Original Article

Anterior fissureless uniport *vs.* posterior intra-fissure triple-port thoracoscopic right upper lobectomy: a propensity-matched study

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Background: This study aimed to assess the efficiency of anterior fissureless uniport (AFU) thoracoscopic lobectomy for early stage right upper non-small cell lung cancer (NSCLC).

Methods: Between June 2014 and Dec 2016, 162 consecutive NSCLC patients who underwent thoracoscopic right upper lobectomy (RUL) by AFU approach (AFU group, n=65) or posterior intra-fissure triple-port dissection (PIFT group, n=97) were enrolled. A propensity-matched analysis was used to compare perioperative outcomes, safety and efficiency between the two groups.

Results: Propensity matching produced 40 pairs in this retrospective study. During the operation, lobectomy took less time in the AFU group compared with the PIFT group, while no statistical differences in mediastinal lymphadenectomy time, intraoperative blood loss, and total of lymph nodes harvested were found between the two groups. Postoperatively, length of hospital stay (LOS) and time of postoperative air leak were significantly reduced in AFU group than in PIFT group. However, the overall complication rate and volume of pleural effusion drainage within 48 h were similar. Compared with the PIFT group, visual analogue scale (VAS) of 3 postoperative days in AFU group was slighter.

Conclusions: In RUL, AFU thoracoscopic approach is safe, efficient and easily maneuverable, which would reduce the duration of lobectomy, LOS and time of postoperative air leak. Postoperative pain is also mild.

Keywords: Thoracoscopic lobectomy; fissureless; triple-port; uniport

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Introduction

In conventional triple-port video-assisted thoracic surgery (VATS) right upper lobectomy (RUL), posterior approach is often selected, dissecting through the fissure in order to produce a tunnel above the pulmonary artery, which may increase the odds of air leak (1). Conversely, anterior fissureless lobectomy, which was first described in open thoracotomy in 1999 (2), decreases the chance of postoperative air leak. However, anterior fissureless lobectomy is rarely applied in triple-port VATS RUL, the mainly reason is that exposure of the superior border in hilum is limited, with the optical source generating a torsion angle not favorable with standard two-dimensional monitors (3).

Uniport VATS lobectomy has become popular in china since 2013 for reducing postoperative pain, length of hospital stay (LOS) and time to return to daily activities (4,5). Meanwhile, exposure of the hilum structure is clear (6) especially in upper lobectomy thanks to the camera in the upper location of the incision; the whole procedure is similar to open thoracotomy. However, performing uniport

VATS lobectomy is also challenging, especially for patient with fused fissure because of the limited space.

In order to reduce postoperative pain, the chance of air leak and improve surgical maneuverability, we firstly combined anterior the fissureless technique and uniport VATS for RUL at the beginning of 2015, and obtained a favorable result. In this study, we performed a retrospective study comparing anterior fissureless uniport (AFU) VATS technique and posterior intra-fissure triple-port (PIFT) VATS dissection for RUL, evaluating the safety and efficacy of these procedures.

Methods

This retrospective propensity matched cohort study was approved by the institutional review board and the ethics committee of Affiliated Hospital of Nantong University, and the data were collected from the hospital's database by trained surgical coordinators. During the period of study, two surgical procedures were conducted by two different senior consultant surgeons, one with 3 years of experience in uniport VATS lobectomy and the other with >4 years of experience in triple-port VATS lobectomy.

Study design

Between June 2014 and Dec 2016, 65 consecutive patients with early stage NSCLC who underwent uniport thoracoscopic RUL with anterior fissureless technique were included. During the same period, another 97 consecutive patients with early stage NSCLC who underwent triple-port thoracoscopic RUL with posterior intra-fissure dissection were also analyzed in order to avoid intention-to-treat selection bias. Preoperative examination, including lung function, electrocardiography, enhanced chest CT scan, head magnetic resonance imaging (MRI), abdominal ultrasound, and bone electroconvulsive therapy (ECT) were performed. Inclusion criteria were: (I) clinically diagnosed stage T1a–cN0M0 NSCLC (AJCC/UICC 8th edition) (7); (II) no previous history of thoracotomy, chemotherapy or radiotherapy; (III) no severe thoracic adhesion; (IV) American Society of Anesthesiologists (ASA) score of I–II.

In this study, we modelled the likelihood of AFU group with logistic regression, and age, gender, body mass index (BMI), tumor size, histology, pulmonary function, fissural grade (8) and co-morbidities were used. Subsequently, PIFT group were matched with the nearest propensity score (within a range of 0.03 on a scale from 0 to 1) (*Table 1*).

Table 1 Original data of preoperative variables

Parameter	AFU (n=65)	PIFT (n=97)	P value
Age	61.5±10.4	63.2±12.1	0.539**
Gender			0.417*
Male	17	28	
Female	48	69	
BMI	21.5±2.7	23.1±2.2	0.782**
Histological type			0.615*
SC	5	12	
AD	60	85	
Clinical TNM stage			0.421*
T1aN0M0	16	29	
T1bN0M0	34	41	
T1cN0M0	15	27	
Tumor size			0.421*
<1 cm	16	29	
1–2 cm	34	41	
2–3 cm	15	27	
Pulmonary function			0.643**
FEV1%	77.8±12.1	75.6±10.8	
DLCO%	65.6±12.7	64.7±11.8	
Fissure grade			
I	9	26	0.017*
II	12	25	0.023*
III	35	40	0.656*
IV	9	6	0.778*
Comorbidity			
Primary hypertension	25	31	0.515*
grade I	12	11	
grade II	13	20	
II type diabetic mellitus	12	18	0.871*

Data are mean ± standard deviation or N (percentage). *, McNemar's test; **, paired Student's *t*-test. FEV1, forced expiratory volume in the first second; DLCO, diffusing capacity of carbon monoxide; SC, squamous cell cancer; AD, adenocarcinoma; AFU, anterior fissureless uniport; PIFT, posterior intra-fissure triple-port; BMI, body mass index.

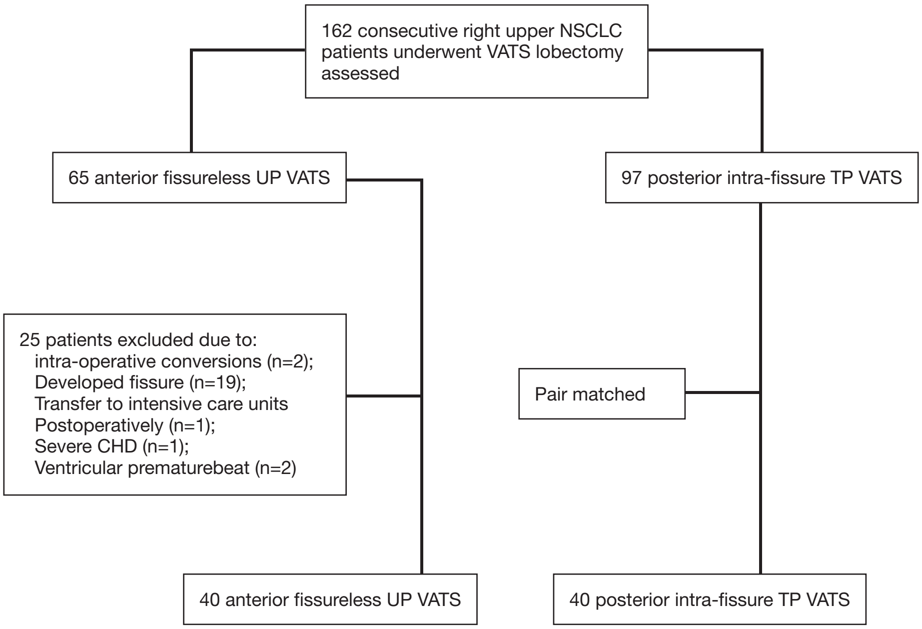

Figure 1 Study flowchart. UP, uniport; TP, triple port; CHD, coronary heart disease; VATS, video-assisted thoracoscopic surgery; NSCLC, non-small-cell lung cancer.

The flowchart summarizing the inclusion and matching procedure was found in *Figure 1*.

Surgical approach

For general anesthesia, a double-lumen tracheal intubation plus intravenous anesthesia was applied in both groups. In AFU group, the surgical incision was performed at the fifth intercostal space along the anterior axillary line, which was approximately 4-cm. In PIFT group, a 1.0-cm camera incision was made at the 8th intercostal space along the mid-axillary line. The main operative incision (3-cm) was made at the fifth intercostal space along the anterior axillary line; a secondary incision was made at the 7th intercostal space along the triangle of auscultation

The surgical procedures in both groups were different. In the AFU group, the first step was involved the opening of the anterior mediastinal pleura with electrocautery to liberate the upper lobe pulmonary artery branch, anterior to the lung tip. This was followed by an approach that sequentially involved the upper lobe bronchus, posterior ascending branch of the pulmonary artery, upper pulmonary vein, and fissure last (*Figure 2*). This procedure is similar to single-direction (9). In PIFT group, the first step was to divide the oblique fissure with a harmonic scalpel (Ethicon Endo-Surgery, Inc, Cincinnati, Ohio, USA) or endoscopic staple if the fissure was fused, and then ascending pulmonary artery and upper lobe bronchus were exposed. After dividing them, the apical and anterior artery branched from the right pulmonary arterial trunk appeared separately and upper pulmonary vein can be dissected easily.

After the resection of the right upper lobe, the 2nd, 4th, 7th, 8th and 9th groups of lymphatic nodes were removed by Harmonic scalpel (Ethicon Endo-Surgery, Inc., Cincinnati, Ohio, USA). Intraoperative air leak were always tested by submerging the residual lung in sterile saline and inflating it to a pressure of 25–30 cmH_2O. Sutures with 4-0 propylene or Fibrin Sealant (5 mL, Guangzhou Bioseal biotech Co, Ltd., China) are often used to minimize the air leak. At the end of both procedures, a 28-French intrathoracic tube was placed in the camera incision with a single stitch.

Criteria of postoperative parameters

We investigated the postoperative complications including pneumonia, atelectasis, chylothorax, arrhythmia, hypoxia, prolonged air leak and Cerebrovascular accident (CVA). Pneumonia and atelectasis were defined by purulent sputum and chest radiography, or computed tomography.

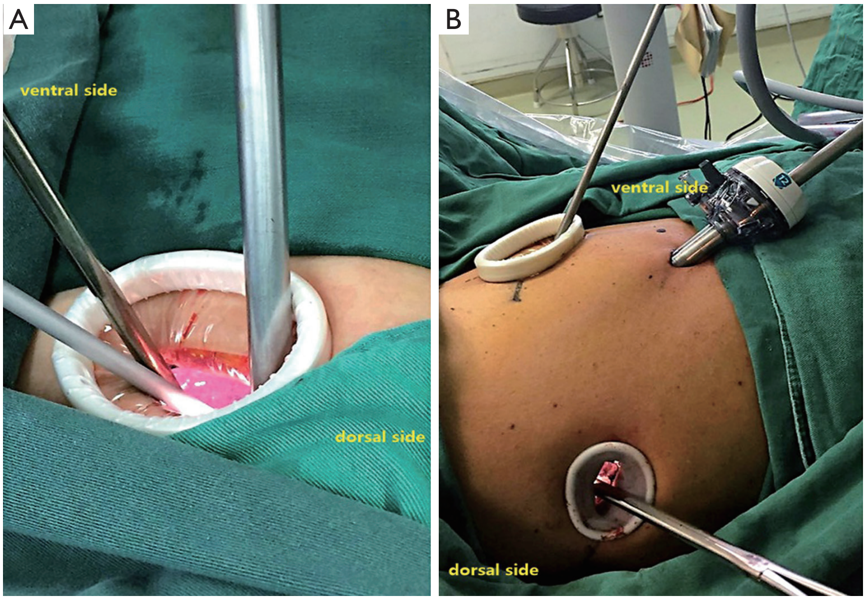

Figure 2 The uniportal access incision (4-cm) was at the 5th intercostal space along the anterior axillary line (A). In triple-port access, camera incision was made at the eighth intercostal space along the mid-axillary line; the main operative incision (3-cm) was made at the fifth intercostal space along the anterior axillary line and the secondary (2-cm) at the 7th intercostal space along the triangle of auscultation (B).

If the pleural effusion appeared lacte and the chyle test was positive, chylothorax was confirmed. Arrhythmia was defined by the need for treatment, and hypoxia by a decline in oxygen saturation, as measured by pulse oximetry, to ≤90%. Air leak was assessed twice daily (during the morning and evening rounds) and the patients were instructed to perform standardised repeated forced expiratory manoeuvres (coughing and blowing). Prolonged air leak was diagnosed when a patient needed chest tube drainage for >5 days. CVA is defined when blood flow to a part of your brain is stopped either by a blockage or the rupture of a blood vessel. Angiogram, CT and MRI are often used for diagnosis in our hospital.

Chest tube was removed if no air leak was detectable, the pleural effusion was less than 100 mL in the last 24 h and chest X-ray showed satisfactory lung expansion. Subsequently, the patients were discharged when routine blood analysis showed no obvious abnormalities.

Pain management and visual analogue scale (VAS) scores

Pain management was the same in both groups, including a vein analgesic protocol and intercostal nerve block using Naropin (7.5 mg/mL, AstraZeneca) postoperatively. VAS from 0 to 10 was used to assess the maximum pain scores; pain scores were recorded at postoperative 1 h and days 1, 3, 7 and 30, respectively (*Figure 3A-F*). After surgery, the patients were followed up for at least 3 months at the outpatient department.

Statistical analysis

Propensity scores were calculated by multivariate logistic regression. Descriptive statistical analysis was performed. Continuous variables were expressed as mean ±standard deviation according to data distribution. Comparisons between the two groups were performed by paired Student's test for continuous variables or McNemar's test with continuity correction for categorical variables, to account for the matching design. Statistical analyses were performed with the SAS software package (SAS Institute, Inc., Cary, NC, USA). Statistical significance was set at $P<0.05$.

Results

Clinical features

From June 2014 and Dec 2016, after propensity scored analysis, 40 AFU VATS RUL were included. Meanwhile, 40 PIFT VATS RUL were matched in this retrospective study. Patients in the two groups were similar in age, gender, BMI, tumor size, clinical TNM stage, pulmonary function,

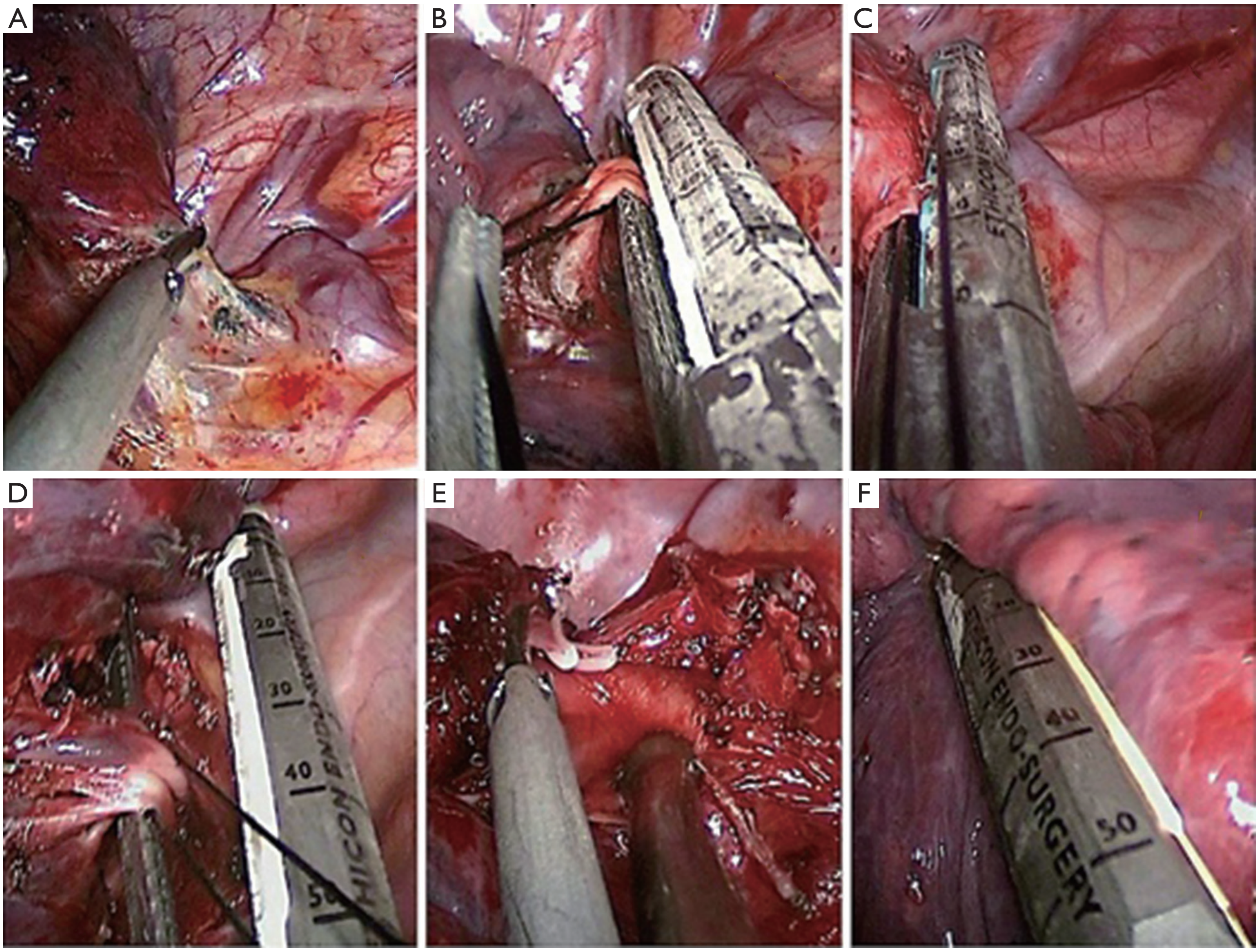

Figure 3 Anterior fissureless uniport thoracoscopic approach for RUL. (A) Opening of the anterior mediastinal pleura; (B) dissection of the pulmonary artery branch anterior to the lung tip; (C) dissection of the bronchus; (D) dissection of the pulmonary vein; (E) dissection of the pulmonary artery ascending branch; (F) completing the fissure.

fissural grade and comorbidities (*Table 2*). Postoperative pathological results revealed that the current patient cohort consisted of 71 adenocarcinoma and 9 squamous carcinoma, respectively. Furthermore, postoperative pathological TNM staging revealed that 29 cases were stage pT1aN0M0, 31 were stage pT1bN0M0, 17 were stage pT1cN0M0, 1were stage pT1bN1M0, and 2 were stage pT1cN1M0. Therefore, the current patient cohort was in principle suitable for assessing the performance of VATS RUL, being representative for clinical practice.

Surgery characteristics

There were no perioperative deaths or conversions to open chest surgery in either groups. Duration of lobectomy (85.2±35.1 *vs.* 116.2±49.2 min; P=0.001), LOS (4.2±1.7 *vs.* 7.5±3.1 d; P=0.048) and postoperative air leak (2.0±1.3 *vs.* 4.4±2.6 d; P=0.014) were significantly reduced in the AFU group compared with the PIFT group. Duration of systemic mediastinal lymphadenectomy, intraoperative blood loss, total lymph nodes harvested and volume of pleural effusion drainage within 48 h were similar in both groups (*Table 3*). There was also no significant difference in complication occurrence (*Table 4*).

Pain scores comparison between the two groups

There were no significant differences in the pain scores at postoperative 1 h and POD 1, 7, and 30. However, at POD 3, a significant difference was found (P=0.011) (*Table 5*). In both groups, only a small number of patients tended to receive normal doses of analgesics (e.g., nonsteroidal anti-inflammatory drugs, NSAIDs) after surgery. No side effects appeared due to these analgesics.

Discussion

Uniport VATS lobectomy (10,11) is widely accepted, especially in East Asia since 2011. There are multiple advantages, such as minimal trauma, beauty of the incision, and mild postoperative pain. In addition, compared with conventional TP VATS, a specific advantage of uniport VATS is exposure especially in upper lobectomy (12). For example, the high camera provides the shortest observation distance to the hilar structure, without overt reversal of the lobe. The sagittal view of the surgical field may be more conductive to anterior operation (13). However, though uniportal VATS has a good visibility, a narrow space often restricts the operative procedure. Many beginners feel uncomfortable in the initial learning curve, and the lobectomy time is not increased (14).

The fissureless technique was applied firstly in open thoracotomy in 1999, and reports related to VATS lobectomy appeared recently (15). In terms of technology, the process is simple and easy to learn, especially for RUL (16). The advantages of this approach are reduced operating time and decreased odds of postoperative air leak. Therefore, in early 2015, we combined anterior the fissureless technique and uniportal VATS in RUL; after a preliminary exploration of 20 cases, our learning curve became stable gradually. In this study, we found AFU VATS RUL was associated with shortened lobectomy time, LOS and postoperative drainage.

In 2013, Gonzalez (17) found that uniport VATS lobectomy has multiple advantages, including shortened operative time, corroborating our findings. Skillful manipulation and good visualization may be crucial factors. Nevertheless, Shen *et al.* (18) performed a propensity-matched study, and showed that the total operation duration, volume of intraoperative blood loss, total of lymph nodes and length of postoperative hospital stay are similar between the single incision and multi-incision VATS groups. The discrepant conclusions may be associated with the proficiency of surgeons. Furthermore, statistical errors may be produced if taking into account all lobes for analysis. Indeed, resection of different lobes has varying complexity because of anatomical structure differences. It would be more accurate if each lobe was assessed separately. In this study, only RUL were enrolled; more cases with shortened lobectomy time were obtained, which may contribute to the

Table 2 Propensity score matching of preoperative variables

Parameter	AFU (n=40)	PIFT (n=40)	P value
Age	59.3±11.2	60.2±11.7	0.639**
Gender			0.597*
Male	7	8	
Female	23	22	
BMI	19.5±2.3	20.7±2.0	0.772**
Histological type			0.655*
SC	3	6	
AD	37	34	
Clinical TNM Stage			0.371*
T1aN0M0	16	13	
T1bN0M0	12	20	
T1cN0M0	12	17	
Tumor size			0.371*
<1 cm	16	13	
1–2 cm	12	20	
2–3 cm	12	17	
Pulmonary Function			0.842**
FEV1%	75.4±11.6	77.6±12.1	
DLCO%	65.6±12.7	64.7±11.8	
Fissure grade			
III	34	35	0.883*
IV	6	5	0.778*
Comorbidity			
Primary hypertension	15	12	0.685*
Grade I	7	5	0.878*
Grade II	8	7	
II type diabetic mellitus	8	7	

Data are mean ± standard deviation or N (percentage). *, McNemar's test; **, paired Student's *t*-test. FEV1, forced expiratory volume in the first second; DLCO, diffusing capacity of carbon monoxide; SC, squamous cell cancer; AD, adenocarcinoma; AFU, anterior fissureless uniport: PIFT, posterior intra-fissure triple-port; BMI, body mass index.

Table 3 Perioperative outcomes in the AFU and PIFT groups

Parameter	AFU (n=40)	PIFT (n=40)	P value
Lobectomy time (min)	85.2±35.1	116.2±49.2	0.001
Mediastinal lymphadenectomy time (min)	23.2±11.5	20.4±13.7	0.336
Total lymph nodes harvest (n)	13±9	16±8	0.882
Intraoperative blood loss (mL)	77.8±33.6	82.5±42.7	0.656
Time of postoperative drainage (d)	2.0±1.3	4.4±2.6	0.014
Volume of chest tube drainage within 48 h (mL)	323.7±155.2	486.5±183.3	0.227
Postoperative hospital stay (d)	4.2±1.7	7.5±3.1	0.048

Table 4 Postoperative complications

Parameter	AFU (n=40)	PIFT (n=40)	P value
Total, n [%]	4 [10]	6 [15]	0.337
Prolonged air leakage (>5 d)	0	3	
Arrhythmia	2	1	
Chylothorax	0	1	
hypoxia	0	0	
Pneumonia	1	1	
Atelectasis	0	0	
Cerebrovascular accident	1	0	

novel surgical process, although we are beginners.

In addition, there were no significant differences between the two groups in terms of mediastinal lymphadenectomy time, intraoperative blood loss, total of lymph nodes harvested, overall complications, and volume of pleural effusion drainage within 48 h, in agreement with other studies (19,20). However, duration of postoperative drainage and hospital stay in the UP group were shorter than the of TP group. This may contribute to the anterior fissureless technique. Ng *et al.* (1) and Refai *et al.* (21) have been verifying its safety and efficacy for many years, although only in open thoracotomy or muscle-sparing lateral thoracotomy. Davor *et al.* (15) recently reported that the fissureless technique applied in VATS lobectomy appears to be superior to conventional VATS lobectomy in terms of preventing postoperative drainage and reducing LOS, corroborating our findings. Nevertheless, the numbers of patients in subgroups were too small for detailed analysis. Therefore, a larger, randomized study is required to confirm our findings.

With respect to postoperative pain, most contrastive studies (22,23) showed either no difference or significant difference in the early postoperative stage, while assessing simple thoracic surgery, e.g., for spontaneous pneumothorax correction. In the current study, the overt alleviation of postoperative pain at POD 3 differed from the above reports. This difference may mainly result from the shortened duration of chest tubes, and likely independent of the number of incision. Before uniport can be recommended as a less painful option than multiport thoracoscopic surgery, higher quality prospective randomized studies, validated pain assessment tools, and longer follow-up are needed.

There were two limitations in this study. Firstly, the number of patients was relatively small, with the lobe type limited. However, after matching for confounding factors, the characteristic results of the comparison were reliable. Secondly, the results were from a single medical center, which limits the generalization of the findings. Multicenter randomized controlled trials are therefore required to confirm the role of the AFU thoracoscopic approach for RUL or the resection of another lobe.

Conclusions

This initial study suggests that the AFU thoracoscopic approach for RUL appears to be safe, efficient and easy to manipulate; therefore, it merits further studies for suitability for the other lobe, or widespread clinical implementation.

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Table 5 Pain scores comparison between the two groups

Groups	Postoperative 1 h	POD 1 d	POD 3 d	POD 7 d	POD 30 d
AFU (n=40)	2.3±0.8	2.4±0.5	2.4±0.3	2.8±0.7	1.3±0.2
PIFT (n=40)	2.5±1.2	2.7±0.6	3.1±0.4	3.5±1.2	1.2±0.7
P value	0.898	0.724	0.011	0.365	0.866

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: Written informed consent was obtained from patients with approval from the Institutional Review Board in Affiliated Hospital of Nantong University, China (2016-K143).

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