Effect of arterial blood bicarbonate (HCO_3^-) concentration on the accuracy of STOP-Bang questionnaire screening for obstructive sleep apnea

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Research article

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Abstract

Background

To evaluate the effect of arterial bicarbonate (HCO_3^-) concentration on the accuracy of STOP-Bang questionnaire (SBQ) screening for obstructive sleep apnea (OSA).

Methods

A total of 144 patients with suspected OSA were included. Polysomnograms (PSG) and blood gas analysis were performed, and the Epworth Sleepiness Scale (ESS), STOP-Bang questionnaire, and Berlin questionnaire were completed. The correlation between the arterial HCO_3^- concentration, apnea hypopnea index (AHI), and other related indicators was analyzed. The scoring results of the ESS, SBQ, and Berlin questionnaire were compared with the PSG results, and the sensitivity and specificity were calculated in the form of a four-cell table. The changes in the sensitivity and specificity of OSA screening after SBQ alone and combined with HCO_3^- concentration were compared, and ROC curves were drawn.

Results

Arterial HCO_3^- concentration was positively correlated with AHI ($r = 0.537$, $P < 0.001$). The ratio of HCO_3^- concentration ≥ 24.6 mmol/L in the non-OSA group was significantly lower than that in the OSA group (25.0% VS 80.8%, $P < 0.001$). The sensitivity of the SBQ was higher than that of the ESS (97.5% VS 81.7%, $P < 0.001$) and the Berlin questionnaire (97.5% VS 79.2%, $P < 0.001$). There was no statistical significance in the specificity of the three scales (25%, 37.5%, 37.5%). A combined SBQ score ≥ 3 and HCO_3^- concentration ≥ 24.6 mmol/L showed increased specificity and decreased sensitivity compared with an SBQ score ≥ 3 alone, with a corresponding AUC of 0.771 ($P < 0.01$) and 0.613 ($P > 0.05$), respectively.

Conclusion

The sensitivity of the SBQ was better than that of the Berlin questionnaire and ESS. After combining arterial blood HCO_3^- concentration, the SBQ questionnaire increased the specificity of OSA prediction and decreased the sensitivity, which improved the accuracy of screening.

Background

Obstructive sleep apnea (OSA), also known as obstructive sleep apnea hypopnea syndrome (OSAHS), is characterized by repeated apnea and hypopnea during sleep[1]. OSA is a common disease in China[2]. Polysomnography monitoring (PSG) is the gold standard for the diagnosis of OSA, but the examination is time-consuming and expensive and most primary hospitals in China do not perform the test. Thus, many

patients cannot be diagnosed in a timely fashion. It is particularly important to adopt simple methods for preliminary screening and diagnosis of OSA. The Berlin Questionnaire, STOP-Bang Questionnaire (SBQ), and Epworth Sleepiness Scale (ESS) are widely used in OSA screening and have good sensitivity [3,4]. Some OSA patients were complicated with chronic daytime hypercapnia[5]. In order to maintain the acid-base balance in the body, the kidney reduces the excretion of HCO_3^-, leading to an increase in arterial blood HCO_3^-. The combination of HCO_3^- and a questionnaire is hypothesized to improve the sensitivity or specificity of questionnaires alone [6]. This study compared the difference between the SBQ, the Berlin questionnaire, and the ESS screening for patients with OSA, and examined the effect of arterial HCO_3^- concentration on SBQ screening.

Methods

Patient selection

Patients who underwent PSG examination at the Sleep Center of the Third Affiliated Hospital of Anhui Medical University (Hefei First People's Hospital) from March 2019 to October 2020 were screened for study inclusion. Inclusion criteria were: (1) age >18 years old; (2) complete autonomous behavior and cognitive ability; (3) arterial blood gas analysis and PSG monitoring performed during hospitalization; and (4) ability to answer the questionnaire completely and accurately. Exclusion criteria were: (1) associated diseases such as chronic obstructive pulmonary disease, acute attacks of asthma, interstitial pulmonary disease, laryngospasm, vocal cord paralysis, tracheal foreign bodies, anemia, and electrolyte disorders that may affect blood gas analysis; (2) other underlying diseases that may affect HCO_3^- concentration, such as liver, kidney, lung, and heart dysfunction; (3) use of a ventilator in the past three months; (4) other common sleep respiratory disorders besides OSA; (5) pregnancy, lactation, puerperium, and mental disorders including a history of depression or anxiety; (6) use of sedatives or antipsychotic treatment in the past three months; and (7) patients with an abnormal EEG. This study was approved by the ethics committee of the third affiliated hospital of Anhui Medical University, and patients gave their informed consent to all the monitoring and questionnaire contents.

PSG recording and analysis

All subjects were monitored employing an Alice6 PSG instrument (Philips Viagra, USA) and analyzed manually by sleep technicians to confirm or exclude OSA. The apnea hypopnea index (AHI), minimum blood oxygen saturation ($LSaO_2$) and mean blood oxygen saturation ($MSaO_2$) were recorded. Respiratory events were determined. OSA was diagnosed according to the Chinese Guidelines for Primary Diagnosis and Treatment of Adult Obstructive Sleep Apnea (2018 Edition)[7]. These include (1) clinical symptoms of any one or more of the following: daytime sleepiness, non-recovery of energy after waking, fatigue, or insomnia; waking up because of breathlessness, poor breathing, or suffocation at night; habitual snoring and breathing interruption; and hypertension, coronary heart disease, stroke, heart failure, atrial fibrillation, type 2 diabetes, mood disorders, or cognitive impairment; (2) PSG monitoring: AHI ≥5 times/h, mainly

blocking events; (3) none of the above symptoms and PSG monitoring: AHI≥ 15 times/h, mainly blocking events. Adult OSA can be diagnosed if criteria (1) and (2) are met or only criterion (3) is met. Grade of disease: AHI: 5–15 times/h is mild, > 15–30 times/h is moderate, and >30 times/h is severe. The percentage of total sleep time when blood oxygen is less than 90% (CT90%), duration of apnea hypopnea in total sleep time (AHT%), average duration of apnea hypopnea (MAD), and duration of apnea hypopnea per hour (HAD) were calculated based on the reported data. PSG is the gold standard for the diagnosis of OSA.

Blood gas analysis

Two milliliters of radial artery blood were collected with a special syringe for blood gas analysis (American Westmed). Samples were obtained from study subjects following PSG monitoring and when they were awake and seated in a quiet room. The sample was mixed and sealed, and blood gas analysis was performed within 30 min to detect HCO_3^-. The process of specimen extraction strictly followed the requirements of aseptic operation.

ESS

The ESS asks individuals to grade their sleepiness during several routine activities including sitting and reading, watching TV, sitting in a public place, a long ride (more than 1 h), talking with people, resting after dinner (not drinking), driving, and reposing at rest in the afternoon. Each condition is divided into four grades: never (0), rarely (1), sometimes (2) and often (3). The subjects will score according to their own conditions, and the researchers will calculate the total score. An ESS score ≥9 was associated with high risk of OSA, and an ESS score <9 was associated with a low risk of OSA.

SBQ

The questionnaire comprised eight characteristics: S, snoring; T, tiredness; O, observed apnea; P, high blood pressure; B, body mass index >35 kg/m^2; A, older than 50 years; N, neck circumference >40 cm; and G, male gender. Patients answered the first four questions (STOP questions), and the staff in the sleep room measured the height, weight, blood pressure, and neck circumference of the patients. Then, the respondents answered the last four questions (BANG questions). The answer was yes (1 points) or no (0 points), and the total score was calculated. A score ≥3 was defined as a high risk of OSA, while a score < 3 was defined as a low risk of OSA.

Berlin Questionnaire

This consisted of snoring frequency, snoring loudness, daytime sleepiness, apnea, wakefulness fatigue, history of hypertension, and body mass index. Some of the questions had to be answered by the patient's family members or co-residents to ensure the accuracy of the answers. Depending on whether the final results were positive or negative, OSA was classified as high-risk or low-risk.

Analytical Methods

Clinical data of the patients were retrospectively analyzed. All patients received PSG monitoring, blood gas analysis, and completed the ESS, SBQ, and Berlin questionnaires. According to AHI and symptoms, the patients were divided into the non-OSA group or the OSA group, and the latter group was further divided into mild (5 times/h≤AHI≤15 times/h), moderate (15 times/h<AHI≤30 times/h), and severe (AHI > 30 times/h). Patients were divided into two groups according to the SBQ: the high-risk OSA group (STOP-Bang questionnaire score ≥3 points) and low-risk OSA group (STOP-Bang questionnaire score < 3 points). Patients were divided into two groups according to ESS: ESS ≥9 was classified as high-risk for OSA, and ESS <9 was classified as low-risk for OSA. According to the Berlin questionnaire, the patients were divided into two groups: positive for the high-risk OSA group and negative for the low-risk OSA group. A correlation analysis between HCO_3^- concentration and AHI, LSAO2, MSAO2, CT90%, AHT%, MAD, and HAD was carried out to judge the correlation degree, and the diagnostic value of HCO_3^- concentration on OSA was analyzed and evaluated. The sensitivity and specificity of the three kinds of questionnaires for screening OSA were compared. Then, the diagnostic value of the STOP-Bang questionnaire score alone and SBQ combined with the HCO_3^- concentration for OSA was further compared.

Statistical Methods

SPSS19.0 statistical software was used for data analysis. Patient information was analyzed by descriptive statistics. The normal distribution data is represented by ±s, and the non-normal distribution data is represented by the median (M) and the interquartile range (P75–P25). Correlation analysis was conducted between the HCO_3^- concentration and AHI, CT90%, AHT%, MAD, and HAD, and the correlation coefficients were calculated. Then, calculation was done for the degree of sensitivity, specific diagnostic test evaluation of the four tables, and sensitivity to the specific degrees of comparison between different methods using the matching c2 test (with P<0.05 for the difference being statistically significant). The optimal truncation value of the HCO_3^- concentration for the diagnosis of OSA was analyzed by Youden index. A ROC curve was used to compare the scores of SBQ alone and the diagnostic value of SBQ combined with HCO_3^- concentration for OSA.

Results

General information

The general morphological data of 144 patients with suspected diagnosis of OSA are shown in Table 1. According to the PSG monitoring results, the 144 patients with suspected diagnosis were divided as follows: 24 in the non-OSA group and 120 in the OSA group, including 17 mild cases, 12 moderate cases, and 91 severe cases.

Table 1
Demographic and physiologic data of the study cohort

Parameters	OSA	non-OSA
Sex		
Male	108	15
Female	12	9
Age (years)	45.0 ± 12.9	39.3 ± 15.7
Neck circumference (cm)	41.9 ± 3.7	37.4 ± 3.7
BMI (kg/m^2)	27.7, 4.8	24.9 ± 4.9
AHI	52.9 ± 27.0	2.4 ± 0.9
CT90 (%)	17.0, 38.0	0.1, 0.3
AHT (%)	40.2 ± 21.7	2.0, 1.7
MAD (s)	27.5 ± 7.5	26.5, 9.1
HAD (s)	1446.7 ± 781.0	72.7, 58.5
HCO_3^- (mmol/L)	25.6 ± 1.3	24.0 ± 1.4
$LSaO_2$ (%)	73.2 ± 13.0	90.0, 3.8
$MSaO_2$ (%)	94.1, 3.0	97.0 ± 1.1
SBQ	5.0, 1.0	3.0, 3.0
ESS	13.8 ± 4.9	9.1 ± 5.2
Berlin Questionnaire		
Positive	95	15
Negative	25	9

Correlation between HCO_3^- concentration and PSG index and its predictive value for OSA

The HCO_3^- concentration was positively correlated with AHI ($r = 0.537$, $P < 0.001$) (Fig. 1A), negatively correlated with $LSaO_2$ ($r = -0.251$, $P = 0.004$) (Fig. 1B), negatively correlated with $MSaO_2$ ($r = -0.394$, $P < 0.001$) (Fig. 1C), positively correlated with CT90 ($r = 0.437$, $P < 0.001$) (Fig. 2A), positively correlated with AHT ($r = 0.433$, $P < 0.001$) (Fig. 2B), positively correlated with HAD ($r = 0.433$, $P < 0.001$) (Fig. 2C), and had no correlation with MAD.

When the HCO_3^- concentration was applied to predict OSA, the corresponding area under the ROC curve (AUC) was 0.80 (Fig. 3A). After calculating the corresponding Yoden index, the HCO_3^- concentration of 24.6 mmol/L had the best cutoff value for screening (Yoden index = 0.558). The ratio with an HCO_3^- concentration ≥ 24.6 mmol/L in the non-OSA group was significantly lower than that in the OSA group (25.0% vs. 80.8%, P < 0.001). The ratio with an HCO_3^- concentration ≥ 24.6 mmol/L in the severe OSA group was significantly higher than that in the mild OSA group (87.9% vs. 52.9%, P = 0.001), while there was no statistically significant difference in the ratio between the severe OSA group and the moderate OSA group (87.9% vs. 66.7%, P = 0.127).

Comparison of sensitivity and specificity of the SBQ, ESS and Berlin questionnaires

The four-grid tables of diagnostic test evaluation of the three scales are presented in Tables 2, 3 and 4.

Table 2
Comparison of SBQ and PSG

STOP-Bang questionnaire	PSG		Total
	Positive	Negative	
High risk	117	18	135
Low risk	3	6	9
Total	120	24	144

Table 3
Comparison of ESS and PSG

ESS	PSG		Total
	Positive	Negative	
High risk	98	15	122
Low risk	22	9	22
Total	120	24	144

Table 4
Comparison of Berlin questionnaire and PSG

Berlin questionnaire	PSG		Total
	Positive	Negative	
High risk	95	15	110
Low risk	25	9	34
Total	120	24	144

The sensitivity of the SBQ questionnaire compared with the ESS questionnaire (97.5% VS 81.7%, $P < 0.001$) was statistically significant. The sensitivity of the SBQ questionnaire compared with the Berlin questionnaire (97.5% vs. 79.2%, $P < 0.001$) was also statistically significant. There was no statistically significant difference in sensitivity between the ESS and Berlin questionnaires (81.7% vs. 79.2%, $P = 0.701$).

There was no statistical significance in the specificity of the three scales (25%, 37.5%, 37.5%).

The value of SBQ alone and SBQ combined with HCO_3^- concentration screening for OSA

The sensitivity and specificity of all OSA, moderate and severe OSA, and severe OSA were calculated, with an SBQ score ≥ 3 as the screening cutoff value, as shown in Table 5. A combined SBQ score ≥ 3 points and HCO_3^- concentration ≥ 24.6 mmol/L showed increased specificity and decreased sensitivity (Table 5).

Table 5
The value of an SBQ ≥ 3 points combined with an HCO_3^- concentration ≥ 24.6 mmol/L for screening for OSA (%)

Cutoff value	SBQ ≥ 3 points	SBQ ≥ 3 points HCO_3^-≥24.6 mmol/L
AHI ≥ 5		
Sensitivity	97.5	79.2*
Specificity	25.0	75.08*
AHI ≥ 15		
Sensitivity	98.1	84.5*
Specificity	17.1	65.9*
AHI ≥ 30		
Sensitivity	98.9	86.8*
Specificity	15.1	58.5*
Annotation: * Compared with an SBQ score ≥ 3 group, $P < 0.01$		

When the SBQ was applied alone to predict OSA, the corresponding AUC of the OSA group was 0.613 ($P > 0.05$). When a combined SBQ score ≥ 3 and the HCO_3^- concentration ≥ 24.6 mmol/L, the corresponding AUC in the OSA group increased to 0.771 ($P < 0.01$) (Fig. 3B).

Discussion

Various examinations and questionnaires exist to evaluate the degree of sleepiness and quality of life to diagnosis OSA. However, none of them can completely satisfy clinical needs. While more accurate, some methods are complex and inconvenient such as PSG, which is the gold standard for the diagnosis of OSA [1,8]. The SBQ, ESS, and Berlin questionnaires are commonly used in the clinical evaluation of OSA and are less expensive and more convenient than PSG [1,9,10].

SBQ is a self-evaluation questionnaire developed by Canadian investigators [11] and sleep medicine experts in 2008. The questionnaire is based on the STOP questionnaire, and includes the common symptoms of OSA (snoring, fatigue, sleep apnea, high blood pressure, BMI, gender, age, and neck circumference) and adopts "yes/no" questions as a second grading method. It is simple to use, can be done in a shorter time, and is easily accepted by subjects. The questionnaire was used for screening OSA patients preoperatively in the sleep clinic with high sensitivity [11, 12]. In keeping with this, we found the SBQ questionnaire more sensitive than the ESS and Berlin questionnaires. However, the specificity of the three scales was equally low. Compared with the SBQ questionnaire alone, the specificity and sensitivity of the SBQ combined with arterial blood HCO_3^- concentration in screening OSA were significantly increased and decreased, respectively. However, by calculating and comparing the AUC, we found that the diagnostic accuracy of the SBQ combined with arterial blood HCO_3^- concentration was significantly better than that of the SBQ questionnaire alone.

Serum HCO_3^- levels increased the specificity of the SBQ in predicting moderate to severe OSA, thereby reducing the number of false positives. Interval nocturnal hypercapnia due to obstructive apnea or hypopnea may result in renal HCO_3^- retention to compensate for respiratory acidosis. This may lead to the elevation of serum HCO_3^- [6]. A serum HCO_3^- of at least 28 mmol/L and an SBQ score of at least 3 were found to improve the specificity of the prediction of moderate to severe OSA, but sensitivity was reduced [13]. In the current study cohort of 144 patients, only 3 cases (2.1%) had an HCO_3^- concentration $\geq$ 28 mmol/L, and the optimal cutoff value of the HCO_3^- concentration was 24.6 mmol/L. A correlation between the BMI and the severity OSA was reported [14]. This finding is relevant, as the BMI of Asians is generally lower than that of Europeans and Americans [15], and may, in part, explain the low HCO_3^- concentration cutoff value in our study. In addition, this study confirmed a significant correlation between AHI and HCO_3^- concentration [16], revealing a certain correlation between the $LSaO_2$, $MSaO_2$, CT90, AHT, HAD, and HCO_3^- concentration.

Improvements and modification of the various questionnaires continue to be pursued. This is especially true of the SBQ questionnaire. In this situation, BMI was a focus of modification in relation to the scoring but the results were inconsistent [17,18]. Indeed, the modified STOP-B28 questionnaire had the same high sensitivity and low specificity as the original SBQ in screening for OSA [19].

Conclusions

In conclusion, the present study indicates that Chinese individuals with a SBQ score ≥ 3 and an arterial HCO_3^- concentration ≥ 24.6 mmol/L should be considered as having OSA, and therefore PSG monitoring should be performed to confirm the diagnosis. This approach is expected to be helpful in more precisely identifying those individuals in which the more intensive technique of PSG will be useful. The combination of the SBQ questionnaire and arterial blood HCO_3^- concentration showed good sensitivity and is much less intrusive than PSG.

There are several limitations to the present study. First, the subjects of this study were all patients who went to the sleep center already with a suspected diagnosis of OSA, so there may have been a selection bias. Second,The time of arterial blood collection was the morning after the completion of PSG, and the proportion of patients diagnosed with severe OSA was relatively high, which may have affected the results. Third, the study included predominantly male participants, limiting its application to the female population. In addition, home sleep tests were not included in the study. This is mainly due to the inability to conduct a more comprehensive examination in the outpatient clinic to determine whether a patient meets the inclusion criteria, as does blood gas analysis. Because in our country most patients need to bear their own outpatient expenses, which is a difficulty.

Abbreviations

SBQ
STOP-Bang questionnaire
OSAHS
obstructive sleep apnea hypopnea syndrome
OSA
obstructive sleep apnea
PSG
Polysomnograms
ESS
Epworth Sleepiness Scale
AHI
apnea hypopnea index
$LSaO_2$
minimum blood oxygen saturation
$MSaO_2$
mean blood oxygen saturation
CT90%
The percentage of total sleep time when blood oxygen is less than 90% AHT%duration of apnea hypopnea in total sleep time

MAD
average duration of apnea hypopnea
HAD
duration of apnea hypopnea per hour

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Third Affiliated Hospital of Anhui Medical University. The informed consent obtained from study participants was written.

Consent for publication

The authors consented to the publication of the manuscript.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that there is no conflict of interest in relation to this manuscript.

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Authors' contributions

CP wrote the manuscript and calculated the data was a major contributor in writing the manuscript. Sy G reviewed and revised the manuscript and is the corresponding author of the paper. All authors read and approved the final manuscript.

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Not applicable

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Figures

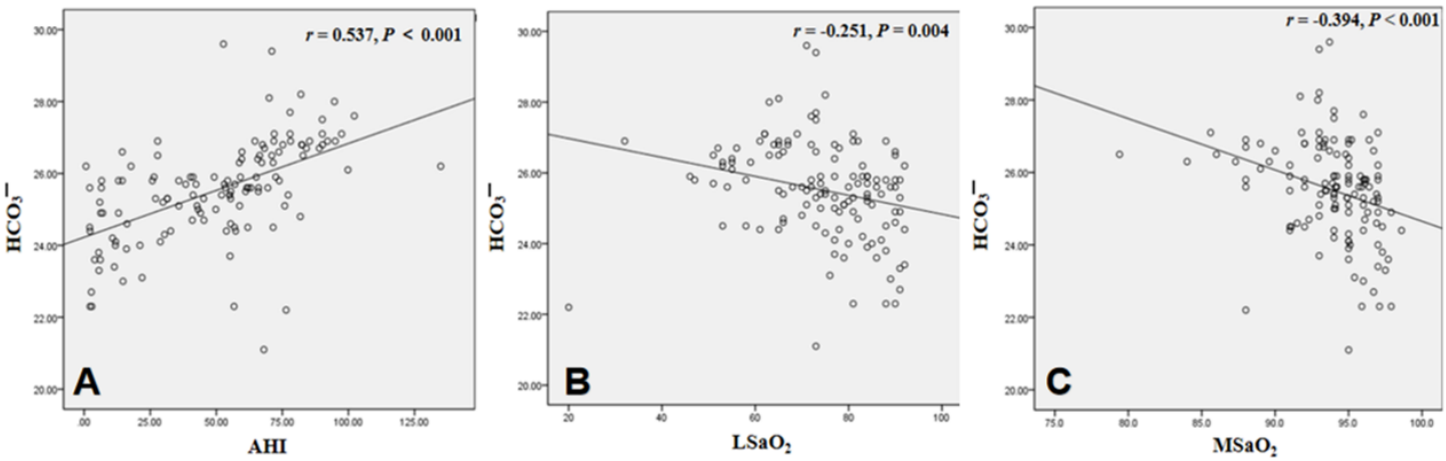

Figure 1

A: HCO3− concentration is positively correlated with AHI (r = 0.537, P < 0.001); B: HCO3− concentration is negatively correlated with LSaO2 (r = −0.251, P = 0.004); C: HCO3− concentration is negatively correlated with MSaO2 (r = −0.394, P < 0.001)

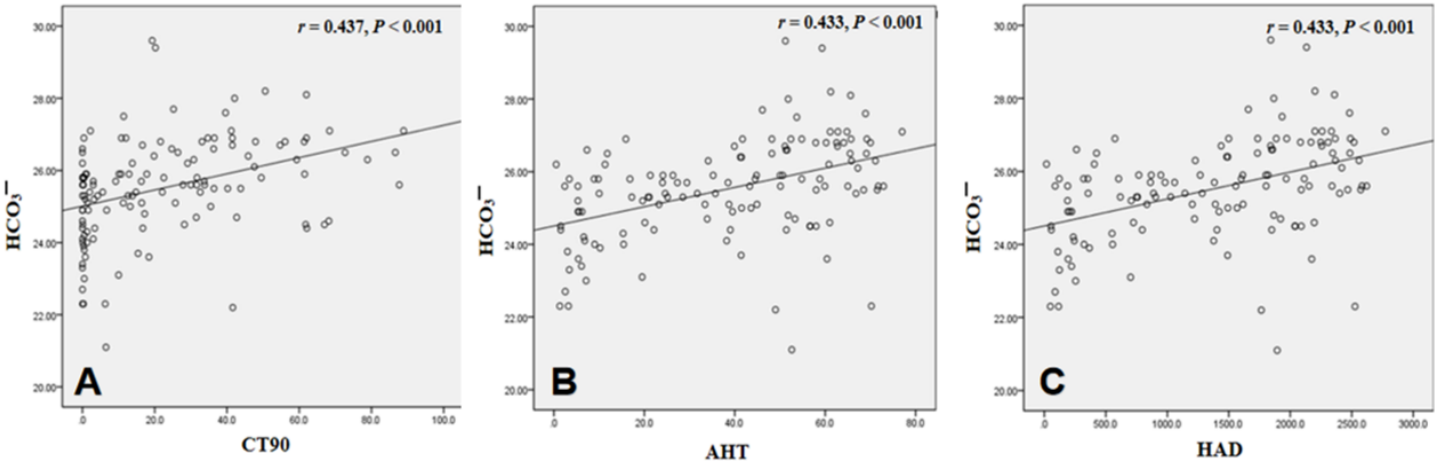

Figure 2

A: HCO3− concentration is positively correlated with CT90 (r = 0.437, P < 0.001); B: HCO3− concentration is positively correlated with AHT (r = 0.433, P < 0.001); C: HCO3− concentration is positively correlated with HAD (r = 0.433, P < 0.001)

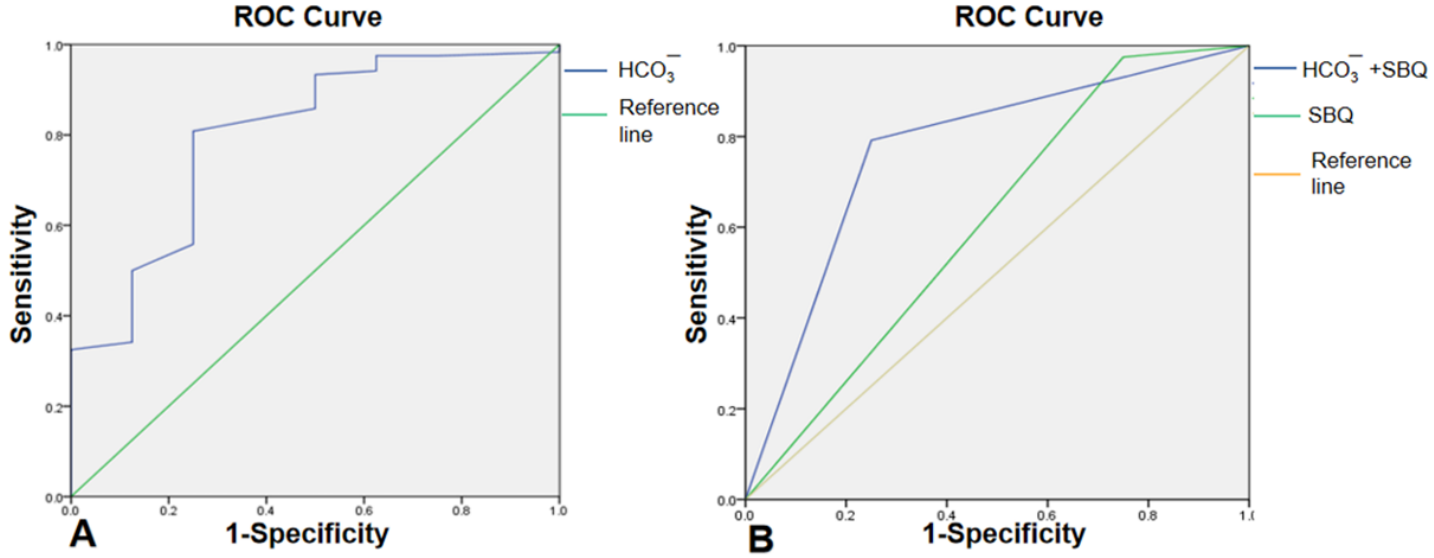

Figure 3

A: HCO3− concentration predicts OSA as demonstrated by the corresponding area under the ROC curve (AUC) being 0.80; B: A combination of the SBQ questionnaire score and arterial HCO3− concentration is more predictive of OSA than either alone. Corresponding AUC of the OSA group was 0.613 (P > 0.05). When the combined SBQ score was ≥3 and the HCO3− concentration was ≥24.6 mmol/L, the corresponding AUC in the OSA group increased to 0.771 (P < 0.01)