Lobectomy by video-assisted thoracic surgery (VATS) versus thoracotomy for lung cancer

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Background: The optimal surgical technique for lobectomy in lung cancer is not well defined. Proponents of video-assisted thoracic surgery (VATS) hypothesize that less trauma leads to quicker recovery, whereas those who advocate thoracotomy claim it as an oncologically superior procedure. However, a well-balanced comparison of the two procedures is lacking in the literature.

Methods: All patients who underwent lobectomy for clinical stage 1A lung cancer by computed tomographic and positron emission tomographic scan were identified from a prospective database. Patient characteristics were compared by the Student *t* test, Pearson χ^2, and Fisher exact test. A propensity score–matched analysis was performed. Survival was assessed by Kaplan–Meier and Cox proportional hazards analysis. Complications were assessed by a multivariate logistic regression model evaluating age, sex, comorbidities, pulmonary function, tumor size, nodal status, surgeon, and histologic characteristics.

Results: From May 2002 to August 2007, 398 patients underwent an attempt at VATS lobectomy and 343 underwent thoracotomy. An ''intent-to-treat'' analysis was performed. There was 1 postoperative death in each group. Survival by Cox model was no different for VATS versus thoracotomy (hazard ratio 0.72; $P = .12$), whereas age (hazard ratio 1.03; $P < .001$), larger tumor size (hazard ratio 1.34; $P < .001$), and higher nodal stage (hazard ratio 1.92; $P < .001$) were associated with worse survival. Logistic regression demonstrated fewer complications for VATS lobectomy (odds ratio 0.73; $P = .06$), whereas age (odds ratio 1.04; $P < .001$) and tumor size (odds ratio 1.2; $P < .020$) correlated with a greater number of complications. Patients undergoing VATS lobectomy demonstrated a 2-day shorter length of stay than patients undergoing thoracotomy ($P < .001$). Propensity score–matched analysis supported these findings.

Conclusions: VATS lobectomy and thoracotomy demonstrated similar 5-year survivals. However, VATS lobectomy was associated with fewer complications and shorter length of hospital stay.

The role of VATS wedge resection for the diagnosis of lung cancer is well established whereas the role of VATS lobectomy for treatment is not well defined. Many case series have demonstrated the feasibility of VATS lobectomy since it was first described in the early 1990s; however, surgeons have been reticent to use the technique because of intraoperative safety and long-term oncologic concerns.[1] The Society of Thoracic Surgeons database demonstrates that only 16% of lobectomies reported in the United States are performed by the VATS method.[2]

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Data from well-designed comparative studies in the literature are scarce. The majority of data is low on the evidence-based scale and the studies are often underpowered.[3] Recently, the demand in our practice for VATS lobectomy appears to be driven by patients and to a lesser extent by resident trainees. The obvious arguments in favor of VATS lobectomy include cosmesis, less postoperative pain, shorter length of stay, and lower overall cost, but there is a paucity of evidence-based data to support these assumptions. At present, no well-balanced comparative studies of sufficient power exist to adequately compare VATS lobectomy with thoracotomy lobectomy.

Therefore, we undertook this study to evaluate whether VATS lobectomy could be performed by a uniform technique among different surgeons with acceptable short- and long-term outcomes when compared with standard thoracotomy on a homogeneous well-balanced large population from a single institution.

METHODS

Data Aquisition

All patients with clinical stage IA non–small cell lung cancer by computed tomographic (CT) and positron emission tomographic (PET) scan were identified from a prospectively maintained institutional thoracic database after institutional review board approval. Excluded patients included those with a history of preoperative chemotherapy; histologic diagnosis of

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Abbreviations and Acronyms

CT = computed tomography
DLCO = diffusing capacity for carbon monoxide
FEV_1 = forced expiratory volume in 1 second
PET = positron emission tomography

benign disease, carcinoid, small cell, or mucoepidermoid carcinoma; procedures other than a lobectomy, such as wedge, segmentectomy, bilobectomy, pneumonectomy, or chest wall resection; and those with multiple primary tumors.

Variables recorded included age, sex, comorbidities, pulmonary function, tumor size, nodal status, and histologic characteristics. Comorbidities included coronary artery disease, valvular heart disease, dysrhythmia, hypertension, chronic obstructive pulmonary disease, asthma, renal insufficiency, and diabetes mellitus. Smoking history was defined as current (any amount), former (>100 cigarettes in a lifetime), and never (0–100 cigarettes in a lifetime) smokers.

All complications were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 (http://ctep.cancer.gov/reporting/ctc.html). Survival was recorded from day of the operation until date of death or last follow-up. Deaths were verified by the Social Security Death Index. Perioperative mortality was defined as death within 30 days of the operation or within the same hospital admission.

Operative Technique

The decision to perform either procedure was made by the individual surgeon. Four surgeons (R.F., V.R., B.P., and N.R.) perform VATS lobectomy for patients with early-stage disease whereas two surgeons (R.D. and M.B.) exclusively perform thoracotomy lobectomy for such patients.

All patients underwent standard anesthesia care with the use of double-lumen endotracheal tubes and perioperative fluid restriction. Postoperative pain relief was provided by continuous epidural administration of fentanyl and bupivacaine and/or intravenous opioid administration.

TABLE 1. Patient characteristics

	VATS (n = 398, 54%)	Thoracotomy (n = 343, 46%)	*P* value
Age, y (mean)	67 (36–90)	67 (35–89)	.59
Male sex	152 (38)	117 (34)	.25
No. of comorbidities			
1	178 (45)	167 (49)	.43
2	66 (17)	57 (17)	
3	8 (2)	11 (3)	
4	1	2	
FEV_1 (%)	92	88	.01
DLCO (%)	90	84	.004
Smoking history			
Current	57 (14)	53 (15)	.77
Former	288 (72)	240 (70)	
Never	53 (13)	50 (15)	
COPD	88 (22)	105 (30)	.01
Cardiac disease	201 (50)	177 (52)	.07
Diabetes mellitus	44 (11)	38 (11)	.42
Chronic renal insufficiency	6 (2)	2 (1)	.31

VATS, Video-assisted thoracic surgery; *FEV_1,* Forced expiratory volume in 1 second; *DLCO,* diffusing capacity for carbon monoxide; *COPD,* chronic obstructive pulmonary disease. Figures in parentheses indicate either range or percent.

VATS lobectomy was performed via a 4-cm utility incision at the anterior axillary line at the third or fourth intercostal space by using standard thoracic instruments without rib spreading, a 2-cm anterior thoracostomy port at the eighth intercostal space at the anterior axillary line for the camera, and a 2-cm posterior port for retraction and stapler insertion. The operation was performed entirely with thoracoscopic visualization. The hilar structures were individually ligated by endovascular staplers, and mediastinal nodal dissection or sampling was performed. The camera port was subsequently used as a thoracostomy tube site. Our technique has been described previously.[4,5] In VATS cases in which the robot was used for assistance in dissection, the same three VATS incisions were used as described in an earlier report.[6]

Thoracotomy lobectomy was performed via a posterolateral thoracotomy incision that spared the serratus anterior muscle. The chest was entered via the fifth intercostal space and a Finochietto retractor was used to gain exposure. Endoscopic staplers were routinely used for the transection of vessels and the completion of the fissures. In all patients an ipsilateral mediastinal dissection or sampling was performed.

Statistical Methods

Patient characteristics and perioperative data were compared by the Student *t* test, Pearson χ^2, and Fisher's exact test. Survival was assessed by Kaplan–Meier and Cox proportional hazards analysis. Conversions from VATS to thoracotomy were analyzed in the VATS cohort by the ''intent-to-treat'' method. Complications were assessed by a multivariate logistic

TABLE 2. Perioperative data

	VATS (n = 398)	Thoracotomy (n = 343)	*P* value
Pathologic stage			
IA	260 (65)	213 (62)	.49
IB	69 (17)	62 (18)	
IIA	19 (5)	17 (5)	
IIB	12 (3)	15 (4)	
IIIA	29 (7)	21 (6)	
IIIB	9 (2)	15 (4)	
Histology			
Adenocarcinoma	159 (40)	122 (36)	.1
Adenocarcinoma w/BAC	179 (45)	145 (42)	
BAC	6 (2)	12 (3)	
Squamous	44 (11)	56 (16)	
Large cell	10 (3)	8 (2)	
Tumor location			
LLL	44 (11)	53 (15)	.196
LUL	115 (29)	86 (25)	
RLL	52 (13)	54 (16)	
RML	21 (5)	23 (7)	
RUL	166 (42)	127 (37)	
Tumor size, cm (mean)	2	2	.55
No. of nodal stations removed	3.6	4.5	<.0001
Complications (any)	96 (24)	104 (30)	.05
LOS (d)	5	7	<.0001
Deaths	1	1	
Median OR time (h)	3:40	3:44	
Conversions	70 (17)		

VATS, Video-assisted thoracic surgery; *BAC,* bronchoalveolar carcinoma; *LLL,* left lower lobe; *LUL,* left upper lobe; *RLL,* right lower lobe; *RML,* right middle lobe; *RUL,* right upper lobe; *LOS,* length of stay; *OR,* operating room. Figures in parentheses indicate percent.

TABLE 3. Reasons for conversion from VATS to thoracotomy

	No.	Percent
Tumor location	22	6
Adhesions	15	4
Bleeding	11	3
Adenopathy	9	2
Anatomy	8	2
Failed lung isolation	4	1
Obesity	1	
Total	70	

regression model evaluating age, sex, comorbidities, pulmonary function, tumor size, nodal status, surgeon, and histologic characteristics; nonsignificant variables were excluded in a stepwise fashion to obtain the final model. STATA 10 software (Stata Corporation, College Station, TX) was used to perform statistical analyses.

A propensity score–matched analysis was performed. Propensity scores were generated for all patients eligible to undergo either VATS or thoracotomy lobectomy. VATS versus thoracotomy was the treatment indicator (dependent variable) and the covariates were age, sex, comorbidities, forced expiratory volume in 1 second (FEV_1), diffusing capacity for carbon monoxide (DLCO), smoking history, stage, histologic characteristics, tumor size, and nodal status. Nearest neighbor matching method was used without replacement. VATS and thoracotomy group covariates were compared by standardized differences. Patients were stratified by propensity score groupings to evaluate survival, complications, and length of stay among the VATS and thoracotomy groups. Cox and logistic regression models were constructed to evaluate the influence of VATS on survival and complications, respectively, adjusting for propensity score. STATA 10/ PSMATCH2 (Leuven and Sianesi) was used to perform statistical analyses.

RESULTS

From 2002 to 2007, 741 patients with clinically staged IA non–small cell lung cancer underwent surgical resection. Of these, 343 underwent thoracotomy and 398 underwent attempted VATS lobectomy, of whom 70 required conversions to thoracotomy. There was one perioperative death in each group and there were no intraoperative deaths. Median follow-up was 28 months in both groups. Patient characteristics and perioperative findings are shown in Tables 1 and 2, respectively.

Of the 64 procedures that were begun as VATS with robotic assistance, 59 were completed by VATS and 5 were converted to thoracotomy. Conversions are outlined in Table 3. A total of 102 adverse events occurred in 96 patients in the VATS group and 123 in the 104 patients undergoing thoracotomy. Eight patients in the VATS group and 13 in the thoracotomy group had grade 3 or higher complications (Tables 4A and 4B).

TABLE 4A. Complications by CTCAE: VATS lobectomy group

	Grade				
Complication	1	2	3	4	5
Atrial arrhythmia		41			
Hemorrhage				5	
Gastrointestinal		2	1		
Respiratory		26	1		1
Empyema					
Prolonged air leak		17			
Pulmonary embolus		3			
Myocardial infarction		1			
Other		4			

CTCAE, Common Terminology Criteria for Adverse Events.

TABLE 4B. Complications by CTCAE: Thoracotomy lobectomy group

	Grade				
Complication	1	2	3	4	5
Atrial arrhythmia		43			
Hemorrhage				2	
Gastrointestinal	2	1			
Respiratory		34	6	1	1
Empyema			1		
Prolonged air leak		18			
Pulmonary embolus		2			
Myocardial infarction	2				
Other	2	6		2	

CTCAE, Common Terminology Criteria for Adverse Events.

Kaplan–Meier analysis demonstrated a 79% 5-year survival for the VATS group and a 75% 5-year survival for the thoracotomy group (log rank; $P = .08$) (Figure 1). A Cox proportional hazards model included age, sex, comorbidities, pulmonary function tests, smoking history, tumor location, surgeon, type of surgical procedure, histologic type, tumor size, and nodal status. Stepwise elimination of insignificant variables yielded the final model shown in Table 5A. The multivariate analyses demonstrated increased age, tumor size, and nodal stage to adversely affect outcome. The intent-to-treat analysis, which included conversions in the thoracotomy group, demonstrated a hazard ratio of 0.72 for the VATS group ($P = .12$). When all three groups were analyzed separately (VATS, thoracotomy, and conversion groups), no significant differences

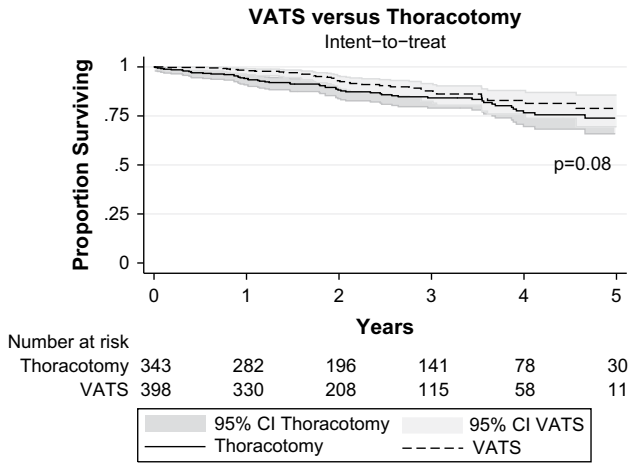

FIGURE 1. VATS versus thoracotomy. Intent to treat. *VATS,* Video-assisted thoracic surgery; *CI,* confidence intervals.

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TABLE 5A. Cox proportional hazards model of all 741 patients

	HR	CI	*P* value
VATS	0.72	0.47, 1.1	.12
Age	1.03	1.01, 1.06	<.001
Tumor size	1.34	1.15, 1.62	<.001
Nodal stage	1.92	1.47, 2.52	<.001

HR, Hazard ratio; *CI,* confidence intervals; *VATS,* video-assisted thoracic surgery. Histology, surgeon, comorbidities, sex, and smoking history were not significant.

TABLE 5B. Logistic regression: Complications as the dependent variable of all 741 patients

	OR	CI	*P* value
VATS	0.73	0.52, 1.01	.06
Age	1.04	1.02, 1.06	<.001
Tumor size	1.2	1.02, 1.40	.02

OR, Odds ratio; *CI,* confidence intervals; *VATS,* video-assisted thoracic surgery. Histology, surgeon, comorbidities, sex, smoking history, and nodal stage were not significant.

in survival were demonstrated ($P = .9$) by Kaplan–Meier analysis. When the conversion group was placed in the thoracotomy group, the survival was no different by Kaplan–Meier analysis ($P = .07$). When the Cox model included the conversions in the thoracotomy group, the hazard ratio for VATS lobectomy dropped to 0.67 ($P = .08$, confidence intervals –0.43, 1.05).

A logistic regression model was created yielding the final model shown in Table 5B. Increased age and tumor size were significant predictors of complications. VATS lobectomy appeared to yield fewer complications (odds ratio = 0.73; $P = .06$) when controlling for tumor size and age. The conversion coefficient in the regression model demonstrated a value of 0.3 ($P = .27$), which was equal and opposite to the sign of the coefficient of VATS of –0.3 ($P = .06$). When conversions were included in the thoracotomy group, ignoring the intent-to-treat principle, the VATS lobectomy odds ratio was 0.64 ($P = .01$; highly significant).

An interaction term of age and tumor size was generated and assessed in both Cox and logistic regression models. The term was insignificant, suggesting no evidence of interaction between the two variables.

The two groups were well balanced with regard to stage. This was the main reason for performing the analysis by the intent-to-treat method. We wanted patients with more complicated disease, and (theoretically) a greater tendency for complications and longer lengths of hospital stay, to be included in the VATS lobectomy group. However, the conversion group demonstrated a similar stage distribution when compared with the VATS and thoracotomy groups: stage IA, 47 patients; stage IB, 8 patients; stage IIA, 2 patients; stage IIB, 3 patients; stage IIIA, 8 patients; and stage IIIB, 2 patients.

A propensity score–matched analysis was performed. Propensity scores were generated for 677 patients; 64 of 741 patients did not receive a propensity score owing to missing variables. After propensity score matching, 51 unmatched patients were excluded, yielding a total of 313 patients in each of the VATS and thoracotomy groups. Covariates were compared by standardized differences (Table 6). Patients were then grouped by propensity scores, which demonstrated similar survival between the VATS and thoracotomy groups but fewer complications and a shorter length of stay for the VATS group (Table 7). Propensity scores were then multiplied by 10 to present hazard ratios in terms of a 10% change in propensity score. A Cox proportional hazards model demonstrated a hazard ratio of 0.8 for the VATS group when adjusted for propensity score (Table 8A). A logistic regression model with complication as the dependent variable demonstrated an odds ratio of 0.67 for the VATS group when adjusted for propensity score (Table 8B).

DISCUSSION

The technique of VATS lobectomy has developed during the past two decades, with most data presented in the form of

TABLE 6. Comparison of baseline characteristics of raw, propensity score–matched, and –unmatched data

	Raw data			Propensity score matching			Unmatched (n = 115)
	VATS (n = 398)	Thoracotomy (n = 343)	Standardized difference*	VATS (n = 313)	Thoracotomy (n = 313)	Standardized difference*	VATS (n = 85); thoracotomy (n = 30)
Age	67	68	10	67	68	10	72
Male sex	152 (38%)	117 (34%)	4	129 (41%)	106 (34%)	7	35 (30%)
No comorbidities	145 (36%)	106 (31%)	5	128 (41%)	95 (30%)	12	28 (24%)
FEV_1 (% predicted)	92	88	17	95	88	31	73
DLCO (% predicted)	90	84	21	93	84	31	70
Never smokers	53 (13%)	50 (14%)	0.01	36 (12%)	47 (15%)	4	20 (17%)
Greater than stage 1	69 (17%)	68 (20%)	4	47 (15%)	63 (20%)	6	26 (23%)
Non-adenocarcinoma histology	54 (14%)	64 (19%)	7	24 (8%)	59 (19%)	16	35 (30%)
Tumor size (cm)	2	2	4	2	2.1	10	2.4
Nodal disease	64 (16%)	55 (16%)	0.3	47 (15%)	50 (16%)	3	21 (18%)

VATS, Video-assisted thoracic surgery; *FEV_1,* forced expiratory volume in 1 second; *DLCO,* diffusing capacity of carbon monoxide. *Standardized difference is the mean difference divided by the pooled SD, expressed as a percentage.

TABLE 7. Propensity score groups (n = 677)

	<0.4	.04–0.59	>0.6
VATS (n)	20	232	112
Thoracotomy (n)	42	212	59
Survival (VATS HR, CI, *P* value)	0.9, CI (0.27, 2.99), $P = .9$	0.9, CI (0.55, 1.6), $P = .8$	0.5, CI (0.15, 1.7), $P = .27$
Complications (VATS, Thor, *P* value)	0.6, 0.4, $P = .1$	0.23, 0.33, $P = .03$	0.16, 0.19, $P = .67$
LOS, d (VATS, Thor, *P* value)	9, 8, $P = .3$	5, 7, $P < .0001$	4, 6, $P = .01$

VATS, Video-assisted thoracic surgery; *HR,* hazard ratio; *CI,* confidence intervals; *Thor,* thoracotomy; *LOS,* length of stay.

large case series that focus on the feasibility of this approach.[1,3,7-10] However, these large series tend to favor VATS lobectomy inasmuch as they do not provide adequate thoracotomy comparison groups and may inadvertently exclude conversions of VATS to thoracotomy. A major problem in comparing VATS lobectomy from one study with thoracotomy survival from other studies is that populations may differ significantly with regard to patient tumor histologic types, sex, and stage. Such factors influence survival results and can mask any differences related to surgical technique. The theoretical advantages of decreased pain, shorter length of stay, better pulmonary function, and preservation of host immunity should lead to improved short- and long-term outcomes. However, VATS lobectomy must be supported by solid data if it is to gain greater acceptance in mainstream thoracic surgery practice.

Current published data comparing VATS with thoracotomy consist of a few underpowered randomized controlled trials. The quality and sample size of these studies do not permit statistically valid conclusions.[11-14] One of the largest retrospective comparative studies from Watanabe and associates,[15] which included more than 100 patients in each group, was imbalanced because of a greater number of T2 lesions in the thoracotomy patient group.

In addition, the vast majority of comparative studies fail to adhere to the intention-to-treat principle, a major design flaw that would inherently bias results in favor of VATS lobectomy. Indeed, many comparative studies demonstrate a survival benefit in favor of VATS lobectomy that is frequently attributed to better outcome from less chest wall trauma.[16-18] However, it is more likely that the thoracotomy group includes converted cases that are likely to be higher stage and more technically difficult then those performed by VATS.

Published conversion rates from VATS to thoracotomy range from 1.6% to 19%.[1,3,8,9] These results may be inaccurate because of retrospective data acquisition. Our study benefits from routine prospective data collections performed weekly by our group with review by the involved surgical attending staff. Indications for VATS lobectomy as well as thresholds for conversions vary among surgeons, and these factors change over time as the surgeon gains more experience with the procedure.

Our cohort of patients was well balanced in all categories between the thoracotomy and VATS lobectomy groups, therefore minimizing bias from known confounders. Preoperative comorbidities were similar. Although more patients were labeled as having chronic obstructive pulmonary disease in the thoracotomy group, smoking history was similar and preoperative FEV_1 and DLCO differed between the two groups by only 4% and 6%, respectively. The thoracotomy group had a mean of one extranodal station sampled; however, there were no significant differences in stage distribution or overall survival. Nodal evaluation is dependent on effort and surgeon and is not due to any technical limitation of VATS. For example, when operating on upper lobe tumors by VATS, we rarely take down the inferior pulmonary ligament and dissect out the level 9 nodes, thus reducing the total number of nodal stations sampled by one. However, the value of such additional sampling is debatable inasmuch as level 9 nodal metastases are rare for upper lobe tumors.

The propensity score–matched analysis supported the results of the raw data. Survival among the different propensity score groupings demonstrated similar survival between VATS and thoracotomy groups and fewer complications and shorter length of stay for the VATS group.

This study also demonstrates that thoracotomy for lung cancer can be performed with an excellent outcome. Interestingly, conversion from VATS to thoracotomy does not appear to pose an increased risk of complications other than those associated with thoracotomy alone. Conversion in the regression model is an interaction term because only patients undergoing VATS can be converted. The regression coefficient of VATS (–0.3) was equal and opposite in sign to that of patients converted from VATS to thoracotomy

TABLE 8A. Cox proportional hazards model of 626 propensity score–matched patients

	HR	CI	*P* value
VATS	0.8	0.27, 1.3	.4
Propensity score	0.68	0.52, 0.88	.004

VATS, Video-assisted thoracic surgery; *HR,* hazard ratio; *CI,* confidence intervals.

TABLE 8B. Logistic regression model of 626 propensity score–matched patients (dependent variable = complications)

	OR	CI	*P* value
VATS	0.67	0.45, 0.98	.04
Propensity score	0.71	0.57, 0.87	.001

VATS, Video-assisted thoracic surgery; *OR,* odds ratio; *CI,* confidence intervals.

(0.3), indicating that complications from the conversion of VATS to thoracotomy were the same as for primary thoracotomy. The small difference in complication rate and low operative mortality underscores the effectiveness of lobectomy by thoracotomy even after conversion; therefore, any VATS case in which oncologic principles may be compromised should be converted to thoracotomy.

Limitations of the Study

Every study has limitations. Our data lack narcotic information, a validated pain scale, and an objective measurement of postoperative pulmonary function. Although the data in this study were gathered prospectively, the analysis was performed retrospectively; therefore, unknown confounding variables and inherent selection biases could exist. The comparisons in this study are inextricably confounded with systematic surgeon selection bias: 100% of the VATS lobectomies are performed by four surgeons whereas two of the surgeons only perform thoracotomy. Thus, complications may be based on unrecorded surgeon-related factors that cannot be separated from those intrinsic to the approach. However, given the experience and the expertise of the two surgeons performing thoracotomy, we believe this is unlikely.

A randomized controlled trial is considered to be the gold standard to demonstrate superiority of one procedure over another, but it may not be feasible in many situations. However, an adequately powered randomized controlled trial on this topic is unlikely because many VATS surgeons are unwilling to randomize patients and many patients tend to seek out surgeons who are willing to perform this procedure.

On the basis of the presented data, VATS lobectomy and thoracotomy are both acceptable procedures for the treatment of lung cancer and are associated with similar long-term survivals. However, VATS lobectomy is associated with fewer complications and a significantly decreased length of hospital stay. Nevertheless, the performance of an oncologically sound operation must take priority over a suboptimal VATS lobectomy, and conversion to thoracotomy should be performed in situations in which the extent of disease mandates an open procedure for complete resection.

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References

1. McKenna RJ, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1,100 cases. *Ann Thorac Surg*. 2006;81:421-6.
2. Boffa DJ, Allen MS, Grab JD, Gaissert HA, Harpole DH, Wright CD. Data from The Society of Thoracic Surgeons General Thoracic Surgery database: the surgical management of primary lung tumors. *J Thorac and Cardiovasc Surg*. 2008; 135:247-54.
3. Flores RM, Alam N. VATS lobectomy, open thoracotomy and the robot for lung cancer. *Ann Thorac Surg*. 2008;85:S710-5.
4. Flores RM. VATS lobectomy for early stage lung cancer. CTSNET Experts' Techniques at www.ctsnet.org [cited 2005 April]. Available from: http://www.ctsnet.org/sections/clinicalresources/thoracic/expert_tech-.html.
5. Weyant MJ and Flores RM. VATS mediastinal nodal dissection. CTSNET Experts' Techniques at www.ctsnet.org [cited 2005 September]. Available from: http://www.ctsnet.org/sections/clinicalresources/thoracic/expert_tech-26.html.
6. Park BJ, Flores RM, Rusch VW. Robotic assistance for video-assisted thoracic surgical lobectomy: technique and initial results. *J Thorac Cardiovasc Surg*. 2006;131:54-9.
7. Swanson SJ, Herndon JE, D'Amico TA, Demmy TL, McKenna RJ, Green MR, et al. Video-assisted thoracic surgery lobectomy: report of CALGB 39802—a prospective, multi-institution feasibility study. *J Clin Oncol*. 2007;25:4993-7.
8. Onaitis MW, Petersen RP, Balderson SS, Toloza E, Burfeind WR, Harpole DH Jr, et al. Thoracoscopic lobectomy is a safe and versatile procedure: experience with 500 consecutive patients. *Ann Surg*. 2006;244:420-5.
9. Nicastri DG, Wisnivesky JP, Little VR, Yun J, Chin C, Dembitzer FR, et al. Thoracoscopic lobectomy: report on safety, discharge independence, pain, and chemotherapy tolerance. *J Thorac Cardiovasc Surg*. 2008;135:642-7.
10. Walker WS, Codispoti M, Soon SY, Stamenkovic S, Carnochan F, Pugh G. Long-term outcomes following VATS lobectomy for non–small cell bronchogenic carcinoma. *Eur J Cardiothorac Surg*. 2003;23:397-402.
11. Kirby TJ, Mack MJ, Landreneau RJ, Rice TW. Lobectomy—video-assisted thoracic surgery versus muscle-sparing thoracotomy: a randomized trial. *J Thorac Cardiovasc Surg*. 1995;109:997-1002.
12. Sugi K, Kaneda Y, Esato K. Video-assisted thoracoscopic lobectomy achieves a satisfactory long-term prognosis in patients with clinical stage IA lung cancer. *World J Surg*. 2000;24:27-31.
13. Craig SR, Leaver HA, Yap PL, Pugh GC, Walker WS. Acute phase responses following minimal access and conventional thoracic surgery. *Eur J Cardiothorac Surg*. 2001;20:455-63.
14. Shigemura N, Akashi A, Nakagiri T, Ohta M, Matsuda H. Complete versus assisted thoracoscopic approach: a prospective randomized trial comparing a variety of video-assisted thoracoscopic lobectomy techniques. *Surg Endosc*. 2004;18: 1492-7.
15. Watanabe A, Koyanagi T, Ohsawa H, Mawatari T, Nakashima S, Takahashi N, et al. Systematic node dissection by VATS is not inferior to that through an open thoracotomy: a comparative clinicopathologic retrospective study. *Surgery*. 2005;138:510-7.
16. Whitson BA, Andrade RS, Boettcher A, Bardales R, Kratzke RA, Dahlberg PS, et al. Video-assisted thoracoscopic surgery is more favorable than thoracotomy for resection of clinical stage I non–small cell lung cancer. *Ann Thorac Surg*. 2007;83:1965-70.
17. Kaseda S, Aoki T, Hangai N, Shimizu K. Better pulmonary function and prognosis with video-assisted thoracic surgery than with thoracotomy. *Ann Thorac Surg*. 2000;70:1644-6.
18. Cattaneo SM, Park BJ, Wilton AS, Seshan VE, Bains MS, Downey RJ, et al. Use of video-assisted thoracic surgery for lobectomy in the elderly results in fewer complications. *Ann Thorac Surg*. 2008;85:231-5.

Discussion

Dr Scott J. Swanson *(New York, NY).* Dr Flores, you are to be congratulated for an excellent report regarding an important topic in lung cancer. Your results are quite impressive.

I would like to highlight a couple of pertinent facts and then ask three questions. Your database shows that 90% of patients have adenocarcinoma and most are women, consistent with the clear-cut change in epidemiology we have all witnessed over the past 20 years. However, approximately 15% of your cohort are never smokers, a trend that is clearly on the rise, very disturbing, and argues for a critical need for translational research funding in this area. It appears that your clinical staging system based on CT and PET was only accurate in about two thirds of the population. Fully 33% to 40% were understaged, and that has been seen elsewhere in the 2008 meeting of The American Association for Thoracic Surgery. Approximately 10% of your patients were found to have stage III disease. About 18% of your patients in the VATS lobectomy

group were converted to thoracotomy. My first question pertains to the last point. Why do you think your conversion rate is higher than most? Ours is approximately 5%. We also use a prospective database. What does tumor location mean, as 22 patients were converted on this basis, and this is in the setting of a mean tumor size of 2 cm? My point about this is that your survival difference between VATS and thoracotomy borders on significance at .08. In fact, if you showed that slide in an oncology meeting, that would be a highly significant slide. If your conversion rate was lower, perhaps you would have seen a significant difference in survival.

Dr Flores. That is a good point about the conversion rate. It is the central point of this presentation. Most of the data out there are retrospective. I think retrospective analyses tend to miss the conversion patients. The most common reasons that patients are converted are theoretically higher stage, adhesions, ambiguous anatomy, and other such findings. Including such patients in the thoracotomy group will skew the results in favor of VATS lobectomy; therefore, we adhered to the intent-to-treat principle and included them in the VATS lobectomy group, which would in theory make the VATS group look worse. Since you mentioned oncology meetings, this is the standard methodology for an oncologic study.

I think our results are pretty consistent with the prospective data, because the CALGB (Cancer and Leukemia Group B) trial, in which you were an investigator, had a 14% conversion rate. That study included surgeons who had substantial experience in performing VATS lobectomy and did not include their learning curves. Therefore, I think the conversion rate of 14% in that series is more realistic for experienced VATS lobectomy surgeons rather than the lower conversion rates reported in the case series literature. In our study, four different surgeons were performing VATS lobectomy. Also included within our reported conversion rate is our learning curve, so that includes the learning curve conversions of all four surgeons. I think it is an honest way of reporting the results. Even though it is a retrospective analysis, these data are gathered prospectively.

Dr Swanson. You might look at survival without the intention-to-treat principle.

Dr Flores. Survival without intention-to-treat data shows that VATS lobectomy is highly significant and superior to thoracotomy, and I do not think that is an appropriate analysis. Many would argue the bias would favor VATS lobectomy.

Dr Swanson. My second question pertains to lymph nodes. I assume none of these patients had mediastinoscopies, but about 10% had stage III disease. Do you think it is important to identify these patients before resection? If so, have you considered doing what we do—performing an initial ipsilateral mediastinal node evaluation using VATS before resection and, if positive, stopping and giving induction therapy before coming back for lobectomy? The morbidity of this approach is not higher than that of mediastinoscopy and allows for chemotherapy or chemoradiation to start within a week. Also of importance, it does not add time to the operation. We have also found that a similar percentage of patients, 5% to 10%, will have positive results. Do you know how this 10% cohort fared in terms of survival? I assume they all received adjuvant therapy.

Finally, in the same vein, do you have a standard approach for sampling lymph nodes? Do you think it is important to harvest the same number of nodes or nodal stations no matter what the approach? As you point out in this paper, about one less station was sampled in VATS than in thoracotomy.

Dr Flores. Those are good points.

I have pondered the question about doing a nodal dissection first and then giving induction therapy, and I think you will find variability among the surgeons in our institution. The new data that have been reported in the medical oncology literature indicate that adjuvant chemotherapy is beneficial. That said, when stage IIIA microscopic nodal disease is identified, after a thorough preoperative staging with CT, magnetic resonance imaging, and PET, I fail to see why stopping the operation and giving the patient induction therapy is better than just doing a nodal dissection and administering postoperative chemotherapy.

From the nodal standpoint, we routinely perform the same nodal dissection sampling with VATS as we do with open thoracotomy. One case scenario is different—and since we had a preponderance of upper lobectomies, I think this is where the decrease among nodal stations takes place. When we have a left upper lobe or right upper lobe, we do not mobilize the inferior pulmonary ligament and we do not take the level 9 lymph node. I think that is where that number difference comes from.

Dr Swanson. My last question pertains to your overall survival and outcome. I do think you should study the pain and functional issues, because these may be key differences between these two approaches if the survival differences that are being suggested are difficult to prove. We have recently published an article showing pain is minimal at 2 weeks and that adjuvant chemotherapy can be delivered at full dose and on time in over 70% of patients undergoing a VATS approach. Why do you think that you had such excellent survival when almost 20% of your patients had stage II or stage III disease? You had about an 80% long-term survival, which seems very good. What methods of follow-up do you use to get your survival figures? Do you depend on the Social Security Death Index to determine whether a patient is alive or dead, or do you do chart follow-up or telephone calls?

Dr Flores. Our primary method of survival is through our institution. The institution monitors these patients closely, and we have a set of data managers who follow up with that. In addition, we look at the Social Security Death Index. However, there is a 6-month lag period with the Social Security Death Index, so that alone is not sufficient when you are evaluating our time period.

Dr Todd L. Demmy *(Buffalo, NY).* An index of the maturity of a VATS lobectomy program is the proportion of total lobes that you are doing thoracoscopically. Do you have the percentage in this time period that were done thoracoscopically?

Dr Flores. No, I do not have that number.

Dr Demmy. Your FEV_1 is in the 80% to 90% range, which suggests that this is a very selective population of patients with good pulmonary function. That tends to lead to better collapse of the lung and a somewhat technically easier VATS lobectomy. Could you comment on that? Since your study has found fewer complications, are you going to now offer VATS lobectomy to the high-risk group in which you expect more complications?

Dr Flores. The FEV_1 point reported is the mean FEV_1. The range goes down as far as 40% of predicted with FEV_1 and DLCO, so the number that you are looking at is the mean. I did not provide the range. However, I think the important point of this paper is that the patients were selected in the same way. The thoracotomy patients and the VATS patients were selected on the basis of the CT scan, PET scan, and pulmonary function tests.

There is no difference among the six surgeons who perform lobectomies at our institution.

Dr Erino A. Rendina *(Rome, Italy).* When comparing thoracotomy with VATS lobectomy, I think it is very important to also give the details about the thoracotomy. It is very important to know whether you are comparing VATS with a small thoracotomy of maybe 9 or 10 cm or with the sternovertebral thoracotomy of our ancestors. Obviously, that might have an impact on the postoperative course.

Dr Flores. Absolutely. I think that is a great point, and that is always my argument. It is discussed in the manuscript. All of these patients had division of the latissimus dorsi, sparing the serratus anterior muscle; the hilar ligation was usually performed with staples, and the fissure was completed with staples as well.

Dr David M. Follette *(Sacramento, Calif).* Dr Flores, we do not really know that patients with microscopic stage IIIA disease do better than the neoadjuvant group. In fact, there is a Southwest Oncology Group (SWOG) trial looking at that with radiation. That is a presumption based on the data we have for adjuvant treatment. My question for you is this: inasmuch as your boss is one of the leaders and proponents of neoadjuvant treatment, what is your ability to give neoadjuvant treatment in terms of patient compliance versus adjuvant treatment in a similar group of patients? That is the important question. At Sloan–Kettering, do you see as large a difference as all the rest of us do in your ability to give neoadjuvant versus adjuvant chemotherapy?

Dr Flores. Sure. That is the biggest argument with induction therapy. You can get more chemotherapy into the patient and complete the cycles giving induction. In cases of obvious stage IIIA disease, we will do mediastinoscopy and try to identify it. We do give induction therapy as well. However, I always teach my fellows that not all stage IIIA disease is same. They stratify by number of nodal stations involved, microscopic versus bulky nodal disease, and so on. I think the patients with stage IIIA disease in the VATS lobe cohort are going to have microscopic disease, usually at a single station when prescreened by CT and PET. There is no right answer. So, the operation has begun. The patient is under general anesthesia. I would remove the diseased lobe and lymph nodes and administer adjuvant therapy. However, I do understand the controversy that exists.

Dr David J. Sugarbaker *(Boston, Mass).* I have just a brief comment on that. We do not need to reinvent or go back to the future. Induction therapy for stage IIIA disease in two randomized trials gives superior survival. Adjuvant chemotherapy in stage IIIA disease, according to Cybulski and some of the other large reports of resected micrometastatic disease, gives 5% to 12% 5-year survival. So even the CALGB trial, which is now being published and of which I am an author, suggests that there is no difference in earlier stage disease between those getting adjuvant therapy and those not. The data for adjuvant chemotherapy in the treatment of stage IIIA disease, whether it be microscopic or not, is inconclusive in terms of its effect on survival. The only data we have that are prospective from both the Roth trial and the Roselle trial indicate that a large difference in survival is seen with induction treatment.

Dr Flores. No, I completely disagree with you on that point. You are quoting antiquated studies published 15 years ago that include patients enrolled well before that. The Roselle trial and the induction trials involved about 100 patients as opposed to the recent adjuvant trials, which involved thousands of patients, and the subset of patients with stage IIIA disease did better with adjuvant therapy than the patients who did not get adjuvant therapy. The numbers you are quoting are very small. I do not agree with your point.

Dr Sugarbaker. Well, Dr Flores, which trial are you talking about?

Dr Flores. The one from France.

Dr Sugarbaker. Who is the author? I do not recall that one.

Dr Flores. There have been numerous prospective studies: ALPI, ANITA, BLT, JBR10, and the LACE meta-analysis, which showed that patients with stage III disease had a hazard ratio of 0.83 with adjuvant therapy. However, the initial one that I was referring to was the LeChevallier study, the International Adjuvant Lung Cancer Trial (IALT), the big one from France that was presented at the American Society of Clinical Oncology meeting, which resurrected adjuvant therapy in lung cancer.

Dr Sugarbaker. That study was underpowered in stage IIIA disease.

Dr Mark J. Krasna *(Towson, Md).* Dr Flores, I will disagree with you on that point. I want to agree with Dr Sugarbaker. There are actually two studies and they are both retrospective. I think one was from MD Anderson almost a decade ago and the other was from Italy. They actually looked at the subpopulation that you are talking about, patients in whom you open the chest, find residual disease, and then go back in after they have received a full dose of neoadjuvant therapy. Thus there are some data, although not prospective. But, again, if you take the subset that Dr Sugarbaker is talking about, which I agree is good prospective data, and you take these other subsets of patients whom you actually close, treat neoadjuvantly, and then resect, I actually agree; I think those patients should be offered the best possible therapy, which is neoadjuvant.

Dr Flores. Well, I guess I have to beat this horse dead although I think this discussion is beyond the scope of this paper. However, to complete my argument, those two trials, the MD Anderson one and the Roselle trial, were performed well before the lung cancer staging system revisions in 1997. They included patients who had T3 N0 lesions that initially were staged as IIIA but have been now downstaged to stage II because of improved survival. Although those older studies are stage IIIA, by today's standards they include stage II disease as well and therefore are inherently flawed, in addition to having very few patients. That is a different subset of inhomogeneous patients, not the microscopic single station nodal disease that we speak about today in stage IIIA lung cancer with VATS lobectomy.