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Can the width of lower tongue base preoperative sonography measurements predict hypoxemia during esophagogastroduodenoscopy under sedation in ASA I-II patients?

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Abstract

Aim: The most common complication during esophagogastroduodenoscopy (EGD) under sedation is hypoxemia. There is a scarcity of indicators to predict the risk of hypoxemia during EGD under sedation accurately. The width of the lower tongue base measured by ultrasound (US) is considered to be a significant predictor of the presence and severity of obstructive sleep apnea syndrome (OSAS), which develops hypoxemia by a similar mechanism to EGD under sedation. This study aimed to observe its ability to predict hypoxemia during EGD under sedation. **Material and methods**: Adult patients undergoing EGD under sedation at our hospital after assessment in the anesthesia clinic were enrolled in the study. The width of the lower tongue base was measured as the distance between the lingual arteries (DLA) on both sides of the inferior lateral margin of the tongue by US. The primary outcome was hypoxemia defined as the SpO2 <90% for longer than 10 seconds during EGD under sedation. **Results**:A total of 304 patients were successfully included, and hypoxemia was reported in 32 patients (10.5%). The DLA prediction criterion for hypoxemia was >31 mm. The DLA was correlated with hypoxemia (Spearman correlation coefficient, 0.455; p<0.001) and owned the highest area under the receiver operating characteristic curve (0.927; 99% CI, 0.891 to 0.953, compared with that of the other predictors, p< 0.001) with hypoxemia. **Conclusions**: The width of the lower tongue base, measured as the DLA by US examination can be used to effectively predict the risk of hypoxemia during EGD under sedation.

Keywords: esophagogastroduodenoscopy; sedation; hypoxemia; ultrasound

Introduction

The frequency of esophagogastroduodenoscopy (EGD) under sedation has been growing rapidly in the outpatient anesthesia work [1]. It is popular among patients and gastroenterologists for its advantages such as comfort, short anesthesia time, less trauma, relieving patients' fears, and improving satisfaction.

Propofol-based intravenous anesthesia is the main component of outpatient implementation of EGD under sedation techniques. However, there are certain risks and complications associated with intravenous anesthesia, the most common being a decrease in pulse oxygen saturation (SpO_2) and even the development of hypoxemia [2]. The sharing of the oropharyngeal cavity for EGD operations and anesthesia management leads to complex airway management and further increases the risk of hypoxemia. The special working conditions of outpatient anesthesia can make it difficult to effectively resuscitate patients if severe complications due to intolerable hypoxemia will appear. Therefore, accurate assessment and prediction of the risk of hypoxemia during EGD under sedation is significant to both anesthesiologists and gastroenterologists.

There is a scarcity of specific indicators to predict the risk of hypoxemia during EGD under sedation [3] and mostly based on exterior characteristics, for instance, increased Mallampati classification [4] and body mass index (BMI) are considered as risk factors [5]. It is pos-

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tulated that obese patients with obstructive sleep apnea may have higher airway collapse with the use of propofol sedation [6,7].

The width of the lower tongue base measured by ultrasound (US) is considered to be a significant predictor of the presence and severity of obstructive sleep apnea syndrome (OSAS) [8]. Patients with OSAS are prone to hypoxemia during sleep, and the physical characteristics of patients with hypoxemia during EGD under sedation are quite similar to those of patients with OSAS, and a large number of patients undergoing EGD under sedation have undiagnosed OSAS. Whether tongue base width measured by UScan be used to effectively predict the risk of hypoxemia during EGD under sedation was not studied.

The purpose of this study was to measure the lower tongue base width using ultrasonography and apply it to the prediction of hypoxemia risk during EGD under sedation, comparing to BMI and Mallampati classification to derive the predictive capacity of this method.

Materials and methods

This study was approved by the Ethics Committee of Anhui Provincial Hospital, affiliated with the Chinese University of Science and Technology, ethics number: 2019KY No. 108, and by the China Clinical Trials Registry, registration number: ChiCTR2000032940. All participants were informed about the whole trial process and signed the informed consent form.

Inclusion and exclusion criteria

We selected patients who intended to undergo EGD under sedation in our hospital after assessment in the anesthesia clinic, ASA physical status I to II, age >18 years. The exclusion criteria were: patients with limited head and neck mobility; patients with baseline SpO_2 levels <95%; patients with fever, upper respiratory tract infection, respiratory tract inflammation and other chronic lung diseases which could cause hypoxemia during sedation and patients who temporarily changed EGD under sedation to ordinary EGD. Eligible subjects scheduled to undergo EGD under sedation were fasted for 8 hours before the examination, and their essential information was recorded, including gender, age, weight, height, and Mallampati classification. The specific assessment method of Mallampati classification is: the patient sat upright, opened the mouth wide, and extended the tongue to the maximum. The patient was then scored according to the pharyngeal structure that could be observed [9].

The width of the lower tongue base measured by US

Before the patient underwent EGD in the outpatient waiting area, the width of the lower tongue base was measured by US (Wisonic, Labat SP, low-frequency convex array probe). With the patient in a seated position, the ultrasonic probe was placed to the skin of the neck in the submental region coronally. When the tongue base was found, lingual arteries were seen with Doppler mode on both sides of lower lateral borders of tongue base and the distance between the lingual arteries (DLA) was measured and considered as the tongue base width [8]. The patients were instructed to remain still and silent and to avoid tongue movements, swallowing, or talking.

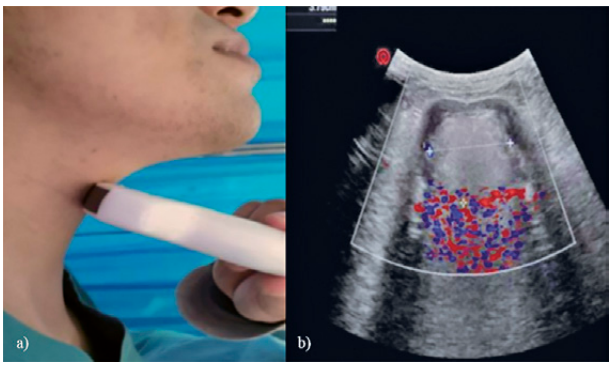

Fig 1. a) The curved probe was placed to the skin of the neck in the submental region coronally; b) The probe was adjusted to obtain the hyoid bone clearly in the screen. In the area between the hyoid bone and the symphysis of the mandible, lingual arteries were seen with Doppler mode on both sides of lower lateral borders of tongue base, the distance between lingual arteries (DLA) can be measured by ultrasound. The DLA of this patient is 37.9 mm as shown in the figure.

All US examinations were performed consecutively and independently by two trained anesthesiologists, respective experience in US examination of the tongue base, blinded to the clinically relevant information with the same standard in the same session. The above measurement was repeated three times for each patient, and an average DLA was taken (fig 1).

The procedure of EGD under sedation

During EGD, the heart rate (HR), blood pressure (BP), bispectral index (BIS) and SpO_2 were continuously monitored. After the intravenous access was established, the patient was placed at the lateral position and instructed to breathe deeply which is the routine practice of our hospital for EGD under sedation. Oxygenation was applied with a nasal tube (3 L/min).

After preoxygenation for 1 minute, anesthesia was induced with an intravenous injection of propofol 2 mg/kg by another anesthesiologist who was blinded to any preoperative evaluation results, until the palpebral reflex had disappeared. The initial dose was slowly infused within 60 s, followed by a maintenance dose at 2–5 mg/kg/h. The aim of BIS is to maintain 50–65 during EGD under sedation. If the BIS was >65, an additional dose of 0.5

mg/kg was injected. All EGD was performed by the same endoscopist. During the gastroscopy, an additional dose of 0.5 mg/kg was injected in the event of signs of body movement. All patients were transferred to post-anesthesia care unit (PACU) under the care of an experienced anesthetist nurse on completion of the EGD.

Study end points

The primary outcome was the incidence of hypoxemia, which was defined as SpO_2 <90% for longer than 10 seconds [10]. The secondary outcomes of the study were the followings: propofol dose and the incidences of adverse reactions. The adverse reactions were cough, body movements and hiccups.

Throughout the EGD, if hypoxemia occurred, the taken measures included [11-13]: stopping the injection of additional propofol, increasing the oxygen flow from 3 to 8 L/min and airway opening with the jaw-thrust maneuver. When the patient's SpO_2 <85%, the gastroscope tube was quickly removed and facemask ventilation was performed. If the patient's SpO_2 did not improve within 1 minute through the above measures, tracheal intubation for mechanical ventilation was realized.

Statistical analysis

The SPSS software version 24.0 (SPSS, Chicago, IL) and the MedCalc version 19.2.0 (MedCalc Software, Mariakerke, Belgium) were used for the statistical analysis. The measurement data were displayed as the means ± standard deviation, and the categorical variable data were presented as frequency/ratio (n/%). For univariate comparison, the independent-sample t test, rank sum test, and chis-quared test were selected, according to specific circumstances. Correlations between the predictors and hypoxemia were analyzed with the Spearman correlation analysis. The Youden index was used to determine criteria for DLA, Mallampati classification and BMI to predict hypoxemia. The odds ratios, sensitivity, specificity, positive predictive value, negative predictive value, and their 95% confidence intervals (95%Cis) for each predictor were calculated. The receiver operating characteristic curve and the area under the curve (AUC) were utilized to analyze the abilities to predict hypoxemia. The comparison of 2 AUCs was performed using the nonparametric test. For the statistical analyses with 2-tailed tests, $p<0.05$ was defined as statistical significance.

Sample size

The sample size was calculated with the MedCalc 19.2.0 statistical software packages. With an $\alpha = 0.05$ and a power of 80%, We conducted a pilot study of 50 patients for sample size assessment. In this pilot study, there were 4 patients with hypoxemia. The incidence of hypoxemia was 8%, a 0.3 difference value of AUC in the pilot study, and a 90% statistic power, a sample size of at least 173, was calculated to detect the difference of receiver operating characteristic curves between DLA and BMI.

Results

General information of patients and the incidence of hypoxemia

During the observation period from June 2020 until August 2020, 317 patients were selected to be performed EGD under sedation, 13 patients were temporarily changed to ordinary gastroscopy due to symptoms of upper respiratory tract infection. Hence, a total of 304 patients were successfully included in this study, including 129 male patients and 32 patients with hypoxemia. All of 32 patients successfully underwent EGD with sedation, employing prompt and efficient interventions. Specifically, 18 patients benefited from an increase in oxygen flow from 3 to 8 L/min, 10 patients received airway opening through the application of the jaw-thrust maneuver, and 4 patients underwent removal of the gastroscope tube followed by facemask ventilation. After group analysis of the patients according to whether they had hypoxemia, weight, body mass index, DLA, cough, Mallampati classification and the total dose of propofol between the two groups were statistically significant ($p<0.05$), while the differences of other adverse reactions were not ($p>0.05$). Descriptive data of the patients and the incidence of hypoxemia were shown in Table I.

The prediction criterion of DLA for hypoxemia determined by Youden index was DLA >31 mm. After group analysis hypoxemia and cough was more frequently en-

Table I. Comparison between the hypoxemia and the non-hypoxemia groups

Variable	Hypoxemia	Non-hypoxemia	p value
	n=32	n=272	
Sex (male/female, n)	17/15	112/160	0.196
Age (y)	51±14	50±13	0.705
Height (cm)	166±7	163±7	0.042
weight (kg)	69±13	60±11	<0.001
Body mass index (kg/m^2)	24.8±3.9	22.4±4.1	<0.001
Mallampati classification (>2/<3, n)	20/12	74/198	<0.001
DLA (mm)	33.0±2.6	26.9±3.4	<0.001
Total dose of propofol (mg)	165.2±43.5	137.2±28.9	<0.001
Adverse reactions, n (%)			
Cough	10 (31.3)	34 (1.1)	0.01
Body movements	7 (21.9)	26 (9.6)	0.069
Hiccups	4 (12.5)	19 (7)	0.446

Data are shown as the means±standard deviation or number (%). DLA, Distance between lingual arteries.

countered in high DLA (>31 mm) group (p<0.05). Descriptive data were shown in Table II.

Comparison between possible predictors and hypoxemia

The *r* values for all the possible predictors, such as BMI, DLA, the total dose of propofol in comparison with the hypoxemia were 0.178(p=0.002), 0.455(p<0.001), 0.251(p<0.001), respectively (Table III).

Comparison between related indicators and DLA

The *r* values for the related indicators, such as BMI, Mallampati classification, cough in comparison with the DLA were 0.393(p<0.001), 0.308(p<0.001), 0.15(p=0.007), respectively (Table IV). The *r* values for BMI, cough in comparison with total dose of propofol were 0.335 and 0.187 (Table V).

The predictive value of each possible predictor to predict hypoxemia

The receiver operating characteristic (ROC) curve analysis showed that the AUC of the BMI, DLA, Mallampati classification and obesity for predicting hypoxemia were 0.667(95% CI, 0.611 to 0.720), 0.927(95% CI, 0.891 to 0.953), 0.7(95% CI, 0.645 to 0.751) and 0.541(95% CI, 0.484 to 0.598) respectively (compared with AUC = 0.5, p<0.01 for all of them). Significant differences were observed between AUCs of the DLA to the other predictors (p<0.001 for all the comparisons) (fig 2).

The prediction criterion of Mallampati classification and BMI for hypoxemia determined by Youden index were Mallampati >2, BMI>22 kg/m^2 respectively. The OR value, sensitivity and specificity, positive predictive value and negative predictive value of each possible predictor were calculated by this criterion. Among them, the predictive value of the DLA was the highest: OR value was 80.4 (95%CI: 23.2-278.6), sensitivity was 0.875 (95%CI: 0.71–0.965), specificity was 0.919 (95%CI: 0.88–0.949), positive predictive value was 0.56 (95%CI: 0.474–0.728), negative predictive value was 0.984 (95%CI: 0.835–0.991) (Table VI).

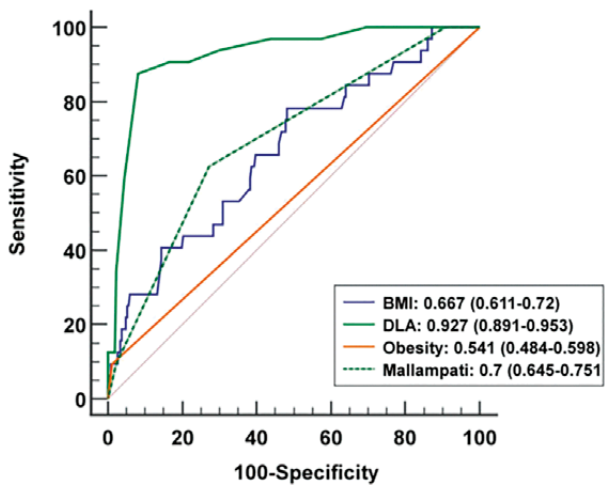

Fig 2. Receiver operating characteristic curve analysis of each predictor for predicting hypoxemia. BMI, Body mass index; DLA, Distance between lingual arteries.

Table II. Comparison between the high distance between lingual arteries (DLA) and low DLA groups.

Adverse reactions, n (%)	High DLA (>31 mm)	Low DLA (≤31 mm)	p value
	n=50	n=254	
Hypoxemia	28 (56)	4 (1.6)	<0.001
Cough	12 (24)	32 (12.6)	0.036
Body movements	7 (14)	26 (10.2)	0.434
Hiccups	7 (14)	16 (6.3)	0.446

Data are shown as numbers (%).

Table III. Correlations between possible predictors and hypoxemia (n=304)

Variable	*r* value	p value
BMI	0.178	0.002
DLA	0.455	<0.001
Total dose of propofol	0.251	<0.001

Spearman correlation analysis was used for all correlations. BMI, Body mass index; DLA, Distance between lingual arteries.

Table IV. Correlation between related indicators and DLA (n=304)

Variable	*r* value	p value
BMI	0.393	<0.001
Mallampati classification	0.308	<0.001
Cough	0.15	0.007

Spearman correlation analysis was used for categorical variable, Pearson correlation analysis was used for continuous variable. BMI, Body mass index; DLA, Distance between lingual arteries.

Table V. Correlation between BMI, cough and total dose of propofol (n=304)

Variable	*r* value	p value
BMI	0.335	<0.001
Cough	0.187	0.001

Spearman correlation analysis was used for cough and total dose of propofol, Pearson correlation analysis was used for BMI and total dose of propofol. BMI, Body mass index.

Discussion

In this prospective observational study, accurate US measurement of the distance between the lingual arteries in the inferior lateral margin of the tongue can predict the occurrence of hypoxemia during sedation of EGD. AUC comparisons showed that DLA had the highest AUC in predicting hypoxemia. We found that the positive predic-

Table VI. Variable values to predict hypoxemia (n=304)

Factors	Odds ratio (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
BMI>22 kg/m^2	0.86 (0.24-3.06)	0.781 (0.6-0.907)	0.478 (0.417-0.539)	0.16 (0.114-0.745)	0.953 (0.625-0.975)
Mallampati>2	4.45 (2.077-9.572)	0.625 (0.437-0.789)	0.728 (0.671-0.780)	0.213 (0.163-0.274)	0.943 (0.913-0.963)
Obesity	7.1 (0.47-105.7)	0.094 (0.02-0.25)	0.989 (0.968-0.998)	0.513 (0.418-0.593)	0.903 (0.846-0.987)
DLA＞31 mm	79.5 (25.6-247.4)	0.875 (0.71 -0.965)	0.919 (0.88-0.949)	0.56 (0.474-0.728)	0.984 (0.835-0.991)

CI, confidence interval; BMI, Body mass index; DLA, Distance between lingual arteries; NPV, negative predictive value; PPV, positive predictive value.

tive value of BMI, Mallampati classification and sensitivity of obesity were low. This implies a high rate of missed diagnosis, which is risky for anesthesiologists. It is noteworthy that the DLA exhibits a substantial positive predictive value and sensitivity.

The incidence of hypoxia has been reported to be highly variable (4–50%) during EGD under sedation [14], which is similar to our study (10.5%). Furthermore, a study by Friedrich-Rust et al [15] indicated that independent risk factors for hypoxemia were high BMI, history of sleep apnea, and increased doses of sedatives, which was consistent with our research results. Weight, body mass index, DLA, cough, and the total dose of propofol between the two groups were statistically significant. Since additional propofol dose was administered for movement, it is likely that coughing during EDG might trigger additional administration of propofol. Hence, we analysed the correlation between the total dose of propofol and cough, the correlation was relatively low. As a consequence, a cough may be a risk factor for hypoxemia by comparing differences between the two groups (hypoxemia and non-hypoxemia). Some authors considered that coughing during EGD under sedation might be a surrogate marker for an increased risk of aspiration-related postoperative infection [16], but this aspect was not demonstrated in other studies [4,17]. The mechanism may be related to the fact that coughing during EGD under sedation can give a rise to an abnormal movement of the glottis and aggravated respiratory depression. Similarly, the dosage of propofol is based on body weight. We suppose that one reason why high BMI increases the risk of hypoxemia may be the increased dosage of propofol by the correlation between BMI and total dose of propofol.

By comparing the group with high DLA and the group with low DLA, we found that the difference in coughing was statistically significant between the two groups. Correlation analysis yielded that the cough was correlated with DLA, but the correlation coefficient was not high, and it was hypothesized that there was a certain likelihood of a cough in patients with a high DLA, but whether high DLA was a high-risk factor for a cough still needs to be confirmed by further studies. BMI and Mallampati classification had relatively high correlation with DLA, further suggesting that DLA is a useful predictor of hypoxemia as well as them.

The cut-off value calculated by the Youden index was BMI >22 kg/m^2, which was due to the low BMI threshold for defining overweight and obesity in China [18]. But even so, the predictive value of BMI was low: the AUC was 0.668, and the PPV was only 0.16. If obesity (BMI >30 kg/m^2) was used as a predictor, there would be a high rate of missed diagnosis. In addition to the different BMI standards for diagnosing obesity in Chinese, a more important reason is the different mechanisms of hypoxemia in Chinese and Caucasians [19], so it is inappropriate to use obesity (BMI >30 kg/m^2) as a prediction standard in China.

It has also been universally acknowledged that pharyngeal stenosis and collapsibility assume greater pathogenic significance in Chinese OSAS subjects [20]. This is similar to the mechanism by which hypoxemia occurs during EGD under sedation: tongue retraction and expansion reduced pharyngeal space with airway collapsibility [21]. In addition, hypoxemia can be aggravated by gastroscopic insertion and aeration [22]. Patients with OSAS assessed by US are more likely to develop hypoxemia during EGD under sedation. The reason may be that a wider tongue wrap around the EDG scope to occlude the airway. The hypoxemia based on this mechanism cannot relieve by adjustment of EGD generally. Therefore, it is feasible to use US to assess the risk of hypoxemia during EGD under sedation, which is also fully illustrated by the results of our study.

Obstructive sleep apnea is considered to be a considerable sedation risk during upper gastrointestinal endoscopy [23]. Polysomnography is the gold standard for diagnosing OSAS, but it is often overlooked by clini-

cians and patients [24]. The large number of outpatients receiving EGD under sedation, including many potential patients with OSAS, has created a crisis in the field of outdoor anesthesia. The width of the lower tongue base, measured as the DLA by US, was considered to be associated with the existence and severity of OSA [8]. As anesthesiologists become more proficient with US, this method can be used quickly and easily to diagnose and screen OSA before EGD under sedation, thus improving safety and ensuring that sedated EGD can be performed safely and at high speed. The cut-off value of DLA in this study was 31 mm, which is almost in line with the cut-off of 30 mm for Yonatan et al [8]. Their study focused on the absolute size of the tongue base, the absolute value of DLA as measured by US, rather than its dimensions relative to other structures in the pharynx, which may play an important role in the pathogenesis of OSAS. Our consistent results further suggest that OSAS and hypoxemia of EGD under sedation have similar mechanisms. As for why our cut-off value of DLA was 1 mm higher, we suspected that it might be related to oxygen inhalation during gastroscopic sedation. After all, OSA patients did not use oxygen during sleep monitoring, which needs to be confirmed by further studies.

In this study, there are still some limitations. First of all, all patients needed to be evaluated by the anaesthesia assessment clinic before sedation during upper gastrointestinal endoscopy. Hence it was impossible for our subjects to be randomly selected, and even if we tried our best with blinding, bias cannot be avoided. Secondly, the mechanism of EGD under sedation hypoxemia and OSA is not exactly the same, and EGD under sedation hypoxemia mechanism could be relatively more complicated because it involves the gastroscope itself operation complications and intravenous anesthesia complications, Therefore, using the diagnosis of OSA indicators by US to predict EGD under sedation hypoxemia has a certain value, but it is not the gold standard. There is no doubt that the prediction of EGD under sedation hypoxemia must be a comprehensive evaluation process, rather than a single indicator. Our findings suggested that intraoperative cough was a risk factor, but whether it was related to the width of the tongue and how to predict intraoperative cough before surgery should be further studied. Next, we can use ultrasound to compare changes in the anatomical structure of the pharynx at the time of hypoxemia occurrence with OSA to identify specific similarities and differences in their mechanisms. Last but not least, due to the difference appearance in Chinese and Caucasian populations, the relationship between DLA and hypoxemia may be different in other populations. This would suggest the need to repeat similar trails in other populations in future.

Conclusions

The width of the lower tongue base, measured as the DLA by US examination can be used to effectively predict the risk of hypoxemia during EGD under sedation. In addition, compared with BMI and Mallampati classification, DLA measured by US examination exhibited an independent and better predictive property.

Conflict of interest: none

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