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Evaluation of indocyanine green inhalation to detect air leak sites during video-assisted thoracoscopic surgery: a prospective study

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Abstract

Background This study aimed to investigate the feasibility and clinical benefits of indocyanine green (ICG) inhalation for detecting air leak sites during video-assisted thoracoscopic surgery (VATS).

Methods Between February 2023 and May 2023, a total of 288 patients underwent VATS were enrolled in this study. Among the population, 72 patients received ICG inhalation test following the traditional submersion sealing test. And 216 patients only underwent the submersion sealing test were matched using 1:3 propensity score matching analysis. The results of ICG inhalation test and the clinical outcomes were compared.

Results In the ICG group, 48 air leak sites were detected in 25 patients (25/72, 34.7%). The conventional submersion sealing test identified 30 air leak sites, while the ICG inhalation test detected 47 sites. Among these detected air leak sites, 34 sites were repaired by suturing or stapling. The postoperative air leak rate in the ICG group (20.8%) was significantly lower than the control group (37.0%, P = 0.011). ICG inhalation test was a favorable factor for reducing postoperative air leaks (OR: 0.40; 95%CI: 0.20–0.78; P = 0.008).

Conclusions The ICG inhalation test facilitates the identification of air leak sites that may have been overlooked in the conventional submersion sealing test. This technique is useful to reduce postoperative air leaks for patients undergoing VATS.

Trial registration Chinese Clinical Trial Registry: ChiCTR2300067603 on January 13rd 2023.

Keywords Air leaks, Video-assisted thoracoscopic surgery, Indocyanine green, Inhalation

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Introduction

Postoperative air leak is a prevalent complication following lung resection, affecting 20%−50% of patients who undergo pulmonary surgery [1, 2]. This condition can prolong hospital stay and delay chest tube removal, potentially increasing the risk of serious complications such as empyema, pneumonia, and respiratory failure [3]. To mitigate the risk of postoperative air leak, it is crucial to identify and repair all air leak sites during surgery [4].

Contrary to the integration of synthetic sealants and ameliorative staplers [5, 6], the methodology for intraoperative detection of air leak sites has remained unchanged for several decades. Up to date, the submersion sealing test is the most common approach for intraoperative evaluation of air leak [7]. Currently, the submersion sealing test remains the most prevalent technique for intraoperative evaluation of air leaks. In the conventional sealing test, the thoracic cavity is filled with saline or other fluids, and air bubbles are examined after the operative lung is ventilated. However, during VATS, the surgical field is significantly restricted by the inflated lung, potentially leading to the oversight of certain air leak sites. Therefore, the development of a novel method that does not impose such limitations would be highly beneficial in reducing postoperative air leaks.

The indocyanine green (ICG)-based near-infrared fluorescence technique has gained widespread acceptance in the field of surgery, particularly in the visualization of various anatomical structures [8–10]. Our institution has reported the use of ICG for near-infrared fluorescent imaging of lung tumors through both intravenous [11, 12] and inhalation administration routes [13]. Furthermore, we have described the application of ICG for near-infrared intraoperative imaging of thoracic sympathetic nerves [14] and interlobar fissures through intravascular administration [15]. Additionally, we have reported on the successful fluorescence imaging of thoracic ducts using subcutaneous injection of ICG [16].

In a recent publication by Yakota et al. [17], the application of intraoperative ICG inhalation for fluorescence imaging of air leak sites during lung resection was reported. The authors demonstrated that after inhaling an ICG aerosol, the dye would accumulate at the air leak sites, exhibiting continuous fluorescence under near-infrared camera observation. This fluorescence persisted even when the lungs were collapsed, suggesting that ICG inhalation may overcome the limitations imposed by conventional submersion sealing tests on surgical field visualization. However, it is important to note that this study was a single-arm trial and did not assess the clinical outcomes associated with this novel sealing test for pleural defects.

In this research, we described a modified intraoperative ICG nebulization method, and this study is the first to compare postoperative air leak in VATS patients utilizing intraoperative ICG inhalation test versus those without ICG inhalation test.

Methods

Study design and patient recruitment

This study aims to assess the effectiveness and clinical outcomes of intraoperative detection of air leak sites using ICG inhalation. Patients aged 18 years or older who underwent VATS at Peking University People's Hospital were eligible for the ICG group, and patients with allergies to iodine or indocyanine green, as well as those with history of asthma, were excluded. The ICG group was continuously enrolled from February to May 2023, including patients who met the inclusion criteria, did not meet the exclusion criteria, and voluntarily signed informed consent forms at our center. Subsequently, the control group was subsequently selected from patients during the same time period by matching based on gender, age, and surgical method using a 1:3 propensity score matching analysis to ensure comparability between the groups. Moreover, all enrolled patients were followed up for 1 month to evaluate the adverse events associated with ICG inhalation.

The primary objectives of this investigation were to evaluate the incidence of postoperative air leak and the duration of air leak exceeding 24 h following surgery, while the secondary endpoints were postoperative air leak of patients underwent wedge resection or anatomic resection, the rate of persistent air leaks (PAL) and the duration of chest tubes. A digital drainage system (Thopaz Chest Drain System, Medela Inc., Baar, Switzerland) was utilized to monitor the postoperative chest tube, which provided consistent suction and accurate measurement of air leak volume. The definition of postoperative air leak was established as an air leak volume recorded by the digital drainage system exceeding 0 ml/min at a suction pressure of −8 cmH_2O upon patient admission to the ward [18]. PAL was defined as postoperative air leak longer than 5 days. This study was registered in Chinese Clinical Trial Registry (ChiCTR2300067603).

Indocyanine green inhalation

ICG is a widely utilized near-infrared contrast agent with US and China Food and Drug Administration approval in near-infrared imaging [12, 19], which was applied as an aerosol in this investigation. All patients in the ICG group were administered aerosolized ICG (Concentration: 2.5 mg/ml. Yichuang Pharmaceutical Co. Ltd, Dandong, China) through a nebulizer system described in our previous study [13], which incorporates a jet nebulizer and a T-shaped tube. The jet nebulizer kit (Flexicare Medical Ltd, UK), driven by oxygen flow at 6L/min, was employed for aerosolizing the ICG, and a T-shaped tube was applied to connect the nebulizer kit and ventilator circuit. We utilized the near-infrared fluorescence thoracoscope system (DPM-ENDOCAM-03 and DPM-LIGHT-03, Zhuhai Dipu Medical Technology Co., Ltd., Zhuhai, China) for intraoperative fluorescent exploration.

Surgical procedure

After resecting the lung tumor, the traditional submersion sealing test was conducted. During this procedure, air bubbles were observed in the ventilated lungs at a pressure of 20 cm H_2O in a chest cavity filled with saline solution. The number and locations of air leak sites were recorded based on the presence of these bubbles. Following this, the chest cavity was dried, and all patients in the ICG group underwent the ICG inhalation test. These patients inhaled an ICG aerosol for approximately four respiratory cycles (20 s) through the aforementioned system while the ventilator was set to volume-controlled mode, maintaining a peak airway pressure of 20–25 cm H_2O at 12 respirations per minute. After the ICG inhalation, single-lung ventilation was resumed, and fluorescent exploration was performed to identify fluorescent sites deposited by ICG, which were recognized as air leak sites detected by the ICG inhalation test. For additional air leak sites identified solely by the ICG inhalation test, a second traditional submersion sealing test was conducted to confirm the presence of air leakage. Intraoperative air leaks were evaluated using the Macchiarini scale score (MSS), which classified the air leak sites as grade 0 (No leak), grade I (Countable bubbles), grade II (Streams of bubbles) and grade III (Coalesced bubbles). MSS grade I and II air leaks were regarded as minor leaks and were managed by synthetic sealants, while grade III air leaks were regarded as major leaks and were repaired by surgical intervention [20, 21].

Statistical analysis

A nearest-neighbor 1:3 propensity score matching with a caliper of 0.1 based on age, gender, extent of surgery and pathology was performed to reduce the potential selection bias. Descriptive statistical methods were employed to elucidate the demographic and clinical features of patients, including the median, range, and proportion. The Mann–Whitney U test and Wilcoxon signed rank sum test were utilized to compare non-normally distributed and paired measurement data, respectively. The chi-square test was implemented to assess the differences in count data between two groups. McNemar's paired chi-square test was applied to evaluate rate disparities between paired samples. Logistic regression analysis was conducted to identify risk factors for postoperative air leakage, with variables exhibiting $P < 0.1$ in univariate logistic regression analysis being incorporated into the multivariate logistic regression model. Statistical analyses were executed using Stata/SE 15.0 (StataCorp, College Station, TX, USA) and GraphPad Prism 9.0 (GraphPad Prism Software Inc., San Diego, CA). All statistical tests were two-tailed, and a P-value < 0.05 was considered statistically significant.

Results

Characteristics of patients

In total, 288 patients were incorporated into this study (Fig. 1). A prospective consecutively enrollment of 72 patients (comprising 34 males and 38 females) with a median age of 63 years (ranging from 33 to 79 years) was conducted in the ICG group, out of which 62 were pathologically confirmed to have primary lung cancer. The majority of these patients ($n = 37$, accounting for 51.39%) underwent wedge resection, while 25 patients (34.72%) underwent lobectomy. Additionally, a total of 216 patients were enrolled in the control group using propensity score matching at a ratio of 1:3, 168 of whom were confirmed to have primary lung cancer. Among the control group, 111 patients (51.39%) underwent wedge resection and 75 patients (34.72%) received lobectomy. The demographic and clinical characteristics of the study population are presented in Table 1.

Features of air leak sites after ICG inhalation

The visualizations of air leaks in four representative scenarios are depicted in Fig. 2A-D. Figure 2a illustrated the images obtained through the traditional submersion sealing test for detecting air leak sites, which can significantly

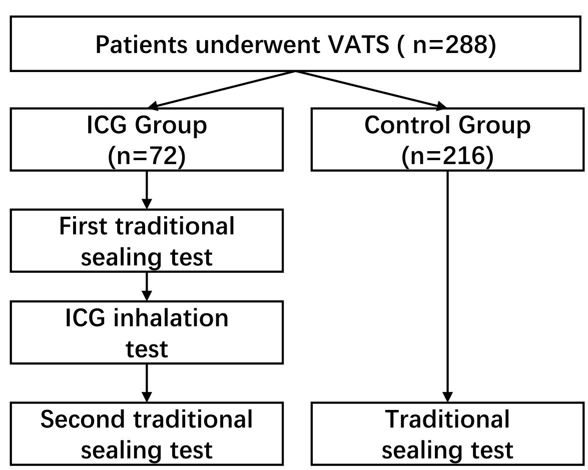

Fig. 1 Flow chart of this study

Table 1 Clinicopathological characteristics of study population

Characteristics	ICG group	Control group	*P*-value
Number of patients, n	72	216	
Age, years, median(range)	63 (33–79)	63 (13–80)	0.52
Gender, n (%)			0.95
Male	34 (47.22)	103 (47.69)	
Female	38 (52.78)	113 (52.31)	
Smoking history	17 (23.61)	60 (27.78)	0.49
Respiratory disease			
COPD	7 (9.72)	18 (8.33)	0.72
ILD	2 (2.78)	2 (0.93)	0.25
Other diseases[a]	3 (4.17)	14 (6.48)	0.47
Extent of surgery, n (%)			1
Wedge resection	37 (51.39)	111 (51.39)	
Segmentectomy	10 (13.89)	30 (13.89)	
Lobectomy	25 (34.72)	75 (34.72)	
Pathology, n (%)			0.29
Benign tumor	9 (12.5)	45 (20.83)	
Metastatic lung tumor	1 (1.39)	3 (1.39)	
Lung cancer	62 (86.11)	168 (77.78)	

ICG indocyanine green, *COPD* chronic obstructive pulmonary disease, *ILD* interstitial lung disease

[a] Including atelectasis and bronchiectasia

impair the field of view under thoracoscopic conditions, and the exact location of the air leak sites could not be determined quickly. Figure 2b showed cases where the visualizations were subsequent to water drainage, under which circumstances the surgeon could not accurately suture repair the air leak sites without the guidance of bubbles. Following inhalation of ICG, the air leak sites were fluorescently labeled (Fig. 2c) and continued to be visualized when the pulmonary was collapsed, which effectively guided surgeons to repair the pleural defect. (Video).

Detection of the air leak sites

In the control group, 82 air leaks sites were detected in 64 patients (64/216, 29.63%), while 48 sites were identified in 25 cases among the ICG group (25/72, 34.72%, $P = 0.462$). In the ICG group, a total of 30 air leak sites were identified during the initial conventional submersion sealing test. The majority of these sites ($n = 12$) were caused by anatomical separation of the interlobular fissures, followed by division of pleural adhesions ($n = 5$) and dissection of lymph nodes ($n = 5$) (Fig. 3). The ICG inhalation test revealed a total of 50 fluorescent sites, with 29 being consistent with the positive results of the initial conventional submersion sealing test. Additionally, 21 fluorescent spots were not detected during the initial submersion sealing test. Upon re-immersion testing, 18 of the 21 fluorescent spots were confirmed to be additional pleural defects (Supplementary Fig. 1), with 5 located near the sites identified during the submersion sealing test, 13 distant from the sites detected during the submersion sealing test, even outside the surgical field. The remaining three fluorescent spots were false positive results that did not produce bubbles during re-immersion testing. One air leak site detected during the initial sealing test was not detected after ICG inhalation and was considered a false negative finding.

From the point of surgical type, 18 air leak sites were found among patients underwent wedge resection, with 12 were detected by saline submersion sealing test and 18 were identified by ICG inhalation test. Thirty air leak sites were revealed among patients received anatomic lung resection, with 18 and 29 were detected by saline submersion sealing test and ICG inhalation test respectively. The overall sensitivity of ICG inhalation for detecting air leak sites was 98%, while the sensitivity of the conventional submersion sealing test was only 60% (Table 2), which was statistically significant ($P < 0.001$). Despite a higher accuracy, the ICG test took significantly less time than the conventional test (95 s vs. 160 s, $P < 0.001$). In the ICG group, the traditional submersion sealing test identified 21 major leaks and 9 minor leaks, while the ICG inhalation test detected 34 major leaks and 13 minor leaks. All major leaks detected by both methods were surgically repaired, while minor leaks were managed with synthetic sealants.

Throughout the study, no intraoperative adverse reactions, including decreases in blood oxygen levels or blood pressure, were observed in patients undergoing the ICG inhalation test. Additionally, during the one-month postoperative follow-up, no ICG-related adverse reactions were reported.

Comparison of the clinical outcomes

Among the intraoperatively detected air leak sites, 57 sites (57/82, 69.51%) in the control group and 34 sites in the ICG group (34/48, 70.83%) were classified as MSS-III leaks and were repaired by suturing or stapling. The postoperative air leak rate was significantly lower in the ICG group (15/72, 20.83%) compared to the control group (80/216, 37.04%, $P = 0.011$), particularly in more complex lung resections, such as lobectomy (9/25, 36% vs 45/75, 60%, $P = 0.037$). Additionally, when comparing the rate of postoperative air leak over 24 h or persistent air leak, the ICG group had a significantly lower risk than the control group (Table 3). In the control group, 13 patients experienced persistent postoperative air leaks, while none of the individuals in the ICG group encountered such occurrences ($P = 0.033$). No significant difference was found in the

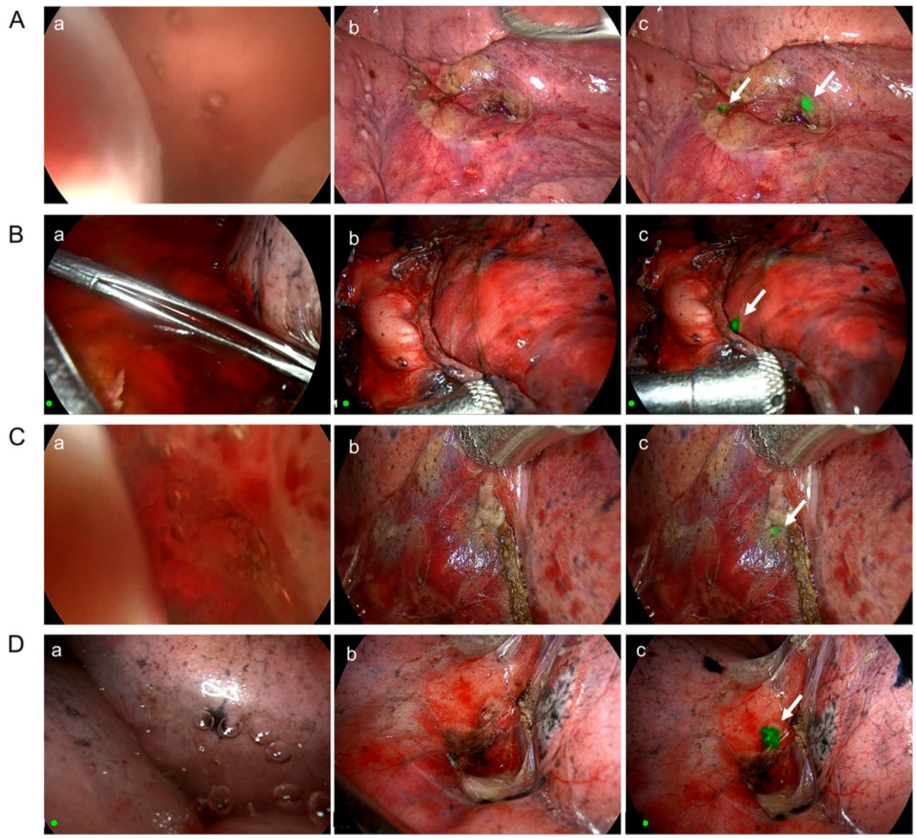

Fig. 2 The visualizations of air leaks in the submersion sealing test and the ICG inhalation test. **a** visions from traditional submersion sealing test. **b** visions subsequent to water drainage. **c** visions after inhalation of ICG

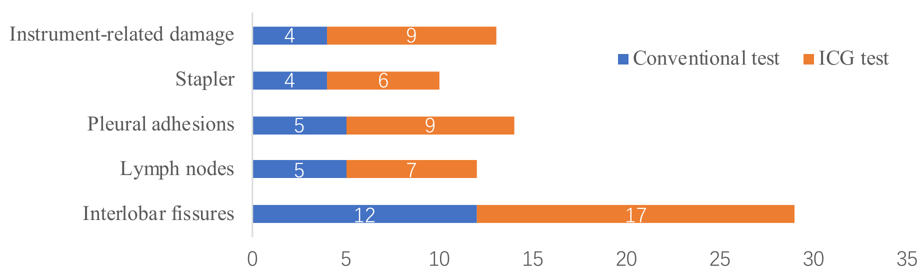

Fig. 3 Causes of air leak sites in the ICG group detected by the conventional test and ICG test

duration of chest tube between two groups ($P = 0.885$), a further subgroup analysis of patients undergoing segmentectomy or lobectomy revealed that the average chest drain duration was 3.142 days in the ICG group versus 3.714 days in the control group ($P = 0.2136$). In the control group, 7 patients developed postoperative pneumonia, which was resolved with antibiotic escalation, and in the ICG group, only 1 patient developed postoperative pneumonia, also resolved with antibiotic treatment. And no other severe complications were found during study. Moreover, 2 patients in the control group underwent interleukin-based chemical pleurodesis because of the PAL.

Factors related to postoperative air leakage

Subsequently, a logistic regression analysis was performed to investigate the correlation between potential clinical/surgical factors and postoperative air leakage. As demonstrated in Supplementary Table 1, patients with a history with chronic obstructive pulmonary disease (COPD) and those undergoing more complex surgical procedures are at a higher risk of

Table 2 Result of air leak sites detection in ICG group

Number of detected sites, n	
Traditional sealing test	30
ICG inhalation test	50
Time for detecting sites, s	
Traditional sealing test	160
ICG inhalation test	95
Status of detected sites by ICG inhalation test, n	
Matched air leak sites	29
Additional air leak sites	18
False positive	3
False negative	1
Total air leak sites, n	48
Detection rate, %	
Traditional sealing test	60%
ICG inhalation test	98%

ICG indocyanine green

developing postoperative air leakage, which aligns with existing knowledge. Furthermore, this study revealed that an ICG inhalation test can significantly reduce the likelihood of postoperative air leakage.

Discussion

In this prospective study, we describe the detailed imaging characteristics of air leak sites using ICG aerosol with a modified atomization technique. Furthermore, we compare the clinical outcomes of this method with those of traditional submersion sealing testing for the first time.

In this investigation, we have developed a novel nebulizing system for ICG aerosol delivery, which incorporates a jet nebulizer and a T-shaped tube. This approach differs from the previously reported nebulization technique by Yokota et al. [17]. Based on our preclinical studies, sufficient fluorescence was observed at air leak sites following 20 s of ICG aerosol inhalation when the ICG concentration was set at 2.5 mg/ml. Notably, our study found that the median time required for the ICG inhalation test was 95 s, which is shorter than that of the traditional submersion sealing test. The nebulizing system and ICG used in this study are both inexpensive and readily available, suggesting that this innovative technique has great potential for widespread application.

The ICG inhalation test offers several advantages over the traditional sealing test. The most notable feature of the ICG inhalation test is air leak sites stained with ICG exhibit a constant fluorescence, particularly when the lung is in a collapsed state. This advantage allows surgeons to conduct a comprehensive exploration of air leak sites without being restricted by the inflated lungs during surgery. This comprehensive approach under collapsed lung conditions ensured thorough sealing of pleural defects, thereby decreasing the likelihood of postoperative air leaks and promoting faster patient recovery. In this study, 18 newly identified fluorescent sites in the ICG group were confirmed as air leak sites through the second submersion sealing test, indicating a higher detection rate for this novel technique. It is worth noting that certain small lung air leak sites, although not requiring surgical intervention, still exhibited noticeable fluorescence after inhalation of ICG, reflecting the high sensitivity of this method. In this study, intraoperative air leaks were evaluated and addressed according to the MSS grade, and the rates of severe air leak sites (grade III) detected by traditional sealing test were similar between two groups, further proving the comparability of these two groups.

In the ICG group, only one air leak site failed to exhibit sufficient fluorescence after inhalation of ICG aerosol and was not detected during intraoperative fluorescent exploration. This air leak point was caused by accidental injury of clamp, which was covered in blood. Yakota et al. [17]. have reported that air leak sites blocked by liquids such as blood or pleural fluid may influence the

Table 3 Clinical outcomes comparison between ICG and control group

Characteristics	ICG group	Control group	*P*-value
Time of traditional sealing test, median (range)	160 (60–440)	180 (100–340)	0.114
Patients with intraoperative air leak, n (%)	25 (34.72)	64 (29.63)	0.462
Postoperative air leak, n (%)			
Overall	15 (20.83)	80 (37.04)	0.011
Wedge resection	3 (8.11)	22 (19.82)	0.1
Segmentectomy	3 (30)	13 (43)	0.456
Lobectomy	9 (36)	45 (60)	0.037
Postoperative air leak over 24 h, n (%)	6 (8.33)	40 (18.52)	0.041
Persistent air leak, n (%)	0 (0)	13 (6.02)	0.033
Chest tube duration (days), median (range)	3 (2–10)	3 (2–13)	0.885

ICG indocyanine green

staining of ICG at alveolar-pleural fistulas. Additionally, three fluorescent points were confirmed not to be air leak sites through repeated traditional submersion sealing tests. The reasons for these false positive findings may be excessive ICG inhalation or local emphysema, which require further research. Therefore, it is necessary to dry the chest cavity and use the proper inhalation dosage of ICG when performing this novel technique.

For patients with extensive pleural adhesions, inhalation of ICG offers distinct advantages over conventional submersion sealing tests for detecting air leak sites. Supplementary Fig. 2 displays intraoperative images of a patient with extensive pleural adhesions that resulted in multiple air leak sites during the division of pleural adhesions. During the initial water immersion test, numerous bubbles were produced, making it challenging to discern the precise number and location of the air leaks. However, after inhalation of ICG, the air leaks were marked with fluorescence, revealing multiple defect sites. With the guidance of fluorescence, the surgeon was able to effectively repair the air leaks, thereby preventing prolonged postoperative drainage time.

Our study demonstrated the safety of the ICG inhalation test, as no adverse reactions were observed intraoperatively or during the one-month postoperative follow-up. However, further studies with larger sample sizes are warranted to fully establish the safety profile of this method.

The underlying mechanism of fluorescent imaging for detecting air leak sites following ICG aerosol inhalation remains elusive. When inhaled, ICG aerosolizes and travels through the respiratory tract. We speculate that ICG may preferentially reach the lung surface through air leak sites as opposed to areas with normal pleural, and the disrupted alveolar-capillary barrier at sites of air leaks allows ICG to bind to plasma proteins within the pleural space. Under near-infrared fluorescence imaging, these areas emit a distinct fluorescent signal, which provides a clear contrast between leaking and non-leaking areas. This hypothesis also implies that the dosage of inhaled ICG should be carefully controlled to prevent false-positive findings due to excessive ICG inhalation.

According to previous studies, postoperative air leak occurs in 20%−50% patients undergoing lung resections, which is similar with the result of control group in this study. We found the incidence of postoperative air leak in the ICG group was significantly lower than that in the control group. Specifically, patients who underwent lobectomy exhibited a significantly lower rate of postoperative air leak in the ICG group, indicating that this novel method may be more advantageous for patients undergoing complex surgeries with a higher risk of air leak. Most air leaks would spontaneously resolve by 24 h because of the slight pleural damage and absorption of residual cavity, especially for patients receiving wedge resections. In fact, only 1 and 6 patients undergoing wedge resections endured air leak after first 24 h. Therefore, to evaluate the clinical impact of air leak appropriately, we compared patients with postoperative air leak beyond 24 h, and these patients were more prevalent among the control group. These findings suggest that this technique may be beneficial in reducing both the incidence and duration of air leak after lung surgeries, thereby reducing the risk of complications related postoperative air leak.

The nebulization system used for ICG delivery is straightforward and can be easily incorporated into the surgical workflow without significant additional training or resources. Furthermore, the cost-effectiveness of ICG, combined with its safety profile demonstrated in our study, supports its adoption as a tool for air leak detection.

In this study, we demonstrated that ICG inhalation test offers distinct advantages over traditional underwater testing, including shorter detection time, higher accuracy, and continuous visualization, which may be particularly beneficial for less experienced thoracic surgeons in identifying and managing air leaks intraoperatively. However, no significant differences were observed in chest drain duration or severe complications between ICG inhalation and the control group in this study. This may be attributed to our center's high surgical volume, advanced thoracoscopic expertise, and the predominance of simple wedge resections in our cohort, who generally have a short chest tube duration. Notably, subgroup analysis revealed a more pronounced reduction in chest tube duration in patients undergoing more complex procedures, such as lobectomy and segmentectomy. Future multicenter studies involving a broader range of complex cases are necessary to further elucidate the clinical benefits of this technique.

A few limitations should be considered in interpreting this study. This study was a single-center study, and the selection bias inherent in this research is unavoidable. Moreover, the ICG inhalation test could not determine the severity of air leaks, and the relationship between the findings of ICG inhalation and the volume of air leaks needs further researches. Furthermore, there may be observer bias in identifying air leaks, as the detection relies on the subjective assessment of the surgical team. Additionally, variations in surgical techniques across different procedures may influence the efficacy of the ICG inhalation method. Future randomized controlled trials with standardized surgical protocols and multi-center participation are necessary to further evaluate the effectiveness and generalizability of the ICG technique in various surgical settings.

Conclusion

The ICG inhalation test facilitates the identification of air leak sites that may have been overlooked in the conventional submersion sealing test. This technique is useful to reduce postoperative air leaks for patients undergoing VATS.

Abbreviations

VATS	Video-assisted thoracoscopic surgery
ICG	Indocyanine green
CI	Confidence interval
PAL	Persistent air leaks
MSS	Macchiarini scale score
COPD	Chronic obstructive pulmonary disease
ILD	Interstitial lung disease

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12893-025-02875-z.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

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Not applicable

Authors' contributions

Zhenfan Wang: Data collection and analysis; Software; Validation; Visualization; Writing-original draft. Xue Tian: Data collection; Editing. Zihan Wei: Data collection; Writing-original draft. Hao Xu: Data collection; Writing—original draft; Editing. Kunshan He: Software; Validation. Chongwei Chi: Software; Validation. Songjing Zhao: Software; Validation. Fan Yang: Methodology; Project administration. Yun Li: Conceptualization; Methodology; Project administration. Jian Zhou: Conceptualization; Methodology; Project administration; Supervision.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate

The study received ethics approval from the Institutional Review Board of Peking University People's Hospital (2022PHB382-001; November 16, 2022) and was conducted in accordance with the Declaration of Helsinki. Prior to undergoing surgery, all participants provided written informed consent in accordance with established ethical guidelines.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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