for BMI (2). The current analysis of risk for incident hypertension reveals an estimated BMI-adjusted association of similar magnitude, but the estimate has a wider CI. The greater degree of imprecision partly reflects the smaller number of participants in the longitudinal analysis, which was limited to the 2,470 subjects without baseline hypertension and with available follow-up data. The earlier cross-sectional analysis included 6,132 participants. In the longitudinal analysis, we did not observe an effect modification by age, while the cross-sectional association between sleep-disordered breathing and hypertension, adjusted for BMI, was limited to participants below 60 years of age (17).

Our results do not confirm the relationship of sleep-disordered breathing to risk for incident hypertension observed in a previous cohort study of sleep-disordered breathing and hypertension incidence by Peppard and coworkers (9). In that study, an AHI of 15 per hour or greater was associated with an OR of 3.15 (95% CI, 1.26–7.84) after adjustment for demographic factors and BMI. The relatively wide confidence intervals in the Peppard study reflect the relatively small numbers of subjects with an AHI of 5 to 14.9 (n = 96) or with an AHI 15 or greater (n = 37) in comparison with the SHHS. We repeated our analysis using the same AHI categories as Peppard and colleagues, and subjects with an AHI of 15 per hour or greater had an OR for incident hypertension of 1.07 (95% CI, 0.62–1.85). Although the 95% CIs around the estimated overall OR for SHHS overlap with those of Peppard and colleagues, the upper bound of the 95% CI observed in our study is below the estimate of 3.15 for subjects with an AHI 15 or greater in the Wisconsin study (9). The Wisconsin study participants (9) were on average 14 years younger and 1.5 kg/m^2 more obese than participants in the SHHS; however, stratified analyses of our data did not reveal significant BMI-adjusted associations among the younger or more obese subjects in our sample. The Wisconsin cohort was recruited from among state employees in one geographical location; by contrast, our study included a diverse population, with all participants in established cohort studies. The differences in study findings might reflect the differing age ranges of the populations, the greater heterogeneity of the SHHS population, the different time of day of blood pressure measurements, or selection factors related to recruitment of the SHHS cohort from existing epidemiologic cohort studies. For example, partic-

TABLE 6. ADJUSTED ODDS RATIOS FOR INCIDENT HYPERTENSION AMONG SLEEP HEART HEALTH STUDY SUBJECTS WHO WERE NORMOTENSIVE AT BASELINE, ACCORDING TO BASELINE APNEA-HYPOPNEA INDEX, STRATIFIED BY EPWORTH SLEEPINESS SCORE

	ESS ⩽11		ESS >11	
Baseline AHI	n	OR (95% CI)	n	OR (95% CI)
0–4.9	1,189	—	221	—
5–14.9	472	0.83 (0.63–1.09)	119	1.31 (0.72–2.38)
15–29.9	178	0.90 (0.62–1.31)	47	2.32 (1.09–4.97)
⩾30	58	1.57 (0.87–2.83)	27	1.50 (0.58–3.85)

Definition of abbreviations: AHI = apnea-hypopnea index; CI = confidence interval; ESS = Epworth Sleepiness Score; OR = odds ratio.

TABLE 7. CHANGE OF SYSTOLIC AND DIASTOLIC BLOOD PRESSURE BETWEEN BASELINE AND SECOND FOLLOW-UP EXAMINATION, ACCORDING TO APNEA-HYPOPNEA INDEX AT BASELINE, AMONG 1,522 SUBJECTS WHO WERE NORMOTENSIVE AT BASELINE AND WERE NEVER TREATED WITH ANTIHYPERTENSIVE MEDICATIONS AT BASELINE OR FOLLOW-UP EXAMINATIONS*

Baseline AHI	Model 1*	Model 2†	Model 3‡
Change in systolic BP, mm Hg			
0–4.9	—	—	—
5–14.9	0.03 (0.90)	0.10 (0.94)	−0.12 (0.99)
15–29.9	0.61 (1.40)	0.84 (1.43)	0.50 (1.48)
⩾30	0.93 (2.16)	1.65 (2.23)	1.39 (2.25)
Change in diastolic BP, mm Hg			
0–4.9	—	—	—
5–14.9	0.26 (0.61)	0.41 (0.64)	0.48 (0.68)
15–29.9	−0.23 (0.95)	−0.02 (0.98)	−0.08 (1.01)
⩾30	−0.65 (1.47)	−0.70 (1.52)	−0.67 (1.54)

Definition of abbreviations: AHI = apnea-hypopnea index; BP = blood pressure.

Values are mean (SE) change in blood pressure in mm Hg estimated by linear models, as described in text.

* Adjusted for age, sex, race, and follow-up interval.

† Adjusted for factors in model 1 plus BMI.

‡ Adjusted for factors in model 2 plus waist/hip ratio and neck girth.

ipants in ongoing cardiovascular disease studies may have increased awareness of cardiovascular health issues and may have modified behaviors that affect risk for hypertension in association with sleep apnea.

Stratified analyses suggested that sleep-disordered breathing may predict future hypertension among women and less obese persons. These potentially significant associations should be interpreted cautiously, however, because they were not tests of *a priori* hypotheses and because the interactions between AHI and sex and AHI and obesity were not statistically significant. Nonetheless, the findings emphasize the need to further assess whether there are groups at greater risk for hypertension associated with sleep-disordered breathing. There was also a suggestion that sleep-disordered breathing may predict hypertension among persons with excessive daytime sleepiness.

Animal (18) and human studies (19) suggest sympathetic nervous system activation caused by hypoxemia (20) and/or arousal from sleep (21) as a potential mechanism linking sleep-disordered breathing and hypertension. Animal models of obstructive sleep apnea demonstrate acute increases in blood pressure during episodes of airway obstruction and arousal (22, 23). In a canine model, intermittent airway occlusion during nocturnal sleep led to increased nighttime and daytime blood pressure (24). In this experiment, the increased blood pressure returned to baseline over several weeks after cessation of the intermittent airway occlusion. In patients with obstructive sleep apnea, nasal CPAP treatment has been shown to reduce blood pressure and plasma norepinephrine when measured as soon as 14 (25) or 42 days (26) after the initiation of treatment. A randomized clinical trial of nasal CPAP therapy in patients with obstructive sleep apnea syndrome revealed that this therapy reduced the ambulatory mean arterial pressure by 2.5 mm Hg (27). Not all clinical trials of nasal CPAP treatment for sleep apnea have shown that this therapy reduces blood pressure (28), and those that have revealed beneficial effects have involved patients with more severe degrees of obstructive sleep apnea and daytime sleepiness (28). These studies of sleep apnea and hypertension appear to conflict with our observation that sleep-disordered breathing is not an independent predictor of hypertension. One possible explanation for this apparent conflict is that animal models and patients requiring CPAP treatment involve more severe degrees of sleep-disordered breathing than that detected in a general population cohort. Another possibility is that persons who are normotensive at baseline despite having sleep-disordered breathing may be relatively resistant to the development of hypertension. That is, sleep-disordered breathing may have a relatively rapid effect to raise blood pressure but relatively little impact on future hypertension risk after excluding persons who are normotensive despite sleep-disordered breathing at baseline.

Participants in the SHHS cohort were recruited from community-based samples, and consequently the distribution of sleep-disordered breathing in this sample is less severe than would be encountered in a clinical sample referred for evaluation of sleep-related symptoms. Thus, our findings cannot necessarily be extrapolated to clinic-based populations with a more severe range of disease. Also, because this cohort was assembled from existing cohort studies, one cannot exclude the possibility that other selection factors make this cohort different from the general population. Another potential limitation of our study is the approximately 5-year follow-up interval, a relatively short period for evaluation of incident hypertension. In addition, in this study as in others, there is a possibility of residual confounding by unmeasured covariates, such as salt intake or physical activity, which could differ between persons with and without sleep-disordered breathing. Finally, although the baseline and second follow-up examination blood pressures were measured with identical technique during early-evening home visits, the blood pressure measurements for most of the participants' first follow-up examination were measured at study clinic visits during the daytime, a setting more similar to a physician's office in which blood pressure would tend to be higher than during an early-evening home visit. Although this might increase the incidence of hypertension at the first follow-up examination compared with the second follow-up examination, this would be a nondifferential effect between subjects with and without sleep-disordered breathing. Our study, like most epidemiology studies with limitations in access to participants dictated by feasibility, did not include the measurement of blood pressure on multiple visits at the time of follow-up, such as clinicians are encouraged to use to when deciding whether to prescribe antihypertensive therapy (29).

In summary, among 2,470 middle-aged and older men and women who were free of hypertension at baseline, sleep-disordered breathing measured at baseline was a not a significant independent predictor of incident hypertension after adjusting for BMI. Although our results do not exclude the possibility of a modest relationship between a baseline AHI greater than 30 and future hypertension, our results do not support the finding of a strong association between sleep-disordered breathing and future hypertension reported previously in another prospective cohort study.

Conflict of Interest Statement: G.T.O. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. B.C does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. A.B.N. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. S.F.Q. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript D.M.R. receives grant support from Restore Medical and Fisher Paykel directly and from ProTech Services, Advanced Brain Monitoring, and Korosensor through NIH SBIR grants. He also holds multiple patents to diagnostic and therapeutic devices for obstructive sleep apnea, which are licensed through New York University to Covidian, Fisher Paykel Healthcare, Advanced Brain Monitoring, and Protech Services and which generate royalties to him through NYU. S.R. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. H.E.R. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. J.S. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. E.S. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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