CHEST

Original Research

SLEEP DISORDERS

Serum Bicarbonate Level Improves Specificity of STOP-Bang Screening for Obstructive Sleep Apnea

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Background: **The STOP-Bang questionnaire is a validated screening tool for the identification of surgical patients with obstructive sleep apnea (OSA). A STOP-Bang score ≥ 3 is highly sensitive but only moderately specific. Apnea/hypopnea during sleep can lead to intermittent hypercapnia and may result in serum bicarbonate (HCO_3^-) retention. The addition of serum HCO_3^- level to the STOP-Bang questionnaire may improve its specificity.**

Methods: **Four thousand seventy-seven preoperative patients were approached for consent and screened by the STOP-Bang questionnaire. Polysomnography was performed and preoperative HCO_3^- level was collected in 384 patients. Study participants were randomly assigned to a derivation or validation cohort. Predictive parameters (sensitivity, specificity, positive and negative predictive values) for STOP-Bang score and serum HCO_3^- level were calculated.**

Results: **In the derivation cohort, with a STOP-Bang score ≥ 3, the specificity for all OSA, moderate/severe OSA, and severe OSA was 37.0%, 30.4%, and 27.7%, respectively. HCO_3^- level of 28 mmol/L was selected as a cutoff for analysis. With the addition of HCO_3^- level ≥ 28 mmol/L to the STOP-Bang score ≥ 3, the specificity for all OSA, moderate/severe OSA, and severe OSA improved to 85.2%, 81.7%, and 79.7%, respectively. Similar improvement was observed in the validation cohort.**

Conclusion: **Serum HCO_3^- level increases the specificity of STOP-Bang screening in predicting moderate/severe OSA. We propose a two-step screening process. The first step uses a STOP-Bang score to screen patients, and the second step uses serum HCO_3^- level in those with a STOP-Bang score ≥ 3 for increased specificity.** ***CHEST 2013; 143(5):1284–1293***

Abbreviations: AHI = apnea-hypopnea index; HCO_3^- = bicarbonate; NPV = negative predictive value; OHS = obesity hypoventilation syndrome; OSA = obstructive sleep apnea; PPV = positive predictive value; PSG = polysomnography

Obstructive sleep apnea (OSA) is the most prevalent breathing disturbance in sleep, affecting 2% to 26% of the general population[1] and 3% to 7% of patients undergoing surgery.[2-5] An estimated 82% of men and 92% of women with moderate/severe OSA remain undiagnosed.[6] Untreated OSA is associated with increased mortality and morbidity.[7,8] Surgical patients with OSA are at higher risk for postoperative complications, ICU admissions, and increased duration of hospital stay.[9-11] A preoperative screening questionnaire may be an important tool to identify patients with undiagnosed OSA.[2,4,5,12]

The STOP-Bang questionnaire is a screening tool validated in surgical patients.[2] It consists of eight yes/no

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questions, with each positive response generating 1 point. A score ≥ 3 yields high sensitivity for moderate and severe OSA and excludes OSA in those patients with a STOP-Bang score < 3.[2] However, a score ≥ 3 only yields a specificity of 43% and 37% for moderate and severe OSA, respectively, suggesting a high false-positive rate.

Chronic daytime hypercapnia ($PaCO_2 \geq 45$ mm Hg) is found in 10% to 38% of patients with OSA.[13] As OSA severity increases (as measured by the apnea-hypopnea index [AHI] or the degree of nocturnal hypoxemia), the risk of chronic daytime hypercapnia may increase.[14] It is plausible that serum bicarbonate (HCO_3^-) may increase in moderate/severe OSA without reaching overt chronic daytime hypercapnia. A mathematical model was proposed in which nocturnal intermittent hypercapnia due to obstructive apnea/hypopnea leads to renal HCO_3^- retention to compensate for acute respiratory acidosis, particularly if the time constant for HCO_3^- excretion was increased.[15]

We hypothesized that the addition of serum HCO_3^- level to the STOP-Bang questionnaire would improve its specificity for detecting OSA. The objective of this study was to evaluate the predictive parameters of the STOP-Bang questionnaire at various levels of serum HCO_3^-.

Materials and Methods

Patient Population

The study was conducted in the preoperative clinics of Toronto Western Hospital and Mount Sinai Hospital, Toronto, Ontario, Canada. Institutional review board approval was obtained from both institutions (MSH: 06-0143-E and 07-0183-E; UHN: 06-0135-AE and 07-0515-AE). Patients aged ≥ 18 years with an American Society of Anesthesiologists physical status of 1 to 4 who were scheduled to undergo elective procedures in general surgery, gynecology, orthopedics, urology, plastics, or ophthalmology were approached for polysomnography (PSG) consent. Patients who did not consent or were expected to have abnormal EEG findings (eg, brain tumor, epilepsy surgery, patients with deep brain stimulator) were excluded.

Preoperative Screening With the STOP-Bang Questionnaire and Polysomnography

The consented patients were asked to complete the STOP questionnaire. BMI, age, neck circumference, and sex (Bang) were collected. Patients then underwent a portable PSG study at home. We analyzed serum HCO_3^- level , if available as part of the screening preoperative process, within 3 months of the date of surgery.

Portable PSG

The portable PSG was performed with a level 2 portable sleep device (Embletta X100), which has been demonstrated to be a reliable alternative for standard PSG in surgical patients, with very low failure rate.[16] The recording montage consisted of two EEG channels (C3 and C4), electrooculogram (left or right), and chin muscle electromyograms. Thoracic and abdominal respiratory effort bands, body position sensors, and pulse oximeter were used. The device was attached to patients by a trained PSG technician and picked up the next morning. The overnight recordings were unattended. A certified polysomnographic technologist scored the recordings under the supervision of a sleep physician. The technologist was blinded to the results of the STOP-Bang questionnaire. The sleep stages and AHI were scored according to the American Academy of Sleep Medicine Task Force recommendations.[17] Apnea was defined as at least 90% drop in airflow from baseline, which lasts at least 10 s. Hypopnea was defined as at least 30% reduction in airflow that lasts at least 10 s and is associated with at least 4% decrease in arterial oxyhemoglobin saturation. Apneas were classified as obstructive if respiratory efforts were present and central if respiratory efforts were absent during the event. OSA was diagnosed if AHI was > 5. Based on AHI values, the severity of OSA was classified as mild (AHI, 5-15), moderate (AHI > 15-30), and severe (AHI > 30).

Derivation and Validation of Prediction Model

Model derivation and validation were based on a half split-sample validation method from a cohort of patients who completed the STOP-Bang questionnaire, underwent PSG, and provided blood for serum HCO_3^- determination. Study participants were randomly assigned to a derivation cohort and validation cohort using a computer random number generator.

Sample Size Calculation

The calculation of sample size was performed according to the method reported by Obuchowski.[18] Briefly, two separate calculations of sample size were performed based on either estimated sensitivity using the precision (potential error) of sensitivity, expected power, a type 1 error, and estimated prevalence; or specificity, the precision of specificity, expected power, type 1 error, and prevalence. The larger number of the two was chosen as the sample size. Based on the previous publication by Chung and colleagues,[2] the following parameters were used to calculate the sample size: a sensitivity of 0.88, a precision of 0.09, an OSA prevalence rate of 25%, a type 1 error of 0.05, and a power of 0.8 were used to calculate the sample size. The result was 200. The number calculated based on a specificity of 0.8 was 101. Therefore, 200 patients were initially chosen as the sample size.

Statistical Analysis

Statistical analyses were performed using SAS version 9.2 (SAS Institute, Inc). Demographic data were described using descriptive statistics. Median and interquartile range were used for non-normally distributed continuous data, and comparisons were done using Mann-Whitney *U* test. Categorical data were described as frequency and percentage with 95% CI, and statistical significance was determined by χ^2 or Fisher exact test. Continuous data that were normally distributed were presented as mean ± SD, and the Student *t* test was used to calculate the *P* value. Comparisons were considered statistically significant if the *P* value was ≤ .05.

The relationship between AHI and serum HCO_3^- level was assessed by Pearson correlation analysis and simple linear regression. To assess the performance of the STOP-Bang score plus serum HCO_3^- level metric, multiple 2×2 contingency tables were used to calculate the sensitivity, specificity, positive predictive values (PPVs), and negative predictive values (NPVs) for each cutoff value. The response was dichotomized using AHI > 5, AHI > 15, and AHI > 30 as the cutoff value. OR was calculated by using logistic regression.

Results

A total of 4,077 patients were approached for consent and screened for OSA by the STOP-Bang questionnaire. Six hundred fifty of 908 consented patients completed the portable PSG. Preoperative HCO_3^- level was measured in 59% (384 of 650) of patients who completed PSG (Fig 1). BMI, age, neck circumference, and sex (Bang) of various patient groups are shown in Table 1. These characteristics are similar between patients who underwent PSG and those who did not. In patients who underwent PSG, these characteristics are also similar between patients with preoperative serum HCO_3^- level determined and those without.

Of the 384 patients who were analyzed, 276 (71.9%) had AHI > 5 (all OSA), 159 (41.4%) had AHI > 15 (moderate/severe OSA), and 73 (19.0%) had AHI > 30 (severe OSA). Pearson correlation analysis showed that there was a statistically significant correlation between AHI and serum HCO_3^- level (correlation coefficient of 0.1255, $P = .0138$) (Fig 2). The 384 patients were dichotomized by a serum HCO_3^- level of 28 mmol/L, which represents the 75th percentile of the cohort. To further evaluate the relationship between serum HCO_3^- level and OSA severity, we classified the cohort into four groups: non-OSA (AHI ≤ 5), mild OSA (AHI > 5-15), moderate OSA (AHI > 15-30), and severe OSA (AHI > 30). As the severity of OSA increases, the proportion of patients with serum HCO_3^- level ≥ 28 mmol/L also increases (Fig 3). There was no significant difference between the group with non-OSA and mild OSA (25.9% vs 30.8%, $P = .42$). However, the proportion of patients with serum HCO_3^- level ≥ 28 mmol/L in moderate or severe OSA were significantly higher than patients without OSA (39.5%/43.8% vs 25.9%, $P < .05$) (e-Table 1).

There were no statistically significant differences in serum HCO_3^- level in patients with or without hypertension (26.4 ± 3 mmol/L vs 26.4 ± 3 mmol/L, $P > .05$), coronary artery disease (26.5 ± 4 mmol/L vs 26.4 ± 3 mmol/L, $P > .05$), smoking history (26.3 ± 3 mmol/L vs 26.4 ± 3 mmol/L, $P > .05$), asthma (26.7 ± 3 mmol/L vs 26.3 ± 3 mmol/L, $P > .05$), COPD (26.4 ± 3 mmol/L vs 26.4 ± 3 mmol/L, $P > .05$), and type 2 diabetes mellitus (26.4 ± 4 mmol/L vs 26.4 ± 3 mmol/L, $P > .05$). There was no statistically significant difference in the serum HCO_3^- level between patients receiving diuretic treatment or not (26.3 ± 3 mmol/L vs 26.6 ± 3 mmol/L, $P > .05$) (e-Table 2).

The cohort was randomly split into 192 patients for the derivation set and 192 for the validation set. The demographic data and the distribution of STOP-Bang score are similar between the two cohorts (Fig 4, Table 2). In the derivation cohort, when serum HCO_3^- level was used to predict OSA, the area under the receiver operating characteristic curve (95% CI) was 0.54 (0.44-0.63), 0.59 (0.51-0.67), and 0.60 (0.50-0.69) for all OSA, moderate/severe OSA, and severe OSA, respectively. Although the areas under the receiver operating characteristic curves do not show perfect

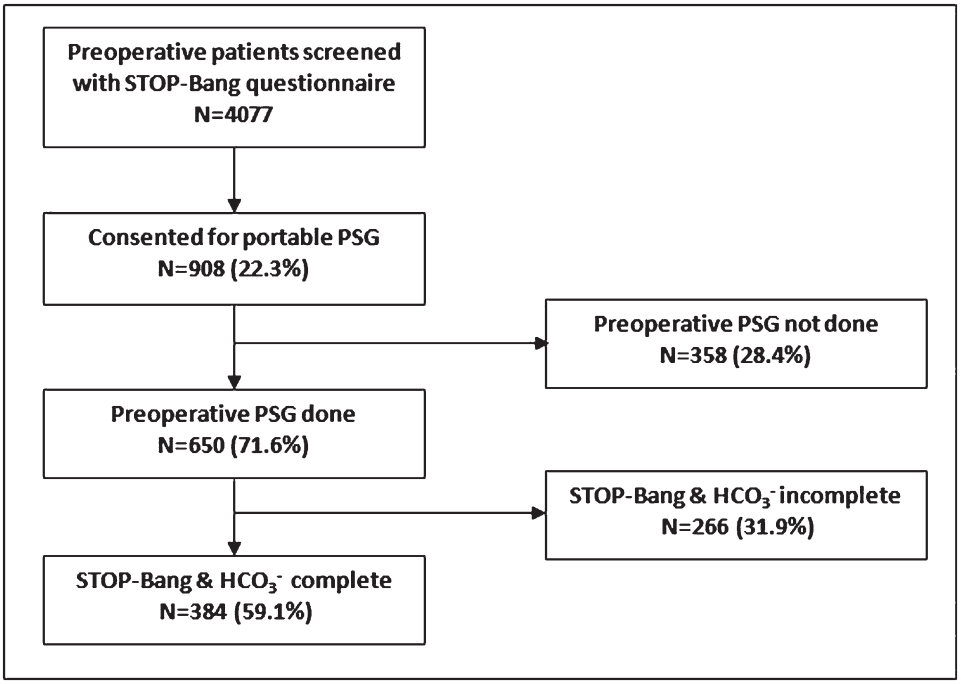

Figure 1. Screening flowchart of patients. Number and percentage of patients are provided for the different groups. HCO_3^- = bicarbonate; PSG = polysomnography.

Table 1—*Characteristic of Patients*

Characteristic	PSG Not Done	PSG Done		
		Total	STOP-Bang and HCO_3^- Measurement Complete	STOP-Bang and HCO_3^- Measurement Incomplete
No.	3,427	650	384	266
Sex, male/female, No. (%)	1,508/1,919 (44/56)	297/353 (46/54)	175/209 (46/54)	122/144 (46/54)
Age, y	58 ± 15	60 ± 12	60 ± 12	59 ± 13
BMI, kg/m²	28.2 ± 6	30.7 ± 7	30.9 ± 7	30.3 ± 7
Neck circumference cm	37.6 ± 5	38.9 ± 4	38.8 ± 4	39.0 ± 3

Data are shown as mean ± SD unless otherwise noted. HCO_3^- = bicarbonate; PSG = polysomnography.

discrimination, the CIs for moderate/severe OSA and severe OSA do not include 0.5, confirming the diagnostic ability of serum HCO_3^- level. The analysis based on the receiver operating characteristic curve shows that a serum HCO_3^- level of 27 mmol/L is the best cutoff. However, the specificity (95% CI) of serum HCO_3^- level ≥ 27 for all OSA, moderate/severe OSA, or severe OSA was low at 57.9% (44.1-70.9), 54.7% (45.2-63.9), and 50.6% (42.6-58.7). On the other hand, serum HCO_3^- level ≥ 28 mmol/L showed greater specificity for all OSA, moderate/severe OSA, or severe OSA at 75.9% (62.4-86.5), 73.0% (64.0-80.9), and 70.3% (62.5-77.4), respectively (e-Table 3).

In the derivation cohort, the specificity (95% CI) of a STOP-Bang score ≥ 3 for OSA, moderate/severe OSA, and severe OSA was 37.0% (24.3-51.3), 30.4% (22.2-39.7), and 27.7% (20.9-35.5), respectively. When serum HCO_3^- level ≥ 28 mmol/L was added to STOP-Bang ≥ 3, the specificity was improved to 85.2% (72.9-93.4), 81.7% (73.5-83.3), and 79.4% (72.1-85.4) for all OSA, moderate/severe OSA, and severe OSA, respectively (Table 3). Similar improvement in specificity was observed in the validation cohort (Table 4). The combination of serum HCO_3^- level ≥ 28 and STOP-Bang score ≥ 3 increased specificity at the expense of sensitivity.

We have recently found that a high STOP-Bang score (≥ 6) is associated with a high probability of moderate/severe OSA.[19] From the derivation cohort, we identified patients with STOP-Bang score ≥ 6. They were different from patients with STOP-Bang score ≥ 3 and serum HCO_3^- level ≥ 28 mmol/L, with some overlap. Eighteen patients have STOP-Bang score ≥ 3 and HCO_3^- level ≥ 28 mmol/L, and 29 patients

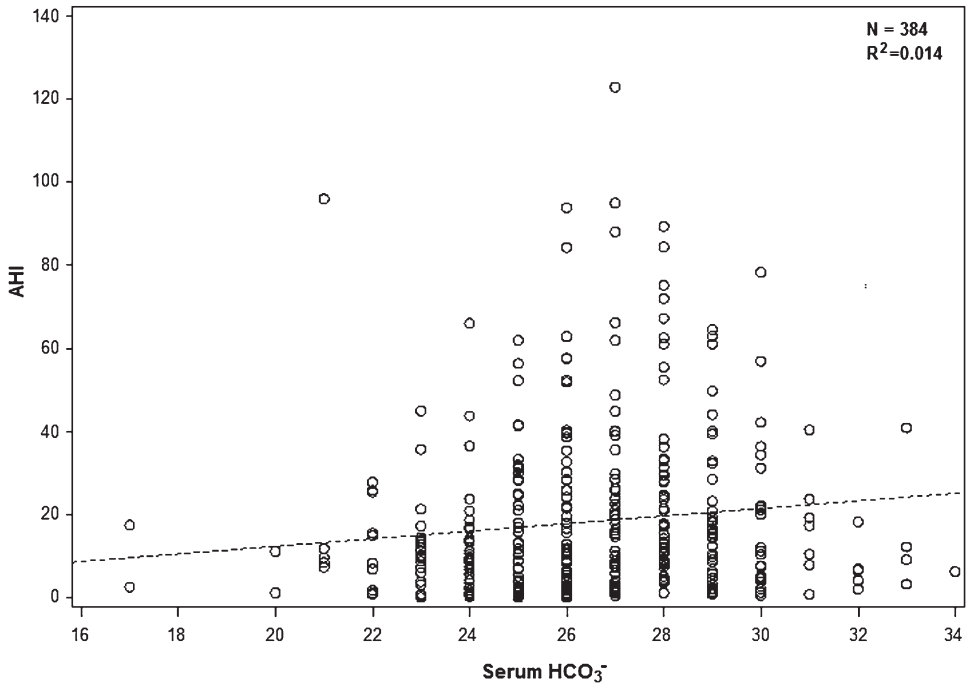

FIGURE 2. Scatterplot matrix of AHI and serum HCO_3^- level. AHI = apnea-hypopnea index. See Figure 1 legend for expansion of other abbreviation.

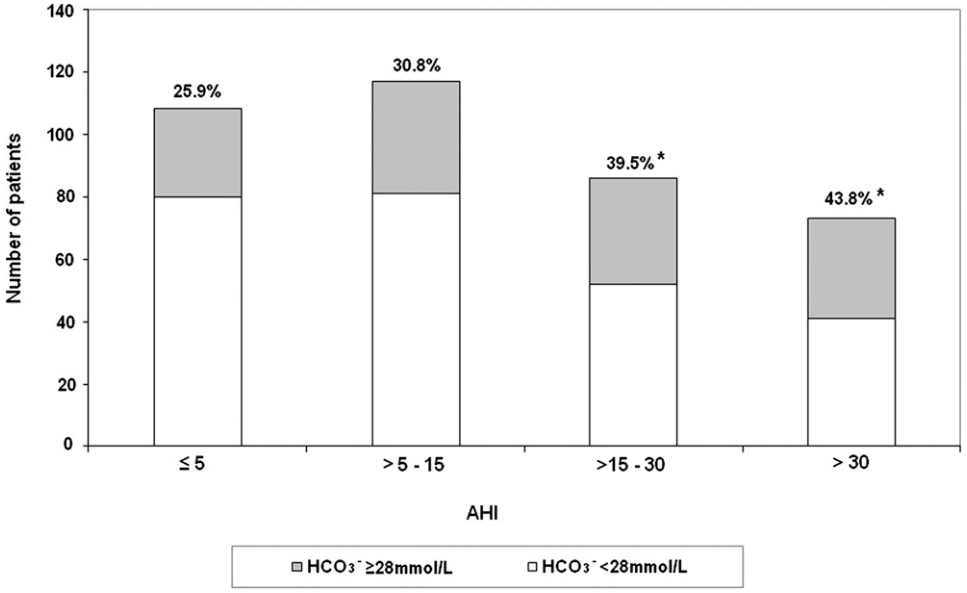

FIGURE 3. Proportion of patients without obstructive sleep apnea (OSA) and patients with mild, moderate, and severe OSA with serum HCO_3^- level ≥ 28 mmol/L. *$P < .05$ for moderate OSA or severe OSA vs non-OSA. See Figure 1 legend for expansion of other abbreviation.

have STOP-Bang score ≥ 6. Eleven patients could be identified by either criterion (Fig 5). Similar result was found in the validation cohort.

Based on the previous analysis, a two-step screening process was developed (Fig 6). The first step consists of using STOP-Bang to screen all 384 patients. In patients with STOP-Bang score < 3, the predicted probability (95% CI) of having OSA, moderate/severe OSA, or severe OSA was determined to be 0.52 (0.41-0.63), 0.24 (0.16-0.34), and 0.06 (0.03-0.14), respectively. These patients were identified as most unlikely to have moderate/severe OSA.

For the 304 patients with STOP-Bang score ≥ 3, the second step applied either STOP-Bang ≥ 6 or serum HCO_3^- level ≥ 28 mmol/L to further identify patients at high risk of OSA. The predictive probability (95% CI) was 0.53 (0.45-0.61) for moderate/severe OSA and 0.31 (0.24-0.39) for severe OSA, respectively (Fig 6). There is a twofold increase in the probability of having severe OSA for patients with STOP-Bang score ≥ 6 or STOP-Bang score ≥ 3 plus serum HCO_3^- level ≥ 28 mmol/L than those who did not meet these criteria (Fig 6).

DISCUSSION

In this study, the addition of serum HCO_3^- level to a STOP-Bang score ≥ 3 significantly improved the specificity of predicting moderate/severe OSA. Using the combination of HCO_3^- level ≥ 28 mmol/L and STOP-Bang score ≥ 3, the specificity for all OSA, moderate/severe OSA, and severe OSA were 85.2%, 81.7%, and 79.4%, respectively. As previously shown in treadmill exercise testing and diagnostic mammography,[20,21] sensitivity and specificity are affected by the severity of the disease and not the prevalence. Similarly, our study demonstrated an increase in specificity from 79.4% to 95.5% for severe OSA in patients with serum HCO_3^- level ≥ 30 mmol/L, compared with those with serum HCO_3^- level ≥ 28 mmol/L. Serum HCO_3^- level is easily measured from a venous blood sample and can be ordered along with other laboratory tests in the preoperative clinic. Thus, it is a valuable and applicable tool in the preoperative OSA risk stratification.

Surgical patients with OSA are at higher risk for postoperative complications.[9,11,22] It is, therefore, imperative to identify these patients preoperatively. The gold standard for OSA diagnosis, an in-laboratory polysomnography, is time consuming and costly. Furthermore, most sleep centers typically have a long waiting list, and it is difficult to establish a timely diagnosis preoperatively. Screening tools become increasingly important as they identify patients at high risk of OSA such that the appropriate testing and treatment can be arranged. Two systematic reviews and meta-analyses of clinical screening tools for OSA identified high methodological quality and easy-to-use features of the STOP-Bang questionnaire,[23,24] thereby facilitating routine application in busy clinical settings, such as preoperative clinics.

Our data clearly show that there is a significant correlation between AHI and serum HCO_3^- level. However, the relationship between AHI and serum HCO_3^- level, although statistically significant, is weak, and there must be several other more important

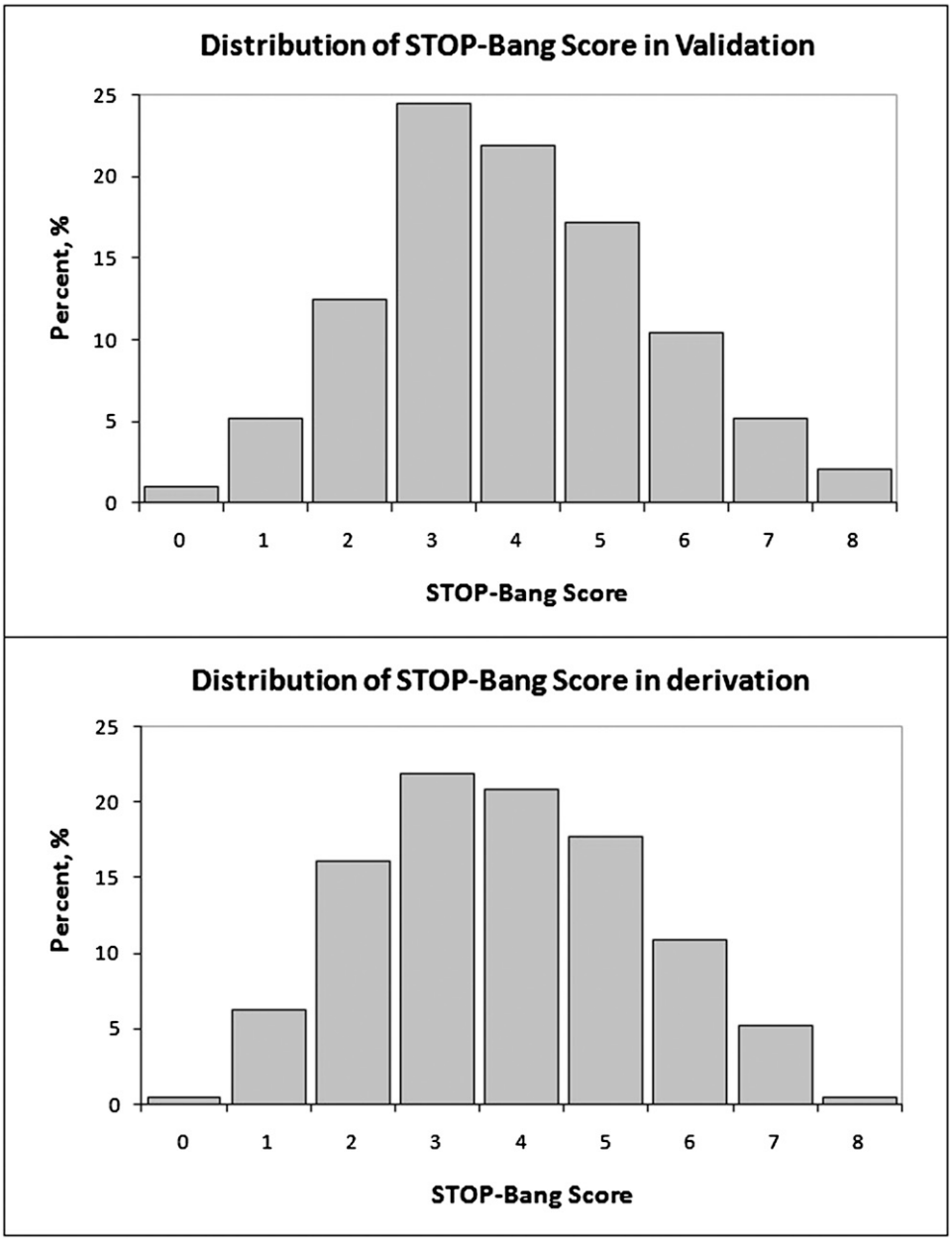

FIGURE 4. Distribution of patients by STOP-Bang score in the derivation and validation cohorts.

factors than the AHI that determine serum HCO_3^- level. Our study, however, was not designed to ascertain what these factors are. It remains unclear whether a higher AHI leads to a higher serum HCO_3^- level or vice versa. The pathophysiologic mechanisms for the increase in serum HCO_3^- level in OSA requires further investigation. Recurrent upper airway obstruction in patients with OSA can lead to acute intermittent hypercapnia during sleep. A compensatory hyperventilatory response after each apneic episode restores CO_2 homeostasis.[25,26] Failure to compensate occurs when obstructive events are too long in duration and repetitive in nature, leading to excessive CO_2 accumulation. In addition, in some patients with OSA, the interapnea hyperventilatory response is inadequate to eliminate the accumulated CO_2. Theoretically, these two mechanisms can lead to CO_2 accumulation during sleep and trigger mild elevations of serum HCO_3^- level without leading to overt daytime hypoventilation. Certain medications (eg, benzodiazepines or opioids) or underlying cardiopulmonary conditions can further increase the risk of hypoventilation during sleep. Impaired HCO_3^- excretion by the kidneys may contribute to the transition between acute to chronic hypercapnia. Elevated serum HCO_3^- level blunts the change in hydrogen ion concentration for a given

Table 2—*Demographic Data of Derivation Cohort and Validation Cohort*

Demographic	Derivation Cohort	Validation Cohort
No.	192	192
Sex, male/female	87/105 (45/55)	88/104 (46/54)
Age, y	60 ± 12	60 ± 11
Neck circumference, cm	38.5 ± 5	39.1 ± 4.0
BMI, kg/m²	30.7 ± 7	31.2 ± 7
ASA physical status		
I	3 (1.6)	2 (1.0)
II	84 (43.7)	85 (44.3)
III	99 (51.6)	99 (51.6)
IV	6 (3.1)	6 (3.1)
AHI, median (IQR)	11.0 (4.0-22.8)	11.8 (4.6-24.8)
No OSA, %	28.1	28.1
Mild OSA, %	31.8	29.2
Moderate OSA, %	20.3	24.0
Severe OSA, %	19.8	18.8
Preoperative HCO_3^- level, mmol/L	26.2 ± 3	26.6 ± 3
Existing conditions		
Hypertension	102 (53.1)	108 (56.3)
CAD	18 (9.4)	15 (7.8)
Smoker	41 (21.4)	40 (20.8)
Asthma	24 (12.5)	29 (15.1)
COPD	7 (3.7)	7 (3.7)
Diabetes mellitus	34 (17.7)	44 (22.9)
Patients on diuretics	28 (14.6)	36 (18.7)
STOP-Bang questionnaire: percentage of " yes" answer		
Q1 (Snoring)	101 (52.6)	110 (57.3)
Q2 (Tired or sleepy)	116 (60.4)	122 (63.5)
Q3 (Observed apnea)	110 (57.3)	101 (52.6)
Q4 (Pressure)	47 (24.5)	60 (31.3)
Score BMI (B)	50 (26.0)	47 (24.5)
Score age (A)	153 (79.7)	153 (79.7)
Score neck (N)	70 (36.5)	73 (38.0)
Score sex (G)	87 (45.3)	88 (45.8)

Data are presented as mean ± SD or No. (%) unless otherwise noted. ASA = American Society of Anesthesiologists; CAD = coronary artery disease; IQR = interquartile range; OSA = obstructive sleep apnea. See Table 1 legend for expansion of other abbreviation.

change in $PaCO_2$, resulting in further reduction of the ventilatory drive.[15,27] In fact, the mechanisms previously stated contribute to the development of obesity hypoventilation syndrome (OHS), defined as chronic daytime hypercapnia in obese patients with sleep-disordered breathing.[26,28] Whether milder forms of nonhypercapnic OSA lead to mild retention of serum HCO_3^- (serum HCO_3^- levels within the upper limits of normal) remains unknown and would require further investigation. We speculate that as the severity of OSA increases, it can result in mild elevations in serum HCO_3^- level. However, in contrast to patients with OHS, the degree of sleep hypoventilation is less severe, and daytime hypoventilation is absent. The cohort is at extremely low risk for OHS given that the mean BMI, AHI, and serum HCO_3^- level were significantly lower than that reported in cohorts of patients

Table 3—*Predictive Value of STOP-Bang Plus Serum Various HCO_3^- Levels Based on the Derivation Cohort*

	Derivation (n = 192)				
Cutoff	STOP-Bang ≥ 3	STOP-Bang ≥ 3 + HCO_3^- Level ≥ 26	STOP-Bang ≥ 3 + HCO_3^- Level ≥ 27	STOP-Bang ≥ 3 + HCO_3^- Level ≥ 28	STOP-Bang ≥ 3 + HCO_3^- Level ≥ 29	STOP-Bang ≥ 3 + HCO_3^- Level ≥ 30
AHI > 5						
Sensitivity, %	82.6 (75.2-88.5)	52.9 (44.2-61.5)	41.3 (33.0-50.0)	30.4 (22.9-38.8)	17.4 (11.5-24.8)	7.2 (3.5-12.9)
Specificity, %	37.0 (24.3-51.3)	64.8 (50.6-77.3)	77.8 (64.4-88.0)	85.2 (72.9-93.4)	88.9 (77.4-95.8)	94.4 (84.6-98.8)
PPV, %	77.0 (69.4-83.5)	79.3 (69.6-87.1)	82.6 (71.6-90.7)	84.0 (70.9-92.8)	80.0 (61.4-92.3)	76.9 (46.2-95.0)
NPV, %	45.5 (30.4-61.2)	35.0 (25.7-45.2)	34.1 (25.8-43.2)	32.4 (24.8-40.8)	29.6 (22.7-37.3)	28.5 (22.0-35.7)
AHI > 15						
Sensitivity, %	88.3 (79.0-94.5)	62.3 (50.6-73.1)	49.4 (37.8-61.0)	37.7 (26.9-49.4)	20.8 (12.4-31.5)	9.1 (3.7-17.8)
Specificity, %	30.4 (22.2-39.7)	61.7 (52.2-70.7)	73.0 (64.0-80.9)	81.7 (73.5-83.3)	87.8 (80.4-93.2)	94.8 (89.0-98.1)
PPV, %	45.9 (37.7-54.3)	52.2 (41.5-62.7)	55.1 (42.6-67.1)	58.0 (43.2-71.8)	53.3 (34.3-71.7)	53.8 (25.1-80.8)
NPV, %	79.5 (64.7-90.2)	71.0 (61.1-79.6)	68.3 (59.3-76.4)	66.2 (57.8-73.9)	62.3 (54.4-69.8)	60.9 (53.3-68.1)
AHI > 30						
Sensitivity,%	97.3 (85.8-99.9)	70.3 (53.0-84.1)	59.5 (42.1-75.3)	48.6 (31.9-65.6)	29.7 (15.9-47.0)	16.2 (6.2-32.0)
Specificity,%	27.7 (20.9-35.5)	57.4 (49.2-65.3)	69.7 (61.8-76.8)	79.4 (72.1-85.4)	87.7 (81.5-92.5)	95.5 (90.9-98.2)
PPV, %	24.3 (17.7-32.1)	28.3 (19.4-38.6)	31.9 (21.2-44.2)	36.0 (22.9-50.8)	36.7 (19.9-56.1)	46.2 (19.2-74.9)
NPV, %	97.7 (88.0-99.9)	89.0 (81.2-94.4)	87.8 (80.7-93.0)	86.6 (79.9-91.8)	84.0 (77.4-89.2)	82.7 (76.3-87.9)

Data are presented as average (95% CI). AHI = apnea-hypopnea index; NPV = negative predictive value; PPV = positive predictive value. See Table 1 legend for expansion of other abbreviation.

Table 4—*Predictive Value of STOP-Bang Plus HCO_3^- Level ≥ 28 mmol/L Based on the Validation Cohort*

	Validation (n = 192)	
Cutoff	STOP-Bang ≥ 3	STOP-Bang ≥ 3 + HCO_3^- Level ≥ 28
AHI > 5		
Sensitivity, %	87.0 (80.2-92.1)	29.7 (22.2-38.1)
Specificity, %	33.3 (21.1-47.5)	79.6 (66.5-89.4)
PPV, %	76.9 (69.5-83.3)	78.8 (65.3-88.9)
NPV, %	50.0 (32.9-67.1)	30.7 (23.2-39.1)
AHI > 15		
Sensitivity, %	87.8 (78.7-94.0)	32.9 (22.9-44.2)
Specificity, %	23.6 (16.1-32.7)	77.3 (68.3-84.7)
PPV, %	46.2 (38.2-54.3)	51.9 (37.6-66.0)
NPV, %	72.2 (54.8-85.8)	60.7 (52.1-68.9)
AHI > 30		
Sensitivity,%	88.9 (73.9-96.9)	36.1 (20.8-53.8)
Specificity,%	20.5 (14.5-27.7)	75.0 (67.5-81.6)
PPV, %	20.5 (14.5-27.7)	25.0 (14.0-39.0)
NPV, %	88.9 (73.9-96.9)	83.6 (76.4-89.3)

Data are presented as average (95% CI). See Table 1 and 4 legends for expansion of abbreviations.

with OSA in whom the prevalence of OHS is between 10% to 20%.[13] In a previous study, the mean serum HCO_3^- level of hypercapnic patients with severe OSA was shown to be 32 mmol/L.[29] The patient population in our study did not exhibit such a high level of serum HCO_3^-; only 1% of patients exhibited a serum HCO_3^- level > 32 mmol/L. Moreover, the patients in our study were less obese than the hypercapnic OSA cohorts.[29]

In our study, it is not surprising that the serum HCO_3^- levels are not different between those taking diuretics or patients with COPD. The patients are undergoing elective surgery and probably do not have severe COPD or require high doses of diuretics. Therefore, metabolic alkalosis due to contraction alkalosis and chloride wasting was not observed.

The results of this study refine the perioperative care plan for patients with suspected OSA. We propose a two-step screening process in which surgical patients are first evaluated with the STOP-Bang questionnaire. Because of its high sensitivity, those who score < 3 are at low risk for OSA. On the other hand, patients with a STOP-Bang score of 5 to 8 have been shown to be at higher risk for moderate to severe OSA.[19] Therefore, patients who screen positive for STOP-Bang (score ≥ 3) can be further risk stratified by serum HCO_3^- level. A STOP-Bang score ≥ 3 plus serum HCO_3^- level ≥ 28 mmol/L indicate a higher risk for moderate/severe OSA than a STOP-Bang score ≥ 3. Ideally, patients deemed at very high risk of moderate/severe OSA should be referred to sleep medicine for PSG and initiation of positive airway pressure therapy before major elective surgery.[30] If this is not feasible, perioperative precautions should be used. These can include preparation for possible difficult airway, use of short-acting anesthetic agents, opioid-sparing analgesic regimen, and empirical positive airway pressure therapy in the postoperative period.[30]

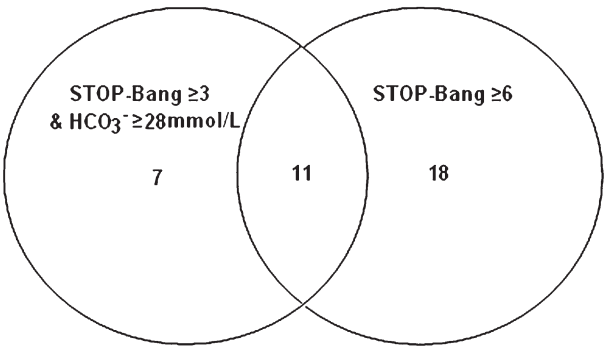

FIGURE 5. Identified patients with moderate/severe obstructive sleep apnea by STOP-Bang score ≥ 3 and HCO_3^- level ≥ 28 mmol/L or STOP-Bang score ≥ 6. See Figure 1 legend for expansion of abbreviation.

Using either STOP-Bang score ≥ 3 and serum HCO_3^- level ≥ 28 mmol/L or STOP-Bang score ≥ 6 as cutoff criteria, we were able to identify different patients with moderate/severe OSA with a small degree of overlap. Therefore, these two criteria can be complementary and may prove to be helpful in reducing the false-positive rate. Given the overall low prevalence of OSA in the general population, our results suggest that judicious use of PSG in patients with a STOP-Bang score ≥ 6 or STOP-Bang score ≥ 3 and HCO_3^- level ≥ 28 mmol/L may save significant resources.

Our study has a few limitations. It is possible that since patients who are coming for surgery are anxious, they may have been less likely to consent for preoperative PSG and participate in our study if they had no OSA symptoms. Subjects who experience OSA-related symptoms may have been more inclined to consent to PSG. Therefore, there may have been a self-selection bias during the patient recruitment process resulting in a high prevalence of patients with OSA in our study population. Also, there may have been an additional selection bias in the cohort. Healthy patients may not have had an HCO_3^- level ordered as part of the preoperative workup. Therefore, those patients who had HCO_3^- testing ordered prior to elective surgery were more likely to have chronic illness and/or be scheduled for major surgery. Thus, the findings may not be applicable to all patients presenting for elective surgery. Second, arterial blood gas sampling was not performed in the majority of patients. Therefore, we were unable to correlate serum HCO_3^- values with the $PaCO_2$ and pH. Moreover, we did not monitor the end-tidal or transcutaneous CO_2 during sleep to prove whether those with mild elevations in serum HCO_3^- level have increased risk of sleep hypoventilation. Finally,

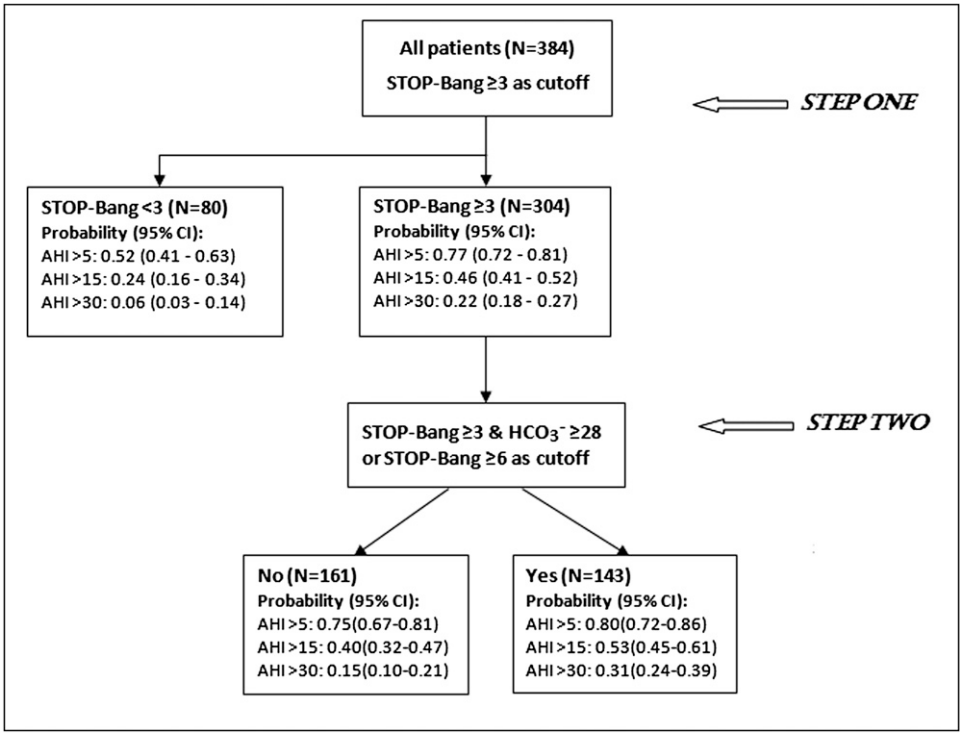

FIGURE 6. Two-steps strategy to identify patients at high risk for obstructive sleep apnea. See Figure 1 and 2 legends for expansion of abbreviations.

the study population consisted of surgical patients presenting to the preoperative clinic. Although our data were internally validated, the results are from a single center, and further validation is required to apply the results of this study to other populations.

In summary, the addition of serum HCO_3^- level ≥ 28 mmol/L to a STOP-Bang score ≥ 3 improves the specificity of predicting moderate/severe OSA but decreases the sensitivity. We propose a two-step screening process. The first step uses STOP-Bang questionnaire as a highly sensitive tool to screen patients for OSA, and the second step uses serum HCO_3^- level ≥ 28 mmol/L in those with STOP-Bang score ≥ 3 for increased specificity. This approach can help physicians to stratify patients according to their risk for OSA and manage them appropriately to minimize perioperative complications.

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Dr Chung: contributed to designing the study, conducting the study, and writing the manuscript.
Dr Chau: contributed to designing the study and writing the manuscript.
Dr Yang: contributed to analyzing the data and writing the manuscript.
Dr Liao: contributed to designing the study.
Dr Hall: contributed to designing the study and writing the manuscript.
Dr Mokhlesi: contributed to designing the study and writing the manuscript.
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Additional information: The e-Tables can be found in the "Supplemental Materials" area of the online article.

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