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Less is More: Video-Assisted Thoracic Surgery (VATS) vs. Open Thoracotomy (OT) in the Management of Resectable Lung Cancer

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Abstract

Background: Video-Assisted Thoracoscopic Surgery (VATS) has become the recommended approach for the treatment of resectable lung cancer. However, no large randomized clinical trial has been conducted formally comparing surgical resections completed by VATS to those done by Open Thoracotomy (OT) in low volume centers. The current study sought to assess differences in Recurrence-Free Survival (RFS), Overall Survival (OS), positive margins and postoperative Length of Stay (LOS) between VATS and OT lobectomies in our center.

Method: A single institution retrospective chart review from May 2005 through May 2015 was conducted. All patients diagnosed with stage I through III lung cancer who received surgical resection were selected. Patient and tumor characteristics recorded included age at diagnosis, sex, tobacco use, tumor location (side and lobe), stage, size and receipt of chemotherapy or radiotherapy. Chi-square and Wilcoxon-Mann-Whitney tests were used to compare demographics, tumor characteristics and LOS. Multiple logistic and Cox regression analyses were used to compute Relative Risk (RR) for positive margins and mortality hazard ratios along with 95% Confidence Intervals (CIs), respectively.

Results: Of the 235 patients, 101 subjects had VATS while OT was performed in 134 patients. Age at diagnosis, sex, tobacco use, tumor location, and size was comparable for VATS and OT. No significant difference was observed in the RR of positive margins for VATS versus OT, RR=0.56 (95% CI=0.26, 1.05). However, VATS had shorter median LOS compared to OT (4 vs. 6 days, respectively), p=0.002. A comparison of VATS versus OT showed no significant difference in the risk of recurrence, HR=1.21 (95% CI=0.74, 2.00), or death, HR=1.34 (95% CI=0.88, 2.06), in the intent-to-treat population. Similarly, no significant differences in recurrence or mortality risk were observed between VATS versus OT for analyses conducted separately for each cancer stage group or those limited to patients with negative margins.

Conclusion: Our study indicates that compared to OT, VATS leads to shorter LOS while achieving comparable margins status, RFS and OS regardless of tumor stage at diagnosis and therefore can be considered as a favorable surgical approach in this group of patients.

Keywords: Video-assisted thoracic surgery; Open thoracotomy; Recurrence-free survival; Overall survival; Positive margins; Postoperative length of stay

Abbreviations: VATS: Video-Assisted Thoracoscopic Surgery; OT: Open Thoracotomy; RFS: Recurrence-Free Survival; OS: Overall Survival; LOS: Length of Stay; RR: Relative Risk; CC: Confidence Interval; DFS: Disease-Free Survival; IQR: Interquartile Rages

Introduction

Lung cancer is the leading cause of cancer-related mortalities around the world [1]. Potentially curable early stage Non-Small-Cell Lung Cancer (NSCLC) can be found in one-third of this patient population [2]. Surgical resection remains the backbone of treatment in resectable lung cancers. The introduction of VATS in 1994 [3] sparked interest in minimally invasive tumor resection. VATS has also been shown to have fewer postoperative complications [4] and has been associated with decreased postoperative pain and increased quality of life compared to OT [5]. Several studies have compared these two approaches indirectly, but no randomized controlled trial has investigated the long-term effect on outcomes. We aim to investigate the long-term Disease-Free Survival (DFS) and OS of patients with lung cancer undergoing lung resection by OT or VATS for resectable stage lung cancer.

Patients and Methods

Surgical methods

VATS lung resections were performed via a three-port incision technique including a 4-centimeter anterior axillary working port. The specimens were removed via the working port. Rib spreading was not required. A hilar dissection proceeding from anterior to posterior was performed for lobectomies. For OT resections, a standard posterolateral thoracotomy was used. Generally, bulky tumors, inability to tolerate one-lung ventilation, dense adhesions, en bloc chest wall resections, sleeve resections, neoadjuvant radiation therapy, or intraoperative

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complications were reasons for selecting an OT approach or for requiring a conversion from VATS to OT.

Study population

Records for patients diagnosed with stage I through III resectable lung cancer treated at Loma Linda University Medical Center from May 2005 through May 2015 were retrieved through a retrospective chart review. Patients were subsequently divided into VATS and OT groups.

Study outcomes

The primary outcome of this study was RFS followed by OS as the secondary outcome. Survival was calculated from the date of surgery to the date of recurrence diagnosis/death or end of study follow-up.

Study covariates

Patient and tumor characteristics included age at diagnosis, sex, tobacco use, tumor location (Side and Lobe), stage, size and type of treatments including chemotherapy or radiotherapy.

Statistical analyses

Tumor and demographic characteristics were compared using Chi-square and Wilcoxon-Mann-Whitney tests. Purposeful variable selection approach was used to identify covariates that were included in the final models. A covariate-adjusted Cox proportional hazards model was used to compare RFS and OS between patients treated with VATS and those treated with OT. Profile likelihood was used to estimate 95% CIs. Proportionality was assessed using Shoenfeld residuals correlations and log-log survival plots. All tests were conducted using R software; R Core Team. R: A language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria.

Results

Study population description

From May 2005 through May 2015, 235 patients were diagnosed with stage I through III lung cancer. Of those, 134 and 101 patients received OT and VATS, respectively (Table 1). Median age at surgery (with Interquartile Rages, (IQR)) was similar for the two groups, OT 69 (IQR=61, 77) and VATS 70 (IQR=63,76), p=0.48. Similarly, no difference in gender distribution was observed, p=0.92. Both VATS and OT had a higher proportion of tumors located in the right lung, 62 (61.39%) and 78 (58.21%) respectively, p=0.31. Additionally, more than half of all tumors were located in the upper lobe with a slightly higher proportion seen for OT [78 (57.58%)] than VATS [53 (52.48%)], p=0.02. In contrast, a higher proportion of stage I cancers was treated by VATS versus OT, p=0.02. There was no significant difference in median tumor size [3 (IQR=2,5) vs. 3 (IQR=2, 4), p=0.41] or percentage of tumors with negative margins [104 (89.66%) vs. 89 (95.70%), p=0.13] between OT and VATS, respectively. Compared to VATS, a higher proportion of OT patients received chemotherapy [38 (28.36%) vs. 13 (12.87%), p=0.02] and radiotherapy [30 (22.39%) vs. 4 (3.96%), p<0.001] [6-17].

Recurrence-free survival (RFS) and overall survival (OS)

No significant differences in RFS (Figure 1) (p=0.23) or OS (Figure 2) (p=0.68) were observed between VATS versus OT in the Kaplan-Meier survival curves. After adjusting for covariates, the Cox regression models (Tables 2 and 3), show no difference in RFS, HR=1.26 (95% CI=0.73, 2.19), or OS, HR=1.34 (95% CI=0.85, 2.10), between VATS and OT.

Patients characteristics	Open thoracotomy (n=134)	VATS (n=101)	p-value
Age at diagnosis ǂ	69 (61-77)	70 (63-76)	0.48
Sex			0.92
Male	50 (37.31%)	37 (36.63%)	
Female	84 (62.69%)	64 (63.37%)	
Side			0.31
Left	53 (39.55%)	39 (38.61%)	
Right	78 (58.21%)	62 (61.39%)	
Bilateral/unknown	3 (2.24%)		
Lobe			0.02
Lower	33 (25.00%)	40 (39.60%)	
Middle	10 (7.58%)	6 (5.94%)	
Upper	76 (57.58%)	53 (52.48%)	
Bilateral/unknown	13 (9.85%)	2 (1.98%)	
Stage †			0.02
1	62 (46.27%)	66 (65.35%)	
2	33 (24.63%)	20 (19.80%)	
3	30 (22.39%)	13 (12.87%)	
Unknown	9 (6.72%)	2 (1.98%)	
Size ǂ	3 (2-5)	3 (2-4)	0.41
Margin status			0.13
Negative	104 (89.66%)	89 (95.70%)	
Positive	12 (10.34%)	4 (4.30%)	
Unknown	18 (13.43%)	8 (7.92%)	
Chemotherapy			0.02
No	85 (63.43%)	80 (79.21%)	
Yes	38 (28.36%)	13 (12.87%)	
Unknown	11 (8.21%)	8 (7.92%)	
Radiotherapy			<0.001
No	99 (73.88%)	97 (96.04%)	
Yes	30 (22.39%)	4 (3.96%)	
Unknown	5 (3.73%)		
Postoperative length of stay	6 (4-7)	4 (3-6)	0.002
ǂ Median with Interquartile Range (IQR); † Pathological stage **Abbreviations-** VATS: Video Assisted Thoracoscopic Surgery			

Table 1: Patient's characteristics by type of procedure.

Length of stay (LOS)

The median LOS was 2 days shorter among patients treated with VATS compared to those treated with OT 4 (3,6) vs. 6 (4,7), p=(0.002) (Figure 3).

Discussion

VATS was performed initially in the 1990's. Since then there have been multiple studies advocating the superiority of VATS over conventional OT in terms of short and long-term side effects as well as hospital LOS [18-20]. However, some surgeons still prefer OT over VATS. In fact, according to the Society of Thoracic Surgeons General Thoracic Surgery Database, the percentage of VATS lobectomies performed in the United States are performed by VATS [21,22] at high volume centers. One explanation for this may be due to the controversial results between several comparative studies in this field [23] since during the resectable years of its development, there was a lack of a clear definition of VATS between thoracic surgeons [24-26]. The goal of this study was to evaluate the outcomes in a low volume university setting over the last 10-year period, 2005-2015, where VATS was initiated in 2009 (Figure 4).

Our study, like other similar articles (Table 4), did not capture any

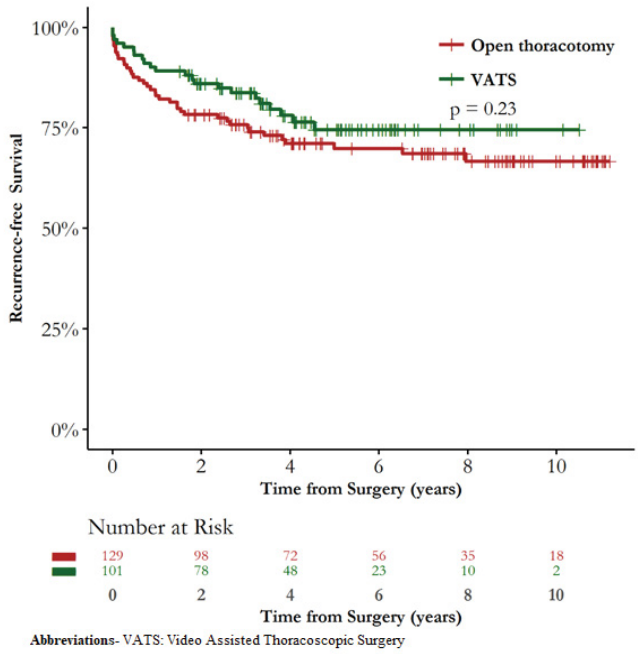

Figure 1: Kaplan-Meier survival curves for recurrence-free survival.

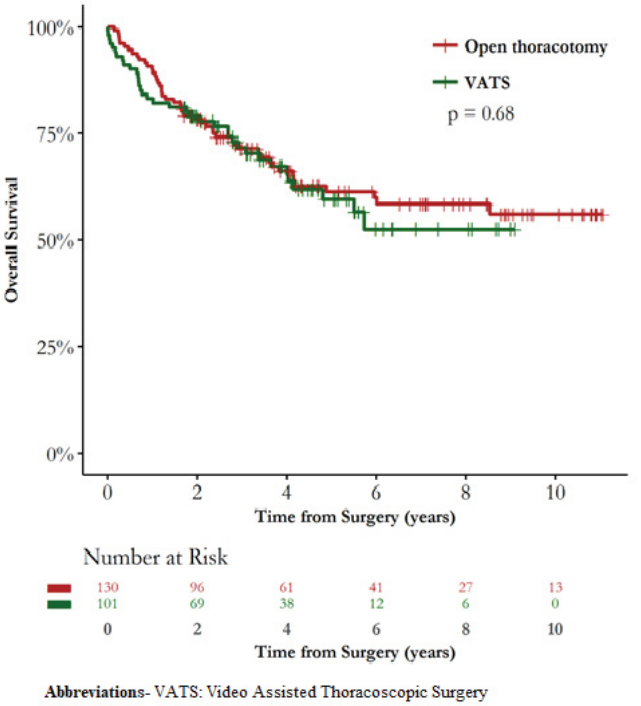

Figure 2: Kaplan-Meier survival curves for overall survival.

statistically significant findings between VATS and OT groups in terms of RFS and OS (p=0.23 and p=0.68, respectively). Also similarly, VATS lobectomy was associated with shorter LOS and non-inferior long-term

Patients characteristics	HR (95% CI)
Procedure	
Open thoracotomy	1
VATS	1.26 (0.73,2.19)
Age	1.10 (0.90,1.35)
Stage	
0-1	1
2	5.71 (2.73,11.93)
3	9.81 (4.87,19.78)
Unknown	3.18 (0.86,11.81)
Margin status	
Negative	1
Positive	2.21 (0.92,5.34)
Unknown	2.21 (1.12,4.38)
Abbreviations-VATS: Video Assisted Thoracoscopic Surgery; HR: Hazard Ratio; CI: Confidence Interval	

Table 2: Covariate-Adjusted cox regression recurrence hazards ratios with 95% Confidence Interval (CI).

Patients characteristics	HR (95% CI)
Procedure	
Open thoracotomy	1
VATS	1.34 (0.85,2.10)
Age	1.36 (1.11,1.68)
Stage	
0-1	1
2	1.82 (1.03,3.19)
3	3.25 (1.90,5.55)
Unknown	3.21 (1.30,7.89)
Margin status	
Negative	1
Positive	2.12 (1.04,4.32)
Unknown	1.10 (0.54,2.25)
Abbreviations-VATS: Video Assisted Thoracoscopic Surgery; HR: Hazard Ratio; CI: Confidence Interval	

Table 3: Covariate-Adjusted cox regression recurrence hazards ratios with 95% Confidence Interval (CI).

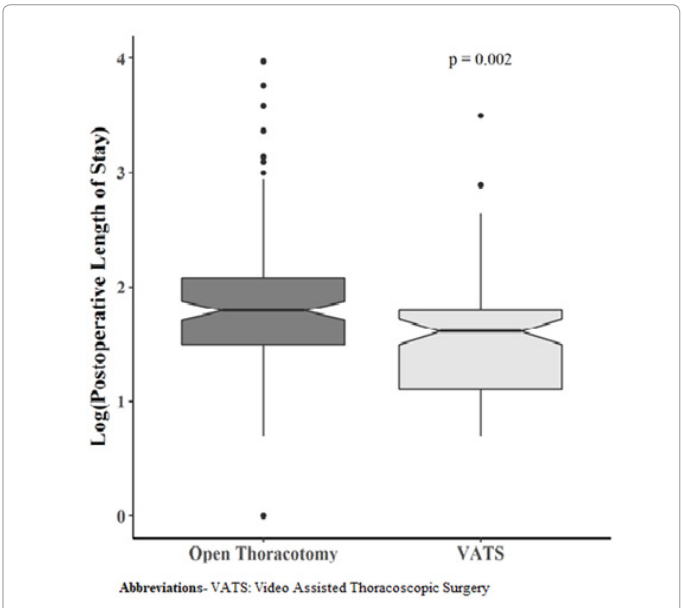

Figure 3: Postoperative length of stay by type of procedure.

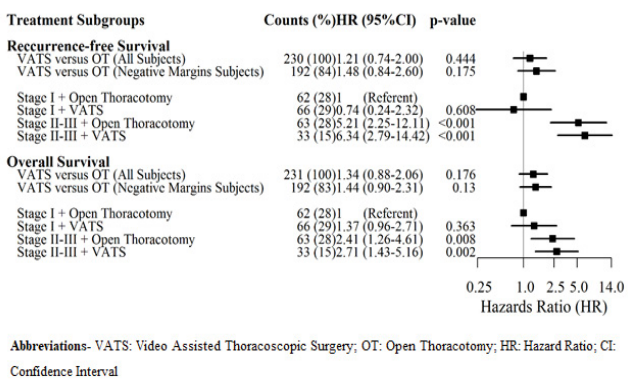

Figure 4: Forest plot for various treatment subgroups.

N=Total Pts	Shorter LOS VATS vs. OT	LOS (p-value)	DFS (p-value)	OS (p-value)	DFS/ OS (years)
N=160 114 VATS 46 OT			No difference p=0.27	No difference p=0.55	5
Propensity score matching 88 per group	VATS 2 days	p<0.05	No difference p=0.63	No difference p=0.27	3
Propensity score matching 175 per group	VATS	p<0.05	No difference p=0.35	No difference p=0.24	5
N=55 25 VATS 30 OT	VATS	p<0.05			
Propensity score matching 1195 per group			No difference p=0.46	p=0.55	3
80 40 VATS 40 OT			No difference p=0.44 (IA) p=0.48 (IB)	No difference p=0.15 (IA) p=0.20 (IB)	5
N=68350 10554 VATS 57796 OT	VATS 2 days	p<0.001			
N=389 63 VATS 326 OT	VATS	p<0.001			
N=287 98 VATS 189 OT	VATS	p<0.001			
N=529 156 VATS 373 OT	VATS 2 days	p<0.05	No difference p=0.43	No difference p=0.76	3
N=136 74 VATS 62 OT	VATS	p<0.001			
N=741 398 VATS 343 OT	VATS 2 days	p<0.001		No difference p=0.12	5
Abbreviations- LOS: Length Of Stay; Vats: Video Assisted Thoracoscopic Surgery: Ot: Open Thoracotomy; DFS: Disease-Free Survival; OS: Overall Survival					

Table 4: Lobectomy associated with shorter LOS.

survival when compared with OT lobectomy. These results support previous findings from smaller single- and multi-institutional studies that suggest that VATS does not compromise oncologic outcomes when used for resectable stage lung cancer [27,28]. Over the last 15 years, there have been multiple studies, which have compared VATS to OT (Table 4). As noted in the table, these studies consistently showed decreased LOS and no difference in three to five-year disease free or OS. Our data is consistent with other data sets retrospectively comparing VATS and OT for resection of resectable non-small cell lung cancer [10,28].

Although our current study did not capture any statistically significant value related to RFS, OS between two surgical modalities but compare to OT, in VATS lobectomy's incisions are smaller with no rib spreading which leads to have a faster recovery. Reviewing the previous studies showed although there was no difference in terms of the timing to receive adjuvant chemotherapy between VATS vs. OT [17] but patients who went under VATS had a better chance to tolerate and complete adjuvant chemotherapy courses, with less need for dose reduction and experiencing less related side effects [29] although still there is lack of data and results about any possible OS benefit [30-32].

Our study has several limitations. First and most importantly, our study is a single institution retrospective study. Specific information on patient selection criteria as well as differences in surgeons' experience is lacking and may have led to selection bias. VATS, like all newly developed minimally invasive surgical techniques, requires skills and experience in which not all surgeons have been trained.

Conclusion

Our study suggests that patients undergoing VATS lobectomy in a low-medium sized university setting have comparable long-term and short-term outcomes compared to national data in terms of DFS, OS, and shorter LOSs. This suggests referrals to high volume centers for lobectomy is not required as even low-medium volume centers with board-certified thoracic surgeons trained in VATS can achieve equivalent outcomes.

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