The New England Journal of Medicine

VOLUME 342 MAY 11, 2000 NUMBER 19

PROSPECTIVE STUDY OF THE ASSOCIATION BETWEEN SLEEP-DISORDERED BREATHING AND HYPERTENSION

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ABSTRACT

Background Sleep-disordered breathing is prevalent in the general population and has been linked to chronically elevated blood pressure in cross-sectional epidemiologic studies. We performed a prospective, population-based study of the association between objectively measured sleep-disordered breathing and hypertension (defined as a laboratory-measured blood pressure of at least 140/90 mm Hg or the use of antihypertensive medications).

Methods We analyzed data on sleep-disordered breathing, blood pressure, habitus, and health history at base line and after four years of follow-up in 709 participants of the Wisconsin Sleep Cohort Study (and after eight years of follow-up in the case of 184 of these participants). Participants were assessed overnight by 18-channel polysomnography for sleep-disordered breathing, as defined by the apnea–hypopnea index (the number of episodes of apnea and hypopnea per hour of sleep). The odds ratios for the presence of hypertension at the four-year follow-up study according to the apnea–hypopnea index at base line were estimated after adjustment for base-line hypertension status, body-mass index, neck and waist circumference, age, sex, and weekly use of alcohol and cigarettes.

Results Relative to the reference category of an apnea–hypopnea index of 0 events per hour at base line, the odds ratios for the presence of hypertension at follow-up were 1.42 (95 percent confidence interval, 1.13 to 1.78) with an apnea–hypopnea index of 0.1 to 4.9 events per hour at base line as compared with none, 2.03 (95 percent confidence interval, 1.29 to 3.17) with an apnea–hypopnea index of 5.0 to 14.9 events per hour, and 2.89 (95 percent confidence interval, 1.46 to 5.64) with an apnea–hypopnea index of 15.0 or more events per hour.

Conclusions We found a dose–response association between sleep-disordered breathing at base line and the presence of hypertension four years later that was independent of known confounding factors. The findings suggest that sleep-disordered breathing is likely to be a risk factor for hypertension and consequent cardiovascular morbidity in the general population. (N Engl J Med 2000;342:1378-84.)

SCREENING studies in the United States, Europe, and Australia have shown that a substantial proportion of the adult population has mild-to-moderate sleep-disordered breathing, a condition characterized by repeated episodes of apnea and hypopnea during sleep.[1-6] Apnea and hypopnea cause temporary elevations in blood pressure in association with blood oxygen desaturation, arousal, and sympathetic activation and may cause elevated blood pressure during the daytime and, ultimately, sustained hypertension.[7] Recent reviews judged the epidemiologic evidence relating sleep-disordered breathing to hypertension to be inconclusive, but they noted that study designs were inappropriate, that there was inadequate control for confounding factors such as obesity, and that there was a dearth of prospective studies.[8,9] Since sleep-disordered breathing is prevalent and treatable and the morbidity and costs of hypertension are profound, a rigorous assessment of the relation between the two conditions remains a priority.

We assessed the association between sleep-disordered breathing and hypertension in a prospective analysis of data from the Wisconsin Sleep Cohort Study. The Sleep Cohort Study is a population-based, longitudinal study of the natural history of sleep-disordered breathing in adults. Participants complete overnight sleep studies at four-year intervals. These studies include assessment of sleep-disordered breathing (by monitored polysomnography), blood pressure, and many potential confounding factors.

METHODS

Overview

The protocols for the Wisconsin Sleep Cohort Study and informed-consent documents were approved by the institutional review board of the University of Wisconsin Medical School. In

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1989, a subgroup of employees of four Wisconsin state agencies was mailed a four-page questionnaire on sleep habits, health history, and demographic information. A stratified random sample of respondents was invited to participate in the study. Participants completed a base-line overnight protocol that included assessments of the physiologic characteristics of sleep by polysomnography, blood pressure, habitus, health history, and other information. Approximately every four years thereafter, participants have been invited for follow-up studies.

Exclusion criteria included pregnancy, unstable or decompensated cardiopulmonary disease, airway cancers, and recent surgery of the upper respiratory tract. For this report, participants were also excluded if they had sleep studies with unusable physiologic measurements, an inadequate period of sleep (less than four hours), no episodes of rapid-eye-movement sleep, or a history of physician-diagnosed stroke or cardiovascular disease, or if they were receiving medical treatment for sleep-disordered breathing.

Participants

As of September 1999, a total of 1189 participants had completed a base-line sleep study and 957 of these participants had been invited for four-year follow-up studies. Of those invited, 709 (74 percent) participated in a follow-up study, 233 (24 percent) declined, and 15 (2 percent) could not be contacted (because they had moved or died). Of the 709 who completed four-year follow-up studies, 219 had been invited for eight-year follow-up studies at the time of our analysis. Of these, 184 (84 percent) completed the second follow-up study, 30 (14 percent) declined, and 5 (2 percent) could not be contacted. Table 1 compares key base-line variables among the participants who completed the base-line sleep study, those who completed the four-year follow-up study, and those who completed the eight-year follow-up study. There were no substantial differences among the three groups, although the percentage of female participants was slightly lower in the subgroup that completed the eight-year follow-up study.

Collection of Data

The overnight sleep studies were conducted at the University of Wisconsin General Clinical Research Center in rooms resembling typical bedrooms. Participants arrived in the early evening. Sleep technicians obtained written informed consent and administered health-history and lifestyle questionnaires. The use of antihypertensive medication was determined on the basis of participants' answers to questions concerning the current use of α-adrenergic antagonists, beta-blockers, calcium-channel blockers, diuretics, and angiotensin-converting–enzyme inhibitors for the treatment of hypertension. After administration of the questionnaires and after participants had been seated for at least 15 minutes, two or three readings of systolic and diastolic (phase V) blood pressure were obtained at 5-minute intervals with the use of conventional mercury sphygmomanometry according to the recommendations of the American Society of Hypertension.[10] Habitus was assessed with the use of standard procedures[11] and included measurements of height (in meters) and weight (in kilograms); waist, hip, and neck circumference (in centimeters); skin-fold thickness (in millimeters) of the biceps, triceps, and subscapular and suprailiac areas with use of a caliper; and body-mass index, which was calculated as the weight in kilograms divided by the square of the height in meters.

After the assessment of blood pressure and habitus, technicians affixed polysomnography leads to each participant and performed calibrations. An 18-channel polysomnographic recording system (model 78, Grass Instruments, Quincy, Mass.) was used to assess sleep state and respiratory and cardiac variables. Sleep state was measured with electroencephalography, electrooculography, and chin electromyography. These signals were used to determine the sleep stage for each 30-second interval of the polysomnographic record, according to conventional criteria.[12] Arterial oxyhemoglobin saturation, oral and nasal airflow, nasal air pressure, and rib-cage and abdominal respiratory motion were used to assess episodes of sleep-disordered breathing. Oxyhemoglobin saturation was continuously recorded with a pulse oximeter (model 3740, Ohmeda, Englewood, Colo.). Stalk-mounted thermocouples (Pro-Tec, Hendersonville, Tenn.) detected oral and nasal airflow. A pressure transducer (Validyne Engineering, Northridge, Calif.) measured air pressure at the nares. Respiratory inductance plethysmography (Respitrace, Ambulatory Monitoring, Ardsley, N.Y.) recorded rib-cage and abdominal excursions. Sleep stage and respiratory events were assessed by trained sleep technicians and reviewed by an expert polysomnographer. Each 30-second interval of the polysomnographic record was inspected visually for episodes of abnormal breathing. Cessation of airflow for at least 10 seconds was defined as an episode of apnea. A discernible reduction in the sum amplitude of the rib-cage plus the abdominal excursions on respiratory inductance plethysmography that lasted at least 10 seconds and that was associated with a reduction in the oxyhemoglobin saturation of at least 4 percent was defined as an episode of hypopnea. The apnea–hypopnea index was defined as the average number of episodes of apnea and hypopnea per hour of objectively measured sleep and was the summary measurement of the occurrence of sleep-disordered breathing.

Statistical Analysis

The primary goal of the study was to estimate the association of sleep-disordered breathing at base line with the presence of hypertension four years later. With this approach, an interpretation of a positive association might be that greater initial degrees of sleep-disordered breathing accelerate the development of hypertension. Actual changes in blood-pressure levels were not modeled, because the prevalent use of antihypertensive medication in the cohort obscures underlying blood-pressure levels in those who use medications, possibly biasing associations.[13] Participants whose blood pressure exceeded a specified cutoff point or who used antihypertensive medication at the time of their studies were classified as being hypertensive. In defining hypertension, we examined cutoff points for blood pressure ranging from 130/85 to 180/110 mm Hg. The cutoff point of primary interest was 140/90 mm Hg, which was defined as stage 1 hypertension by the sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.[14] Other cutoff points were also examined to determine whether the associations depended on the choice of cutoff point.

Among 709 participants who completed base-line and four-year follow-up sleep studies, 184 also completed eight-year follow-up studies, yielding data on 893 sets of four-year sleep studies for analysis. We used logistic-regression analysis with the SAS GENMOD procedure[15] to estimate the odds ratios for the presence of hypertension at follow-up according to the level of sleep-disordered

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PARTICIPANTS WHO COMPLETED THE BASE-LINE SLEEP STUDY, THE FOUR-YEAR FOLLOW-UP STUDY, AND THE EIGHT-YEAR FOLLOW-UP STUDY.*

CHARACTERISTIC AT BASE LINE	BASE-LINE STUDY (N=1189)	FOUR-YEAR FOLLOW-UP STUDY (N=709)	EIGHT-YEAR FOLLOW-UP STUDY (N=184)
Apnea–hypopnea index (events/hr)	4±10	4±9	4±9
Stage 1 or worse hypertension	28	27	27
Female sex (%)	45	45	40
Age (yr)	46±8	46±7	46±8
Body-mass index	29±7	29±6	29±5

*Plus–minus values are means ±SD. The body-mass index was calculated as the weight in kilograms divided by the square of the height in meters.

breathing at base line. We used the generalized-estimating-equations approach[16,17] to incorporate correlations between observations resulting from the inclusion of the 184 participants assessed at all three times. The significance of logistic-regression coefficients was determined with two-sided P values with use of an α level of 0.05 for main effects and of 0.01 for interactions between the covariates and the apnea–hypopnea index.

The degree of sleep-disordered breathing was characterized by the apnea–hypopnea index. We examined whether untransformed values for the apnea–hypopnea index at base line, log-transformed values (apnea–hypopnea index + 1), the square of the values, and categorization of values (0, 0.1 to 4.9, 5.0 to 14.9, and 15.0 or more events per hour) were predictors of the presence of hypertension at follow-up. The category of 0 events per hour was included because a substantial proportion of the participants had no episodes of apnea or hypopnea at base line. The cutoff points of 5.0 and 15.0 events per hour have been used in previous epidemiologic studies of sleep-disordered breathing. Further subdivision of the highest category was impractical because few participants had more than 15.0 events per hour.

Because of variability within subjects and measurement error in assessing blood pressure, some misclassification of hypertension status was inevitable. Thus, we could not precisely identify a cohort of participants who were free of hypertension at base line to follow for a determination of the incidence of hypertension. Instead, in all models, we controlled for hypertension status at base line. This approach allowed us simultaneously to examine the association between sleep-disordered breathing at base line and hypertension at follow-up in participants classified as normotensive at base line and the association between sleep-disordered breathing and persistent hypertension in participants classified as hypertensive at base line. We used an interaction term to assess whether these two associations were different. As a check for a possible bias resulting from the misclassification of hypertension, we performed Monte Carlo simulations in which a random error was added to the measurement of participants' blood pressure. Using conservative (larger than likely) estimates of the error in blood-pressure measurements calculated from the variability between participants' base-line and follow-up measurements, we determined that the misclassification of hypertension might lead to slight underestimates of the odds ratios for the likelihood of hypertension at follow-up.

We examined the following base-line variables as covariates: age, sex, body-mass index, neck circumference, waist circumference, waist-to-hip ratio, skin-fold measurements, smoking status (current smoker, former smoker, or no history of smoking; the number of pack-years; and the current number of packs smoked per week), extent of alcohol use (based on the participant's usual weekly consumption), hours of regular exercise per week, and menopausal status. Base-line covariates that substantially altered regression coefficients for the apnea–hypopnea index at base line were included in the final models. Interactions between the covariates and the apnea–hypopnea index were tested for statistical significance.

RESULTS

Table 2 presents key characteristics at base line and follow-up according to the apnea–hypopnea index at base line. When data on all 893 follow-up studies were analyzed, there was a decrease in mean blood pressure from base line to follow-up (from 125/82 mm Hg to 123/79 mm Hg) and an increase in the prevalence of stage 1 or worse hypertension (from 28 percent to 31 percent). These changes were due, in part, to a net increase in the use of antihypertensive medications (from 10 percent to 17 percent).

Odds ratios for the presence of hypertension at follow-up according to the apnea–hypopnea index at base line are given in Table 3. Results from four models are presented. The first model adjusted for hypertension status at base line, the second controlled for this variable as well as for age and sex (nonmodifiable risk factors), the third controlled for all these variables as well as for habitus, and the fourth controlled for all the preceding variables as well as for weekly alcohol consumption and cigarette use. Within each model there was a linear increase in the logarithm of the odds ratios for successively higher strata of the apnea–hypopnea index. These models fit better than alternative models that used continuous measures of the apnea–hypopnea index. No higher-order terms (e.g., linear squared or cubed) for the strata of the apnea–hypopnea index were statistically significant.

Table 3 reveals that age and sex minimally confounded the association between sleep-disordered breathing and hypertension: the odds ratios remained essentially unchanged after adjustment for age and sex. Adjustment for habitus variables did reduce the odds ratios, but further adjustment for alcohol and cigarette use did not. Other variables examined did not appreciably alter the odds ratios. No interaction terms for sleep-disordered breathing and the covariates examined, including base-line hypertension status, were significant.

Odds ratios obtained with the use of a more conservative definition of hypertension (blood pressure of at least 160/100 mm Hg or the use of antihypertensive medications) were similar to those in Table 3. After adjustment for base-line hypertension status, age, sex, body-mass index, waist and neck circumference, and weekly alcohol and cigarette use, the odds ratio associated with an apnea–hypopnea index of 0.1 to 4.9 events per hour as compared with none was 1.39 (95 percent confidence interval, 1.04 to 1.84), the odds ratio associated with an apnea–hypopnea index of 5.0 to 14.9 events per hour was 1.92 (95 percent confidence interval, 1.09 to 3.39), and the odds ratio associated with an apnea–hypopnea index of 15.0 or more events per hour was 2.66 (95 percent confidence interval, 1.13 to 6.25). Odds ratios based on other cutoff points for blood pressure (ranging from 130/85 to 180/110 mm Hg) were similar.

As a check for possible bias resulting from the dropout of participants from the study, we analyzed data after excluding all eight-year follow-up data and adjusting for base-line hypertension status, age, sex, body-mass index, waist and neck circumference, and weekly alcohol and cigarette use. The resulting odds ratios for the presence of hypertension at the four-year follow-up study were 1.40 (95 percent confidence interval, 1.09 to 1.81) with an apnea–hypopnea index of 0.1 to 4.9 events per hour at base line, 1.97 (95 percent confidence interval, 1.19 to 3.27) with an apnea–hypopnea index of 5.0 to 14.9 events per hour at base line, and 2.77 (95 percent confidence interval, 1.30 to 5.92) with an apnea–hypopnea in-

TABLE 2. CHARACTERISTICS OF THE PARTICIPANTS WHO COMPLETED ONE OR BOTH FOLLOW-UP SLEEP STUDIES, ACCORDING TO THE APNEA–HYPOPNEA INDEX AT BASE LINE.*

CHARACTERISTIC	BASE-LINE APNEA–HYPOPNEA INDEX				ENTIRE GROUP (N=893)
	0 (N=187)	0.1–4.9 (N=507)	5.0–14.9 (N=132)	≥15.0 (N=67)	
Sex — no. (%)					
Female	107 (57)	226 (45)	41 (31)	15 (22)	389 (44)
Male	80 (43)	281 (55)	91 (69)	52 (78)	504 (56)
Age — yr					
At base line	45±7	46±8	50±8	49±8	47±8
At follow-up	49±7	50±8	54±8	53±8	51±8
Apnea–hypopnea index — events/hr					
At base line	0	2±1	9±3	31±16	5±9
At follow-up	2±4	4±6	12±15	27±22	6±12
Median value at base line	0	1.1	8.1	24.6	1.2
Median value at follow-up	0.3	1.6	8.4	23.5	1.9
Systolic blood pressure — mm Hg					
At base line	120±14	124±14	130±14	135±16	125±15
At follow-up	118±15	123±15	131±18	129±16	123±16
Diastolic blood pressure — mm Hg					
At base line	79±9	82±9	84±9	88±11	82±10
At follow-up	75±10	79±11	82±11	81±10	79±11
Use of antihypertensive medications — no. (%)					
At base line	12 (6)	38 (7)	23 (17)	15 (22)	88 (10)
At follow-up	18 (10)	72 (14)	33 (25)	30 (45)	153 (17)
Stage 1 or worse hypertension (blood pressure ≥140/90 mm Hg or use of antihypertensive medications) — no. (%)					
At base line	34 (18)	121 (24)	59 (45)	40 (60)	254 (28)
At follow-up	32 (17)	142 (28)	64 (48)	40 (60)	278 (31)
Stage 2 or worse hypertension (blood pressure ≥160/100 mm Hg or use of antihypertensive medications) — no. (%)					
At base line	13 (7)	52 (10)	31 (23)	24 (36)	120 (13)
At follow-up	19 (10)	87 (17)	37 (28)	33 (49)	176 (20)
Body-mass index					
At base line	27±5	29±5	32±6	35±7	29±6
At follow-up	29±6	30±6	33±7	36±8	30±7
Alcoholic drinks — no. of drinks/wk					
At base line	3±5	4±7	4±6	5±8	4±6
At follow-up	3±4	4±5	4±5	4±6	4±5
Current cigarette smoker — no. (%)					
At base line	34 (18)	88 (17)	23 (17)	8 (12)	153 (17)
At follow-up	32 (17)	76 (15)	18 (14)	8 (12)	134 (15)

*Data are from 893 follow-up sleep studies: 709 participants completed the four-year follow-up study, and 184 also completed the eight-year follow-up study. For the 184 participants who completed both the four-year and the eight-year follow-up studies, four-year follow-up data were used to calculate the base-line values and eight-year follow-up data were used to calculate the follow-up values. Plus–minus values are means ±SD.

dex of 15.0 or more events per hour at base line. In each case the reference category was an apnea–hypopnea index of 0 events per hour. These odds ratios were similar to those in Table 3.

DISCUSSION

We found a relation between sleep-disordered breathing and hypertension, measured over a four-year period, after adjustment for habitus, age, sex, and cigarette and alcohol use. Persons with few episodes of apnea or hypopnea (0.1 to 4.9 events per hour) at base line had 42 percent greater odds of having hypertension at follow-up than did persons with no episodes. Persons with mild sleep-disordered breathing (as defined by an apnea–hypopnea index of 5.0 to 14.9 events per hour) and those with more severe sleep-disordered breathing (as defined by an apnea–hypopnea index of 15.0 or more events per hour) had approximately two and three times, respectively, the odds of having hypertension at follow-up of those with no episodes of apnea or hypopnea. Our findings, if accurate and reflective of a causal relation, are particularly important because of the high prevalences of sleep-disordered breathing and hypertension.

Dropout of participants, the possibility of confounding, and error in assessing key study factors are important features of our study that may be relevant to the accuracy of our results. Among the participants who were invited for the four-year and eight-

TABLE 3. ADJUSTED ODDS RATIOS FOR HYPERTENSION AT A FOLLOW-UP SLEEP STUDY, ACCORDING TO THE APNEA–HYPOPNEA INDEX AT BASE LINE.*

BASE-LINE APNEA–HYPOPNEA INDEX	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS AND NONMODIFIABLE RISK FACTORS (AGE AND SEX)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, AND HABITUS (BMI AND WAIST AND NECK CIRCUMFERENCE)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, HABITUS, AND WEEKLY ALCOHOL AND CIGARETTE USE
	odds ratio (95% confidence interval)			
0 events/hr†	1.0	1.0	1.0	1.0
0.1–4.9 events/hr	1.66 (1.35–2.03)	1.65 (1.33–2.04)	1.42 (1.14–1.78)	1.42 (1.13–1.78)
5.0–14.9 events/hr	2.74 (1.82–4.12)	2.71 (1.78–4.14)	2.03 (1.29–3.19)	2.03 (1.29–3.17)
≥15.0 events/hr	4.54 (2.46–8.36)	4.47 (2.37–8.43)	2.89 (1.47–5.69)	2.89 (1.46–5.64)
P for trend‡	<0.001	<0.001	0.002	0.002

*Hypertension was defined as a blood pressure of at least 140/90 mm Hg or the use of antihypertensive medications. Data on 893 follow-up sleep studies from 709 participants were analyzed. The odds ratios and confidence intervals were adjusted for the fact that 184 participants completed two follow-up sleep studies. BMI denotes body-mass index.

†This category served as the reference group.

‡P values are for the linear trend of the logistic-regression coefficients ($\log_e$ of the odds ratios).

year follow-up studies, 74 percent and 84 percent, respectively, completed the studies. The odds ratios for hypertension at follow-up that were calculated from base-line and all follow-up data were similar to those that excluded eight-year follow-up data, indicating that factors influencing participation in the eight-year follow-up studies did not lead to biased associations. If similar factors influenced participation in the four-year follow-up studies, then it would be unlikely that an important bias related to dropout affected the findings.

The associations between sleep-disordered breathing and hypertension may be confounded by variables that cause both sleep-disordered breathing and hypertension. We measured and controlled for established confounding factors (age, sex, and habitus) as well as several additional variables. In our sample, measures of habitus, but not age or sex, were strong confounding variables. Previous cross-sectional studies of sleep-disordered breathing and hypertension have been faulted for not adjusting for smoking or alcohol use.[8] We found no evidence that these factors were important confounders.

Measurement error in assessing sleep-disordered breathing, blood pressure, or other covariates may have reduced the accuracy of our findings. Random error in measuring sleep-disordered breathing is likely to produce a bias toward the absence of an association.[18] Our Monte Carlo simulations indicated that a random error in blood-pressure measurement might also produce a bias toward a reduced association. If the accuracy of the classification of hypertension was related to the degree of sleep-disordered breathing or to important covariates such as obesity, then underestimates or overestimates of association could occur. Incomplete control of confounding due to, for example, measurement error in assessing habitus may produce a bias toward an overestimate of associations between sleep-disordered breathing and hypertension.[18]

The fact that our study was prospective lends support to the evidence of a causal role of sleep-disordered breathing in hypertension. We found that the presence of sleep-disordered breathing was predictive of the presence of hypertension four years later. This finding may indicate that sleep-disordered breathing accelerates the progression of blood-pressure levels commonly present in middle-aged adults in the United States. However, our findings do not offer comprehensive insight into the natural history of the association. Sleep-disordered breathing changes blood pressures acutely.[19-22] Nocturnal exposure to sleep-disordered breathing may lead to elevations in blood pressure that last throughout the morning or the entire day.[23] A daytime pressor response that outlasts experimentally induced nocturnal hypoxia has been demonstrated in humans.[24] It has also been hypothesized that sleep-disordered breathing could cause permanent changes in blood pressure by remodeling the systemic vasculature.[25]

We did not have data that could be used to model the dynamic relation between sleep-disordered breathing, habitus, and hypertension. For example, although there have been few relevant studies, there has been speculation that sleep-disordered breathing has a causal role in obesity.[26] If this is the case, then our efforts to control for confounding by including measures of obesity in our models may have led to a partial overadjustment of the association between sleep-

disordered breathing and hypertension and thus to an underestimate of the association.

We found no evidence of a threshold of the apnea–hypopnea index below which hypertension was not related to sleep-disordered breathing. Even persons with minimal sleep-disordered breathing (as defined by an apnea–hypopnea index of 0.1 to 4.9 events per hour) had higher odds of hypertension than those with no episodes of sleep-disordered breathing. If even those with minimal sleep-disordered breathing are at higher risk for hypertension, then the proportion of cases of hypertension that are attributable to this factor may be substantial.

Previous epidemiologic studies of sleep-disordered breathing and hypertension that focused on subjects from the general population and patients from sleep-disorders clinics have reached conflicting conclusions, although none have precluded the existence of a moderate association.[9] Studies that involved cross-sectional samples from sleep-disorders clinics[26-34] have typically used high-quality methods to assess sleep-disordered breathing (multichannel polysomnography). However, unknown factors that influence referral to a sleep-disorders clinic may have made these studies incapable of accurately assessing the relations. Conversely, most cross-sectional population-based studies[5,35-43] have used samples that were epidemiologically more rigorous but used instruments with poor or unknown validity to assess sleep-disordered breathing. Two recent population-based cross-sectional analyses from the Wisconsin Sleep Cohort Study[44] and the Sleep Heart Health Study,[45] which used polysomnography to assess sleep-disordered breathing, reported moderate, statistically significant associations between sleep-disordered breathing and hypertension. In a recent prospective study, Hu and colleagues[46] assessed a large number of normotensive women and found that snoring, a cardinal (but nonspecific) symptom of sleep-disordered breathing, significantly increased the risk of hypertension. As compared with the risk in nonsnorers, the risk of hypertension was increased by 29 percent in occasional snorers and by 55 percent in those who snored regularly.

As evidence builds of a causal role of sleep-disordered breathing in hypertension and other health outcomes, there is a growing need to understand the natural history of and risk factors for sleep-disordered breathing. Continued development and refinement of medical treatments for sleep-disordered breathing are also priorities. Available treatments, such as continuous positive airway pressure, can be effective. However, these therapies may be overly burdensome for the treatment of mild cases of asymptomatic sleep-disordered breathing. Little is known about the effectiveness of risk-factor intervention for mild-to-moderate sleep-disordered breathing, and this is an important area for future research.

In this prospective analysis, we found an association between laboratory-assessed sleep-disordered breathing and hypertension. Important elevations in the odds of hypertension were observed even in participants with mild-to-moderate sleep-disordered breathing. Because sleep-disordered breathing is highly prevalent, afflicting as many as 9 percent of women and 24 percent of men in the United States,[1] a causal association could be responsible for a substantial number of cases of hypertension and its sequelae, such as cardiovascular and cerebrovascular morbidity and mortality.

Supported by grants (R01HL62252, P01HL42242, RR03186, and R01CA53786) from the National Institutes of Health.

We are indebted to Jerome Dempsey, Ph.D., Steven Weber, Ph.D., Laurel Finn, Tony Jacques, Linda Evans, Kathy Pluff, Deborah Brown, Andrea Darner, Kathy Kenison, Leah Steinberg, Marty Kanarek, Ph.D., and Richard Chappell, Ph.D., for their contributions and technical expertise.

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