



# Development and validation of a nomogram for difficult laryngoscopy at visual laryngoscopy: a prospective nested case-control study

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**Background:** Unsuccessful airway management is associated with increased perioperative morbidity and mortality. Difficult laryngoscopy is a leading cause of unanticipated difficult airways and presents a challenge for anesthesiologists. Airway ultrasound assessment can be used as a priority diagnostic strategy for difficult laryngoscopy because of its diagnostic performance in difficult airways. This study was designed to develop a comprehensive model based on multivariate statistical analysis (including bedside examination tests and ultrasonography) for difficult laryngoscopy.

**Methods:** This study was conducted from December 27, 2021, to September 16, 2022. All patients underwent an airway ultrasonographic measurement with a standard operating procedure. The baseline characteristics and bedside examination tests were also recorded. Laryngoscopy with a Cormack–Lehane (CL) grade of 1–2 was defined as “easy laryngoscopy”, whereas “difficult laryngoscopy” was based on a CL grade of 3–4. The prediction model was built by using baseline characteristics, bedside examination tests, and ultrasonographic measurements as independent variables and easy/difficult laryngoscopy as the dependent variable.

**Results:** A total of 516 patients were eligible, and 456 patients were finally enrolled in the study. A 4-variable analysis, including inter-incisor gap (IIG), thyromental distance (TMD), the distance from the skin to the tongue root, and airway-related diseases, was performed to construct the optimum prediction model. The area under curve (AUC) value of the prediction model was 0.933 [95% confidence interval (CI): 0.770 to 0.935] in the training set and 0.956 (95% CI: 0.915 to 0.997) in the validation set.

**Conclusions:** The comprehensive model and nomogram, especially the integration of tongue root thickness, can predict the risk of difficult laryngoscopy more accurately and reliably than any other screening method alone, allowing for reasonable individualized regimen decision-making.

**Keywords:** Nomogram; ultrasound; difficult laryngoscopy; difficult airway

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## Introduction

Unsuccessful airway management is associated with increased perioperative morbidity and mortality (1-3). Unforeseen difficult laryngoscopy is the main reason for unanticipated difficult airways, which may lead to severe hypoxia, hypoxic brain damage, and even intraoperative death (4-8). In clinical practice, difficult laryngoscopy is a challenge for anesthesiologists.

The incidence of airway management failure can be greatly reduced if difficult laryngoscopy is predicted with high specificity and sensitivity. However, predicting difficult laryngoscopy is not a simple task. Many anatomical structures and functional units are involved in the formation of difficult laryngoscopy (9). The diagnosis of a difficult laryngoscopy is a subjective process and highly dependent on the anesthesiologist's experience. There is a pressing need to develop methods of predicting difficult laryngoscopy conveniently, quickly, and accurately in clinical practice (10).

Current guidelines provide several approaches to predict the risk of difficult laryngoscopy (11). There has been considerable heterogeneity among studies of bedside examination tests in predicting difficult laryngoscopy, with no single feature being identified as more predictive than another (12). Most of the commonly used bedside examination tests for predicting difficult laryngoscopy are based on body surface anatomical markers, and these tests cannot truly reflect the internal anatomy of the upper airway. A comprehensive score combining a patient's history and bedside test results can improve the accuracy of predicting difficult airways, including the STOP-Bang questionnaire and Wilson score. However, both single examinations and comprehensive scores have only relatively low sensitivities and slightly higher specificities (13). These standard airway screening tests should be interpreted with caution because they seem not to be considered superior screening tests. Therefore, although several assessment strategies have been developed, including a single bedside examination or a comprehensive score, they still cannot completely meet the current clinical requirements (14-16).

Imaging techniques, including X-ray (17), computed tomography (CT) (18), magnetic resonance imaging (MRI) (19), and ultrasound (20), can visualize the anatomical features of the upper airways. Such techniques have been recommended for predicting the risk of difficult airways in guidelines and expert consensus (1,11,21). Studies have shown that the diagnostic performance and area under the

curve (AUC) of ultrasound in difficult airways are similar to those of CT and X-ray (21).

Ultrasonography might facilitate a new direction in difficult airway research, as it may reflect the internal anatomical characteristics of a patient's upper airway, and can be used as a priority diagnostic strategy for difficult laryngoscopy owing to its easy availability, low cost, and no radiation hazard (11,21). Previous clinical practice and observations have found that some ultrasound image features such as pretracheal soft tissue thickness and tongue thickness are associated with difficult laryngoscopy (22-26). However, most current studies have only analyzed the association between each predictor and difficult laryngoscopy independently. Furthermore, the results of most studies are based on direct laryngoscopy, which is not consistent with a medical environment in which visual laryngoscopy dominates. Therefore, this study was designed to develop a comprehensive model based on multivariate statistical analysis (including bedside examination tests and ultrasonography) for difficult laryngoscopy at visual laryngoscopy. We present this article in accordance with the TRIPOD reporting checklist (available at <https://qims.amegroups.com/article/view/10.21037/qims-23-95/rc>).

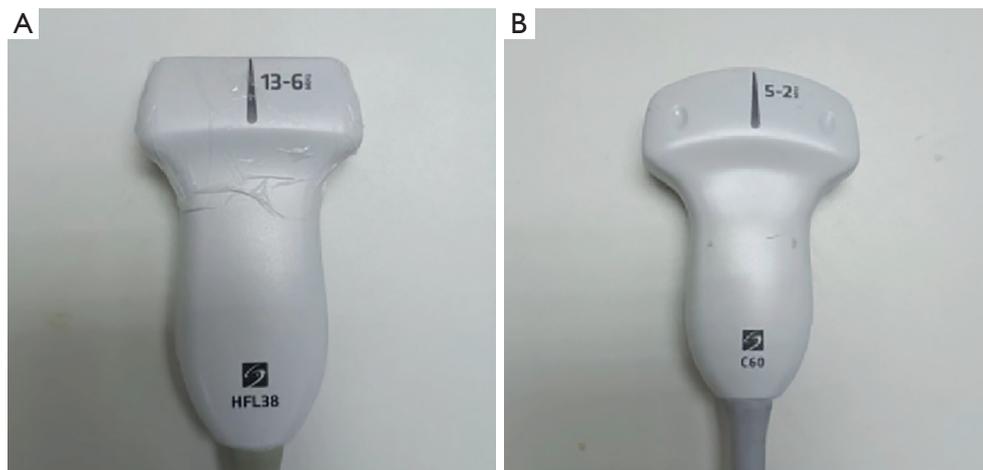
## Methods

### Participants

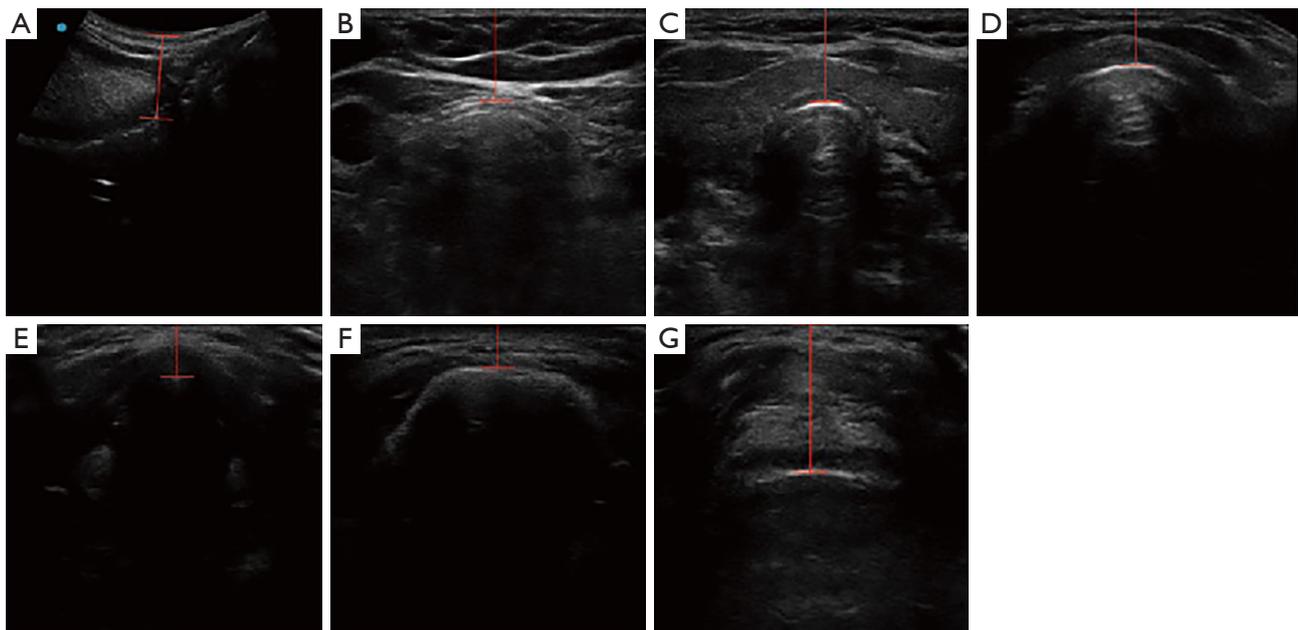
The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee of Shanghai Ninth People's Hospital, Shanghai, China approved the research protocol (No. SH9H-2021-T356-2). All patients provided their written informed consent before enrolment in this prospective nested case-control study. This study was conducted from December 27, 2021, to September 16, 2022, at Shanghai Ninth People's Hospital. The following inclusion criteria were applied: (I) adult patients ( $\geq 18$  years of age); (II) scheduled for elective surgery with American Society of Anesthesiologists Physical Status (ASA-PS) 1-3; (III) required tracheal intubation at visual laryngoscopy. Patients were excluded based on the following criteria: (I) language communication disorders; (II) cervical spine fractures or cervical spine diseases; (III) head and neck injury; (IV) emergency surgery; (V) allergy to related drugs.

### Airway assessments

All patients underwent an ultrasonographic examination



**Figure 1** Two types of ultrasonic probe. (A) High-frequency probe (13-6 MHz); (B) low-frequency probe (5-2 MHz).



**Figure 2** Ultrasound images. (A) DSTR; (B) DSTJ; (C) DSTI; (D) DSCM; (E) DSAC; (F) DSHB; (G) DSE. DSTR, distance from the skin to the tongue root; DSTJ, distance from the skin to the trachea at the jugular notch; DSTI, distance from the skin to the thyroid isthmus; DSCM, distance from the skin to the cricothyroid membrane; DSAC, distance from the skin to the anterior commissure of the vocal cords; DSHB, distance from the skin to the hyoid bone; DSE, distance from the skin to the epiglottis.

(SII; SonoSite Corporation, Bothell, WA, USA). The ultrasonographic measurements were performed by 2 experienced researchers using 2 ultrasound probes (*Figure 1*). Before ultrasonographic measurement, each patient was placed in the supine position with neck hyperextension by lifting the shoulders using a hard pillow. The ultrasound

measurements were selected based on previous studies and systematic reviews (22,27-29). The following ultrasonographic methods were used: (I) distance from the skin to the tongue root (DSTR; *Figure 2A*), (II) distance from the skin to the trachea at the jugular notch (DSTJ; *Figure 2B*), (III) distance from the skin to the thyroid isthmus (DSTI;

Figure 2C), (IV) distance from the skin to the cricothyroid membrane (DSCM; Figure 2D), (V) distance from the skin to the anterior commissure of the vocal cord (DSAC; Figure 2E), (VI) distance from the skin to the hyoid bone (DSHB; Figure 2F), and (VII) distance from the skin to the epiglottis (DSE; Figure 2G). All ultrasound measurements conformed strictly to a standard operating procedure. The ultrasound system was adjusted to Steep Needle Profiling (SNP) mode before the measurement. The ultrasound images were saved after all measured targets were displayed completely and clearly. The depth was set to 3.3 cm for high-frequency probe and 9.2 cm for low-frequency probe.

Before tracheal intubation, standard airway assessment was performed by a specific team comprising specially trained anesthesiologists and nurses. The results of baseline characteristics, medical history, and classic airway bedside examinations of each patient were recorded. The whole airway assessment process was mainly based on the 2022 American Society of Anesthesiologists Practice Guidelines for Management of the Difficult Airway (11). The definitions and details of baseline characteristics, medical histories, and classic airway bedside examinations are shown in Table S1.

### Induction of general anesthesia

Patients were routinely monitored with electrocardiography, pulse oximetry, and non-invasive blood pressure measurement. They were administered with midazolam 2–3 mg, fentanyl 2–4 µg/kg, propofol 2–2.5 mg/kg, and rocuronium 0.6 mg/kg intravenously before tracheal intubation. After preoxygenation with mask-pressurized ventilation for approximately 3 minutes, tracheal intubation was performed using a visual laryngoscope (McGrath MAC; Aircraft Medical Co., Ltd., Edinburgh, UK), which is being increasingly utilized and gradually replacing direct laryngoscope.

During tracheal intubation, the Cormack–Lehane (CL) grade was evaluated (grade 1 represents a complete view of the glottis, grade 2 represents a partial view of the glottis or arytenoids, grade 3 represents only the visibility of the epiglottis, and grade 4 represents the absence of epiglottis visibility) (30). The CL grade was assessed by anesthesiologists with more than 3 years of experience who were blinded to the results of the ultrasonographic measurements. The classification was based on the CL grade, with grades 1–2 classified as “easy laryngoscopy”

and grades 3–4 classified as “difficult laryngoscopy”. The airway assessments and CL evaluations were performed by different well-trained researchers, and they were both blinded to each other’s assessment results.

### Sensitivity analysis

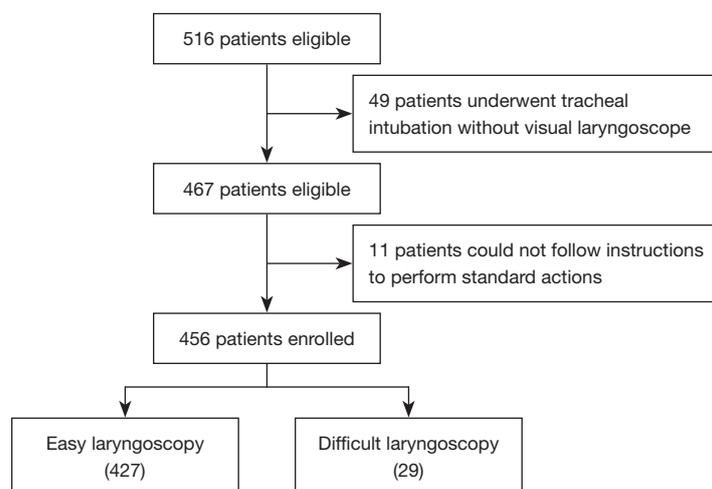
To examine the adequacy of the sample size, we performed a sensitivity analysis by performing a saturation analysis. Different sized datasets (from 10% to 100%) were used to evaluate the same model for the same outcome (difficult laryngoscopy). The relationship between dataset size and model performance can be summarized throughout the analysis (31).

### Statistical analysis

Continuous variables were expressed as the median (quartile) or the mean ± standard deviation. Categorical variables were expressed as frequencies and percentages. Statistical analyses were conducted to assess group differences using different methods. Median values were analyzed using the Kruskal–Wallis H test, means were analyzed using Student’s *t*-test, and categorical variables were analyzed using chi-square analysis. The statistical analysis was performed using the software SPSS 25.0 (IBM Corp., Armonk, NY, USA) and R version 4.2.1 (The R Foundation for Statistical Computing, Vienna, Austria; <https://www.r-project.org/>).

A few missing values were filled using the missRanger algorithm in R. The data were randomly divided into a training set and a validation set (at a ratio of 7:3). Using the least absolute shrinkage and selection operator (LASSO) method (32), variables with a P-value of ≤0.1 in the univariate logistic regression analysis were considered, and the most significant risk factors were selected for prediction modeling. We performed 10-fold cross-validation to determine the optimal parameter configuration, and ‘*typ. measure*’ was set to ‘deviance’. The non-zero coefficient features were determined based on the  $\lambda$  value corresponding to a standard error of the minimum distance deviation. The development of the prediction model involved performing multivariable logistic regression analysis, and the optimal model was obtained by stepwise regression (33,34).

Following the establishment of the optimal model, the nomogram underwent bootstrapping validation using 1,000 bootstrap resamples. A calibration curve was plotted to evaluate the model’s calibration. Differential efficacy



**Figure 3** Flow diagram of the study.

was evaluated by receiver operating characteristic (ROC) curve analysis, and clinical decision curve analysis (DCA) was performed to evaluate the clinical application value of the model. We then quantified the net income within the threshold probability range. Finally, the constructed model was verified in the validation set.

## Results

### Participant characteristics

A total of 516 patients were eligible for the study. Of these, 49 patients who underwent tracheal intubation without a visual laryngoscope were excluded, and another 11 patients were excluded because they could not follow instructions to perform standard actions. Finally, 456 patients aged between 18 and 82 years old, including 287 females and 169 males, were enrolled in the study (Figure 3). The incidence of difficult laryngoscopy (CL grade of 3–4) was 6.4% (29 patients). Some 8 patients were intubated using an alternative device, such as a fiberoptic bronchoscope. No complications occurred during tracheal intubation. The characteristics of patients in the training and validation sets are shown in Table S2 and Table S3, respectively.

### Feature selection

Univariate binary logistic regression analysis was applied for all variables. A cutoff P value of 0.1 was utilized, resulting in the identification of 23 variables associated with difficult laryngoscopy, as listed in Table 1. Through the utilization of

LASSO analysis and stepwise regression, a 4-variable [interincisor gap (IIG), thyromental distance (TMD), DSTR, and airway-related diseases] analysis was formulated as the optimal prediction model (Figure 4). The thresholds, AUCs and odds ratios (ORs) of the included variables are shown in Table 2.

### Prediction model

An independent predictive model was developed and represented as a nomogram, incorporating relevant predictors (Figure 5). The predictive capability of the model for difficult laryngoscopy was assessed using ROC curve analysis. In the training set, the AUC value of the prediction model was 0.933 [95% confidence interval (CI): 0.770 to 0.935] with a sensitivity of 0.889 (95% CI: 0.744 to 1.000), a specificity of 0.860 (95% CI: 0.821 to 0.900), and an accuracy of 0.862 (95% CI: 0.861 to 0.863). Meanwhile, in the validation set, the AUC value of the prediction model was 0.956 (95% CI: 0.915 to 0.997), with a sensitivity of 1.000 (95% CI: 1.000 to 1.000), a specificity of 0.817 (95% CI: 0.750 to 0.885), and an accuracy of 0.832 (95% CI: 0.830 to 0.834) (Figure 6, Table 3).

The calibration plot revealed good predictive accuracy between the actual probability and predicted probability (Figure 7). The DCA showed that intervention (i.e., advanced difficult airway strategy) in patients based on the prediction model leads to greater benefits than the alternative strategies, except for a small range of low preferences (Figure 8).

**Table 1** LASSO regression of the 23 variables

Variable	Regression coefficient	P value
ASA-PS		
1		
2	1.309	0.032
3	-14.599	0.992
4	-14.599	0.997
Age	0.048	0.001
BMI	0.135	0.03
Education		
1		
2	-1.569	0.025
3	-1.303	0.016
HBP (%)	1.339	0.051
Airway-related diseases (%)	1.992	0.001
Smoking (%)	1.019	0.052
Tumor (%)	1.768	0.005
NC	0.141	0.027
ULBT		
1		
2	0.929	0.074
3	1.216	0.149
MMT	1.225	0.002
IIG	-1.204	<0.001
LT	-0.539	0.03
THD	-0.736	0.003
TMD	-1.013	<0.001
SMD	-0.438	0.001
JD	-0.995	0.029
DSCM	4.747	<0.001
DSE	1.214	0.054
DSTI	2.168	0.017
DSHB	2.737	0.001
DSAC	2.69	0.018
DSTR	2.397	<0.001

LASSO, least absolute shrinkage and selection operator; ASA-PS, American Society of Anesthesiologists Physical Status; BMI, body mass index; HBP, hypertension; NC, neck circumference; ULBT, upper lip bite test; MMT, modified Mallampati test; IIG, inter-incisor gap; LT, length of tongue; THD, thyroid and hyoid distance; TMD, thyromental distance; SMD, sternomental distance; JD, jaw depth; DSCM, distance from skin to cricothyroid membrane; DSE, distance from skin to epiglottis; DSTI, distance from skin to thyroid isthmus; DSHB, distance from skin to the hyoid bone; DSAC, distance from skin to anterior commissure of the vocal cord; DSTR, distance from the skin to the tongue root.

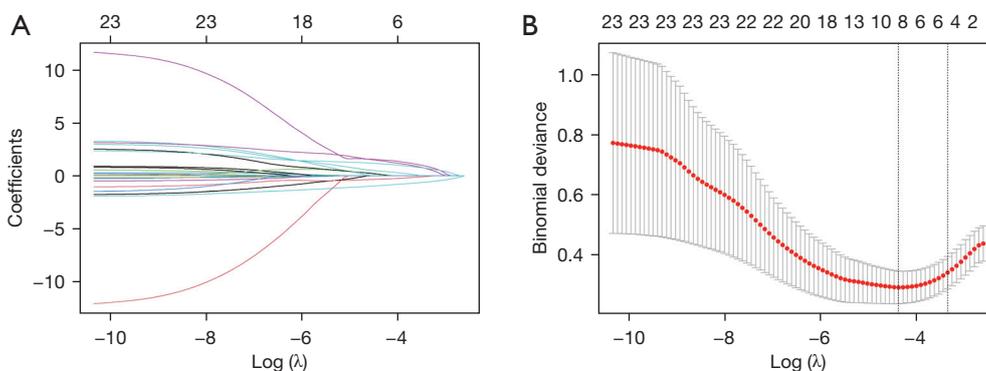
### Sensitivity analysis

By performing saturation analysis, saturation level was reached at about 70% of our current sample size (Figure 9). In other words, a larger sample size would not produce any different result, and the current sample size is sufficient to represent the statistical stability of a larger sample size.

### Discussion

Difficult laryngoscopy is the main reason for unanticipated difficult airways, and represents a challenge for anesthesiologists. Recently, a study developed a nomogram based on direct laryngoscope to predict difficult laryngoscopy and difficult intubation (35). However, as the utilization of visual laryngoscope increases, that of direct laryngoscope is gradually decreasing worldwide, diminishing the suitability of a direct laryngoscope-based nomogram for current clinical practice. This article reports the first time that most of the bedside examination tests and ultrasonographic measurements were combined to develop and validate a visual laryngoscope-based nomogram for clinical application. In this study, we evaluated the value of the nomogram for predicting difficult laryngoscopy at visual laryngoscopy and found a high correlation between CL grade and 4 clinical variables, including IIG, TMD, DSTR, and airway-related diseases. After multivariable logistic regression analysis, we developed a novel nomogram. The internal validation revealed good discrimination and correction ability. The high AUC value obtained from the interval validation demonstrated that the nomogram could be frequently and precisely used.

The utilization of video laryngoscope has steadily increased and is gradually replacing direct laryngoscope. However, no single device can solve all problems. It is notable that the utilization of awake intubation techniques has not declined significantly since the introduction of video laryngoscopy (36), indicating that visual laryngoscopy is still not a substitute for awake intubation techniques (37). We also noticed that most of the current studies on difficult airways still utilize direct laryngoscopy, which does not adhere to the clinical practice (24,38,39). Ultrasonography may facilitate new directions in difficult airway research when standard airway assessment provides inadequate predictive performance. Ultrasound has become an important tool in the operating room and intensive care unit to provide important information for diagnosis and prediction (40-42). In recent years, the application of ultrasound in airway management has gradually increased.

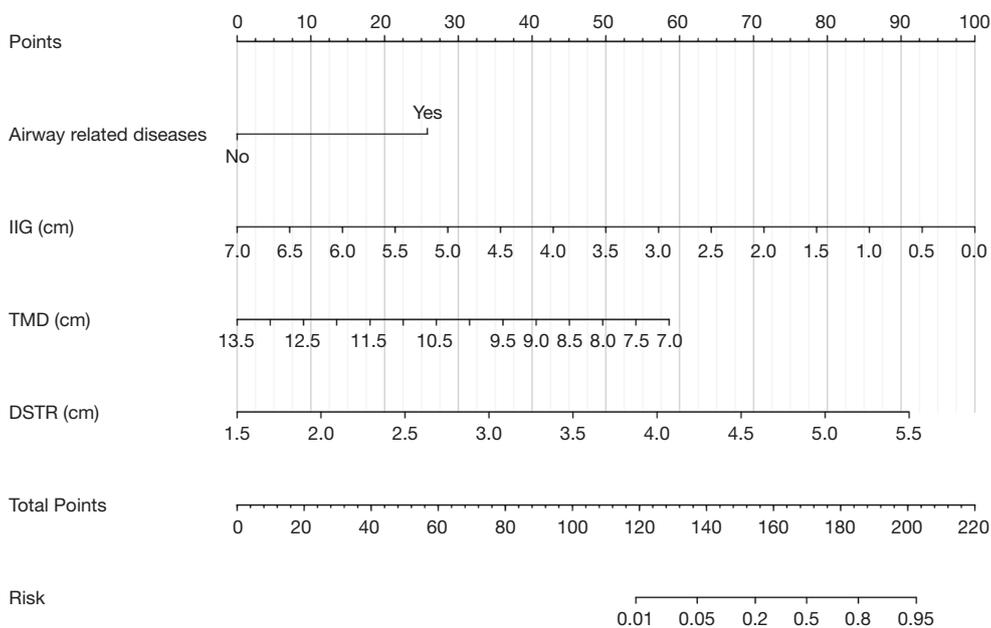


**Figure 4** LASSO regression for variable selection and regularization. (A) LASSO regression was performed on 23 variables. (B) Cross-validation is utilized to fine-tune parameter selection in LASSO regression. LASSO, least absolute shrinkage and selection operator.

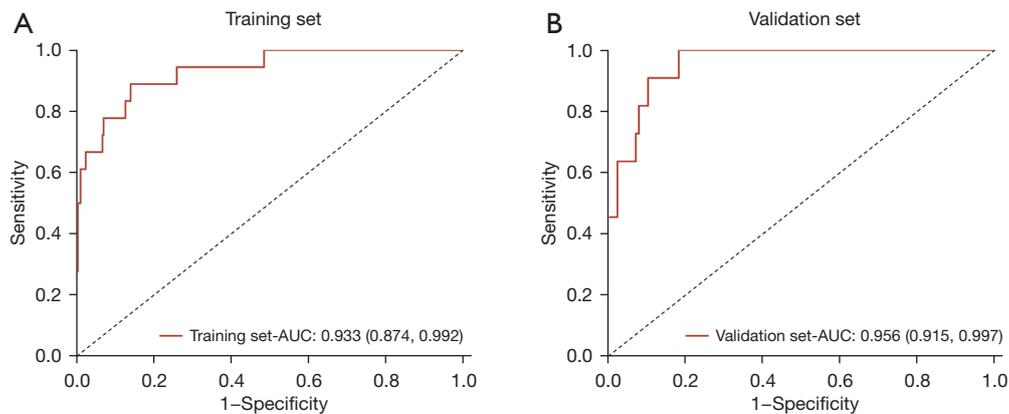
**Table 2** Predictive factors of difficult laryngoscopy

Variable	Threshold	AUC (95% CI)	OR (95% CI)	P value
Airway-related diseases	0.500	0.614 (0.507, 0.721)	10.246 (2.133, 53.319)	0.004
IIG	4.150	0.798 (0.687, 0.909)	0.276 (0.135, 0.488)	<0.001
TMD	9.550	0.781 (0.694, 0.868)	0.444 (0.205, 0.877)	0.027
DSTR	3.950	0.844 (0.736, 0.953)	7.797 (2.379, 32.509)	0.002

AUC, area under the curve; OR, odds ratio; CI, confidence interval; IIG, inter-incisor gap; TMD, thyromental distance; DSTR, distance from the skin to the tongue root.



**Figure 5** Nomogram developed for difficult laryngoscopy. The nomogram for difficult laryngoscopy was developed using IIG, TMD, DSTR, and airway-related diseases. IIG, inter-incisor gap; TMD, thyromental distance; DSTR, distance from the skin to the tongue root.

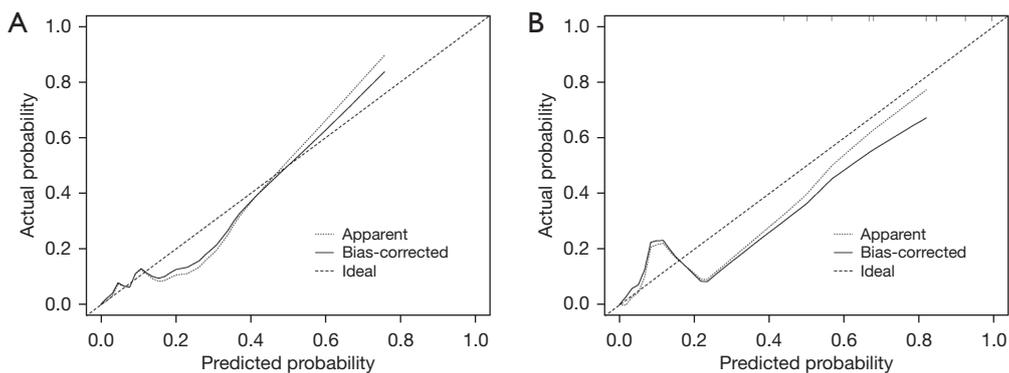


**Figure 6** ROC curve analysis for difficult laryngoscopy. (A) ROC curve for difficult laryngoscopy in the training set; (B) ROC curve for difficult laryngoscopy in the validation set. ROC, receiver operating characteristic; AUC, area under the curve.

**Table 3** The AUC, specificity, sensitivity, and accuracy of the training and validation sets

Dataset	AUC (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Accuracy (95% CI)
Training set	0.933 (0.874, 0.992)	0.889 (0.744, 1.000)	0.860 (0.821, 0.900)	0.862 (0.861, 0.863)
Validation set	0.956 (0.915, 0.997)	1.000 (1.000, 1.000)	0.817 (0.750, 0.885)	0.832 (0.830, 0.834)

AUC, area under the curve; CI, confidence interval.

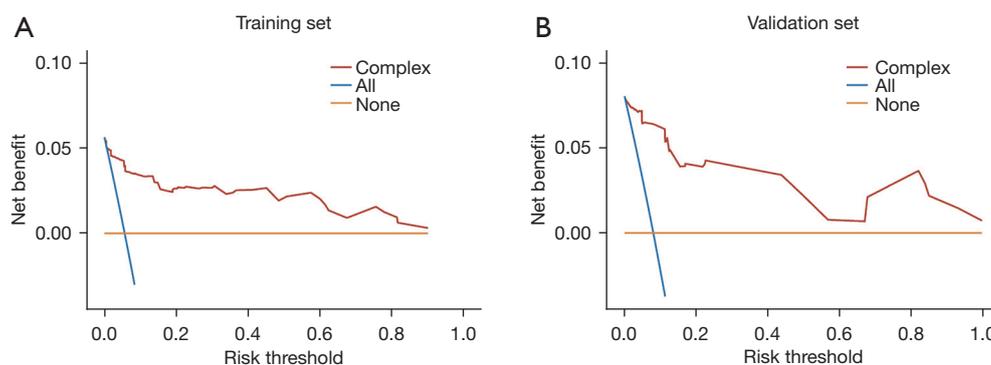


**Figure 7** Calibration curves of the risk nomogram. (A) Calibration curves of the risk nomogram in the training set; (B) calibration curves of the risk nomogram in the validation set. Dashed diagonal lines demonstrate the excellent estimations of the ideal model. The nomogram performance is represented by the solid line; the closer the solid line is to the diagonal dotted line results reflects a more desirable estimation.

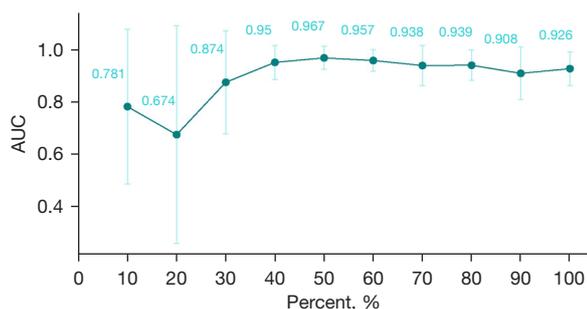
It can be used to determine the correct position of the endotracheal tube (43,44), predict the suitable diameter of the endotracheal tube (45,46), and determine the position of the cricothyroid membrane for the front-of-neck airway (47). Several authors have used ultrasound to predict difficult intubation or difficult laryngoscopy (23,24,27,38,48); however, there is still no consensus regarding which ultrasound assessment is the best predictor, and high-quality

evidence is also scarce.

We found that the DSTR was significant for predicting the classification of CL grade upon visual laryngoscopy. Most previous studies have measured the maximum thickness of the tongue (38,48,49), and their results showed that a thicker tongue (>6.1 cm, evaluated by ultrasonography) was an independent predictor for difficult tracheal intubation and difficult laryngoscopy, especially



**Figure 8** DCA for the predictive model; orange line: intervention for none; blue line: intervention for all. (A) DCA in the training set; (B) DCA in the validation set. DCA, decision curve analysis.



**Figure 9** Result of saturation analysis: this figure shows the trend between the size of the dataset and the estimated model performance, with the green dots representing the results of the evaluation of the model performance. AUC, area under the curve.

for direct laryngoscopy (24). However, most previous studies have used direct laryngoscope, rather than visual laryngoscope, during tracheal intubation (24,38,39). Visual laryngoscopes and direct laryngoscopes differ in their approach to laryngeal exposure. When using a direct laryngoscope, the anesthesiologist's view of the larynx is angled. At this moment, the largest factor interfering with laryngeal exposure is the midsection of the tongue, which is generally the maximum thickness of the tongue. When using a visual laryngoscope, the laryngoscope blade has crossed over the midsection of the tongue and the camera (the camera is usually placed at the front of the blade) is positioned relatively horizontal to the larynx. Thus, maximum tongue thickness is no longer an influencing factor for DL, whereas DSTR has the greatest effect on laryngeal exposure.

The maximum thickness of the tongue varied greatly when the patient was awake, and even when the patient had

been instructed to maintain a uniform posture (keeping their mouth closed and placing the tongue tip to slightly touch the incisors, with the tongue relaxed) (24). There is a significantly greater variability between the maximum thickness of the tongue ( $3.5 \pm 2.5$  vs.  $1.2 \pm 3.4$  mm,  $P=0.018$ ) depending on whether the specified posture is performed or not (50). The tongue root is fixed by muscles, ligaments, lingual frenulum, and other structures. Therefore, the DSTR has less variation than the maximum thickness of the tongue, and the result based on the DSTR has lower heterogeneity and better prediction performance. Overall, the high correlation between DSTR and visual laryngoscopy and the low variability were 2 important reasons for utilizing this factor as a modeling variable.

Several studies have shown a correlation between difficult airways and the increased thickness of pretracheal soft tissue (51), which is not consistent with our present results. Studies have also indicated that a soft tissue thickness of the anterior neck at the thyrohyoid plane  $>2.8$  cm is correlated with the difficulty of laryngoscope exposure, and the DSE of 2–2.5 cm had the highest accuracy in predicting difficult laryngoscopy (23,25,52,53). However, although the soft tissue thickness (DSTJ, DSTI, DSCM, DSAC, and DSHB) and DSE were also considered to have predictive value in our study, their predictive power was lower than that of the IIG and TMD. There are 2 possible reasons for such a difference. First, as mentioned earlier, most of the previous studies were based on direct laryngoscopy rather than visual laryngoscopy, and the visualization approach of these 2 laryngoscopes is different. Second, ultrasound results are strongly examiner-dependent, and each examiner varies in technique and experience.

Our results indicated that the IIG and TMD had the

best discrimination ability of the bedside examination tests. The institution that conducted this study is a medical institution that specializes in stomatology. Therefore, many of the patients included in this study had oral and maxillofacial diseases, such as temporomandibular joint disease, which presents with limited mouth opening. During the research process, 8 patients were intubated using an alternative device, among which 6 patients were intubated with a fiberoptic bronchoscope because their IIGs were very small (or even zero). The increased incidence of limited mouth opening is significant for IIG in predicting the classification of the CL grade. A short IIG refers to impaired mouth opening. When IIG is limited, it is difficult to insert the laryngoscope blade. TMD is another common bedside examination test; during the measurement, the anesthesiologist needs to measure the distance from the chin process to the notch of the thyroid cartilage with the patient's neck extended. A short TMD represents impaired neck mobility or a short neck, which lead to difficult airways. Previous studies have yielded similar results and conclusions regarding TMD (54-56).

Some diseases can lead to challenges in airway management. In our study, rheumatoid arthritis, ankylosing spondylitis, degenerative osteoarthritis, obstructive sleep apnea syndrome, Pierre–Robin syndrome, Klippel–Feil syndrome, Treacher–Collins syndrome, Down's syndrome, and airway masses were considered airway-related diseases. This list of airway-related diseases is primarily based on the 2022 American Society of Anesthesiologists Practice Guidelines for Management of the Difficult Airway, which are currently the most authoritative list of recommendations worldwide (11). These diseases may result in upper airway obstruction, abnormal airway anatomy, and limited neck mobility in patients. After multivariable logistic regression analysis, airway-related diseases showed a high correlation with the AUC between the CL grade at visual laryngoscopy. Almost all consensus of experts, guidelines, and systematic reviews with high quality and high recognition agree that a history of related diseases plays a critical role in difficult airways (1,2,11,12,57-59), and we reached the same conclusion. However, the airway anatomy is so complex that even the most authoritative guidelines currently do not cover all difficult airway-related diseases.

By dividing the dataset into the training and validation set and obtaining high AUC values on both datasets, the robustness of the model was validated. In addition, after performing saturation analysis, we found that the model sample size has similar predictive performance at about

70% of the samples with 100% of the samples, which further demonstrates the robustness of the model and the adequacy of the sample size (31). Compared with another similar study, our model has similar performance with lower model complexity (35), resulting in easier generalization and application. However, because this study is a single-center prospective study, it is almost impossible to collect information from other centers, and therefore no external validation could be performed to demonstrate its generalizability and transportability.

The model developed in our study included only 4 risk factors, but achieved a very high predictive performance, which is very helpful for clinical practice. However, it may still be unrealistic to perform ultrasound measurements for each patient. We suggest performing an additional DSTR measurement in a patient with suspected difficult laryngoscopy to further validate the risk of difficult airway in that patient. In actual clinical practice, the anesthesiologist's judgment of a difficult airway is often based on experience, especially if the bedside examination results are ambiguous. Generally, the anesthesiologist has 2 options. The first option is to attempt tracheal intubation and then perform airway rescue after a difficult airway has occurred (intervention for none in DCA). The second option is to immediately pre-prepare for difficult airway resuscitation or directly perform awake intubation techniques (intervention for all in DCA). Neither strategy is the best option, because the former is too conservative, and the latter is too aggressive. At this moment, it may be a good strategy to perform an ultrasound examination and assess the patient's airway risk based on the nomogram, as ultrasound is available and completely non-radioactive.

Our study has several limitations. Firstly, our study included a relatively small sample size. Larger patient populations are needed to explore further applications of the comprehensive model in patients with difficult laryngoscopy. Secondly, our study has the inherent limitations of a single-center study, including a restricted patient population and the unavoidable risk of bias, which may limit the generalizability of our results to the global population. In the future, we plan to expand the sample size and study population and introduce deep learning to develop artificial intelligence-based predictive models for further research.

## Conclusions

Compared with a single predictor of difficult laryngoscopy,

the comprehensive model and nomogram, especially through the integration of tongue root thickness, can predict the risk of difficult laryngoscopy more accurately and reliably, allowing for reasonable individualized regimen decision-making.

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### Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee of Shanghai Ninth People's Hospital, Shanghai, China approved the research protocol (No. SH9H-2021-T356-2). Written informed consent forms were obtained from the patients before enrolment in this prospective nested case-control study.

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**Table S1** Description of Airway Assessments

Variable	Detail
<b>Baseline characteristics</b>	
Age	Age of the patient
Gender	Gender of patient
ASA-PS	ASA-Physical Status: ASA-PS 1: in good health; ASA-PS 2: with mild comorbidities; ASA-PS 3: with severe comorbidities and limited activity ability; ASA-PS 4: with severe comorbidities and no activity ability
Height	Height of the patient
Weight	Weight of the patient
BMI	BMI of the patient
Education	Education level of the patient Education 1: Uneducated; Education 2: Junior high school or below; Education 3: High school education or above
History of alcohol	Whether the patient had a drinking habit.
History of smoking	Whether the patient had a smoking habit.
<b>Medical history</b>	
History of heart diseases	Whether the patient has a previous history of cardiovascular diseases.
History of lung diseases	Whether the patient has a previous history of respiratory diseases.
History of DM	Whether the patient has a previous history of diabetes.
History of HBP	Whether the patient has a previous history of hypertension.
Airway-related diseases	The definition of airway-related diseases is mainly based on 2022 American Society of Anesthesiologists Practice Guidelines for Management of the Difficult Airway, including rheumatoid arthritis, ankylosing spondylitis, degenerative osteoarthritis, obstructive sleep apnea syndrome, Pierre-Robin syndrome, Klippel-Feil syndrome, Treacher-Collins syndrome, Down's syndrome, and airway masses.
History of rhinitis	Whether the patient has a previous history of rhinitis.
Nasal obstruction	Whether the patient is currently suffering from nasal obstruction.
History of snoring	Whether the patient has a previous history of snoring.
History of radiotherapy and chemotherapy	Whether the patient has a previous history of radiotherapy and chemotherapy.
History of surgery	Whether the patient has a previous history of surgery history.
History of mandibular surgery	Whether the patient has a previous history of mandible operation history.
History of tumors	Whether the patient has a previous history of maxillofacial tumors.
History of trauma	Whether the patient has a previous history of maxillofacial trauma.
buck teeth	Whether the patient currently has buck teeth.
epiglottis swelling	Whether the patient is currently suffering from epiglottis swelling.
<b>Bedside examinations</b>	
NC	neck circumference: circumference of the neck at the level of the thyroid cartilage.
CSM	cervical spine mobility CSM 1: > 90° CSM 2: 90° CSM 3: < 90°
MP	mandibular protrusion: the range of movement of the mandible; MP 1: The lower incisors extend beyond the upper incisors; MP 2: The lower incisors are flush with the upper incisors; MP 3: The lower incisors extend within the upper incisors;
ULBT	upper lip bite test: measured by asking patients to bite their upper lip with their lower incisors; UBLT 1: the lower incisors extend beyond the vermilion border of the upper lip; UBLT 2: the lower incisors bite the lip but cannot extend above the vermilion border; UBLT 3: the lower incisors cannot bite the upper lip;
MMT	modified Mallampati test: a grading system used to rate the visibility of the structures in the oropharynx, including the uvula, faucial pillars, and soft palate when the mouth is opened; MMT 1: the soft palate, the pharyngopalatine arch, the uvula, and the hard palate are visible; MMT 2: the soft palate, the uvula, and the hard palate are visible; MMT 3: the soft palate and the hard palate are visible; MMT 4: only hard palate is visible;
IIG	inter-incisor gap: the maximal distance between the upper and lower incisors.
LT	length of tongue: the maximum length of the tongue outside the mouth.
THD	thyroid and hyoid distance: the distance between the thyroid and the hyoid with the neck extended
HMD	hyomental distance: the distance between the hyoid bone and the mentum with the neck extended
TMD	thyromental distance: the distance between the upper-most border of the thyroid cartilage and the mentum with the neck extended.
SMD	sternomental distance: the distance between the upper border of the sternum and the tip of the jaw with the neck fully extended
ML	mandible length: the length of mandible.
JD	jaw depth: the distance of the edge of lower lip and chin
UIL	upper incisor length: the length of upper incisor.

BMI, body mass index; ASA-PS, American Society of Anesthesiologists Physical Status; MMT, modified Mallampati test; ULBT, upper lip bite test; MP, mandibular protrusion; NC, neck circumference; LT, length of tongue; JD, jaw depth; ML, mandible length; CSM, cervical spine mobility; IIG, inter-incisor gap; UIL, upper incisor length; TMD, thyromental distance; SMD, sternomental distance; THD, thyroid and hyoid distance; HMD, hyomental distance.

**Table S2** The characteristics of patients in the training set

Characteristics	Easy laryngoscopy (n=301)	Difficult laryngoscopy (n=18)	Overall P value
Age	27.81 (22.01, 39.13)	46.51 (35.40, 59.22)	<0.001
Gender			1.000
Female	180 (59.80%)	11 (61.11%)	
Male	121 (40.20%)	7 (38.89%)	
ASA-PS			0.146
1	272 (90.37%)	14 (77.78%)	
2	21 (6.98%)	4 (22.22%)	
3	7 (2.33%)	0 (0.00%)	
4	1 (0.33%)	0 (0.00%)	
Height	1.67 (1.61, 1.73)	1.65 (1.62, 1.72)	0.632
Weight	60.00 (51.00, 70.00)	62.50 (57.00, 69.25)	0.112
BMI	21.22 (19.03, 23.83)	22.59 (20.76, 26.20)	0.044
Education			0.023
1	50 (16.61%)	8 (44.44%)	
2	90 (29.90%)	3 (16.67%)	
3	161 (53.49%)	7 (38.89%)	
History of alcohol			0.540
No	248 (82.39%)	14 (77.78%)	
yes	53 (17.61%)	4 (22.22%)	
History of smoking			0.091
No	255 (84.72%)	12 (66.67%)	
Yes	46 (15.28%)	6 (33.33%)	
History of heart disease			0.478
No	291 (96.68%)	17 (94.44%)	
Yes	10 (3.32%)	1 (5.56%)	
History of lung disease			1.000
No	296 (98.34%)	18 (100.00%)	
Yes	5 (1.66%)	0 (0.00%)	
History of DM			0.375
No	294 (97.67%)	17 (94.44%)	
Yes	7 (2.33%)	1 (5.56%)	
History of HBP			0.072
No	286 (95.02%)	15 (83.33%)	
Yes	15 (4.98%)	3 (16.67%)	
Airway-related diseases			0.003
No	286 (95.02%)	13 (72.22%)	
Yes	15 (4.98%)*	5 (27.78%)**	
History of rhinitis			0.789
No	220 (73.09%)	14 (77.78%)	
Yes	81 (26.91%)	4 (22.22%)	
Nasal obstruction			1.000
0	280 (93.02%)	18 (100.00%)	
1	10 (3.32%)	0 (0.00%)	
2	7 (2.33%)	0 (0.00%)	
3	4 (1.33%)	0 (0.00%)	
History of Snoring			0.204
No	172 (57.14%)	7 (38.89%)	
Yes	129 (42.86%)	11 (61.11%)	
History of radiotherapy and chemotherapy			0.296
No	296 (98.34%)	17 (94.44%)	
Yes	5 (1.66%)	1 (5.56%)	
History of surgery			0.699
No	140 (46.51%)	7 (38.89%)	
Yes	161 (53.49%)	11 (61.11%)	
History of mandibular surgery			1.000
No	291 (96.68%)	18 (100.00%)	
Yes	10 (3.32%)	0 (0.00%)	
History of tumor			0.013
No	287 (95.35%)	14 (77.78%)	
yes	14 (4.65%)	4 (22.22%)	
History of trauma			0.411
No	293 (97.34%)	17 (94.44%)	
Yes	8 (2.66%)	1 (5.56%)	
Buck teeth			0.208
No	298 (99.00%)	17 (94.44%)	
Yes	3 (1.00%)	1 (5.56%)	
Epiglottis swelling			1.000
No	295 (98.01%)	18 (100.00%)	
yes	6 (1.99%)	0 (0.00%)	
NC	34.10 (32.00, 37.60)	36.15 (34.67, 38.65)	0.050
CSM			1.000
1	299 (99.34%)	18 (100.00%)	
2	2 (0.66%)	0 (0.00%)	
MP			0.112
1	277 (92.03%)	15 (83.33%)	
2	21 (6.98%)	2 (11.11%)	
3	3 (1.00%)	1 (5.56%)	
UBLT			0.077
1	189 (62.79%)	7 (38.89%)	
2	96 (31.89%)	9 (50.00%)	
3	16 (5.32%)	2 (11.11%)	
MMT			0.002
1	99 (32.89%)	0 (0.00%)	
2	56 (18.60%)	2 (11.11%)	
3	138 (45.85%)	15 (83.33%)	
4	8 (2.66%)	1 (5.56%)	
IIG	4.40 (4.00, 5.00)	3.60 (2.55, 4.00)	<0.001
LT	4.50 (4.00, 5.20)	4.00 (3.80, 4.50)	0.015
THD	4.90 (4.00, 5.70)	4.00 (3.28, 4.27)	0.003
HMD	4.34 (0.79)	4.58 (0.90)	0.280
TMD	10.01 (1.09)	8.89 (0.86)	<0.001
SMD	17.97 (1.90)	16.39 (2.06)	0.005
ML	9.00 (8.70, 9.50)	9.15 (8.80, 9.75)	0.399
JD	3.90 (3.50, 4.30)	3.65 (3.50, 4.00)	0.046
DSCM	0.70 (0.60, 0.70)	0.80 (0.70, 0.95)	0.001
DSE	1.90 (1.70, 2.20)	2.00 (1.80, 2.28)	0.083
DSTI	0.70 (0.60, 0.80)	0.85 (0.60, 1.08)	0.068
DSTJ	1.10 (1.00, 1.30)	1.30 (1.00, 1.50)	0.143
DSHB	0.80 (0.70, 1.00)	1.00 (0.83, 1.40)	0.003
DSAC	0.70 (0.50, 0.80)	0.70 (0.60, 0.88)	0.079
DSTR	3.20 (2.80, 3.80)	4.25 (4.00, 4.45)	<0.001

ASA-PS, American Society of Anesthesiologists Physical Status; BMI, body mass index; DM, diabetes mellitus; HBP, hypertension; NC, neck circumference; CSM, cervical spine mobility; MP, mandibular protrusion; UBLT, upper lip bite test; MMT, modified Mallampati test; IIG, inter-incisor gap; LT, length of tongue; THD, thyroid and hyoid distance; HMD, hyomental distance; TMD, thyromental distance, SMD, sternomental distance; ML, mandible length; JD, jaw depth; DSCM, distance from skin to cricothyroid membrane; DSE, distance from skin to epiglottis; DSTI, distance from skin to thyroid isthmus; DSTJ, distance from skin to trachea at jugular notch; DSHB, distance from skin to the hyoid bone; DSAC, distance from skin to anterior commissure of the vocal cord; DSTR, distance from the skin to the tongue root; ASA-PS 1: in good health; ASA-PS 2: with mild comorbidities; ASA-PS 3: with severe comorbidities and limited activity ability; ASA-PS 4: with severe comorbidities and no activity ability; \*: 12 patients with airway masses, 2 patients with obstructive sleep apnea syndrome, and 1 patient with rheumatoid arthritis. \*\*: 4 patients with airway masses and 1 patient with obstructive sleep apnea syndrome.

**Table S3** The characteristics of patients in the validation set

Characteristics	Easy laryngoscopy (n=126)	Difficult laryngoscopy (n=11)	Overall P value
Age	24.75 (21.22, 34.46)	37.10 (27.92, 60.94)	0.036
Gender			0.733
Female	89 (70.63%)	7 (63.64%)	
Male	37 (29.37%)	4 (36.36%)	
ASA-PS			0.022
1	115 (91.27%)	7 (63.64%)	
2	7 (5.56%)	3 (27.27%)	
3	4 (3.17%)	1 (9.09%)	
Height	1.67 (1.62, 1.72)	1.65 (1.59, 1.72)	0.600
Weight	57.00 (50.00, 65.88)	52.50 (49.50, 70.00)	0.748
BMI	20.08 (18.38, 22.82)	20.28 (19.26, 23.37)	0.724
Education			0.035
1	15 (11.90%)	3 (27.27%)	
2	31 (24.60%)	5 (45.45%)	
3	80 (63.49%)	3 (27.27%)	
History of alcohol			0.690
No	101 (80.16%)	10 (90.91%)	
Yes	25 (19.84%)	1 (9.09%)	
History of smoking			0.056
No	110 (87.30%)	7 (63.64%)	
Yes	16 (12.70%)	4 (36.36%)	
History of heart disease			0.287
No	123 (97.62%)	10 (90.91%)	
Yes	3 (2.38%)	1 (9.09%)	
History of lung disease			1.000
No	118 (93.65%)	11 (100.00%)	
Yes	8 (6.35%)	0 (0.00%)	
History of DM			0.346
No	122 (96.83%)	10 (90.91%)	
Yes	4 (3.17%)	1 (9.09%)	
History of HBP			0.099
No	121 (96.03%)	9 (81.82%)	
Yes	5 (3.97%)	2 (18.18%)	
Airway-related diseases			0.045
No	118 (93.65%)	8 (72.73%)	
Yes	8 (6.35%)*	3 (27.27%)**	
History of rhinitis			0.172
No	85 (67.46%)	10 (90.91%)	
Yes	41 (32.54%)	1 (9.09%)	
Nasal obstruction			0.179
0	113 (89.68%)	9 (81.82%)	
1	6 (4.76%)	0 (0.00%)	
2	4 (3.17%)	2 (18.18%)	
3	3 (2.38%)	0 (0.00%)	
History of Snoring			0.312
No	89 (70.63%)	6 (54.55%)	
Yes	37 (29.37%)	5 (45.45%)	
History of radiotherapy and chemotherapy			0.155
No	125 (99.21%)	10 (90.91%)	
Yes	1 (0.79%)	1 (9.09%)	
History of surgery			0.899
No	66 (52.38%)	5 (45.45%)	
Yes	60 (47.62%)	6 (54.55%)	
History of mandibular surgery			0.540
No	118 (93.65%)	10 (90.91%)	
Yes	8 (6.35%)	1 (9.09%)	
History of tumor			0.155
No	119 (94.44%)	9 (81.82%)	
Yes	7 (5.56%)	2 (18.18%)	
History of trauma			1.000
No	123 (97.62%)	11 (100.00%)	
Yes	3 (2.38%)	0 (0.00%)	
Buck teeth			0.540
No	118 (93.65%)	10 (90.91%)	
Yes	8 (6.35%)	1 (9.09%)	
Epiglottis swelling			0.224
No	124 (98.41%)	10 (90.91%)	
yes	2 (1.59%)	1 (9.09%)	
NC	33.00 (31.50, 35.95)	31.60 (31.25, 35.10)	0.394
CSM			1.000
1	125 (99.21%)	11 (100.00%)	
3	1 (0.79%)	0 (0.00%)	
MP			0.108
1	110 (87.30%)	8 (72.73%)	
2	14 (11.11%)	2 (18.18%)	
3	2 (1.59%)	1 (9.09%)	
UBLT			0.012
1	79 (62.70%)	2 (18.18%)	
2	40 (31.75%)	8 (72.73%)	
3	7 (5.56%)	1 (9.09%)	
MMT			<0.001
1	39 (30.95%)	0 (0.00%)	
2	26 (20.63%)	0 (0.00%)	
3	59 (46.83%)	8 (72.73%)	
4	2 (1.59%)	3 (27.27%)	
IIG	4.30 (3.80, 4.80)	2.80 (1.75, 3.50)	<0.001
LT	4.47 (0.96)	3.27 (1.35)	0.015
THD	4.97 (1.10)	4.05 (1.07)	0.018
HMD	4.23 (0.77)	3.88 (0.57)	0.080
TMD	10.00 (9.50, 11.00)	8.50 (7.10, 9.00)	<0.001
SMD	18.28 (1.78)	15.72 (2.03)	0.002
ML	9.02 (0.67)	8.94 (1.04)	0.806
JD	3.84 (0.61)	3.46 (0.41)	0.014
DSCM	0.70 (0.60, 0.70)	0.70 (0.65, 0.70)	0.189
DSE	1.80 (1.60, 2.00)	2.10 (1.70, 2.25)	0.166
DSTI	0.70 (0.52, 0.80)	0.80 (0.70, 0.90)	0.017
DSTJ	1.10 (1.00, 1.30)	1.10 (1.00, 1.25)	0.534
DSHB	0.70 (0.70, 0.90)	1.00 (0.80, 1.05)	0.030
DSAC	0.60 (0.60, 0.70)	0.60 (0.50, 0.70)	0.567
DSTR	3.13 (0.64)	3.99 (0.54)	<0.001

ASA-PS, American Society of Anesthesiologists Physical Status; BMI, body mass index; DM, diabetes mellitus; HBP, hypertension; NC, neck circumference; CSM, cervical spine mobility; MP, mandibular protrusion; UBLT, upper lip bite test; MMT, modified Mallampati test; IIG, inter-incisor gap; LT, length of tongue; THD, thyroid and hyoid distance; HMD, hyomental distance; TMD, thyromental distance, SMD, sternomental distance; DSTI, distance from skin to thyroid isthmus; DSTJ, distance from skin to trachea at jugular notch; DSHB, distance from skin to the hyoid bone; DSAC, distance from skin to anterior commissure of the vocal cord; DSTR, distance from the skin to the tongue root; \* 6 patients with airway masses and 2 patient with obstructive sleep apnea syndrome; \*\* 3 patients with airway masses.