

Sleep and Sleep-disordered Breathing in Adults with Predominantly Mild Obstructive Airway Disease

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Neither the association between obstructive airways disease (OAD) and sleep apnea-hypopnea (SAH) nor the sleep consequences of each disorder alone and together have been characterized in an adult community setting. Our primary aims were (1) to determine if there is an association between OAD and SAH and (2) identify predictors of oxyhemoglobin desaturation during sleep in persons having OAD with and without SAH. Polysomnography and spirometry results from 5,954 participants in the Sleep Heart Health Study were analyzed. OAD was defined by a FEV₁/FVC value less than 70%. Assessment of SAH prevalence in OAD was performed using thresholds of respiratory disturbance index (RDI) greater than 10 and greater than 15. A total of 1,132 participants had OAD that was predominantly mild (FEV₁/FVC 63.81 ± 6.56%, mean ± SD). SAH was not more prevalent in participants with OAD than in those without OAD (22.32 versus 28.86%, with and without OAD, respectively, at RDI threshold values greater than 10; and 13.97 versus 18.63%, with and without OAD, respectively, at RDI threshold value greater than 15). In the absence of SAH, the adjusted odds ratio for sleep desaturation (> 5% total sleep time with saturation < 90%) was greater than 1.9 when FEV₁/FVC was less than 65%. Participants with both OAD and SAH had greater sleep perturbation and desaturation than those with one disorder. Generally mild OAD alone was associated with minimally altered sleep quality. We conclude that (1) there is no association between generally mild OAD and SAH; (2) exclusive of SAH and after adjusting for demographic factors and awake oxyhemoglobin saturation, an FEV₁/FVC value less than 65% is associated with increased risk of sleep desaturation; (3) desaturation is greater in persons with both OAD and SAH compared with each of these alone; and (4) individuals with generally mild OAD and without SAH in the community have minimally perturbed sleep.

Keywords: sleep; chronic obstructive pulmonary disease; sleep apnea; sleep disorders; sleep-disordered breathing

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Obstructive airway disease (OAD) has been estimated to affect 14 to 16 million individuals in the United States, causing substantial morbidity and mortality (1–4). Sleep apnea-hypopnea (SAH) is also prevalent in the community (5–10). By chance alone, some persons would be expected to have both conditions, previously termed an “overlap syndrome” (11). Chaouat and coworkers have suggested that the prevalence of OAD in patients with SAH exceeds the prevalence of OAD in the general population (12). Conversely, an unexpectedly high prevalence of SAH has also been reported in patients with OAD (13).

A putative association between OAD and SAH could be due to the role of tobacco smoking. Some, but not all, studies have suggested that tobacco use is a risk factor for both entities (14–20). In addition, OAD has been associated with nocturnal hypoxemia, poor sleep quality, and insufficient or disrupted sleep (21–25). The sleep-related physiologic disturbances in patients with OAD may be relevant to the pathogenesis of SAH. Some investigations have implied that these disturbances may be associated with abnormal ventilatory control and upper airway instability during sleep (26–31). A number of studies have suggested that the presence of both OAD and SAH leads to greater blood gas and pulmonary hemodynamic perturbations than found in individuals with OAD or SAH alone (12, 32–35), thereby increasing risk for cor pulmonale. On the basis of these studies as well as data suggesting a specific association between OAD and SAH, some authors have suggested that a diagnostic evaluation for OAD should be conducted in all SAH patients (12).

Prior studies of breathing during sleep and objectively assessed sleep quality in patients with OAD have evaluated relatively small samples, have focused on patients with severe disease, or have included individuals referred to sleep laboratories or pulmonary clinics, introducing the potential of a selection bias (21–24). The baseline data of the Sleep Heart Health Study (SHHS), which includes polysomnography (PSG) and spirometry results on a large and diverse middle-aged to elderly community population, provide a unique opportunity to examine the interrelationships between OAD, sleep, and SAH. The two primary objectives of this analysis were (1) to test the hypothesis that OAD and SAH coexist more often in a community sample than would be expected by chance alone, and (2) to identify predictors of sleep-related oxyhemoglobin desaturation in community-dwelling OAD patients with and without objective evidence of SAH. The secondary aim of this analysis was to characterize sleep quality and architecture in OAD patients in the community who do not have SAH.

METHODS

Study Participants

This investigation uses data from the SHHS, a prospective multicenter cohort study that was initiated to assess whether sleep-disordered

breathing is a risk factor for hypertension and cardiovascular disease in adults. Details regarding the design and methodology have been reported (36–38). In brief, participants were recruited from ongoing cohort studies, including the Cardiovascular Health Study (39), the Framingham Heart Study (40), the Tucson Epidemiologic Study of Obstructive Airways Disease (41), the Strong Heart Study (42), the Atherosclerosis Risk in Communities Study (43), the Health and Environment Cohort Study in Tucson, as well as three New York City cohorts undergoing evaluation for the impact of psychosocial risk factors on cardiovascular disease. Criteria for inclusion in SHHS included age of 40 years or older and having not received positive airway pressure treatment for sleep apnea, a tracheostomy, or supplemental oxygen. Oversampling of participants younger than 65 years who had a history of snoring was conducted to increase the prevalence of SAH in the study group and optimize the statistical power. Participants underwent unattended PSG at home between December 1995 and January 1998.

Polysomnography

Unattended home PSGs were performed with the Compumedics PS-2 system (Compumedics Pty. Ltd, Abbotsville, Australia). The recorded variables included the electroencephalogram (montage: C_3/A_1 and C_4/A_2), right and left electrooculograms, submental electromyogram using bipolar electrodes, nasal/oral airflow recorded by thermocouple (Protec, Woodenville, WA), rib cage and abdominal movement recorded by inductive plethysmography, oxyhemoglobin saturation (S_pO_2) by pulse oximetry (Nonin, Minneapolis, MN), and electrocardiogram using a bipolar lead. In addition, a mercury gauge recorded body position, and a light sensor recorded ambient light. Leg movements were not recorded. Standardized techniques for sensor attachment and quality assurance were used and have been previously described (36, 44). PSG data were stored on PCMCIA cards and sent to a central scoring center.

PSG Scoring and Sleep Parameters

Scoring of sleep stages followed the guidelines of Rechtschaffen and Kales (45). Arousals were identified according to criteria published by Bonnet and coworkers (46). Apnea was defined as complete or almost complete cessation of airflow (to $\leq 25\%$ of baseline) and associated with 4% desaturation or more. Hypopnea was defined as a decrease to less than 70% of baseline on either inductance plethysmography channel or thermocouple channels, for 10 seconds or longer and associated with 4% desaturation or more. The Respiratory Disturbance Index (RDI) was calculated by computing the average number of apneas plus hypopneas per hour of sleep.

The arousal index was calculated as the average number of arousals per hour of sleep. Approximately 15% of studies were identified by the scorer to have potentially unreliable arousal data due to difficulties in discerning episodic changes in electroencephalogram from fluctuations in background electroencephalogram or less often because of difficulties in reliably distinguishing specific sleep stages due to excessive electroencephalogram artifact. Therefore, analyses of arousal data were restricted to 4,670 individuals in whom the electroencephalogram data were deemed to be of sufficient quality to permit reliable identification of arousals. Sleep latency was defined as the interval between “lights-out” and the first three consecutive 30-second intervals (epochs) scored as sleep. This measure was available for 3,612 participants in whom the light meter indicated a clear transition of ambient light before sleep onset. Sleep efficiency was defined as the percent of the Total Sleep Time (TST) divided by the time from lights-out until the final morning awakening. Analyses of sleep efficiency were restricted to those individuals in whom the total sleep period was considered to have been captured during the recording (i.e., the subject awoke before termination of the recording, and no intervening periods of lost data were identified between sleep onset and final awakening).

Spirometry

Spirometry was performed either as part of the parent study protocol or specifically for SHHS in accordance with published guidelines (39, 47–51).

Questionnaire and Demographic Data

At the time of the PSG, participants completed a health questionnaire that included queries regarding underlying medical conditions (includ-

ing OAD) and relevant exposures such as smoking. The questionnaire also included the Epworth Sleepiness Scale, which was used to assess sleep propensity during normal daily activities (36, 52–54). Participants' weight was measured using a calibrated scale at the time of PSG. Race was determined by self-report. Participants' height was taken from parent study data obtained within 3 years of the sleep study and used to calculate the body mass index (BMI) (kg/m^2).

Statistical Analyses

Home PSG was performed on 6,443 SHHS participants (including data from two individuals aged 37 and 39 years). One hundred and twenty four participants (2%) with self-reported congestive heart failure were excluded from analyses. Of the remaining participants, 5,954 had complete spirometry data. OAD was defined as the ratio of the FEV_1 to FVC being less than 70% (55–57). Predicted values for the FEV_1 were calculated from the formulas of Hankinson and colleagues (58). The formula described for white individuals was applied to the “other” category of our study population (usually reflecting participants of mixed ancestry and those who were uncertain of their racial background).

Because of the variable time interval between spirometry and PSG (3.03 ± 2.4 years, mean \pm SD, before PSG), analyses were repeated with the data obtained from the 3,496 (59%) participants who had spirometry within 3 years of the PSG. Results based on the restricted population were similar to those obtained from the entire sample, and therefore analyses based on the entire sample are presented.

Additional statistical methodology is described in the online supplement. All analyses were performed using SAS for Windows Version 6.12. Data are presented as mean \pm SD.

The SHHS has been approved by the institutional review board at each participating site. Informed written consent has been obtained from all participants.

RESULTS

Characteristics of the Study Population

The overall FEV_1/FVC for the sample population was $75.5 \pm 7.9\%$ (mean \pm SD). Participants classified as having OAD had a mean FEV_1/FVC of $63.8 \pm 6.6\%$, and those without OAD had a mean FEV_1/FVC of $78.3 \pm 5.3\%$. The distribution of FEV_1/FVC ratio values across the entire study population shows that only a small number of participants ($n = 226$, 3.8%) had an FEV_1/FVC ratio less than 60% (Figure 1).

The characteristics of participants with and without spirometric evidence of OAD regardless of SAH status are shown in

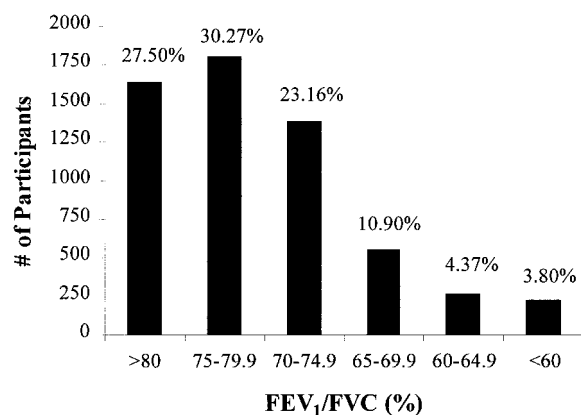


Figure 1. Distribution (by number and percentage) of the FEV_1/FVC in the study population.

TABLE 1. CHARACTERISTICS OF ENTIRE STUDY POPULATION BY SPIROMETRIC EVIDENCE OF OBSTRUCTIVE AIRWAY DISEASE

	FEV ₁ /FVC ≥ 70% (n = 4,816)	FEV ₁ /FVC < 70% (n = 1,138)
Age, yr (mean ± SD)*	62.24 ± 10.9	66.46 ± 9.79
Men, % [†]	44.95	57.21
Race, % [‡]		
White	77.63	79.0
African American	7.60	8.44
Native American	9.26	9.49
Other	5.50	3.08
BMI, (mean ± SD)*	28.78 ± 5.44	27.42 ± 4.96
Smoking status, % [§]		
Never	50.0	30.85
Former	40.34	51.95
Current	9.66	17.20

Definition of abbreviation: BMI = body mass index.

* p < 0.0001.

[†] p < 0.001.

[‡] p = 0.0089.

[§] p = 0.005, overall p value difference for the χ -square test.

TABLE 2. CHARACTERISTICS OF THE STUDY POPULATION BY SPIROMETRIC EVIDENCE OF OBSTRUCTIVE AIRWAYS DISEASE, EXCLUDING THOSE WITH RESPIRATORY DISTURBANCE INDEX GREATER THAN 15

	FEV ₁ /FVC ≥ 70% (n = 3,917)	FEV ₁ /FVC < 70% (n = 979)
Age, yr (mean ± SD)*	61.75 ± 11.0	66.32 ± 9.96
Men, %*	40.59	53.12
Race, % [†]		
White	78.12	78.96
African American	7.58	8.48
Native American	8.50	9.40
Other	5.80	3.17
BMI, (mean ± SD)*	28.11 ± 5.09	26.92 ± 4.64
Smoking status (%) [‡]		
Never	50.64	32.13
Former	39.21	49.74
Current	10.15	18.13

For definition of abbreviations see Table 1.

* p < 0.0001.

[†] p = 0.0071.

[‡] p < 0.001.

Table 1. The characteristics of those individuals with and without OAD who did not have SAH (RDI ≤ 15) are shown in Table 2.

Considering the entire study group (regardless of SAH status), participants with OAD (FEV₁/FVC < 70%) were significantly older, more likely to be male, and had a lower mean BMI compared with those without OAD (Table 1). In the absence of SAH, participants with OAD were predominantly male and had a lower BMI than those without OAD (Table 2).

Association between OAD and SAH

Participants with OAD had a significantly lower mean and median RDI than those without OAD. In addition, the percentage of participants with an RDI greater than 10 and an RDI greater than 15 was significantly lower in the group of participants with OAD compared with those without OAD (Table 3). However, after stratification by BMI quartile, RDI values were similar in the participants with and without OAD (Table 4). As expected, the RDI increased with higher BMI quartile in participants with and without OAD.

The relationship between RDI and FEV₁/FVC was also evaluated by analysis of variance after adjusting for BMI, age, sex, and race as well as smoking status. The multivariable models revealed no significant interaction between BMI and FEV₁/FVC (p = 0.40) in their relationship with RDI. However, there was a significant positive relationship between RDI and the FEV₁/

FVC ratio ($\beta = 2.05$, 95% confidence interval = 0.44 to 3.66), suggesting that a lower FEV₁/FVC ratio is independently associated with a lower RDI.

We considered the possibility that some normal, elderly individuals might be misclassified as having OAD by defining this disorder as existing when the FEV₁/FVC ratio is less than 70%. Therefore, we also examined and compared the mean and median RDI, as well as the percentage of participants with RDI greater than 10 and RDI greater than 15 employing a threshold value of FEV₁/FVC at less than 65% versus greater than or equal to 65%. The results were similar to those described previously.

The Impact of OAD on Sleepiness and Sleep Variables in Participants with and without SAH

The Epworth Sleepiness Scores (ESS) and sleep variables in participants with OAD only, SAH only, neither disorder, and both disorders are shown in Table E1 in the online supplement. In the absence of SAH, after adjusting for age, sex, height, weight, race, and smoking status, there were statistically significant but small differences between participants with and without OAD with regard to TST, but no differences were observed with regard to ESS, sleep latency, sleep efficiency, and %TST spent in rapid eye movement or in Stages 1, 2, 3/4, or the arousal index (Table E1 in the online supplement, comparing values in Columns 1 and 2).

TABLE 3. RESPIRATORY DISTURBANCE INDEX BY SPIROMETRIC EVIDENCE OF OBSTRUCTIVE AIRWAYS DISEASE

	FEV ₁ /FVC ≥ 70% (n = 4,816)	FEV ₁ /FVC < 70% (n = 1,138)
RDI		
Mean ± SD	9.13 ± 12.59	7.49 ± 11.87*
Median (interquartile range) [†]	4.51 (1.36, 11.59)	3.51 (1.35, 8.81) [‡]
Participants with RDI > 10 events/hr, %	28.86	22.32*
Participants with RDI > 15 events/hr, %	18.63	13.97 [§]

Definition of abbreviations: RDI = respiratory disturbance index.

[†] Median (interquartile range) is presented due to the skewed RDI distribution.

* p < 0.0001.

[‡] p < 0.001.

[§] p < 0.0002.

TABLE 4. MEDIAN RESPIRATORY DISTURBANCE INDEX (INTERQUARTILE RANGE) DETERMINED BY SPIROMETRIC EVIDENCE OF OBSTRUCTIVE AIRWAY DISEASE AND BODY MASS INDEX QUANTILES

BMI Quartile (Interquartile Range)	Median RDI (Range) FEV ₁ /FVC ≥ 70% (n = 4,816)	Median RDI (Range) FEV ₁ /FVC < 70% (n = 1,138)
1 (9.78–24.84)	1.94 (0.52–6.26)	1.79 (0.64–5.02)*
2 (24.85–27.76)	3.37 (1.08–8.99)	2.89 (1.04–6.64)*
3 (27.77–31.20)	5.18 (1.95–11.64)	4.7 (1.83–9.24)*
4 (31.21–58.88)	8.62 (3.75–18.17)	7.96 (3.17–17.12)*

Definition of abbreviations: BMI = body mass index; RDI = respiratory disturbance index.

* No significant difference.

To examine the impact of coexistent OAD and SAH on sleepiness and sleep architecture, we compared data from participants having both disorders with data from participants with each disorder alone. After adjusting for age, sex, height, weight, race, and smoking status, significant but small differences were observed between participants who had SAH alone and those who had both disorders (SAH + OAD). The former group had higher sleep efficiency and lower %TST in Stage 1 (see Table E1 in the online supplement). In contrast, differences between participants with both SAH and OAD and those with OAD alone were expressed more broadly across sleep variables (see Table E1 in the online supplement). After adjusting for age, sex, height, weight, race, and smoking status, participants who had both SAH and OAD had significantly higher ESS, lower TST, lower sleep efficiency, lower %TST in Stages rapid eye movement and 3/4 sleep, greater %TST in Stage 2 sleep, and higher arousal index than those with OAD alone.

Comparison of participants with single disorders (e.g., OAD only, SAH only) (see Table E1 in the online supplement) indicated that those with SAH alone had greater perceived sleepiness by ESS, lower %TST in rapid eye movement as well as in Stage 3/4 sleep, and greater %TST in Stage 2 sleep than those with OAD alone. In addition, individuals with SAH alone had a markedly higher arousal index than those with only OAD. Thus, the most notable differences in sleep variables across the four participant groups were reflected in the comparisons between groups with and without SAH, regardless of whether or not there was coexistent OAD.

To determine if sleepiness and sleep architecture are influenced by the severity of OAD in the absence of SAH, data from the 976 participants with OAD (defined by an FEV₁/FVC

TABLE 5. ADJUSTED ODDS RATIO* FOR GREATER THAN 5% TOTAL SLEEP TIME WITH OXYHEMOGLOBIN SATURATION LESS THAN 90% BY FEV₁/FVC, EXCLUDING PARTICIPANTS WITH RESPIRATORY DISTURBANCE INDEX GREATER THAN 15

FEV ₁ /FVC (%)	n	Adjusted Odds Ratio (95% Confidence Interval)
≥ 80	1,298	1.00 (Reference)
75.0–79.9	1,458	0.92 (0.60, 1.44)
70.0–74.9	1,155	1.01 (0.66, 1.56)
65.0–69.9	552	1.32 (0.81, 2.14)
60–64.9	224	1.92 (1.10, 3.34)
< 60	197	3.36 (1.98, 5.70)

* Adjusted for age, sex, height, weight, smoking, and awake oxyhemoglobin saturation.

ratio < 70%) but without SAH were analyzed by quartile of percent-predicted FEV₁. TST and sleep efficiency were slightly but statistically less in the lowest compared with highest FEV₁ quartile. No other significant differences were noted from the highest to lowest percent-predicted FEV₁ quartiles (see Table E2 in the online supplement). Similar findings were obtained from analyses of the 421 participants with OAD, defined as existing when the FEV₁/FVC ratio is less than 65% (see Table E3 in the online supplement).

The Impact of OAD on Sleep-related Oxyhemoglobin Saturation in Participants with and without Coexistent SAH

After adjusting for age, sex, height, weight, smoking status, and awake S_pO₂, the odds ratios (OR) for experiencing more than 5% of TST with S_pO₂ less than 90% were calculated across a range of FEV₁/FVC values. In the absence of SAH, the adjusted OR for nocturnal oxyhemoglobin desaturation increased at levels of FEV₁/FVC below 65% (Table 5). In participants with an FEV₁/FVC of 60 to 65% the adjusted OR for desaturation to less than 90% for more than 5% TST was 1.92 (confidence interval: 1.1, 3.34). The adjusted OR conferred by an FEV₁/FVC less than 60% was 3.36 (confidence interval: 1.98, 5.7).

To examine the degree to which OAD and SAH independently and conjointly contribute to desaturation during sleep we assessed the risk for spending more than 5% of TST with S_pO₂ less than 90% and less than 85%, respectively, in the presence of single and combined disorders. After adjusting for age, sex, height, weight, race, smoking status, and awake S_pO₂, the OR for oxyhemoglobin desaturation below threshold levels of less than 90% and less than 85% for more than 5% of TST was considerably increased in the presence of SAH, with a relatively lower OR conferred by OAD in the absence of SAH (Table 6). The OR for desaturation below 85% for greater than 5% TST was approximately 20-fold greater in participants with SAH alone compared with those who had neither disorder, and increased to approximately 30-fold in participants with both disorders (Table 6). A separate model examining the individual effects of OAD and SAH revealed no interaction between the two disorders. Thus, the observed effect of coexistent disorders on sleep desaturation was not greater than that which is expected based on the individual risks conferred by each alone.

DISCUSSION

The principal results of our study are (1) the prevalence of SAH, defined either as an RDI greater than 10 or greater than 15 is not greater in community-dwelling adults with objective evidence of predominantly mild OAD than in those without OAD; (2) in the absence of SAH, individuals with objective evidence of generally mild OAD do not perceive themselves to have greater sleep propensity during usual daily conditions than those without OAD; (3) in the absence of SAH, there are only minor differences in sleep quality and architecture between community-dwelling adults with generally mild OAD and those without OAD, and these may not be clinically significant; (4) independent of SAH and awake S_pO₂, the presence of OAD characterized by an FEV₁/FVC ratio less than 65% is associated with an increased risk of oxyhemoglobin desaturation during sleep; and (5) the proportion of participants with notable sleep desaturation as well as the degree to which sleep is perturbed is greater in the presence of both disorders but is largely related to the contribution of SAH.

Our analyses support the hypothesis that when generally mild OAD and SAH coexist, it is on the basis of aggregation by chance rather than through a pathophysiologic linkage. In fact, the prevalence of individuals with an RDI greater than 10 or

TABLE 6. ADJUSTED ODDS RATIO OF DESATURATION BASED ON OBSTRUCTIVE AIRWAY DISEASE AND SLEEP APNEA-HYPOPNEA STATUS

	SAH (+)		SAH (-)	
	OAD (+) (n = 254)	OAD (-) (n = 897)	OAD (+) (n = 884)	OAD (-) (n = 3,919)
> 5% TST spent with $S_pO_2 < 90\%$				
People, %*	42.91	47.94	11.43	6.30
Odds ratio (CI) [†]	8.06 (5.55, 11.69)	8.98 (6.86, 11.74)	1.80 (1.33, 2.45)	1.0 (Reference)
Odds ratio (CI) [§]	8.28 (5.78, 11.86)	9.26 (7.14, 12.02)	1.89 (1.40, 2.54)	
> 5% TST spent with $S_pO_2 < 85\%$				
People, %*	11.02	10.59	0.79	0.41
Odds ratio (CI) [†]	30.08 (13.21, 73.18)	15.83 (7.23, 34.67)	3.15 (1.07, 9.26)	1.0 (Reference)
Odds ratio (CI) [§]	28.73 (12.56, 65.70)	15.18 (7.17, 32.14)	2.85 (0.99, 8.18)	

Definition of abbreviations: CI = confidence interval; OAD = obstructive airways disease; SAH = sleep apnea-hypopnea; TST = total sleep time.

* Overall chi-square comparison significant at < 0.0001 level.

[†] OR (95% CI) adjusted for age, sex, height, weight, race, smoking status (former and current); comparison group for each is -OAD/-SAH.

[‡] Adjusted for awake oxyhemoglobin saturation.

[§] Unadjusted for awake oxyhemoglobin saturation.

greater than 15 was lower in adults with OAD, compared with those without OAD. Although the participants with OAD had a significantly lower BMI, this did not completely explain the difference in RDI between the groups. Across all BMI strata, the median RDI was consistently, although not significantly, lower in participants with OAD. Furthermore, after accounting for age, race, sex, resting S_pO_2 , and BMI, RDI tended to be lower as the FEV₁/FVC ratio decreased. This surprising observation requires confirmation by further studies.

OAD and SAH are both prevalent health problems with well-defined effects on health-related quality of life and cognitive function (59–65). A clinical view that OAD is inherently associated with poor sleep quality, daytime sleepiness, insomnia, and nocturnal desaturation has evolved from some investigations addressing these issues (24, 25, 66–75). The SHHS study participants represent a community population that was not identified by virtue of health care-seeking efforts and that has generally mild OAD, with a relatively small proportion of individuals having more severe disease. This large study population provides a unique opportunity to resolve existing controversies regarding the impact of mild OAD, with and without SAH, on sleep quality.

Our data suggest that after excluding individuals with SAH, community-dwelling adults with objective evidence of OAD do not perceive themselves to be sleepier than those without OAD, at least as measured by ESS. Moreover, although individuals with OAD alone had a shorter TST, there were no other significant differences in sleep architecture compared with participants with neither OAD nor SAH.

Although in general, the study population of OAD patients had predominantly mild disease severity, some individuals had more severe degrees of obstruction, with 3.8% of participants having FEV₁/FVC less than 60%. Aside from a shorter TST, there were no apparent trends regarding ESS or parameters of sleep architecture from the highest to the lowest percent-predicted FEV₁ quartiles either in participants with an FEV₁/FVC less than 70% or in those with an FEV₁/FVC less than 65%. This suggests no difference in these regards with increasing OAD severity (see Tables E2 and E3 in the online supplement). To the extent that comparisons of certain quartile pairs yielded significant differences at p values less than 0.05, it should be recalled that no correction was made for multiple comparisons, reinforcing the absence of meaningful differences. In this light, although not normal, sleep architecture was remarkably well preserved in those SHHS participants with generally mild OAD, suggesting that clinicians should not conclude that sleep-related

complaints in patients with similar degrees of OAD are attributable to the underlying OAD *per se* without exploring other diagnostic possibilities.

Identifying patients who experience sleep-related oxyhemoglobin desaturation is clinically important due to the known adverse physiologic and clinical health consequences of hypoxemia as well as the therapeutic benefits of supplemental oxygen. It is noteworthy in this regard that the threshold degree and duration of sleep-related desaturation that results in adverse health outcomes has not been established. As recently described by Gries and Brooks (76), there is considerable variability in reported normative values of sleep-related S_pO_2 during sleep. Based on evidence of reduced survival in OAD patients who experienced overnight desaturation to less than 90% for 5 minutes, reaching a nadir of less than or equal to 85% at least once (77, 78), we elected to examine the prevalence of desaturation across our study groups employing the criteria of greater than 5% of TST spent with S_pO_2 less than 90% and less than 85%. Uncertainties regarding the threshold defining unacceptable sleep-related oxyhemoglobin desaturation notwithstanding, considerable efforts have been made to predict which OAD patients experience hypoxemia during sleep (23, 79–83). Many, but not all of these, studies found that awake S_pO_2 was the best predictor of sleep-related desaturation. We observed that an FEV₁/FVC ratio less than 65% was associated with a considerably increased OR for spending more than 5% TST with S_pO_2 less than 90% even after adjusting for awake oxyhemoglobin saturation and other factors (Table 6). Thus, our observations suggest that even when SAH is not clinically suspected, overnight oximetry should be considered in OAD patients with this degree of disease.

Our data reinforce the results of previous studies indicating greater perturbations of sleep quality and architecture and increased risk of notable sleep desaturation in individuals with both SAH and even generally mild OAD (overlap syndrome) relative to each disorder alone. The abnormalities are mostly, although not exclusively, attributable to the SAH. Thus, although OAD is not a risk factor for SAH or the converse, when one of these disorders is diagnosed, clinicians should consider the possible independent presence of the other due to the risk for additional adverse physiologic impact.

Considerations and Potential Limitations of the Study

Several issues and potential limitations were considered in interpreting our data: (1) the SHHS population in this study consisted of community-dwelling individuals, none of whom were under

treatment with continuous positive airway pressure or supplemental oxygen. The relatively low percentage of subjects with severe OAD may limit the generalizability of our findings to more severely impaired individuals. Nonetheless, our data are representative of a heterogeneous middle-aged and older community population, unencumbered by potential selection bias associated with recruitment of individuals who were seeking health care in pulmonary, general medical, or sleep clinics or laboratories. Published studies have addressed sleep and breathing in patients with severe OAD, but none to our knowledge provide insight with respect to a patient population with predominantly mild OAD. (2) As previous investigators have done, we defined OAD as occurring when the FEV₁/FVC ratio is less than 70%, (48, 55–57, 84). Because a decline in this ratio may accompany normal aging, it is possible that some normal participants were misclassified as having OAD. However, our data indicate that at least in individuals with generally mild OAD but without SAH, sleep quality, architecture, and continuity are not notably impaired (see Table E2 in the online supplement). Similarly, irrespective of the value of the FEV₁/FVC ratio that was chosen as the threshold for defining OAD, in the absence of SAH, the risk of sleep-related desaturation increased as the ratio declined (Table 5). Due to the relatively small number of participants with FEV₁/FVC less than 60% without SAH (n = 197) we were unable to analyze subquartiles of the ratio below this value. Similarly, the number of individuals with more than 5% TST spent with S_pO₂ less than 85% was too small to stratify further by severity of OAD. (3) We considered the possibility that our conclusions might be influenced by survival bias. Such a bias could result in failure to detect an association between OAD and SAH due to underrepresentation of participants with both disorders in the study population on the basis of mortality. We believe, however, that the large size and heterogeneity of the study population as well as the wide age distribution make selection bias unlikely. We are not certain why there seems to be a higher than expected percentage of nonsmokers among those participants with spirometrically evident airway obstruction. Perhaps this is a consequence of misclassification due to the nature of self-reported smoking data. It is also possible that the prevalence of non-smokers with FEV₁/FVC less than 70% reflects an effect of survival bias. Individuals participating in the SHHS represent a group of individuals (survivors, if you will) from other epidemiologic studies. Thus, those participants who smoked (current and past) and had a lower FEV₁/FVC may have experienced a higher mortality, leaving those individuals with a FEV₁/FVC ratio less than 70% and never-smokers behind. (4) Sleep monitoring was performed in an unattended environment with consequent potential limitations regarding completeness of data collection and quality. However, rigorous quality control measures maximized conformity in the performance and interpretation of PSGs (37, 38). Furthermore, studies were coded regarding possible problems with signals or interpretability to identify potentially unreliable studies. Incomplete information on sleep latency and sleep efficiency occurred predominantly due to problems in interpreting data from the light meter (requiring proper calibration, positioning on the recording garment, and ambient light conditions in the participants' bedrooms that parallel "time in bed"). However, the group of subjects excluded from these subanalyses appears similar to those included. Likewise, the overall parallel findings for sleep stage differences (available for more subjects) with differences in sleep efficiency did not suggest a bias in representation within this subsample. (5) We did not analyze our data with respect to medications. Indeed, OAD patients may receive medications that could alter sleep quality and architecture. In this light, however, our observation of minimal differences in sleep quality and architecture

between individuals with and without chronic obstructive pulmonary disease (in the absence of SAH) as well as across quartiles of %predicted FEV₁ is even more interesting. (6) Although there is no consensus regarding normative data, on initial inspection we noted that the arousal index in our study population, even in the absence of SAH and OAD, seemed relatively high. Whether this reflects our polysomnographic monitoring or scoring technique, inclusion of an elderly population, or other unaccounted factors is not clear. Considerable care was exercised to analyze only the arousal data that were based on reliable scoring (36–38). It should also be noted that our analyses did not identify and exclude participants on the basis of snoring, periodic limb movement disorder, psychiatric/neurologic diagnoses, medication, or caffeine consumption before PSG. It is reassuring, however, that the arousal frequency in our data set is similar to that observed by others in an unselected community population undergoing a first night of in-laboratory PSG (85) and in normal individuals after an acclimatization night (86). In addition, the arousal index in SHHS is similar to that which would be observed by combining the data reported by Boselli and colleagues in healthy, middle-aged (arousal index: 17.8 ± 2) and elderly (27.1 ± 3.3) individuals without SAH, medical or psychological disorders, or periodic limb movement disorder (87).

In conclusion, our data indicate that the associations between generally mild OAD and SAH occurs by chance and not by pathophysiologic linkage. The risk of oxyhemoglobin desaturation for more than 5% of sleep time in patients with coexistent OAD and SAH is equal to the combined risk from each disorder alone. We also observed that sleep is only marginally perturbed in patients with milder OAD without SAH. Consequently, attribution of sleep-related symptoms to underlying generally mild OAD without considering the possibility of other etiologies is not warranted.

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