Propensity-matched comparison of video-assisted thoracoscopic with thoracotomy lobectomy for locally advanced non–small cell lung cancer

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ABSTRACT

Objective: We evaluated whether video-assisted thoracoscopic lobectomy for locally advanced non–small cell lung cancer could be performed safely and with acceptable long-term outcomes by our improved technique and compared with standard thoracotomy lobectomy in a well-balanced population.

Methods: Patients with clinical stage II and III A non–small cell lung cancers who received lobectomy were reviewed. Video-assisted thoracoscopic lobectomies were all performed with Wang's technique by the surgeons who had overcome the learning curve and achieved proficiency. By using propensity-matched analysis, perioperative outcomes and long-term survival were compared.

Results: Matching based on propensity scores produced 120 patients in each group. Conversion rate to thoracotomy was 11.7%. After thoracoscopic lobectomy, hospital length of stay was shorter compared with thoracotomy (9.2 vs 12 days; $P = .014$) despite similar rates of postoperative complications (30/125 [25%] vs 34/125 [28.3%]; $P = .56$). Disease-free survival (49.1% vs 42.2%; $P = .40$) and overall survival (55.0% vs 57.1%; $P = .73$) at 5 years were similar between groups. Although advanced pathologic stage (hazard ratio [HR], 2.018; 95% confidence interval [CI], 1.330–3.062) and no postoperative chemotherapy (HR, 1.880; 95% CI, 1.236–2.858) were independently associated with increased hazard of death in multivariable Cox regression at each time point in follow-up, thoracoscopic lobectomy was not (HR, 1.075; 95% CI, 0.714–1.620; $P = .73$).

Conclusions: With continued experience and optimized technique, video-assisted thoracoscopic lobectomy can be performed in the majority of cases without compromising perioperative outcomes and oncologic efficacy. (*J Thorac Cardiovasc Surg* 2017;153:967–76)

DFS between VATS and thoracotomy groups.

Central Message

With continued experience and optimized technique, VATS lobectomy can be performed without compromising perioperative outcomes and oncologic efficacy.

Perspective

This is the first well-balanced comparative study to adequately compare VATS with thoracotomy lobectomy for locally advanced NSCLC. All the VATS were conducted by thoracic surgeons who had achieved proficiency in the improved technique, which ensured VATS at a consistent level. VATS lobectomy can be performed safely with similar long-term survival compared with thoracotomy in non–stage I NSCLC.

See Editorial Commentary page 977.

Growing evidence has suggested that video-assisted thoracoscopic surgery (VATS) lobectomy is a preferred approach for patients with early-stage non–small cell lung cancer (NSCLC) with superior short- and long-term outcomes.^{1,2} However, most previous studies for VATS in lung cancer were limited to early-stage disease in which the results of

VATS for patients with other disease stages were not clear. Some studies involved a mixture of stages, and results showed that VATS was not inferior to thoracotomy.^{3,4} However, because a majority of patients in these studies were stage I disease, the results of VATS for patients with other disease stages may have been overestimated. We cannot draw any conclusion regarding VATS and thoracotomy for those patients with non–stage I lung cancer.

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Abbreviations and Acronyms

CI	= confidence interval
CT	= computed tomography
DFS	= disease-free survival
HR	= hazard ratio
NSCLC	= non-small cell lung cancer
OS	= overall survival
VATS	= video-assisted thoracoscopic surgery

With the continuous development of surgical instruments, such as high-definition cameras and display devices (1080P), new-generation endoscopic staplers with rotating heads, and retraction instruments, technical difficulties for advanced cases have been gradually overcome.⁵ Thoracic surgeons with increasing experience have made VATS safer and have expanded the indications for thoracoscopic resection. Tumors once thought unapproachable by thoracoscopic techniques are now frequently resected by VATS.

Hennon and Demmy⁵ confirmed the safety of thoracoscopic lobectomy in locally advanced lung cancer. We have previously presented our thoracoscopic experience in patients with tumors larger than 5 cm.⁶ However, because there have been no well-balanced comparative studies with sufficient evidence to adequately compare VATS lobectomy with thoracotomy lobectomy for locally advanced NSCLC, several concerns regarding completeness of oncologic resection, technical challenges, and potential safety have limited the use of minimally invasive techniques for more advanced stages of lung cancer. Therefore, we conducted this study to evaluate whether VATS lobectomy by our improved technique could be performed with acceptable short- and long-term outcomes when compared with standard thoracotomy for patients with locally advanced NSCLC in a well-balanced large population from a multi-institutional database.

MATERIALS AND METHODS

Patient Eligibility

We reviewed our lung cancer surgery database, which was prospectively maintained and included a consecutive cohort of patients who underwent curative surgery of lung cancer in our institution and a series of other hospitals in China. This prospective multi-institutional database was established on the basis of 2 other prospective studies since 2010, which required that for patients enrolled in this database, each hospital had to adopt the same protocols for diagnosis and perioperative management. All of the patients underwent contrast-enhanced thoracic computed tomography (CT) scans before surgery. Other routine preoperative examinations included chest radiograph, cardiopulmonary function tests, abdominal and adrenal gland ultrasonography or CT, brain magnetic resonance imaging or CT, and a bone scan. If mediastinal lymph node enlargement was demonstrated on chest CT, endobronchial ultrasound transbronchial needle aspiration or mediastinoscopic biopsy was performed first. Positron emission tomography/CT was not mandatory in every patient.

The inclusion criterion of this study was patients who underwent a lobectomy for lung cancer with clinical locally advanced stage (stage IIa, IIb, or IIIa) by the 7th American Joint Committee on Cancer TNM staging system.

We reviewed the database from January 2010 to December 2012 and identified 524 patients from 7 high-level comprehensive cancer hospitals in China. Patients who underwent bilobectomy, pneumonectomy, or sleeved lobectomy were excluded. Patients who had small cell lung cancer or incomplete data were also excluded. In all, 411 patients were included, of whom 250 had a VATS lobectomy and 161 had a thoracotomy were identified. The hospital accumulated data with prospective patient permission on the scientific use of collected data, and the protocols of this study were approved by the Institutional Review Board of Peking University People's Hospital.

Clinical Variables

We collected clinical variables of patients, including age, gender, comorbidities, forced expiratory volume in 1 second, diffusing capacity for carbon monoxide, smoking history (<100 cigarettes defined as nonsmokers), TNM stage, tumor histology, and tumor location and size measured by CT. Postoperative complications were described according to the Common Terminology Criteria for Adverse Events Version 3.0. A prolonged air leak was one that lasted more than 7 days postoperatively. All of the hospitals in our multi-institutional database adopted the same indication to remove the chest tube when the drainage was less than 200 mL/d for 2 days.

Chest CT scan and abdominal ultrasound/CT are performed on follow-up visits every 6 months after operation for 5 years. Magnetic resonance imaging and bone scan are performed every year for 5 years or any time that the patient has symptoms. The overall survival (OS) was estimated from the date of surgical resection to death of any cause or the date of last follow-up. Disease-free survival (DFS) was defined as the time from the day of surgery until the first event (relapse, metastasis, or death from any cause) or last follow-up. Perioperative mortality was defined as death within 30 days of the operation.

Operative Technique

More than 90% of lobectomies were performed by VATS at Peking University People's Hospital. Because of the relatively higher morbidity of tuberculosis and infection, Chinese patients with lung cancer present with more severe adhesions between lymph nodes and blood vessels than patients in many other countries.⁷ This situation has caused us to develop more efficient and safer methods to undertake these difficult surgeries. Peking University People's Hospital is an experienced center; thus, we summarized and optimized our technique for the long-term minimally invasive thoracic surgical treatment for lung cancer, and we developed our improved technique (Wang's technique), which has been described.^{7,8} The major features of our technique are as follows (Video 1): (1) a specially made

VIDEO 1. VATS right upper lobectomy by Wang's technique. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(16\)31671-3/addons](http://www.jtcvsonline.org/article/S0022-5223(16)31671-3/addons).

TABLE 1. Patient characteristics

	VATS (n = 250)	Thoracotomy (n = 161)	P value
Age, y ± SD	62.2 ± 10.3	60.2 ± 9.6	.05
Sex, n (%)			
Male	121 (62.4)	156 (75.2)	.007
Tumor size, cm ± SD	3.3 ± 1.6	4.8 ± 2.2	<.001
FEV1%	78.2	79.6	.14
DLCO%	82.6	81.1	.25
Comorbidities, n (%)			
No comorbidities	147 (58.8)	117 (72.7)	.004
Diabetes mellitus	24 (9.6)	11 (6.8)	.33
Hypertension	74 (29.6)	29 (18)	.008
History of MI	27 (10.8)	4 (2.5)	.002
COPD	8 (60.8)	6 (3.7)	.77
Renal insufficiency	11 (4.4)	5 (3.1)	.51
Neoadjuvant, n (%)	6 (2.4)	11 (6.8)	.028
Smoking history, n (%)	108 (43.2)	98 (60.9)	<.001
cTNM, n (%)			.065
IIA	113 (45.2)	61 (37.9)	
IIB	32 (12.8)	34 (21.1)	
IIIA	105 (42)	66 (41)	
cT stage, n (%)			.002
T1	60 (24)	26 (16.1)	
T2	159 (63.6)	94 (58.4)	
T3	29 (11.6)	34 (21.1)	
T4	2 (2.2)	7 (4.3)	
cN stage, n (%)			.87
N0	72 (28.8)	50 (31.1)	
N1	84 (33.6)	51 (31.7)	
N2	94 (37.6)	60 (37.3)	
Tumor location, n (%)			.07
Right upper	81 (32.4)	49 (30.4)	
Right middle	18 (7.2)	4 (2.5)	
Right lower	53 (21.2)	27 (16.8)	
Left upper	65 (26.0)	49 (30.4)	
Left lower	33 (13.2)	32 (19.9)	

VATS, Video-assisted thoracoscopic surgery; SD, standard deviation; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity for carbon monoxide; MI, myocardial infarction; COPD, chronic obstructive pulmonary diseases.

2-curved suction and an electrocautery hook are handled concurrently through a single incision and double-crossed in the same direction. (2) A perivascular tunnel is created for interlobar fissure division. (3) Cutting off the bronchial artery is a priority. (4) Vessels are freed in their subadventitial plane. (5) The mediastinal pleura is unfolded around the hilum of the lung. All of the VATS lobectomies in this study were conducted by the thoracic surgeons who had overcome the learning curve and achieved proficiency of VATS lobectomy (>200 lobectomies independently), which has been published.^{9,10}

Thoracoscopy was performed at the beginning of all operative procedures to assess the extent of disease. Conversions were defined as operations that began with thoroscopic dissection and were concluded as a rib-spreading thoracotomy. Thoracoscopic evaluation without structural dissection that continued as an open case did not qualify as a conversion and was considered a planned thoracotomy. The patients who converted from VATS to thoracotomy were analyzed in the VATS cohort for the reason of “intent-to-treat” method.¹¹ All of the thoracotomy lobectomies were performed via a standard posterolateral thoracotomy incision.

Systematic mediastinal lymph nodal dissection or sampling was mandatory. Lymph nodes in groups 2, 4, 7, and N1 were resected for the right-side

lesion, and lymph nodes in groups 5, 6, 7, and N1 were resected for the left-side lesion.

Statistical Analysis

Univariate analysis of categorical data between VATS and thoracotomy groups was conducted using the Fisher exact test or Pearson’s chi-square test. Student *t* test or Mann–Whitney *U* test was used to assess for 2-group comparisons of continuous variables, which are expressed as the mean values and standard deviations. Propensity score matching was performed to balance the baseline of the patients by logistic regression model. VATS versus thoracotomy was the treatment indicator, and the variables were age, sex, each comorbidity, forced expiratory volume in 1 second, diffusing capacity for carbon monoxide, smoking history, clinical T stage, clinical N stage, clinical stage, neoadjuvant treatment, tumor size, and tumor location. VATS and thoracotomy pairs with a nearest propensity score were matched 1 to 1 with a caliper width of 0.2 of standard deviation (Figures E1 and E2). Postoperative outcomes from the matched cohorts were then compared. OS and DFS were evaluated by Kaplan–Meier survival analysis. Log-rank tests were used to determine the statistical significance of survival between the 2 groups. Univariable and multivariable analyses using the Cox proportional hazards models were constructed to

TABLE 2. Propensity score–matched comparison of baseline characteristics between video-assisted thoracoscopic surgery and thoracotomy groups

	VATS (n = 120)	Thoracotomy (n = 120)	SD before	SD after
Age, y $\pm$ SD	60.3 $\pm$ 10.2	60.9 $\pm$ 9.3	0.196	−0.075
Sex, n (%)				
Male	81 (67.5)	86 (71.7)	−0.263	−0.086
Tumor size, cm $\pm$ SD	3.8 $\pm$ 1.8	4.1 $\pm$ 1.8	−0.991	−0.127
FEV1%	79.0	79.2	−0.166	−0.023
DLCO%	81.3	80.9	0.105	−0.051
Comorbidities, n (%)				
Diabetes mellitus	10 (8.3)	9 (7.5)	0.094	−0.056
Hypertension	25 (20.8)	26 (21.7)	0.253	0.018
History of MI	5 (4.2)	4 (3.3)	0.267	0.134
COPD	4 (3.3)	5 (4.2)	−0.030	0.047
Renal insufficiency	5 (4.2)	5 (4.2)	0.063	0.000
Neoadjuvant, n (%)	4 (3.2%)	5 (4%)	−0.289	0.000
Smoking history, n (%)	68 (56.7)	67 (55.8%)	−0.356	−0.084
cTNM, n (%)			−0.067	−0.009
IIA	52 (43.3%)	52 (43.3%)		
IIB	24 (20%)	18 (15%)		
IIIA	44 (36.7%)	50 (41.7%)		
cT stage, n (%)			−0.398	−0.068
T1	23 (19.2)	25 (20.8)		
T2	81 (67.5)	75 (62.5)		
T3	15 (12.5)	16 (13.3)		
T4	1 (0.8)	4 (3.3)		
cN stage, n (%)			0.032	0.010
N0	34 (28.3)	32 (26.7)		
N1	42 (35.0)	40 (33.0)		
N2	44 (36.7)	48 (40.0)		
Tumor location, n (%)			−0.181	0.063
Right upper	35 (29.2)	40 (33.3)		
Right middle	3 (2.5)	3 (2.5)		
Right lower	33 (27.5)	19 (15.8)		
Left upper	35 (29.2)	39 (32.5)		
Left lower	14 (11.7)	19 (15.8)		

Differences < -0.25 and > 0.25 are significant (at least $P < .05$). VATS, Video-assisted thoracoscopic surgery; SD, standard deviation; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity for carbon monoxide; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease.

assess the potential independent effects on DFS and OS. Predictors ($P < .2$) in univariable analysis were incorporated into a multivariable analysis. We used PASW SPSS for Windows version 22.0 (IBM, Chicago, Ill) and R version 2.15.3 (R Foundation for Statistical Computing, Vienna, Austria) for statistical analysis.

RESULTS

The medical records of 411 patients with locally advanced NSCLC who underwent lobectomy were included, 250 patients underwent VATS, and 161 patients underwent thoracotomy. Patient characteristics are shown in Table 1.

Perioperative Outcomes

After propensity score matching, 120 patients from the thoracotomy group were matched and compared with 120 patients from the thoracoscopic group (Table 2). There was 1 perioperative death in each group and no

intraoperative deaths. All patients were R0 resected. Fourteen patients (11.7%) in the VATS group were converted to thoracotomy. Reasons for conversions were bleeding ($n = 2$), large tumor size ($n = 2$), lymph node calcification ($n = 7$), margins that needed to be extended ($n = 1$), and failed fissure dissociation ($n = 2$).

Median surgery time, blood loss, and tube duration were not significantly different between the 2 groups. When the conversion group was placed in the thoracotomy group, the blood loss (141 vs 184 mL, $P = .006$) was significantly less in the VATS group than in the thoracotomy group. A total of 37 adverse events occurred in 30 patients in the VATS group, and 45 adverse events occurred in the 34 patients undergoing thoracotomy. Thoracoscopic lobectomy was associated with a shorter length of hospital stay (9.2 vs 12 days, $P = .014$) (Table 3).

To evaluate the thoroughness of lymph node clearance by VATS or thoracotomy, both the mean number of lymph

TABLE 3. Comparison of perioperative outcomes between video-assisted thoracoscopic surgery and thoracotomy groups

	VATS (n = 120)	Thoracotomy (n = 120)	P value*
Surgery time, min, median (range)	183 (90-465)	200 (90-535)	.64
Blood loss, mL, median (range)	147 (20-1000)	180 (40-1100)	.06
Tube duration, d, median (range)	6.6 (2-24)	7 (3-16)	.94
LOS, d, median (range)	9.2 (4-35)	12 (4-26)	.014
Complication, n (%)			
Any complication	30 (25)	34 (28.3)	.56
Prolonged air leak	17 (14.2)	22 (12.5)	.70
Bleeding	2 (1.7)	2 (1.7)	1.0
Atelectasis	2 (1.7)	2 (1.7)	1.0
Pneumonia	2 (1.7)	3 (2.5)	1.0
Atrial arrhythmia	5 (4.2)	8 (6.7)	.39
Heart failure	1 (0.8)	1 (0.8)	1.0
Chylothorax	3 (2.5)	1 (0.8)	.62
Wound infection	2 (1.7)	4 (3.3)	.68
Others	3 (2.5)	2 (1.7)	1.0
Histology, n (%)			.19
Adenocarcinoma	84 (70)	72 (60)	
Squamous carcinoma	34 (28.3)	47 (39.2)	
Others	2 (1.7)	1 (0.8)	
pStage, n (%)			.95
IA	3 (2.5)	3 (2.5)	
IB	6 (5.0)	7 (5.8)	
IIA	44 (36.7)	43 (35.8)	
IIB	16 (13.3)	16 (13.3)	
IIIA	48 (40.0)	50 (41.7)	
IIIB	3 (2.5)	1 (0.8)	
Lymph nodes, mean ± SD			
Total stations	5.5 ± 1.8	5.5 ± 1.6	.85
Total lymph nodes	15.6 ± 9.2	14.7 ± 7.9	.42
N1 stations	2.2 ± 0.9	2.0 ± 0.8	.09
N1 lymph nodes	5.3 ± 4.0	5.3 ± 3.7	.96
N2 stations	3.3 ± 1.2	3.5 ± 1.4	.17
N2 lymph nodes	10.3 ± 7.0	9.4 ± 5.8	.27

VATS, Video-assisted thoracoscopic surgery; LOS, length of hospital stay; SD, standard deviation. *P values are based on Mann–Whitney U tests for abnormal distributed continuous data.

nodes and nodal stations removed were compared between the 2 groups. There were no differences in the number and stations of N1, N2, or total lymph nodes between the 2 surgical approaches. When we separated our patients into 2 groups according to the operation time, similar to Lee and colleagues’ recent study,¹² our data also showed an increase in nodal harvest by VATS as time progressed. In the early group (January 2010 to June 2011), no differences were found between VATS and thoracotomy, except that more total nodal stations (5.8 vs 5.2, $P = .037$) and N2 stations (3.7 vs 3.3, $P = .046$) were resected by thoracotomy than VATS. Compared with the early group, a greater number of total nodal stations (5.8 vs 5.1 $P = .046$), lymph nodes (16.5 vs 12.2 $P = .011$), N1 stations (2.4 vs 1.8, $P < .001$), N1 lymph nodes (5.7 vs 4.3, $P = .048$), and N2 lymph nodes (10.8 vs 8.0, $P = .042$) were retrieved by VATS than thoracotomy in the late group (July 2011 to December 2012).

Because most of the patients in this study had stage II or III disease, adjuvant chemotherapy was recommended. The chemotherapy regimens administered in the 2 groups were similar, which included gemcitabine, pemetrexed, docetaxel plus cisplatin, or paclitaxel plus carboplatin every 3 weeks. It seemed that more patients in the VATS group could tolerate all 4 (or more) cycles at the fully planned dose on schedule, but this difference was not significant (Table 4).

Oncologic Efficacy

The last follow-up was completed in January 2016. The median follow-up period was 45 months (range, 1-72). The location of recurrence was not significantly different between the 2 groups (Table 5). Three-year DFS was 50.1% in the open thoracotomy group and 54.8% in the VATS group. Five-year DFS was 42.2% in the open thoracotomy group and 49.1% in the VATS group. There was no

TABLE 4. Chemotherapy compliance after lobectomy by different approaches

	VATS (n = 120)	Thoracotomy (n = 120)	P value
Adjuvant chemotherapy, n (%)	84 (70.0)	78 (65.0)	.41
Receive full dose on schedule, n (%)	62 (51.7)	51 (42.5)	.16
Time to start chemotherapy, d, mean $\pm$ SD	33.9 $\pm$ 3.0	34.5 $\pm$ 3.4	.21
Cycles completed, mean $\pm$ SD	2.4 $\pm$ 1.8	2.2 $\pm$ 2.0	.33

VATS, Video-assisted thoracoscopic surgery; SD, standard deviation.

significant difference in recurrence between the 2 groups ($P = .40$) (Figure 1, A). The overall 3-year survival was 72.6% in the thoracotomy group and 78.2% in the VATS group. The overall 5-year survival was 57.1% in the thoracotomy group and 55% in the VATS group. There was no significant difference in survival between the 2 groups ($P = .73$) (Figure 1, B). When the conversions were placed in the thoracotomy group, the VATS group seemed to have a better 5-year DFS (51.7% vs 40.7%, $P = .124$) (Figure 2, A) and OS (57.9% vs 54.5%, $P = .182$) (Figure 2, B) according to the curves, but there was no significant difference. By comparing the clinical stages, there was no difference between the VATS group and thoracotomy group in 5-year DFS (stage IIa, 50% vs 53%, $P = .988$; stage IIb, 51.8% vs 40%, $P = .814$; stage IIIa, 44.2% vs 30%, $P = .386$) and OS (stage IIa, 56.4% vs 66.8%, $P = .606$; stage IIb, 62% vs 72.2%, $P = .914$; stage IIIa, 48.4% vs 41.4%, $P = .291$).

Multivariable Cox regression analysis of DFS and OS showed that 2 independent predictors were pathologic stage and adjuvant chemotherapy, whether the conversions were placed in the VATS group or thoracotomy group. The worse DFS (hazard ratio [HR], 2.365; 95% confidence interval [CI], 1.618-3.458; $P < .001$) and OS (HR, 2.018; 95% CI, 1.330-3.062; $P = .001$) occurred in patients with advanced pathologic stage and patients without adjuvant chemotherapy (DFS, HR, 1.609; 95% CI, 1.094-2.366; $P = .016$) (OS, HR, 1.880; 95% CI, 1.236-2.858; $P = .003$) (Tables 6 and 7).

DISCUSSION

Although thoracoscopic resection for advanced-stage NSCLC has been reported,¹³ few studies have been designed specifically to validate the potential benefits of VATS for advanced lung cancer. We attempted to be as objective as possible in comparing the 2 approaches. First, our study benefitted from a multi-institutional prospective data collection that was reviewed every week by the attending surgical staff, which should have been more accurate than acquisition of retrospective data. Second, our VATS technique has been described,^{7,8} and all VATS were conducted by thoracic surgeons who had achieved proficiency (>200 lobectomies) in this improved technique (Wang's technique).¹⁰ Most previous studies comparing VATS and thoracotomy did not show all surgeons being proficient in the surgery.¹⁴ As a traditional surgery, the thoracotomy lobectomy techniques were almost the same and were conducted with consistent standard posterolateral thoracotomies in different hospitals. Therefore, we could minimize bias by the skills of the surgeons and equally compare the 2 approaches.

After matching, our cohort of patients were well balanced in all categories between the thoracotomy and VATS lobectomy groups, which minimized bias from known confounders. Cao and colleagues⁴ performed a large matched study of VATS versus thoracotomy; however, the study lacked detailed data, perioperative outcomes, oncologic efficacy, and DFS were not compared. Therefore, we consider our study the first well-balanced comparative study to

TABLE 5. Summary of recurrence patterns between the 2 groups

	All patients (n = 240)	VATS (n = 120)	Thoracotomy (n = 120)	P value
Overall recurrence	123	58	65	.87
Locoregional, n (%)	51	24 (41.4)	27 (41.5)	
Ipsilateral lung	31	13	18	
Lymph node	20	11	9	
Distant, n (%)	57	26 (44.8)	31 (47.7)	
Contralateral lung	5	3	2	
Brain	19	10	9	
Bone	20	7	13	
Liver	6	2	4	
Others	7	4	3	
Local and distant, n (%)	15	8 (13.8)	7 (10.8)	

VATS, Video-assisted thoracoscopic surgery.

FIGURE 1. A, DFS between thoracotomy and VATS groups ($P = .40$). B, OS between thoracotomy and VATS groups ($P = .73$). VATS, Video-assisted thoracoscopic surgery; DFS, disease-free survival; CI, confidence interval; OS, overall survival.

adequately compare VATS lobectomy with thoracotomy lobectomy for locally advanced NSCLC. In recent clinical guidelines such as the American College of Chest Physicians, we could only conclude that “For patients with clinical stage I NSCLC, a minimally invasive approach such as

video-assisted thoracic surgery is preferred over a thoracotomy...”¹ Our study provides evidence comparing VATS and thoracotomy for non-stage I NSCLC. In the current study, the conversion rate from VATS to thoracotomy was not greater than published VATS

FIGURE 2. A, DFS between thoracotomy and VATS groups (conversions in the thoracotomy group) ($P = .12$). B, OS between thoracotomy and VATS groups (conversions in the thoracotomy group) ($P = .18$). VATS, Video-assisted thoracoscopic surgery; DFS, disease-free survival; CI, confidence interval; OS, overall survival.

TABLE 6. Univariable and multivariable Cox analyses for disease-free survival

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	0.985 (0.968-1.003)	.097	0.988 (0.972-1.004)	.150
Sex				
Female/male	1.204 (0.828-1.753)	.33		
Tumor size	0.964 (0.872-1.066)	.47		
Smoking history				
No/yes	1.414 (0.993-2.015)	.055	1.244 (0.851-1.820)	.26
Comorbidity				
No/yes	1.136 (0.772-1.670)	.52		
Histology				
Nonadenocarcinoma/adenocarcinoma	0.779 (0.53-1.146)	.21		
FEV1%	0.990 (0.973-1.007)	.24		
DLCO%	0.987 (0.974-1.000)	.058	0.987 (0.973-1.001)	.063
Location				
Left/right lobe	0.775 (0.541-1.111)	.17	0.834 (0.569-1.222)	.35
Middle or lower/upper lobe	0.741 (0.509-1.078)	.12	0.693 (0.466-1.033)	.072
Lymph node dissection				
Stations	0.956 (0.865-1.056)	.38		
Number	0.989 (0.966-1.013)	.39		
N1 stations	0.867 (0.710-1.058)	.16	0.953 (0.740-1.228)	.71
N1 number	0.958 (0.908-0.011)	.12	0.968 (0.903-1.038)	.36
N2 stations	0.978 (0.857-1.115)	.74		
N2 number	0.996 (0.966-1.027)	.80		
Adjuvant Chemotherapy				
No/yes	1.388 (0.958-2.012)	.083	1.609 (1.094-2.366)	.016
Cycles completed	0.956 (0.870-1.050)	.35		
pStage				
III/II, I	2.490 (1.735-3.575)	<.001	2.365 (1.618-3.458)	<.001
Group				
Thoracotomy/VATS	1.162 (0.815-1.657)	.41		

HR, Hazard ratio; CI, confidence interval; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity for carbon monoxide; VATS, video-assisted thoracoscopic surgery.

conversion rates ranging from 0% to 22.5%.¹⁵ In contrast to the study by Puri and colleagues,¹⁶ the main cause of conversion was lymph node calcification, which may have been due to the high rate of tuberculosis and inflammation in Chinese people. Meta-analyses showed that the overall complication rates for NSCLC was lower in the VATS group than in the thoracotomy group.^{2,17} In our study, the incidence of postoperative complications was lower in the VATS group than in the thoracotomy group, but statistical significance was not achieved, which may have been due to the small sample size.

Our patients had a longer chest tube duration and longer length of stay than are usually reported because of different indications for removing the tube in Chinese and Western countries. Most Chinese doctors are conservative in treatment and worry about resetting the tube. Thus, they tend to remove the tube later (<150-200 mL/d) than in Western hospitals, which leads to a longer length of stay in the hospital. However, we do not think this difference affected our study. We did not compare the exact length of stay in the hospital between Chinese patients and patients in other

countries. We compared the 2 groups who adopted the same criteria for removing the chest tube (<200 mL/day for at least 2 days). The length of hospital stay and duration of chest tube were similar to those in other studies from China.¹⁸ In addition, we have adopted western practices of earlier tube removal in recent years, and the length of stay of patients in our department is shorter than before.

There was no difference in performance status or comorbidities between the patients who did and did not receive adjuvant chemotherapy. In accordance with Lee and colleagues' study,¹⁹ the VATS group trended toward better compliance with adjuvant chemotherapy without a reduced dose, but there was no significant difference. A possible explanation may be lower postoperative pain and lighter psychologic burden with side effects in the VATS group.

The possibility of technique-dependent recurrence rate in VATS lobectomy concerns many surgeons, who consider that factors such as cancer dissemination during manipulation, insufficient surgical margin, or lymph node dissection affect the recurrence rate. The meta-analysis by Zhang and colleagues²⁰ revealed that the difference in mean total

TABLE 7. Univariable and multivariable Cox analyses for overall survival

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	0.993 (0.972-1.013)	.49		
Sex				
Female/male	1.013 (0.649-1.580)	.96		
Tumor size	0.993 (0.885-1.114)	.90		
Smoking history				
No/yes	0.968 (0.658-1.425)	.87		
Comorbidity				
No/yes	1.076 (0.714-1.623)	.73		
Histology				
Nonadenocarcinoma/adenocarcinoma	0.958 (0.623-1.471)	.84		
FEV1%	0.993 (0.973-1.013)	.47		
DLCO%	0.991 (0.976-1.007)	.28		
Location				
Right/left lobe	0.791 (0.521-1.201)	.27		
Middle or lower/upper lobe	0.858 (0.558-1.318)	.48		
Lymph node dissection				
Stations	1.003 (0.887-1.134)	.96		
Number	0.995 (0.969-1.022)	.72		
N1 stations	0.888 (0.703-1.120)	.32		
N1 number	0.985 (0.928-1.046)	.63		
N2 stations	1.049 (0.890-1.237)	.57		
N2 number	0.996 (0.962-1.031)	.82		
Adjuvant Chemotherapy				
No/yes	1.729 (1.140-2.622)	.01	1.880 (1.236-2.858)	.003
Cycles completed	0.892 (0.800-0.995)	.04	1.036 (0.824-1.303)	.76
pStage				
III/II, I	1.882 (1.244-2.848)	.003	2.018 (1.330-3.062)	.001
Group				
Thoracotomy/VATS	1.075 (0.714-1.620)	.73		

HR, Hazard ratio; CI, confidence interval; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity for carbon monoxide; VATS, video-assisted thoracoscopic surgery.

lymph node dissection or lymph node sampling numbers between VATS and thoracotomy was not significant in early-stage NSCLC ($P = .14$). However, systematic lymph node dissection is more complicated and mandates a stricter thorough clearance in locally advanced NSCLC than in the early stage. Lee and colleagues³ compared the 2 approaches for all stages of NSCLC and showed that both the number of lymph nodes and the number of lymph node stations removed were less in VATS than in thoracotomy. However, their study reviewed patients over more than 2 decades. Lee and colleagues¹² showed that a greater number of lymph nodes and nodal stations were sampled in the later period than in the earlier period and indicated a learning curve in VATS nodal dissection, which is similar to our data. Cumulative experience could positively affect the adequacy of lymph node resection. Few studies have reported the incidence of procedure-related tumor dissemination during VATS. Kim and colleagues²¹ compared VATS lobectomy with thoracotomy and did not see an increase in the risk of procedure-related pleural dissemination in patients with VATS. Long-term survival and pattern of recurrence were

similar between the 2 groups in 2 recent studies.^{3,21} In comparison, although our study had more patients with advanced-stage disease, there were also no significant differences in both locoregional and distant recurrence. These results may eliminate some apprehension about technique-dependent recurrence rate related to VATS.

Multivariable regression analysis indicated similar DFS and OS with the VATS approach compared with thoracotomy. When the conversions were placed in the thoracotomy group, the VATS group had less blood loss and seemed to have a better survival, although there was no significant difference. In view of a shorter length of hospital stay, likely better compliance with adjuvant chemotherapy, and cumulative experience, we believe VATS showed a suggestion of benefit for patients with locally advanced NSCLC.

Study Limitations

First, although the data in this study were gathered prospectively, the analysis was performed retrospectively. Second, as in most studies comparing the 2 approaches, it is difficult to eliminate the surgeon's selection bias.

Complicated tumors (eg, centrally located) may be preferred for thoracotomy. However, because a prospective randomized controlled trial between VATS and open thoracotomy seemed unlikely to be conducted, we believe this propensity analysis minimized bias as much as possible. Third, we did not have data on how many patients received postoperative radiation therapy or targeted therapy, which play important roles in advanced NSCLC and may affect the OS. However, with similar clinical characteristics and number of recurrences between the 2 groups, we considered they might have had the same opportunities to use these therapies, which would not change our results.

CONCLUSIONS

VATS lobectomy for locally advanced-stage NSCLC can be performed safely with a shorter length of hospital stay and showed similar long-term survival compared with thoracotomy. With continued experience and optimized technique, VATS lobectomy can be performed in the majority of cases without compromising perioperative outcomes and oncologic efficacy.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: lung cancer, video-assisted thoracoscopic lobectomy, locally advanced

FIGURE E1. Histogram of propensity scores for patients between VATS and thoracotomy groups (A) unmatched patients who received VATS, (B) matched patients who received VATS, (C) unmatched patients who received thoracotomy, and (D) matched patients who received thoracotomy. Matched groups have similar propensity score distributions.

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FIGURE E2. Standardized differences of variables between patients who received VATS and patients who received thoracotomy. *Hollow diamond* symbolizes differences before propensity matching, and *black diamond* symbolizes differences after propensity matching. Propensity matching effectively reduced heterogeneity among variables between the 2 surgical approaches in comparison. *FEV1*, Forced expiratory volume in 1 second; *DLCO*, diffusing capacity for carbon monoxide; *HTN*, hypertension; *MI*, myocardial infarction; *COPD*, chronic obstructive pulmonary disease; *RI*, renal insufficiency; *Chemo*, neoadjuvant chemotherapy.