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Original Article

Equivalency of oncological outcomes during lobectomy by video-assisted thoracoscopic surgery versus thoracotomy

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Abstract: The aim of this study was to compare the results of oncological outcomes during lobectomy during video-assisted thoracoscopic surgery (VATS) versus thoracotomy for clinical stage I non-small cell lung cancer (NSCLC). We retrospectively reviewed clinical and follow-up data from 401 consecutive patients undergoing lobectomy for clinical stage I NSCLC by VATS or thoracotomy, between January 2008 and December 2013. In total, 401 lobectomies for clinical stage I NSCLC were performed, including 185 lobectomies by VATS and 216 lobectomies by thoracotomy. Patient demographic data, type of resection, histological type, and pathological data were comparable between the two groups. There was less blood loss ($P < 0.05$), less post-operative analgesia needed ($P < 0.05$), shorter duration of chest drainage ($P < 0.05$), and earlier hospital discharge ($P < 0.05$) in the VATS group than in the thoracotomy group ($P < 0.05$), although operative time was significant longer for VATS than for thoracotomy ($P < 0.05$). The entirety of lymphadenectomy was comparable between the two groups. Overall survival and recurrence-free survival were similar in both groups. The current results indicate that VATS lobectomy results in oncological outcomes that are equivalent to open surgery for clinical stage I NSCLC.

Keywords: Non-small cell lung cancer, lymphadenectomy, minimally invasive surgery, video-assisted thoracoscopic surgery, thoracotomy

Introduction

Lung cancer is one of the most commonly diagnosed malignancies worldwide and is the leading cause of cancer-related mortality in China [1]. In recent years, the incidence of early stage (stage I by the TNM system) lung cancer has been increasing rapidly because of the development of diagnostic techniques, increase in life expectancy, smoking, and air pollution [2]. Despite the introduction of multimodality therapy for lung cancer, recurrence and mortality rates remain high. For clinical stage I non-small cell lung cancer (NSCLC), lobectomy with mediastinal lymph node dissection is the main treatment method [3]. Conventionally, lobectomies have been performed by thoracotomy [4-6]. Although effective, thoracotomy has some shortcomings, such as a longer thoracotomy incision, poor cosmetic results, major trauma, and slower recovery. Video-assisted thoracoscopic surgery (VATS) lobectomy, first reported in the 1990s, has become established as an appropriate method for shorter incision, minor trauma, and faster recovery. As instruments have improved, VATS lobectomies have become more frequent over the past decade [7].

Mediastinal lymph node dissection during VATS lobectomy is technically difficult, and as a consequence, some reports have expressed concerns over the entirety of lymphadenectomy and long-term survival [8]. Although some investigators have performed VATS lobectomy, only a few reports have examined the specific oncological outcomes arising from VATS lobectomy [9-13]. To the best of our knowledge, there have been no studies yet which have directly compared oncological outcomes between VATS and thoracotomy in a Chinese population in a

Table 1. Patient demographics for patients who underwent VATS and open lobectomy

	VATS (*n* = 185)	Thoracotomy (*n* = 216)	*P* value
Age (y)	65.0 (50-73)	64.0 (49-70)	0.685
Gender (Male:Female)	113:72	126:90	1.000
Comorbidity			1.000
Chronic obstructive pulmonary disease	6	7	
Hypertension	23	26	
Diabetes Mellitus	12	23	
Smoking	89	102	
Atrial fibrillation	1	2	
Earlier myocardial infarction	1	2	
FEV1 (observed to predicted) %	86.0 (76-95)	86.0 (80-98)	0.855
Tumor size (cm)	2.00 (0.8-3.9)	1.90 (1.0-6.5)	0.384
Clinical stage			1.000
IA	79	98	
IB	106	108	
Mediastinoscopy	2	2	1.000
ASA score			1.000
I	89	96	
II	93	115	
III	3	5	

Table 2. Surgical and pathological data of VATS and open lobectomy

	VATS (*n* = 185)	Thoracotomy (*n* = 216)	*P* value
Type of resection			1.000
Left upper lobectomy	42	45	
Left lower lobectomy	53	49	
Right upper lobectomy	44	76	
Right middle lobectomy	10	13	
Right lower lobectomy	36	33	
Operative time (min)	300.0 (190-380)	230.0 (180-360)	0.000
Blood loss (mL)	160.0 (100-320)	205.0 (110-500)	0.000
Histological type			1.000
Adenocarcinoma	157	180	
Squamous cell carcinoma	18	23	
Others	10	13	
Pathological stage			1.000
IA	52	66	
IB	82	89	
IIA	26	38	
IIB	13	7	
IIIA	12	16	
Residual tumor (R0/R1/R2)	185/0/0	216/0/0	1.000
Post-operative analgesia (d)	2.0 (1.0-5.0)	5.0 (1.0-6.0)	0.000
Duration of chest drainage (d)	6.0 (3-9)	7.0 (5-13)	0.000
Hospital stay (d)	8.0 (6-13)	16.0 (11-30)	0.000
Post-operative complications	39	46	0.958
Severity of complications			0.005
Major (3, 4 and 5)	3	15	
Minor (1 and 2)	36	31	

single institution. Therefore, in this study, we assessed oncological outcomes via VATS versus thoracotomy in 401 consecutive resections in a single institution.

Patients and methods

Patient evaluation

We retrospectively reviewed data from 401 consecutive patients with clinical stage I NSCLC undergoing lobectomy in our treatment group at the Department of Thoracic Surgery, The Fourth People's Hospital of Changzhou from January 2008 to December 2013. Our hospital is a tertiary cancer center in the city of Changzhou. All patients underwent tumor marker tests, biochemical examination, blood coagulation tests, cardiovascular and pulmonary function tests, bronchoscopy, endobronchial ultrasound along with computed tomographic scans of the brain, neck, chest, and upper abdomen to determine the clinical stage and to exclude tumor metastases. Mediastinoscopy was not necessary except in cases showing positive mediastinal or hilar lymph nodes upon chest computed tomographic scans. Positron emission tomography-computerized tomography (PET-CT) and bone scanning were performed in selected cases. The clinical stage was based on the 7th edition

Table 3. Nodes and stations harvested of VATS and open lobectomy

	VATS (*n* = 185)	Thoracotomy (*n* = 216)	*P* value
Number of harvested lymph node stations	8.0 (6-8)	8.0 (6-8)	0.449
Mediastinal lymph node stations dissected	5.0 (3-5)	5.0 (3-5)	0.344
Number of harvested lymph nodes	28.0 (22-36)	28.0 (22-40)	0.164
Mediastinal lymph nodes dissected	17.0 (12-23)	17.0 (12-28)	0.110
Number of harvested lymph nodes on both sides			
Left side	26.0 (23-29)	26.0 (22-34)	0.723
Right side	30.0 (22-36)	30.0 (23-40)	0.604
Distribution of harvested lymph nodes in the main stations			
Left side			
5+6	5.0 (3-6)	4.0 (3-6)	0.460
7	6.0 (4-7)	6.0 (3-8)	0.134
8L+9L	4.0 (3-8)	5.0 (3-7)	0.533
10L+11L+12L	11.0 (9-14)	11.0 (9-18)	0.086
Right side			
2R+4R	10.0 (6-13)	10.0 (7-20)	0.186
7	5.0 (3-6)	5.0 (3-6)	0.717
8R+9R	4.0 (3-6)	4.0 (2-6)	0.549
10R+11R+12R	11.0 (6-13)	11.0 (9-13)	0.879

Table 4. Literature review of mediastinal lymph node dissection by VATS versus thoracotomy (mean)

Study	Number of Patients	Lymph nodes	N1 lymph nodes	N2 lymph nodes	Lymph node stations
Watanabe A (2005, Japan) [15]	VATS 191	33.8	NR	23.4	NR
	Open 159	30.9		21.0	
Ramos R (2012, France) [16]	VATS 96	22.6	NR	17.7	5.1
	Open 200	25.4		18.2	4.5
Yang H (2013, China) [17]	VATS 31	28.2	9.5	18.6	6.8
	Open 31	29.8	8.4	21.4	6.7
Palade E (2013, Germany) [18]	VATS 32	25.1	10.5	NR	NR
	Open 32	25.2	8.9		

NR, not reported.

of the TNM [3] classification of lung cancer, which was proposed by Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC), and the mediastinal lymph node staging was based on the newest lymph node map proposed by International Association for the Study of Lung Cancer (IASLC) [3]. For patients operated before 2009, their staging was recalculated to match the 7th edition of TNM classification of lung cancer.

Surgical technique

All surgery, including VATS and thoracotomy, were performed by one senior surgeon (Jianrong Yu) with proven expertise in lung cancer treatment. The surgical approach was selected by patients and their families after the advantages and disadvantages of VATS and thoracotomy had been discussed. Resection was considered as curative intention (R0) in all cases. Only trocar and endoscopic instruments were used in VATS lobectomy and no rib spreading was applied. All patients underwent single-lung ventilation and were placed in the lateral decubitus position. We did not prepare intra-operative lymph node frozen sections. On the left side tumor, lymph node station 5, 6, 7, 8, 9, 10, 11 and 12 were systematically cleared. On the right side tumor, lymph node station 2R, 4R, 7, 8, 9, 10, 11, and 12 were also dissected. The surgical procedure has been described elsewhere [9].

Surgical outcome and post-operative complications

The overall number of mediastinal lymph nodes, mediastinal stations harvested in both sides, and lymph nodes harvested in the main nodal stations of both sides was assessed. We

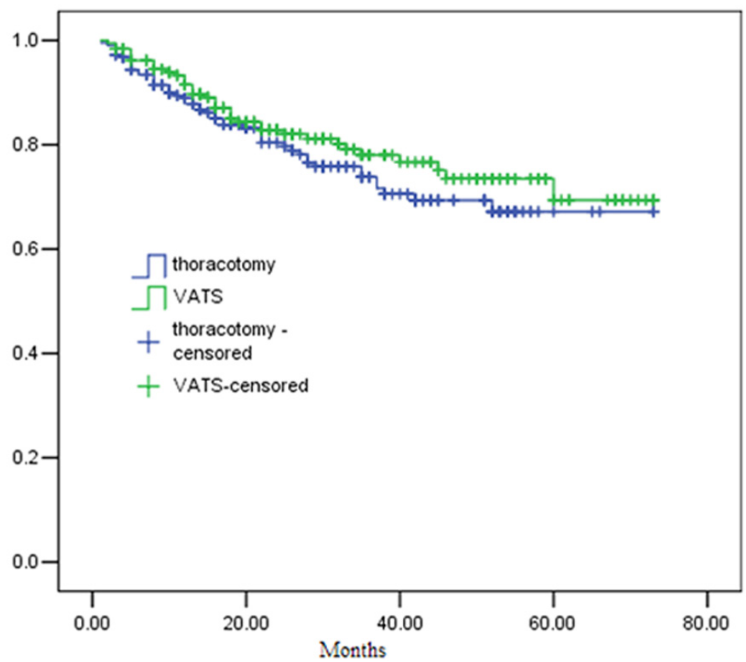

Figure 1. Overall survival in relation to approach of lobectomy in 401 consecutive patients.

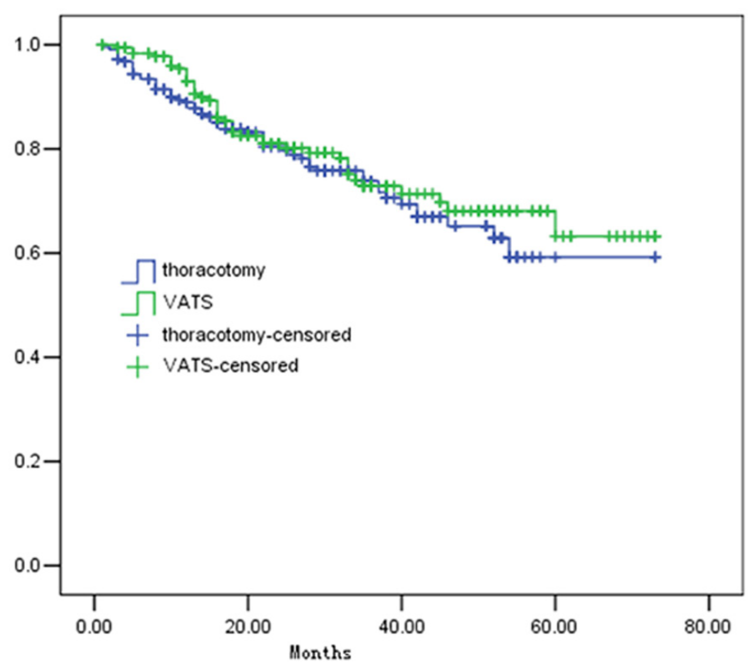

Figure 2. Recurrence-free survival in relation to approach of lobectomy in 401 consecutive patients.

also reviewed the type of resection, operative time, blood loss, histological type, pathological stage, residual tumor, results of lymphadenectomy, post-operative analgesia, duration of chest drainage, hospital stay, and post-operative complications. Post-operative complications were graded as being either major or minor using the Clavien-Dindo classification [14]. Major complications were defined as grades 3, 4, and 5, whereas minor complications were classified as 1 and 2. Operative death was defined as mortality within 30 days or during hospitalization after surgery.

Follow up

During the first year after treatment, patients were seen every 3 months in the outpatient department. In the second year, follow-up took place every 6 months, and then follow-up was performed at the end of each year after treatment. During follow-up, diagnostic investigations were performed. All patients received a CT scan of the chest before discharge and before each follow-up visit. Any post-operative complications and medical conditions requiring hospitalization were reviewed. The last follow up occurred in March 2014. Overall survival was assessed from the date of surgery until the last follow up or death of any cause. The recurrence-free survival was calculated from the date of surgery until the date of cancer recurrence or death of any cause.

Statistical analysis

For statistical analysis, SPSS 14.0 (SPSS Inc., Chicago, IL, USA) was applied. Data were presented as mean and standard deviations for variables following normal distribution and were analyzed by *t* test. For variables following non-normal distribution, results were expressed as median and range and were compared by nonparamet-

Table 5. Comparison of recurrence pattern and site after lobectomy

	VATS (n = 185)	Thoracotomy (n = 216)	P value
Overall recurrence n (%)	22 (11.9%)	28 (13.0%)	1.000
Locoregional n (%)	15 (8.1%)	14 (6.5%)	1.000
Mediastinal lymph node	4	3	
Pleura	5	5	
Ipsilateral lung	6	6	
Distant n (%)	7 (3.8%)	14 (6.5%)	1.000
Brain	3	6	
Liver	3	6	
Adrenal gland	1	2	
Time to recurrence (median)	17 months	14 months	0.363

ric test. Differences of semi-quantitative results were analyzed by Mann-Whitney *U*-test. Differences of qualitative results were analyzed by chi-square tests or Fisher exact test where appropriate. Survival rates were analyzed using the Kaplan-Meier method; differences between the two groups were analyzed with the log-rank test. $P < 0.05$ was considered statistically significant.

Results

Patient demographics

Demographic data are summarized in **Table 1**. During this study, 185 lobectomies were performed by VATS and 216 lobectomies by thoracotomy. There were no significant differences in age, gender, co-morbidity, FEV1 (observed to predict), tumor size, clinical stage, mediastinoscopy, and ASA (American Society of Anesthesiologists) score ($P > 0.05$).

Surgical and pathological characteristics

Surgical procedures and pathological outcomes are summarized in **Table 2**. There were no operative deaths. While the operative time was significant longer for VATS than thoracotomy ($P = 0.000$), there was less blood loss during VATS than thoracotomy ($P = 0.000$). Patients in the VATS group experienced a faster recovery, including less requirement for post-operative analgesia ($P = 0.000$), shorter duration of chest drainage ($P = 0.000$), and earlier hospital discharge ($P = 0.000$). The rate of post-operative complications was similar in both groups ($P = 0.958$). However, when the severity of complications was compared, more complications were classified as major in patients undergoing thoracotomy ($P = 0.005$). There were no significant differences in type of resection, histological type, pathological stage or residual tumor ($P > 0.05$). No positive resection margin was obtained in our series.

There were no significant differences when comparing the number of harvested lymph node stations and the overall number of harvested lymph nodes ($P > 0.05$) (**Table 3**). There were no significant differences in left- and right-sided harvested lymph nodes ($P > 0.05$) (**Table 3**). The distribution of harvested lymph nodes in the main stations was similar in both groups ($P > 0.05$) (**Table 3**). Our results were similar to other studies (**Table 4**).

Follow-up results

The overall survival and recurrence-free survival were a particular focus of our attention. After a median follow-up period of 35 months, the 5-year cumulative overall survival rate in the VATS group was 71%, compared to 68% in the thoracotomy group. Overall survival analysis indicated no significant difference in the overall survival rate when compared between the two groups (**Figure 1**; $P = 0.298$).

The recurrence-free 5-year survival rate was 63% in the VATS group and 60% in the thoracotomy group, respectively, with no significant differences between the two groups (**Figure 2**; $P = 0.424$). The location of recurrence and the time for recurrence to occur were not significantly different when compared between the two groups (**Table 5**). There was no port-site recurrence in patients undergoing VATS lobectomy. Our follow-up results were similar to other large sample size studies performed by other surgeons (**Table 6**).

Discussion

Although VATS lobectomy for NSCLC is a popular technique because of its proven benefits [19], this technique remains controversial because of the question of oncological outcomes and the absence of multicenter randomized controlled trials. In this study, we compared

Table 6. Literature review of follow-up results by VATS versus thoracotomy for early stage NSCLC

Study	Clinical stage	Approach	*n*	Overall survival	Recurrence-free survival
Thomas P (2002, France) [10]	I	VATS	110	VATS: 5-yr: 62.9%	NR
		Open	404	Open: 5-yr: 62.8%	
Shiraishi T (2006, Japan) [11]	I	VATS	81	VATS: 5-yr: 89.1%	VATS: 5-yr: 79.0%
		Open	79	Open: 5-yr: 77.7%	Open: 5-yr: 80.2%
Flores RM (2009, USA) (12)	I	VATS	398	VATS: 5-yr: 79.0%	NR
		Open	343	Open: 5-yr: 75.0%	
Lee PC (2013, USA) [9]	I	VATS	188	VATS: 3-yr: 87.4%	VATS: 3-yr: 77.7%
				5-yr: 76.5%	5-yr: 61.1%
		Open	187	Open: 3-yr: 81.6%	Open: 3-yr: 76.9%
				5-yr: 77.5%	5-yr: 72.1%
Stephens N (2014, USA) [13]	I	VATS	307	VATS: 5-yr: 78.0%	NR
		Open	307	Open: 5-yr: 73.0%	

NR, not reported.

VATS lobectomy to thoracotomy lobectomy in a consecutive series of patients who were operated on by dedicated thoracic surgeons with extensive experience in VATS lobectomy and open lobectomy. We demonstrated that there was no evidence of any differences in terms of oncological outcome for the VATS group versus thoracotomy group, and this is consistent with most published reports.

The key point of success of any oncological surgery is the long-term survival outcome, measured by overall survival and recurrence-free survival. Our overall survival and recurrence-free survival rates were similar to other published reports concerning VATS versus open lobectomy for Clinical Stage I NSCLC [10-13]. Over time, thoracic surgeons have become more skilled in VATS and increasingly recognized its benefits, such as faster recovery, better cosmetic outcomes, and less trauma. However, the establishment of prospective randomized multicenter trials to compare VATS and thoracotomy has proved problematical because of the difficulty to enroll a sufficient number of patients. Previous reports have shown slightly improved long-term survival and recurrence-free survival following VATS [10-13]. In our series, patients undergoing VATS exhibited slightly improved long-term survival and recurrence-free survival, albeit with no significant difference. This phenomenon may be explained by the fact that the reduced level of trauma incurred by VATS lobectomy may lead to quicker recovery, earlier administration of adjuvant therapy, more compliance of adjuvant chemotherapy, and more routine of adjuvant therapy [20]. Some surgeons have hypothesized that reduced immunological suppression following VATS may increase the patient's ability to scavenge residual cancer cells shed into the blood or lymphatic system at resection [21]. However, further studies are warranted concerning this phenomenon in the future.

Apart from the technical feasibility and favorable results of VATS lobectomy, the quality of mediastinal lymph node dissection is an important issue in performing this particular. Most previous studies have failed to demonstrate differences in the quality of mediastinal lymph node clearance when comparing VATS to open lobectomy [15-18]. However, some reports have found that the quality of lymph node dissection was inferior to thoracotomy, especially in the early literature. In the CALGB 39802 study [22], a prospective and multicenter study, proposed by Scott J. Swanson and his hospital colleagues, results showed that more than 50% of patients undergoing VATS had less than two stations sampled and around 15% of patients undergoing VATS had no lymph nodes harvested. This result was far from the recommendation proposed by IASLC [23], which states that at least 6 lymph node stations should be removed or sampled in radical lobectomy for NSCLC. The IASLC also recommends that three of these lymph node stations should be mediastinal lymph nodes [23].

In the present study, as a way of comparing the quality of mediastinal lymph node clearance, we compared the number of surgically dissected lymph node stations, including mediastinal lymph node stations, lymph nodes including mediastinal lymph nodes, and the distribution of lymph nodes in the main stations. Our results showed that the number of dissected lymph node stations, lymph nodes, and the distribution of lymph nodes in the main stations were similar in VATS than thoracotomy. That is to say that VATS lobectomy is oncologically compatible with thoracotomy in terms of mediastinal lymph node dissection. In our series, a median of 28 lymph nodes were lymph nodes, whereas a median of 17.0 lymph nodes were mediastinal. Similar results have been reported by Asian and European surgeons specializing in thoracic surgery (**Table 4**). The reason for this is that VATS exhibits some advantages for mediastinal lymph node dissection, such as allowing different angles of vision and offering a perfect view in areas that are hidden by tissues.

This study has several limitations. First, our study was based on a single-center, not multiple centers, and was based on retrospective non-randomized analysis, not prospective randomized analysis. Consequently, we cannot exclude bias from patients and surgical approach selection. Prospective randomized trials are not easy to carry out to compare VATS and thoracotomy because VATS lobectomy is technologically difficult to grasp. Second, the size of the sample is relatively small, only 185 patients by VATS and 216 patients by thoracotomy, which should be considered when interpreting the results.

In conclusion, this study demonstrates that VATS for NSCLC is feasible and safe with equal oncological outcomes. Further prospective randomized multicenter trials are warranted before incorporating VATS into routine surgical care.

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Discourse of conflict of interest

None.

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