SCIENTIFIC INVESTIGATIONS

Obesity Hypoventilation Syndrome: Early Detection of Nocturnal-Only Hypercapnia in an Obese Population

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Study Objectives: Hypoventilation in obesity is now divided into five stages; stage 0 (pure obstructive sleep apnea; OSA), stages I/II (obesity-related sleep hypoventilation; ORSH) and stages III/IV (awake hypercapnia, obesity hypoventilation syndrome; OHS). Hypercapnia during the day may be preceded by hypoventilation during sleep. The goal of this study was to determine the prevalence and to identify simple clinical measures that predict stages I/II ORSH. The effect of supine positioning on selected clinical measures was also evaluated.

Methods: Ninety-four patients with a body mass index $> 40 \text{ kg/m}^2$ and a spirometric ratio > 0.7 were randomized to begin testing either in the supine or upright seated position on the day of their diagnostic sleep study. Arterialized capillary blood gases were measured in both positions. Oxygen saturation measured by pulse oximetry was also obtained while awake. Transcutaneous CO_2 monitoring was performed during overnight polysomnography.

Results: Stages I/II ORSH had a prevalence of 19% in an outpatient tertiary hospital setting compared with 61%, 17%, and 3% for stages 0, III/IV, and no sleep-disordered breathing respectively. Predictors for sleep hypoventilation in this group were an awake oxygen saturation of $\leq 93\%$ (sensitivity 39%, specificity 98%, positive likelihood ratio of 22) and a partial pressure of carbon dioxide $\geq 45 \text{ mmHg}$ (sensitivity 44%, specificity 98%, positive likelihood ratio of 24) measured in the supine position.

Conclusions: ORSH has a similar prevalence to OHS. Awake oxygen saturation and partial pressure of carbon dioxide performed in the supine position may help predict obese patients with sleep hypoventilation without awake hypercapnia.

Commentary: A commentary on this article appears in this issue on page 1455.

Clinical Trial Registration: Registry: Australian New Zealand Clinical Trials Registry, Identifier: ACTRN 12615000135516, URL: <https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=367493&isReview=true>, Title: A cross-sectional study to identify obese patients who are at risk for developing obesity hypoventilation syndrome (OHS) by investigating the relationship between daytime measures (including supine hypercapnia, distribution of body fat and lung volumes) with the presence of hypoventilation during sleep

Keywords: body weights and measures, early diagnosis, obesity hypoventilation syndrome

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BRIEF SUMMARY

Current Knowledge/Study Rationale: The prevalence and clinical predictors of obesity-related sleep hypoventilation (ORSH) without daytime hypercapnia is unknown. Detection and multimodal management of patients at this stage may potentially prevent the development of advanced obesity hypoventilation syndrome and its related complications.

Study Impact: Our study demonstrates that stages I/II ORSH and stages III/IV obesity hypoventilation syndrome have a similar prevalence in a tertiary sleep referral center setting, with awake oxygen saturation and partial pressure of carbon dioxide obtained in a supine position shown to be the best predictors for nocturnal-only hypoventilation. Simple measures using supine positioning help predict sleep hypoventilation in a morbidly obese population, where ORSH is underrecognized.

INTRODUCTION

Obesity hypoventilation syndrome (OHS) is traditionally diagnosed in patients with a body mass index (BMI) $> 30 \text{ kg/m}^2$ and daytime hypercapnia (partial pressure of carbon dioxide; $\text{PCO}_2 > 45 \text{ mmHg}$) without other known causes of hypoventilation. Its prevalence increases with BMI.¹ OHS is associated with increased morbidity and mortality compared with obstructive sleep apnea (OSA) but is underdiagnosed.^{2–4}

In a recent European Respiratory Society (ERS) task force report, hypoventilation in obesity is now divided into

five stages. Stage 0 encompasses the pure OSA population without evidence of nocturnal-only hypoventilation or daytime hypercapnia. In stages I and II, only obesity-related sleep hypoventilation (ORSH) is present. Patients in stage I and II also have a bicarbonate level of less than 27 mmol/L or $\geq 27 \text{ mmol/L}$, respectively. Daytime hypercapnia is only present in the most advanced OHS stages of III and IV.⁵ Patients in stage IV have concurrent comorbidities whereas those in stage III do not. Similar to patients with neuromuscular and chest wall restriction, it is believed that in patients with nocturnal hypoventilation without daytime

hypercapnia, advanced OHS and diurnal hypercapnia may eventually develop.^{6,7}

There are only limited publications that include patients known to have stages I/II ORSH.^{8,9} The ability to detect patients who may be at risk of the development of stages III/IV OHS in a timely manner may allow earlier multimodal treatment initiation and potentially prevent the development of advanced OHS pathophysiology and cardiometabolic morbidity.^{10,11} Not only does OHS carry a significantly higher morbidity and mortality than OSA, the raised mortality persists despite positive airway therapy.¹⁰ In fact, the main cause of death in OHS is cardiovascular disease rather than respiratory failure. Comorbidities are also often present before advanced OHS is diagnosed.¹¹ The goal of this study was to determine the prevalence of stages I/II ORSH in morbidly obese patients referred to a sleep unit for assessment of sleep-disordered breathing and to identify simple daytime clinical measures that may predict ORSH. The effect of awake supine positioning on these measures was also evaluated. We hypothesize that evaluating the effect of awake supine positioning will allow earlier detection of ORSH.

METHODS

Participants

Patients between the ages of 18 and 75 years with a BMI > 40 kg/m² and able to lie flat were recruited from sleep and obesity clinics at Royal Prince Alfred Hospital as well as other local and regional sleep centers for assessment of sleep-disordered breathing. Those with major psychiatric or neurological disorders, obstructive lung disease (forced expiratory volume in 1 second [FEV1]/forced vital capacity [FVC] < 0.7) or uncontrolled medical conditions, such as cardiac failure, were excluded. The study protocol was approved by the Human Research Ethics Committee of the Sydney Local Health District (X14-0386 & HREC/14/RPAH/512) at Royal Prince Alfred Hospital (Sydney, NSW, Australia). All subjects gave written informed consent prior to study participation. This trial was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN 12615000135516).

Study Design

Patients were randomized to begin testing either in the supine or upright seated position during the afternoon of their in-laboratory diagnostic sleep study. Each position was maintained for 30 minutes prior to arterialized capillary blood gas testing and all patients were tested in both the upright and supine positions while awake.¹² Slow vital capacity was also measured in each position in random order.

Instrumentation and Measurements

Neck, hip, and waist circumference were measured with the participant standing upright. Waist circumference was measured at the level of the umbilicus. The sagittal height of the abdomen was measured in centimeters with the patient in a supine position. A spirit level was positioned on a flat surface of the bed and a second level was positioned on the patient's

abdomen during the sagittal height measurement. The distance between these two points was recorded.

FEV1 and FVC and spirometric ratio (FEV1/FVC) were measured as per the American Thoracic Society/ERS guidelines using a bedside EasyOne spirometer (nidd Medical Technologies, Andover, Massachusetts, United States).¹³ Patients were advised to perform a maximal inspiratory and expiratory maneuver in an unforced manner.

A pea-sized drop of vasodilating cream containing nonivamide, butoxyethyl nicotinate, and sorbic acid was applied 30 minutes before arterialized capillary blood sampling to the inferolateral part of the ear lobe (Finalgon Boehringer Ingelheim, North Ryde, Australia). Blood was collected with a capillary tube (SafeClinitubes, Radiometer Medical Aps, Bronshøj, Denmark). The sample was analyzed within 10 minutes using the blood gas analyzer flex mode (Radiometer ABL800FLEX, Radiometer, Bronshøj, Denmark).

Oxygen saturation measured by pulse oximetry (Rad-5 Masimo pulse oximeter, Irvine, California, United States) used within the sleep unit was obtained from the patient admission and sleep study observation charts. Admission oxygen saturation was obtained with the patient in the seated upright position whereas the sleep observation chart recorded the oxygen saturation when the patient was in a supine position before and during sleep. Oxygen saturation while in a supine position was obtained when the patient was awake and before the first epoch of sleep was recorded on polysomnography.

Nocturnal transcutaneous CO₂ (TcCO₂) monitoring occurred concurrently with the diagnostic sleep study (SenTec Ag Digital Monitoring System, Therwil, Switzerland). The diagnosis of sleep-disordered breathing and nocturnal hypoventilation was based on standard scoring techniques.^{14,15} Nocturnal hypoventilation was scored when the TcCO₂ was > 55 mmHg for ≥ 10 minutes or there was an increase in the TcCO₂ ≥ 10 mmHg (in comparison with an awake supine value) to a value exceeding 50 mmHg for ≥ 10 minutes.¹⁵ Patients with fewer than 5 obstructive events/h without hypoventilation received a diagnosis of OSA. Those with a daytime partial pressure of carbon dioxide (PcCO₂) ≥ 45 mmHg without other known causes of hypoventilation received a diagnosis of stages III/IV OHS, whereas patients with nocturnal-only hypoventilation with a PcCO₂ < 45 mmHg, were categorized as having stages I/II ORSH.

Statistical Methods

Analysis of patient demographics, anthropometrics, upright and supine spirometry and blood gases, and sleep study parameters were performed on the 94 patients who participated in the study. A one-way analysis of variance and Bonferroni analysis were used to compare three groups: pure OSA (stage 0), ORSH (stages I/II), and advanced OHS (stages III/IV). For data without a normal distribution, Kruskal-Wallis one-way analysis of variance was performed.

To determine the best predictors of stages I/II ORSH, variables that were significantly different between patients with early OHS and pure OSA were identified. These were then further analyzed with a backward step-wise logistic regression. The most significant variables were further analyzed with receiver operating characteristic (ROC) curves.

Statistical significance was set at $P < .05$ (two-tailed). Data were analyzed with the statistical software package STATA version 14 (StataCorp, College Station, Texas, United States), and the pROC package of R for the comparisons between ROC curves.¹⁶

RESULTS

Table 1 outlines patient characteristics of the entire study cohort. **Figure 1** describes the study design and sleep-disordered breathing categories of the cohort. Stages I/II ORSH had a prevalence of 19.1% (95% confidence interval [CI] 0.12–0.29) whereas stage III/IV OHS, pure OSA, and patients without sleep-disordered breathing had prevalences of 17% (95% CI 0.1–0.26), 60.6% (95% CI 0.5–0.7), and 3.2% (95% CI 0.01–0.1), respectively.

Multiple significant differences between the three groups were found (**Table 2**). In relation to the stages I/II ORSH versus

Table 1—Characteristics of all patients with a BMI > 40 kg/m².

Patient Characteristics (n = 94)

Age (years), mean ± SD [range]	49 ± 12.5 [26–75]
Male, n (%)	43 (45.7)
BMI (kg/m ²), median (IQR) [range]	52.4 (14.9) [39.8–89.6]
Ethnicity, n (%)	
Caucasian	61 (64.9)
Pacific Islander	12 (12.7)
Aboriginal	9 (9.6)
Other	12 (12.8)
Epworth Sleepiness Scale score, mean ± SD [range]	12 ± 5.8 [0–24]
Never smoker, n (%)	42 (44.7)
Pack-years, median (IQR) [range]	15 (21) [1–50.0]

BMI = body mass index, IQR = interquartile range, SD = standard deviation.

Figure 1—Study design and prevalence of sleep-disordered breathing.

BMI = body mass index, FEV1/FVC = forced expiratory volume in 1 second/forced vital capacity, OHS = obesity hypoventilation syndrome, ORSH = obesity-related sleep hypoventilation, OSA = obstructive sleep apnea, TcCO₂ = transcutaneous carbon dioxide monitoring.

Table 2—Patient characteristics, anthropometrics, spirometry, blood gas and sleep study parameters: hypoventilation in obesity stages 0-IV.

	Stage 0 Pure OSA	Stages I/II ORSH	Stages III/IV OHS	P
Characteristics				
Number (%)	57 (61)	18 (19)	16 (17)	
Age (years)	49 ± 12	45 ± 11	51 ± 14	ns
Male (%)	51	39	44	ns
BMI (kg/m ²)	50 (43–56)	56 (51–63)	58 (51–65)	.01†
Caucasian (%)	74	50	44	ns
Epworth Sleepiness Scale score	10 ± 5	15 ± 5	13 ± 7	.009*
Smoking history (%)	46	72	69	ns
Pack-years	5 (2–30)	20 (12–25)	15 (11–25)	ns
Upright awake SpO ₂ (%)	96 (95–97)	95 (93–97)	93 (90–95)	< .001*,§
Supine awake SpO ₂ (%)	96 (94–97)	93 (91–94)	90 (87–92)	< .001‡,§
Difference in supine versus upright SpO ₂ (%)	0.6 ± 1.9	2.5 ± 3.8	1.9 ± 5.5	ns
Waist to hip ratio	0.98 ± 0.08	0.96 ± 0.11	0.98 ± 0.07	ns
Neck (cm)	47.9 ± 5.3	51.3 ± 5.5	52.8 ± 6.3	.008†
Abdominal sagittal height (cm)	30 (27–32)	31 (29–35)	30 (30–33)	ns
Spirometry				
Upright SVC (L)	2.90 ± 0.87	2.57 ± 0.83	2.11 ± 0.70	.004†
Supine SVC (L)	2.80 ± 0.93	2.49 ± 0.85	1.89 ± 0.70	.001†
FVC (L)	3.07 ± 0.92	2.08 ± 1.04	2.23 ± 0.78	.006†
FVC (% predicted)	81.73 ± 16.2	77.4 ± 15.4	65.6 ± 17.9	.003†
Capillary Blood Gas				
Upright PcCO ₂ (mmHg)	37.8 (36–40)	41.5 (39–43)	48.8 (47–52)	< .001‡,§
Supine PcCO ₂ (mmHg)	38.0 (36–42)	44.8 (41–46)	48.7 (47–54)	< .001‡,§
HCO ₃ (mmol/L)	24.8 ± 1.9	26.6 ± 1.8	30.3 ± 2.4	< .001‡,§
Sleep Study Parameters				
AHI (events/h)	53 (20–83)	79 (58–97)	91 (36–128)	.005†
Minimum oxygen saturation (%)	77 (68–82)	51 (39–60)	46 (40–60)	< .001‡
TcCO ₂ > 50 mmHg (minutes)	0 (0–0)	107 (28–249)	435 (334–488)	< .001‡,§
TcCO ₂ > 55 mmHg (minutes)	0 (0–0)	0 (0–30)	29 (155–409)	< .001†,§
Oxygen saturation time < 90% (minutes)	29.3 (9–77)	270.0 (84–345)	338.6 (232–413)	< .001‡,§
Oxygen saturation time < 80% (minutes)	1.1 (0–8)	46.7 (22–180)	96.5 (17–161)	< .001‡

Data presented as mean ± standard deviation, median (interquartile range) or frequency as indicated. AHI = apnea-hypopnea index, BMI = body mass index, FVC = forced vital capacity, HCO₃ = serum bicarbonate, ns = not significant, OHS = obesity hypoventilation syndrome, ORSH = obesity-related sleep hypoventilation, OSA = obstructive sleep apnea, PcCO₂ = capillary carbon dioxide tension, SpO₂ = oxygen saturation measured by pulse oximetry, SVC = slow vital capacity, TcCO₂ = transcutaneous carbon dioxide monitoring. Italicized words = paired variables obtained in the upright and supine position. Bold words = to indicate categories of data. * = *P* value comparison between stage 0 and stages I and II; † = *P* value comparison between stage 0 and stages III and IV; ‡ = *P* value comparison between stage 0 and stages I, II, III and IV; § = *P* value comparison between stages I and II and stages III and IV.

Table 3—Hypoventilation in obesity stages 0-IV: OSA severity.

OSA severity	Stage 0	Stages I/II	Stages III/IV
Mild n (%)	9 (16)	1 (< 1)	3 (19)
Moderate n (%)	7 (12)	0 (0)	0 (0)
Severe n (%)	41 (72)	17 (94)	13 (81)

OSA = obstructive sleep apnea.

pure OSA (stage 0), the Epworth Sleepiness Scale (ESS) score, awake upright and supine oxygen saturation and PcCO₂, serum bicarbonate, minimum oxygen saturation, total sleep time

with oxygen saturation below 80% and 90% during polysomnography and time with TcCO₂ > 50 mmHg were significantly different. After adjusting for AHI and BMI, one variable with the best odds ratio and *P* value, from a group of variables that demonstrated collinearity, was included in the backward stepwise logistic regression. The variables included in the final logistic regression were supine awake oxygen saturation, supine PcCO₂, ESS, and bicarbonate. Awake supine oxygen saturation and PcCO₂ were the best variables to predict nocturnal hypoventilation in stages I/II ORSH. To confirm arterialization of capillary blood gases, the upright pH, partial pressure of oxygen, and oxygen saturation of the cohort as a whole were 7.42, 78 mmHg, and 95%, respectively. Severity of obstructive

Figure 2—ROC curve analysis for supine SpO₂ for the dependent variable of hypoventilation, for stages I/II ORSH and pure OSA.

Supine SpO ₂	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR-
≤ 90	11	100	100	82	*	0.89
≤ 92	27	100	100	85	*	0.72
≤ 93	39	98	85	87	22.17	0.62
≤ 94	56	91	61	89	6.33	0.49
≤ 96	94	56	35	98	2.15	0.09

* = unable to calculate due to 100% specificity. LR = likelihood ratio, NPV = negative predictive value, ORSH = obesity-related sleep hypoventilation, OSA = obstructive sleep apnea, PPV = positive predictive value, ROC = receiver operating characteristic, SpO₂ = oxygen saturation measured by pulse oximetry.

events in stages 0-IV of hypoventilation in obesity are shown in **Table 3**.

An awake supine oxygen saturation ≤ 93% had a poor sensitivity (39%) but good specificity and positive likelihood ratio (LR) for nocturnal hypoventilation in stages I/II ORSH. The area under the curve (AUC) for this analysis was 0.87 (**Figure 2**). In addition, a supine partial pressure of carbon dioxide ≥ 45 mmHg had a sensitivity of 44% but a specificity of 98%, positive LR of 24, and an AUC of 0.86 (**Figure 3**). For both **Figure 2** and **Figure 3**, ROC curve analysis for supine SpO₂ and P_cCO₂ were performed using logistic regression, for the dependent variable of hypoventilation, for stages I/II ORSH and pure OSA.

Using a logistic regression model with both variables, supine oxygen saturation and partial pressure of carbon dioxide were significant predictors of nocturnal hypoventilation in stages I/II ORSH with a sensitivity of 61%, specificity of 98%, positive predictive value of 93%, and the AUC of 0.93 at a threshold of 70%. The probability of nocturnal hypoventilation in stages I/II ORSH can be estimated in this sample as follows:

Probability = $e^x / (1 + e^x)$, where $x = 67.314 + (0.457 \times \text{PcCO}_2 \text{ supine}) - (0.925 \times \text{O}_2 \text{ supine})$

ROC curves (**Figure 2** and **Figure 3**) were compared using DeLong and Bootstrap tests. The AUC derived from the two-variable predictive model was significantly better than the

AUC for supine PCO₂ alone ($P < .05$), but not the AUC for supine SpO₂ ($P = .07$).

DISCUSSION

This is the first study to identify a morbidly obese population with nocturnal-only hypoventilation, demonstrating a similar prevalence to OHS with daytime hypercapnia, in a tertiary sleep center cohort of obese patients with a BMI ≥ 40 kg/m² referred for assessment of sleep-disordered breathing. Predictors of nocturnal hypoventilation in stages I/II ORSH are an awake oxygen saturation of ≤ 93% and a P_cCO₂ ≥ 45 mmHg, both performed while in a supine position. This is also the first study to report on the effect of awake supine positioning in stages I/II ORSH, which may have important clinical implications in the early detection of patients who may be at risk of the development of OHS and its associated comorbidities.

The prevalence of stages III/IV OHS in this study was 20% of all those with obstructive events, which is similar to previously reported cohorts from sleep clinics where an aggregate prevalence of 17% was obtained from 10 studies.³ The prevalence of stages I/II ORSH has not previously been reported to our knowledge. The best predictors of stages I/II ORSH in our study were readily measurable in an outpatient setting.

Figure 3—ROC curve analysis for supine PcCO_2 for the dependent variable of hypoventilation, for stages I/II ORSH and pure OSA.

Supine PcCO_2	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR-
≥ 38	100	46	32	100	1.82	0.12
≥ 40	83	61	35	94	2.00	0.36
≥ 42	67	83	50	91	4.00	0.40
≥ 45	44	98	86	88	24.00	0.57

LR = likelihood ratio, NPV = negative predictive value, ORSH = obesity-related sleep hypoventilation, OSA = obstructive sleep apnea, PcCO_2 = capillary carbon dioxide tension, PPV = positive predictive value, ROC = receiver operating characteristic.

Supine SpO_2 and the predictive model combining both SpO_2 and PcCO_2 performed in a supine position were comparable in predicting nocturnal hypoventilation in stages I/II ORSH but the two-variable predictive model had an improved sensitivity. The primary purpose of this model was to help rule in or predict disease rather than as a screening tool to exclude patients not likely to have ORSH. Upright and supine SpO_2 using oximetry have been previously studied in OHS (BMI $> 30 \text{ kg/m}^2$) and very obese populations (BMI $> 50 \text{ kg/m}^2$) respectively.^{17,18} Only weak correlations were found between clinic SpO_2 or partial pressure of arterial carbon dioxide (PaCO_2), and BMI in a prior observational study in patients with OHS.¹⁸ Forced vital capacity also predicted daytime hypercapnia in that population but did not predict nocturnal-only hypoventilation in our cohort. In our study, SpO_2 measured in the supine position while awake had a better AUC than daytime upright SpO_2 (AUC 0.66).

Supine positioning significantly increased PcCO_2 in stages I/II ORSH only ($P < .01$). From a practical perspective, this suggests that patients with a BMI $\geq 40 \text{ kg/m}^2$ may benefit from a blood gas performed after 30 minutes in a supine position. A recent study in an obese population with a mean BMI of 40 kg/m^2 also showed a higher PaCO_2 after 15 minutes in a supine position.¹⁹ This cohort had an OHS prevalence of 57% with a total of 50 subjects in the study.¹⁹ At the higher altitude of Mexico City (2,240 meters above sea level), there was a mean increase of 5 mmHg when the patient was placed in a supine position. Although there was a statistically significant reduction in SpO_2

in the supine position in both stages I/II ORSH and OSA, the reduction in the OSA group was clinically marginal. A recent retrospective study in a population with a BMI $> 50 \text{ kg/m}^2$ also showed that SpO_2 in a supine position was helpful in predicting daytime hypercapnia but not sleep-disordered breathing.¹⁷ No comparative SpO_2 measured in an upright position was presented. Our threshold of 93% is marginally higher than the 91% cutoff (sensitivity 34.8%, specificity 96.6%) in the study by Chung et al.¹⁷ but is lower than the upright overall SpO_2 94% cutoff (sensitivity 83%, specificity 63%) in another study in stages III/IV OHS.¹⁸

The lack of effect of supine positioning in stage III/IV OHS raises the possibility of a more decompensated ventilatory response in this cohort compared to stages I/II ORSH,⁷ such that a positional change has less influence on awake gas exchange. Multiple prior studies have shown reduced ventilatory responses to hypoxia and hypercapnia in stages III/IV OHS.^{20,21} The higher the proportion of REM sleep hypoventilation in stages III/IV OHS, the more insensitive the CO_2 ventilatory response is during wakefulness.²¹ This blunted ventilatory response may initially develop in subjects with nocturnal-only hypoventilation and lead to future diurnal hypoventilation with retention of bicarbonate and subsequent alkalosis suppressing awake ventilation.^{22–24} Once diurnal hypoventilation with retention of bicarbonate and subsequent alkalosis suppressing awake ventilation occurs, it could explain the lack of positional change from an upright to supine position and vice versa, and a persistently raised PCO_2 and reduced SpO_2 .

Although 134 patients were screened for the study, 30% were excluded. The most common reason was a spirometric ratio < 0.7 . Although it is part of the definition of OHS to exclude obstructive lung disease (obesity-related asthma and chronic obstructive lung disease), these criteria may exclude some morbidly obese patients where airflow limitation instead of a predominant restrictive physiology has been described.²⁵ Patients who currently or previously smoked, however, were not excluded if their FEV1/FVC was higher than 0.7. Arterialized capillary blood gases were used in this study. This simple and less painful technique has been validated against arterial blood gas for pH and CO₂ levels but the use of partial pressure of oxygen is limited to the exclusion of hypoxia.²⁶ More recently, capillary bicarbonate levels have been shown to correlate with arterial levels.^{27,28} The ERS task force report also used evening versus morning PCO₂ levels to detect stages I and II of hypoventilation in obesity while we used overnight transcutaneous capnometry. The task force did, however, indicate that nocturnal hypercapnia can be monitored with long-term transcutaneous capnometry. The same pulse oximeter was used for daytime and nighttime assessments; however, varying brands of oximeters may result in differences in absolute cutoff values to predict ORSH. Revalidation in other devices may be necessary and measurement error within oximeters exists. A further limitation is that we did not include patients with a BMI between 30 and 39 kg/m². Subsequent studies on nocturnal or diurnal hypoventilation may benefit from the addition of this group to determine if more patients with pure hypoventilation will be detected. Last, we did not include the three patients without sleep-disordered breathing in the predictive analysis. Most patients without daytime hypercapnia received a diagnosis of either stages I/II ORSH or pure OSA.

In summary, obesity-related sleep hypoventilation without daytime hypercapnia is currently underrecognized. Measurements of SpO₂ and PcCO₂ obtained in a supine position were positive predictors of nocturnal hypoventilation in stages I/II ORSH. A predictive model combining both variables obtained in a supine position had improved sensitivity. Adequate management of hypoventilation during stages I/II ORSH may prevent the development of advanced OHS decompensated ventilatory responses and allow earlier initiation of multimodal treatment. It is possible that stages I/II ORSH may represent distinct OHS phenotypes rather than a less advanced stage within a spectrum of OHS severity. Further studies on the natural history of this group would be instructive but not necessarily feasible as most would require concurrent treatment for OSA.

ABBREVIATIONS

AHI, apnea-hypopnea index
 AUC, area under the curve
 BMI, body mass index
 ESS, Epworth Sleepiness Score
 FEV1, forced expiratory volume in 1 second
 FVC, forced vital capacity
 HCO₃, serum bicarbonate

LR, likelihood ratio

OHS, obesity hypoventilation syndrome

ORSH, obesity-related sleep hypoventilation

OSA, obstructive sleep apnea

PcCO₂, capillary carbon dioxide tension

ROC, receiver operating characteristic

SpO₂, oxygen saturation measured by pulse oximetry

TcCO₂, transcutaneous carbon dioxide monitoring

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