The Prediction of Fissure Integrity by Quantitative Computed Tomography Analysis

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Abstract

Background Incomplete interlobar fissure may increase the difficulty of thoracoscopic lobectomy. Herein, we compared the accuracy of visual versus quantitative analysis to predict fissure integrity in lung cancer patients undergoing thoracoscopic lobectomy and evaluated the effects of fissure integrity on surgical outcome.

Methods This was a single-center retrospective study including consecutive patients undergoing VATS (video-assisted thoracoscopic surgery) lobectomy for lung cancer. The target interlobar fissures were classified as complete or incomplete by visual and quantitative analysis. Using the intraoperative finding as the reference method, the diagnostic accuracy of the two methods to define fissure completeness (dependent variable) was calculated and statistically compared. Yet, we evaluated differences in postoperative outcomes between patients with complete and incomplete fissure integrity.

Results A total of 93 patients were included in the study; 33/93 (36%) presented complete fissure. Visual and quantitative analyses correctly identified complete fissure in 19/33 (57%) and 29/33 (88%) patients, respectively, and incomplete fissure in 56/60 (93%) and 58/60 (96%) patients, respectively. Quantitative analysis had better diagnostic accuracy than visual analysis (81 vs. 93%; $p = 0.01$). Patients with incomplete fissure compared with those with complete fissure had a higher conversion rate (6 vs. 13%; $p = 0.43$), higher persistent air leak rate (0/33 vs. 14/60; $p = 0.03$), and longer hospitalization (12.6 ± 3.8 vs. 7.1 ± 2.4 days; $p = 0.01$).

Conclusion Quantitative analysis accurately predicted the fissures' integrity; it may be useful for selecting suitable cases for thoracoscopic lobectomy especially for surgeons with limited minimally invasive experience.

Keywords
- computed tomography
- CT scan
- lung cancer
- minimally invasive surgery
- thoracoscopy
- VATS

Introduction

Lobectomy is still the treatment of choice for early-stage lung cancer. Actually, video-assisted thoracoscopic surgery (VATS) lobectomy is the preferred approach due to less postoperative morbidity and mortality, and similar oncologic results compared with open lobectomy.[1–4] However, VATS lobectomy is a demanding procedure and the degree of pulmonary fissure integrity (FI) is an important issue that thoracic surgeons always deal with. Incomplete interlobar fissures can increase the surgical difficulty, and negatively affect postoperative outcomes.[5,6]

High-resolution computed tomography (CT) scan in multiplanar reconstruction is currently used for the evaluation of degree of FI, but the interobserver variability and the

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operator's experience limit the diagnostic accuracy of this strategy.[7] In the last years, there has been a growing interest in defining the degree of FI by quantitative CT (QCT) scan for selection of emphysematous patients scheduled for bronchoscopic lung volume reduction (BLVR) with one-way endobronchial valves (EBVs).[8,9]

In the present study, we compared the accuracy of visual CT analysis with that of QCT analysis to define the degree of FI in patients undergoing VATS lobectomy; then, we evaluated the effects of the FI on surgical outcome.

Materials and Methods

Study Design

This was a retrospective single-center study included all consecutive patients undergoing VATS lobectomy for non-small cell lung cancer (NSCLC) between September 2019 and January 2022. We excluded from the analysis the clinical data of: (1) patients with incomplete data regarding FI visual-CT analysis, QCT analysis, and intraoperative analysis; and (2) patients with incomplete data on postoperative outcomes.

The preoperative chest CT scans of each patient were reviewed by visual and QCT analyses, and the target interlobar fissure was classified as complete or incomplete. The visual detection was performed by two independent observers blinded to the QTC analysis and intraoperative results. The discordant results were resolved by a third observer. Using the intraoperative findings as the reference method, the diagnostic accuracy of visual and QCT methods to define fissure completeness (dependent variable) was calculated and statistically compared (primary end point). The effects of FI on surgical outcome were also defined (secondary end point).

The study was approved by the local ethics committees of our institution (approval number 225/18). All patients included in the study gave a written informed consent for the VATS lobectomy and they were aware that their data could be used anonymously for scientific purposes only.

Study Population

Patients with early stage of lung cancer (stages I and II) were scheduled for VATS lobectomy based on standard oncologic principles. All patients had preoperative exams such as iodinated contrast CT whole body and positron emission tomography (PET) imaging. Patients with suspected neoplastic involvement of the mediastinal lymph nodes on CT and/or PET underwent endobronchial ultrasound biopsy with fine needle aspiration and/or mediastinoscopy to exclude involvement of the N2 station lymph nodes. Standard cardiopulmonary tests were performed to define if the patient was fit or not for surgery.

For each patient, demographic data (age at the time of surgery, sex), body mass index, exposure to risk factors, smoking habit, preoperative comorbidity, lung function status, and characteristics of the tumor (side and size) were recorded. Data related to perioperative and postoperative outcomes were also acquired, including operative time (minutes), intraoperative blood loss (mL), blood transfusion, chest drainage duration (days), length of hospital stay (LHOS) (days), major morbidity (defined as Grade 3 or higher according to the Clavien–Dindo classification system[10]), and mortality within 30 days.

Visual CT Fissure Analysis

All CT exams were acquired using a 64-multi detector CT (64-MDCT) unit with injection of the contrast medium, in full inspiration and apnea. The acquired data were reconstructed using standard and high-resolution filters, in 1 mm sections at 0.5 mm intervals. Subsequently, the fissure between the target lung lobe and the adjacent lung lobe was analyzed in sagittal, axial, and coronal sections. In cases where the target lobe corresponded to a lower (right or left) or upper left lobe, the FI score was evaluated on the oblique fissure. When the target lobe corresponded to a right upper lobe, the FI was evaluated on the upper half of the oblique fissure and contextually on the horizontal fissure. A fissure was defined as complete or as incomplete whether the FI score was $\geq$90% or $<$90%, respectively, in the sagittal, axial, and coronal planes.

QCT Fissure Analysis

QCT analysis was performed using StratX software (PulmonX Inc., Redwood City, California, United States).[11] The preoperative CT images were uploaded in the DICOM format to the StratX platform. The data were analyzed using validated algorithms and the results were ready within 2 to 3 business days. The final report illustrated information regarding FI, pulmonary emphysema density, and inspiratory lobar volume. In this study we evaluated only data regarding FI, classified into three subgroups: FI $\geq$ 95% (continuous black line), FI between 80 and 95% (continuous gray line), and FI $<$ 80% (dotted gray line). As previously reported,[9] fissure was defined as complete or as incomplete depending on whether the FI score was $\geq$95% or $<$95%, respectively.

Intraoperative Fissure Analysis

A standard anterior triportal approach was used in all cases and lung resection followed the classic principles of lobectomy.[12,13] At the end of operation, a complete lymph node resection was performed. A single chest tube was placed, and it was removed in absence of air leaks and if the fluid drained was $<$200–250 mL in 24 hours. A same surgeon (A.F.) performed all the procedures and defined the degree of FI using the following standardized score system[14,15]:

- Grade 0: well-separated lobes by fully complete fissure.
- Grade 1: complete visceral cleft with more than 70% completeness of FI.
- Grade 2: partly evident visceral cleft with 30 to 70% completeness of FI.
- Grade 3: no evident fissural line with absent 30% completeness of FI.

As previously reported by Li et al,[16] fissure was defined as complete or incomplete in case of score 0–1 or of score $\geq$2, respectively.

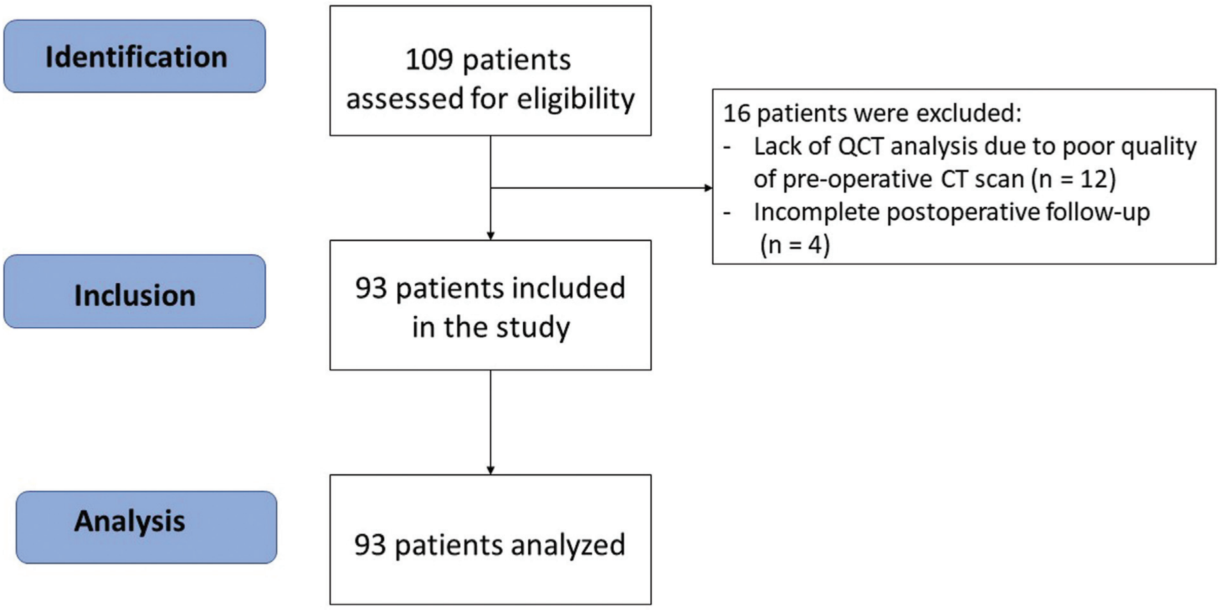

Fig. 1 Flow chart of the study.

Statistical Analysis

Data were expressed as mean ± standard deviation for continuous variables and absolute number and percentage for categorical variables. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy to define complete fissure (dependent variable) were calculated for each method having intraoperative finding as the reference method. The agreement between visual and QCT analyses with intraoperative analysis was defined by the K index; the difference in diagnostic accuracy was evaluated using the McNemar's exact test while *t*-test and chi-square test were used for comparison of continuous and categorical variables, respectively. A *p*-value of <0.05 was considered statistically significant. The MedCalc statistical software (Version 12.3, Broekstraat 52, Mariakerke, Belgium) was used for this analysis.

Results

During the study period, 109 patients underwent VATS lobectomy. Twelve patients were excluded due to lack of QCT evaluation for the poor quality of preoperative CT scan and four patients because of incompleteness of data on postoperative outcomes. Therefore, our study population included 93 patients (►**Fig. 1**). As summarized in ►**Fig. 2**, 7 (7.5%) patients had Grade 0, 26 (28%) Grade 1; 42 (45%) Grade 2; and 18 (19%) Grade 3 based on intraoperative analysis. Thus, 33 patients (36%) had a complete fissure and 60 (64%) incomplete fissures. The characteristics of study groups are summarized in ►**Table 1**. The mean age was 69 ± 8.5 years; of these, most were male (79%). Right upper lobectomy was performed in 26 (28%) patients, left upper lobectomy in 28 (30%); right lower lobectomy in 20 (21.5%), and a left lower lobectomy in 19 (20.5%). The two study groups did not show statistically significant differences in demographic variables, preoperative comorbidities, lung function, and tumor characteristics.

Diagnostic Accuracy of the Visual CT Analysis and QCT Analysis to Define FI

Visual analysis: this method correctly identified the presence of complete fissures in 19 out of 33 (58%) cases and of incomplete fissures in 56 out of 60 (93%) cases. The sensitivity, specificity, PPV, NPV, and diagnostic accuracy were 58, 93, 83, 80, and 81%, respectively.

QCT fissure analysis: this strategy correctly identified the presence of complete fissures in 29 out of 33 (88%) cases and of incomplete fissures in 58 out of 60 (97%) cases. The sensitivity, specificity, PPV, NPV, and diagnostic accuracy were 88, 96, 93, 93, and 93%, respectively.

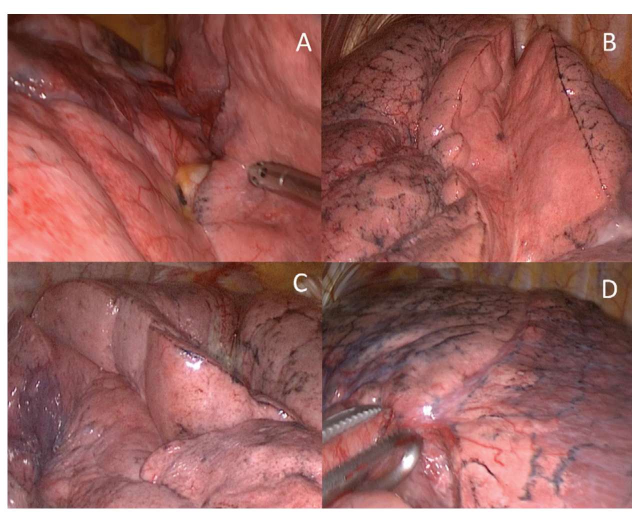

Fig. 2 Our study population included 7 (7.5%) patients with Grade 0 (**A**), 26 (28%) with Grade 1 (**B**); 42 (45%) with Grade 2 (**C**); and 18 (19%) with Grade 3 (**C**) fissure integrity based on intraoperative analysis.

Table 1 Characteristics of the study population

Variables	Study population ($n=93$)	Complete fissure ($n=33$)	Incomplete fissure ($n=60$)	p-Value
Age (y), mean ± SD	69 ± 8.5	69 ± 5.5	69 ± 9.8	0.87
Smokers, *n* (%)	89 (96)	31 (94)	58 (97)	0.74
Sex (male/female), *n* (%)	73 (79)/20 (21)	23 (70)/10 (30)	50 (83)/10 (17)	0.58
Previous comorbidity, *n* (%)				
• Diabetes	14 (15)	4 (12)	10 (17)	0.58
• Hypertension	40 (43)	14 (42)	26 (43)	0.47
• Cardiac	20 (21)	6 (18)	14 (23)	0.39
• Cerebral	2 (2)	0 (0)	2 (3)	0.21
• BPCO	49 (53)	20 (60)	30 (50)	0.13
• Neoplastic	8 (9)	2 (6)	6 (10)	0.31
Respiratory function, mean ± SD				
• FEV_1%	89 ± 11	89 ± 8.6	89 ± 7.6	0.69
• FVC%	88 ± 8.6	88 ± 5.6	88 ± 11	0.71
• DLCO%	85 ± 4.8	89 ± 5.7	85 ± 8.9	0.56
• 6MWT (m)	385 ± 48	384 ± 81	385 ± 112	0.67
Tumor size (mm), mean ± SD	38 ± 4.7	38 ± 3.7	38 ± 5.7	0.46
Site, *n* (%)				
• RUL	26 (28)	6 (18)	20 (33)	0.97
• RLL	20 (21)	8 (24)	12 (20)	0.98
• LUL	28 (30)	7 (21)	20 (33)	0.78
• LLL	19 (20)	12 (36)	8 (13)	0.94

Abbreviations: 6MWT, 6-minute walk test; DLCO, diffusing capacity for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced volume capacity; LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RUL, right upper lobe; SD, standard deviation.

QCT compared with visual-CT analysis showed a higher K value (0.85 vs. 0.55) with intraoperative finding and better diagnostic accuracy (93 vs. 81%; $p=0.01$). Examples are reported in ►**Figs. 3** and **4** with concordant results between visual analysis, QCT analysis, and intraoperative analysis, while ►**Fig. 5** shows concordant results between QCT and intraoperative analyses alone.

Surgical Outcome

The results are summarized in ►**Table 2**. No major intraoperative complications or deaths occurred. Incomplete compared with complete fissure was associated with significant longer operative time (248 ± 37 vs. 174 ± 25 minutes; $p=0.003$), prolonged chest tube duration (11.8 ± 2.5 vs. 6.3 ± 1.3 days; $p=0.01$), LHOS (12.6 ± 3.8 vs. 7.1 ± 2.4; $p=0.01$), and higher rate of postoperative air leaks (23 vs. 0%; $p=0.03$). In all cases, persistent air leaks resolved spontaneously, without needing of further interventions.

Discussion

Incomplete fissure represented a challenge for thoracic surgeons and increased the difficulty of VATS lobectomy, especially for surgeons during the early phase of learning curve. Incomplete fissure in addition to dense adhesions, silicotic adenopathies, and anatomic malformation represented the main reasons for conversion during VATS lobectomy.[17,18] Several authors[14–16] used standard CT scans to define the FI, but the interobserver variability, the operator's experience, and the presence of pulmonary diseases such as emphysema limit the accuracy and the reproducibility of this method. To overcome these limits, in this study we evaluated the diagnostic accuracy of QCT analysis to define the FI in patients undergoing VATS lobectomy, an issue not been reported so far.

First, our study showed the higher accuracy of QCT analysis compared with visual CT analysis for defining the degree of FI. These results were in line with previous studies,[8,9] which found that QCT analysis was superior to visual CT analysis for scoring FI in emphysematous patients scheduled for BLVR with EBVs. However, in these studies the accuracy of QCT analysis to define the FI was indirectly demonstrated by the lung atelectasis obtained after valve treatment, but the real anatomical integrity of the fissures was not defined as all patients underwent lung volume reduction by bronchoscopy. Conversely, the novelty and the strength of the present article were that the results of QCT analysis were correlated with the intraoperative findings of interlobar fissure seen during thoracoscopy. Thus, the results of previous studies were a starting point for

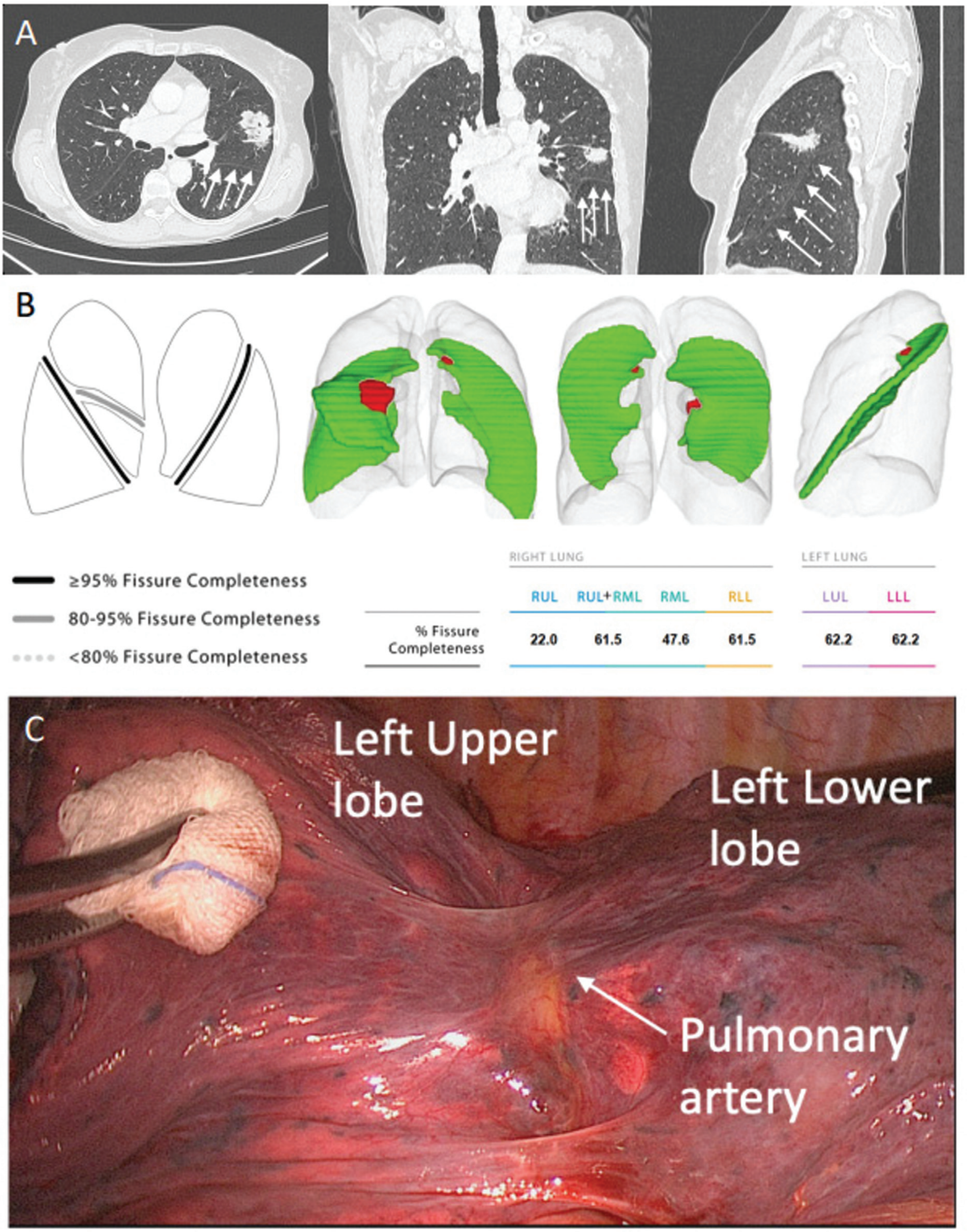

Fig. 3 Visual (**A**), quantitative (**B**), and intraoperative (**C**) analyses confirmed the presence of complete fissure integrity in a 73-year-old man undergoing thoracoscopic left upper lobectomy for adenocarcinoma. The pulmonary artery is clearly visible at the bottom of the fissure.

developing this work, in which we used the same strategy as the assessment of FI by QCT analysis in comparison with visual analysis but in a different clinical context as patients scheduled for thoracoscopic lobectomy. Similarly, Schieman et al[19] and Kent et al[20] evaluated the agreement between visual CT analysis and intraoperative analysis to define the degree of FI in patients undergoing lung resection. In both studies,[19,20] the visual analysis was unable to accurately predict the completeness of the lung fissure discovered during surgery. However, in our series QCT analysis failed to identify the presence of complete fissures in 4 out of 33 cases and of incomplete fissures in 2 out of 60 cases. In

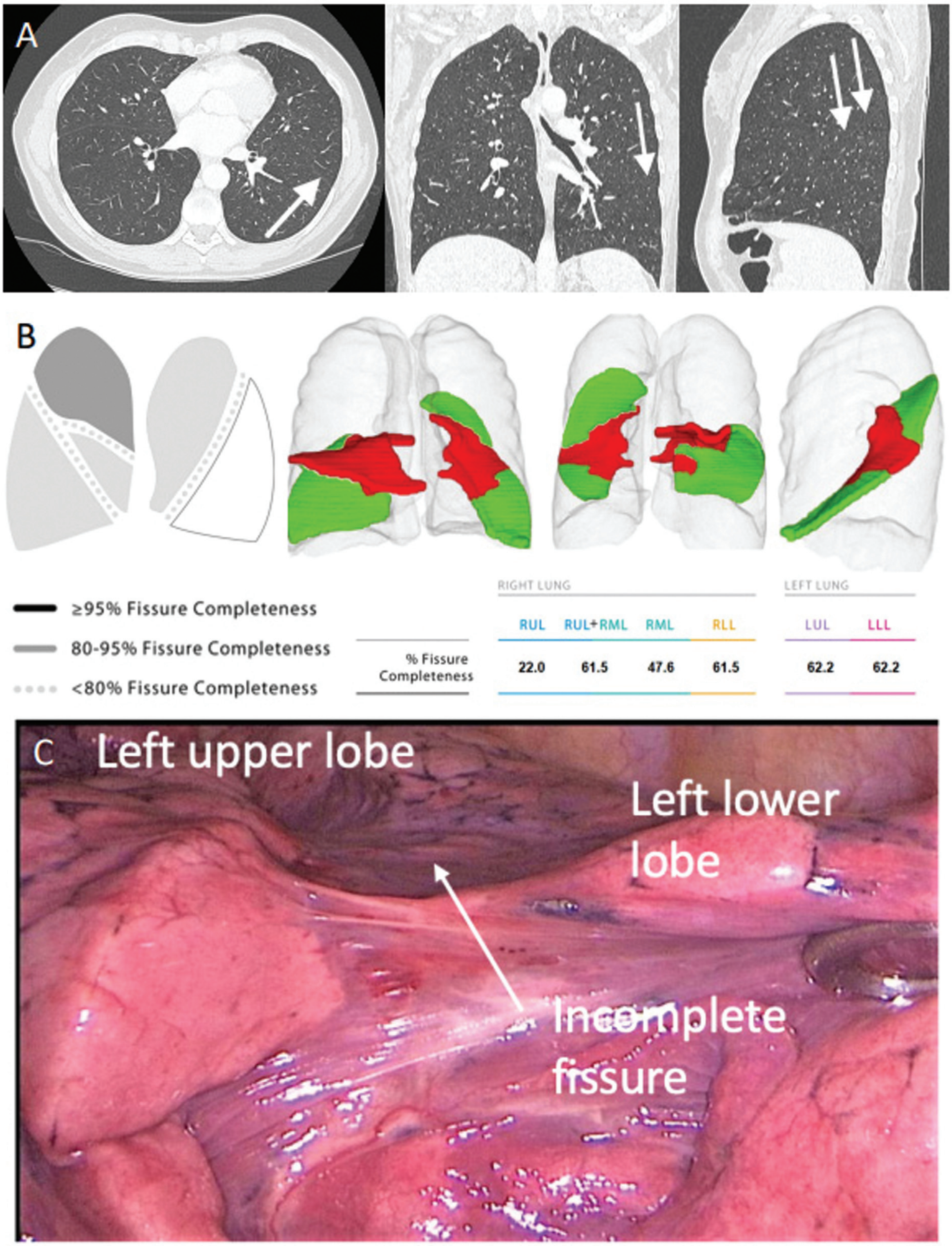

Fig. 4 Visual (**A**), quantitative (**B**), and intraoperative (**C**) analyses confirmed the presence of incomplete fissure in a 67-year-old woman undergoing thoracoscopic left lower lobectomy for adenocarcinoma.

theory, computer analysis identified the presence of small gaps in the fissure that could be missed by human intraoperative analysis during surgery. The poor quality of preoperative CT scan was an additional explanation. Being a retrospective study, the preoperative CT protocol was not designed for input to StratX analysis, and thus it could be suboptimal for QCT analysis, resulting in underestimation of FI scores.

Second, our results confirmed that the presence of incomplete fissure increased the difficult of VATS lobectomy, as

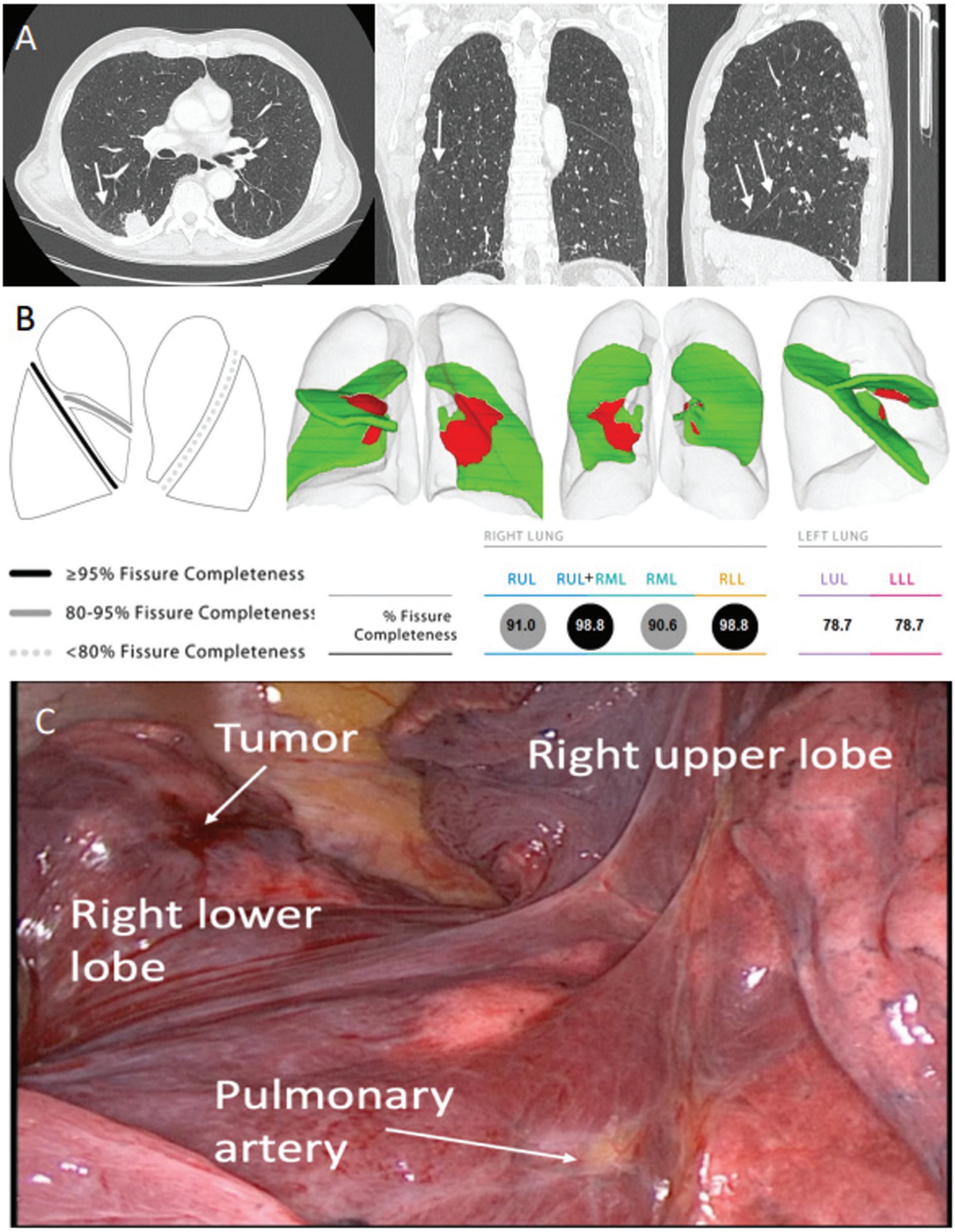

Fig. 5 Visual analysis (**A**) showed the presence of incomplete fissure between upper and lower right lobes that resulted to be complete on quantitative analysis (**B**) and intraoperative analysis (**C**). The 71-year-old man underwent thoracoscopic right lower lobectomy for squamous cell carcinoma.

demonstrated by the longer operative time and higher blood loss. Additionally, patients with incomplete fissure presented a higher persistent air leak rate, resulting in a longer chest tube drainage and hospital stay. Technically, the presence of incomplete fissure obscured the pulmonary artery, resulting in an increased risk of lung injury and of postoperative air leaks. Our results were in line with those of Li et al,[16] who retrospectively analyzed the clinical results of 563 patients undergoing VATS lobectomy for NSCLC. Patients with incomplete fissure ($n = 190$) compared with those

Table 2 Comparison of surgical outcome

Variables	Complete fissure ($n = 33$)	Incomplete fissure ($n = 60$)	*p*-Value
Operative times (min)	174 ± 25	248 ± 37	0.003
Blood loss (mL), mean ± SD	150 ± 19	200 ± 31	0.43
Number of staplers for fissure	1.4 ± 0.7	3.5 ± 1.2	0.001
Conversion to thoracotomy, *n* (%)	2 (6)	8 (13)	0.43
Persistent air leaks, *n* (%)	0 (0)	14 (23)	0.03
Length of chest drainage (d),	6.3 ± 1.3	11.8 ± 2.5	0.01
Length of hospital stay (d),	7.1 ± 2.4	12.6 ± 3.8	0.01

Abbreviation: SD, standard deviation.

with complete fissure ($n = 373$) had a significantly higher overall morbidity rate and longer hospital stay. Obviously, the retrospective nature of the study did not allow us to demonstrate the real impact of the preoperative evaluation of FI by QCT analysis on the surgical outcome. However, we suppose that our strategy may improve surgical outcome by selecting the most suitable patients for VATS lobectomy. Incomplete interlobar fissure increases the surgical difficulty of VATS lobectomy and is a predictive factor of major and minor postoperative morbidity. The risk of injury to visceral pleura during the interlobar approach of pulmonary arteries may result in prolonged postoperative air leaks that lead to prolonged hospital stay and delayed adjuvant treatment.[21] Thus, to know the presence of incomplete fissure before the operation may be very useful especially for surgeons with limited experience in minimally invasive surgery. This allows surgeons to plan an alternative strategy to conventional lobectomy as fissure-last approach to successfully handle incomplete fissure, prevent persistent postoperative air leaks, and contribute to reduce the conversion rate for incomplete interlobar fissure cases.[16,22]

Study Limitations

This study had several limitations that should be taken in account before drawing definitive conclusions. (1) The retrospective nature of the study and the small sample size were the main limitations. (2) The results of visual-CT analysis and of intraoperative analysis depended by the decision of the radiologist and surgeon, respectively, making difficult their reproducibility. Additionally, this study involved only one surgeon who defined the grade of fissures, which were then correlated with QCT and visual analysis. Thus, the lack of interobserver agreement by two surgeons could affect the results. (3) Despite the StratX quantified separately the integrity of oblique fissures and horizontal fissures, in our analysis we included only the oblique fissures. This decision was based on the fact that horizontal fissures are almost always incomplete, and from a technical point of view to know if they are complete or not is irrelevant for the surgery as an approach to the pulmonary artery (PA) is never obscured by small fissures.[23,24] (4) The results of StratX could be suboptimal for the evaluation of patients scheduled for anatomical lung resections. Specifically, the QCT analysis defined fissure as complete or incomplete, but it was unable to identify in which part the fissure was incomplete. This missing information could be useful for surgeons especially in patients scheduled for sublobar resections as segmentectomy.

Conclusion

The preoperative evaluation of degree of FI may be useful especially for surgeons in the early learning curve as the presence of incomplete interlobar fissure increased the difficulty of the VATS lobectomy and the risk of persistent airleaks. QCT analysis better defined the FI than visual-CT analysis, and it could be added to standard preoperative work-up to select the most appropriate candidates for VATS lobectomy. Obviously, due to retrospective nature of the study and the small sample size, our results should be confirmed by further and prospective studies.

Conflict of Interest
None declared.

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