Review Article

True Video-Assisted Thoracic Surgery for Early-Stage Non-Small Cell Lung Cancer

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ABSTRACT Since its inception, minimally invasive surgery has made a dramatic impact on all branches of surgery. Video-assisted thoracic surgery (VATS) lobectomy for early-stage non-small cell lung cancer (NSCLC) was first described in the early 1990s and has since become popular in a number of tertiary referral centers. Proponents of this relatively new procedure cite a number of potentially favorable perioperative outcomes, possibly due to reduced surgical trauma and stress. However, a significant proportion of the cardiothoracic community remains skeptical, as there is still a paucity of robust clinical data on long-term survival and recurrence rates.

The definition of 'true' VATS has also been under scrutiny, with a number of previous studies being considered 'mini-thoracotomy lobectomy' rather than VATS lobectomy . We hereby examine the literature on true VATS lobectomy, with a particular focus on comparative studies that directly compared VATS lobectomy with conventional open lobectomy.

KeyWords: Video-assisted thoracic surgery, VATS, non-small cell lung cancer, lobectomy.

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Since the first laparscopic cholecystectomy in the late 1980s, minimally invasive surgery has revolutionised many branches of surgery. After the first video-assisted thoracic surgery (VATS) lobectomy for early stage non-small-cell lung cancer (NSCLC) was simultaneously described by several institutions in the early 1990s (1-3), several studies have demonstrated potential advantages associated with this new technique, possibly due to reduced trauma encountered during surgery (Table1) (4-13). To date, two randomised controlled trials (RCTs) have been completed, demonstrating the safety and feasibility of VATS lobectomy compared to conventional open lobectomy (1,4). Perhaps more importantly, a recent systematic review and meta-analysis suggested that VATS lobectomy does not differ significantly to open lobectomy in locoregional recurrence rate, and might even be associated with a reduced systemic recurrence rate and an improved overall 5-year mortality rate (14). From such reports, it is not surprising that the utility of VATS lobectomy has steadily increased over the last decade, especially amongst high-volume centers (15).

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Despite the encouraging results for VATS lobectomy, it has been recognised that heterogeneous practice exists between institutions, including significant differences in patient selection, the use of rib spreaders or retractors, and the length of access. Indeed, the very definition of VATS has been under scrutiny, with some techniques being considered 'video-assisted mini-thoracotomy' rather than true non-rib spreading VATS lobectomy (4). In response, there has been a concerted effort by the International Society of Minimally Invasive Cardiothoracic Surgery to standardize the definition of VATS (16). Based on these definitions, only a limited number of non-randomised comparative studies have directly evaluated the true VATS approach for early stage lung cancers. We hereby review the current literature on the safety and efficacy of VATS lobectomy, with a particular focus on the results of these non-randomized comparative studies.

Safety

Perioperative mortality and morbidity

As with any new surgical technique, avoidable adverse outcomes might be expected to arise as a result of inexperience (17). However, from the available data, VATS lobectomy has been found to have an extremely low perioperative mortality rate. In deed, no comparative studies have shown any significant difference in postoperative mortality rates comparing VATS lobectomy to the conventional open technique (Table 2). This was further support-

Table 1 Summary of trials directly comparing true video-assisted thoracic surgery (VATS) versus open lobectomy in patients with early-stage non-small cell lung cancer

Study	Year	Study	n	Staging	Access
Sugi et al.[4]	2000	RCT	100	cIA	8cm
Sugiura et al.[5]	1999	OC	44	cIA (36), cIB (8)	6cm
Inada et al.[6]	2000	OC	54	cIA+B	7cm
Yim et al.[7]	2000	OC	36	cIA+B	NR
Koizumi et al.[8]	2002	OC	87	cIA+B	10cm
Muraoka et al.[9]	2006	OC	85	cIA	8cm
Sakuraba et al.[10]	2007	OC	140	cIA	5cm
Petersen et al.[11]	2007	OC	100	pI (40), pII (24)	5cm
Whitson et al.[12]	2007	OC	147	cIA+B	6cm
Park et al.[13]	2007	OC	244	cIA+B	4cm

RCT, randomized controlled trial; OC, observational cohort; NR, not reported.

Table 2 Perioperative outcomes and postoperative complications following video-assisted thoracic surgery (VATS) or open lobectomy for early-stage non-small-cell lung cancer

Study	Mortality		Conversion rate	Persistent air leak		Pneumonia		Arrhythmia		Operating time (hours)		Blood loss (mL)		Chest drain (days)		Hospital stay (days)	
	VATS	Open		VATS	Open	VATS	Open	VATS	Open	VATS	Open	VATS	Open	VATS	Open	VATS	Open
Sugi et al.[4]	NR	NR	4%	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Sugiura et al.[5]	0/22	0/22	12%	2/22	3/22	2/22	0/22	NR	NR	3.8	3.3	150	300	NR	NR	23	22
Inada et al.[6]	NR	NR	NR	0/24	0/30	NR	NR	NR	NR	4.7	3.7	201	244	6.5	5.7	15.4	12.2
Yim et al.[7]	0/18	0/18	0%	1/18	1/18	NR	NR	NR	NR	1.3	1.4	NR	NR	3.2	4.1	4.1	5.3
Koizumi et al.[8]	0/52	0/35	NR	4/52	2/35	0/52	4/35	11/52	4/35	4.7	4.5	253	443	NR	NR	NR	NR
Muraoka et al.[9]	0/43	0/42	9%	1/43	3/42	1/43	1/42	2/43	10/42	4.8	4.9	151	362	3	3.9	NR	NR
Sakuraba et al.[10]	0/84	0/56	8%	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Petersen et al.[11]	0/57	0/43	5%	NR	NR	1/57	3/43	8/57	3/43	NR	NR	NR	NR	3.1	4.7	4.2	5.3
Whitson et al.[12]	/59	/88	16%	8/59	10/88	2/59	17/88	8/59	9/88	3.8	3.5	251	255	5	6.1	6.4	7.7
Park et al.[13]	0/122	3/122	NR	4/122	7/122	NR	NR	15/122	20/122	3.7	3	NR	NR	NR	NR	4.9	7.2

NR, not reported.

e d by McKenna et al. (18) in their large series of 1100 VATS lobectomy patients, with an acceptable postoperative mortality rate of 0.8%.

Complication rates have been shown to have a significant impact on quality of life, and can affect the length of stay as well as physical and social function (19). Muraoka et al. (9) and Park et al. (13) both reported a significantly lower overall morbidity rate in their VATS lobectomy group when compared to open lobectomy. Possibly related to this, Petersen et al. (11) and Park et al. (9) also reported a significantly shorter length of stay for patients in their respective VATS lobectomy groups. Furthermore, McKenna et al. (18) reported a mean length of stay of less than 5 days in patients who underwent VATS lobectomy (19).

Arrhythmia

Atrial fibrillation(AF) and other arrhythmias have been recognized to be associated with increases in morbidity and length of stay for patients undergoing noncardiac thoracic surgery (20). Muraoka et al. (9) reported a significantly reduced incidence of postoperative arrhythmia in their VATS lobectomy patients (RR 0.20, 95% CI 0.05 to 0.84), but was unable to ascertain any specific reasons for this finding. Reduction in the incidence of cardiac overload secondary to blood transfusions and preservation of the cardiac branches of the vagal nerve during selective lymphadenectomy in the VATS lobectomy group have been postulated as possible explanations. On the contrary, a larger study by Park et al. (13) matched 122 patients in their VATS lobectomy group with an open thoracotomy group, and found no significant difference in the incidence of postoperative AF. They suggested that the autonomic denervation and stress-mediated neurohumoral mechanisms resulting from pulmonary resection, rather than incision-related effects, were responsible for the pathogenesis of AF in these patients. This is supported by a number of other studies, which found no significant difference in the incidence of postoperative arrhythmias (8, 11, 12). However, these results should be interpreted with caution, as defi

nitions of arrhythmias, preventative strategies and monitoring techniques differ between institutions.

Pneumonia

Whitson et al. (12) found significantly fewer cases of postoperative pneumonia in their VATS lobectomy arm (RR 0.18, 95% CI 0.04 to 0.73), and suggested that this may be due to a combination of reduced postoperative inflammation, less pain, and fewer secretions. Although a number of other studies did not find any significant difference in the incidence of pneumonia between VATS and open lobectomy groups (8, 11, 13), Muraoka et al. (9) did report a significant difference in sputum retention (p=0.026), and attributed this to reduced postoperative pain in their VATS lobectomy patients, which was also credited for a reduction in other respiratory complications, including atelectasis and ARDS.

Pain

Postoperative pain management has a significant effect on patient recovery and is essential for optimization of postoperative care (21). A number of studies have shown that minimally invasive techniques are associated with reduced postoperative pain (22, 23). Yim et al. (7) and Maraoka et al. (9) both reported reduced levels of postoperative pain for patients in their VATS lobectomy groups. Despite a relatively small number of patients, Yim et al. (7) reported a significantly reduced amount of parenteral narcotics required by patients in their VATS lobectomy arm. Similarly, Muraoka et al. (9) evaluated postoperative pain by means of epidural tube duration, additional analgesic requirement, and visual analogue pain scale, and reported significantly less postoperative pain in their VATS lobectomy group. In addition, they commented that all patients who underwent VATS lobectomy in their study were able to stand up beside their bed in the intensive care unit on postoperative day 1. In contrast, patients in the open thoracotomy group were not able to achieve this, even though both groups received the same pain control regimen by continuous epidural infusion of bupivacine. Muraoka further commented that this finding was particularly important for an earlier recovery of activities of daily living.

Inflammatory markers

To support the hypothesis that VATS lobectomy causes less surgical trauma and stress to patients, a number of studies have compared postoperative serum markers of inflammation between the VATS and open groups. Yim et al. (7) found significantly lower levels of IL-6 and IL-8 in patients in their VATS lobectomy arm in the first 48 hours postoperatively. However, these patients were also found to have significantly lower levels of IL-10, an anti-inflammatory cytokine. From these results, Yim suggested that open thoracotomy may be associated with an increased imbalance of pro-inflammatory and anti-inflammatory mediators due to an increased extent of inflammatory injury. Muraoka et al. (9) recorded the maximum levels of white cell count and C-reactive protein postoperatively, and found significantly lower levels inpatients who underwent VATS lobectomy. However, it should be noted that they did not find significantly lower IL-6 and IL-8 levels on the first postoperative day, as reported by Yim et al.

Conversion

Conversion rates of VATS lobectomy to open lobectomy varied greatly between different institutions, ranging from 0% to 16% (4-13). A contentious point is the grouping of patients who had to convert to open thoracotomy after a failed VATS lobectomy. In their RCT, Kirby et al. (1) excluded 3 patients from their VATS lobectomy arm after encountering difficulty in safely dissecting either the interlobar pulmonary artery or incomplete fissures. Another RCT conducted by Sugi et al. (4) initially randomized 50 patients to each arm of their study, but transferred two patients from the VATS lobectomy group to the open thoractomy group for statistical analysis after they experienced intraoperative bleeding and required conversion. It has been argued that this transfer was unfair, as these two patients suffered a complication of VATS requiring an open procedure and should be included in the VATS group (4).

Proponents of VATS lobectomy emphasize a number of other potential benefits associated with the minimally invasive technique, including reduced intraoperative blood loss (5, 9), shortened chest tube duration (9), and length of stay (11). In addition to a potential improvement in the quality of life, these factors may also be of significant value in clinical management. For example, Petersen et al. (11) found that patients in their VATS lobectomy group were more compliant with their adjuvant chemotherapy regimens, and a higher proportion of patients were able to tolerate a higher dose of chemotherapy agents. This was possibly related to their reduced postoperative complications and quicker recovery from their VATS surgery.

Efficacy

Although there is increasing evidence that suggests VATS lobectomy can be associated with short-term outcomes such as reduced morbidity, less postoperative pain and quickened recovery, the ultimate question remains to be whether these parameters can be achieved without compromising the long-term oncologic efficacy in the form of survival and locoregional and systemic recurrence rates.

A number of comparative studies found no significant differences in either locoregional or systemic recurrence (4, 8, 10). The results of these studies can be seen in Table 3. A recent meta-analysis(14) actually reported a reduced systemic recurrence rate (p=0.03) for VATS lobectomy when compared to open surgery.

Similar to the findings on locoregional and systemic recurrence

Table 3 Summary of long-term survival and locoregional and systemic recurrence rates of patients after video-assisted thoracic surgery (VATS) versus open lobectomy for early-stage non-small cell lung cancer

Study	All-cause 5-yr mortality		Local recurrence		Systematic recurrence	
	RR	95% CI	VATS	Open	VATS	Open
Sugi et al.[4]	0.90	0.29-2.77	3/48	3/52	2/48	7/52
Koizumi et al.[8]	0.75	0.30-1.89	2/45	4/32	4/45	7/32
Sakuraba et al.[10]	0.72	0.37-1.41	1/84	1/56	6/84	5/56

rates, all-cause 5-year mortality rates have been found to be non-significant between VATS lobectomy and open lobectomy groups in a number of studies (4, 8, 10). Indeed, a meta-analysis (14) indicated a more favourable 5-year mortality rate for VATS lobectomy patients (p=0.04).

DISCUSSION

Not long after the first reports of VATS lobectomy, Kirby et al. (1) conducted the first RCT to assess the safety and potential benefits associated with this new technique. This trial included 61 patients with clinical stage I NSCLC who underwent VATS lobectomy or muscle sparing thoracotomy, and found significantly lower postoperative complication rates in the VATS lobectomy group (6% vs 16%), but not a significant decrease in the duration of chest tube drainage, blood loss, length of hospital stay, or postoperative pain. It should be noted that rib spreading was not avoided in all patients in the VATS group and mini-thoracotomy was performed for an unknown number of patients. The second RCT by Sugi et al. (4) randomized 100 patients with clinical stage I/A lung cancer for VATS lobectomy and mediastinal lymph node dissection or posterolateral open thoracotomy. This study found no significant differences in recurrence and survival rates, with overall 5-year survival rates of 90% and 85% in the VATS and open groups, respectively. Although the results from these reports have been encouraging, both RCTs have been scrutinized for a number of reasons. Firstly, the precise definition of VATS lobectomy has been questioned by some surgeons (4). The blurry line between 'true' VATS lobectomy and mini-thoracotomy was addressed by the multi-institutional study conducted by the Cancer and Leukemia Group B (CALGB) 39802 prospective trial (24), which chose to define VATS lobectomy as a true anatomic lobectomy with individual ligation of lobar vessels and bronchus, as well as hilar lymph node dissection or sampling, without the use of retractors or rib spreading. Another criticism encountered by both RCTs has been the designation of patients into study arms for statistical analysis, as both studies excluded or transferred patients from their respective VATS lobectomy groups after a conversion to open thoracotomy was performed.

In addition to the RCTs, a number of non-randomized, comparative studies have been conducted to assess a number of parameters between VATS and open lobectomy surgeries (4-13). These studies have indicated a number of potential advantages associated with the VATS procedure, including reduced arrhythmias, pneumonia, intraoperative bleeding, posteroperative pain, inflammatory response, chest drain duration, length of stay, and overall complications. Overall, the current literature suggests that VATS lobectomy performed in qualified centres is a valid alternative to open surgery for early-stage NSCLC, and can be associated with reduced morbidity, without any evidence of compromise to overall survival or recurrence rates. However, robust clinical data is still lacking for a direct comparison between true VATS lobectomy and conventional open lobectomy, and it remains difficult to ascertain the benefits associated with this relatively new procedure without further studies involving appropriately defined patients. Future studies should focus on recruiting a larger number of patients, preferably in the form of well designed RCTs.

References

1. Kirby TJ, Rice TW. Thoracoscopic lobectomy. Ann Thorac Surg 1993; 56: 784-6.
2. Lewis RJ. The role of video-assisted thoracic surgery for cancer of the lung: wedge resection to lobectomy by simultaneous stapling. Ann Thorac Surg 1993; 56: 762-8.
3. Walker WS, Carnochan, FM, Pugh GC. Thoracoscopic pulmonary lobectomy. J Thorac Cardiovasc Surg 1993; 106: 1111-7.
4. 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.
5. Sugiura H, Morikawa T, Kaji M, Sasamura Y, Kondo S, Katoh H. Long-term benefits for the quality of life after video-assisted thoracoscopic lobectomy in patients with lung cancer. Surg Laparosc Endosc Percutan Tech 1999; 9: 403-8.
6. Inada K, Shirakusa T, Yoshinaga Y, Yoneda S, Shiraishi T, Okabayashi K, et al. The role of video-assisted thoracic surgery for the treatment of lung cancer: lung lobectomy by thoracoscopy versus the standard thoracotomy approach. Int Surg 2000; 85: 6-12.
7. Yim AP, Wan S, Lee TW, Arifi AA. VATS lobectomy reduces cytokine responses compared with conventional surgery. Ann Thorac Surg 2000; 70: 243-7.
8. Koizumi K, Haraguchi S, Hirata T, Hirai K, Mikami I, Fukushima M, et al. Video-assisted lobectomy in elderly lung cancer patients. Jpn J Thorac Cardiovasc Surg 2002; 50: 15-22.
9. Muraoka M, Oka T, Akamine S, Tagawa T, Nakamura A, Hashizume S, et al. Video-assisted thoracic surgery lobectomy reduces themorbidity after surgery for stage I non-small-cell lung cancer. Jpn J Thorac Cardiovasc Surg 2006; 54: 49-55.
10. Sakuraba M, Miyamoto H, Oh S, Shiomi K, Sonobe S, Takahashi N, et al. Video-assisted thoracoscopic lobectomy vs. conventional lobectomy via open thoracotomy in patients with clinical stage IA non-small-cell lung carcinoma. Interact Cardiovasc Thorac Surg 2007; 6: 614-7.

11. Petersen RP, Pham D, Burfeind WR, Hanish SI, Toloza EM, Harpole DH Jr, et al. Thoracoscopic lobectomy facilitates the delivery of chemotherapy after resection for lung cancer. Ann Thorac Surg 2007; 83: 1245-9.
12. 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.
13. Park BJ, Zhang H, Rusch VW, Amar D. Video-assisted thoracic surgery does not reduce the incidence of postoperative atrial fibrillation after pulmonary lobectomy. J Thorac Cardiovasc Surg 2007; 133: 775-9.
14. 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.
15. 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.
16. Downey R, Cheng D, Kernstine K,Stanbridge R, Shennib H, Wolf R, et al. Video-assisted thoracic surgery in lung cancer resection: a consensus statement of the International Society of Minimally Invasive Cardiothoracic Surgery (ISMICS) 2007. Innov: Technol Tech Cariothorac Vasc Surg 2007; 2: 293-302.
17. Krahenbü hl L, Sclabas G, Wente MN, Sch?fer M, Schlumpf R, Bü chler MW. Incidence, risk factors, and prevention of biliary tract injuries during laparoscopic cholecystectomy in Switzerland. World J Surg 2001; 25: 1325-30.
18. McKenna RJ Jr, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1,100 cases. Ann Thorac Surg 2006; 81: 421-5.
19. Avery KN, Metcalfe C, Nicklin J, Barham CP, Alderson D, Donovan JL, et al. Satisfaction with care: an independent outcome measure in surgical oncology. Ann Surg Oncol 2006; 13: 764-5.
20. Passman RS, Gingold DS, Amar D, Lloyd-Jones D, Bennett CL, Zhang H, et al. Prediction rule for atrial fibrillation after major noncardiac thoracic surgery. Ann Thorac Surg 2005; 79: 1698-703.
21. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg 2003; 97: 534-40.
22. Darzi SA, Munz Y. The impact of minimally invasive surgical techniques. Annu Rev Med 2004; 55: 223-37.
23. Massard G, Thomas P, Wihlm J. Minimally invasive management for first and recurrent pneumothorax. Ann Thorac Surg 1998; 66: 592-9.
24. Swanson SJ, Herndon JE 2nd, D'Amico TA, Demmy TL, McKenna RJ Jr, 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.