

# Video-Assisted Thoracic Surgery (VATS) Lobectomy: the Evidence Base

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## ABSTRACT

**Background:** Video-assisted thoracic surgery (VATS) lobectomy provides a minimally invasive alternative for management of early stage non-small cell lung cancer, but is still only performed in a few specialized centers around the world. Questions about the safety of the surgery and its adequacy as a cancer operation remain hurdles for many surgeons.

**Methods:** We performed a systematic review of the literature on VATS lobectomy to assess these questions. The MEDLINE database was queried and the papers analyzed.

**Results:** Four randomized control trials, 11 case-control series, and 10 case series were reviewed. A variety of VATS techniques are used, making generalization of results difficult. The weight of this evidence suggests that VATS lobectomy can be safely performed and is an adequate cancer operation for early stage non-small cell lung cancer. There is also evidence that patients experience less pain with VATS, but that length of hospital stay is similar.

**Conclusion:** In expert hands, VATS lobectomy appears to be a safe procedure. However, the published evidence is thin and ongoing study is required, preferably with standardization of VATS techniques.

**Key Words:** VATS, Lobectomy, Minimally invasive surgery, Lung cancer.

## INTRODUCTION

The earliest reports of minimally invasive lobectomies were published more than a decade ago.<sup>1,2</sup> Although video-assisted thoracic surgery (VATS) has become the method of choice for many procedures formerly done via thoracotomy, the use of VATS for major lung resections has lagged substantially behind. The reasons are manifold. Performing anatomic lung resections by VATS is more complex than the relatively simple open operation and may require the use of special instruments. The intraoperative costs are higher. Perhaps most importantly, because lung cancer is the most common indication for performing lobectomy, the question of adequacy of the operation in satisfying surgical oncologic principles remains a hurdle in many surgeons' minds. The main considerations, therefore, in assessing whether to perform a minimally invasive lobectomy are adequacy as a cancer operation (as manifested by equivalent survival), safety in terms of complications and mortality, relative cost (including intraoperative and length of stay considerations), and benefits for the patients in terms of decreased pain and improved quality of life.

The definition of a VATS major lung resection can be problematic, or at least vague. In the literature, VATS lobectomy is a term used to describe a spectrum of operations from a mini-thoracotomy with rib-spreading and direct visualization through the wound to a completely minimally invasive approach with no rib-spreading and use of only thoracoscopic instruments. In interpreting studies of VATS lobectomy, careful review of the Methods section usually sheds light as to the nature of the operation performed. This needs to be taken into account when evaluating the evidence and forming conclusions.

## METHODS

A systematic review of the literature was performed by accessing the MEDLINE database from 1966 through June 2005. The subject heading search terms "carcinoma, non-small-cell lung," "lung non small cell cancer," "lung adenocarcinoma," "lung alveolus cell carcinoma," "lung squamous cell carcinoma," "surgery," "cancer surgery," "lung surgery," "thoracic surgery, video-assisted," and "pneumo-

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nectomy” were combined with the following phrases used as text words: “non small cell lung,” “lobectomy,” “pneumonectomy,” “VATS,” “surgery,” “thoracoscopy,” “thoracoscopic,” and “minimally invasive.” These terms were then combined with the search terms for the following publication types and study designs: practice guidelines, systematic reviews, metaanalyses, randomized control trials (RCTs), phase III clinical trials, and major clinical studies.

Relevant articles (published in English) and abstracts were selected and reviewed by the authors, and the reference lists from those sources were searched for additional trials. Studies were divided into the following groups: RCTs, case-control studies, and case series. Patient consent and Internal Review Board approval were not required.

**RESULTS**

The literature published to date on VATS lobectomy or major lung resections is scant and largely of a lesser weight on the evidence scale. A few authors from various centers around the world are responsible for a large share of the studies, and the majority of the data is in the form of case series.

**Randomized Control Trials**

Few randomized control trials exist in this area (Table 1).<sup>3-6</sup> Of the 3 published trials comparing open to VATS lobectomies, 2 examine clinical outcomes and 1 investigates biochemical markers.<sup>3-5</sup> The first and most well-known RCT was published by Kirby and colleagues.<sup>3</sup> They randomized 61 patients with clinical stage I non-small cell lung cancer (NSCLC) to undergo lobectomy by VATS (31 patients) or muscle-sparing thoracotomy (30

patients). The VATS were performed without rib-spreading. One patient in the open group and 2 patients in the VATS group had benign disease and were excluded from analysis. In addition, 3 patients in the VATS group required conversion to thoracotomy and were also excluded from the analysis leaving 30 in the open and 25 in the VATS groups. There were few differences between the groups. The incidence of postoperative complications was less in the VATS group (6% versus 16%). There were no significant differences in operating time, blood loss, duration of chest tube placement, length of hospital stay, and incidence of disabling postthoracotomy pain (2 in the open versus 1 in the VATS group).

The other RCT comparing clinical outcomes between open and VATS lobectomy was published by a Japanese group.<sup>4</sup> Sugi and colleagues<sup>4</sup> randomized 100 patients with clinical stage IA lung cancer to open (52 patients) or VATS (48 patients) lobectomy and mediastinal lymph node dissection. The additional 2 patients in the open group were conversions from VATS and were analyzed in the open group. There were no significant differences in the recurrence rates or survival. The reported 3- and 5-year survivals were 93% and 85% in the open group and 90% and 90% in the VATS group, respectively. Of note, this is the only RCT to examine survival differences between VATS and open lobectomies.

A study comparing acute phase responses randomized 22 patients to VATS and 19 patients to open lobectomy.<sup>5</sup> They used a nonrib-spreading technique, and all patients had mediastinoscopy preoperatively. Blood samples were taken before and at various times in the first week after surgery. Both operations increased acute phase response

**Table 1.**  
Randomized Control Trials of VATS Major Lung Resections

Study	Patients	Outcomes	Results	Comment
Kirby <sup>3</sup> 1995	25 VATS 30 Open	LOS, OR time, Complications	Less complications in VATS, no other differences	Stage I tumors, 3 VATS excluded due to conversion
Sugi <sup>4</sup> 2000	48 VATS 52 Open	Survival, recurrences	No differences	All pts had MLND
Craig <sup>5</sup> 2001	22 VATS 19 Open	Acute phase reactants	Lower CRP and IL-6 in VATS	
Shigemura <sup>6</sup> 2004	18 Complete VATS 16 Assisted VATS	OR time, LOS, pain, complications, markers	Longer OR, Shorter LOS, lower CRP with complete	Complete VATS— no spreading

markers, but VATS was associated with lower rises in C-reactive protein (CRP) and interleukin (IL)-6.

A final RCT was performed comparing complete VATS (c-VATS) to assisted VATS (a-VATS).<sup>6</sup> The authors randomized patients with clinical stage I lung cancer to either a nonrib-spreading approach (c-VATS, 18 patients) or a mini-thoracotomy approach with rib-spreading (a-VATS, 16 patients). The authors found significantly shorter length of stay (11 versus 15 days), longer OR times, less blood loss, and lower serum markers (CRP, white blood cells) in the c-VATS group.

### Case-Control Studies

A number of case-control studies examining a variety of outcomes have been performed on VATS major lung resections (**Table 2**).<sup>8-14,25-27</sup> Two studies investigating the effects of VATS lobectomies in high-risk patients have been performed.<sup>7,8</sup> A Japanese case-control study

done with patients 80 or older with 17 VATS cases and 15 open controls showed no significant difference in survival or complications with trends favoring the VATS group.<sup>7</sup> Demmy<sup>8</sup> performed a case-control study comparing VATS lobectomy patients with matched controls who had open surgery. VATS was only offered to patients who were deemed high risk based on either poor pulmonary function tests (PFTs) or poor function. There were 19 patients in each group. Despite having higher risk patients, the VATS group had a shorter length of stay, a quicker return to activity, and less pain 3 weeks postoperatively than did the open group.

A number of other case-control series examining pain, changes in PFTs, nocturnal hypoxemia, and various markers of inflammation have been performed and are summarized in **Table 2**.<sup>10-14</sup> They generally favored VATS approaches, but the selection of controls was problematic. For example, in one study of cytokines before and after

**Table 2.**  
Case-Control Series of VATS Major Lung Resections

Study	Patients	Outcomes	Results	Comment
Shiraishi <sup>25</sup> 2006	10 VATS 9 mini 19 Open	Mediastinal LNs, LOS, pain by visual analog scale	Equal Mediastinal LN resected, Less pain in VATS	Clinical Stage IA, pain less in VATS vs. Open on POD 2
Watanabe <sup>27</sup> 2005	191 VATS 159 Open	Number of mediastinal LNs, mortality, recurrence	Mediastinal LNs equal, 5 year recurrence free survival similar	Groups not equivalent, more T2 in open
Muraoka <sup>26</sup> 2006	43 VATS 42 Open	Surgical invasiveness parameters, complications	Less blood loss, shorter chest tube duration, less pain, lower WBC and CRP all in VATS	An overall decreased morbidity rate in VATS (25.6% vs. 47.6%), Clinical stage I
Demmy <sup>8</sup> 1999	19 VATS 19 Open	LOS, Return to activity, pain	All favor VATS	High risk pts, 3 deaths in VATS, 1 in control
Koizumi <sup>7</sup> 2003	17 VATS 15 Open	Complications, survival	Trend favors VATS	Pts age >80
Demmy <sup>9</sup> 2004	20 VATS 38 Open	Discharge independence, LOS	Shorter LOS, less pain, fewer transfers to care facilities	Groups well matched
Kawai <sup>10</sup> 2005	10 VATS 11 Open	Nocturnal hypoxemia POD 3 and 14	Less hypoxemia at POD 14 with VATS	Open were >2 cm, VATS were < 2 cm
Nagahiro <sup>11</sup> 2001	13 VATS 9 Open	PFTs, pain, cytokines	Less pain, lower IL-6 in VATS	Open were T2, VATS were T1
Nakata <sup>12</sup> 2000	10 VATS 11 Open	PFTs, early and late	PFTs better for VATS pod 7, no change at 1 year	Selection of controls ill-defined, spreading used
Yim <sup>13</sup> 2000	18 VATS 18 Open	Cytokines, analgesic requirement	IL-6, IL-8, IL-10 lower and less IV narcotic in VATS	Controls were initially attempted VATS
Kaseda <sup>14</sup> 2000	44 VATS 77 Open	PFTs 3 months post-op, survival	PFT changes and Stage I survival better for VATS	Historical controls not well defined

surgery, the control group was made up of T2 tumors and the VATS cases were T1.<sup>10</sup>

**Case Series**

Numerous case series have been published, many of which have been updated reflecting the ongoing experience of the authors, follow-up of patients, and modifications in technique. The series published in English with more than 100 patients are reviewed in **Table 3**.<sup>15-24</sup>

Roviaro and colleagues<sup>1</sup> from Milan have been publishing on their experience with VATS for major lung resections since 1993. Their most recent update looked at their 11-year experience with 344 patients (278 with NSCLC, 6 metastases, 68 benign) that went to surgery for VATS major resection. In patients with lung cancer, their indications were clinical stage I with peripheral tumors <3 cm in diameter.<sup>15</sup> Their technique does not use rib-spreading

and involves 3 incisions to 4 incisions with the largest being 5cm for withdrawal of the specimen.

Two recent case series have been published from different centers in Japan.<sup>16,17</sup> Iwasaki and colleagues<sup>16</sup> published their experience with 140 procedures (100 lobes, 40 segments). Their technique did not involve rib-spreading, and their indications were clinical stage I disease with peripheral tumors <3 cm. They reported a 5-year survival of 77.3% for the VATS patients with 80.9% for stage I and 70.3% for stage II tumors.

The other Japanese case series involved 106 patients, 95 of whom had a VATS procedure and the other 11 of whom were converted to thoracotomy (10% conversion rate).<sup>17</sup> Their main indication was clinical stage I. Tumor size was not a criterion. Their technique involved the use of a mini-thoracotomy and rib-spreading. They reported a 3-year survival of 93%, but only included the 82 patients

**Table 3.**  
Case Series of VATS Major Lung Resections

Study	Patients (ITT)	Technique	Survival	LOS Days	Comment
Roviaro <sup>15</sup> 2004	259 (344)	No spreading	5y 68.9	5	78 (23%) conversions, 2 deaths
Iwasaki <sup>16</sup> 2004	140	No spreading	5y 77.3% I 80.9% II 70.3%	NR	100 lobes, 40 segments
Ohtsuka <sup>17</sup> 2004	95 (106)	Spreading	3y 93%	7.6	Survival in only 82 patients, 1 death, 10% conversion
Walker <sup>18</sup> 2003	158 (178)	No spreading	5y I 77.9% II 51.4%	6	1.8% 30d mortality, 11% conversion
Gharagozloo <sup>23</sup> 2003	179	Simultaneous stapling, no spreading	5y 83%	4.1	1 death
Solaini <sup>19</sup> 2001	112 (125)	No spreading	3y 85% I 90	6.2	Survival in 86 patients with NSCLC, 10% conversion
Lewis <sup>22</sup> 1999	250	Simultaneous stapling, no spreading	3y 83%	2.8	About half of patients were stage II
Yim <sup>20</sup> 1998	214 (266)	Spreading	2y 93%	NR	1.8% 30d mortality, 19% conversion
McKenna <sup>21</sup> 2006	1100	No spreading	5y I~80% II~60%	3 med 4.78 mean	0.8% mortality, 2.5% conversion, port site recurrence-0.6%
Onaitis <sup>24</sup>	500	No spreading	2y 80%	3	1% mortality, 1.6% conversion

for whom they had follow-up data for more than 6 months. Yim and colleagues<sup>20</sup> from Hong Kong published their series of 266 patients with tumors <5 cm for whom they attempted VATS resections. They converted to thoracotomy 19% of the time, and completed 214 VATS major lung resections. A rib-spreader was used. They reported a 22% incidence of nonfatal complications, 1 postoperative death, and 93% of patients alive at 2 years.

In the largest series of VATS major lung resections, McKenna and colleagues<sup>21</sup> reported on their experience of 1100 patients for whom they performed 1072 procedures with a conversion rate of 2.5%. There were no intraoperative deaths, and their mortality was only 0.8%. The complication rate was 15.3% with the most common complications being prolonged air leak and atrial fibrillation. Kaplan-Meier survival curves are presented, and extrapolation shows 5-year survivals for stage I and II cancers of approximately 80% and 60%, respectively. The incidence of port-site recurrence was 0.6%.

Finally, 2 independent series<sup>22,23</sup> using forms of simultaneous stapling have been published. This technique involves no rib-spreading, but variations on stapling the bronchus and vascular structures together without formal dissection. Lewis<sup>22</sup> reported a complication rate of 11.2% and 3-year survival of 83%. Of note, almost half of the patients were stage II. Gharagozloo<sup>23</sup> reported on 179 patients with a 5-year survival of 83%. They performed 29 right upper and middle bilobectomies (16%) in the series. This high number was performed as a conscious decision after some early recurrences in the N1 nodes between upper and middle lobes.

## DISCUSSION

As detailed above, the bulk of the evidence is in the form of case series and case-control studies with few published RCTs. Synthesizing the data, some conclusions can be drawn:

- VATS lobectomy can be performed safely with equivalent mortality and complication rates to that of open lobectomy. This is based on the results of 2 small RCTs and a number of case-control trials and case series.<sup>3,4,7,8,14–27</sup>
- The survival of patients with stage I lung cancer following VATS lobectomy is equivalent to that of patients having open surgery. This is based on one small RCT, case-control studies, and the case series.<sup>4,7,14–27</sup>
- Patients experience less pain with VATS based on case-control studies.<sup>1,8,9,25,26</sup>
- Length of hospital stay is similar to that of open proce-

dures. One RCT showed no difference, and 3 case-control studies suggested it was shorter with VATS.<sup>3,8,9,26</sup>

Because the published evidence is thin, no definite recommendations can be made. The reality of the situation is that many surgeons are performing the procedure and many patients are requesting it. The data support that VATS lobectomy can be done safely and that the survival of early-stage patients is equivalent to that of thoracotomy. In terms of the postoperative course, although the data are mixed, there seems to be a suggestion that VATS patients have less pain and shorter hospital stays.

Differences in indications, technique, and extents of lymph node dissection make comparing across studies difficult. If one can perform the same operation in terms of anatomic dissection and lymph node removal as done through thoracotomy, then it would seem reasonable to offer a VATS lobectomy. The therapeutic role of lymph node dissection will remain unanswered for the time being until the survival results of the recently completed American College of Surgeons Oncology Group (ACOSOG) Z0030 study, comparing mediastinal lymph node dissection to sampling, are maturing. In the interim, few thoracic surgical oncologists would dispute the importance of lymph node dissection, particularly in view of the evidence that it does not increase morbidity or mortality and it aids in the selection of patients for adjuvant chemotherapy in the presence of lymph node involvement.<sup>28</sup> With that in mind, it would seem the real question of whether or not to perform VATS lobectomies hinges on the completeness of the lymph node dissection.

Few studies have been performed to assess the adequacy of lymph node dissection in VATS lobectomy. Sagawa and colleagues<sup>29</sup> conducted an interesting study by performing a VATS lobectomy and mediastinal lymph node dissection (with rib-spreading) followed by a conversion to thoracotomy at the same operation to assess the residual lymphatic tissue that remained unresected. In 29 patients, the mass of lymphatic tissue “missed” by VATS lobectomy was <3% of the amount resected, which they judged to be an adequate result. In a more conventional retrospective analysis, Watanabe et al<sup>27</sup> compared 191 VATS lobectomy patients with 159 thoracotomy patients. They demonstrated that the number of nodes dissected was similar in both groups. Shiraishi and colleagues<sup>25</sup> also noted in their small case-control study that the number of mediastinal lymph nodes dissected was similar in VATS and open groups. It should be noted that Japanese surgeons are generally regarded as being particularly aggressive in their lymph node dissections. This importance on lymphade-



nectomy is reflected by the fact that all 3 studies addressing this issue in VATS lobectomy are from Japan.

Our practice has been to offer VATS lobectomy using no rib-spreading to patients with clinical stage I cancers with peripheral tumors <3 cm in diameter. Contraindications include the use of preoperative chemotherapy or radiotherapy. Lobectomy remains the standard of care for all early lung cancers. As such, the use of simultaneous stapling techniques is probably not warranted particularly in light of the increased number of bilobectomies performed by one center due to the inadequacy of their lymph node removals. It would seem that this is not the same operation as an open lobectomy.

## CONCLUSION

There is certainly a need for further study. A large multicenter randomized trial comparing open lobectomy to VATS lobectomy would be ideal. However, the myriad of techniques used by different surgeons would make the standardization of the VATS arm difficult or impossible. Quality of life studies with validated instruments need to be performed to ascertain the impact of VATS. Another interesting avenue of investigation that has been embarked on but requires further study is the use of VATS in higher risk groups to see whether they fare better. Also, with the recent shift in clinical practice to adjuvant chemotherapy for more and more of our patients, there may be some additional benefit to VATS lobectomy if patients are better able to tolerate chemotherapy postoperatively. This should also be a subject of future studies.

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