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Age-Dependent Associations Between Sleep-Disordered Breathing and Hypertension

Importance of Discriminating Between Systolic/Diastolic Hypertension and Isolated Systolic Hypertension in the Sleep Heart Health Study

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***Background*—**Sleep-disordered breathing (SDB) is associated with hypertension in the middle-aged. The association is less clear in older persons. Most middle-aged hypertensives have systolic/diastolic hypertension, whereas isolated systolic hypertension (ISH) is common among persons over 60 years. Mechanistically, only systolic/diastolic hypertension is expected to be associated with SDB, but few studies of SDB and hypertension distinguish systolic/diastolic hypertension from ISH. Prior investigations may have underestimated an association between SDB and systolic/diastolic hypertension in the elderly by categorizing individuals with ISH as simply hypertensive.

***Methods and Results*—**We conducted cross-sectional analyses of 6120 participants in the Sleep Heart Health Study, stratified by age: 40 to 59 (n=2477) and ≥60 years. Outcome measures included apnea-hypopnea index (AHI; average number of apneas plus hypopneas per hour of sleep), systolic/diastolic hypertension (≥140 and ≥90 mm Hg), and ISH (≥140 and <90 mm Hg). With adjustment for covariates, ISH was not associated with SDB in either age category. In those aged<60 years, AHI was significantly associated with higher odds of systolic/diastolic hypertension (AHI 15 to 29.9, OR=2.38 [95% CI 1.30 to 4.38]; AHI ≥30, OR=2.24 [95% CI 1.10 to 4.54]). Among those aged ≥60 years, no adjusted association between AHI and systolic/diastolic hypertension was found.

Conclusions*—**SDB is associated with systolic/diastolic hypertension in those aged <60 years. No association was found between SDB and systolic/diastolic hypertension in those aged ≥60 years or between SDB and ISH in either age category. These findings have implications for SDB screening and treatment. Distinguishing between hypertensive subtypes reveals a stronger association between SDB and hypertension for those aged <60 years than previously reported. (Circulation*. 2005;111:614-621.**)

Key Words: epidemiology ■ hypertension ■ risk factors ■ sleep apnea syndromes

Sleep-disordered breathing (SDB) is strongly associated with hypertension.[1–3] More recently, prospective data demonstrate SDB to be an independent risk for future hypertension.[4] Although the link between SDB and hypertension is clear, the majority of evidence has been obtained in middle-aged populations. Less certainty exists about the risk of SDB for hypertension in the elderly, although both hypertension and SDB are more common in the elderly than in the middle-aged.[3,5–9]

The combination of systolic and diastolic hypertension is common in middle-aged hypertensive patients, whereas isolated systolic hypertension (ISH) is predominately a disease of elderly hypertensives.[10] It is estimated that ISH accounts for nearly 60% of hypertension in older populations, and its treatment results in as much as a 35% reduction in cardiovascular events.[11,12] Although both systolic/diastolic hypertension and ISH predict adverse cardiovascular events, each reflects different underlying pathophysiological processes. Systolic/diastolic hypertension represents multiple etiologic factors, with evidence to suggest that the sympathetic nervous system is an important mediator.[13] ISH results from the age-dependent loss of arterial compliance, manifested clinically by a widened pulse pressure.[14]

Activation of the sympathetic nervous system is an important mechanism linking SDB to hypertension; the loss of arterial compliance has not been implicated mechanistical-

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ly.[15,16] Therefore, because the proposed mechanisms linking SDB to hypertension might be expected to engender systolic/diastolic hypertension but not ISH, distinguishing the hypertensive condition as systolic/diastolic hypertension or ISH may be important when evaluating the risk of hypertension posed by SDB. Few studies have distinguished between systolic/diastolic hypertension and ISH when examining the association between SDB and hypertension. Indeed, most of the well-designed, large cross-sectional and prospective studies have defined the hypertensive condition as a systolic blood pressure (SBP) ≥140 mm Hg or a diastolic blood pressure (DBP) ≥90 mm Hg (or the presence of antihypertensive medication use).[1,3,4,6] However, because most elderly patients have ISH rather than systolic/diastolic hypertension, prior studies that used either SBP ≥140 or DBP ≥90 mm Hg as diagnostic criteria for hypertension may have erroneously categorized elderly patients with ISH as simply hypertensive, thereby reducing the likelihood of detecting a true relationship between systolic/diastolic hypertension and SDB. We hypothesized that prior studies may not have found a relationship between SDB and hypertension in the elderly because most elderly patients have ISH and the pathophysiology of ISH is not related to SDB. Furthermore, we hypothesized that SDB is associated with increased risk for systolic/diastolic hypertension in all groups. We sought to examine the relation between SDB and hypertension by categorizing patients with systolic/diastolic hypertension or ISH across age groups. Specifically, we tested whether SDB was associated with systolic/diastolic hypertension or ISH stratified by age using cross-sectional data from the baseline examination of the Sleep Heart Health Study (SHHS).

Methods

Parent Cohorts and Study Sample

The aims and design of the SHHS have been reported[17] (also available at http://www.jhucct.com/shhs/). Briefly, SHHS subjects were recruited from ongoing cohort studies of cardiovascular or respiratory disease. From these parent cohorts, a sample of individuals who met the inclusion criteria (age ≥40 years; no history of treatment of SDB with continuous positive airway pressure; no tracheostomy; no current home oxygen use) were invited to participate in SHHS. Selection and recruitment procedures varied by study site according to logistical considerations and participants' characteristics.[18] To optimize statistical power, snorers were oversampled in sites that recruited individuals between 40 and 70 years of age.

Among 11 053 eligible participants in the parent cohorts, 3394 (30.7%) refused to participate in SHHS; 818 (7.4%) could not be located or were unable to participate because of illness. The remaining 6841 participants (62%) completed the SHHS baseline sleep study in their homes between November 1995 and January 1998. Sleep studies that met acceptability criteria (≥4 hours of interpretable signals on respiratory channels and sufficient electroencephalogram data to distinguish sleep from awake) were available for 6441 individuals (94.1%).[19] The present analyses are based on the 6120 participants with complete information on age, gender, race, blood pressure (BP), and body mass index (BMI).

Baseline SHHS Examination

A home visit was conducted that included a health interview, assessment of current medication use, BP and anthropometric measurements, and a full unattended polysomnograph study (PSG).[20] Resting BP was measured in the arm after a 5-minute rest with a mercury sphygmomanometer. The first and last Korotkoff sounds determined SBP and DBP, respectively. The average of the second and third of 3 consecutive measurements determined the BP. If participants were taking antihypertensive medications, BP measurements were made while on treatment. Weight was measured in light clothes on a portable scale. Neck circumference was measured below the laryngeal prominence by standard methods.[21] Polysomnography was conducted with a Compumedics PS-2 system (Compumedics Pty Ltd) with the following montage: 2 central electroencephalograms, bilateral electro-oculograms, chin electromyogram, single bipolar ECG, finger pulse oximetry, chest and abdominal excursion (by respiratory inductance plethysmography), airflow measures by oronasal thermocouples, body position, and ambient light. Sensors were placed and equipment calibrated during the evening home visit by centrally certified technicians. Data were stored in real time on PCMCIA (Personal Computer Memory Card International Association) cards. The equipment was retrieved the next morning by study staff.

Study Variables

Hypertensives were classified as having either systolic/diastolic hypertension (SBP ≥140 and DBP ≥90 mm Hg) or ISH (SBP ≥140 and DBP <90 mm Hg). Eighty-four participants (1.4%) had isolated diastolic hypertension (SBP <140 and DBP ≥90 mm Hg) and were included in the systolic/diastolic hypertension group.

The protocol for centralized scoring of sleep stages, arousals, and respiratory events has been described.[19] SDB was assessed with the apnea-hypopnea index (AHI), defined as the average number of apneic plus hypopneic episodes per hour of sleep. Apnea was defined as a complete or an almost complete cessation of airflow and hypopnea as a decrease in airflow or thoracoabdominal excursion of at least 30% of baseline for 10 seconds or more, each accompanied by a ≥4% oxygen desaturation. The percentage of sleep time with oxygen saturation below 90% (alternatively referred to as hypoxic sleep time) was also measured. The night-to-night reproducibility of sleep and respiratory patterns for SHHS subjects is acceptable.[22] The AHI scoring reliability has been reported previously.[23] The AHI as defined herein showed high interscorer reliability (intraclass correlation coefficient 0.99).

Age was considered continuously and categorically as age groups of 40 to 59 years and ≥60 years. A cutoff of 60 years was chosen for the primary analyses because longitudinal data suggest age 60 is when arterial stiffness engenders a characteristic fall in DBP with continued rise in SBP, manifested clinically as ISH.[24] In addition, antihypertensive trials of ISH have used age 60 for age dichotomization.[25–27] Analyses were also repeated using 65 years for dichotomization, which created age groups 40 to 64 years and ≥65 years. Smoking and diabetes histories were obtained from health interview. Usual alcohol intake, waist and hip circumferences, and height were obtained from the parent studies. BMI was calculated as weight in kilograms divided by the square of height in meters. Medication use was determined according to a standardized protocol in which participants were asked to gather all medications taken in the past 2 weeks.[20]

Statistical Analyses

For continuous variables, bivariate comparisons between participants aged 40 to 59 years and ≥60 years were conducted with *t* tests. Differences between the means and the 95% CIs for the differences are reported. Differences in AHI levels, which are highly skewed, were assessed with the Kruskal-Wallis test. ORs were calculated for categorical variables by logistic regression. Age-stratified χ^2 tests were performed to compare AHI category by hypertension category.

General linear models were used to measure SDB (AHI, percent hypoxic sleep time) for hypertension categories after adjustment for hypertensive medication use, gender, race, age, smoking, alcohol consumption, diabetes, BMI, and waist-to-hip ratio. A priori contrasts were conducted to test for differences between the normotensive group and the systolic/diastolic hypertension group and between the normotensive group and ISH group. AHI was log-transformed (log e [x+0.01]) to normalize the distribution. The resulting adjusted mean log AHI was exponentiated to approximate adjusted geometric mean AHI. The interaction between hypertension and age was evaluated with a model that included age, the systolic/diastolic hypertension contrast, the ISH contrast, and the interaction of age and each of the contrasts. A further model was used to test for the interactions after adjustment for hypertensive medications, gender, race, age, smoking, alcohol consumption, diabetes, BMI, and waist-to-hip ratio.

Logistic regression was used to calculate ORs for hypertension by AHI category (0 to 1.4 [reference category], 1.5 to 4.9, 5 to 14.9, 15 to 29.9, and ≥30) while adjusting for confounding variables. Separate models were run to compare participants categorized as having ISH to normotensives and to compare systolic/diastolic hypertensives to normotensives for both age groups. Partially adjusted models included presence of hypertensive medication, gender, age, and race as covariates. Fully adjusted models additionally included diabetes, BMI, waist-to-hip ratio, smoking status, and alcohol consumption as covariates. These logistic regressions were repeated to calculate adjusted ORs for hypoxic sleep time (0 to 0.049 [reference category], 0.05 to 0.49, 0.5 to 3.9, 4 to 11.9, and ≥12). Age-stratified general linear models were used to model pulse pressure as a function of AHI and hypoxic index after adjustment for covariates. Pearson correlations between all covariates were calculated. Although many of the covariate correlations were statistically significant, none had high correlation coefficients. All statistical analyses were conducted with SAS 8.01 software (SAS Institute).

Results

Sample Characteristics

The majority (60%) of participants were ≥60 years of age (Table 1). Nearly 20% of those aged ≥60 years had at least

TABLE 1. Characteristics of Sample Compared by Age Grouping

Variable	Age 40–59 y (n=2477)	Age >60 y (n=3643)	Mean Difference or OR (95% CI) Comparing Age ≥60 to Age 40–59 y
Normotensive, %	82.2	66.6	1.00
Systolic/diastolic hypertension, %	7.6	4.0	0.64 (0.51–0.81)*
ISH, %	10.2	29.5	3.56 (3.07–4.13)*
Age, y, mean (SD)	52.2 (5.3)	70.2 (6.9)	18.0 (17.7–18.3)
Race, %			
White	69.1	83.2	1.00
Black	7.2	7.4	0.85 (0.70–1.04)†
Native American	12.9	7.6	0.49 (0.42–0.59)†
Other	10.8	1.9	0.14 (0.11–0.19)†
Diabetes, %	8.8	11.9	1.41 (1.18–1.68)
Gender, % male	45.7	48.1	1.10 (1.00–1.22)
BMI, kg/m^2, mean (SD)	28.9 (5.9)	28.2 (5.0)	−0.7 (−1.0 to −0.4)
Waist:hip ratio, mean (SD)	0.91 (0.21)	0.94 (0.09)	0.03 (0.02–0.04)
Smoking, %			
None	46.2	46.3	1.00
Former	38.3	45.5	1.19 (1.06–1.32)‡
Current	15.5	8.3	0.53 (0.45–0.63)‡
AHI category, %			
<1.5	36.8	21.4	1.00
1.5 to <5	26.2	26.4	1.73 (1.50–1.98)§
5 to <15	22.5	32.4	2.47 (2.15–2.83)§
15 to <30	9.3	13.0	2.40 (2.00–2.83)§
≥30	5.1	6.7	2.25 (1.78–2.85)§
BP medication, %			
β-Blockers	6.9	15.1	2.39 (1.99–2.86)
Calcium channel blockers	7.8	17.9	2.56 (2.16–3.04)
ACE inhibitors	10.9	14.3	1.37 (1.17–1.61)
Diuretics	8.0	20.3	2.93 (2.48–3.46)
Any BP medication	25.8	49.0	2.77 (2.48–3.09)
Alcohol, %			
None	55.2	61.4	1.00
1 or 2 drinks/wk	17.4	14.1	0.73 (0.63–0.84)‖
3 to 7 drinks/wk	15.9	13.6	0.77 (0.64–0.89)‖
>7 drinks/wk	11.6	10.9	0.84 (0.71–0.99)‖

*Odds of systolic/diastolic hypertension, referenced to normotensives.
†Odds of race, referenced to white race.
‡Odds of smoking category, referenced to never smokers.
§Odds of AHI category, referenced to AHI <1.5.
‖Odds of alcohol consumption category, referenced to nondrinkers.

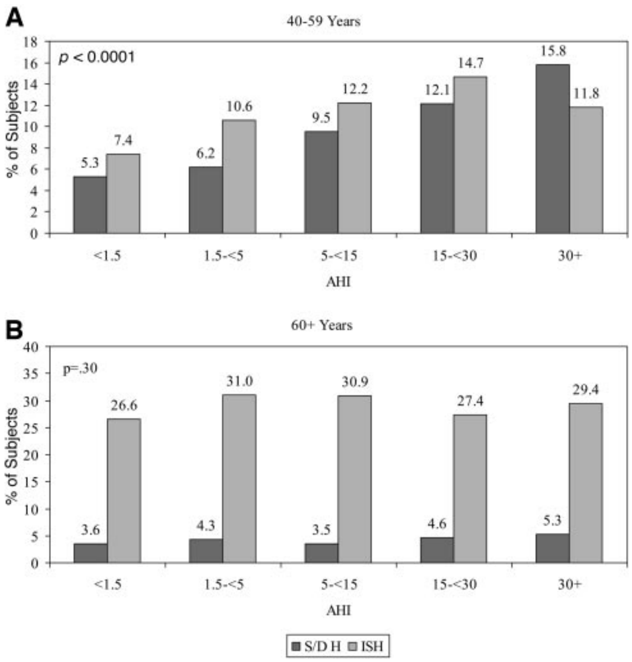

Figure 1. Unadjusted proportion of hypertensive conditions distributed by worsening AHI and age. S/D H indicates systolic/diastolic hypertension.

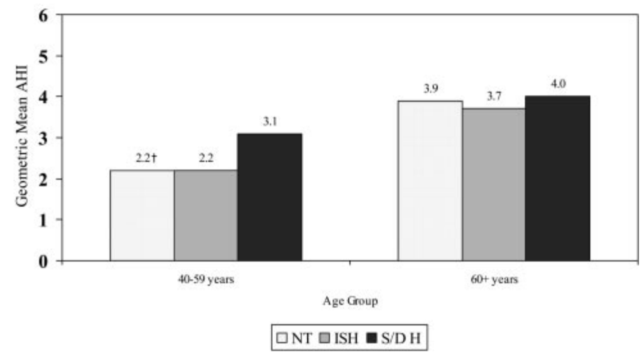

Figure 2. Adjusted geometric mean of log-transformed AHI according to BP category and age group. NT indicates normotensive; S/D H, systolic/diastolic hypertension. Adjusted for gender, race, age, smoking, alcohol use, diabetes, BMI, waist-to-hip ratio, and hypertensive medication use. †$P<0.05$ compared with 40- to 59-year-old S/D H group.

moderate SDB (AHI ≥15), as compared with 14.3% of those aged 40 to 59 years ($P<0.001$). The median AHI for the older group was 5.4 compared with 2.9 for the younger group ($P<0.001$). Approximately one third of the older participants were classified as hypertensive (either systolic/diastolic hypertension or ISH), compared with 17.8% of the 40- to 59-year-old group. Participants were more likely to be classified as having ISH than systolic/diastolic hypertension in both age groups; however, the distribution of hypertensive type differed significantly across age groups. ISH was observed in 88% of older participants with hypertension compared with 57% of younger hypertensives. Nearly half of the older participants were taking antihypertensive medications compared with 26% of younger participants.

AHI and Hypertension

With regard to AHI, there were statistically significant interactions between age and both systolic/diastolic hypertension ($P=0.005$) and ISH ($P=0.0001$) in the unadjusted model. The interaction was significant in the fully adjusted model for systolic/diastolic hypertension ($P=0.02$). Among the younger age group with AHI ≥15, 27.3% were hypertensive, with 13.5% classified with systolic/diastolic hypertension and 13.8% with ISH. Among the older cohort with an AHI ≥15, 4.9% had systolic/diastolic hypertension compared with 28.1% with ISH. Figure 1 demonstrates the unadjusted distribution of BP categorizations within AHI category. Despite similar numbers of systolic/diastolic hypertensives in both age groups (n=146 [4%] for ages ≥60 years; n=188 [7.6%] for ages 40 to 59 years), only in the younger cohort was systolic/diastolic hypertension significantly more prevalent as AHI severity worsened. There was no association between AHI and either systolic/diastolic hypertension or ISH in those aged ≥60 years ($P=0.30$). Figure 2 demonstrates the associations of AHI with BP classification according to age group, adjusted for covariates. Geometric mean AHI was significantly higher among younger participants with systolic/diastolic hypertension than among normotensives. In contrast, among those aged ≥60 years, no significant differences were observed in geometric mean AHI when the normotensive group was compared with the systolic/diastolic hypertension and ISH groups, respectively.

Table 2 presents the OR for being classified as having either ISH or systolic/diastolic hypertension (relative to normotensive) as a function of AHI, according to age group. Among the 40- to 59-year-olds, the odds of systolic/diastolic hypertension increased significantly with AHI. In the older age group, no increased risk was observed for either systolic/diastolic hypertension or ISH with AHI.

Other Measures of SDB and Hypertension

Among those 40 to 59 years of age, the average hypoxic sleep time was significantly higher among participants categorized with systolic/diastolic hypertension than among the normotensive group (Figure 3). In the older group, systolic/diastolic hypertensives had more hypoxic sleep time (on average) than normotensives. No significant difference existed in hypoxic sleep time between the normotensive and ISH groups in the younger cohort; however, in the older group, there was significantly more hypoxic sleep time in the normotensive group than in the ISH group (Figure 3). Table 3 shows that for the younger group, the odds of systolic/diastolic hypertension increased significantly with more hypoxic sleep time, whereas there was no relation between systolic/diastolic hypertension and increasing hypoxic sleep time in the older group. In the fully adjusted model, the odds of ISH decreased significantly with more hypoxic sleep time for those aged ≥60 years but not for the younger cohort.

Effect of BP Medication

We repeated the analyses excluding participants treated for hypertension. The analyses presented in Tables 2 and 3 were repeated excluding those individuals taking BP medications (n=1860 and n=1840 for the older and younger groups,

TABLE 2. Adjusted OR for ISH and Systolic/Diastolic Hypertension as a Function of Worsening AHI According to Age, Dichotomized at 60 Years

BP Group	Age, y	AHI	N	OR Adjusted for Demographics* (95% CI)	OR Fully Adjusted† (95% CI)
ISH vs NT	40–59	0 to <1.5	863	1.00 (Reference)	1.00 (Reference)
		1.5–4.9	610	1.41 (0.98–2.03)	1.18 (0.79–1.76)
		5–14.9	505	1.49 (1.02–2.17)	1.14 (0.75–1.75)
		15–29.9	203	1.66 (1.03–2.67)	1.25 (0.74–2.13)
		30+	107	1.09 (0.58–2.06)	0.63 (0.30–1.31)
		P (trend)		0.12	0.76
	60+	0 to <1.5	753	1.00 (Reference)	1.00 (Reference)
		1.5–4.9	921	1.21 (0.98–1.51)	1.22 (0.97–1.52)
		5–14.9	1139	1.15 (0.93–1.42)	1.12 (0.90–1.39)
		15–29.9	453	0.98 (0.75–1.28)	0.94 (0.71–1.24)
		30+	232	1.07 (0.77–1.50)	1.03 (0.72–1.46)
		P (trend)		0.95	0.63
S/D H vs NT	40–59	0 to <1.5	844	1.00 (Reference)	1.00 (Reference)
		1.5–4.9	581	1.11 (0.71–1.72)	1.30 (0.80–2.12)
		5–14.9	490	1.61 (1.04–2.47)	1.78 (1.09–2.92)
		15–29.9	197	1.99 (1.18–3.36)	2.32 (1.27–4.24)
		30+	112	2.17 (1.19–3.96)	2.27 (1.13–4.56)
		P (trend)		0.001	0.002
	60+	0 to <1.5	573	1.00 (Reference)	1.00 (Reference)
		1.5–4.9	664	1.22 (0.74–2.00)	1.14 (0.69–1.91)
		5–14.9	815	0.91 (0.55–1.49)	0.93 (0.55–1.55)
		15–29.9	345	1.08 (0.60–1.94)	1.04 (0.56–1.94)
		30+	173	1.18 (0.59–2.37)	1.30 (0.63–2.71)
		P (trend)		0.96	0.78

NT indicates normotension; S/D H, systolic/diastolic hypertension.

*Adjusted for gender, race, age, and BP medication use.

†Adjusted for gender, race, age, BP medication use, diabetes, BMI, waist:hip ratio, smoking, and alcohol consumption.

respectively). Significant associations were observed only between SDB and systolic/diastolic hypertension and only in the younger age group.

Effect of Central Sleep Apneas

The prevalence of participants with central sleep apnea was low in the SHHS sample. For central apneas, the mean central apnea index for the younger age group was 0.2 (SD=1.1), and for the older group, it was 0.4 (SD=1.9). For both groups, the median central apnea index for central apneas was 0.0. Nonetheless, we repeated the analyses presented in Table 2 excluding those participants with central apnea. The results obtained were nearly identical to those in Table 2, with significant associations observed between systolic/diastolic hypertension and AHI in the younger group only. There was no observed association between ISH and AHI for either age group with central apneas excluded.

Effect of Dichotomizing Age at 65 Years

Because central arterial stiffening and ISH become more prevalent with aging, we explored the effect of dichotomizing the present sample at a later age. When age groups were dichotomized at age 65 years, there was no association between ISH and AHI in either age group. In the younger age group (40 to 64 years), the odds of being classified with systolic/diastolic hypertension remained significantly increased for those with AHI >15; however, it was attenuated. No risk was observed for being classified with systolic/diastolic hypertension among the older group (≥65 years), as was the case when the sample was dichotomized at 60 years. Thus, the effect of dichotomizing at age 65 was to attenuate the level of the association between systolic/diastolic hypertension and AHI that was observed when the sample was dichotomized at age 60.

Discussion

In the general population, SDB is common, although largely undiagnosed.[28] It is important to understand clearly the true impact of SDB on hypertension, because both the diagnosis (via sleep study) and treatment (continuous positive airway pressure) of SDB are highly resource consuming. The main findings of the present cross-sectional analysis of the SHHS baseline data are that although SDB and systolic/diastolic

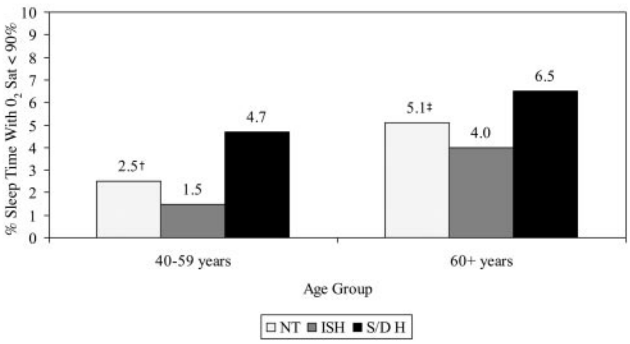

Figure 3. Adjusted average percentage of sleep time with oxygen saturation (% Sleep Time O_2 Sat) <90% according to BP category and age group. NT indicates normotensive; S/D H, systolic/diastolic hypertension. Adjusted for gender, race, age, smoking, alcohol use, diabetes, BMI, waist-to-hip ratio, and hypertensive medication use. †$P<0.05$ compared with 40- to 59-year-old S/D H group; ‡$P<0.05$ compared with ≥60-year-old ISH group, $P<0.05$ compared with ≥60-year-old S/D H group.

hypertension were significantly associated in those aged 40 to 59 years, there were neither significant nor consistent relationships between hypertension and SDB among those ≥60 years of age, even when ISH was distinguished from systolic/diastolic hypertension. Moreover, no association was observed between SDB and ISH in either age group. The present findings add new insight into the complex relation between SDB and hypertension and help define those individuals at risk for SDB-related cardiovascular morbidity. However, because survival biases may influence disease associations in cross-sectional studies, especially those of older populations, prospective studies are required to establish the natural history of SDB in aging populations.

With regard to hypertension, our findings suggest that SDB may have different clinical implications for older participants. Why this should be is less clear, although such age-related differences are reported in the literature. Follow-up studies of middle-aged cohorts have shown that SDB worsens in severity with time.[29] In the elderly, however, SDB is not progressive.[30] In a community-based study of elderly patients (age range 65 to 77 years), SDB had a predictive value of only 50% for SDB assessed 4 to 8 years later.[30] Furthermore, strong correlates of SDB in the middle-aged, such as neck circumference, BMI, and breathing pauses, are less strongly associated with SDB in the elderly.[31] In a population-based sample of men, the prevalence of SDB increased monotonically with age.[5] However, the SDB syndrome, defined as AHI ≥10 plus daytime sleepiness, hypertension, or other cardiovascular complication, followed a quadratic distribution: 1.2% of the young cohort, 4.7% of the middle aged, and 1.7% of the elderly. Thus, there is evidence that the prevalence of sleep apnea increases with age, but the cardiovascular significance of sleep apnea decreases with age.

SDB may present distinctly in populations of different ages owing to several factors, including differences in underlying risk factors for SDB (for example, relative contributions of obesity compared with ventilatory control abnormalities), or owing to differences in physiological responses to intermittent upper-airway occlusion. For example, hypertension may be mediated in part by arousal and sympathetic nervous system responses and/or intrathoracic pressure swings that result from upper-airway occlusion. The observed reduction in prevalence of snoring (potentially explained by diminished inspiratory efforts) in older populations is supportive of the latter hypothesis.[32] Another explanation for the observed differences in the relationship between AHI and systolic/diastolic hypertension between age groups may relate to potential differences in the physiological characteristics of breathing disturbances in population subgroups. For example, older subjects may have a greater proportion of central apneas, which occur in association with cardiovascular or neurological diseases. Although central apneas, as identified by the absence of effort on both respiratory inductance channels in this study, constituted only a small proportion of total breathing events, it is possible that more sensitive measures of central events may have led to a greater proportion of older subjects being classified as having central apneas. If hypertension is more strongly associated with obstructive than central apneas, then such misclassification may have contributed to age differences in the observed associations with systolic/diastolic hypertension. However, even when alternative indices of physiological stress were used as exposure measures (such as percentage of hypoxic sleep time), differences between older and younger participants in the present study were still observed. Finally, we cannot rule out that there was insufficient power to detect an association between sleep apnea and systolic/diastolic hypertension in those ≥60 year of age. However, the number of systolic/diastolic hypertensives was similar in both age groups, yet only in those aged <60 years was there an association with SDB.

Effects of Antihypertensive Treatment

It is important to consider any biases that may have been introduced by the inclusion of participants taking antihypertensive medications in the analyses. There are 3 possible effects of an antihypertensive medication on an individual categorized as having systolic/diastolic hypertension: (1) They may be rendered normotensive and reclassified as such; (2) they may have a proportionate reduction in DBP, resulting in reclassification as ISH; or (3) they may fail to reduce their BP below 140/90 mm Hg and therefore continue to be classified as having systolic/diastolic hypertension. Bias may be introduced in the first 2 scenarios, because participants with SDB and systolic/diastolic hypertension will be classified as normotensive or as having ISH, respectively. The effect in either case is to decrease the probability of observing any true associations between SDB and systolic/diastolic hypertension. The effect of such biases, however, would be present in both the younger and older cohorts. We cannot exclude the possibility that we did not see an association between SDB and systolic/diastolic hypertension in those aged ≥60 years because of such biases. However, because of the observed associations between SDB and systolic/diastolic hypertension in the younger group, and because misclassification biases would be expected to apply equally to both age groups, the present results suggest (at least) a stronger association between SDB and systolic/diastolic hypertension in those aged 40 to 59 years compared with those ≥60 years

TABLE 3. Adjusted OR for ISH and Systolic/Diastolic Hypertension as a Function of Increasing Percentage of Sleep Time With Oxygen Saturation <90%, According to Age

BP Group	Age, y	Hypoxic Sleep Time*	N	OR Adjusted for Demographics† (95% CI)		OR Fully Adjusted‡ (95% CI)	
ISH vs NT	40–59	0–0.049	1015	1.00	Reference	1.00	Reference
		0.05–0.49	520	1.34	0.95–1.89	1.16	0.80–1.70
		0.5–3.9	438	1.16	0.79–1.69	0.88	0.58–1.35
		4–11.9	140	1.69	1.03–2.76	1.29	0.75–2.24
		≥12	103	0.95	0.49–1.85	0.46	0.21–1.05
		P (trend)		0.29		0.33	
	60+	0–0.049	1071	1.00	Reference	1.00	Reference
		0.05–0.49	791	1.03	0.84–1.26	1.01	0.82–1.24
		0.5–3.9	921	0.96	0.79–1.17	0.91	0.74–1.12
		4–11.9	385	0.97	0.75–1.26	0.90	0.69–1.19
		≥12	330	0.78	0.59–1.04	0.72	0.54–0.97
		P (trend)		0.16		0.04	
S/D H vs NT	40–59	0–0.049	1036	1.00	Reference	1.00	Reference
		0.05–0.49	507	1.26	0.83–1.91	1.46	0.93–2.29
		0.5–3.9	423	1.31	0.85–2.02	1.30	0.79–2.13
		4–11.9	144	2.21	1.28–3.82	2.54	1.37–4.73
		≥12	114	2.69	1.55–4.69	2.73	1.45–5.15
		P (trend)		<0.001		0.001	
	60+	0–0.049	788	1.00	Reference	1.00	Reference
		0.05–0.49	573	0.91	0.56–1.49	0.86	0.52–1.44
		0.5–3.9	675	1.00	0.64–1.57	1.04	0.65–1.67
		4–11.9	280	0.96	0.52–1.74	1.07	0.57–2.01
		≥12	254	1.13	0.63–2.02	1.31	0.71–2.43
		P (trend)		0.74		0.37	

NT indicates normotension; S/D H, systolic/diastolic hypertension.

*Percentage of sleep time with hemoglobin oxygen saturation <90%.

†Adjusted for gender, race, age, and BP medication use.

‡Adjusted for gender, race, age, BP medication use, diabetes, BMI, waist:hip ratio, smoking, and alcohol consumption.

of age. Nonetheless, we repeated our analyses excluding participants taking antihypertensive medications; significant associations were found only between SDB and systolic/diastolic hypertension and only in those aged <60 years.

Implications for Future Research

By restratifying the age groups at age 65, the observed associations between AHI and systolic/diastolic hypertension were markedly attenuated. Thus, the present analyses suggest that studies that (1) fail to distinguish systolic/diastolic hypertension from ISH and (2) include participants aged >60 years may dilute the true association between SDB and systolic/diastolic hypertension among middle-aged individuals. For example, in a previous analysis of SHHS data, a significant association was found between hypertension and SDB, where hypertension was defined as either SBP >140 mm Hg, DBP >90 mm Hg, or use of antihypertensive medication by the participant.[1] The investigators determined the adjusted OR for hypertension for those in the highest compared with the lowest AHI grouping to be 1.37. In comparison, in the present analysis, the adjusted OR for systolic/diastolic hypertension among 40- to 59-year-olds with AHI ≥30 was 2.27, with no association observed in those >60 years of age. The stronger association observed for the 40- to 59-year-old group in the present analysis may be due to our exclusion of older subjects, in whom no association was observed, and our differentiation of systolic/diastolic hypertension and ISH. However, the fully adjusted model used in the present analysis differed from the previous one by additionally controlling for BP medication use and presence of diabetes.[1]

The large, uniformly studied, ethnically and geographically diverse cohort of men and women in the SHHS is well suited for investigating the association between SDB and hypertension across age groups, because subjects ranged from early middle age to nonagenarians. To the best of our knowledge, this is the first study to examine the relation between SDB and hypertension with a large sample of participants aged >60 years in whom hypertensive conditions are distinguished as systolic/diastolic hypertension or ISH. This is a survival cohort, however; the older group is distinguished by not having succumbed to a disease at a younger age. The comparison of the 2 age groups is thus a comparison of 2 distinct and different groups. It is not a longitudinal comparison of an aging population, and hence we cannot exclude the possibility that the reason we failed to observe any association between SDB and hypertension in the elderly was because those affected did not survive.

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