Clinical Significance of Sleep Desaturation in Hypoxemic Chronic Obstructive Pulmonary Disease: Studies in 130 Patients

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We studied 130 patients with hypoxemic chronic obstructive lung disease to determine if nocturnal desaturation aggravates hypoxia-induced complications. All had tests of neuropsychological and physiological function known to be affected by chronic hypoxia. Of the 130 patients, 25 had complete polysomnography and 105 had their sleep judged visually and arterial oxygen saturation recorded continuously. Severe and mild desaturation groups were defined relative to the mean for both mean and maximal sleep desaturation, and the severity of waking complications were compared. No significant differences were noted between patients with mild and severe mean desaturation or maximal desaturation for hematocrit, neuropsychological tests, maximal exercise tolerance, or measures of quality of life. Waking pulmonary artery pressure did not differ significantly between patients with mild and severe mean desaturation or maximal desaturation, except in 20 patients with the most severe mean desaturation during sleep. We conclude that nocturnal desaturation does not aggravate hypoxia-induced complications in most patients who are chronically hypoxemic from chronic obstructive pulmonary disease. (Henry Ford Hosp Med J 1988;36:16-23)

Arterial oxygen desaturation occurs frequently during sleep in patients with chronic obstructive pulmonary disease (COPD) (1-7). In some patients, episodes of hypoxemia during sleep are prolonged and severe. Causes of hypoxemia include hypoventilation (2,6) and, rarely, episodes of upper airway obstruction and central apnea (5,7). Frequently, hypoxemia may occur without any abnormalities in breathing patterns, suggesting alterations in the distribution of ventilation perfusion ratios (1,6).

Although desaturation has been well described and appears to be common, its clinical significance is unclear. Episodes of desaturation are accompanied by transient elevations in pulmonary artery pressure (8,9), but sustained pulmonary hypertension and cor pulmonale have not been causally linked to episodes of sleep desaturation. Furthermore, the effect of nocturnal desaturation on other complications of hypoxia, such as polycythemia, neuropsychological impairment, and exercise intolerance, has not been evaluated. To examine the role of sleep desaturation on hypoxemia-induced complications, we monitored continuously arterial oxygen saturation (SaO_2) during sleep in a well-defined population of patients with severe hypoxemic COPD. Our purpose was to determine if patients with severe nocturnal desaturation had more severe complications of chronic hypoxemia than those with less severe desaturation and whether routine clinical and laboratory features might offer clues to the presence of severe sleep desaturation.

Methods

Patients

From the 203 hypoxemic patients enrolled in a multicenter nocturnal oxygen therapy trial (NOTT), data on 130 who slept for more than two hours were selected for analysis. Complete

entry criteria and methods for the NOTT have been previously published (10). All patients had a history compatible with COPD and a forced expiratory volume in one second (FEV_1) after inhaled bronchodilators of less than 70% of predicted normal and total lung capacity at least 80% of predicted normal. To be considered hypoxemic, a patient had to demonstrate either a partial pressure of PaO_2 of less than 55 mm Hg or a PaO_2 of less than 59 mm Hg with either significant ankle edema or ECG evidence of p-pulmonale. This degree of hypoxemia had to be maintained for at least three weeks of infection-free clinical stability with the patient on an intensive bronchodilator regimen.

Protocol summary

The following procedures were done within five days after the three-week stabilization period: standardized history and physical examination, sleep studies, quality of life questionnaires, neuropsychological tests, pulmonary function tests, hemodynamic measurements, and arterial blood gas measurements. Medical records were reviewed to document a history of hospitalization in the year preceding the patient's entry into the study and to determine the reason for each hospitalization. Aspects of quality of life were determined by two standard self-report questionnaires: the

Profile of Mood States (11), which serves as a measure of current mood; and the Sickness Impact Profile (12), which measures 12 categories of physical and psychosocial activities likely to be affected by illness. The latter includes a sleep-rest category which contains questions such as "I sleep less at night, for example, wake up too early, awaken frequently," and "I am sleeping or dozing most of the time—day and night." During the five days in the hospital, patients retired at their normal time and slept until their normal time of arising. Sleep studies were performed during one night of this hospitalization while the patients were breathing room air. All received a theophylline preparation and an inhaled beta-adrenergic agonist, and none received sedative or psychotropic drugs during the study. Each patient gave informed consent to the study.

Sleep recordings

We performed the sleep studies by two separate methods. In the first method, 25 of the patients selected consecutively from two centers were studied in a fully equipped sleep laboratory. The EEG was recorded with gold-plated surface electrodes applied at positions C_3, C_4, A_1, and A_2 (according to the international 10-to-20 system) (13). Similar electrodes were applied around the eyes to obtain the electrooculogram and under the chin to obtain the electromyogram of submental muscles. The impedance of the applied electrodes was measured with an electrode impedance meter (Grass Instrument Co, Quincy, MA) and was always less than 10 Ω. Other variables measured were breathing pattern (using inductance pneumography or abdominal and chest strain gauges), SaO_2 (using a fiberoptic ear oximeter [Hewlett-Packard]), airflow detection at the nose and mouth (using an infrared CO_2 analyzer, or thermistors), and an ECG. The data were recorded on a multichannel polygraph at a paper speed of 10 mm/sec. Awake SaO_2 was obtained during 15 minutes of supine wakefulness. Mean SaO_2 (referred to as basal sleep SaO_2) was obtained for a 30-second period every 2.5 minutes throughout the night. We recorded the number of times the SaO_2 reached 10% less than the awake SaO_2. The lowest SaO_2 for the entire sleep period was also obtained.

The second method consisted of studying 105 subjects who slept at night in a darkened room with a qualified observer in constant attendance. Sleep was judged visually, and SaO_2 was measured by a fiberoptic ear oximeter (Hewlett-Packard) and recorded continuously on a single channel recorder. From these records, similar measurements were made of awake, basal sleep, 10% dips, and lowest sleep SaO_2. Although we tried to record at least four hours of sleep, instrumentation prevented this in some cases. All patients were judged to sleep for more than two hours during the period they were observed.

Statistical analysis

Pairwise associations between variables were examined by Pearson correlation coefficients or χ^2 tests as appropriate. The relationship between one variable and several others was examined by multiple regression analysis. Student's t test was used to test the equality of mean values between two groups. Mean values for two groups were compared after adjustment for a covariate by analysis of covariance (14). The survival experience for two groups was compared by the log-rank test (15). In addition to these inferential procedures, basic, descriptive information

Table 1
Clinical and Physiologic Characteristics of 130 Patients with Hypoxemic Chronic Obstructive Pulmonary Disease

Characteristics	Nonpolygraphic Mean	Nonpolygraphic SD	Polygraphic Mean	Polygraphic SD
Age (years)	66	8.5	66	8.8
PaO_2 (mm Hg)	51.7	4.4	52.4	4.5
$PaCO_2$ (mm Hg)	42.2	7.2	44.7	8.2
FEV_1* (L)	0.75	0.3	0.7	0.4
Total sleep time† (minutes)	195.5	40.3	256.1	93.4
Awake supine SaO_2 (%)	86.2	4.6	87.8	4.7
Mean sleep SaO_2 (%)	83.2	6.9	82.9	7.2
Lowest sleep SaO_2 (%)	69.1	13.6	69.0	13.2
Sex (male/female)	83/22		20/5	

*FEV_1 = forced expiratory volume in one second.
†$P < 0.001$; all other differences $P > 0.1$.

such as means and standard deviations were provided for the most relevant variables.

Results

The 105 patients who underwent nonpolygraphic sleep studies and the 25 patients who were studied with complete polysomnography were similar in terms of pulmonary function and degree of arterial oxygen desaturation during sleep (Table 1). The mean total sleep time was one hour longer in the latter group. Rapid eye movement (REM) sleep, recorded in 21 of these 25 patients, accounted for 10% of their total sleep time. Patients in both groups ranged in age from 41 to 84 years (mean 65.7 years) and weighed from 40 to 104 kg (mean 64.2 kg). They had severe obstructive lung disease with associated hypoxemia and borderline hypercapnia. Their other characteristics were similar to those previously recorded for patients enrolled in the NOTT (10).

Terms and definitions

Desaturation was expressed as either basal desaturation (awake SaO_2 minus mean sleep SaO_2) or maximal desaturation (awake SaO_2 minus lowest sleep SaO_2). We separated the patients into severe and mild desaturation groups for both the basal and maximal desaturation measures. The groups were defined relative to the mean for both basal and maximal desaturation. This arbitrary division allowed for approximately equal numbers in each group, yet recognized the clustering of patients toward a mild degree of desaturation (Figs 1 and 2). The basal desaturation during sleep exceeded 3% in 49 patients and was ≤ 3% in 81 patients. Maximal desaturation was ≥ 17% in 53 patients and < 17% in 77 patients. A total of 66 patients had either severe basal or severe maximal desaturation, but only half (36/66) had severe abnormalities for both measures of desaturation. Because of this divergence, both measures of desaturation were analyzed.

Degree of desaturation during sleep

The mean awake SaO_2 ± SD in 130 patients was 86.5% ± 4.7%. The mean basal desaturation was 3.4% ± 4.0% (Fig 1), and the mean maximal desaturation was 17.4% ± 11.4% (Fig 2).
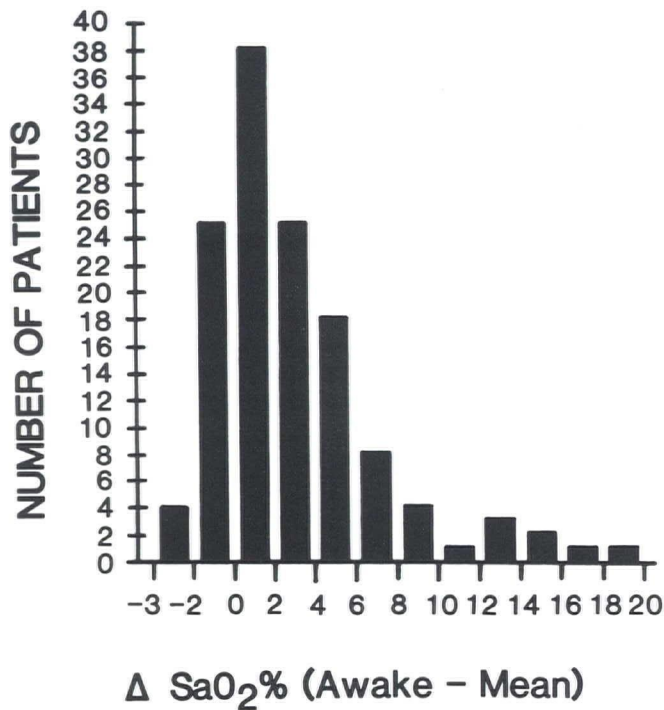
Δ SaO$_2$% (Awake − Mean)

Fig 1—Distribution of basal sleep desaturation abscissa: change in SaO$_2$ from awake supine to the mean value during sleep.

Δ SaO$_2$% (Awake − Lowest)

Fig 2—Distribution of maximal sleep desaturation abscissa: change in SaO$_2$ from awake supine to the lowest during sleep.

The maximal fall in SaO$_2$ recorded in a single patient during sleep was 61%, and 11 patients experienced SaO$_2$ less than 50% during sleep. All patients experienced desaturation at some time during sleep (Fig 2). More frequent episodes of desaturation of > 10% occurred in patients with severe desaturation. The mean frequency of SaO$_2$ dips > 10% per night was 7.6 in patients with severe maximal desaturation compared to 1 for patients with mild maximal desaturation (P < 0.001). The frequency was 5.9 in those with severe basal desaturation and 2.5 if basal desaturation was mild (P < 0.02). In 67 patients, the mean sleep SaO$_2$ was similar to or marginally greater than the awake SaO$_2$. Although the severity of desaturation varied considerably in these patients (Figs 1 and 2), the distribution was skewed in the direction of more severe desaturation. This abnormal distribution is not solely due to the shape of the oxyhemoglobin dissociation curve since the waking SaO$_2$ of most of our patients was at or near the steep portion of the curve. This finding suggests that some patients with COPD develop unusually severe desaturation during sleep.

In 70% (92/130) of our patients, basal desaturation did not occur or was < 4% (Fig 1), which indicates that a marked, prolonged depression in SaO$_2$ during sleep does not regularly occur in COPD. However, at least one large dip in saturation occurred commonly with 66% (86/130) of the patients, demonstrating a maximal desaturation of greater than 10%.

No repetitive periods of apnea were observed in any of the patients, nor was significant apnea documented polygraphically. In the 25 patients who had polygraphic studies, the SaO$_2$ decreased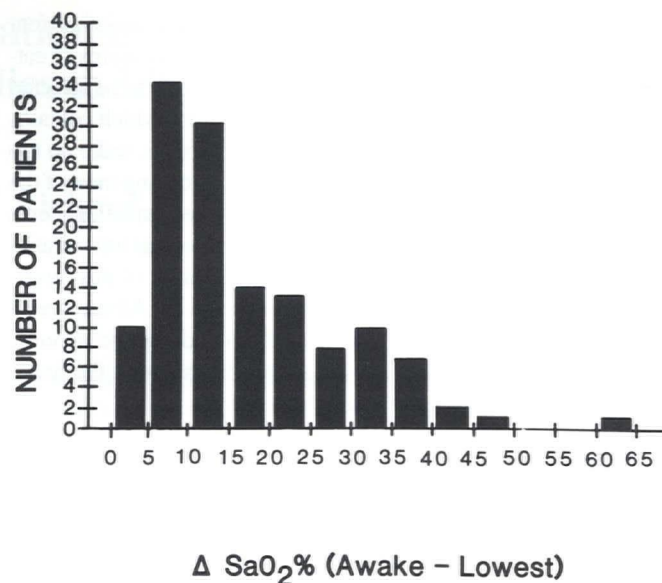 from awake in all sleep stages but was severe only in REM sleep. Maximal desaturation occurred during REM sleep in 21 of the patients who experienced this sleep stage. A more detailed description of the sleep data in these 25 patients was reported by Fleetham et al (16).

Prediction of desaturation during sleep

To evaluate those factors that predict the degree of desaturation in sleep, both maximal and basal desaturation were correlated with clinical and laboratory data (Table 2). The most significant relationship existed between awake PaCO$_2$ and both measures of desaturation. The correlation was higher for maximal desaturation (r = 0.38, P < 0.001) than for basal desaturation (r = 0.26, P < 0.003). The awake PaO$_2$ correlated with basal desaturation (r = −0.25, P < 0.005) nearly as well as the awake PaCO$_2$ but was not useful for predicting maximal desaturation. Based on multiple regression analysis, the combination of PaO$_2$ and PaCO$_2$ was not significantly more predictive of basal and maximal desaturation than PaCO$_2$ alone.

No relationship existed between the degree of desaturation and complaints of sleep disturbance which were provided by analysis of individual questions or the overall sleep-rest scale of the Sickness Impact Profile. There was also no relationship between degree of desaturation and the observations of troubled sleep based on responses to the KATZ Adjustment Scale administered to relatives of the patients. Other clinical and laboratory data were also unrelated to the degree of desaturation. These included age, sex, and weight as well as analysis of measures of pulmonary function such as spirometry, airway resistance, functional residual capacity, and physical findings such as heart and respiratory rate, wheezing and degree of edema, and the presence of cough or volume of sputum produced per day.

The relationship of PaCO$_2$ to both measures of desaturation shows considerable scatter (Figs 3 and 4). Patients with low
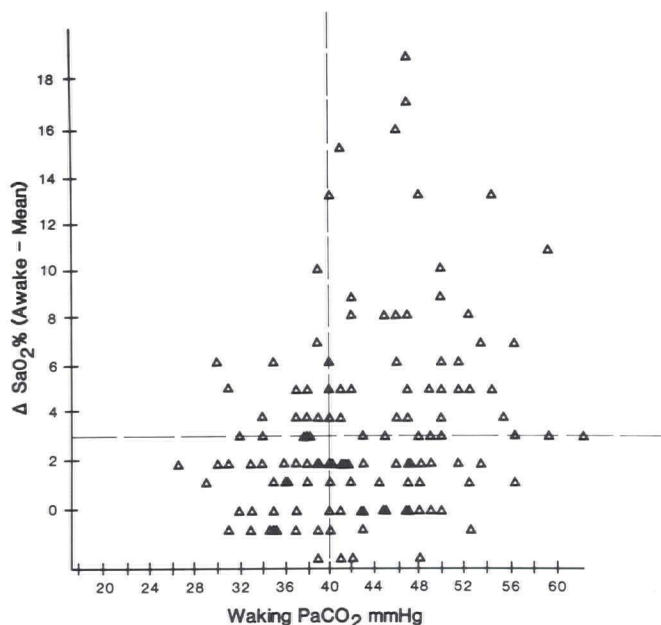
Fig 3—Relationship between waking $PaCO_2$ and basal desaturation during sleep in 130 patients with hypoxemic COPD.
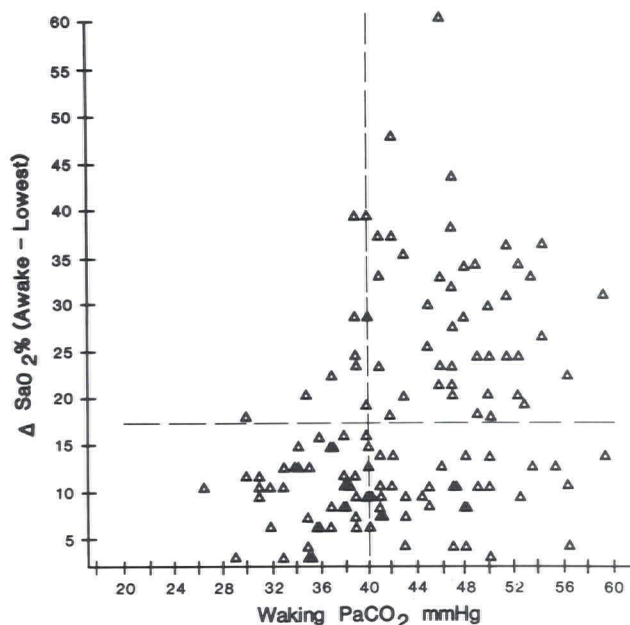

Fig 4—Relationship between waking $PaCO_2$ and maximal desaturation during sleep in 130 patients with hypoxemic COPD.

$PaCO_2$ tended not to desaturate. A $PaCO_2 \geq 40$ mm Hg had high sensitivity but low specificity in predicting severe desaturation. Of the patients with severe basal desaturation ($> 3\%$), 77% (37/48) had a $PaCO_2 \geq 40$ mm Hg. However, of the patients with mild basal desaturation ($\leq 3\%$), only 43% (35/82) had a $PaCO_2 < 40$ mm Hg (Fig 3). The results are slightly better for predicting severe maximal desaturation ($\geq 17\%$) with a sensitivity of 86.5% (45/52) and specificity of 50% (39/78) (Fig 4). A low $PaCO_2$ may be a useful screening tool to indicate that an individual is unlikely to develop severe desaturation during sleep. However, even this test is not generally useful to reliably ascertain the degree of desaturation at night.

Significance of sleep desaturation

We examined the complications of chronic hypoxemia to determine if they were more severe when marked desaturation occurred during sleep. A low but significant correlation ($r = 0.30$, $P < 0.001$) occurred between basal desaturation, but not maximal desaturation, and the mean pulmonary artery pressure at rest. A low correlation also occurred between the number of hospitalizations in the year before the patients entered the study and both measures of desaturation ($r = 0.20$, $P < 0.03$). No relationship was observed between either measure of desaturation and hematocrit, maximal exercise tolerance, the results of neuropsychological tests, or measures of the quality of life.

Table 2
Relationship Between Clinical and Laboratory Data and Desaturation During Sleep

Characteristics	N	Mean	SD	Maximal Desaturation Correlation Coefficient	P	Basal Desaturation Correlation Coefficient	P
$PaCO_2$ (mm Hg)	129	42.7	7.5	0.381	0.001	0.262	0.003
PaO_2 (mm Hg)	129	51.8	4.4	−0.104	0.24	−0.252	0.004
pH	129	7.4	0.046	0.151	0.09	−0.122	0.17
Age (years)	130	65.7	8.5	−0.076	0.39	0.012	0.90
Weight (kg)	130	64.2	13.5	0.076	0.39	0.036	0.68
FVC (% predicted)	127	53.2	18.6	−0.115	0.20	0.051	0.57
FEV_1 (% predicted)	127	28.7	13.9	−0.123	0.17	0.063	0.48
SIP sleep-rest scale (normal value = 2.1)	121	35.6	26.9	0.058	0.53	−0.095	0.30

	Maximal Desaturation Mean	SD	P	Basal Desaturation Mean	SD	P
Sex						
Male (N = 103)	17.1	11.3		3.2	3.8	
Female (N = 27)	18.7	11.7	0.52	4.3	4.6	0.19

FEV_1 = forced expiratory volume in one second, FVC = forced vital capacity, SIP = Sickness Impact Profile, and SD = standard deviation.

| Characteristics | N* | Maximal Desaturation | | | Basal Desaturation | | |
		Mild < 17%	Severe ≥ 17%	P	Mild ≤ 3%	Severe > 3%	P
Number of patients		77	53		81	49	
Gas exchange							
PaO_2 (mm Hg)	129	52.4	50.9	0.06	52.4	50.9	0.06
$PaCO_2$ (mm Hg)	129	40.2	46.3	< 0.001	41.3	44.9	< 0.01
pH	129	7.41	7.39	0.02	7.41	7.40	0.31
Pulmonary hemodynamics							
Mean pulmonary artery pressure at rest (mm Hg)	122	27.0	29.5	0.10	26.7	30.2	< 0.03
Quality of life characteristics							
Number of hospitalizations in year prior to entry	129	0.82	1.4	< 0.003	0.98	1.2	0.28
Number of episodes of heart failure in year prior to entry	129	0.32	0.62	0.04	0.43	0.47	0.78
Sickness Impact Profile (N = 3.1)	120	23.7	24.7	0.70	23.8	24.7	0.73
Profile of Mood States (N = 26.4)	118	38.8	37.7	0.86	38.7	37.7	0.87
Hematocrit (%)	130	47.7	47.8	0.90	47.5	48.3	0.41
Maximal exercise tolerance (WATTS)	129	38.0	40.6	0.42	38.3	40.2	0.56
Neuropsychological characteristics							
Global rating (N = 3.5)	123	4.2	4.4	0.35	4.2	4.4	0.30
Halstead impairment index (N = 0.63)	118	0.71	0.76	0.25	0.71	0.76	0.32
Cumulative survival (%)							
Nocturnal oxygen therapy		0.126	0.142	0.67	0.133	0.185	0.40
Continuous oxygen therapy		0.099	0.098	0.60	0.084	0.117	0.88

*N < 130 due to incomplete data.
All entries are mean values unless otherwise indicated.

To examine these relationships further, the severe and mild desaturation groups were analyzed for differences in severity of hypoxia-induced complications (Table 3). Pulmonary hypertension was more severe in patients with severe desaturation during sleep (Table 3). This difference was significant only for the basal desaturation determination. The mean pulmonary artery pressure in the group with severe basal desaturation was only 3.5 mm Hg higher than in those with mild basal desaturation. Although patients with severe maximal desaturation had less severe abnormalities of pulmonary hemodynamics than patients with severe basal desaturation, they had significantly more hospitalizations in the year preceding entry into the study. This was due to more frequent hospitalizations for episodes of right heart failure. No differences were noted in hospitalization rates or heart failure between the patients with severe and those with mild basal desaturation.

The severity of desaturation had no effect on other manifestations of chronic hypoxemia such as erythrocytosis, exercise intolerance, neuropsychological impairment as measured by the Halstead-Reitan battery of tests, or the quality of life as measured by the Sickness Impact Profile and the Profile of Mood States. There was also no effect on individual scales in each of these tests.

The awake $PaCO_2$ was significantly higher in patients with severe desaturation, but this was well compensated, as manifested by similar pH values in both groups. The hypercarbia resulted in a slightly lower PaO_2 for patients with severe desaturation. Because of these differences in waking blood gases, the effect of basal desaturation on pulmonary artery pressure was further examined by analysis of covariance to control for differences in PaO_2 or $PaCO_2$. After adjustments were made for waking $PaCO_2$, patients with severe basal desaturation still had significantly higher adjusted mean values for pulmonary artery pressure at rest (30 versus 26.9 mm Hg, P < 0.05). However, after adjustments were made for waking PaO_2, the adjusted mean pulmonary artery pressure at rest was 29.7 mm Hg in patients with severe baseline desaturation and 27.1 mm Hg in those with mild baseline desaturation (P < 0.08).

Effect of desaturation in selected patients

The effect of basal desaturation on waking pulmonary artery pressure was determined in a group of 53 patients with a waking PaO_2 between 54 and 59 mm Hg (Table 4). Of these, 15 had severe basal desaturation (> 3%) and mean arterial blood gases similar to the 38 with mild basal desaturation (≤ 3%). Their mean pulmonary artery pressure was 3.7 mm Hg higher than that of the patients with less severe nocturnal desaturation, but these differences were not significant in this group of patients.

In another group, 20 patients with the most severe nocturnal desaturation (basal desaturation > 6%) were compared to 110 patients with less severe desaturation (Table 4). Their mean PaO_2 was similar to and the mean $PaCO_2$ was higher than that of patients with less severe desaturation. Their mean pulmonary artery pressure was significantly higher than that of the patients with less severe nocturnal desaturation. No significant dif-

Table 4
Effect of Nocturnal Desaturation on Pulmonary Hemodynamics
in Select Patient Populations

Characteristic		Very Severe Desaturation Basal Desaturation				Waking PaO$_2$ 54-59 mm Hg Basal Desaturation		
	N	$\leq$ 6%	> 6%	P	N	$\leq$ 3%	> 3%	P
Number of patients		110	20			38	15	
Gas exchange								
PaO$_2$ (mm Hg)	129	52.1	50.5	0.16	53	55.6	56.4	0.14
PaCO$_2$ (mm Hg)	129	41.8	47.2	0.003	53	41.5	42.2	0.73
pH	129	7.41	7.39	0.19	53	7.41	7.41	0.94
Pulmonary artery								
pressure at rest (mm Hg)	123	27.2	32.9	0.008	51	24.3	28.0	0.16

All entries are mean values unless otherwise indicated.

ferences in the severity of other hypoxia-induced complications were found. The 25 polygraphically monitored patients were analyzed separately. No significant correlations were found between hypoxia-induced complications and either measure of desaturation.

Mortality

The presence of severe desaturation in patients, obtained while they were breathing room air, was not a predictor of subsequent mortality while they were receiving home oxygen therapy. This therapy included the use of oxygen during sleep in all cases. Since the type of oxygen therapy has been shown to affect mortality (10), before we calculated survival rates the patients were separated into two groups based on the type of therapy they were receiving (nocturnal versus continuous). After a follow-up period of at least 12 months (mean 19.3 months), the life table cumulative survival rates were similar for patients with mild and severe desaturation (Table 3). The initiation of treatment would affect any influence that desaturation would have on mortality. This finding merely indicates that severe nocturnal desaturation prior to therapy does not predict a poor response to oxygen therapy.

Discussion

The degree of sleep arterial oxygen desaturation did not differ between our two groups of patients with and without polygraphic recordings (Table 1). Although we did not document sleep by EEG in all patients, it is reasonable to assume that these patients did in fact sleep. For this reason, we believe the two groups could be combined to examine relationships between sleep desaturation and other physiological variables. Our patients slept an average of three to four hours, and 21 of the 25 polygraphically monitored patients demonstrated REM sleep. These conditions are adequate to document typical sleep desaturation in this population.

Complications of chronic hypoxemia such as erythrocytosis, exercise intolerance, brain dysfunction, and impaired life quality as measured by standardized questionnaires were not aggravated by nocturnal desaturation. Similarly, no relationship was observed between the *maximal* desaturation during sleep and waking pulmonary hypertension. Patients with severe maximal desaturation also had more frequent SaO$_2$ dips > 10%. This in-

dicates that these isolated physiologic challenges are of insufficient duration to produce permanent hemodynamic changes. This is not surprising since these brief, dramatic events occur exclusively in REM sleep which comprises a minor fraction (2% to 5%) of the day for patients with COPD (16-18).

The mean level of SaO$_2$ prevailing throughout sleep is probably more relevant to the development of sustained pulmonary hypertension since the pulmonary vasculature is exposed to this SaO$_2$ for a longer period. This average desaturation throughout sleep was examined as the basal desaturation. A correlation was found between basal desaturation and pulmonary artery pressure. However, two factors should be considered in evaluating this relationship and attempting to determine if there is an independent effect of basal desaturation on waking pulmonary hypertension. The degree of basal desaturation is related to the waking PaO$_2$ (Table 2): the lower the waking PaO$_2$, the more severe the basal desaturation during sleep. Since all of these patients had waking hypoxemia which could produce pulmonary hypertension alone, an independent effect of nocturnal desaturation may be difficult to determine. The group with severe basal desaturation (Table 3) had a mean waking pulmonary artery pressure only 3.5 mm Hg higher than that of the patients with mild desaturation, but this difference was not significant after adjusting for the waking PaO$_2$ difference in these two groups.

These results also apply to patients with moderate waking hypoxemia (PaO$_2$ 54 to 59 mm Hg). These patients would be expected to be more susceptible to nocturnal desaturation since they have less pulmonary hypertensive stimulus during waking hours. Finally, in the 20 patients with the most severe basal desaturation (> 6%), we found their mean pulmonary artery pressure to be significantly higher (5.7 mm Hg) than that of patients with less severe desaturation. This suggests that at some degree of severity nocturnal desaturation can aggravate hypoxemia-induced pulmonary hypertension.

The lack of a significant relationship between nocturnal desaturation and waking pulmonary hypertension is surprising. Numerous studies have confirmed that in awake patients with COPD a close relationship exists between chronic hypoxemia and pulmonary hypertension. By combining data from several reports, Burrows (19) demonstrated that mean pulmonary artery pressure progressively increases as waking SaO$_2$ falls below

Table 5
Nocturnal Desaturation in Chronic Obstructive Pulmonary Disease

Reference	Number of Patients and Type	Mean Waking SaO$_2$ (%)	Mean PaCO$_2$ (mm Hg)	Mean Maximal Desaturation (%)	Mean Basal Desaturation (%)
Flick and Block (4)	10 IPD	95	—	26	—
Wynne et al (5)	7 IPD/OPD	89	40	17	—
Douglas et al (6)	12 OPD	83	53	30	—
Littner et al (22)	9 OPD	91	42	15	—
DeMarco et al (23)	4 BB	81	49	30	3.2
	6 PP	92	37	5	0
Calverly et al (18)	13 BB	80	51	41	9
	7 PP	94	36	16	2.1
NOTT (10)	130 OPD	86	43	17	3

IPD = hospitalized subjects, OPD = ambulatory subjects, BB = "blue bloater," PP = "pink puffer," and NOTT = nocturnal oxygen therapy trial.

85%. Moreover, periodic episodes of desaturation during sleep in COPD (8,9) as well as in sleep apnea (20) have been shown to produce transient increases in pulmonary artery pressure. It has also been postulated that nocturnal desaturation may produce sustained pulmonary hypertension and cor pulmonale (21). Although we did not measure pulmonary artery pressure during sleep, the mean wake saturation of our patients was in the range defined by a relationship between pulmonary hypertension and SaO$_2$. It is reasonable to assume that our patients with lower SaO$_2$ during sleep had greater increases in pulmonary artery pressure during sleep. However, our results show that transient changes in saturation and associated pulmonary hypertension during sleep *usually* do not produce chronic hemodynamic changes in severe COPD beyond the effect attributable to the daytime level of desaturation.

These results may not apply to nocturnal desaturation in other disorders such as sleep apnea and in COPD with borderline hypoxemia (PaO$_2$ > 60 mm Hg). Since patients with these disorders generally do not have a sustained pulmonary hypertensive effect during waking hours, they may be more susceptible to chronic hemodynamic changes produced by basal desaturation during sleep. Nevertheless, our results indicate that more work is necessary in this area before concluding that nocturnal desaturation alone will produce sustained pulmonary hypertension.

Patients with severe maximal desaturation had more hospitalizations and episodes of right heart failure. These patients also had more frequent dips in saturation greater than 10%. Transient episodes of pulmonary hypertension associated with these dips might have had an adverse effect on right ventricular function that produced more severe right ventricular hypertrophy. However, left ventricular dysfunction that produced greater lability in nocturnal saturation may have been more common in patients with severe maximal desaturation. Since this group did not have more severe waking pulmonary hypertension, this finding is difficult to explain.

Our results demonstrate that marked desaturation during sleep is unusual in an unselected population of stable patients with severe hypoxemic COPD. The mean basal desaturation was only 3.4% ± 4.0%. This is a more comprehensive measure of nocturnal desaturation and indicates that desaturation throughout the night is less severe than previously indicated. The wide difference between maximal and mean desaturation is due to serious desaturation occurring mostly in the brief periods of REM sleep in this patient population (16). Maximal arterial oxygen desaturation in our patients was comparable to that reported in previous studies of patients with COPD (Table 5). In our study, the mean maximal desaturation was 17.4% ± 11.4%, and earlier reports of the mean maximal desaturation ranged from 5% to 41% (4-6,18,22,23). Since similar recording techniques were used in all of these studies, the great variability in degree of sleep arterial oxygen desaturation is probably related to differences in patient population in terms of clinical stability, severity of hypercarbia, and proportion of "blue bloater"-type patients.

None of our patients demonstrated significant periodic apnea or the characteristic features of the sleep apnea syndrome such as hypersomnolence and frequent arousals (24). This is consistent with earlier reports (4-6,22) in which only two of 28 patients with COPD demonstrated significant obstructive apnea, but it conflicts with the data of Guilleminault et al (7) who found significant apnea in 23 of 26 patients with COPD. However, the unusual incidence of sleep apnea in their patients may be because they were referred primarily for evaluation of a sleep disorder and were unusually obese (mean weight 96 kg) for patients with severe COPD.

Previous studies of sleep and breathing in normal subjects have demonstrated that oxygen desaturation or irregular breathing during sleep is more severe in men and increases with age and weight (25-27). However, we found no such relationship in our subjects, possibly because patients with severe obstructive lung disease are a more homogeneous group of elderly, thin people. Only four patients were under 50 years old, and only 14 were greater than 130% of their ideal weight. Also, all except one of our female patients were postmenopausal, and breathing during sleep in postmenopausal women may be similar to that of men (28). Complaints of sleep disturbance were also unrelated to the degree of desaturation during sleep. Although these com-

plaints were common among our patients, as confirmed by the Sickness Impact Profile (sleep-rest scale, mean 35.6, normal 2.1), the disturbance was most likely caused by factors other than desaturation, which could include coughing, hypercarbia not associated with significant desaturation, effects of medication, and other chronic disease. Arousals in the patients are common and often unassociated with significant desaturation, which supports this explanation (16).

The awake PaO_2 and $PaCO_2$ were the only clinical or laboratory tests associated with sleep desaturation. Even these tests were not reliable as a generally useful tool for predicting the degree of nocturnal desaturation (Figs 3 and 4). The $PaCO_2$ relation was a permissive one, that is, patients with low $PaCO_2$ usually do not have severe desaturation, whereas patients with a higher $PaCO_2$ may or may not have severe desaturation. Sleep desaturation has a similar relationship to the hypercapnic drive to breathe (29). Patients with high hypercapnic drive generally do not have large dips in SaO_2. Those with low drive had either little desaturation or severe desaturation, although all those with severe desaturation had low drives. This is consistent with the notion that low hypercapnic drives do not cause sleep desaturation but permit the process which causes desaturation to occur.

In stable patients with chronic hypoxemia and severe COPD, the following four conclusions can be made: 1) the mean nocturnal desaturation is mild in most patients; 2) desaturation during sleep does not aggravate hypoxia-induced polycythemia, exercise intolerance, or neurophysiological impairment; 3) waking pulmonary hypertension is increased by nocturnal desaturation, but this effect is clinically and statistically significant in only a few patients with very severe decreases in mean saturation during sleep ($> 6\%$); and 4) although the awake PaO_2 and $PaCO_2$ were the only clinical parameters associated with sleep desaturation, even these tests were not reliable predictors of nocturnal desaturation; however, a low $PaCO_2$ indicates that severe desaturation during sleep is unlikely.

Acknowledgments

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