CHEST

Original Research

SLEEP MEDICINE

Obstructive Sleep Apnea Is Common in Idiopathic Pulmonary Fibrosis

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Background: **From 1984 to 2006, studies of sleep in patients with interstitial lung disease revealed disturbed sleep, frequent nocturnal desaturations, nocturnal cough, and obstructive sleep apnea (OSA). Our goal was to analyze OSA in an outpatient population of stable patients with idiopathic pulmonary fibrosis (IPF).**

Methods: **Patients with IPF who had been followed up in the Vanderbilt Pulmonary Clinic were asked to participate. All patients were given a diagnosis of IPF by the 2000 American Thoracic Society consensus statement criteria. Subjects completed an Epworth sleepiness scale (ESS) questionnaire and a sleep apnea scale of sleep disorders questionnaire (SA-SDQ) before undergoing nocturnal polysomnography (NPSG). OSA was defined as an apnea-hypopnea index (AHI) of > 5 events per hour.**

Results: **Fifty subjects enrolled and completed a NPSG. The mean age was 64.9 years, and the mean BMI was 32.3. OSA was diagnosed in 88% of subjects. Ten subjects (20%) had mild OSA (AHI, 5 to 15 events per hour), and 34 subjects (68%) had moderate-to-severe OSA (AHI, > 15 events per hour). Only 6 subjects (12%) had a normal AHI. One patient was asymptomatic as determined by ESS and SA-SDQ, but had an AHI of 24 events per hour. The sensitivity of the ESS was 75% with a specificity of 15%, whereas the SA-SDQ had a sensitivity of 88% with a specificity of 50%. BMI did not correlate strongly with AHI ($r = 0.30$; $p = 0.05$).**

Conclusions: **OSA is prevalent in patients with IPF and may be underrecognized by primary care providers and specialists. Neither ESS nor SA-SDQ alone or in combination was a strong screening tool. Given the high prevalence found in our sample, formal sleep evaluation and polysomnography should be considered in patients with IPF.** ***(CHEST 2009; 136:772–778)***

Abbreviations: AHI = apnea-hypopnea index; ANOVA = analysis of variance; CI = confidence interval; CPAP = continuous positive airway pressure; DLCO = diffusing capacity of the lung for carbon monoxide; ESS = Epworth sleepiness scale; GERD = gastroesophageal reflux disease; ILD = interstitial lung disease; IPF = idiopathic pulmonary fibrosis; MP = Mallampati; NPSG = nocturnal polysomnography; OSA = obstructive sleep apnea; PFT = pulmonary function test; REM = rapid eye movement; SA-SDQ = sleep apnea scale of sleep disorders questionnaire

Obstructive sleep apnea (OSA) is estimated to occur in approximately 20% of older adults.[1] The prevalence of OSA appears to increase with age and plateau around the age of 65 years; although, the reported prevalence rates in the elderly vary widely.[2] Since the first descriptions of OSA in the 1960s were obtained by using nocturnal polysomnography (NPSG), much has been learned about OSA and its need for treatment. The complications of OSA include hypertension, increased insulin resistance, pulmonary arterial hypertension, increased inflammatory cytokines, and exacerbated gastroesophageal reflux disease (GERD).[3–5] OSA is prevalent in patients with chronic lung diseases such as COPD in the overlap syndrome.[6]

Similar to COPD, idiopathic pulmonary fibrosis (IPF) is a chronic lung disease that is associated with oxygen desaturations and pulmonary arterial hypertension. IPF is a restrictive fibrotic lung disease of unknown etiology that is associated with hypoxemia progressing to respiratory failure and death. GERD, a complication of OSA, has been linked to IPF.[7] No effective therapy for IPF is available.[8] The few studies describing sleep in patients with interstitial

lung disease (ILD) include small numbers of patients and are primarily descriptive.

No studies that we are aware of have adequately described the prevalence of OSA in a large population of patients with IPF. Our goal was to analyze OSA in an outpatient population of clinically stable patients with IPF. We hypothesized that OSA, which was defined as an apnea-hypopnea index (AHI) of > 5 events per hour, would be highly prevalent in patients with IPF.

Materials and Methods

Subjects

This study was approved by the Vanderbilt Institutional Review Board. Sixty-eight subjects visiting the Vanderbilt Pulmonary Clinic for the follow-up of IPF between August 2006 and February 2008 who met study criteria were asked to participate. The study criteria included the following: age > 18 years; ability to provide informed consent; stable dyspnea; and a confirmed diagnosis of IPF by the American Thoracic Society 2000 consensus statement criteria.[8] To include an unbiased representative sample of our clinic population, patients with prior diagnoses of OSA were not excluded. Fifty-nine subjects agreed to participate and voluntarily signed consent forms, with seven subjects withdrawing consent prior to undergoing overnight NPSG. Three of these seven subjects had been previously given a diagnosis of OSA or were subsequently given a diagnosis locally of NPSG. Two of the 52 subjects could not participate due to transportation difficulties. Therefore, a total of 50 NPSGs were completed.

Subjects who were not previously given a diagnosis of OSA were asked to complete the Epworth sleepiness scale (ESS) questionnaire and the sleep apnea scale of sleep disorders questionnaire (SA-SDQ). Both questionnaires have been validated, and are commonly used tools for measuring daytime sleepiness and assessing the risk for sleep apnea.[9–14] Any subject with excessive daytime sleepiness shown on the ESS or increased risk for OSA shown on the SA-SDQ was considered to be at risk for sleep-disordered breathing.[9,10] These subjects were referred to a sleep specialist prior to completing a NPSG at the Vanderbilt Sleep Disorders Center. Those patients without positive scores on the sleep questionnaires were considered not to be at risk for sleep-disordered breathing. These patients completed a NPSG at the Vanderbilt Sleep Research Center located in the Vanderbilt General Clinical Research Center. Identical NPSG protocols were used at both centers. Any subjects who received a diagnosis of OSA prior to signing a consent form and had completed a NPSG locally repeated a NPSG within the Sleep Research Core (without continuous positive airway pressure [CPAP] therapy). All patients had their upper airway assessed by the IPF physician, sleep physician, or IPF nurse practitioner according to the Mallampati (MP) classification for difficult intubation. All providers were trained using this scoring system prior to the start of the study.[15]

Overnight Polysomnography

Overnight NPSG was performed using digital systems (Nihon-Kohden; Foothill Ranch, CA), and included standard sleep channels of EEG (C3, C4, O1, and O2), two channels of electrooculogram, two channels of electromyogram, thermistor and nasal pressure transducer monitoring to measure airflow, thoracic and abdominal wall motion to measure respiratory effort, oximetry to measure oxygen desaturations, ECG, a microphone for snoring, and anterior tibialis monitoring.

An apnea was defined as a cessation of airflow ($\geq 90\%$ compared with baseline) for ≥ 10 s. An hypopnea was defined as a clear amplitude reduction of 50 to 90% in either the thermistor or the nasal pressure transducer channel during sleep that was associated with either an oxygen desaturation of $\geq 3\%$ and/or an EEG arousal.[16,17] OSA was defined as an AHI of > 5 events per hour.[18] Patients who were receiving home oxygen therapy stopped receiving oxygen at the start of their study and were titrated per the standard of care oxygen titration protocol that is used in our laboratory. Patients were titrated up on oxygen for persistent and not transient desaturations.

All NPSGs were scored by one of eight sleep technologists who were either registered polysomnography technicians or were board eligible. Six of these eight sleep technologists are registered polysomnography technicians. Reliability checks among the sleep technologists are performed routinely to ensure consistency in scoring. All NPSGs were given a second review of scoring by one of the authors.

Pulmonary Function Testing

Pulmonary function test (PFT) data were captured for all subjects who had completed this testing at the Vanderbilt Pulmonary Clinic prior to the diagnosis of OSA. Measurements were performed according to current guidelines, and included spirometry (FEV_1 and FVC), total lung capacity by body box plethysmography, and diffusing capacity of the lung for carbon monoxide (Dlco).[19]

Statistical Analysis

Categorical variables (*eg*, gender, race, and snoring assessment) are reported as percentages and were analyzed by using Fisher exact test. Means and SDs were calculated for the normally distributed continuous variables, while medians and intraquartile ranges are reported for the variables without normal distributions. Continuous outcome variables, such as AHI, were analyzed with a one-way analysis of variance (ANOVA). Correlations were analyzed by using Spearman testing. All p values were two tailed, and values ≤ 0.05 were considered statistically significant.

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Table 1—*Demographics: Personal Characteristics*

Characteristics	No OSA (AHI 0–5 events/h) [n = 6]	Mild OSA (AHI 5.1–15 events/h) [n = 10]	Moderate-to-Severe OSA (AHI > 15 events/h) [n = 34]	p Value*
Age, yr	69 ± 8.1	64 ± 8.9	64 ± 8.4	0.47
Male gender, %	50	60	73	0.44
BMI	26 ± 2	33 ± 6.7	33 ± 6.4	0.05
Mean weight, lb	175 ± 32.2	207 ± 51.2	218 ± 41	0.09
Neck circumference, inches	15 ± 1.9	17 ± 1.1	17 ± 1.7	0.1
MP score, %				0.04
I	25	12	0	
II–IV	75	87	100	
Medical history, %				
GERD	50	80	68	0.46
Diabetes mellitus, type II	0	20	21	0.47
Hypertensive heart disease	66	70	65	0.95
Systolic or diastolic dysfunction	16	30	21	.078
Coronary artery disease	16	30	18	0.68
Hypothyroidism	33	20	18	0.68
Alcohol use, %	17	20	38	0.38
Medications, %				
Prescription sleeping pills	67	20	9	0.003
Prescription narcotics	50	40	12	0.04
IPF medications				
Prednisone	0	20	24	0.41
Other†	67	20	18	0.05

Values are given as the mean ± SD or %, unless otherwise indicated.
*Comparison among all groups in the ANOVA.
†Includes interferon-γ 1b, pirfenidone, and imuran.

Results

Forty-four of 50 subjects (88%) had OSA as defined by an AHI of > 5 events per hour. Ten subjects (20%) had mild OSA (AHI, 5 to 15 events per hour), and 34 subjects (68%) had moderate-to-severe OSA (AHI > 15 events per hour). The subject demographic data in relation to the AHI are shown in Table 1. Age was well matched across AHI categories. The BMI and neck circumference increased with an increase in AHI. The BMI only weakly correlated (BMI: $r = 0.30$; $p = 0.05$; Neck circumference: $r = 0.23$; $p = 0.1$). OSA was noted in patients with normal BMIs[20–25] (5 of 44 patients; 11%). Forty-one of 50 patients had MP scores reported. Only one subject with OSA had an MP score of < 2. Medical diseases associated with OSA were common, although not significantly different across groups.

Thirty of 44 subjects (68%) with sleep apnea (AHI > 5 events per hour) did not require home oxygen therapy but had documented nocturnal desaturations consistent with sleep-disordered breathing (Table 2). The mean minimum oxygen saturation for patients not receiving home oxygen was 79%, whereas their mean baseline awake oxygen saturation was 94% prior to the start of the NPSG.

Pulmonary Physiology

Spirometry, lung volumes, and DLCO did not inversely correlate with the AHI or severity of sleep-disordered breathing (Table 2). In the subgroup of patients undergoing echocardiography (n = 12), no significant difference in the calculated systolic pulmonary artery pressure was found in subjects with and without OSA.[20]

Polysomnography

Total sleep time, sleep latency, and sleep efficiency were well matched across the AHI groups (Table 3). A predominance of stage 2 sleep was seen in all groups. All groups noted reduced sleep efficiency, slow-wave sleep, and rapid eye movement (REM) sleep. No significant difference in the amount of REM sleep was noted between subjects with OSA and without OSA. Increased arousals were noted as the AHI rose ($p < 0.001$).

Hypopneas were more commonly noted than apneas. The mean AHI for subjects without OSA was 1.6. The mean AHI for subjects with mild OSA was 10.7, whereas the mean AHI for moderate-to-severe sleep apnea was 39, highlighting a predominance of severe OSA in this latter group. More sleep-disordered breathing events (apneas and hypopneas) were noted during

Table 2—*Demographics: Physiologic Characteristics*

Physiologic Characteristics	No OSA (AHI 0–5 events/h) [n = 6]	Mild OSA (AHI 5.1–15 events/h) [n = 10]	Moderate-to-Severe OSA (AHI > 15 events/h) [n = 34]	p Value*
Supplemental oxygen therapy received at home, %	50	30	29	0.6
PFT results				
FVC, L	2.2 ± 0.9	2.2 ± 0.5	3.0 ± 0.8	0.01
FVC %	58 ± 10.5	63 ± 18.4	73 ± 13.7	0.03
FEV_1, L	1.77 ± 0.7	1.8 ± 0.4	2.4 ± 0.6	0.006
TLC, L	3.5 ± 1.9 (n = 2)	3.3 ± 0.6 (n = 10)	4.4 ± 1.3 (n = 30)	0.07
DLCO, mL/mm Hg/min	12.2 ± 4.7	10.4 ± 2.8	14.5 ± 3.8	0.03
DLCO, % predicted	43 ± 13.8	38 ± 12.8	48 ± 11.1	0.11
Echocardiogram				
Calculated SPAP, mm Hg	34 (n = 1)	33 ± 6.4 (n = 4)	38 ± 9.5 (n = 7)	0.72

Values given as mean ± SD, unless otherwise indicated. FVC% = percent predicted FVC; SPAP = systolic pulmonary artery pressure; TLC = total lung capacity.
*Comparison among all groups in the ANOVA.

REM sleep in the groups with lower AHI. Events during REM sleep and non-REM sleep were more balanced in subjects with moderate-to-severe OSA.

Baseline awake oxygen saturations at the start of the NPSG were similar across groups. Sixteen of the 50 patients required oxygen at the time of the study. All patients began their study breathing room air. Oxygen was added (per the standard of care protocol for our laboratory) for persistent, sustained hypoxemia and not for transient dips in oxygenation as would be seen with OSA. Individuals who received oxygen during their sleep study and had sleep-disordered breathing still continued to show transient dips and hypopneas that were consistent with OSA, although their desaturations may have been blunted by the additional oxygen. The mean minimum oxygen saturation during sleep worsened with the rise in AHI.

Sleep Questionnaires

ESS scores of ≥ 10 are believed to be consistent with excessive daytime sleepiness (Table 4).[9]

Table 3—*Sleep Architecture*

Variables	No OSA (AHI 0–5 events/h) [n = 6]	Mild OSA (AHI 5.1–15 events/h) [n = 10]	Moderate-to-Severe OSA (AHI > 15 events/h) [n = 34]	p Value*
Polysomnography				
Latency to sleep, min	22.5 ± 13.7	20.7 ± 25.2	21.8 ± 26.3	0.99
Sleep efficiency, %	77.2 ± 12.8	75.9 ± 13.7	69.8 ± 18.7	0.45
Stage 1 sleep, %	10.4 ± 5.1	16.2 ± 7.7	22.3 ± 11.2	0.02
Stage 2 sleep, %	70.1 ± 5.1	62.9 ± 18.2	63.9 ± 11.7	0.54
Stage 3/4 sleep, %	3.2 ± 5	1.5 ± 3.1	0.2 ± 0.4	0.007
Stage REM sleep, %	16.5 ± 9.6	14.2 ± 6.6	12.6 ± 7.6	0.47
Arousal index	6.4 ± 5	20.2 ± 14.7	38.1 ± 20.2	< 0.001
Periodic Limb Movement index	22.4 ± 34.8	4.0 ± 6.3	12.5 ± 20	0.22
Respiratory analysis				
Total AHI	1.6 ± 1.6	10.7 ± 2.1	39.4 ± 25.9	< 0.001
AHI non-REM	0.9 ± 1.5	8.9 ± 4.1	37.5 ± 26.6	< 0.001
AHI REM	4.4 ± 5.8	23.6 ± 14.1	26.1 ± 32.5	0.04
Hypopnea index	1.5 ± 1.5	10.0 ± 2.0	26.6 ± 19.2	0.001
Hypopneas with arousals, % of total	19.4 ± 21.9	52.2 ± 30.2	54.8 ± 21.6	0.012
Hypopneas				
Hypopneas with desaturations, % of total hypopneas	80.6 ± 21.9	47.8 ± 30.2	45.2 ± 21.5	0.012
Apnea index	0.1 ± 0.2	0.8 ± 1.1	7.1 ± 11.4	0.09
Minimum saturation, %	87.3 ± 6.9	81.6 ± 6.8	78.7 ± 7.3	0.03
Saturation at start of NPSG, %	92.8 ± 6.2	94.2 ± 1.9	94.9 ± 2.2	0.29
Desaturation index	4.6 ± 5.1	9.3 ± 5.3	35 ± 19.4	< 0.001

Values given as the mean ± SD, unless otherwise indicated.
*Comparison among all groups in the ANOVA.

Table 4—*Sleep Questionnaires*

Questionnaires	No OSA (AHI 0–5 events/h) [n = 6]	Mild OSA (AHI 5.1–15 events/h) [n = 10]	Moderate-to-Severe OSA (AHI > 15 events/h) [n = 34]	p Value*
ESS				
Mean	8.2 ± 5.3 (n = 6)	5.8 ± 1.7 (n = 4)	8.3 ± 5.3 (n = 25)	0.64
No. with ESS ≥ 10, %	33	0	28	0.45
SA-SDQ				
Mean	27.8 ± 3.7 (n = 6)	29.7 ± 4.2 (n = 4)	37.1 ± 8.4 (n = 21)	0.03
Men scoring ≥ 29, %	67	100	87	0.56
Women scoring ≥ 26, %	33	100	83	0.18

Values given as mean ± SD unless otherwise indicated. A score of ≥ 10 on the ESS is consistent with excessive daytime sleepiness, and is a risk factor for sleep-disordered breathing. Scores of ≥ 29 for men and scores ≥ 26 for women on the SA-SDQ are consistent with increased risk for sleep-disordered breathing.

*Comparison among all groups in the ANOVA.

SA-SDQ scores of > 29 for men and > 26 for women are believed to represent a positive risk for sleep-disordered breathing.[10] Of the 50 patients included in this study, 35 completed the ESS and/or SA-SDQ prior to undergoing the NSPG. Thirty-one patients scored as a positive risk for sleep apnea, whereas four patients scored as no risk. Of the 31 patients who scored as a positive risk for OSA by the SA-SDQ, 26 were found to have OSA by NPSG (84%). Three of the four patients (75%) who scored as having no risk for OSA on their questionnaires had OSA as determined by their NPSG findings. The ESS score did not correlate with the severity of OSA ($r = 0.14$; $p = 0.43$). The mean ESS scores for patients given a diagnosis of OSA did not denote significant excessive daytime sleepiness. One patient was asymptomatic by ESS and SA-SDQ but had an AHI of 24. The SA-SDQ correlated better with the severity of OSA ($r = 0.45$; $p = 0.01$) [Table 4]. The positive predictive value and the negative predictive value for the ESS were 21% (95% confidence interval [CI], 10 to 38%) and 67% (95% CI, 30 to 90%), respectively. The positive predictive value of the SA-SDQ was 88% (95% CI, 70 to 96%) with a negative predictive value of 50% (95% CI, 19 to 81%). Only 10 of the 44 patients with OSA (22%) were given a diagnosis prior to referral to our facility, either by their primary care physician or pulmonologist.

Discussion

We believe that our study represents the first prospective study of OSA in patients who were given a diagnosis of IPF according to the American Thoracic Society 2000 consensus statement criteria.[8] The vast majority of patients (88%) had OSA as defined by an AHI of > 5 events per hour. Sleep-disordered breathing in this population predominantly manifested as hypopneas rather than apneas. Neither oxygen saturation nor oxygen use predicted AHI or the severity of desaturation. FVC, lung volumes, and DLCO did not inversely correlate with the AHI as expected. Daytime sleepiness as measured by the ESS did not correlate with the severity of OSA. The SA-SDQ better predicted OSA in this population. Neither test had a high enough negative predictive value to support its use as a screening test in this population.

Few articles have been published on sleep in IPF patients. Small studies[21–26] of sleep in ILD patients have revealed nocturnal desaturation, tachypnea, and disrupted sleep architecture. In 2001, Clark et al[27] studied 48 patients with IPF via overnight oximetry and noted that nocturnal hypoxia was common and affected quality of life. The actual incidence of sleep apnea in patients with ILD has varied depending on the study. Aydogdu et al[28] studied 37 patients with ILD by using overnight polysomnography and found disrupted sleep architecture and nocturnal hypoxia in all with 24 patients meeting the definition of OSA. Hypopneas were predominantly noted. No difference was found between BMIs in patients with and without OSA.[28] Mermigkis et al[29] found a similarly high percentage of OSA in 18 hospitalized patients with IPF. AHI positively correlated with BMI and negatively correlated with FEV_1 and FVC. A recent study by Krishnan et al[23] evaluated 41 patients with IPF assessing sleep quality by the Pittsburgh Sleep Quality Index and the ESS. They found that patients with IPF noted poor sleep quality and daytime sleepiness. Poor sleep quality did not correlate with BMI. A small study[30] of sleep quality in 15 patients with IPF found 67% had an AHI > 5 (D. Bouros; personal communication; April 2009). Our study expands on this knowledge by investigating these issues in a large study of well-defined patients with IPF.

Prior studies have demonstrated an interdependence between upper airway size in OSA and lung volumes. Snorers with OSA were found to have a more dramatic fall in measured pharyngeal cross-sectional area as lung volume decreased.[31] Sériès et al[32] in 1988 placed a subject with OSA in a poncho-type respirator after 8 months of oral medroxyprogesterone therapy and applied negative extrathoracic pressure. By increasing the functional residual capacity (0.5 L), they found that there was a significant reduction in the AHI and an improvement in sleep architecture. This was further illustrated in 2005 in 17 subjects with severe OSA (mean AHI, 42.6 events per hour) who were placed in a negative-pressure chamber with neck and upper airway outside of the rigid apparatus. Lung volume was manipulated by using negative extrathoracic pressure while upper airway airflow limitation was monitored. Increases in lung volumes resulted in decreased CPAP levels, which were required to overcome upper airway flow limitation. As lung volume increased, the AHI and the 3% desaturation index improved.[33] A study[34] in 20 rabbits similarly demonstrated that increases in lung volume resulted in caudal tracheal traction that mediated a decrease in upper airway collapsibility due to a decrease in upper airway extraluminal tissue pressure. Our study in a stable outpatient population of patients with IPF did not demonstrate an inverse relationship between FVC and AHI. The lack of inverse correlation between the PFTs and the severity of sleep apnea may be explained by the use of PFTs performed with the patient in the upright or standing position. FVCs obtained with the patient in the supine position may be more accurate at predicting sleep lung volumes and may better display interdependence between the upper airway and lung volumes during sleep.

Comorbidities, such as GERD, were common. GERD has been closely linked with IPF and OSA. Prior studies[35] have shown improvement in patients with GERD by treating the OSA with CPAP. Treating OSA with CPAP may simultaneously treat GERD in the patient with IPF, which may play a role in disease progression.

Our study is limited by its size and the lack of a standard definition for hypopneas used in research or clinical practice. The definition of hypopnea can vary in flow limitation, percent desaturation, and whether concurrent arousals are recognized. Similar to Mermigkis et al,[29] we utilized the alternate American Academy of Sleep Medicine diagnosis for the definition of hypopneas. This definition, by having a 3% desaturation instead of a 4% desaturation, may allow for the scoring of more hypopneas and elevate the AHI. Additional scoring by using the different definitions of hypopneas or ultimately standardizing a definition of hypopnea for research and clinical care will help us to better understand the true prevalence of OSA in patients with IPF. Hypopneas may be scored more frequently in patients with underlying parenchymal lung disease because their underlying ventilation perfusion abnormalities make them more prone to desaturate. Additional ventilation-perfusion mismatching in patients who already sit on the steep slope of the oxygen dissociation curve may result from the upper airway flow limitation of OSA coupled with reduced tidal volumes during sleep. However, it is important to note that not just desaturation alone, but the finding of concurrent flow limitation due to upper airway obstruction is necessary to identify and score a hypopnea.

Although additional studies will be necessary to further understand the prevalence of sleep-disordered breathing in IPF patients and its consequences, this study identifies OSA as a highly prevalent comorbidity in this disease and suggests that all patients with IPF be screened for OSA with NPSG. In a disease with no available therapy, treating OSA via nocturnal ventilation may improve breathing and impact quality of life for patients with few therapeutic options.

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Author contributions: Drs. Lancaster, Rice, Loyd, Milstone, Collard, and Malow, Ms. Mason, and Mr. Parnell meet the criteria of authorship as a group, as outlined by *CHEST* Authorship and Contributorship requirements. As the principal investigator, Dr. Lancaster had complete access to all the data, and takes full responsibility for the reliability of the data and the accuracy of the data analysis. Ms. Mason, the corresponding author, bears full responsibility for the absolute integrity of the abstract, article, and tables.

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References

1 Hiestand DM, Britz P, Goldman M, et al. Prevalence of symptoms and risk of sleep apnea in the US population: results from the National Sleep Foundation Sleep in America 2005 Poll. Chest 2006; 130:780–786

2 Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002; 165:1217–1239

3 Parish JM, Somers VK. Obstructive sleep apnea and cardiovascular disease. Mayo Clin Proc 2004; 79:1036–1046

4 Vgontzas AN, Bixler EO, Chrousos GP. Sleep apnea is a manifestation of the metabolic syndrome. Sleep Med Rev 2005; 9:211–224

5 Ing NJ, Ngu MC, Breslin AB. Obstructive sleep apnea and gastroesophageal reflux. Am J Med 2000; 108:S120–S125
6 Weitzenblum E, Chaouat A, Kessler R, et al. Overlap syndrome: obstructive sleep apnea in patients with chronic obstructive pulmonary disease. Proc Am Thorac Soc 2008; 5:237–241
7 Raghu G. The role of gastroesophageal reflux in idiopathic pulmonary fibrosis. Am J Med 2003; 115:60–64
8 American Thoracic Society. Idiopathic pulmonary fibrosis: diagnosis and treatment. Am J Respir Crit Care Med 2000; 161:646–664
9 Johns M. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991; 14:540–545
10 Douglass AB, Bornstein R, Nino-Murcia G, et al. The Sleep Disorders Questionnaire: creation and multivariate structure of SDQ. Sleep 1994; 17:160–167
11 Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep 1992; 15:376–381
12 Johns MW. Daytime sleepiness, snoring, and obstructive sleep apnea: the Epworth Sleepiness Scale. Chest 1993; 103:30–36
13 Johns MW. Sleepiness in different situations measured by the Epworth Sleepiness Scale. Sleep 1994; 17:703–710
14 Weatherwax KJ, Lin X, Marzec ML, et al. Obstructive sleep apnea in epilepsy patients: the Sleep Apnea scale of the Sleep Disorders Questionnaire (SA-SDQ) is a useful screening instrument for obstructive sleep apnea in a disease-specific population. Sleep Med 2003; 4:517–521
15 Mallampati SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: a prospective study. Can Anaesth Soc J 1985; 32:429–434
16 Iber C, Ancoli-Israel S, Stuart Quan M. The American Academy of Sleep Medicine manual for the scoring of sleep and associated events: rules, terminology, and technical specifications. Westchester, IL: American Academy of Sleep Medicine, 2007
17 Flemons WW, Buysse D, Redline S, et al. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research: the report of an American Academy of Sleep Medicine Task Force. Sleep 1999; 22:667–689
18 Strollo PJ, Rogers RM. Obstructive sleep apnea. N Engl J Med 1996; 334:99–104
19 Miller MR, Crapo R, Hankinson J, et al. General considerations for lung function testing. Eur Respir J 2005; 26:153
20 Abbas AE, Fortuin DF, Schiller NB, et al. Echocardiographic determination of mean pulmonary artery pressure. Am J Cardiol 2003; 92:1373–1376
21 Bye PTP, Issa F, Berthon-Jones M, et al. Studies of oxygenation during sleep in patients with interstitial lung disease. Am Rev Respir Dis 1984; 129:27–32
22 Hira HS, Sharma RK. Study of oxygen saturation, breathing pattern and arrhythmias in patients of interstitial lung disease during sleep. Indian J Chest Dis Allied Sci 1997; 39:157–162
23 Krishnan V, McCormack M, Mathai SC, et al. Sleep quality and health-related quality of life in idiopathic pulmonary fibrosis. Chest 2008; 134:693–698
24 Perez-Padilla R, West P, Lertzman M, et al. Breathing during sleep in patients with interstitial lung disease. Am Rev Respir Dis 1985; 132:224–229
25 McNicholas WT, Coffey M, Fitzgerald MX. Ventilation and gas exchange during sleep in patients with interstitial lung disease. Thorax 1986; 41:777–782
26 Midgren B, Hansson L, Eriksson L, et al. Oxygen desaturation during sleep and exercise in patients with interstitial lung disease. Thorax 1987; 42:353–356
27 Clark M, Cooper B, Singh S, et al. A survey of nocturnal hypoxaemia and health related quality of life in patients with cryptogenic fibrosing alveolitis. Thorax 2001; 56:482–486
28 Aydogdu M, Ciftci B, Firat GS, et al. Assessment of sleep with polysomnography in patients with interstitial lung disease. Tuberk Toraks 2006; 54:213–221
29 Mermigkis C, Chapman J, Golish J, et al. Sleep-related breathing disorders in patients with idiopathic pulmonary fibrosis. Lung 2007; 185:173–178
30 Mermigkis C, Stagaki E, Amfilochiou A, et al. Sleep quality and associated daytime consequences in patients with idiopathic pulmonary fibrosis. Med Princ Pract 2009; 18:10–15
31 Bradley TD, Brown IG, Grossman RF, et al. Pharyngeal size in snorers, nonsnorers, and patients with obstructive sleep apnea. N Engl J Med 1986; 315:1327–1331
32 Sériès F, Cormier Y, Lampron N, et al. Increasing the functional residual capacity may reverse obstructive sleep apnea. Sleep 1988; 11:349–353
33 Heinzer RC, Stanchina ML, Malhotra A, et al. Lung volume and continuous positive airway pressure requirements in obstructive sleep apnea. Am J Respir Crit Care Med 2005; 172:114–117
34 Kairaitis K, Byth K, Parikh R, et al. Tracheal traction effects on upper airway patency in rabbits: the role of tissue pressure. Sleep 2007; 30:179–186
35 Shepherd KL, Holloway RH, Hillman DR, et al. The impact of continuous positive airway pressure on the lower esophageal sphincter. Am J Physiol Gastrointest Liver Physiol 2007; 292:G1200–G1205