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ORIGINAL ARTICLE

Thoracoscopic lobectomy is associated with improved short-term and equivalent oncological outcomes compared with open lobectomy for clinical Stage I non-small-cell lung cancer: a propensity-matched analysis of 963 cases[†]

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Abstract

OBJECTIVES: Previous literature has reported lower morbidity for video-assisted thoracoscopic surgery lobectomy (VL) compared with open lobectomy (OL); however, most comparative studies have been retrospective and have failed to compare well-matched patient groups, therefore allowing selection bias to influence results. Furthermore, oncological adequacy of VL has recently been questioned, particularly with respect to lymphadenectomy. This study aimed to evaluate short- and long-term outcomes of a large cohort of consecutive patients with c-stage I non-small-cell lung cancer (NSCLC) that underwent either VL or OL.

METHODS: Consecutive patients with c-stage I NSCLC who underwent lobectomy without preoperative therapy were reviewed. Univariable, multivariable and propensity-matched analyses were performed. VL patients who underwent conversion to OL were analysed within the VL group.

RESULTS: VL was performed in 307 (32%) patients and OL in 656 (68%). Twenty-two (7%) patients converted from VL to OL. Although there were no differences in overall p-stage grouping, there were fewer patients with pT2 tumours in the VL group (39 vs 48%, $P = 0.012$) and fewer patients with squamous cell histology (26 vs 18%, $P = 0.006$). These differences resolved after propensity matching. In unmatched and matched analyses, VL was associated with less overall morbidity, less pulmonary morbidity, fewer atrial arrhythmias, shorter chest tube duration and shorter hospital stay than patients who had OL. Thirty-day in-hospital mortality was 0.3 and 1.4%, for VL and OL groups, respectively (P = NS). In unmatched analysis (log rank), 5-year survival favoured VL (78 vs 68%, $P = 0.007$); however, after propensity matching there was only a trend towards improved survival with VL (78 vs 73%, $P = 0.071$). Multivariable Cox regression analysis revealed VL (hazard ratio (HR) 0.64, 95% confidence interval (CI) 0.46–0.92), male sex (HR 1.43, 95% CI 1.10–1.86), Zubrod performance status (HR 3.42, 95% CI 1.26–9.29) and increasing age (HR 1.04, 95% CI 1.03–1.06) to be independent predictors of survival.

CONCLUSIONS: Patients with clinical Stage I NSCLC undergoing VL have less perioperative morbidity compared with matched OL controls. Regional lymphadenectomy, nodal upstaging, overall and disease-free survival were similar between VL and OL groups. In experienced centres, VL is an acceptable operation for patients with c-stage I NSCLC.

Keywords: Thoracoscopy • Thoracotomy • Lobectomy • Non-small-cell lung cancer • Survival

INTRODUCTION

Lobectomy performed by thoracotomy is the standard of care for fit patients with clinical Stage I non-small-cell lung cancer (NSCLC) [1]; however, the last two decades have seen increasing adoption of video-assisted thoracoscopic surgery (VATS) lobectomy by thoracic surgeons [1–7]. VATS lobectomy (VL) avoids the trauma of rib spreading and reported advantages of VL over open lobectomy (OL) include preservation of pulmonary function, less postoperative pain, a lower rate of atrial fibrillation, shorter chest tube duration and a shorter hospitalization [2]. Despite a growing adoption by thoracic surgeons of VL, there are no large prospective studies comparing the efficacy of VL to OL. Most comparative studies have been retrospective and have failed to compare well-matched patient groups, therefore allowing selection bias to influence results. Furthermore, the majority of studies have focused on short-term rather than on oncological outcomes [1–10]. In this study, we aimed to examine both short-term and long-term outcomes in a homogenous group of patients with NSCLC (all clinical

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Stage I) who underwent lobectomy by either VATS or open technique. To account for potential changes in management over time, we limited analysis to a 10-year period when both open and VATS were being performed, and to minimize selection bias we performed propensity score-based matching to generate two homogenous groups for comparison.

MATERIALS AND METHODS

The study was approved by the Institutional Review Board of the University of Texas M.D. Anderson Cancer Center and waiver of informed consent approved. A retrospective analysis was performed of a prospectively maintained database. We identified 963 consecutive patients with c-stage I NSCLC who underwent lobectomy between January 2002 and December 2011. VL was performed in 307 (32%) patients and OL in 656 (68%). Clinical staging was performed according to the sixth edition of the American Joint Commission on Cancer (AJCC), as most of the prospectively collected patient data predated the current seventh edition of the staging system. Pathological staging was according to the AJCC seventh Edition. Patients were routinely staged with both computed tomography (CT) and positron emission tomography (PET) but mediastinoscopy was used only selectively (13% in each group, P = NS). Patients who received preoperative chemotherapy or radiotherapy were excluded. We also excluded patients who underwent robotic lobectomy, bilobectomy, sleeve lobectomy or lobectomy with accompanying vascular, chest wall or diaphragm resection. VL was performed using a 4–5 cm anterior non-rib spreading access incision and one to three additional port sites. All specimens were removed via the access incision using an impervious specimen retrieval bag. OL was performed via a posterolateral thoracotomy through the fifth interspace. In all cases, the serratus anterior muscle was preserved and division of the latissimus dorsi was performed in a minority of cases. Mediastinal nodal evaluation included dissection of all hilar (N1) and at least three mediastinal (N2) nodal stations. Postoperatively patients were extubated in the operating room, transferred to the postanaesthesia recovery unit and then to the thoracic ward with continuous electrocardiographic telemetric monitoring until discharge from hospital. All patients were managed according to the same standardized postoperative pulmonary resection protocol. Chest drains were typically removed when there was no air leak and the volume was less than 400 cc/day.

Perioperative mortality was defined as death within 30 days of lobectomy or during initial hospitalization. Pulmonary morbidity included any of the following: atelectasis requiring bronchoscopy, pneumonia, adult respiratory distress syndrome (ARDS), respiratory arrest, bronchopleural fistula, initial ventilator support longer than 48 h, reintubation, tracheostomy, air leak longer than 5 days. VL was successfully performed in 285 (93%) patients, but in 22 patients the procedure required conversion to thoracotomy because of intraoperative bleeding (12), incomplete fissures (4), tumour extent (3), poor lung isolation (2) and dense lymphadenopathy (1). These patients were included in the VATS group and considered as 'intention to treat' for analysis purposes. Local recurrence was defined as recurrence within the ipsilateral haemothorax and/or mediastinum.

Comparisons of preoperative characteristics between groups were made using the two-sample non-parametric McNemar's and Fisher exact tests. To identify correlates of survival, logistic regression analyses were performed. When developing the multivariable model, we first considered univariable logistic regressions to evaluate associations of each variable with survival. The multivariable model initially considered variables with a univariable probability value of less than 0.25. To account for differences between the open and VATS groups in an additional way, 1 : 1 propensity matching was performed. We formulated an augmented model that identified the common denominators of group membership (VATS or open). The initial variables included were: age, gender, coronary artery disease, chronic obstructive airway disease, diabetes, hypertension, renal insufficiency, cerebrovascular disease, performance status, sidedness, lobe resected, histology and c-T-stage. Renal insufficiency, cerebrovascular disease and lobe resected were subsequently excluded from the final model because they prevented convergence. The propensity score was used as the sole criterion for matching pairs of patients. A matched pair was formed when a patient was selected from the open (control) group whose propensity score was nearest to that of a patient in the VATS (case) group.

RESULTS

Patient characteristics

Univariate analysis revealed no significant differences in age; gender; pulmonary, cardiac, neurological and renal comorbidities or performance status between VATS and open groups; however, there were more patients with diabetes in the open group (9 vs 13%, P = 0.027) (Table 1). Preoperative predicted forced expiratory volume in one second (FEV1)% (89.3 vs 86.3%, P = 0.007), but not diffusion capacity of the lung for carbon monoxide (DLCO)% (mean 83.5 vs 81.1%, P = 0.136), was significantly higher in the VATS group. More patients in the VATS group had adenocarcinoma (75 vs 65%, P = 0.006), clinical T1 stage tumours (75 vs 59%, P < 0.001) and pathological T1 stage tumours (58 vs 48%, P = 0.012) compared with the open group. Distribution of lobes resected was similar apart from a non-significant trend towards more patients with left upper lobectomy in the OL group (Table 2). Because of differences in physiological and tumour-related variables between groups 1 : 1 propensity score-based case matching was performed. This resulted in two patient groups (n = 307 each) that were similar in age, gender, performance status, comorbidities, pulmonary function, histology, tumour diameter and c-stage (Table 3).

Perioperative outcomes

In univariate analysis of non-matched groups, VL was associated with lower incidence of new onset atrial arrhythmias (12 vs 20%, P = 0.001), fewer major pulmonary events (9 vs 17%, P = 0.003), lower overall morbidity (19 vs 36%, P < 0.001), shorter chest tube duration (median 2 vs 3 days, P < 0.001) and shorter hospitalization (median 4 vs 6 days, P < 0.001). VL was associated with a slightly higher incidence of reoperation (3 vs 1%, P = 0.018) and a slightly longer operative time (median 173 vs 160 min, P < 0.001) (Table 3).

Univariate analysis of matched controls showed that VL remained highly associated with a lower incidence of postoperative atrial arrhythmias (12 vs 21%, P = 0.003), major pulmonary events (9 vs 19%, P = 0.001), overall morbidity (19 vs 37%, P < 0.001), longer operative time (median 173 vs 159 min,

Table 1: Patient characteristics in patients undergoing lobectomy

Characteristics	VATS (*n* = 307)	Open (unmatched, *n* = 656)	*P*-value	Open (matched, *n* = 307)	*P*-value
Age, year	66 ± 10	67 ± 10	0.12	66 ± 10	0.49
Male gender, *n* (%)	134 (44)	320 (49)	0.14	129 (42)	0.73
CAD, *n* (%)	45 (15)	107 (16)	0.51	39 (13)	0.56
HTN, *n* (%)	152 (50)	307 (47)	0.43	150 (50)	0.93
DM, *n* (%)	26 (9)	88 (13)	0.03	39 (5)	0.13
CVD, *n* (%)	14 (5)	24 (4)	0.50	10 (3)	0.52
COPD, *n* (%)	42 (14)	93 (14)	0.94	39 (14)	1.0
Zubrod score, *n* (%)					
0	193 (51)	385 (58)	0.27	193 (50)	1.0
1	110 (36)	266 (41)		112 (37)	
2	4 (13)	5 (1)		2 (1)	
FEV1% predicted (mean)	89.3	86.3	0.007	87.3	0.093
DLCO% predicted (mean)	83.5	81.1	0.136	81.7	0.51
Histology, *n* (%)					
Adenocarcinoma	231 (75)	427 (65)	0.006	240 (78)	0.28
Squamous cell	54 (18)	172 (26)		50 (16)	
NSCLC, other	22 (7)	57 (9)		17 (6)	
Clinical T stage, *n* (%)					
T1	229 (75)	384 (58)	0.0001	217 (71)	0.13
T2	78 (25)	272 (42)		90 (29)	
Tumour diameter, mean	2.5 ± 1	3.2 ± 2	0.0001	2.8 ± 2	0.18

Data are presented as mean + standard deviations where shown.
Open: conventional thoracotomy; VATS: video-assisted thoracoscopic surgery; CAD: coronary artery disease; HTN: hypertension; DM: diabetes mellitus; CVD: cerebrovascular disease; COPD: chronic obstructive pulmonary disease; NSCLC: non-small-cell lung cancer; FEV1: forced expiratory volume in one second; DLCO: diffusion capacity of the lung for carbon monoxide.

Table 2: Anatomic distribution of lobectomies (*n* = 963)

Anatomic distribution	Open (*n* = 656)	VATS (*n* = 307)	*P*-value
Right upper lobectomy, *n* (%)	223 (36)	110 (36)	0.098
Right middle lobectomy, *n* (%)	35 (5)	21 (7)	
Right lower lobectomy, *n* (%)	89 (14)	55 (18)	
Left upper lobectomy, *n* (%)	196 (30)	69 (23)	
Left lower lobectomy, *n* (%)	103 (16)	52 (17)	

Open: conventional thoracotomy; VATS: video-assisted thoracoscopic surgery.

P = 0.007), shorter chest tube duration (median 2 vs 3 days, *P* < 0.001) and shorter hospitalization (median 4 vs 6 days, *P* < 0.001) (Table 3). In addition, more patients in the open group required transfusion in the postoperative period (7 vs 4%, *P* = 0.048).

Lymphadenectomy

There was no difference in the mean number of lymph node stations sampled between the VATS and open groups (4.2 vs 4.3, *P* = 0.621) or in the number of N1 (2.5 vs 1.6, *P* = 0.262) or N2 stations (2.6 vs 2.5, *P* = 0.139). There was similar distribution between groups of the individual nodal stations that were sampled with the exception of Stations 2 and 12, which were sampled more frequently in the VATS group, and Station 9, which was sampled more often in the open group (Table 4). Overall upstaging of clinical stage occurred in 35% of the VATS group and in 38% of the open group (*P* = 0.51) with no statistical differences seen in either tumour (24 vs 23%, *P* = 0.16) or nodal (15 vs 20%, *P* = 0.83) upstaging. No significant differences were identified between groups in final pathological stage groupings (AJCC seventh edition) (Table 5).

Recurrence and survival

Recurrence data were unavailable for 7 matched pairs leaving 300 patients in each group for analysis. No significant differences in overall (16 vs 11%), local (3 vs 3%), regional (7 vs 5%) or distant recurrence (5 vs 4%) were found in the VL and OL groups, respectively. Multivariate analysis revealed VL to be an independent predictor of survival along with, gender, performance status, age and pathological stage (Table 6). In analysis of unmatched patients (*n* = 963), there was a statistically significant difference in overall

Table 3: Postoperative events in patients undergoing lobectomy

Postoperative event	VATS (*n* = 307)	Open (unmatched, *n* = 656)	*P*-value	Open (matched, *n* = 307)	*P*-value
Atelectasis	5 (2)	21 (3)	0.20	5 (2)	1.0
Air leak >5 days, *n* (%)	13 (4)	51 (8)	0.15	30 (10)	1.0
Pneumonia, *n* (%)	17 (6)	55 (8)	0.12	28 (9)	0.12
Bronchopleural fistula, *n* (%)	0 (0)	2 (<1)	1.0	1 (<1)	1.0
Tracheostomy, *n* (%)	3 (1)	12 (2)	0.41	7 (2)	0.34
Reintubation, *n* (%)	7 (2)	18 (3)	0.67	8 (3)	1.0
Respiratory arrest, *n* (%)	2 (1)	9 (1)	0.51	5 (2)	0.45
ARDS, *n* (%)	3 (1)	9 (1)	0.76	6 (2)	0.51
MI, *n* (%)	2 (1)	8 (1)	0.52	4 (1)	0.68
Atrial arrhythmia, *n* (%)	36 (12)	132 (20)	0.001	64 (21)	0.003
Ventricular arrhythmia, *n* (%)	0 (0)	4 (1)	0.31	2 (1)	0.50
CVA, *n* (%)	1 (<1)	3 (1)	1.0	0 (0)	1.0
PE, *n* (%)	1 (<1)	1 (<1)	0.54	0 (0)	1.0
DVT, *n* (%)	0 (0)	0 (0)	1.0	0 (0)	1.0
Bleeding, *n* (%)	3 (1)	7 (1)	1.0	3 (1)	1.0
Empyema, *n* (%)	0 (0)	3 (1)	1.0	1 (<1)	1.0
Sepsis, *n* (%)	3 (1)	10 (2)	0.77	8 (3)	0.23
Renal failure, *n* (%)	1 (<1)	12 (2)	0.07	7 (2)	0.07
Reoperation, *n* (%)	9 (3)	6 (1)	0.02	4 (1)	0.27
Chest tube duration, median days	2 ± 4	3 ± 20	0.0001	3 ± 19	0.0001
Operative time, median minutes	173 ± 57	160 ± 57	0.0001	159 ± 56	0.0001
Length of stay, median days	4 ± 8	6 ± 7	0.0001	6 ± 8	0.0001
Pulmonary morbidity	29 (9)	110 (17)	0.003	59 (19)	0.001
Overall morbidity	59 (19)	220 (34)	0.0001	114 (37)	0.0001
Thirty-day/in-hospital death	1 (<1)	9 (1)	0.18	5 (2)	0.22
Ninety-day death	3 (1)	16 (2)	0.13	8 (3)	0.23

Data are presented as mean + standard deviations where shown.
Open: conventional thoracotomy; VATS: video-assisted thoracoscopic surgery; ARDS: acute respiratory distress syndrome; MI: myocardial infarction; CVA: cerebrovascular accident; PE: pulmonary embolus; DVT: deep venous thrombosis.

Table 4: Number of nodal stations after propensity score-based matching by location and approach (*n* = 614)

Nodal LN stations	VATS (*n* = 307)	Open (matched, *n* = 307)	*P*-value
1	5 (2)	6 (2)	1.0
2	49 (16)	24 (8)	0.003
3	14 (5)	8 (3)	0.82
4	189 (62)	182 (59)	0.60
5	93 (30)	72 (23)	1.0
6	29 (9)	34 (11)	0.60
7	258 (84)	268 (87)	0.30
8	33 (11)	35 (11)	0.89
9	107 (35)	164 (53)	0.001
10	184 (60)	182 (59)	0.94
11	234 (76)	218 (71)	0.18
12	74 (24)	50 (16)	0.02
Mean ± SD	4.18 ± 1.3	4.28 ± 1.8	0.61
Median	4.0	4.0	

Open: conventional thoracotomy; VATS: video-assisted thoracoscopic surgery; LN: lymph node; SD: standard deviation.

survival at 5 years, favouring the VATS group (5-year survival 78 vs 68%, $P = 0.007$); however, when only matched groups were compared there was no difference (5-year survival 78 vs 73%, $P = 0.071$) (Fig. 1A and B). Similarly, disease-free survival was significantly greater in the VATS group but only when unmatched patients were considered (Fig. 2A and B).

DISCUSSION

Thoracoscopic (VATS) lobectomy has been associated with reduced perioperative morbidity in numerous single institution as well as large database/registry series. However, many of these studies fail to take into account inherent biases in patient selection

Table 5: Pathological stage after propensity score-based matching ($n = 614$)

Pathological stage (AJCC seventh edition)	VATS ($n = 307$)	Open (matched, $n = 307$)	*P*-value
Tumour stage, *n* (%)			
T1	179 (58)	172 (56)	0.21
T2	117 (38)	116 (38)	
T3	7 (2)	13 (4)	
T4	4 (1)	6 (2)	
Nodal stage, *n* (%)			
N0	261 (85)	247 (81)	0.17
N1	27 (9)	36 (12)	
N2	19 (6)	24 (8)	
Metastasis stage, *n* (%)			
M0	306 (100)	305 (99)	1.0
M1	1 (<1)	2 (1)	
Overall p-stage			
IA	152 (50)	143 (47)	0.078
IB	90 (29)	76 (25)	
IIA	32 (10)	44 (14)	
IIB	9 (3)	9 (3)	
IIIA	23 (8)	33 (11)	
IIIB	0 (0)	0 (0)	
IV	1 (<1)	2 (1)	

Open: conventional thoracotomy; VATS: video-assisted thoracoscopic surgery.

Table 6: Multivariate analysis for survival

Variable	Hazard ratio	95% confidence interval	*P*-value
VATS	0.68	0.48–0.97	0.014
Male gender	1.39	1.07–1.81	0.004
Zubrod score			0.004
1	1.44	1.11–1.87	0.007
2	3.17	1.16–8.63	0.024
Age	1.04	1.04–1.06	0.0001
Pathological stage			0.001
II	1.35	0.98–1.87	0.071
III	2.14	1.48–3.12	0.0001
IV	4.38	1.79–10.73	0.001

VATS: video-assisted thoracoscopic surgery.

related to differences in variables such as clinical stage, comorbid conditions and performance status and histology, which may greatly influence not only short-term but also long-term outcomes. Furthermore, many studies exclude from analysis patients who have undergone conversion from VL to OL or analyse these patients in the open group, thus biasing results in favour of VATS. Although it is impossible in any retrospective study to fully take into account all of the factors that may influence the choice of VATS or open procedure, we attempted to minimize selection bias by limiting our initial analysis to only patients with clinical Stage I NSCLC who underwent simple lobectomy (the most common group of patients who would be considered for VL). In addition, since stage and histology are critical determinants of long-term outcomes, we controlled for these variables by performing propensity score-based matching. As preoperative staging and operative management of patients with NSCLC may change over time, we limited the study to a recent 10-year period, during which there was uniform use of preoperative imaging (PET and CT). Furthermore, this study reports all consecutive patients who underwent VL during this period and includes our initial learning experience. During the study period of seven thoracic surgeons, two exclusively performed OL. Importantly, we considered patients who underwent conversion from VL to OL as belonging to the VATS group, analysing on an intention to treat basis to avoid biasing results against OL.

Our results are strikingly consistent with those of other recent studies. In both unmatched and match analyses, overall morbidity was significantly reduced (by over 45%). This is similar to the 55% reduction in morbidity observed by Kirby *et al.* [11] who performed one of only three prospective randomized studies ever performed comparing outcomes of VATS with those of OL. Two recent propensity-matched studies have also reported significant reductions in overall morbidity. In a series of 1079 patients who underwent lobectomy for Stage I–III NSCLC Villamizar *et al.* [12] reported a significant difference in overall morbidity rates between patients undergoing VL and OL (30 vs 50%, $P = 0.0001$), and, as in our study, this difference was maintained in a comparison of matched cohorts (31 vs 49%, respectively, $P = 0.0001$). Similarly, a retrospective intention to treat analysis of 741 patients with clinical Stage IA NSCLC by Flores *et al.* [8] showed significant reduction in overall morbidity associated with VL when compared with a matched cohort of OL patients (23 vs 33%, $P = 0.03$). Reductions in operative morbidity have also been confirmed in large multicentre database studies. In a retrospective subset analysis of patients enrolled in ACOSOG ZD0030, 66 patients who underwent VL were compared with 686 that had an OL [13]. Morbidity was significantly less in the VATS group (27 vs 48%, $P < 0.05$). In an analysis of outcomes from the Society of Thoracic Surgeons (STS) database, Paul *et al.* [14] reported less overall morbidity in 1281 patients (45% of which had clinical Stage I) undergoing VL compared with a 1 : 1 matched group of patients who had thoracotomy (26 vs 35%, $P < 0.001$). Lastly, an analysis of the National Inpatient Sample Database showed that patients who underwent VATS had fewer complications than unmatched patients who had OL (38 vs 44%, $P < 0.001$) [7]. On multivariable analysis, the

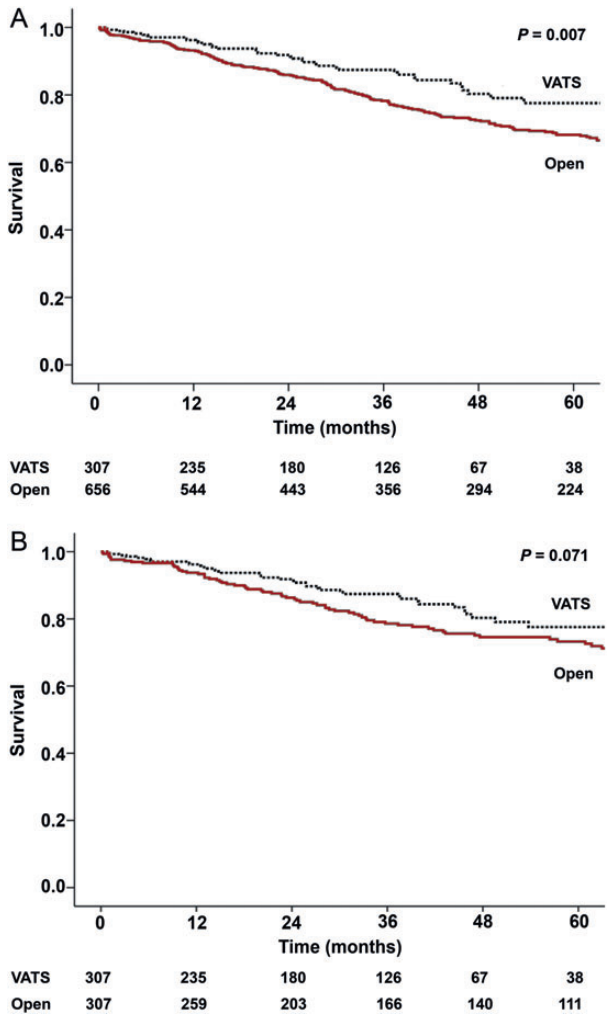

Figure 1: Kaplan–Meier overall survival estimates of VL and OL in (**A**) unmatched analysis ($n = 963$) and (**B**) propensity-matched analysis ($n = 614$).

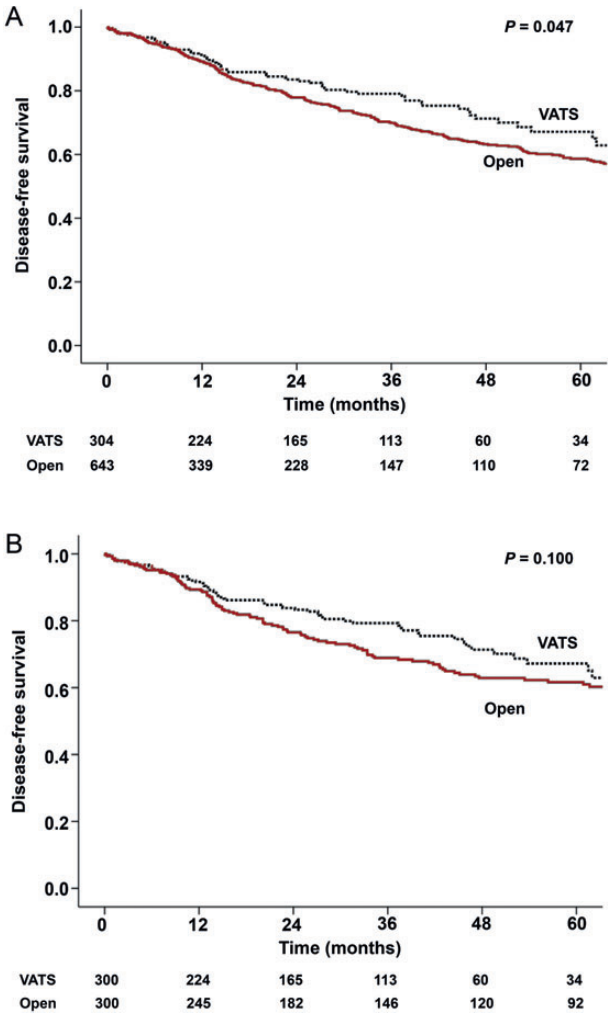

Figure 2: Kaplan–Meier disease-free survival estimates of VL and OL in (**A**) unmatched analysis ($n = 944$) and (**B**) propensity-matched analysis ($n = 600$).

authors found that VATS was independently associated with lower risk of morbidity. The majority of the reduction in overall morbidity that we observed related to differences in the incidence of pulmonary complications and atrial arrhythmias, which is consistent with other published reports [2, 12, 14]. With respect to the findings of shorter duration of chest tube and hospitalization, this has been reported by several other authors; however, as the proportion of VL to OL was greater in the latter half of the study period, it is certainly possible that observed differences may be related to subtle changes in postoperative management over the study period rather than to the procedure itself [2, 12–14].

Although the superiority of VATS in terms of immediate postoperative outcomes is increasingly appreciated, there remains concern regarding whether it is an operation that is oncologically equivalent to OL. In particular, proponents of OL have criticized the ability of VL to achieve an adequate lymphadenectomy [15]. For instance, a recent (non-matched) analysis of 1513 patients with clinical Stage I from the Danish Lung Cancer Registry showed that more patients who underwent OL were upstaged to pN1 (13 vs 8%, $P < 0.001$) and pN2 (12 vs 4%, $P < 0.001$) [16]. In contrast, a larger analysis of 11 531 patients with clinical Stage I NSCLC from the STS database showed that N0–N2 upstaging was similar between patients who underwent VL or OL (4.9 vs 5.0%, respectively) [17]. We did not find that VATS was inferior to OL with regard to either hilar or mediastinal nodal sampling. We found no significant differences in the mean number of N1 and N2 stations biopsied and nodal upstaging was similar for VATS and open groups (15 vs 20%, P = NS). We specifically did not analyse the number of nodes resected at each nodal station, as this measure is virtually meaningless because of fragmentation of nodal specimens and the likelihood of over-counting by pathologists. The ability of VATS to achieve nodal sampling equivalent to OL has been shown by several other investigators. D'Amico *et al.* [18] compared 199 patients with NSCLC (mostly clinical Stage I) with 189 patients who underwent OL and showed that similar numbers of N1 and N2 stations were resected in each group (mean 4.8 and 4.4, respectively, $P = 0.06$) and Ramos *et al.* [19] documented a higher total number of nodal stations biopsied with VATS compared with OL (5.1 vs 4.5, $P < 0.001$) in a non-matched study of patients who underwent either VL ($n = 96$) or OL ($n = 200$). A recent single-centre prospective study compared nodal specimens removed in patients randomized to either VATS ($n = 34$) or OL ($n = 32$). No differences were identified between groups in the mean number of nodes removed or in the number of nodes resected per station [20].

Studies evaluating survival differences between VL and OL have reported varying results. A single randomized study prospectively examined 5-year survival among patients with clinical Stage-I

NSCLC who underwent either VL (n = 48) or OL (n = 52) [21]. No significant difference in 5-year survival was noted between the VATS and open groups, with 5-year survival of 90 and 85%, respectively, though was underpowered. In an analysis of survival outcomes using Surveillance, Epidemiology and End Results Medicare data, Farjah *et al*. [22] found that in patients undergoing lobectomy for lung cancer between 1994 and 2002, only 6% underwent VL and survival was similar in these patients as those who underwent OL (hazard ratio (HR) 0.97, 95% confidence interval (CI) 0.88–1.07). Two single-institution studies have compared survival retrospectively among patients with Stage I NSCLC. Yang *et al*. [23] performed VL on 43 patients and OL on 98 patients with p-stage I NSCLC and found no significant survival difference at 5 years (79 vs 82%, respectively). A larger series performed from Memorial Sloan Kettering Cancer Center, reported similar 5-year survival rates in propensity-matched patients with c-stage I NSCLC who underwent VL (n = 398) or OL (n = 343) (79 and 75%, respectively, P = NS) [8].

In contrast, three separate meta-analyses have each reported statistically significant differences in survival benefit favouring VL. Whitson *et al*. [9] evaluated 39 studies with a cumulative sample size of 6370 patients and reported a 4-year survival of 88% for patients that underwent VATS compared with 71% for patients after an OL (P = 0.003). Similarly, the analysis by Yan *et al*. [1], revealed a relative risk reduction of 0.66 (95% CI 0.45–0.97) in terms of death at 5-years. Most recently, Taioli *et al*. [24] reported a meta-analysis of 20 observational studies and concluded that VL was associated with an absolute survival advantage of 5% over OL at 5 years, identical to the difference we observed in the comparison of matched VATS and open groups (78 vs 73%, P = 0.071) and similar to differences reported in other single-institution series. It should be noted that most of the studies that have been used in meta-analyses derive from retrospective studies of non-matched patients with a high likelihood of inherent selection bias. Therefore, any conclusions regarding influence of VL on survival must be tempered with the realization that there may be confounding variables (known and unknown) that might influence survival and that observed differences may not be related to the procedure performed but rather to factors that led to procedure selection. As evidenced by our study, multivariate analysis and propensity matching may lessen this bias but it cannot be avoided entirely.

In summary, in patients with clinical Stage I NSCLC treated in a high volume, experienced centre VL was associated with reduced perioperative morbidity, shorter hospital stay and equivalent oncological outcomes compared with OL. We believe that when performed with maintenance of oncological surgical principles VL is an acceptable alternative to OL. Ultimately, a larger, prospective trial comparing survival in a highly controlled, stage equivalent and homogenous group of patients would be required to reveal statistically and clinically relevant differences in long-term survival.

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REFERENCES

[1] Yan TD, Black D, Bannon PG, McCaughan BC. Systematic review and meta-analysis of randomized and nonrandomized trials on safety and efficacy of video-assisted thoracic surgery lobectomy for early-stage non-small-cell lung cancer. J Clin Oncol 2009;27:2553–62.

[2] Handy JR Jr, Asaph JW, Douville EC, Ott GY, Grunkemeier GL, Wu Y. Does video-assisted thoracoscopic lobectomy for lung cancer provide improved functional outcomes compared with open lobectomy? Eur J Cardiothorac Surg 2010;37:451–5.

[3] McKenna RJ Jr, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1,100 cases. Ann Thorac Surg 2006;81:421–5.

[4] 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.

[5] 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.

[6] Park JS, Kim K, Choi MS, Chang SW, Han WS. Video-assisted thoracic surgery (VATS) lobectomy for pathologic stage I non-small cell lung cancer: a comparative study with thoracotomy lobectomy. Korean J Thorac Cardiovasc Surg 2011;44:32–8.

[7] Park HS, Detterbeck FC, Boffa DJ, Kim AW. Impact of hospital volume of thoracoscopic lobectomy on primary lung cancer outcomes. Ann Thorac Surg 2012;93:372–9.

[8] Flores RM, Park BJ, Dycoco J, Aronova A, Hirth Y, Rizk NP *et al*. Lobectomy by video-assisted thoracic surgery (VATS) versus thoracotomy for lung cancer. J Thorac Cardiovasc Surg 2009;138:11–8.

[9] Whitson BA, Groth SS, Duval SJ, Swanson SJ, Maddaus MA. Surgery for early-stage non-small cell lung cancer: a systematic review of the video-assisted thoracoscopic surgery versus thoracotomy approaches to lobectomy. Ann Thorac Surg 2008;86:2008–16.

[10] Kim K, Kim HK, Park JS, Chang SW, Choi YS, Kim J *et al*. Video-assisted thoracic surgery lobectomy: single institutional experience with 704 cases. Ann Thorac Surg 2010;89:S2118–22.

[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;109:997–1001.

[12] Villamizar NR, Darrabie MD, Burfeind WR, Petersen RP, Onaitis MW, Toloza E *et al*. Thoracoscopic lobectomy is associated with lower morbidity compared with thoracotomy. J Thorac Cardiovasc Surg 2009;138:419–25.

[13] Scott WJ, Allen MS, Darling G, Meyers B, Decker PA, Putnam JB *et al*. Video-assisted thoracic surgery versus open lobectomy for lung cancer: a secondary analysis of data from the American College of Surgeons Oncology Group ZD0030 randomized clinical trial. J Thorac Cardiovasc Surg 2010;139:976–81.

[14] Paul S, Altorki NK, Sheng S, Lee PC, Harpole DH, Onaitis MW *et al*. Thoracoscopic lobectomy is associated with lower morbidity than open lobectomy: a propensity-matched analysis from the STS database. J Thorac Cardiovasc Surg 2010;139:366–78.

[15] Denlinger CE, Fernandez F, Meyers BF, Pratt W, Zoole JB, Patterson GA *et al*. Lymph node evaluation in video-assisted thoracoscopic lobectomy versus lobectomy by thoracotomy. Ann Thorac Surg 2010;89:1730–5.

[16] Licht PB, Jørgensen OD, Ladegaard L, Jakobsen E. A national study of nodal upstaging after thoracoscopic versus open lobectomy for clinical stage i lung cancer. Ann Thorac Surg 2013;96:943–50.

[17] Boffa DJ, Kosinski AS, Paul S, Mitchell JD, Onaitis M. Lymph node evaluation by open or video-assisted approaches in 11,500 anatomic lung cancer resections. Ann Thorac Surg 2012;94:347–53.

[18] D'Amico TA, Niland J, Mamet R, Zornosa C, Dexter EU, Onaitis MW. Efficacy of mediastinal lymph node dissection during lobectomy for lung cancer by thoracoscopy and thoracotomy. Ann Thorac Surg 2011;92:226–31.

[19] Ramos R, Girard P, Masuet C, Validire P, Gossot D. Mediastinal lymph node dissection in early-stage non-small cell lung cancer: totally thoracoscopic vs thoracotomy. Eur J Cardiothorac Surg 2012;41:1342–8.

[20] Palade E, Passlick B, Osei-Agyemang T, Günter J, Wiesemann S. Video-assisted vs open mediastinal lymphadenectomy for Stage I non-small-cell lung cancer: results of a prospective randomized trial. Eur J Cardiothorac Surg 2013;44:244–9.

[21] 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;24:27–30.

[22] Farjah F, Wood DE, Mulligan MS, Krishnadasan B, Heagerty PJ, Symons RG *et al*. Safety and efficacy of video-assisted versus conventional lung resection for lung cancer. J Thorac Cardiovasc Surg 2009;137:1415–21.

[23] Yang X, Wang S, Qu J. Video-assisted thoracic surgery (VATS) compares favorably with thoracotomy for the treatment of lung cancer: a five-year outcome comparison. World J Surg 2009;33:1857–61.

[24] Taioli E, Lee DS, Lesser M, Flores R. Long-term survival in video-assisted thoracoscopic lobectomy vs open lobectomy in lung-cancer patients: a meta-analysis. Eur J Cardiothorac Surg 2013;44:591–7.