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Postoperative Complications in Patients With Unrecognized Obesity Hypoventilation Syndrome Undergoing Elective Noncardiac Surgery

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BACKGROUND: Among patients with OSA, a higher number of medical morbidities are known to be associated with those who have obesity hypoventilation syndrome (OHS) compared with OSA alone. OHS can pose a higher risk of postoperative complications after elective noncardiac surgery (NCS) and often is unrecognized at the time of surgery. The objective of this study was to retrospectively identify patients with OHS and compare their postoperative outcomes with those of patients with OSA alone.

METHODS: Patients meeting criteria for OHS were identified within a large cohort with OSA who underwent elective NCS at a major tertiary care center. We identified postoperative outcomes associated with OSA and OHS as well as the clinical determinants of OHS (BMI, apnea-hypopnea index [AHI]). Multivariable logistic and linear regression models were used for dichotomous and continuous outcomes, respectively.

RESULTS: Patients with hypercapnia from definite or possible OHS and overlap syndrome are more likely to experience postoperative respiratory failure (OR, 10.9; 95% CI, 3.7-32.3; $P < .0001$), postoperative heart failure (OR, 5.4; 95% CI, 1.9-15.7; $P = .002$), prolonged intubation (OR, 3.1; 95% CI, 0.6-15.3; $P = .2$), postoperative ICU transfer (OR, 10.9; 95% CI, 3.7-32.3; $P < .0001$), and longer ICU (β-coefficient, 0.86; SE, 0.32; $P = .009$) and hospital (β-coefficient, 2.94; SE, 0.87; $P = .0008$) lengths of stay compared with patients with OSA. Among the clinical determinants of OHS, neither BMI nor AHI showed associations with any postoperative outcomes in univariable or multivariable regression.

CONCLUSIONS: Better emphasis is needed on preoperative recognition of hypercapnia among patients with OSA or overlap syndrome undergoing elective NCS.

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KEY WORDS: hypercapnia; obesity hypoventilation syndrome; obstructive sleep apnea; postoperative

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ABBREVIATIONS: ABG = arterial blood gas; AHI = apnea-hypopnea index; CCHS = Cleveland Clinic Health System; CHF = congestive heart failure; EMR = electronic medical record; GA = general anesthesia; NCS = noncardiac surgery; OHS = obesity hypoventilation syndrome; PFT = pulmonary function test; PSG = polysomnography

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A small cohort of studies has reported the prevalence of obesity hypoventilation syndrome (OHS) in the general population to be around 0.3% to 0.4%.[1] Among the only surgical series to report prevalence of OHS is a study in premenopausal women presenting for bariatric surgery with an 8% prevalence of OHS.[2] Among patients with known OSA, the reported prevalence of OHS is between 10% and 20% and is known to increase with obesity to as high as 50% with BMI > 50 kg/m^2.[3] OHS usually is associated with many medical comorbidities and often is undiagnosed or undertreated before elective noncardiac surgery (NCS). The main aims of this study were (1) to characterize the types of postoperative complications associated with elective NCS among patients with known or undiagnosed OHS and (2) to evaluate their association with the main defining characteristics of OHS, that is, BMI, hypercapnia, and apnea-hypopnea index (AHI).

Materials and Methods

The study protocol was approved by the Cleveland Clinic Institutional Review Board, #12-625.

Cohort Identification

A retrospective cohort study was performed with Cleveland Clinic Health System (CCHS) data obtained with the help of Explorys Inc. The Explorys platform provides access to anonymous patient information and can create a large database of electronic medical records (EMRs), allowing for large-scale population studies. The database was queried for all patients with BMI ≥ 30 kg/m^2 who underwent polysomnography (PSG) and NCS and who had arterial blood gases (ABGs) drawn on more than one occasion through CCHS. Laboratory records of ABGs done at various times during these patients' preoperative course and interoperative periods were used to identify the cohort of patients with definite and possible OHS.

Inclusion Criteria: The study inclusion criteria were as follows:

1. BMI > 30 kg/m^2
2. Diagnosis of OSA by PSG at any time before and within 5 years after surgery
3. Arterial hypercapnia ($Paco_2$ ≥ 45 mm Hg) at two separate intervals prior to NCS, single recorded hypercapnia before surgery with persistent hypercapnia (two or more) recorded values at two separate intervals > 30 days apart after NCS, or hypercapnia observed postoperatively from two separate ABGs preceding the index surgery
4. Elective NCS

Among patients selected, those with BMI ≥ 30 kg/m^2; AHI ≥ 5; $Paco_2$ ≥ 45 mm Hg; and absence of significant lung disease, including COPD (FEV_1/FVC < 70%) and very severe restrictive lung disease (FVC < 30%)[4,5] were identified as having definite OHS. To identify those with possible OHS, data were collected among patients who had missing pulmonary function test (PFT) information as long as they met the study inclusion criteria. Patients who met the first three inclusion criteria and underwent NCS were labeled as hypercapnic OSA. Patients with OSA (inclusion criterion 2) undergoing NCS who did not meet the ABG criteria were labeled as OSA (Fig 1). For patients who underwent multiple surgeries, procedures performed closest to the date of PSG and time of ABG were chosen. Data were also collected for patients who may have been primarily admitted with hypercapnia from underlying chronic respiratory failure if they underwent elective NCS during that hospitalization.

Exclusion Criteria: The study exclusion criteria were as follows:

1. Cardiac surgery
2. Thoracic surgery
3. Surgery for upper airway or tracheostomy
4. AHI < 5

Definition of Main Postoperative Outcomes

An EMR review was performed to identify postoperative complications, including prolonged intubation, respiratory failure, reintubation, hypoxemia, tracheostomy, heart failure, and death from the time of surgery until discharge. These data were obtained from the EMR, operative notes, postanesthetic care unit records, and discharge summary notes. Postoperative respiratory failure was defined as the need for prolonged mechanical ventilation (> 24 h), need for endotracheal reintubation, or tracheostomy. Postoperative congestive heart failure (CHF) was defined as new pulmonary edema, elevated jugular venous pressure > 10 mm Hg, use of diuretic or afterload or preload reducing agents, or physician documentation of CHF. Postoperative myocardial infarction was defined as appearance of new Q waves > 0.04 s wide and 1 mV in depth accompanied by elevated levels of troponin T (≥ 0.03 ng/mL) and creatine kinase MB (> 100 IU/L).

Statistical Analysis

Categorical variables are described as numbers and proportions. Continuous variables are described as mean ± SD or median (interquartile range). Comparisons between hypercapnic OSA and OSA groups were done with the χ^2 or Fisher exact test for categorical variables and *t* or Wilcoxon rank sum test for continuous variables. Comparisons among three groups were done with the χ^2 and Kruskal-Wallis tests, respectively. The associations between the type of patient (hypercapnic OSA vs OSA) or the determinants of OHS (BMI, AHI) and individual postoperative outcomes were evaluated with multivariable logistic and linear regression models for dichotomous and continuous outcomes, respectively. Variables included in multivariable models were age, sex, smoking, preoperative positive airway pressure use, type of anesthesia, and history of cardiovascular and respiratory disease. $P < .05$ was considered statistically significant. SAS 9.2 software (SAS Institute Inc) was used for all analyses.

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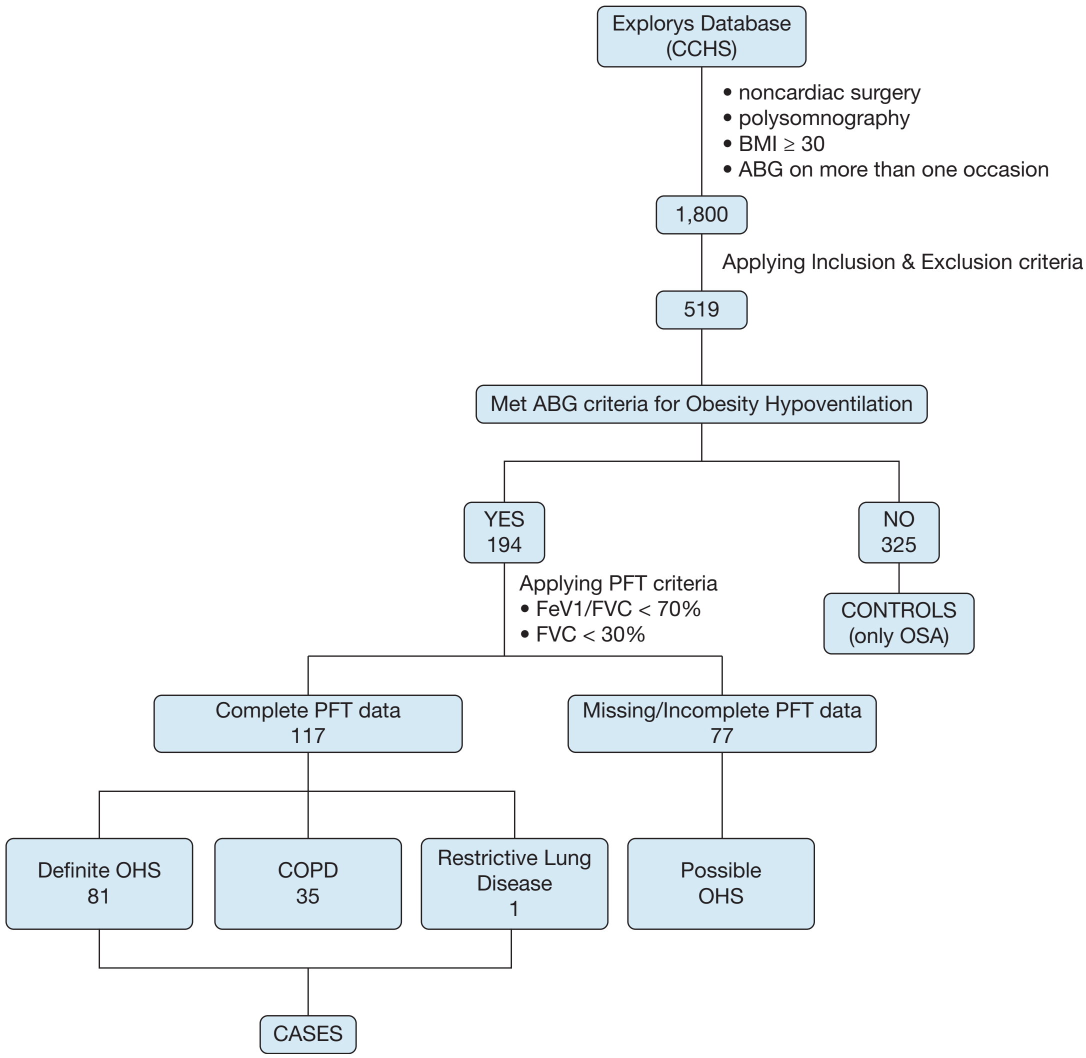


Figure 1 – *Flow diagram for OHS cohort identification and patient selection. ABG = arterial blood gas; CCHS = Cleveland Clinic Health System; OHS = obesity hypoventilation syndrome; PFT = pulmonary function test.*

Results

A total of 1,800 patients with BMI ≥ 30 kg/m^2 who underwent PSG, NCS, and ABG analysis on more than one occasion were identified. One hundred ninety-four met criteria for possible or definite OHS per study protocol. Of these, 139 (72%) had OSA at the time of elective surgery, and the remaining patients (28%) received an OSA diagnosis after PSG within 1 to 5 years postsurgery. Another cohort of 325 had OSA around the time of NCS but either did not meet the ABG criteria for OHS or did not have an ABG drawn at any time during the course of treatment. These patients served as control subjects (OSA group).

Identification of OHS Within the Cohort

Of the 194 patients with OHS identified in the cohort, 117 had complete PFT data. Among these patients, 35 met the criteria for COPD on PFT (FEV_1/FVC < 70%), and one met the criteria of very severe restrictive lung disease (FVC < 30%). Another 81 patients did not meet criteria for COPD (FEV_1/FVC > 70%) and were identified as having definite OHS. The remaining 77 patients had either missing or no PFT data and were identified as having possible OHS (Fig 1). Among the entire cohort of 194 patients, 112 (57%) met the study criteria for obesity hypoventilation with hypercapnia at the time of elective surgery.

Preoperative Morbidity and Postoperative Outcomes

Patients with definite or possible OHS were older and more likely to be men with hypertension, diabetes mellitus, coronary artery disease, CHF, chronic renal failure, COPD, atrial fibrillation or flutter, pulmonary

TABLE 1] Baseline Characteristics of Case and Control Groups

Variable	Hypercapnic OSA (n = 194)	OSA (n = 325)	*P* Value
Age, y	62.7 ± 11.4	57.7 ± 12.6	< .0001
Male sex	86 (49)	142 (45)	.5
AHI	42.27 ± 31.3	37.08 ± 29.8	.08
BMI, kg/m^2	41.35 ± 9.5	38.03 ± 11.0	.001
Preoperative positive airway pressure use	57 (24)	8 (2)	< .0001
History			
Coronary artery disease	87 (46)	64 (20)	< .0001
Myocardial infarction	26 (14)	9 (3)	< .0001
Congestive heart failure	81 (43)	30 (9)	< .0001
COPD	83 (45)	39 (12)	< .0001
Asthma	38 (40)	57 (18)	.4
Atrial fibrillation or flutter	42 (22)	21 (6)	< .0001
Pulmonary hypertension	14 (8)	8 (2)	.006
Hypertension	157 (83)	221 (68)	.0003
Diabetes	101 (53)	96 (30)	< .0001
Chronic renal failure	54 (29)	18 (6)	< .0001
Stroke	25 (13)	17 (5)	.001
Smoking			< .0001
Current	16 (9)	14 (4)	...
Past	80 (43)	85 (26)	...
No	90 (48)	226 (70)	...
Type of surgery			...
General	55 (28)	131 (40)	...
Orthopedic	42 (22)	83 (26)	...
Vascular	37 (19)	17 (5)	...
Neurologic	22 (11)	25 (8)	...
Urologic	21 (11)	18 (6)	...
Colorectal	7 (4)	15 (5)	...
Gynecologic	4 (2)	27 (8)	...
Other	6 (3)	9 (3)	...
Type of anesthesia			< .0001
General	126 (69)	256 (82)	...
Spinal	20 (11)	31 (10)	...
Epidural, spinal + epidural	4 (2)	16 (5)	...
Paravertebral block	2 (1)	3 (1)	...
MAC, local + MAC	31 (17)	6 (2)	...
OSA severity			...
AHI 5-15	30 (15)	84 (26)	.3
AHI > 15-30	45 (23)	88 (27)	.17
AHI > 30	78 (40)	151 (46)	.18

Data are presented as mean ± SD or No. (%). AHI = apnea-hypopnea index; MAC = monitored anesthesia care.

hypertension, and stroke compared with patients with OSA (Table 1). General anesthesia (GA) was used less often in patients known or suspected to have OHS prior to NCS (69% vs 82%, $P < .0001$). Monitored anesthesia care and monitored anesthesia care with local anesthesia were used more often in patients with known or suspected OHS (17% vs 2%, not statistically significant). Patients with hypercapnia from definite or possible OHS

TABLE 2] Adjusted Risk of Postoperative Outcomes in Patients With Definite OHS, Possible OHS, and Overlap Syndrome Versus Patients With OSA

Postoperative Outcome	Hypercapnic OSA (n = 194)	OSA (n = 325)	OR (95% CI)	*P* Value
Respiratory failure	39 (21)	8 (2)	10.9 (3.7-32.3)	< .0001
Heart failure	15 (8)	0	5.4 (1.9-15.7)	.002
Prolonged intubation	24 (13)	12 (4)	3.1 (0.6-15.3)	.2
Reintubation	12 (6)	5 (2)	1.7 (0.2-13.4)	.6
Tracheostomy	4 (2)	3 (1)	3.8 (1.7-8.6)	.002
ICU transfer	41 (21)	19 (6)	10.9 (3.7-32.3)	< .0001
Death at 30 d	2 (1)	0	...[a]	...
Death at 1 y	10 (5)	2 (0.6)	0.9 (0.1-7.5)	.9

Data are presented as No. (%) unless otherwise indicated. Adjusted for all patient variables in Table 1. IQR = interquartile range; OHS = obesity hypoventilation syndrome.
[a]Scarce number of events.

and overlap syndrome were more likely to experience postoperative respiratory failure (OR, 10.9; 95% CI, 3.7-32.3; *P* < .0001), postoperative heart failure (OR, 5.4; 95% CI, 1.9-15.7; *P* = .002), prolonged intubation (OR, 3.1; 95% CI, 0.6-15.3; *P* = .2), postoperative ICU transfer (OR, 10.9; 95% CI, 3.7-32.3; *P* < .0001), and longer ICU (β-coefficient, 0.86; SE, 0.32; *P* = .009) and hospital (β-coefficient, 2.94; SE, 0.87; *P* = .0008) lengths of stay (Tables 2, 3). Among the clinical determinants of OHS, neither BMI nor AHI showed associations with any postoperative outcomes in univariable or multivariable regression analyses (Table 4). In obese patients (BMI ≥ 30 kg/m^2) with OSA, the presence of hypercapnia regardless of whether it was a consequence of obesity hypoventilation or associated COPD seemed to contribute the most to poor postoperative outcomes compared with patients with OSA without hypercapnia. We also explored the association between OSA severity categories (mild, moderate, and severe based on AHI) and outcomes and found no association (data not shown).

Discussion

Among patients with OSA by PSG, significantly worse postoperative outcomes were noted if patients were previously known to be hypercapnic from OHS with or without overlap syndrome. In our experience, this study is the first to report perioperative outcomes in patients with known or suspected OHS. The only other time postoperative outcomes have been reported among patients with a high likelihood of OHS was with the use of the Obesity Surgery Mortality Risk Score in those undergoing bariatric surgery. The Obesity Surgery Mortality Risk Score assigns one point to each of five preoperative variables, namely male sex, BMI > 50 kg/m^2, pulmonary hypertension, OHS, prior thromboembolism, or presence of an inferior vena cava filter.[6] Mortality rates ranged from 0.2% (in low-risk class of no or one comorbidity) to 2.4% (in high-risk class of four to five comorbidities). We previously reported a higher likelihood of postoperative complications, especially respiratory failure, compared with eucapnic OSA (44% vs 2.6%, respectively).

The present study demonstrates that compared with patients with OSA, those with presumed or definite OHS have higher associated medical morbidities as shown previously.[7,8] Additionally, although we demonstrate the association of preoperative hypercapnia (regardless of

TABLE 3] Adjusted Length of ICU and Hospital Postoperative Stay in Patients With Definite OHS, Possible OHS and Overlap Syndrome Versus Patients With OSA

Variables	Hypercapnic OSA (n = 194)	OSA (n = 325)	β ± SE	*P*
ICU length of stay, d			0.86 ± 0.32	.009
Median (IQR)	0 (0-0)	0 (0-0)		
Mean ± SD	0.12 (0.93)	1.04 (3.8)		
Hospital length of stay, d			2.94 ± 0.87	.0008
Median (IQR)	5 (3-9)	0 (0-4)		
Mean ± SD	7.3 (8.2)	2.8 (5.1)		

Data are presented as No. (%) unless otherwise indicated. Adjusted for all patient variables in Table 1. See Table 2 legend for expansion of abbreviations.

TABLE 4] Independent Effect of BMI and AHI on Postoperative Outcomes in Patients With Definite and Possible OHS and Overlap Syndrome

Postoperative Outcome	BMI		AHI[a]	
	Adjusted Statistic	*P* Value	Adjusted Statistic	*P* Value
Respiratory failure	0.99 (0.95-1.03)	...	1.01 (0.99-1.02)	...
Heart failure	0.94 (0.85-1.04)	...	1.00 (0.98-1.02)	...
Prolonged intubation	1.01 (0.97-1.05)	...	1.00 (0.99-1.02)	...
Reintubation	0.99 (0.93-1.05)	...	1.01 (0.99-1.02)	...
ICU transfer	0.99 (0.96-1.02)	...	1.01 (1.00-1.02)	...
ICU length of stay	0.0073 ± 0.01	.80	0.009 ± 0.004	.006
Hospital length of stay	0.006 ± 0.03	.90	0.009 ± 0.01	.40

Data are presented as OR (95% CI) or β ± SE. See Table 1 and 2 legends for expansion of abbreviations.
[a]Models were adjusted for BMI.

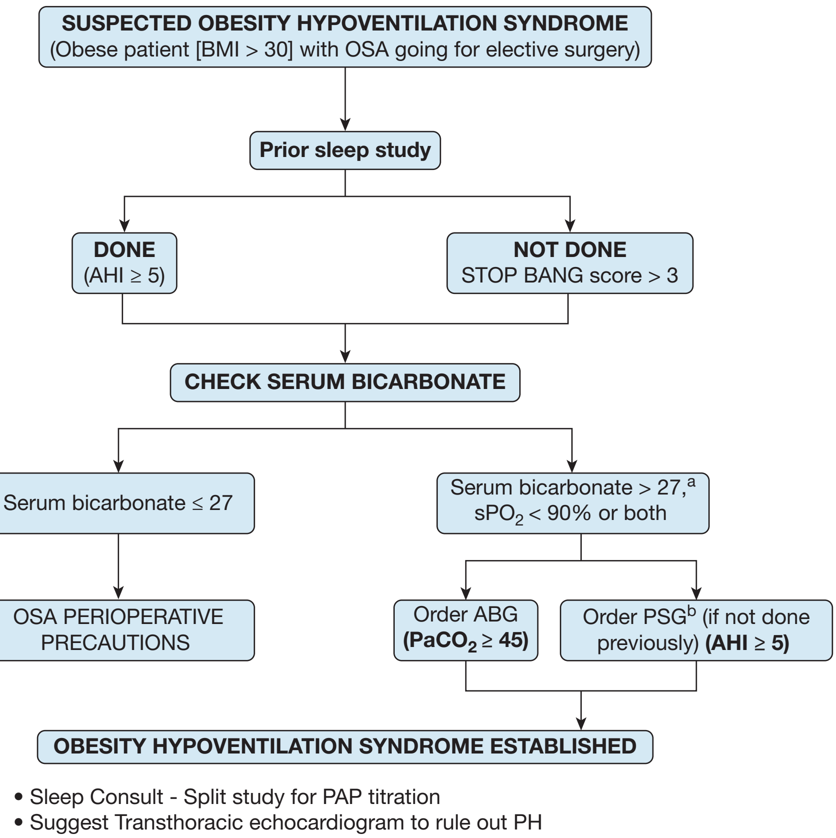
contributing etiology) with adverse postoperative outcomes, we cannot say whether the hypercapnia by itself or the associated imposed severe hypoxia is the causal factor for worse postoperative outcomes in patients with OHS. Borel et al[9] outlined hypoxemia-induced activation of the inflammatory cascade, endothelial dysfunction, and organ dysfunction in patients with OHS. Although numerous reports of the presence of OSA as a risk factor for postoperative complications exist, OSA severity as measured by AHI has not been shown to correlate with postoperative complications.[10-12] BMI, on the other hand, has been more controversial as posing any kind of perioperative risk.[13,14] Furthermore, it is possible that the lower incidence of postoperative respiratory failure in the current OSA cohort (2%) compared with our previous study cohort (4.9%)[11] may be most likely due to reclassification of some patients with OSA to OHS over the years 2002 to 2013. Although it is possible that the majority of respiratory complications in patients with OSA undergoing NCS are dominated by the presence of underlying hypercapnia, the incidence of ICU transfer (6%) and reintubation (2%) remain unchanged in the OSA groups in both studies.

In the present study, poor outcomes were noted among patients with OHS or overlap syndrome, regardless of preferentially lesser use of GA among patients known or suspected to have OHS or overlap syndrome. We propose that prior diagnosis or suspicion of OHS must have possibly led to lesser use of GA among these patients compared with those with OSA alone. Until now, however, no data have supported this practice, which may represent a general sense of caution on the part of the anesthesiologist to minimize cardiopulmonary complications. The American Society of Anesthesiologists advisory on preoperative management had recommended preferred use of regional anesthesia over GA among patients known to have OSA.[15] Given that recommendation, we are still surprised by the frequent use of GA (82%) among patients with OSA in the present study, although not all patients were known to have OSA at the time of surgery. In its revised guidelines, however, the American Society of Anesthesiologists recommends preferred use of GA with a secure airway over deep sedation without a secure airway, particularly for procedures that may mechanically compromise the airway.[16] Memtsoudis et al[17] reported that the use of neuraxial anesthesia has been associated with a decreased rate of major complications among patients with OSA.

The more crucial issue to emphasize is that most patients in the present study were not known to have OHS at the time of elective NCS. OHS is characterized by a triad of chronic daytime hypercapnia ($Paco_2$ $\geq$ 45 mm Hg), sleep-disordered breathing, and obesity with a BMI > 30 kg/m^2.[3] ABG measurements are important for confirming chronic diurnal hypercapnia; however, these often cannot be obtained in routine outpatient preoperative settings. Moreover, the diagnosis of OHS can only be established after excluding other possible causes of hypercapnia, such as severe obstructive airway disease, severe kyphoscoliosis, or interstitial lung disease and neuromuscular disorders. Given these practical difficulties in establishing the diagnostic cohort, no studies to date have reported postoperative outcomes among patients with OHS.

The current results suggest that wherever postoperative respiratory failure occurs in an obese patient with OSA and without other explanation, the possibility of sleep-related hypoventilation should be considered. Obese patients (mean BMI, 39 kg/m^2) known to have severe

Figure 2 – *Preoperative decision tree in patients with suspected obesity hypoventilation syndrome. [a]When metabolic alkalosis is not explained by causes other than chronic respiratory acidosis. [b]Whenever possible, PSG should be arranged before surgery in this situation. AHI = apnea-hypopnea index; PAP = positive airway pressure; PH = pulmonary hypertension; PSG = polysomnography; sPO$_2$ = oxygen saturation as measured by pulse oximetry. See Figure 1 legend for expansion of other abbreviation. (Adapted with permission from Kaw et al.[18])*



OSA (mean AHI, 64) and restrictive chest mechanics (FEV$_1$ < 71% predicted, FVC < 85% predicted) are more likely to have OHS.[1] In a cohort of obese patients referred to a sleep laboratory for suspected OSA, a serum bicarbonate threshold of 27 mEq/L was 92% sensitive in predicting hypercapnia on ABG analysis.[3] Because BMI in that range is invariably associated with restrictive lung mechanics, diurnal oxygen desaturations < 90% (corresponding Pao$_2$ < 60-65 mm Hg) and serum bicarbonate > 27 mEq/L (in the absence of any other explanation) help to increase the suspicion for diurnal hypercapnia, which may then be confirmed by obtaining an ABG before the patient goes for any kind of surgery (Fig 2).[18] Recent data, however, have proposed a spectrum of OHS among obese patients with only elevated serum bicarbonate levels and no diurnal hypercapnia.[19] Additionally, measurement of end-tidal CO$_2$, where possible, can be used as a substitute for ABG, especially in the group with no diurnal hypercapnia.[20]

Among obese patients who have not been previously tested for OSA at the time of surgery, the STOP-Bang questionnaire is a validated screening tool; however, at scores > 3, it loses the specificity for moderate (43%) and severe OSA (37%). Chung et al[21] showed that the addition of a serum bicarbonate level > 28 mmol/L increases the specificity of all OSA severities to 85.2% and that of severe OSA to 79.4%. Greater AHI has been reported among patients with OHS compared with those with eucapnic OSA (mean difference, 12.51; 95% CI, 6.59-18.44; P < .0001).[1] Hence, if OSA is suspected in obese preoperative patients based on clinical signs and symptoms and a STOP-Bang score > 3, serum bicarbonate > 27 mEq/L should prompt a preoperative PSG before elective NCS whenever possible (Fig 2).

The most important limitation of this study is that OHS was, for the most part, unrecognized at the time of surgery. Although all cohort participants were obese (BMI ≥ 30 kg/m^2), some were given a diagnosis of OSA within a certain time frame after surgery, and suspicion of OHS rested on hypercapnia based on ABG drawn in relation to NCS as outlined in the inclusion criteria. The best way to establish these outcomes is by way of a prospective study where ABGs are routinely drawn on patients with suspected OHS before surgery, which will require preoperative and postoperative management of hypercapnia and possible reduction in adverse postoperative outcomes. This, in fact, is the main point of the current observational data; ABGs, even among obese patients, are obtained only when significant desaturations are noted or patients become symptomatic before surgery. Another limitation is that the OSA study population did not have ABGs drawn, so it is possible that some cases of OHS may have existed in the OSA group. However, assuming that happened, the study would show even worse outcomes among the OHS cohort compared with patients with OSA alone. We also did not have pulmonary function data on all patients, so contributions from severe restrictive lung disease and underestimation of the role of undiagnosed obstructive lung disease are possible. Finally, the outcomes are limited to the hospital course until discharge after NCS. Given that OHS is a chronic condition with a dismal outcome, we cannot comment on the impact of NCS on survival at 6 months or 1 year in patients with known or suspected OHS.

Conclusions

Among patients with OSA, a higher number of medical morbidities are known to be associated with those who have OHS compared with OSA alone. Consequently, a higher number of postoperative complications are expected in this group, regardless of BMI or AHI. The risk and frequency of postoperative complications are also higher in patients with OSA and COPD (overlap syndrome) and appear to be no different than that associated with OHS.

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Author contributions: R. K. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. R. K. contributed to the study conception, data collection, data analysis and interpretation, and writing and final approval of the manuscript; P. B., H. P., A. R., and A. D. contributed to the data collection and approval of the final manuscript; A. V. H. contributed to the statistical analysis and writing and final approval of the manuscript; and L. S. A. contributed to the study design, data interpretation, and writing and final approval of the manuscript.

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