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# Comparison of video-assisted thoracoscopic surgery with thoracotomy in bronchial sleeve lobectomy for centrally located non-small cell lung cancer

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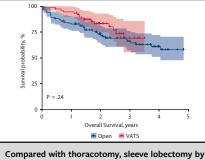
## ABSTRACT

**Objectives:** The aim of this study was to investigate the adequacy of bronchial sleeve lobectomy by video-assisted thoracoscopic surgery in perioperative outcomes and its oncological efficacy by comparing with thoracotomy in a balanced population.

**Methods:** A total of 363 patients who received bronchial sleeve lobectomy for nonsmall cell lung cancer from January 2013 to December 2017 were included and placed in the thoracotomy (n = 251) and video-assisted thoracoscopic surgery (n = 112) groups. Statistical analyses were performed to compare patients' demographics, perioperative outcomes, and survival between the 2 groups.

**Results:** A total of 116 thoracotomy cases were matched with 72 video-assisted thoracoscopic surgery cases by propensity score. Compared with thoracotomy, patients in the video-assisted thoracoscopic surgery group after matching had less intraoperative blood loss (P < .01) and length of postoperative hospital stay (P < .01), duration of chest tube drainage (P < .01), and intensive care unit stay (P = .03) despite comparable operative time, complication rate, and 30- to 90-day mortality rate. The overall survival and recurrence-free survival were similar in patients who received sleeve lobectomy by thoracotomy and video-assisted thoracoscopic surgery (log-rank, P = .24 and .20, respectively) at 3 years. Although advanced TNM stage was independently associated with worse overall survival and recurrence-free survival in multivariable analysis, older age was only predictive for worse overall survival (hazard ratio, 1.04; 95% confidence interval, 1.01-1.07; P = .02). Body mass index was also found be a predictive factor (overall survival: hazard ratio, 0.93; 95% confidence interval, 0.86-0.99, P = .03; recurrence-free survival: hazard ratio, 0.93; 95% confidence interval, 0.87-0.99, P = .02).

**Conclusions:** With appropriate patient selection and continued experience, videoassisted thoracoscopic surgery appears to be safe in the short-term perioperative period and does not appear to comprise oncologic outcomes in performing sleeve lobectomy. (J Thorac Cardiovasc Surg 2021;161:403-13)



VATS did not compromise oncologic survival.

#### CENTRAL MESSAGE

Compared with thoracotomy, VATS is a safe and reliable surgical procedure for sleeve lobectomy in selected patients with centrally located NSCLC without compromising perioperative and oncologic outcomes.

#### PERSPECTIVE

The safety and feasibility of bronchial sleeve lobectomy by VATS have been reported by several case series. However, studies comparing VATS and thoracotomy sleeve lobectomy were limited. This study presented 188 propensity scorematched cases and demonstrated the equivalence of perioperative and oncologic outcomes of VATS bronchial sleeve lobectomy compared with thoracotomy.

See Commentaries on pages 414, 415, and 417.

Sleeve resection is an established surgical procedure with better perioperative outcomes without sacrificing the oncological results compared with pneumonectomy in non– small cell lung cancer (NSCLC).<sup>1-4</sup> The standard approach to perform a sleeve lobectomy is through thoracotomy. In the evolution of video-assisted thoracoscopic surgery (VATS) in the past decade, VATS has been routinely adopted for early-stage NSCLC in a large population. By comparing

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Abbreviations and Acronyms							
CI	= confidence interval						
CT	= computed tomography						
HR	= hazard ratio						
ICS	= intercostal space						
ICU	= intensive care unit						
IQR	= interquartile range						
NSCLC	= non-small cell lung cancer						
OS	= overall survival						
RFS	= recurrence-free survival						
VATS	= video-assisted thoracoscopic surgery						

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with conventional thoracotomy, it was reported that VATS was associated with better perioperative outcomes, including shorter length of hospital stay, lower postoperative pain score, decreased duration for chest tube drainage, and reduced rate of postoperative complications.<sup>5-10</sup>

the

VATS sleeve lobectomy remains a challenging operation, with major concerns for the feasibility of radical resection and safety. After the first reported case of sleeve lobectomy by VATS in 2002,<sup>11</sup> several attempts on sleeve lobectomy via VATS have confirmed its safety and feasibility in sleeve lobectomy for NSCLC.<sup>12</sup> However, controversies remain about the surgical and oncological outcomes of sleeve lobectomy by VATS compared with thoracotomy. In this study, we performed a propensity-matched analysis to compare the surgical and oncological outcomes of sleeve lobectomy under thoracotomy and the VATS technique.

# MATERIALS AND METHODS

## **Study Population**

The Institutional Review Board of Shanghai Pulmonary Hospital approved our retrospective study and waiver of informed consent. Consecutive patients who received bronchial sleeve lobectomy for centrally located NSCLC between January 2013 and December 2017 were included. Patients with angioplasty, sleeve pneumonectomy, or additional lesion excision were excluded (Figure 1). All patients had preoperative workups, including pulmonary function test, flexible bronchoscopy, chest x-ray and computed tomography (CT) scan/contrast-enhanced CT, abdominal/brain CT scan, and bone scan. Positron emission tomography or endobronchial ultrasoundguided transbronchial needle aspiration was performed if necessary.

The medical data of patients were collected and reviewed, including patients' demographics, preoperative investigations, and perioperative variables. All tumors were restaged according to the eighth edition of the TNM staging for lung cancer.<sup>13</sup> Comorbidity was described according to Charlson Comorbidity Index (CCI).<sup>14</sup> Postoperative complications were described according to the Clavien-Dindo Classifications.<sup>15</sup> Prolonged air leakage was defined as lasting for more than 7 days after surgery. Perioperative mortality was defined as death within 30 days of the operation. Postoperative care was standardized for all patients regardless of the surgical approach. Follow-up was conducted through outpatient examinations or telephone calls. Chest CT scan and abdominal ultrasound/CT are performed on follow-up visits within a duration of 3, 6, and 12 months after operation and annually thereafter for 5 years. Magnetic resonance imaging for cerebrum and bone scan were annually performed for 5 years or when the patient had signs or symptoms of recurrence. The positron emission tomography/CT scan or biopsy was recommended to confirm recurrence. The overall survival (OS) was defined as the time from the date of surgery to death of any cause or the date of last follow-up. Recurrence-free survival (RFS) was estimated from the date of surgical reaction to the progress (relapse or metastasis) or death of any cause or last follow-up. All patients completed follow-up for the present study up to January 25, 2019.

## **Surgical Techniques**

Patients were placed in the lateral decubitus position and intubated with a double-lumen tube. Operation was carried out under general anesthesia and single lung ventilation. The decision to perform sleeve lobotomy by either approach was based on surgeon's preference. For thoracotomy, traditional posterolateral incision was made at the fourth or fifth intercostal space (ICS). For tri-portal VATS, we adopted incisions similar to those in a standard VATS lobectomy: 1 camera port of 1 cm at the seventh ICS of midaxillary line, 1 utility incision of 3 to 5 cm at the fourth ICS of anterior axillary line, and one 2-cm incision at the seventh ICS of subscapular line for retraction or stapling. For uniportal VATS, a 3- to 5-cm utility incision was made at the fourth or fifth ICS of anterior axillary line. A wound protector was placed in the utility incision without rib spreading.

During operation, pulmonary vessels and fissures were first handled in a similar way as in routine thoracoscopic lobectomy, and the bronchus was treated last. First, the bronchus was transected with at least a 0.5-cm proximal and distal margins that were confirmed to be tumor-free by frozensection analysis. The inferior pulmonary ligament was released before the bronchial anastomosis to reduce anastomotic tension, and hilar release with a "C" incision at the bottom of inferior pulmonary vein on pericardium was performed according to the tension of the anastomosis. Systematic dissection of mediastinal lymph nodes was usually completed before reconstructing the bronchus to avoid unnecessary traction of the anastomosis.

End-to-end bronchial anastomoses were performed usually by 3-0 Prolene running suture in VATS or by 3-0 Vicryl interrupted sutures in thoracotomy. The suture started at the deepest point of the posterior bronchial wall and ended at the midpoint of the anterior wall. Intercostal muscle flap or thymic tissue was used for anastomosis coverage for patients after induction therapy. After completing anastomosis, air leakage was tested under water and bronchoscopy was introduced to evaluate the anastomosis and clear the airway secretion (Video 1). Usually, 2 chest tubes were placed for drainage before closing thoracic cavity.

# **Statistics**

Normally distributed continuous variables were exhibited as mean  $\pm$  standard deviation, and skewed data were exhibited as median with interquartile range (IQR). Categoric variables were presented as frequency and percentage. Means were compared by Student t test for data obeying normal distribution and by Mann-Whitney U test for skewed data. The proportions of categoric outcomes were assessed by Pearson chi-square test and Fisher exact test.

To balance the baseline of patients, propensity score matching was performed by a logistics regression model. The VATS group was treated as the treatment group, and the variables were age, sex, CCI, forced expiratory

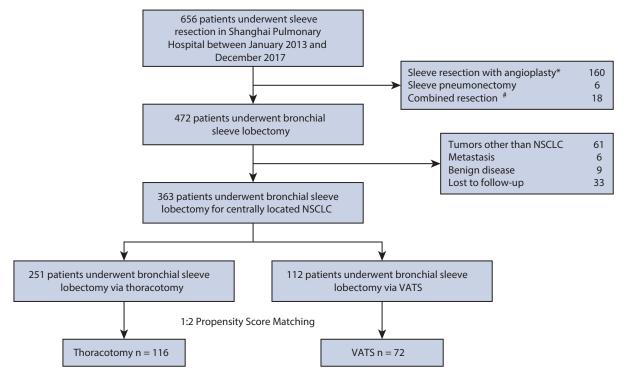


FIGURE 1. Flowchart demonstrating patient inclusion and cohort propensity score matching. Patients with angioplasty,\* sleeve pneumonectomy, or additional lesion excision other than sleeve lobectomy# were excluded. *NSCLC*, Non–small cell lung cancer; *VATS*, video-assisted thoracoscopic surgery.

volume in 1 second, forced expiratory volume in 1 second percentage of predicted value, smoking history, squamous histology, lower location of tumor, surgeons, and overall TNM stage. Thoracotomy and VATS pairs with a nearest propensity score were matched 1 to 2 with a caliper width of 0.1 of standard deviation (Figure E1). Perioperative and survival outcomes from the matched cohorts were then compared. OS and RFS were analyzed using the Kaplan-Meier method, and the difference of survival between the 2 groups was compared by the log-rank test. Median follow-up time was calculated by reverse Kaplan-Meier survival curves. Univariable and multivariable Cox proportional hazards models were adopted to identify the significant prognosis predictors. Predictors (P < .1) in univariable analysis and known prognostic factors were incorporated into a multivariable analysis. Results of univariable and multivariable analyses were presented as hazard ratio (HR) and 95% confidence interval (CI). Statistical analyses were conducted using SPSS 22.0 (IMB-SPSS Inc, Armonk, NY) and R version 3.5.3 (https://www.r-project.org/).



**VIDEO 1.** Uniportal VATS sleeve lobectomy for left upper lobe. Video available at: https://www.jtcvs.org/article/S0022-5223(20)30719-4/ fulltext.

## **RESULTS**

Between January 2013 and December 2017, 363 patients consecutively underwent bronchial sleeve lobectomy for centrally located NSCLC (Figure 1). There were 325 men (89.5%) and 38 women (10.5%) with a median age of 63 (38-83) years. Of them, 112 patients (30.9%) received sleeve resection via VATS and 251 (69.1%) via conventional thoracotomy. In thoracoscopic cases, 78 (69.6%) were performed via uniportal VATS and 34 (30.4%) were via standard VATS. Patients with thoracotomy were mostly male (93.2% vs 81.3%, P < .01) with a higher rate of tobacco use (76.9% vs 66.1%, P = .03) and had a lower forced expiratory volume in 1 second of predicted value  $(80.51\% \pm 17.00\% \text{ vs } 86.39\% \pm 13.93\%, P < .01)$ (Table 1). More squamous cell carcinomas were found in the thoracotomy group (82.5% vs 67.9%, P < .01). Distribution of surgeons (P < .01) between the 2 groups was significantly different. Other variables, including body mass index, comorbidities, and neoadjuvant treatment, were similar between the 2 groups. Five patients with VATS sleeve lobectomy (4.5%) were converted to thoracotomy because of calcified hilar lymph node (n = 2) and adhesion (n = 3). Conversion cases were placed in the VATS group. All patients obtained a R0 resection with no intraoperative death. Propensity score matching generated 116 matched cases from the thoracotomy group with 72 cases from the VATS group. After propensity score matching, matched cohort was well balanced (Figure E1) in all

TABLE 1.	Patient demographie	cs before and a	fter propensity s	core matching

	All patient	ts (n = 363)		Matched cohort (n = 188)			
Characteristics	Thoracotomy $(n = 251)$	<b>VATS</b> (n = 112)	Р	Thoracotomy (n = 116)	<b>VATS</b> (n = 72)	Р	
Age, y $\pm$ SD*	$62.1\pm7.6$	$62.7\pm8.8$	.53	$62.6\pm8.5$	$61.9\pm8.4$	.59	
Sex, n (%)†			<.01			.98	
Male	234 (93.2)	91 (81.3)		103 (88.8)	64 (88.9)		
Female	17 (6.8)	21 (18.8)		13 (11.2)	8 (11.1)		
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD*	$23.2\pm3.9$	$23.3\pm3.4$	.73	$23.2\pm4.2$	$23.6\pm2.7$	.42	
Smoking history, n (%)†			.03			.86	
Never	58 (23.1)	38 (33.9)		32 (27.6)	19 (26.4)		
Ever	193 (76.9)	74 (66.1)		84 (72.4)	53 (73.6)		
Pulmonary function, mean $\pm$ SD*							
FEV1 (L)	$2.2\pm0.5$	$2.3\pm0.5$	.16	$2.3\pm0.5$	$2.3\pm0.4$	.28	
FEV1% (of predicted)	$80.5\pm17.0$	$86.4\pm13.9$	<.01	$83.7\pm16$	$84.1\pm13.3$	.85	
CCI, n (%)†;‡			.20			.85	
0	15 (6.0)	8 (7.1)		10 (8.6)	6 (8.3)		
1	58 (23.1)	25 (22.3)		24 (20.7)	18 (25)		
2	120 (47.8)	47 (42.0)		53 (45.7)	32 (44.4)		
3	52 (20.7)	23 (20.5)		25 (21.6)	12 (16.7)		
4	6 (2.4)	8 (7.1)		4 (3.4)	4 (5.6)		
5	0 (0)	1 (0.9)		-	-		
Surgeons, n (%)†			<.01			.72	
А	41 (16.3)	11 (9.8)		21 (18.1)	9 (12.5)		
В	20 (8.0)	8 (7.1)		11 (9.5)	8 (11.1)		
С	43 (17.1)	8 (7.1)		15 (12.9)	8 (11.1)		
D	58 (23.1)	12 (10.7)		22 (19)	12 (16.7)		
E	23 (9.2)	55 (49.1)		23 (19.8)	23 (31.9)		
F	20 (8.0)	2 (1.8)		3 (2.6)	2 (2.8)		
G	19 (7.6)	4 (3.6)		10 (8.6)	4 (5.6)		
Н	27 (10.8)	12 (10.7)		11 (9.5)	6 (8.3)		
Neoadjuvant chemotherapy, n (%)†	26 (10.4)	10 (8.9)	.67	13 (11.2)	8 (11.1)	.98	
Tumor location, n (%)†			.07			.77	
LUL	51 (20.3)	13 (11.6)		23 (19.8)	10 (13.9)		
LLL	40 (15.9)	27 (24.1)		22 (19)	15 (20.8)		
RUL + RML	141 (56.2)	60 (53.6)		64 (55.2)	43 (59.7)		
RLL	19 (7.6)	12 (10.7)		7 (6)	4 (5.6)		
Squamous histology, n (%)†			<.01			.93	
Yes	207 (82.5)	76 (67.9)		88 (75.9)	55 (76.4)		

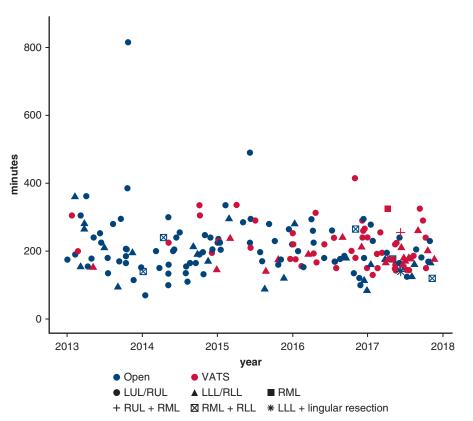
*VATS*, Video-assisted thoracoscopic surgery; *SD*, standard deviation; *BMI*, body mass index; *FEV1*, forced expiratory volume in one second; *CCI*, Charlson Comorbidity Index; *LUL*, left upper lobe; *LLL*, left lower lobe; *RUL*, right upper lobe; *RML*, right middle lobe; *RLL*, right lower lobe. \*Variables compared by Student *t* test. †Variables compared by chi-square test. ‡Variables compared by Fisher exact test.

categories, and baseline characteristics between the 2 groups were similar (Table 1). In the VATS group, 43 (59.7%) thoracoscopic cases were performed via uniportal VATS and 29 (40.3%) via standard VATS.

# **Perioperative Outcomes**

Before propensity score matching, patients in the VATS group were associated with less intraoperative blood loss (100 [IQR, 62.5-150] vs 200 [IQR, 100-300] mL, P < .01), shorter postoperative hospital stay (6 [IQR, 5-7] vs 7 [IQR, 6-9] days, P < .01), chest tube drainage duration (5 [IQR, 4.25-6] vs 6 [IQR, 5-8] days, P < .01), and intensive care unit stay (1 [IQR, 1-1] vs 1 [IQR, 1-2] days, P = .01) compared with that of the thoracotomy group, which is

consistent after matching. Proportions of cases that required postoperative transfusion (28.7% vs 14.3%, P < .01), bilobectomy (8% vs 1.8%, P = .04), and flap use (35.9% vs 17%, P < .01) were higher in the thoracotomy group of the unmatched cohort, which were insignificantly statistically different in the matched cohort. As shown in Figures 2 and E2, the VATS group had a similar operative duration as the thoracotomy group (before matching: 190.5 [IQR, 160-240] vs 197 [IQR, 160-240] minutes, P = .86; after matching: 195 [IQR, 161.25-240] vs 192.5 [IQR, 160-240] minutes, P = .58). In the matched cohort, the mostly used flap tissue was mediastinal pleura (19.7%), followed by thymic/pericardial fat tissue (6.4%) and intercostal muscle (3.7%) as shown in Table E1. There was no significant



**FIGURE 2.** Operative time distribution of the matched cohort based on different resected lobes between thoracotomy and VATS approach. Operative duration was similar between 2 groups (P = .16). More VATS sleeve cases were performed in recent years. *VATS*, Video-assisted thoracoscopic surgery; *LUL*, left upper lobe; *RUL*, right upper lobe; *RLL*, left lower lobe; *RLL*, right lower lobe; *RML*, right middle lobe.

difference between thoracotomy and VATS group in terms of number of removed lymph nodes and lymph node stations. Distribution of pathological T, N, and overall stages was similar in the 2 groups.

Postoperative complications are listed in Table 2. In the unmatched cohort, the overall complication rate was 9.6% (n = 35/363). The primary complication in both groups was prolonged air leak (n = 16, 4.4%). Three patients (1.2%) in the thoracotomy group and 2 patients (1.8%) in the VATS group had hemothorax and required reoperation. In the thoracotomy group, 1 patient experienced bronchial anastomotic fistula, in whom the stump was covered by serratus anterior muscle. The patient then developed severe pulmonary infection and died of hemoptysis on postoperative day 39. In addition, 6 patients (2.4%) with thoracotomy sleeve resection presented chylothorax, of whom 1 patient required thoracic duct ligation while the rest were recovered after conservative treatments. One patient (0.4%) experienced rupture of bullae in the residual lung with persistent air leak, and he received reoperation for the bleb transfixion. In the VATS group, 2 patients (1.8%) experienced bronchopleural fistula with 1 requiring reoperation for fistula repair, and the 2 patients (1.8%) were both discharged successfully. Additionally, among patients with VATS, 1 patient with a history of deep vein thrombosis and cerebral infarction died of

pulmonary embolism despite of perioperative anticoagulation management. In the matched cohort, the overall complication rate was 9.0% (n = 17/188). The primary complication in both groups was prolonged air leak (n = 7, 3.7%). One patient in the thoracotomy group (0.9%) and 1 patient in the VATS group (1.4%) experienced hemothorax that required reoperation. In the VATS group, 1 patient (1.4%) experienced bronchopleural fistula who was discharged successfully after conservative treatment. One patient died of pulmonary embolism.

No significant difference was found in mortality within 30/90 days and disease progression. Adjuvant chemotherapy was recommended for advance-stage disease. The proportions of patients who received adjuvant chemotherapy and radiotherapy were similar between the 2 groups. The adjuvant chemotherapy regimens administered were consistent in both groups, which was platinum-based 2-drug regimens including paclitaxel, gemcitabine, vinorelbine, taxotere, or pemetrexed every 3 weeks for 4 cycles. Adjuvant radiotherapy was recommended for N2 diseases at a median dose of 50 Gy in 2 Gy fractions.

## Survival Analysis in the Matched Cohort

The overall median follow-up time of the matched cohort was 32.2 months. In the thoracotomy group, median follow-

TABLE 2. Perioperative outcomes comparisons between thoracotomy and video-assisted thoracic surgery groups before and after propensity score matching

	All p	atients (n = 363)	Matched cohort $(n = 188)$			
	Thoracotomy			Thoracotomy		
Perioperative outcomes	(n = 251)	VATS (n = 112)	P	(n = 116)	VATS (n = 72)	P
Operation time (min), median (IQR)*	197 (160-240)	190.5 (160-240)	.86	192.5 (160-240)	195 (161.25-240)	.58
Estimated blood loss (mL), median (IQR)*	200 (100-300)	100 (62.5-150)	<.01	200 (100-237.5)	100 (100-200)	<.01
Require for postoperative transfusion, n (%) $^{\dagger}$	72 (28.7)	16 (14.3)	<.01	26 (22.4)	12 (16.7)	.34
Bilobectomy, n (%)‡	20 (8)	2 (1.8)	.04	7 (6)	1 (1.4)	.25
Lymph nodes, mean $\pm$ SD						
Total stations§	$5.9 \pm 1.3$	$5.8 \pm 1.3$	.28	$5.9 \pm 1.2$	$6.0 \pm 1.3$	.70
Total numbers§	$12.8\pm4.2$	$12.2\pm4.7$	.28	$12.6\pm3.8$	$12.3\pm4.8$	.66
Flap use, n (%)†	90 (35.9)	19 (17)	<.01	39 (33.6)	17 (23.6)	.16
T stage, n (%) $^+$			.28			.38
1	16 (6.4)	7 (6.3)		11 (9.5)	6 (8.3)	
2	169 (67.3)	86 (76.8)		76 (65.5)	55 (76.4)	
3	55 (21.9)	16 (14.3)		23 (19.8)	8 (11.1)	
4	11 (4.4)	3 (2.7)		6 (5.2)	3 (4.2)	
N stage, n (%)†			.96			.78
0	156 (62.2)	71 (63.4)		68 (58.6)	42 (58.3)	
1	41 (16.3)	17 (15.2)		17 (14.7)	13 (18.1)	
2	54 (21.5)	24 (21.4)		31 (26.7)	17 (23.6)	
pStage, n (%) <sup>+</sup>			.71			.21
1	104 (41.4)	48 (42.9)		48 (41.4)	28 (38.9)	
2	72 (28.7)	35 (31.3)		29 (25)	23 (31.9)	
3A	56 (22.3)	24 (21.4)		25 (21.6)	18 (25)	
3B	19 (7.6)	5 (4.5)		14 (12.1)	3 (4.2)	
Postoperative stay (d), median (IQR)*	7 (6-9)	6 (5-7)	<.01	7 (6-8)	6 (5-7)	<.01
Drainage (d), median (IQR)*	6 (5-8)	5 (4.25-6)	<.01	6 (5-7)	6 (5-6)	<.01
ICU stay (d), median (IQR)*	1 (1-2)	1 (1-1)	.01	1 (1-2)	1 (1-1)	.03
Clavien-Dindo Grades, n (%)‡			.43			.41
0	225 (89.6)	103 (92)		104 (89.7)	67 (91.7)	
1	13 (5.2)	2 (1.8)		6 (5.2)	1 (1.4)	
2	6 (2.4)	2 (1.8)		4 (3.4)	2 (2.8)	
3B	4 (1.6)	3 (2.7)		1 (0.9)	1 (1.4)	
4A	2 (0.8)	0 (0)		1 (0.9)	0 (0)	
5	1 (0.4)	1 (0.9)		0 (0)	1 (1.4)	
Complications, n (%)‡			.14			.08
Bronchopleural fistula	1 (0.4)	2 (1.8)		0	1 (1.4)	
Prolonged air leak	14 (5.6)	2 (1.8)		6 (5.2)	1 (1.4)	
Chylothorax	6 (2.4)	0		5 (4.3)	0	
Hemothorax	3 (1.2)	2 (1.8)		1 (0.9)	1 (1.4)	
Pulmonary embolism	2 (0.8)	2 (1.8)		1 (0.9)	2 (2.8)	
Pneumonia Descriptores failure	3 (1.2)	0		3 (2.6)	0	
Respiratory failure	1(0.4)	0 0		1 (0.9)	0 0	
Cardiac arrhythmia Pulmonary bullae rupture	2 (0.8) 1 (0.4)	0		0 0	0	
Mortality within 30 d, n (%)‡	1 (0.4)	1 (0.9)	1	0 (0)	1 (1.4)	.38
Mortality within 90 d, n (%)†	12 (4.8)	1 (0.9)	.13	7 (6)	1 (1.4)	.38
Adjuvant chemotherapy, n (%)†	12 (4.8)	79 (70.5)	.15	82 (70.7)	50 (69.4)	.25
		. ,				
Adjuvant radiotherapy, n (%) $\dagger$	8 (3.2)	4 (3.6)	1	5 (4.3)	1 (1.4)	.50
Progression, n (%)			.61			.14

	All patients (n = 363) Thoracotomy			Matched cohort $(n = 188)$			
				Thoracotomy			
Perioperative outcomes	(n = 251)	<b>VATS</b> (n = 112)	Р	(n = 116)	<b>VATS</b> (n = 72)	Р	
Recurrence	85 (33.9)	34 (30.4)		37 (31.9)	16 (22.2)		
Local-regional	41 (16.3)	19 (17)		17 (14.7)	10 (13.9)		
Distant	44 (17.5)	15 (13.4)		20 (17.2)	6 (8.3)		
No recurrence	166 (66.1)	78 (69.6)		79 (68.1)	56 (77.8)		

#### **TABLE 2. Continued**

VATS, Video-assisted thoracoscopic surgery; IQR, interquartile range; SD, standard deviation; T, tumor; N, lymph node; ICU, intensive care unit. \*Variables compared by Mann-Whitney U test. †Variables compared by chi-square test. ‡Variables compared by Fisher exact test. §Variables compared by Student t test.

up time was 40 months, the 3-year OS estimate was 65.9% (95% CI, 56.4-75.4), and the 3-year RFS estimate was 53.9% (95% CI, 43.8-63.8). In the VATS group, median follow-up time was 24.7 months, 3-year OS estimate was 68.8% (95% CI, 53.7-83.9), and 3-year RFS estimate was 60.8% (95% CI, 45.1-76.5). Figure 3 shows the Kaplan-Meier curves of OS and RFS. There was no significant difference in the 3-year OS (log-rank P = .24) and RFS (log-rank P = .20) between the 2 groups.

To determine the predictors of OS and RFS, we performed univariable and multivariable analyses (Table 3). In multivariable analysis, higher pathological stage diseases were found to be a predictive factor of worse OS and RFS, and older age was only predictive for worse OS (HR, 1.04; 95% CI, 1.01-1.07; P = .02). Body mass index, which suggested nourishment status, was found to be an independently predictive factor predicting OS (HR, 0.93; 95% CI, 0.86-0.99; P = .03) and RFS (HR, 0.93, 95% CI, 0.87-0.99; P = .02).

#### DISCUSSION

VATS has been widely adopted in the management of early-stage lung cancer and demonstrated equivalent oncological results.<sup>5,7,9,16,17</sup> Until the early 21st century, sleeve lobectomy has been considered a contraindication for VATS. In an attempt to offer the benefits of minimally invasive surgery, several experienced centers have described the surgical feasibility of sleeve lobectomy by VATS.<sup>12,18-21</sup> In this study, we compared the perioperative and oncologic outcomes of patients receiving sleeve lobectomy under VATS and thoracotomy (Figure 4). Our results revealed that VATS sleeve lobectomy could be safely performed with less intraoperative bleeding and shorter duration of chest tube drainage, whereas morbidity and OS were not compromised.

The difficulty of bronchial anastomosis is the main hurdle of VATS sleeve resection. In the initially reported cases of VATS sleeve lobectomies, surgeons simply conducted

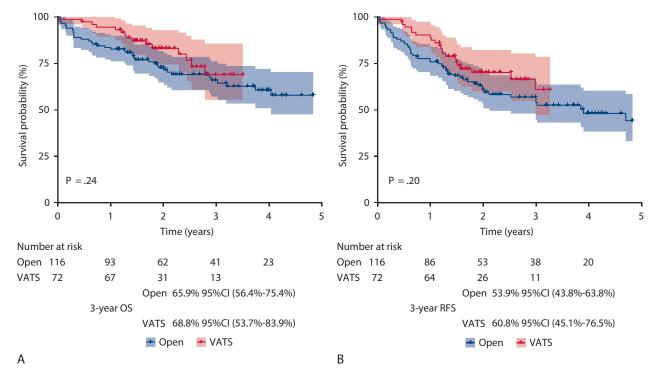


FIGURE 3. Three-year OS (A) and RFS (B) curves of patients received thoracotomy and VATS in the matched cohort (OS, P = .24; RFS, P = .20). VATS, Video-assisted thoracoscopic surgery; *CI*, confidence interval.

TABLE 3. Univariable and multivariable analyses of overall and recurrence-free survival

	OS			RFS				
	Univariable analysis Multivariable analysis		Univariable and	alysis	Multivariable analysis			
Variables	HR (95% CI)	Р	HR (95% CI)	Р	HR (95% CI)	Р	HR (95% CI)	Р
Age	1.03 (1.00-1.07)	.05	1.04 (1.01-1.07)	.02	1.02 (0.99-1.05)	.13		
Sex (male)	1.16 (0.46-2.91)	.76			1.27 (0.58-2.76)	.55		
Smoking history (ever)	1.02 (0.55-1.87)	.96			1.11 (0.66-1.87)	.69		
Surgical approach (VATS)	0.71 (0.39-1.27)	.24	0.75 (0.41-1.35)	.34	0.73 (0.44-1.19)	.20	0.74 (0.45-1.21)	.23
BMI	0.91 (0.85-0.98)	.02	0.93 (0.86-0.99)	.03	0.92 (0.86-0.98)	.01	0.93 (0.87-0.99)	.02
CCI	1.22 (0.92-1.62)	.16			1.12 (0.89-1.42)	.34		
Neoadjuvant chemotherapy	1.01 (0.40-2.54)	.99			1.20 (0.60-2.42)	.61		
Pulmonary function FEV1 FEV1%	0.58 (0.32-1.04) 1.00 (0.98-1.02)	.07 1	0.78 (0.39-1.57)	.49	0.64 (0.39-1.06) 1.00 (0.98-1.01)	.08 .56	0.61 (0.36-1.02)	.06
Location Upper or middle vs lower lobe Left vs right lobe	1.20 (0.62-2.33) 0.74 (0.42-1.31)	.58 .3			1.09 (0.63-1.87) 0.75 (0.46-1.22)	.76 .24		
Squamous histology	0.61 (0.34-1.08)	.09	0.61 (0.32-1.16)	.13	0.68 (0.42-1.12)	.13		
Lymph nodes Total stations Total numbers	1.11 (0.89-1.39) 0.99 (0.93-1.06)	.36 .83			0.97 (0.81-1.18) 0.97 (0.92-1.03)	.79 .36		
Pathological stages								
Stage I	reference		reference		reference		reference	
Stage II	2.84 (1.31-6.16)	.01	2.91 (1.34-6.32)	.01	2.83 (1.53-5.26)	<.01	2.88 (1.55-5.36)	<.01
Stage IIIA	4.20 (1.96-8.97)	<.01	4.70 (2.19-10.10)	<.01	3.47 (1.84-6.54)	<.01	3.91 (2.05-7.45)	<.01
Stage IIIB	4.88 (1.85-12.85)	<.01	6.00 (2.25-15.94)	<.01	3.72 (1.59-8.72)	<.01	3.67 (1.56-8.64)	<.01
Adjuvant therapy	0.97 (0.55-1.71)	.92			1.12 (0.68-1.85)	.65		

OS, Overall survival; RFS, recurrence-free survival; HR, hazard ratio; CI, confidence interval; VATS, video-assisted thoracoscopic surgery; BMI, body mass index; CCI, Charlson Comorbidity Index; FEV1, forced expiratory volume in 1 second.

interrupted sutures as they did in thoracotomy sleeve lobectomy. As experience in conducting bronchial anastomosis grew, continuously running suture was reported to be a safe approach without increasing the risk of anastomotic complications.<sup>22</sup> According to our experience, conducting the bronchial anastomosis with running suture could save time and avoid entanglement of suture. Zhou and colleagues<sup>23</sup> reported their initial experience of VATS sleeve lobectomy in 10 patients and concluded that sleeve lobectomy could be safely performed under VATS with better postoperative outcomes and similar survival compared with open sleeve lobectomy. However, because of longer operative time and comparable blood loss, they found no strong benefit of VATS in intraoperative outcome for patients receiving sleeve resection.<sup>23</sup> A recent study by Gao and colleagues<sup>24</sup> compared short- and long-term outcomes to evaluate the safety and efficacy of VATS sleeve lobectomy by propensity score matching. In their study, the VATS group was associated with longer operative duration (300 vs 221 minutes, P < .01) as affected by learning curves, but with less intraoperative blood loss, shorter drainage duration, and postoperative hospital stay. In contrast, our study showed no statistically significant difference in the operative time of

sleeve resection between VATS and thoracotomy after adjusting for the indication to perform VATS by surgeon, which was the most important confounder in a retrospective study. We first adopted VATS sleeve lobectomy in 2010 and completed 4 initial cases with a mean operative time of  $268 \pm 83$  minutes.<sup>25</sup> Until the start of this study, a total of 56 VATS sleeve lobectomies were performed. As our experience increased in thoracoscopic surgery, we found VATS sleeve lobectomy could be safely performed with equivalent operative time to standard thoracotomy sleeve lobectomy. Mahtabifard and colleagues<sup>12</sup> reported 13 cases of VATS sleeve lobectomy with a relatively short operative time of 167 minutes, which is similar to the operative time for VATS lobectomy. In addition, VATS sleeve lobectomy in our study had a significantly shorter length of postoperative hospital stay and intensive care unit stay, which would reduce hospitalization cost.

As a merit of minimally invasive approach, sleeve lobectomy performed by VATS showed an advantage over thoracotomy on postoperative complication. Previous studies reported a morbidity rate of 22.9% to 45.2% after sleeve lobectomy.<sup>26-31</sup> The major complication rate of sleeve lobectomy in the present study is 9.7%. There

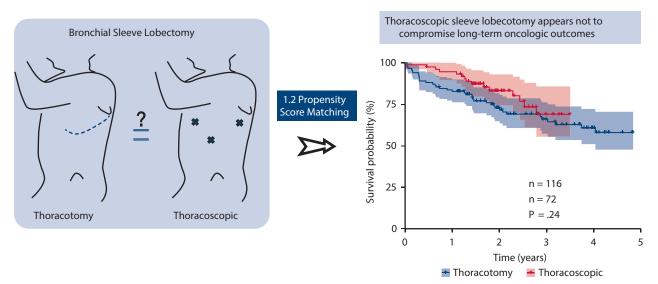


FIGURE 4. Compared with thoracotomy, VATS is a safe and reliable surgical procedure for sleeve lobectomy in selected patients of centrally located NSCLC without compromising perioperative and oncologic outcomes.

was no difference in morbidity rate between the thoracotomy and VATS groups after matching (10.3% vs 6.9%, P = .43). In our study, the most common complication occurred in both the matched and unmatched cohorts, prolonged air leak (3.7% and 4.4%, respectively), which was acceptable compared with the previously reported rate of 2.2% to 6.7%. 23,27,29,31 Anastomotic complication, such as bronchopleural fistula and anastomotic stricture, is the major concern in sleeve lobectomy. In the present study, bronchopleural fistula occurred in 2 patients in the VATS group. The anastomotic complication rate after sleeve lobectomy via thoracotomy was reported to be 2.0% to 6.9%, <sup>26-30</sup> whereas the rate of VATS sleeve resection was only reported by limited studies with small sample size and varied from 0% to 15.4%.<sup>12,23</sup> In our study, pedicled flap was commonly used for anastomosis coverage (Table E1), especially for cases after induction therapy to prevent bronchial anastomotic fistula.<sup>31</sup>

Okada and colleagues<sup>32</sup> found that lymph node metastasis status is the most important factor influencing long-term survival in cases of sleeve lobectomy. There are concerns about the adequacy of lymph node dissection by VATS. Our results showed no difference in terms of the number of dissected lymph nodes and lymph node stations between the thoracotomy and VATS groups. Our finding is in line with previous data from the American College of Surgeons Oncology Group Z0030 trial that showed no significant difference in the number of lymph node dissected in the VATS group compared with thoracotomy in standard lobectomy.<sup>33</sup> In our study, the 5-year OS and the locoregional recurrence rates were comparable among the 2 groups. The Kaplan–Meier survival curves showed

no significantly statistical difference for OS and RFS, which demonstrated that VATS sleeve lobectomy could procure a radical resection and did not compromise the oncologic outcome.

# **Study Limitations**

Several limitations of this study should be considered. First, the retrospective nature of the study has selection bias, and the study was confounded by indication. As the surgical decision was made by surgeons on the basis of the preoperative examination and their own preference, complicated cases might be preferred for an open surgery. Therefore, we attempted to minimize biases by adjusting known confounders through propensity score matching. Second, although the VATS group showed an advantage in less blood loss and shorter duration of chest tube drainage, more evidence is required to confirm the results through prospective study. Last, patients in this study came from a single center and had a relatively short follow-up period; therefore, long-term follow-up data from other institutions were needed to validate the equivalent oncologic outcome of VATS sleeve resection.

# CONCLUSIONS

Bronchial sleeve lobectomy can be safely performed by VATS with a similar operative time and shorter postoperative hospital stay compared with thoracotomy after years of experience. With appropriate patient selection and adequate surgical experience, VATS does not compromise perioperative and oncologic outcomes in sleeve lobectomy for centrally located NSCLC. You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/med ia/19 AM/Monday\_May6/201DF/201DF/S84 - Locally adv anced lung cancer/S84\_4\_webcast\_024344531.mp4.



## **Conflict of Interest Statement**

Authors have nothing to disclose with regard to commercial support.

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Key Words: sleeve lobectomy, video-assisted thoracoscopic surgery, lung cancer

# Discussion Presenter: Dr Jiajun Deng



**Dr Matthew Bott** (*New York, NY*). You alluded to my comment, which is the sheer volume of cases in the series. You identified 350 patients who had sleeve lobectomy over a 4-year period, and that's after you excluded 160 because they had a sleeve lobectomy and arterial work! So that's approxi-

mately 100 sleeve lobectomies per year. Our fellows would love to have that sort of opportunity. As far as my questions go, you answered some of them during the course of your talk, but it seemed like from the abstract that you are performing both open and VATS lobectomies over the study period. Can you tell us a bit about how you select patients for one of those operations versus the other. I think there were some indications that tumor size comes into play. What sort of things do you look at when you're planning these procedures?



**Dr Jiajun Deng** (*Shanghai, China*). You can see in the scatter plot before 2015, we mostly perform via thoracotomy. After 2016, about less than half of the sleeve lobectomy cases were performed by VATS. It's really not related to the characteristics of the patients, it's related to the surgeons. If we are confi-

dent and get enough experience in VATS, it seems we might do it.

Dr Bott. So you'd say it's mostly surgeon preference.

Dr Deng. Yeah, it is mostly the surgeon's decision.

**Dr Bott.** Okay, and then I was going to ask you about the anastomotic technique between the VATS and open. It sounded like you discussed that a bit, so running technique in the minimally invasive cases and then interrupted sutures maybe in the open cases? I was impressed to see that the operative time really wasn't different. Perhaps modifying the technique is helpful for keeping operative time consistent. But the other thing I think it speaks to is where you guys probably were in the learning curve when you were operating on these patients. You're probably well along. So for those of us who don't necessarily do these VATS sleeve lobectomies routinely, what does it take in terms of proficiency for us to feel comfortable doing these sort of cases. Can you give us some insight there?

**Dr Deng.** I couldn't take any credit for this kind of surgery or the technical part to give you a suggestion. I can say that most of these operations, especially those performed after 2015, were done by uniportal procedure. I think it's based on your training.

**Unidentified Speaker.** Were you asking about the learning curve?

**Dr Bott.** Yes, how many procedures do you think it would take? With the number of cases you do, it looks like 3 days (sic).

**Dr Deng.** I think the learning curve occurs before this study period.

**Dr Bott.** Dr Cerfolio made the point this morning during the plenary session that perioperative outcomes are important, but in cancer operations, long-term survival is critical and I'm glad you showed the data about RFS in the 2 procedures. The only thing I didn't see you discuss was completeness of resection. Do you have data on R 0 versus R 1 and 2 resection for the 2 different procedures and were they equivalent?

**Dr Deng.** I don't have the point about the long-term outcome. More than 50% of patients were operated after 2015. I'd say the follow-up is kind of short, less than 3 years. All these patients have been R0 resected.

Dr Bott. Okay. Thanks a lot.

**Unidentified Speaker.** When I see videos on VATS sleeve resection, they always show the reconstruction phase, the anastomosis, and they seldom show the resection phase, which most of the time is more demanding and difficult. So this matches with the question that Dr Bott asked concerning the operative time. I was also surprised that the operative times were comparable between the 2 techniques. Now my inference is that probably you select the most difficult cases for open and leave easier cases for VATS. Is my inference correct?

**Dr Deng.** It might be possible because all the surgical decisions were based on the surgeons' preference. It might be possible that more challenged and complicated cases might be more likely to be operated through thoracotomy. That's a limitation of this study.

**Unidentified Speaker.** Do you have any data on conversion?

**Dr Deng.** There were 5 conversions.

**Unidentified Speaker.** You had 2 bronchopleural fistulas?

Dr Deng. There were 2 patients in each group.

**Unidentified Speaker.** In each group. Were they from the anastomosis?

**Dr Deng.** One patient in the thoracotomy group died 3 days postoperatively.

# TABLE E1. Details of flap used in the matched cohort

N (%)	Thoracotomy $(n = 116)$	<b>VATS</b> (n = 72)
Mediastinal pleura	25 (22)	12 (17)
Intercostal muscle	5 (4)	2 (3)
Thymic/pericardial fat tissue	9 (8)	3 (4)

VATS, Video-assisted thoracoscopic surgery.



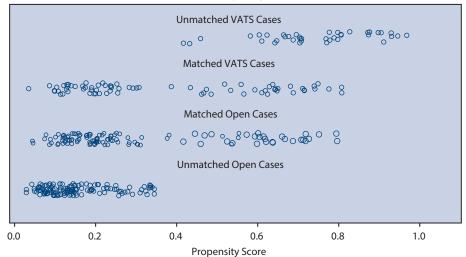
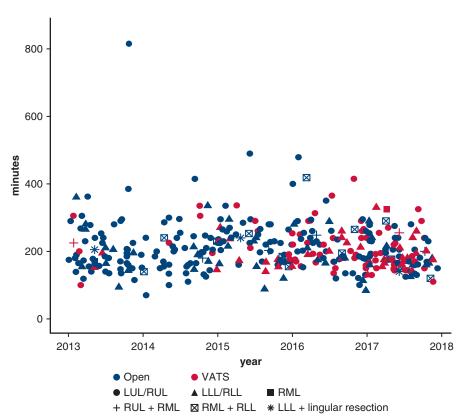


FIGURE E1. Distribution of propensity score of variables between the matched and unmatched cohort between thoracotomy and VATS group. VATS, Video-assisted thoracoscopic surgery.



**FIGURE E2.** Operative time distribution of the whole cohort based on different resected lobes between thoracotomy and VATS approach. Operative duration was similar between 2 groups (P = .86). VATS, Video-assisted thoracoscopic surgery; LUL, left upper lobe; RUL, right upper lobe; LLL, Left lower lobe; RLL, right lower lobe; RLL, right middle lobe.