

Indocyanine green fluorescence-navigated thoracoscopy versus traditional inflation-deflation approach in precise uniportal segmentectomy: a short-term outcome comparative study

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Background: Uniportal video-assisted thoracoscopic surgery (VATS) segmentectomy is widely used in the field of thoracic surgery. However, anatomical variations in the bronchi and lung vessels may be critical obstacles during precise pulmonary segmentectomy. Thus, it is necessary to optimize uniportal VATS segmentectomy and to accurately identify the plane between lung segments by precisely transecting the bronchi and blood vessels of the lung segments. The indocyanine green fluorescence (ICGF)-based method has the potential to be a feasible and effective technique to facilitate the uniportal VATS segmentectomy. The present study aims at comparing the short-term outcomes of ICGF versus the traditional inflation-deflation method for uniportal VATS segmentectomy.

Methods: The perioperative clinical data in 200 consecutive patients undergoing uniportal VATS segmentectomy from December 2018 to August 2020 at Shanghai Chest Hospital were analyzed retrospectively. The targeted segment structures were identified and dissected precisely by using ICGF-based (N=100) or the traditional inflation-deflation (N=100) methods. The parameters of intraoperative blood loss and operation time, postoperative drainage volume, air leakage time, drainage tube retention time, length of hospital stay, and complications in the ICGF group were collected. Further, the operation time between the ICGF and the inflation-deflation groups was compared. The data summary and statistical analysis were performed by SPSS 19.0. P value <0.05 was considered statistically significant.

Results: No massive hemorrhage, hypoxemia, allergy, conversion to lobectomy, or wedge resection was noted during the surgery. ICGF groups resulted in a shorter operative time (90 ± 11.46 vs. 118 ± 10.59 min, P<0.001). No postoperative complications were observed, e.g., bronchopleural fistula, hemoptysis, or atelectasis. All patients were discharged as routinely scheduled. No disease recurrence or metastasis was found during the follow-ups.

Conclusions: Our study indicated that the ICGF-based navigation approach is a simple, effective, and reliable technique that can greatly facilitate the uniportal VATS segmentectomy.

Keywords: Indocyanine green (ICG); uniport; fluorescence thoracoscopy; segmentectomy

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Introduction

With the broad application of low-dose spiral computed tomography (CT), more and more lung cancer has been detected as small lung nodules, especially ground-glass nodules (GGN). Segmentectomy could achieve complete tumor resection while preserving as much functioning pulmonary tissue as possible. However, compared with lobectomy, precise segmentectomy faced more challenges. On the one hand, anatomical variations are common in the bronchi and blood vessels of the lung segments. On the other hand, the lung segments are separated by the intersegmental boundary line that varies from person to person. Although there are multiple ways to identify intersegmental boundary lines during segmentectomy, two main methods have been widely used to create an intersegmental boundary: inflation-deflation and nearinfrared fluorescence imaging with intravenous indocyanine green (ICG) (1).

Due to the highly restricted space of the uniportal videoassisted thoracoscopic surgery (VATS) operation, the ICGF-based method has been considered to be superior to the traditional inflation-deflation method in identifying the intersegmental boundary line. ICGF-based navigation can provide a clear surgical field by allowing maintenance of the deflated state of the lung and can achieve a high rate of accurate identification of the intersegmental line. Another important issue with segmentectomy is how to achieve an accurate resection. Modified uniportal VATS segmentectomy has been performed to solve these issues. For instance, Mimics software has been successfully used to perform a three-dimensional (3D) reconstruction of the lung before surgery, which facilitates the accurate identification of the bronchi and blood vessels of the lung segment where the lung nodule is located. As such, combined ICGF-based method and Mimics software-based 3D reconstruction is expected to enable the accurate and quick identification of the intersegmental plane. Here, we describe our experience in applying ICGF-based method and Mimics software-based 3D reconstruction for uniportal VATS segmentectomy and its advantage (2,3). We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/ article/view/10.21037/jtd-22-292/rc).

Methods

Study design and patients

Study design

The clinical and imaging data of 200 patients undergoing uniportal VATS segmentectomy under ICGF-navigated (N=100) or inflation-deflation (N=100) methods were analyzed, retrospectively, at Shanghai Chest Hospital from December 2018 to August 2020.

Patients

This study was approved by the Institutional Review Board of Shanghai Chest Hospital (#KS1972). All patients had signed informed consent to include their clinical data and specimens in our Lung Biobank and for use in research projects, according to the recommendation of the Institutional Review Board of Shanghai Chest Hospital. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

The inclusion criteria

(I) aged 18–75 years; (II) with adenocarcinoma *in situ* sized <2 cm, with a GGO proportion of 50% or more or tumor doubling time >400 days; (III) patients had not received any preoperative neoadjuvant treatment such as chemotherapy, radiotherapy, or traditional Chinese medicine therapies; (IV) a preoperative assessment according to the National Comprehensive Cancer Network (NCCN) guidelines confirmed that the patient's cardiopulmonary function could tolerate the surgery.

Exclusion criteria

There were no distant metastases, serious underlying diseases, or any other contraindications to surgery. Both inclusion and exclusion criteria were the same in the two groups. The general information was summarized in *Table 1*.

Interventions

A thin spiral CT (slice thickness: 1 mm) scan was performed preoperatively. Based on the CT images, the branches of the trachea, pulmonary artery, and pulmonary vein in the target segment where the lung nodule was located were reconstructed in three dimensions using Mimics software (Materialise, Beijing HuanZhongRuiChi Technology Co.,

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Table 1 Basic information of the enrolled patients

Variables	Data
General information	
Age (years) (mean \pm SD)	54±11.25
Gender (male/female) (n)	53/47
Tumor size (mm) (mean \pm SD)	12.9±3.04
Surgical sites (n)	
Left upper lobe apicoposterior segment	15
Left upper lobe anterior segment	10
Left upper lobe inherent segment	4
Left upper lobe lingual segment	7
Left lower lobe dorsal segment	9
Right upper lobe apical segment	11
Right upper lobe posterior segment	12
Right upper lobe anterior segment	13
Right lower lobe dorsal segment	8
Right lower lobe basal segment	11

SD, standard deviation.

Ltd., Beijing, China). All patients were found to have operable peripheral lung GGNs on health check-ups. Segmentectomy was feasible for these patients.

Operations of ICGF-based method group

The patient was placed on the unaffected side under general double-lumen endotracheal intubated anesthesia. A 4.0-cm incision was created in the 5th intercostal space between the anterior axillary line and the midaxillary line at the diseased side. The incision protector was placed at the observation and operation port. During the surgery, one-lung ventilation was applied to the unaffected side. The uniportal VATS segmentectomy was performed as scheduled. First, the pulmonary artery, pulmonary vein, and bronchus in the target segment were fully mobilized sequentially according to the reconstructed 3D images and transected separately with a cutter/stapler; alternately, these structures were clamped with a Hem-o-lok clip, followed by ultrasonic knife dissection. The intersegmental veins were preserved. Then, the anesthesiologist injected 5 mL of ICG into the peripheral vein. The fluorescence thoracoscope mode was switched from "Normal mode" to "Fluorescence mode" to observe the color border of the lung surface. The intersegmental plane was judged according to the color border. After the intersegmental plane was marked with argon plasma coagulation or an electrocoagulation hook, the target segment was completely resected using a cutter/ stapler along the plane. The lymph nodes were sampled, and the target lung segments were sent for frozen section examination. After complete hemostasis, a 24-gauge closed chest tube and a drainage tube were left in place.

Operations of inflation-deflation method group

In addition, 100 patients who underwent uniportal VATS segmentectomy with the inflation-deflation method in our center during the same period were retrospectively selected as the control group. The same inclusion criteria, surgical indications, number of selected target lung segments, preoperative reconstruction method, anesthesia method, and surgical process were applied in this group. However, the intersegmental plane was judged by using the inflation-deflation method. After the pulmonary artery, pulmonary vein, and bronchus in the target lung segment were transected, the anesthesiologist was asked to inflate the lung with pure oxygen. When the lung was completely re-expanded, one-lung ventilation on the healthy side was continued. Twenty minutes later, the junction line between the target segment, which had not collapsed, and the nontarget segment, which had completely collapsed, was identified as the intersegmental plane.

Assessments

After surgery, the postoperative drainage volume, postoperative air leakage time, postoperative drainage tube retention time, length of hospital stay, bronchopleural fistula, pulmonary infection/pleural effusion, and tumor recurrence/metastasis were recorded. The operative time was compared between the ICGF and the control groups, and intraoperative blood loss was recorded.

Statistical analysis

Normally distributed continuous variables were presented as the mean \pm standard deviation (SD) or median and range. Categorical variables were shown as numbers and percentages. The operative time between the ICGF and control groups was compared using the two-sided Student's *t*-test for continuous variables. The data summary and statistical analysis were performed using SPSS software (version 19.0; IBM-SPSS Inc., Chicago, IL, USA). A P value <0.05 was considered statistically significant.



Figure 1 All lung tissues except the target segment turn green after the injection of indocyanine green via a peripheral vein.



Figure 2 Intersegmental plane marked according to the color border.

Results

In the ICGF group, after the pulmonary artery, pulmonary vein, and bronchus in the target segment were mobilized and transected, ICG injection via a peripheral vein immediately revealed that all lung tissues except the target segment turned green, while the target segment remained in its original color; thus, a clear boundary was visible. The intersegmental plane was marked with argon plasma coagulation or an electrocoagulation hook, and the target segment was completely removed along this plane with a cutter/stapler (*Figures 1,2*). Lymph node sampling was performed, and the intraoperative frozen section pathology confirmed the presence of adenocarcinoma in situ. Standard segmentectomy was completed in all cases. No major bleeding was noted. The intraoperative vital signs were normal, including stable heart rate, rhythm, and blood pressure. The surgery was smooth. No postoperative complications occurred, such as hemoptysis, pulmonary artery embolism, pulmonary atelectasis, bronchopleural fistula, hypoxemia, or celiac disease. Postoperative pathology revealed negative mediastinal and intrapulmonary lymph nodes, and all patients were discharged successfully. Postoperative chest CT scans at 1 month, 3 months,

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Table 2 Com	parison of	operative time	between the ICGF	and inflation-defla	tion groups
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Group	Operative time (minutes) (mean \pm SD)	Patient number	P value	
ICGF group	90±11.46	100	<0.001	
Inflation-deflation group	118±10.59	100		

P value was calculated using a two-sided Student's t-test. ICGF, indocyanine green fluorescence; SD, standard deviation.

Table 3 Intra- and post-operative measures

Intra- and post-operative indicators	Data
Operative time (minutes) (mean ± SD)	90±11.46
Intraoperative blood loss (mL) (mean \pm SD)	94±19.59
Postoperative drainage volume (mL) (mean \pm SD)	215±56.64
Duration of postoperative air leak (days) (mean \pm SD)	1.9±0.45
Duration of postoperative drainage tube retention (days) (mean \pm SD)	2.45±0.50
Duration of hospital stay (days) (mean \pm SD)	3.85±0.73
Bronchopleural fistula (n)	0
Peritoneal effusion (%)	1 (0.01)
Pulmonary infection (%)	2 (0.02)

SD, standard deviation.

6 months, and 1 year showed good expansion of the remnant lungs and normal lung function. No recurrence or metastasis of the tumor was observed (*Tables 2,3*).

Discussion

GGNs are manifestations of early-stage lung cancer, with relatively low harm and a high probability of surgical cure. An increasing number of retrospective studies support the feasibility of performing a less extensive sublobar resection in these patients, preserving as much normal lung tissue as possible while completely removing the tumor; thus protecting lung function, reducing trauma, and improving quality of life (4-7). Sublobar resection includes two procedures: wedge resection and segmentectomy. Although wedge resection is easy to perform, it has limited indications and is only applicable to resection of pulmonary nodules located in the peripheral one-third of the lung; furthermore, it cannot remove the intrapulmonary lymph nodes. Thus, wedge resection is feasible only for a small proportion of patients with strict indications. Pulmonary segmentectomy has unique advantages. On the one hand, it has an anatomical basis, in which the bronchi and pulmonary vessels in each lobe are subdivided into segmental bronchi

and segmental vessels, and there are intersegmental planes separating the different lung segments; on the other hand, segmentectomy enables not only the removal of pulmonary tumors but also the dissection of intrapulmonary lymph nodes (8-10).

Therefore, in recent years, pulmonary segmentectomy has become a hot research topic in thoracic surgery. However, compared with lobectomy, precise segmentectomy is far more challenging. First, segmentectomy requires the dissection of the lung parenchyma, and the surgical trauma surface is prone to bleeding, making the operation more difficult. Second, anatomical variations are common in the bronchi and blood vessels of the lung segments. If the operation is entirely based on the operator's experience, the bronchi and blood vessels may be transected by mistake, which occurs frequently and unpredictably; as a result, patients may experience serious complications such as bleeding, air leak, hemoptysis, and even death. In addition, the intersegmental plane that separates the lung segments varies from person to person, and the presence of numerous communicating branches of lung tissue among lung segments results in no absolute intersegmental plane, which also poses an obstacle to precise segmental resection (10,11).

Segmentectomy based on a surgeon's personal

experience is difficult to standardize, and the learning curve is long. Postoperative complications, such as hemoptysis and air leak, frequently occur, and the longterm outcome of residual lung re-expansion is not ideal. Thus, achieving precise lung segment resection for earlystage lung cancer poses a significant challenge to surgeons. Preoperatively, reconstruction can be performed using Mimics software, which accurately locates the lung segment where the lung nodule is located and enables 3D reconstruction of the trachea and blood vessels in the target lung segment. This allows the trachea and blood vessels to be correctly identified intraoperatively, thus ensuring the precise mobilization and transection of these structures. After transection of the trachea and blood vessels, intersegmental plane determination is challenging in precise segmentectomy. Ideally, a precise resection can remove all lung tissue in the target segment and preserve all tissue outside the target segment. However, there are no clear demarcation lines among lung segments due to a large number of airway passages among the lung segments. The inflation-deflation method and modified inflation-deflation method are two conventional strategies, which often require a lengthy waiting time (typically 20-30 minutes). In our retrospective analysis, we also found that the operative time to complete lung segment resection was significantly longer in the control group (using the inflation-deflation method) than in the ICGF group, mainly because of the need to wait more than 20 minutes to collapse the lung after expansion in the control group. In contrast, the intersegmental plane could be determined within seconds by applying fluorescence thoracoscopy in the ICGF group. In particular, the result of intersegmental plane determination by the inflation-deflation method is unsatisfactory for patients with emphysema, which makes precise segmentectomy extremely difficult (11). In addition, both the inflation-deflation method and the modified inflation-deflation method led to the incomplete collapse of some lung tissues, affecting the surgical field and prolonging the operative time.

In recent years, the fluorescence imaging technique has been used in liver segment resection by intravenous injection of ICG, a specific visualizing agent that is a sterile, watersoluble tricarbocyanine dye. ICG rapidly binds to plasma proteins after intravenous injection, with a peak spectral absorption at 800–810 nm in blood plasma or blood. The distribution area of ICG can be seen through a special fluorescence endoscope for real-time visualization (12). During segmentectomy, ICG is injected through a peripheral vein after accurate transection of the pulmonary artery in the target segment; 20–30 seconds later, the fluorescence endoscope shows lung tissue outside the target segment has turned a clear green fluorescent color while the target segment has no fluorescent distribution, allowing rapid determination of the intersegmental plane (13,14). In our current retrospective analysis, we found that fluorescencenavigated uniportal VATS segmentectomy not only shortened the operative time but also had no postoperative complications. No tumor recurrence or metastasis was seen in multiple postoperative follow-up visits. Therefore, the intersegmental planes were accurately determined, and the resection of the target lung segments could ensure sufficient surgical margins.

The experience of ICGF-navigated uniportal VATS segmentectomy in our center may be summarized as follows: (I) the indications for lung segmentectomy must be strictly followed according to the guidelines; (II) 3D reconstruction must be performed preoperatively to locate the lung segment in which the nodule is located and to reconstruct the trachea and related blood vessels in the target segment to observe whether there are anatomical variations of the trachea and blood vessels; (III) the trachea and related vessels of the target segment must first be mobilized and transected. Any mistransection, undertransection, or overtransection, especially for the pulmonary artery, must be avoided as these errors can result in the wrong confirmation of the intersegmental plane of the target segment after the ICG is injected via the peripheral vein; (IV) ICG may be intravenously injected at a dose of 4-5 mL, although the color development is poor with lower doses. The color change occurs 20-30 seconds after injection and can last 3-5 minutes; (V) intravenous injection of ICG should not be too fast; otherwise, the intersegmental plane may not be detected (15); and (VI) before the intravenous injection of ICG, the fluorescence thoracoscopy is switched from normal mode to fluorescence mode; after the injection, lung tissue other than the target segment turns green within a short period. The intersegmental plane should be immediately marked with argon plasma coagulation or an electrocoagulation hookotherwise, the lung tissue in the target segment may also turn green in a few minutes, which may be due to the diffusion of the ICG along the communicating branches.

Preoperative 3D reconstruction combined with uniportal VATS for standard lung segmentectomy has the following advantages: (I) it maximizes the preservation of lung function while removing lung lesions; (II) it mobilizes the trachea and blood vessels in strict accordance with

the anatomical structure of the lung segment and resects the target lung segment along the actual intersegmental plane, which reduces the occurrence of postoperative complications; (III) it shortens the operative time because it only takes 20-30 seconds to determine the intersegmental plane using the fluorescence thoracoscopy (in contrast, the inflation-deflation method requires at least 15-20 minutes to determine the intersegmental plane); (IV) the inflationdeflation method affects the surgical field after re-expansion, but the fluorescence thoracoscopy does not. In addition, the inflation-deflation method cannot be applied in surgeries for patients with co-existing emphysema, whereas fluorescence thoracoscopy typically will not be affected by emphysema; (V) after the intersegmental plane is accurately determined, standard lung segmentectomy can be performed along the intersegmental plane, which reduces postoperative complications, such as air leak, hemoptysis, and pulmonary atelectasis. Furthermore, it avoids the unnecessary loss of lung function due to excessive resection of lung tissue; and (VI) ICG has no known metabolites in the body and is excreted in its original form, which is not harmful to humans (16,17).

Conclusions

Uniportal fluorescence thoracoscopy combined with preoperative 3D reconstruction is valuable for precise lung segmentectomy. It has excellent results with a short operative time, simple, safe, reliable surgery, and few postoperative complications. Thus, this method can be widely applied in lung segment surgeries.

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Footnote

Reporting Checklist: The authors have completed the

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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) and approved by the Institutional Review Board of Shanghai Chest Hospital (No. #KS1972). Informed consent was obtained from all participants involved in the study.

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