



Quantitative lung CT indicators have good predictive ability for hypoxemia during one-lung ventilation in radical resection for lung cancer

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Abstract

Purpose We aimed to identify the preoperative risk factors for hypoxemia during one-lung ventilation (OLV) in patients who underwent thoroscopic radical resection for lung cancer and to establish a prediction model.

Methods This retrospective study included 268 patients who underwent video-assisted thoroscopic surgery (VATS) radical resection for lung cancer at Yunnan Cancer Hospital from October 2021 to June 2022. Logistic regression analysis was performed to identify independent preoperative risk factors for hypoxemia during OLV. A prediction model was established, and its predictive efficacy was evaluated with the consistency index (C-index) and the area under the receiver operating characteristic curve (AUC).

Results The multivariate analysis demonstrated that the ratio of dependent lung FLV to total lung FLV (odds ratio [OR] 0.8434; 95% confidence interval [CI] 0.7281–0.9623), dependent lung HU value (OR 0.9676; 95% CI 0.9419–0.9895), dependent lung LAV% (OR 1.1838; 95% CI 1.0856–1.3138), and DLCO% pred (OR 0.9632; 95% CI 0.9353–0.9864) were independent preoperative risk factors affecting OLV hypoxemia. The prediction model that was constructed by this indicator was internally validated, with a C-index of 0.963, an AUC of 0.96 (95% CI 0.94–0.99) for the training set, and an AUC of 0.92 (95% CI 0.83–1) for the test set.

Conclusion CT-based quantitative indicators of the dependent lung are strong predictors of hypoxemia during OLV for lung cancer patients. This prediction model helps anesthesiologists to intuitively and accurately identify patients who may experience hypoxemia during OLV before surgery and develop individualized management strategies.

Keywords Hypoxemia · OLV · Quantitative CT · Preoperative risk factors

Abbreviations

AUC	Area under the curve	BMI	Body mass index
ASA	American Society of Anesthesiologists	CI	confidence interval
		COPD	Chronic obstructive pulmonary disease
		CPAP	Continuous positive airway pressure
		CT	Computed tomography

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DLCO	Diffusing capacity for carbon dioxide
DLCO% pred	Actual DLCO as a percentage of the predicted DLCO
DLT	Double-lumen tube
FEV1	Forced expiratory volume in 1 s
FEV ₁ % pred	Actual FEV1 as a percentage of the predicted FEV1
FiO ₂	Fraction of inspired oxygen
FLV	Functional lung volume
FVC	Forced vital capacity
Hb	Hemoglobin
HU	Hounsfield unit
LAV%	Low attenuation volume
OR	Odds ratio
OLV	One-lung ventilation
PaCO ₂	Arterial carbon dioxide partial pressure
PaO ₂	Partial pressure of arterial oxygen
PEEP	Positive end-expiratory pressure
PFT	Pulmonary function test
ROC	Receiver operating characteristic
SPO ₂	Peripheral pulse oxygen saturation
VATS	Video-assisted thoracoscopic surgery

Introduction

Lung cancer is not only the most prevalent cancer in China in terms of morbidity and mortality but also represents a significant global health concern [1]. One-lung ventilation (OLV) represents the most fundamental approach to anesthetic management in the context of radical lung cancer surgery, whereby anesthesiologists select an appropriate airway management tool (usually a double-lumen tube [DLT]) to collapse the surgical lung, and the ventilated lung is designated the dependent lung [2]. Hypoxemia is the most common complication of OLV, with an incidence rate of approximately 10–24% [3, 4]. This is primarily attributable to partial lung collapse, which results in a diminished ventilation/perfusion ratio (V/Q) and augmented intrapulmonary shunts [5]. Hypoxemia is challenging to rectify in approximately 5–10% of patients [6], and persistent intraoperative hypoxemia markedly elevates the risk of postoperative complications and mortality [7].

Accurate preoperative prediction of the risk of hypoxemia during OLV is of great concern to anesthetists, and the prediction results will greatly benefit the selection of airway tools. For high-risk patients, DLT intubation for OLV is not the best option. Anesthesiologists should choose a bronchial blocker to selectively block a single lobe. Compared with a DLT, this tool can increase the ventilated lung volume and thus improve the oxygenation status during OLV, even though it has the disadvantages of ‘easy to shift’ and ‘inconvenient for aspirating sputum’ [8].

Previous studies [9–12] on the preoperative predictors of OLV hypoxemia risk have mainly focused on preoperative pulmonary function test (PFT) indicators. However, the results of relevant studies are controversial, and it is difficult to guide anesthesiologists in making respiratory management decisions before surgery. The reasons for this are mainly related to the limitations of PFT [13]; specifically, the respiratory symptoms of lung cancer patients often affect the accuracy of PFT results, and PFT results reflect the overall function of the lungs, with the bilateral lung functions of patients with lung cancer often being asymmetric [14]. Patients in which overall lung function mainly depends on the OLV-dependent lung are more likely to develop hypoxemia during surgery; however, their preoperative PFT results may be completely normal. In addition, another limitation of previous studies is that the surgical population and type of surgery were not limited, thus resulting in many confounding factors. Therefore, the ability of other factors that have been mentioned in several previous studies to predict the risk of hypoxemia in patients with OLV has not been confirmed.

The development of computed tomography (CT) image post-processing technology has made it possible to apply CT for the evaluation of local lung function (one side/individual lung lobe), which is a useful complement to PFT for the evaluation of lung function [15]. The quantitative indicators of lung CT mainly include functional lung volume (FLV) [16], lung density [17] and the low attenuating volume ratio (LAV%) [17], which can reflect pulmonary ventilation, local microcirculation and the degree of emphysema. In recent years, an increasing number of studies [15–17] have confirmed the accuracy of using the above indicators to evaluate lung function. However, to our knowledge, no OLV hypoxemia prediction model incorporates quantitative lung CT data. Therefore, this study retrospectively analyzed patients who underwent thoracoscopic radical resection of lung cancer by the same surgical team, combined with their preoperative clinically important factors and lung CT quantitative indicators, to determine the preoperative risk factors for a high risk of OLV hypoxemia. This study was performed to provide a basis for anesthesiologists to formulate appropriate thoracic anesthesia management strategies.

Patients and methods

Patients and surgery

This study was approved by the Institutional Review Board of Yunnan Cancer Hospital (KYLX2023-191, December 18, 2023), and the requirement for written informed consent was waived. A retrospective analysis was conducted on the clinical data of 283 lung cancer patients who underwent video-assisted thoracoscopic surgery (VATS) for radical resection

at Yunnan Cancer Hospital between October 2021 and June 2022. The same surgical team was responsible for all surgical procedures. All of the patients who underwent surgery met the surgical standards recommended by the National Comprehensive Cancer Network guidelines [18]. The utilized surgical method was VATS lobectomy + systematic lymph node dissection without rib resection. The American Society of Anesthesiologists (ASA) physical status classifications were I–II. The exclusion criteria were as follows: (1) no DLT was used or hypoxemia was caused by improper positioning of the DLT; (2) serious accidents occurred during the operation, such as massive blood loss or anaphylactic shock; (3) had a history of lung resection; (4) Lack of preoperative CT images; (5) arterial blood gas analysis was not performed during the operation; (6) preoperative peripheral pulse oxygen saturation (SpO_2) < 90%. Fifteen of the 283 patients were excluded for the following reasons: lack of preoperative CT images ($N=3$), lack of intraoperative arterial blood gas analysis results ($N=3$), history of lung resection ($N=3$), preoperative $SPO_2 < 90%$ ($N=2$), no DLT placed ($N=2$) or hypoxemia caused by abnormal positioning of the DLT ($N=2$). The final analysis included data from 268 patients. All of the patients were randomly divided into a training set ($n=187$) and a test set ($n=81$) at a ratio of 7:3 (Fig. 1). All clinical data pertaining to the patients was

obtained from the hospital's medical record system. This included age, gender, body mass index (BMI), history of smoking, history of hypertension, preoperative hemoglobin (Hb), PFT indices and partial pressure of arterial oxygen (PaO_2) levels. BMI was calculated as $\text{weight}/\text{height}^2$, and the smoking history was defined as either still smoking or having smoked for more than 1 year prior to the surgical procedure. [19].

Anesthesia management and determination of hypoxemia

All patients underwent invasive monitoring of arterial pressure prior to the induction of anesthesia. The anesthesia was induced with etomidate, rocuronium and sufentanil, and maintained with propofol and remifentanil or sufentanil. The DLT (Shiley™ endobronchial tube accessories; Covidien, Mansfield, US) was placed under fiberoptic bronchoscopy guidance and the correct position of the DLT was confirmed. The decision regarding the use of DLT is dependent on the side of the thoracotomy. For instance, a left DLT would be selected for a right thoracotomy, and vice versa. A ventilation mode with a small tidal volume combined with positive end-expiratory pressure (PEEP) was routinely used during OLV. Mechanical ventilation parameters were set as follows:

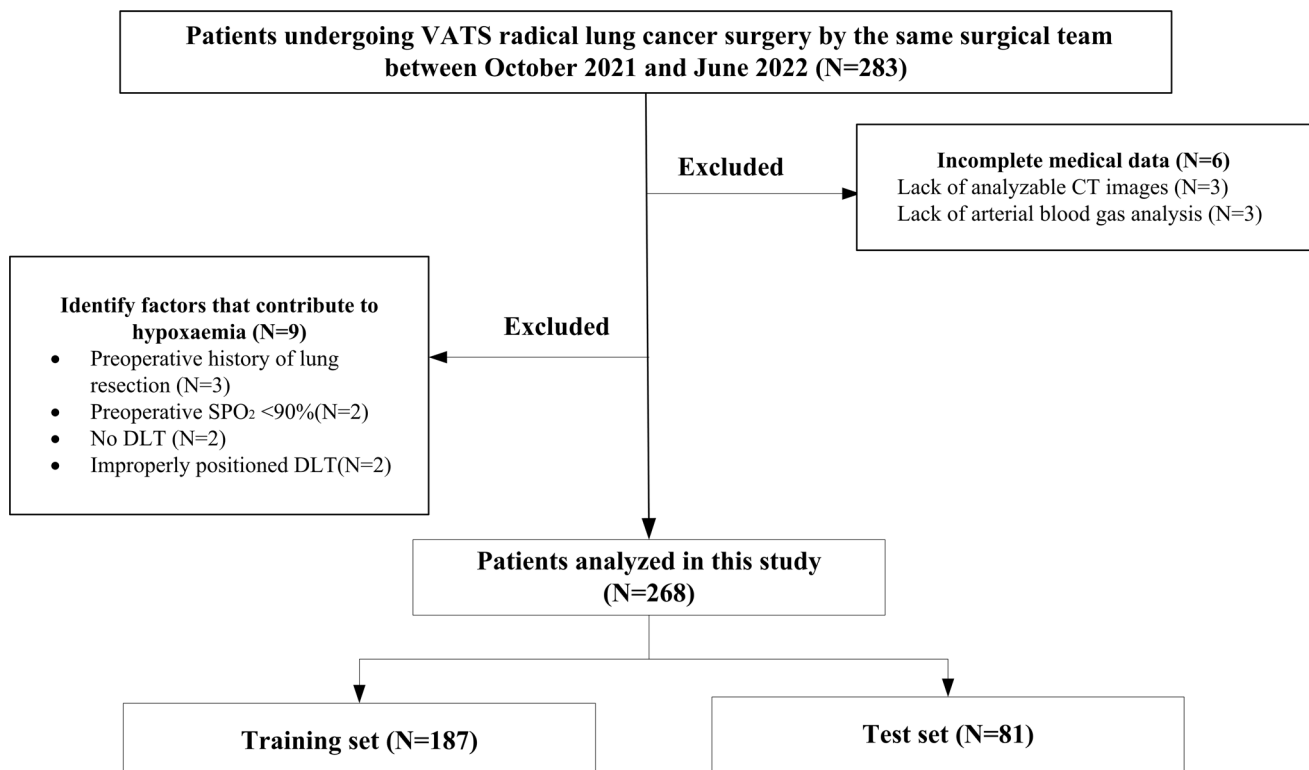


Fig. 1 Patient flowchart. *CT* computed tomography, *DLT* double-lumen tube, *SpO₂* peripheral pulse oxygen saturation, *VATS* video-assisted thoracoscopic surgery

tidal volume was set to 5–6 ml/kg according to the patients' ideal body weight, respiratory rate was set to 10–14/min, and PEEP was adjusted to between 5 and 10 cmH₂O. Maintain peak airway pressure below 30 cmH₂O and normal partial pressure of carbon dioxide in arterial blood (PaCO₂) during ventilation. PEEP was not used in patients with chronic obstructive pulmonary disease (COPD). If the patient was at risk of lung injury before surgery, pressure-controlled ventilation was used. The fraction of inspired oxygen (FiO₂) was 100% during the whole operation. In accordance with the established anesthetic protocol of our institution, arterial blood was sampled 30 min following the commencement of OLV and analyzed immediately via a blood gas analyzer. (Cobas b 221, Roche Diagnostic, India).

Given that 100% pure oxygen was inhaled during surgery, we conducted a review of previous studies [20, 21] on pure oxygen inhalation during OLV and set PaO₂ < 80 mmHg as the standard for hypoxemia during OLV. Furthermore, as PaO₂ frequently reaches its lowest point at OLV 20–30 min [22], this study selected PaO₂ at OLV 30 min as the basis for detecting hypoxemia. In the event of hypoxemia, the anesthesiologists employed a series of measures to improve oxygenation to a safe range. These included implementing the alveolar recruitment strategy, applying continuous positive airway pressure (CPAP) to the collapsed lung, and using bilateral lung low tidal-volume ventilation.

PFT indicator data collection

Preoperative PFT was performed by using a plethysmograph, JAEGER® MasterScreen Body (CareFusion Germany 234 GmbH, Hoechberg, Germany). Patients needed to wear a nose clip and follow the doctor's instructions to complete breathing movements. The following lung function parameters were collected: forced vital capacity (FVC); FEV₁/FVC, which is the ratio of forced expiratory volume in 1 s (FEV₁) to FVC; FEV₁% pred, which is the actual FEV₁ as a percentage of the predicted FEV₁; DLCO% pred, which is the actual diffusion capacity of carbon dioxide (DLCO) as a percentage of the predicted DLCO.

CT scan and image analysis

All chest scans were performed using a 128-slice CT scanner (SOMATOM Definition AS+, Siemens Healthcare, Erlangen, Germany) in the supine position, with full inspiration and breath-holding for whole lung scanning. The scanning parameters were as follows: tube current of 110 mAs, collimation of 0.6 mm, rotation time of 0.5 s, and pitch of 1.2. With an iterative algorithm confirmed by sinograms, the CT image was reconstructed into 1-mm thick cross-axis slices by using a 512×512 image matrix. The reconstructed CT image data were uploaded to the syngo.via workstation

(VB20A, Dual Energy, Siemens Healthineers), after which image analysis was performed by using CT Pulmo 3D software (syngo.via, Siemens Healthineers, Germany). The software is available for CT diagnostic equipment from different manufacturers and allows the acquisition of quantitative CT metrics including FLV and LAV% [23]. The results are similar and reproducible to those of other measurement software (3DSlicer, CT Lung Density Analysis) [24]. Attenuation values are expressed in Hounsfield units (HU), which are generally considered to represent lung density. According to the literature [25], the threshold for automatic segmentation of lung tissue by the software was set as –600 to –910 HU, and soft tissue, large blood vessels, and pathological lung tissue (such as tumor tissue, pulmonary fibrosis, atelectasis, or emphysema) were excluded. This radiologically defined lung volume is known as the functional lung volume (FLV) [26]. The lung tissue segmentation was verified by a thoracic radiologist with 5 years of experience and manually corrected when the software recognition was inaccurate. LAV was defined as a lung volume < –950 HU, and LAV% was defined as the percentage of the LAV to the total volume of both lungs [27]. The quantitative lung CT indicators that were obtained in this study mainly involved OLV-dependent lung parameters, including the proportion of FLV to total lung FLV (FLV%), HU value and LAV%.

Statistical analysis

Based on previous research findings [9, 10, 28], we prioritized the inclusion of key indicators of lung function, including FVC, FEV₁/FVC, FEV₁% pred, and DLCO% pred. The study also included demographic characteristics and important preoperative factors, such as age, sex, BMI, smoking history, hypertension history, preoperative hemoglobin count, and preoperative PaO₂. In addition, we included new CT quantitative indicators of the OLV-dependent lung, including the ratio of the FLV to the total lung FLV (%), the HU value, and the LAV%.

All data were analyzed using R statistical software (version 4.1.3, R studio, Boston, MA, USA). The Kolmogorov–Smirnov test was used to test the normality of the quantitative data. Normally distributed continuous variables are expressed as the mean ± standard deviation, non-normally distributed continuous variables are expressed as the median and interquartile range, and independent sample *t* tests or Mann–Whitney *U* tests were used for comparisons between the groups. Categorical variables are expressed as frequencies or percentages, and comparisons between groups were performed by using the chi-square test. First, a univariate analysis was performed on the training set to screen out statistically significant indicators as independent variables, after which a multivariate logistic regression analysis was performed. A nomogram was constructed based

on the results of multivariate regression analysis, and its predictive efficacy was verified in the test set. The bootstrap method was used to verify the predictive performance of the nomogram model. The area under the receiver operating characteristic (ROC) curve (AUC) and the consistency index (C-index) were used to evaluate the accuracy of the model's prediction results: 0.50–0.70 indicated low accuracy, 0.71–0.90 indicated moderate accuracy, and > 0.90 indicated high accuracy. $P < 0.05$ was considered to indicate statistical significance.

Results

Baseline characteristics of the included patients

A total of 283 patients were included in the initial study, of whom 3 patients had a history of lung resection before surgery, 2 patients had a preoperative $SpO_2 < 90\%$, 2

patients had a difficult airway without the use of a double-lumen tube, 2 patients had intraoperative hypoxemia due to improper double-lumen tube position, 3 patients had preoperative CT scans that could not be analyzed, and 3 patients lacked arterial blood gas analysis results during surgery. A total of 15 patients were excluded from the analysis, and 268 patients were ultimately included in the study. No serious adverse events occurred during the operation in any of the patients. The specific process is shown in Fig. 1. The median age of all of the patients was 54.50 years (range 49.00–61.75 years); 115 patients (42.91%) were males, and 44 patients (16.42%) developed hypoxemia during intraoperative OLV. A comparison of variable characteristics between the training set ($n = 187$) and the test set ($n = 81$) is shown in Table 1. There was no significant difference in the incidence of hypoxemia during OLV between the two groups (16.58 vs. 16.05%, $P > 0.05$). In the intergroup comparison between the non-hypoxemia group and the hypoxemia group in the training set, the proportion of FLV in the dependent lung

Table 1 Clinical baseline characteristics of 268 patients

Features	Train cohort		<i>P</i>	Test cohort		<i>P</i>
	Hypoxemia ($n = 187$)			Hypoxemia ($n = 81$)		
	NO	Yes		NO	Yes	
Number, n (%)	156 (83.4)	31 (16.58)		68 (83.95)	13 (16.05)	
Male, n (%)	63 (40.38)	16 (51.61)	0.248	31 (45.59)	5 (38.46)	0.636
Age (years), median (IQR)	54.00 (49.00, 60.00)	53.00 (46.00, 66.00)	0.701	55.00 (50.00, 64.00)	54.00 (49.50, 61.00)	0.487
BMI (kg/m^2), median (IQR)	22.74 ± 2.50	22.35 ± 2.47	0.512	22.85 (20.80, 24.85)	20.80 (19.65, 22.95)	0.054
Smoke, n (%)	50 (32.05)	10 (32.26)	0.982	21 (30.88)	3 (23.08)	0.572
Hypertension, n (%)	32 (20.51)	5 (16.13)	0.576	16 (23.53)	1 (7.70)	0.199
Hb (g/dl), median (IQR)	14.30 (13.60, 15.30)	14.80 (14.10, 16.10)	0.052	14.40 (13.80, 15.15)	13.80 (13.50, 14.55)	0.086
Preoperative PaO_2 (mmHg), median (IQR)	71.00 (66.00, 74.90)	68.30 (63.00, 75.80)	0.484	69.05 (65.00, 72.88)	65.80 (61.35, 71.90)	0.280
Dependent lung FLV%, median (IQR)	50.10 (46.40, 54.30)	47.30 (45.50, 53.40)	0.048*	47.85 (45.23, 52.88)	47.40 (45.40, 48.95)	0.723
Dependent lung HU	− 823.61 ± 38.61	− 866.03 ± 22.20	< 0.001*	− 828.00 (− 857.75, − 795.00)	− 856.00 (− 872.00, − 833.00)	0.019*
Dependent lung LAV%	20.40 ± 9.50	35.45 ± 7.04	< 0.001*	19.85 ± 9.21	32.42 ± 7.41	< 0.001*
FEV_1 (% predicted), median (IQR)	98.50 (85.70, 106.35)	97.00 (86.10, 107.50)	0.763	91.45 (82.25, 105.40)	97.40 (79.80, 105.20)	0.857
FVC (L), median (IQR)	2.73 (2.35, 3.33)	3.00 (2.42, 3.71)	0.101	2.91 ± 0.76	2.99 ± 0.59	0.723
FEV_1/FVC (%), median (IQR)	89.46 (83.79, 94.43)	90.04 (78.99, 91.50)	0.132	87.94 (80.30, 92.54)	88.24 (80.46, 93.15)	0.882
DLCO (% predicted), mean (SD)	111.90 ± 23.81	94.00 ± 19.07	< 0.001*	112.25 ± 23.45	85.60 ± 13.14	< 0.001*

BMI body mass index, *DLCO* diffusing capacity for carbon dioxide, *FLV* functional lung volume, *FEV₁* forced exhalation volume in 1 s, *FVC* forced vital capacity, *Hb* hemoglobin, *HU* Hounsfield unit, *LAV* low attenuation volume, *IQR* interquartile range, *PaO₂* partial pressure of oxygen in arterial blood, *SD* standard deviation

*The asterisk indicates that the variable was statistically significant

to the total FLV in the lung (50.10 vs. 47.30%, $P=0.048$), the HU value of the dependent lung (-823.61 ± 38.61 vs. -866.03 ± 22.20 , $P<0.001$), the dependent lung LAV% (20.40 ± 9.50 vs. 35.45 ± 7.04 , $P<0.001$), and the preoperative DLCO% pred (111.90 ± 23.81 vs. 94.00 ± 19.07 , $P<0.001$) were significantly different. In the comparison between the non-hypoxemia group and the hypoxemia group in the test set, there were significant differences in the dependent lung HU value ($-828.00 [-857.75, -795.00]$ vs. $-856.00 [-872.00, -833.00]$, $P=0.019$), the dependent lung LAV% (19.85 ± 9.21 vs. 32.42 ± 7.41 , $P<0.001$) and the preoperative DLCO% pred (112.25 ± 23.45 vs. 85.60 ± 13.14 , $P<0.001$). There was no significant difference in the FLV% of the dependent lung between the two groups in the test set (47.85 vs. 47.40%, $P=0.723$).

Univariate analysis of preoperative risk factors for OLV hypoxemia in patients

As shown in Table 2, univariate analysis of the test set demonstrated that 4 preoperative variables, including dependent lung FLV% (OR = 0.9137, 95% CI 0.8377–0.9967), dependent lung HU value (OR = 0.9484, 95% CI 0.9283–0.9688), dependent lung LAV% (OR = 1.2267, 95% CI 0.9283–0.9688), and DLCO% pred (OR = 0.9626, 95% CI 0.9443–0.9812), were significantly related to OLV hypoxemia ($P<0.05$).

Table 2 Results of univariate analysis of preoperative risk factors for OLV hypoxemia

Characteristics	OR	95% CI	<i>P</i> value
Sex	0.6351	0.293–1.3766	0.25
Age	0.9962	0.9765–1.0162	0.71
BMI	0.9485	0.8107–1.1098	0.51
Smoke	1.0095	0.4425–2.3029	0.98
Hypertension	0.7452	0.2652–2.0936	0.58
HbG	0.9907	0.9534–1.0295	0.63
Preoperative PaO ₂	0.9752	0.93–1.0226	0.3
Dependent lung FLV%	0.9137	0.8377–0.9967	0.04*
Dependent lung HU	0.9484	0.9283–0.9688	<0.001*
Dependent lung LAV%	1.2267	1.1374–1.323	<0.001*
FEV ₁ (% predicted)	0.9996	0.9774–1.0223	0.97
FVC	1.6713	0.9666–2.8898	0.07
FEV ₁ /FVC	0.9659	0.9303–1.0029	0.07
DLCO (% predicted)	0.9626	0.9443–0.9812	<0.001*

BMI body mass index, CI confidence interval, DLCO diffusing capacity for carbon dioxide, FEV₁ forced exhalation volume in 1 s, FLV functional lung volume, FVC forced vital capacity, Hb hemoglobin, HU Hounsfield unit, LAV low attenuation volume, OR odds ratio, PaO₂ partial pressure of oxygen in arterial blood

*The asterisk indicates that the variable was statistically significant

Results of multivariate logistic regression analysis of preoperative risk factors for OLV hypoxemia

The four risk factors with $P<0.05$ in the univariate analysis were included as independent variables, and multivariate logistic regression analysis was performed with the occurrence of hypoxemia during OLV as the dependent variable. The results showed that the dependent lung FLV% (OR = 0.8434, 95% CI 0.7281–0.9623), dependent lung HU value (OR = 0.9676, 95% CI 0.9419–0.9895), dependent lung LAV% (OR = 1.1838, 95% CI 1.0856–1.3138), and preoperative DLCO% pred (OR = 0.9632, 95% CI 0.9353–0.9864) were independent risk factors for hypoxemia during OLV ($P<0.05$) (Table 3).

Establishment and validation of an OLV hypoxemia prediction model for patients undergoing radical resection for lung cancer

We plotted the ROC curves for the training set and the test set (Fig. 2a). The training set AUC was 0.96 (95% CI 0.94–0.99), the test set AUC was 0.92 (95% CI 0.83–1), and the C-index of the prediction model was 0.963, thus indicating good predictive performance. Based on the results of multivariate logistic regression analysis, a nomogram was constructed by using R software to predict the risk of OLV hypoxemia in patients undergoing radical resection of lung cancer. As shown in Fig. 2b, the left side of the nomogram shows the four screened variables, including dependent lung FLV%, dependent lung HU value, dependent lung LAV% and DLCO% pred. A longer corresponding line segment indicates a greater impact of the variable on the outcome event. For example, ‘dependent lung LAV%’ was shown to have the greatest impact on the risk of hypoxemia, corresponding to 100 points. The scale of each variable in the corresponding line segment corresponds to a single score. The total score is obtained by summing the scores of the four variables. The corresponding number in the ‘‘Hypoxemia Risk’’ column is the predicted probability.

Table 3 Results of multiple logistic regression analysis of risk factors for OLV hypoxemia

Characteristics	OR	95% CI	<i>P</i> value
Dependent lung FLV%	0.8434	0.7281–0.9623	0.0156*
Dependent lung HU	0.9676	0.9419–0.9895	0.0076*
Dependent lung LAV%	1.1838	1.0856–1.3138	0.0005*
DLCO (% predicted)	0.9632	0.9353–0.9864	0.0055*

CI confidence interval, DLCO diffusing capacity for carbon dioxide, FLV functional lung volume, HU Hounsfield unit, LAV low attenuation volume, OR odds ratio

*The asterisk indicates that the variable was statistically significant

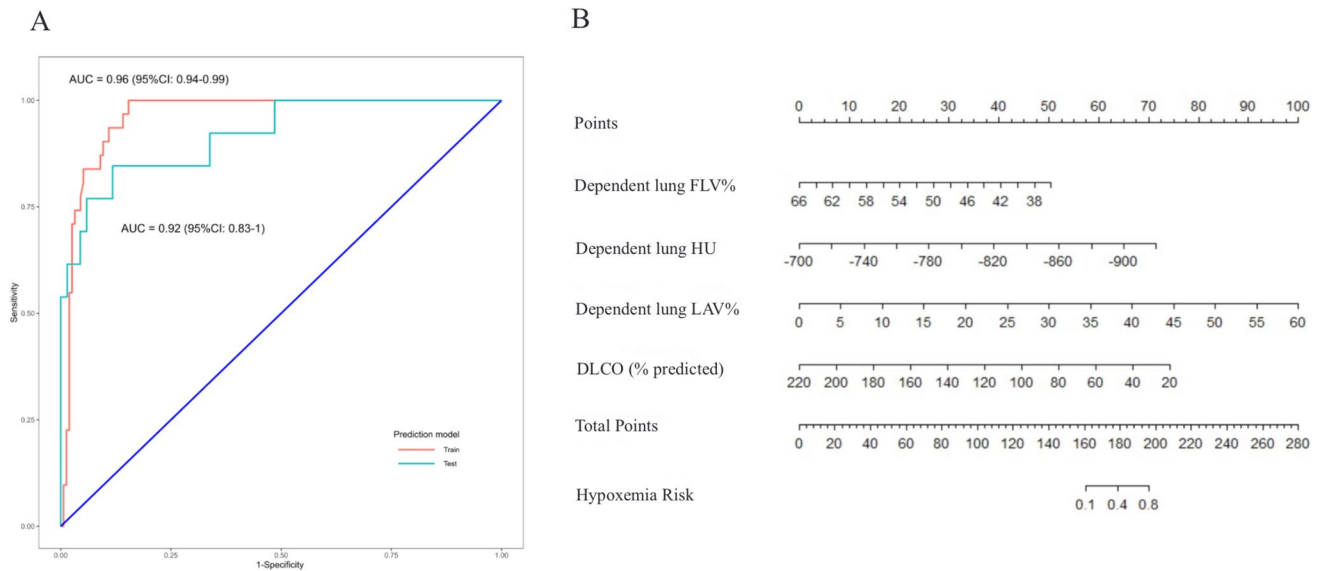


Fig. 2 ROC curves of the training set and test set (a) and nomogram for predicting OLV hypoxemia (b). a: the AUC in the training set was 0.96. In the test set, the AUC was 0.92. b: a nomogram containing four predictors provided an individual score for the risk of developing

OLV hypoxemia in VATS radical resection for lung cancer. AUC area under the curve, DLCO diffusing capacity for carbon dioxide, FLV functional lung volume, HU Hounsfield unit, LAV% low attenuation volume%

Discussion

Accurate prediction of the risk of hypoxemia due to OLV before lung cancer surgery is crucial for anesthesiologists because it affects the choice of airway tools and the decision-making of respiratory management. Our study demonstrated that preoperative dependent lung FLV%, dependent lung HU value, dependent lung LAV% and preoperative DLCO% pred were found to be independent risk factors for hypoxemia during OLV in VATS for radical resection of lung cancer. The predictive ability of three quantitative lung CT indicators for the risk of OLV hypoxemia represents a new discovery of this study (to our knowledge), which has not been previously reported. Among them, the dependent lung LAV% had the greatest impact on OLV hypoxemia, and we developed a new nomogram based on this finding. The results of the nomogram showed good risk prediction ability in the internal test set, which not only helps anesthesiologists to select appropriate lung isolation tools before surgery but also allows them to formulate personalized respiratory management strategies in advance to avoid the occurrence of OLV hypoxemia.

Three lung CT quantitative indicators are significantly related to the risk of OLV hypoxemia

The main finding of this study is that three quantitative lung CT indicators are significantly associated with the risk of OLV hypoxemia. The first indicator (the dependent lung FLV%) is significantly negatively correlated with the risk

of OLV hypoxemia. FLV reflects normal functional lung tissue, which is closely related to lung function [29]. Ueda et al. [26] found that the increase in the FLV was consistent with the improvement in lung function. Furthermore, the ratio of unilateral/single-lung FLV to total-lung FLV can help in evaluating the contribution of a single lung lobe to overall lung function. Fan et al. [29] calculated the ratio of the FLV of a single lung lobe to the FLV of the lung and used this ratio as a basis for predicting lung function after lung resection and achieved good results. This measurement emphasizes the contribution of removed lung tissue to overall lung function. Similarly, in this study, the ratio of the dependent lung FLV to the total lung FLV reflected the contribution of the dependent lung to overall lung function during OLV. The smaller the ratio, the less the dependent lung contributes to overall lung function and the more likely hypoxemia is to occur during OLV.

The second indicator (the dependent lung HU value) was significantly negatively correlated with the risk of OLV hypoxemia. The CT HU value is obtained by measuring the relative proportions of gas, blood, extracellular fluid and lung tissue. It is generally believed that the lung HU value reflects the density of the lungs [30]. Some research has shown that lung HU values are closely related to different pathological types of lung tissue [31] and PFT indicators, such as FEV₁ [32]. The results of this study showed that within the FLV range, a smaller HU value of the dependent lung corresponded to a greater risk of OLV hypoxemia. We speculate that lung cancer sometimes causes local airway obstruction, resulting in gas retention in the dependent

lungs, as evidenced by decreased lung density and consequent decrease in HU values. The ventilatory efficiency of the dependent lungs may also decrease significantly during OLV, thereby increasing the risk of hypoxemia.

The third indicator (dependent lung LAV%) was significantly positively correlated with the risk of OLV hypoxemia. Due to the fact that the threshold of -950 HU can distinguish normal lung tissue from emphysema lesions, the LAV% is considered to quantify emphysema [33]. A higher value indicates a more severe emphysema lesion. Emphysema is associated with many pathological changes in lung tissue. Studies have shown that the LAV% is closely related to lung function in patients with chronic obstructive pulmonary disease [34] and lung cancer [35]. Our study indicated that the degree of emphysema in the dependent lung has a significant impact on the incidence of hypoxemia during OLV. It is recommended that anesthesiologists focus on the predictive role of LAV% on the risk of OLV hypoxemia.

All three of these are common radiological indices used to measure lung status and are widely used in the management of COPD [33, 34] as well as in the prediction of perioperative lung function [26, 29, 32]. With the help of measurement software, these indicators are easy to obtain and can generally be calculated by anesthesiologists themselves after simple training; In the presence of specific lung conditions such as severe obstructive lung atelectasis, the anesthesiologist may request the radiologist to manually delineate the lung area before using the software to take measurements. The three quantitative lung CT metrics demonstrated in the results of this study are easily accessible and valuable in the prediction of hypoxemia in OLV.

The preoperative DLCO% pred is significantly related to the occurrence of OLV hypoxemia

The results of this study demonstrated a significant negative correlation between preoperative DLCO% pred and the risk of OLV hypoxemia, which is consistent with previous studies [9]. Lung diffusion dysfunction is the primary cause of hypoxemia in various lung diseases. DLCO% pred is an index that primarily reflects the diffusion function of the lungs. Other PFT indicators that we included (such as FEV₁ and FVC) were not found to be significantly correlated with outcome indicators, which is consistent with the results of several previous studies [36, 37]. However, another study [11] demonstrated that FVC or FEV₁ was significantly related to arterial blood oxygenation status during OLV. We believe that the reason for the inconsistent research results is that FEV₁ and FVC reflect the overall ventilation function of the lungs, whereas the oxygenation status of OLV mainly depends on the dependent lung. Patients with impaired ventilation of the dependent lung may exhibit hypoxemia during OLV, yet may demonstrate normal overall lung function

indices, rendering them challenging to identify. Furthermore, other preoperative factors that have been previously identified in other studies, including Hb, hypertension, and smoking status, were included in this study and were not found to be significantly associated with the risk of OLV hypoxemia. This discrepancy may be attributed to the fact that this study restricted the surgical team and type, and the distribution of the research population and the sample size differed from those of previous studies.

Construction and validation of the nomogram

A column-line diagram of intraoperative OLV hypoxemia in patients who underwent radical lung cancer surgery was established by using quantitative lung CT and PFT data. This diagram can help clinical doctors in making individualized predictions of hypoxemia during OLV in patients who underwent VATS radical resection for lung cancer. In the subsequent internal validation, the C-index and the areas under the ROC curve of the training and test sets were > 0.90 , indicating that the nomogram can accurately predict the likelihood of hypoxemia during OLV in radical lung cancer surgery.

Limitations of this study

There were two main limitations of our study. Firstly, this was a single-center retrospective study with a small sample size. Secondly, the failure to obtain expiratory phase CT images may have resulted in some degree of inaccuracy in the CT quantitative index measurements. In conclusion, this was a preliminary exploratory study. In the future, we intend to conduct a large-sample, multicenter prospective study and further improve the nomogram model.

Conclusion

The results of this study indicate that the dependent lung FLV%, dependent lung HU value, dependent lung LAV% and preoperative DLCO% pred are independent risk factors for hypoxemia during OLV in radical lung cancer surgery patients. Furthermore, a nomogram was constructed for risk assessment based on the aforementioned risk factors. Chest CT is a routine imaging method for the diagnosis and treatment of lung cancer patients. We recommend quantitative analysis of chest CT images of lung cancer patients before surgery. The combined use of CT quantitative indexes and DLCO% pred will facilitate the intuitive and accurate prediction of the risk of OLV hypoxemia during radical lung cancer surgery. This will assist anesthesiologists in making informed decisions regarding anesthesia for high-risk

patients, reducing the incidence of OLV hypoxemia and ensuring the safety of patients to a greater extent.

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Data availability The data that support the findings of this study are available upon request from the corresponding author. These data are not publicly available due to privacy or ethical restrictions.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of the Third Affiliated Hospital of Kunming Medical University Institutional Review Board (KYLX2023-191, December 18, 2023). Written informed consent was waived from individual or guardian participants.

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