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Indocyanine green fluorescence identification of the intersegmental plane by the target segmental vein-first single-blocking during thoracoscopic segmentectomy

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Abstract

Background Innovative attempt to explore the feasibility and accuracy of using indocyanine green fluorescence (ICGF) to identify the intersegmental plane by the target segmental veins preferential ligation during thoracoscopic segmentectomy.

Methods A retrospective analysis was conducted on clinical data of 32 consecutive patients who underwent thoracoscopic segmentectomy with intersegmental plane identification using both ICGF and inflation-deflation method after target segmental veins prioritized blocking at Nanjing Chest Hospital from December 2022 to June 2023. Preoperative three-dimensional reconstruction was used to identify the target segment and the anatomical structure of the arteries, veins, and bronchi. After ligating the target segmental veins during surgery, the first intersegmental plane was immediately identified and marked with an electrocoagulation device using an inflation-deflation method. Subsequently, the second intersegmental plane was determined using the ICGF method. Finally, the consistency of the two intersegmental planes was evaluated.

Results All the 32 patients successfully completed thoracoscopic segmentectomy without ICG-related complications and perioperative death. The average operation time was (98.59 ± 20.72) min, the average intraoperative blood loss was (45.31 ± 35.65) ml, and the average postoperative chest tube removal time was (3.5 ± 1.16) days. The average postoperative hospital stay was (4.66 ± 1.29) days, and the average tumor margin width was (26.96 ± 5.86) mm. The intersegmental plane determined by ICGF method was basically consistent with inflation-deflation method in all patients.

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Conclusion The ICGF can safely and accurately identify the intersegmental plane by target segmental veins preferential ligation during thoracoscopic segmentectomy, which is a beneficial exploration and important supplement to the simplified thoracoscopic anatomical segmentectomy.

Keywords Segmentectomy, Pulmonary vein, Fluorescence, Indocyanine green, Pulmonary circulation

Background

Thoracoscopic anatomical lung segmentectomy not only requires skilled surgical techniques but also precise identification of segmental anatomical structures and accurate excision of lung parenchyma guided by intersegmental plane delineation. Recent studies have introduced the pulmonary circulation single-blocking method for distinguishing the intersegmental plane during segmentectomy and have further explained the principles underlying the inflation-deflation method [1–3]. In fact, the decisive factor influencing the formation of intersegmental planes using the inflation-deflation method is the interruption of pulmonary circulation. Blocking either the arterial or venous blood flow to the target segment can terminate the pulmonary blood circulation and gas exchange, resulting in a distinct boundary between lung expansion and collapse [1]. However, there are controversies after the introduction of this novel method, primarily focusing on the accuracy of identifying the intersegmental plane. Previous research has demonstrated that the intersegmental planes formed after the single target artery occlusion are as accurate as those formed using the modified inflation-deflation method [4], and are also consistent with those formed using the ICGF method [5]. Additionally, our previous study has also confirmed a high degree of concordance between the intersegmental plane formed by the ICGF method and the modified inflation-deflation method [6]. However, all the above methods are based on occlusion of the target segmental artery. Now we know that a single occlusion of the target segmental veins, followed by inflation-deflation method, can emerge an intersegmental plane after a several minutes. Is the intersegmental plane emerged by target segment veins preferentially single-blocking using inflation-deflation method is concordant with ICGF method? We have reviewed a large number of literatures and found no relevant reports about the intersegmental plane identified by ICGF after target segmental veins single-blocking.

In this study, we designed an experiment to compare whether the intersegmental plane displayed after target segmental veins preferentially single-blocking using the inflation-deflation and ICGF method are consistent, and evaluate the feasibility and accuracy of using ICGF to identify the intersegmental plane by the target segmental veins preferential ligation during thoracoscopic segmentectomy.

Materials and methods

General information

This study was approved by the Ethics Committee of Nanjing Chest Hospital, and written informed consent was obtained from all patients before surgery. A retrospective analysis of clinical data from 32 consecutive patients with pulmonary nodules who underwent thoracoscopic anatomical lung segmentectomy at Nanjing Chest Hospital using both ICGF and inflation-deflation method to display the intersegmental plane after prioritizing segmental veins occlusion from December 2022 to June 2023. Inclusion criteria: (1) Evaluation of preoperative chest CT for pulmonary nodules meeting the indications for segmentectomy according to the NCCN guidelines; (2) Normal preoperative cardiopulmonary function examination; (3) No preoperative adjuvant chemotherapy or other antitumor comprehensive treatments; (4) Lung segmentectomy performed with prioritized single blockade of the target segmental veins. Exclusion criteria: (1) History of allergy to iodine contrast agents or indocyanine green; (2) Concurrent severe liver cirrhosis or liver dysfunction.

Methods

For patients requiring preoperative localization of pulmonary nodules, they were first scheduled to undergo precise and painless localization of pulmonary nodules under basic anesthesia guidance in the mobile CT room [7]. Subsequently, they were seamlessly transferred directly to the operating room for general intravenous anesthesia with double-lumen endotracheal intubation to maintain single-lung ventilation on the healthy side. Typically, a single incision of approximately 3 cm in length was made between the 4th or 5th rib in the mid-axillary line for thoracoscopic anatomical lung segmentectomy. Based on the dynamic target segmental images generated by the preoperative pulmonary nodules three-dimensional reconstruction software Mimics 22.0 (Materialise Medical, Leuven, Belgium) (typically placed in front of the thoracoscopic display screen for real-time intraoperative navigation), precise anatomical identification and disconnection of all pulmonary vein branches within the target segment were prioritized during surgery (Fig. 1a).

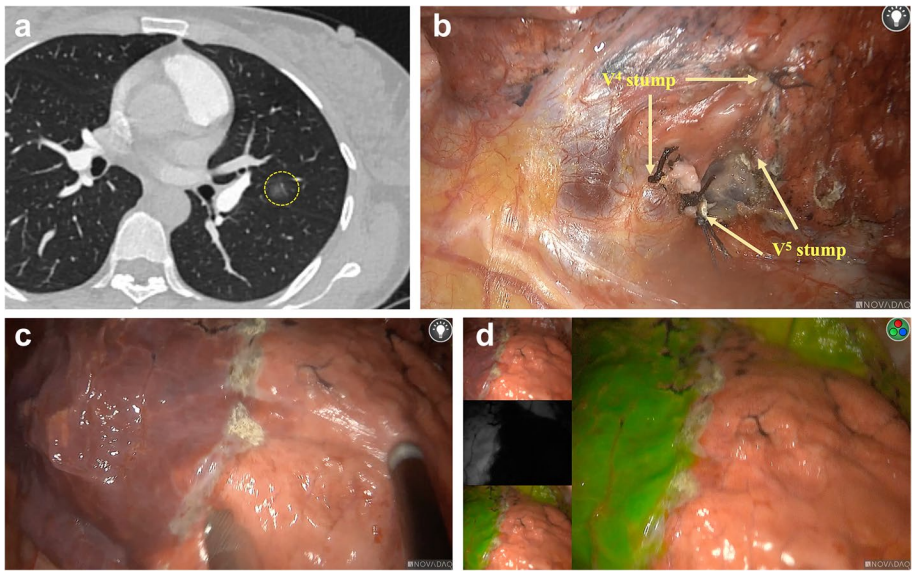

Fig. 1 **a** A 40-year-old female patient with thin-section CT showing a 14 mm ground glass opacity (GGO) in the lingual segment (S^{4+5}) of the left upper lung. **b** Preoperative three-dimensional reconstruction image indicating that the lingual segment vein consists of two branches (V^4 and V^5), V^4 and V^5 were severed respectively. **c** The inflation-deflation plane formed after anatomically disconnecting the lingual veins, marked using an electrocoagulation device. **d** The visualization of intersegmental plane by indocyanine green fluorescence method

Subsequently, the anesthesiologist was instructed to control the airway pressure at 20 cmH_2O and perform complete lung inflation with 100% pure oxygen (Fig. 1b), followed by resumption of single-lung ventilation on the healthy side. During the waiting period for intersegmental plane visualization, further dissection of the segmental structures could be performed without division. After waiting for approximately 10–15 min, a distinct demarcation line between the deflated surrounding segments and the inflated target segment was formed, and this demarcation line no longer changed over time. It was marked as the first plane using an electrocoagulation device (Fig. 1c). After marking, 5 mg/body of ICG (Eisai Liaoning Pharmaceutical, Liaoning, China; drug approval number H20045514, China Food and Drug Administration) was immediately injected into the peripheral vein by the circulating nurse. Subsequently, the fluorescence mode of the PINPOINT thoracoscopic fluorescence imaging system (NOVADAQ, Ontario, Canada) was activated, revealing a clear demarcation line between the stained and unstained areas, which was designated as the second plane (Fig. 1d). The alignment between the demarcation line marked by the electrocoagulation device and the two intersegmental planes were carefully assessed by visual inspection. After visualizing and contrasting the two intersegmental planes, the target segmental bronchus and pulmonary artery branches within the intersegmental plane area were resected, and the "work-plane extension and gate opening" technique was used with energy instruments combined with a cutting and suturing device for tailoring the segmental junction interface along the inter-segmental pulmonary veins [8].

In this study, we identified that the inflation-deflation method for identifying the intersegmental plane after target segmental veins occlusion is accurate and reliable. The target segmental veins—those venous branches in close proximity to the target segment where the pulmonary nodule was located, namely the intra-segmental veins.

Statistical analysis

Statistical data analysis was conducted using SPSS 22.0 software (SPSS Inc, Chicago, IL, USA). The continuous data were presented as mean ± standard deviation (SD). The categorical variables were presented by frequency and percentage (%).

Results

Consistency of both methods

All 32 patients underwent single-port thoracoscopic lung segmentectomy smoothly. After prioritizing the blockade of the target segmental veins, the inflation-deflation planes observed were essentially consistent with those determined by ICGF, with the heights of the two intersegmental planes matching on visual inspection in all 32 cases. The operative findings of each method are

Table 1 Distribution of pulmonary nodules in target segment positions

Right side	Cases	Left side	Cases
S^{2}	3	S^{3}	3
S^{3}	4	S^{4}	1
S^{2b+3a}	2	S^{4+5}	5
S^{7+8}	1	S^{5}	1
S^{8+9}	2	S^{8}	1
S^{9}	1	S^{8+9+10}	1
S^{9+10}	2	S^{9+10}	2
S^{10}	2	S^{10}	1

shown in Figs. 1c and 1d. The distribution of pulmonary nodules in target segment positions is detailed in Table 1.

Surgical outcomes

All 32 patients obtained sufficient tumor margins, meeting the requirement of margins ≥ 2 cm or ≥ the maximum diameter of the tumor. The average tumor margin width was (26.96 ± 5.86) mm, the average lung segment operation time was (98.59 ± 20.72) min, the average intraoperative blood loss was (45.31 ± 35.65) ml, the average postoperative chest tube removal time was (3.5 ± 1.16) days, and the average postoperative hospital stay was (4.66 ± 1.29) days. The final pathological diagnosis for all enrolled patients was early-stage lung cancer, including 5 cases of adenocarcinoma in situ, 18 cases of minimally invasive adenocarcinoma, and 9 cases of invasive adenocarcinoma.

There were no ICG-related complications and no perioperative deaths. Detailed perioperative data for the 32 lung segmentectomy cases are shown in Table 2.

Table 2 Perioperative data for 32 cases of lung segmentectomy

Clinical Data	Data
Age (Yeas)	58.69 ± 11.84
Sex [n (%)]	
Male	14 (43.8)
Female	18 (56.3)
Smoking history [n (%)]	
Yes	8 (25)
No	24 (75)
Tumor diameter (mm)	11.22 ± 3.97
FEV_1 (L)	2.46 ± 0.67
Surgical duration (min)	98.59 ± 20.72
Intraoperative blood loss (ml)	45.31 ± 35.65
Chest tube duration (d)	3.5 ± 1.16
Postoperative hospital stay (d)	4.66 ± 1.29
Postoperative complications [n (%)]	
Persistent pulmonary air leak (> 7d)	0
Hemoptysis	0
Atelectasis	0
Indocyanine green-related complications	0
Pathology results [n (%)]	
AIS	5 (15.6)
MIA	18 (56.3)
IAC	9 (28.1)
Margin width (mm)	26.96 ± 5.86

FEV1 Forced expiratory volume in one second, *AIS* Adenocarcinoma in situ, *MIA* Minimally invasive adenocarcinoma, *IAC* Invasive adenocarcinoma

Discussion

Results from the two largest prospective randomized controlled trials, JCOG0802 and CALGB140503, suggest that for peripheral non-small cell lung cancer (NSCLC) with diameters ≤ 2 cm, sublobar resection is not inferior to lobectomy in terms of long-term recurrence rate and oncological outcomes [9, 10]. This may lead to sublobar resection replacing lobectomy as the standard surgical approach for early-stage peripheral NSCLC with a diameter ≤ 2 cm. Furthermore, with the increasing number of patients with ground-glass opacity (GGO) nodules, multiple primary lung cancers, and multifocal lung cancers, thoracoscopic segmentectomy, by enabling curative resection of early lung cancers while preserving more normal lung parenchyma, has become increasingly favored by contemporary thoracic surgeons [11–13].

However, it is important to note that the non-inferiority of segmentectomy to lobectomy in long-term oncological outcomes is contingent upon achieving a sufficient margin width of ≥ 2 cm or ≥ the maximum diameter of the nodule during parenchymal dissection guided by intersegmental planes [14]. Although the JCOG0802 study implemented rigorous quality control measures for segmentectomy, there were still 22 cases in the segmentectomy group that were transferred to lobectomy due to lymph node metastasis or positive margins after randomization. Additionally, the segmentectomy group had a higher overall recurrence rate (12.1% vs 7.9%, $p = 0.020$) and local recurrence rate (10.5% vs 5.4%, $p = 0.002$) compared to the lobectomy group [9]. This may be attributed to the lack of preoperative three-dimensional reconstruction of pulmonary nodules at enrollment, resulting in inaccurate identification of the target segment location or incomplete recognition of segmental anatomy, leading to considerable subjectivity in determining the boundary between the intersegmental planes and difficulty in ensuring tumor-free margins. Moreover, at enrollment, segmentectomy was performed based on standard lung segments as the minimum resection unit. For

some nodules located near the intersegmental plane, if a standard lung segment resection is performed, it may be difficult to ensure negative margins. Anatomical segmentectomy techniques have undergone technological optimization and development over the decades since JCOG0802, with lung subsegments now considered the minimum resection unit, which is more conducive to controlling tumor margins [15]. Therefore, proficient thoracic surgical skills, accurate identification of segmental anatomy, and intersegmental planes are crucial for implementing precise anatomical segmentectomy.

This study innovatively attempted to identify the intersegmental planes using the ICGF method after target segmental vein-first single-blocking during thoracoscopic segmentectomy. This approach was successfully implemented in all 32 patients, demonstrating satisfactory stained intersegmental planes. Moreover, the results of our study suggest that the intersegmental plane generated by the ICGF method during vein-first resection is concordant with the inflation-deflation method. There were no ICG-related intraoperative or postoperative complications, nor were there any perioperative deaths. All patients underwent precise lung segment resection under the guidance of the intersegmental plane navigation lines and achieved safe and reliable tumor margins without removing an unreasonable amount of pulmonary parenchyma.

In the past, most scholars both domestically and internationally have proposed that the decisive factor for precise identification of the intersegmental planes lies in the accurate disconnection of the target segmental artery [4, 5, 15, 16]. They believe that there is extensive segmental venous collateral circulation between lung segments, known as "non-uniqueness," and only by disconnecting the target segmental veins cannot the intersegmental plane be formed. This study provides the first evidence that the ICGF method can produce clear intersegmental planes after target segmental vein-first single-blocking, and the boundary lines formed are basically matched with those of the inflation-deflation planes. The possible mechanism underlying the formation of the intersegmental plane is the blockage of blood flow in the target segment following pulmonary vein occlusion, preventing ICG from entering the target artery. Due to its advantages of simplicity, speed, accuracy, low requirement for lung quality, and significant reduction in operative and anesthesia time, the ICGF method for visualizing the intersegmental planes is increasingly being promoted and used by thoracic surgeons [17]. However, currently, the clinical application of the ICGF method to visualize intersegmental planes is mainly based on the target segmental artery-first resection. The exploration in this study suggests that termination of the segmental pulmonary circulation and formation of accurate and reliable intersegmental planes can be achieved by target segmental vein-first single-disconnecting during segmentectomy, challenging the theory of "non-uniqueness" of venous collateral circulation. Additionally, it provides surgeons with more flexible options in preoperative planning based on the location of pulmonary nodules within lung segments and their anatomical characteristics, whether from the target pulmonary artery-first resection or the target pulmonary vein-first resection, which has important clinical significance to popularize segmentectomy.

Before the operation, three-dimensional reconstruction is used to determine the branches of the target pulmonary veins. During the operation, precise identification and blockade of these branches are achieved. After the blockade, peripheral venous injection of ICG reveals a clear intersegmental plane between the stained areas (segments to be preserved) and the unstained areas (segments to be removed). This intersegmental plane delineates the drainage area of the segment that needs to be removed, followed by anatomical dissection and disconnection of segmental bronchi and pulmonary arteries. The innovative aspects of this method and their implications for pulmonary segmentectomy are significant, which provided thoracic surgeons with more options based on the vascular-centered resection of different segments and pulmonary nodule locations. For instance, in these specific lung segments (such as the anterior segment, lingual segment, basal segment), the target segmental veins are more anatomically separable than their corresponding segmental arteries and bronchi. As a result, it is easier to combine venous occlusion and ICG injection in these segments to visualize the intersegmental plane. In addition, intrapulmonary lymph nodes are usually accompanied by the target segmental arteries and bronchi. For segmentectomy involving portal nail intrapulmonary lymph nodes, if the target segmental artery-first single-blocking approach is chosen, the interference of portal nail intrapulmonary lymph nodes may increase the difficulty of anatomical dissection and impede the progress of surgery. In such cases, the approach of the target segmental vein preferential-blocking may be an effective alternative [18]. Compared to some other methods, the preferentially ligating the segmental vein branches approach has unique advantages. First, after disconnecting the target segmental veins, the intersegmental plane was visualized immediately by ICG injection. On this basis, combined with the results of preoperative three-dimensional reconstruction, the remaining segmental structures (bronchi and pulmonary artery branches) within the intersegmental plane are anatomically identified and dissected, which is a

"double-confirmation" modified ICGF-guided segmentectomy procedure, avoiding errors in the target segmental structure identification and facilitating precise anatomical segmentectomy, effectively reducing surgical difficulty [19]. Second, preferentially ligating of the target segmental pulmonary vein is more in line with oncological requirements [20]. The theoretical basis is that after blockade of the segmental vein, circulating tumor cells are less likely to enter the bloodstream, reducing the risk of intraoperative tumor dissemination caused by compression. Third, temporary, reversible venous occlusion, rather than division, can be a reasonable approach for performing the ICG test in cases of doubt, and the preservation of the vasculature can be readily ascertained by observing the timely ICG counterstaining of the corresponding tissue after terminating the venous occlusion.

The ICGF identification of the intersegmental plane using the target segmental vein-first single-blocking technique presents several potential challenges. First, the visualization lasts for approximately 30 s before fading, and unlike the target segmental artery-first single-blocking approach, it cannot be repeated by intravenous ICG injection in the short term. Second, due to complex venous anatomy or extensive collateral circulation, the vein-first approach can sometimes be more technically challenging than the artery-first approach. As a result, preoperative three-dimensional reconstruction is crucial for assessing the complexity of venous variations in the target segment. If multiple branching communications and anatomical variations are identified and deemed difficult to recognize intraoperatively, this could impede the progress of segmentectomy, making the vein-first occlusion a potential pitfall. Third, misidentifying the target vein complicates repeated ICG injections, making accurate intersegmental plane identification more difficult, in contrast to the inflation-deflation method. Furthermore, this method indicated that the display time of the intersegmental plane is shorter, but still sufficient to outline the boundary line before it vanishes. The factors influencing the duration of ICG diffusion and its underlying mechanisms remain undetermined.

This study has a few limitations. First, the sample size is small; however, our study could be a meaningful preliminary experience showing that the ICGF identification of the intersegmental plane formed by incising the target vein is feasible and concordant with the inflation-deflation method. Second, there is no randomized control group. Third, the consistency of the two methods in this study was evaluated by comparing the details on the image by visual inspection, which was lacking an exhaustive and quantifiable standard. Fourth, the series of cases is only observed through clinical phenomena, and will be verified at the histologic proofs of intersegmental plane in subsequent studies.

Conclusion

This study preliminarily confirms that the ICGF method can safely and accurately identify the intersegmental plane by target pulmonary veins preferential ligation in thoracoscopic segmentectomy, which is a beneficial exploration and important supplement to the simplified thoracoscopic anatomical segmentectomy. However, the successful application of this method in the series of segmentectomy cases in the presented study should not lead to the generalized assumption that it works uniformly across all segments. Further studies are needed to explore its histologic proofs, formation principles, characteristics, and potential applications.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12893-024-02582-1.

Supplementary Material 1.

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Authors' contributions

Feng Shao and Qiang Zhang conceived and designed the study. Yungang Sun, Qiang Zhang, and Feng Shao performed the experiments. Siyang Jiao, Mengxu Yao, Yu Zhuang, and Zhao Wang analyzed the data. Yungang Sun and Yu Zhuang contributed analysis tools. Yungang Sun and Feng Shao provided critical inputs on design, analysis, and interpretation of the study. All the authors had access to the data. All authors reviewed the manuscript as submitted.

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Availability of data and materials

The datasets used and analyzed during this study are available from the corresponding author on reasonable request. The data are not publicly available due to privacy or ethical restrictions.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Nanjing Chest Hospital and was performed in accordance with the Declaration of Helsinki (Approval number: 2022-KY146-01). All methods were carried out in accordance with relevant guidelines and regulations. Written informed consent was obtained from all patients before surgery.

Consent for publication

Informed consent was obtained for the publication of pictures.

Competing interests

The authors declare no competing interests.

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