

Thoracoscopic versus open lobectomy debate: the pro argument

Thorakoskopische versus offene Lobektomie: das pro-Argument

Abstract

Introduction: Controversy persists about the role of VATS lobectomy for patients with lung cancer. This is particularly true in Europe, where VATS (video assisted thoracic surgery) lobectomy is performed for lung cancer less often than in the USA or Japan. This article reviews existing data comparing the results of VATS vs. open lobectomy for the treatment of lung cancer in order to provide a scientific basis for a rational assessment of this issue.

Methods: The review of the data presented here draws heavily from a 2007 metaanalysis by Cheng et al. [1] published in 2007, as it employed rigorous methodology in performing a systematic review and metaanalysis, and involved a detailed analysis of many major and minor endpoints on an intent to treat basis. This included 36 trials, three of them randomized, and 3589 patients, reported between 1995 and 2007. Summary results for individual endpoints are shown as a mean value with 95% confidence intervals (CI). These values are taken from the summary results of the Forrest plots in the source article. Dichotomized variables are expressed as an Odds Ratio, with values <1 being in favor of VATS lobectomy. Continuous variables are reported as weighted mean differences.

Results: The operative time for a VATS lobectomy was statistically longer, but only by 16 minutes. The conversion rate from VATS to open was 6%. There was no significant difference in the rates of major bleeding, blood transfusion or re-operation. VATS lobectomy was associated with a significantly lower rate of complications in general and pulmonary complications in particular. Postoperative pain was reduced, functional outcome was better, whereas overall quality of life was not. Mediastinal staging was equal with regard to the number of nodes or the number of nodal stations sampled. The ability of patients to receive adjuvant chemotherapy was improved following VATS. There was no difference in survival at 1 and 3 years for lung cancer (all stages combined). There was no difference in survival at 5 years for each tumor stage, and no difference in the rate of deaths at maximal follow-up.

Conclusion: The data suggests that VATS lobectomy for NSCLC is safe, results in fewer complications, less pain, and more rapid return of normal functioning. There appears to be either no difference or a slight benefit in long term survival after VATS lobectomy. These conclusions are demonstrated by a comprehensive, rigorous metaanalysis of the controlled clinical trials, but are weakened by the fact that most of the studies were not randomized. However, because a large randomized trial is not likely to ever be conducted, this represents the best assessment of the value of VATS lobectomy that is available.

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Zusammenfassung

Einführung: An der thorakoskopischen Lobektomie scheiden sich die Geister, ganz besonders, wenn es um die Therapie des Bronchialkarzinoms geht. Diese Kontroverse ist in Europa, wo wesentlich weniger onkologische VATS (videoassistierte Thorakoskopie)-Lobektomien

durchgeführt werden als in den USA oder Japan, besonders ausgeprägt. Der vorliegende Artikel möchte eine rationale Bewertung erleichtern, indem er die Ergebnisse der offenen und thorakoskopischen Lobektomie bei Bronchialkarzinom anhand der aktuellen Datenlage gegenüberstellt.

Methoden: Die hier vorgestellte Übersicht lehnt sich an eine 2007 von Cheng et al. [1] publizierte Metaanalyse an, die sich durch ihre rigorose Methodik, die genaue Analyse aller relevanten Endpunkte und die eingeschlossene Anzahl von 36 Studien, darunter drei randomisierte, und 3589 Patienten auszeichnet. Zur übersichtlichen Darstellung einzelner Endpunkte wurde der Mittelwert mit einem 95% Konfidenzintervall (CI) gewählt; die Werte wurde den Forrest Plots der Quellenartikel entnommen. Kategorielle Daten wurden durch Odds Ratios abgebildet, wobei eine Odds Ratio <1 einen Vorteil für die VATS Lobektomie ausdrückt. Quantitative Daten wurden als gewichtete Mittelwerte dargestellt.

Ergebnisse: Thorakoskopische Lobektomien dauerten statistisch gesehen 16 Minuten länger als offene. Die Konversionsrate betrug 6%. Hinsichtlich der Häufigkeit von Blutungskomplikationen, Transfusionen und Revisionseingriffen gab es keine signifikanten Unterschiede. Die Häufigkeit allgemeiner und pulmonaler Komplikationen war beim thorakoskopischen Vorgehen signifikant geringer. Weitere signifikante Vorteile zeigte das thorakoskopische Vorgehen bei postoperativen Schmerzen und funktionellem Ergebnis, allerdings ohne Niederschlag in Lebensqualitätsanalysen. Das intraoperative mediastinale Lymphknotensampling zeigte hinsichtlich Anzahl untersuchter Lymphknoten und Lymphknotenstationen keinen signifikanten Unterschied. Adjuvante Chemotherapien sind nach thorakoskopischer Lobektomie besser durchführbar. Überleben nach einem und drei Jahren (alle Tumorstadien) sowie stadienspezifisches Überleben nach 5 Jahren und maximaler Beobachtungszeit waren nicht signifikant verschieden.

Schlussfolgerung: Die bisher umfassendste Metaanalyse kontrollierter klinischer Studien lässt folgende Schlüsse zu: Die thorakoskopische Lobektomie zur Behandlung geeigneter Stadien des Bronchialkarzinoms ist sicher durchführbar und verursacht im Vergleich zum offenen Vorgehen weniger Komplikationen, weniger Schmerzen und weniger Funktionseinschränkungen. Das Langzeitüberleben ist der offenen Lobektomie zumindest gleichwertig. Einerseits darf nicht übersehen werden, daß in diese Analyse lediglich drei randomisierte Studie eingeschlossen werden konnten. Andererseits ist die Durchführung einer großen randomisierten Studie sehr unwahrscheinlich, so daß es vernünftig erscheint, die Ergebnisse der Metaanalyse im Moment als bestmögliche Bewertung der thorakoskopischen Lobektomie zu akzeptieren.

Introduction

The first lobectomies performed using Video-Assisted Thoracic Surgery (VATS, also called thoracoscopy) were reported over 15 years ago [2], [3], [4]. Since then, multiple large series have been reported, including several systematic reviews and metaanalyses [1], [5], [6], [7], [8], [9]. The scope of what can be successfully performed thoracoscopically includes pneumonectomy [10], [11], segmentectomy [12], sleeve lobectomy [13], and esophagogastrectomy [14]. However, in the US, VATS lobectomy is done in only about 20% of major academic centers [15], although in those centers that perform VATS lobectomy the vast majority of lung cancer resections are performed thoracoscopically.

Most of the published data on VATS lobectomy involves institutional series, and only a few small randomized trials

have been reported [16], [17], [18]. No large randomized trial comparing these techniques has ever been initiated, and it is highly unlikely that this will ever be done. A randomized trial was under consideration at the National Institutes of Health in the USA for several years, but after analysis of the data from phase II studies it was deemed not to be a worth the effort. This is because outcomes data for the two approaches were so similar that a trial would have to include a large number of patients only to demonstrate equivalence.

Nevertheless, controversy persists about the role of VATS lobectomy, particularly for patients with lung cancer. This is particularly true in Europe, where VATS lobectomy is performed for lung cancer less often than in the USA or Japan. This article reviews existing data comparing the results of VATS vs. open lobectomy for the treatment of

lung cancer in order to provide a scientific basis for a rational assessment of this issue.

Methods

The review of the data presented here draws heavily from a metaanalysis of reported data, which included published and unpublished controlled trials that compared VATS to open lobectomy for lung cancer [1]. This study [1] offers a concise review of a large amount of data. Pertinent individual studies or corroborating studies are cited as needed. I have chosen to highlight this particular metaanalysis because it employed rigorous methodology in performing a systematic review and metaanalysis, and involved a detailed analysis of many major and minor endpoints on an intent to treat basis. Many of the individual studies reported results according to slightly different definitions; however, the authors of this metaanalysis were able to thoughtfully combine some of the data and thereby partially overcome this difficulty. Furthermore, the authors achieved a good compromise between including only comparable patients or studies, and allowing some flexibility in order to have a larger amount of data to analyze (e.g. allowing series that included a limited number [$<20\%$] of wedge resections or segmentectomies, and allowing series that included a limited number of patients [$<20\%$] that did not have lung cancer). The metaanalysis involved 36 trials and 3589 patients, reported between 1995 and 2007. Only 3 of these were randomized trials, which included a sum total of 205 patients [16], [17], [18]. All of the studies included in the metaanalysis involved an anatomic lobectomy, with dissection and individual division of the arteries, veins and bronchus [1].

In order to be concise, I have primarily shown summary results for individual endpoints as a mean value with 95% confidence intervals (CI). These values are taken from the summary results of the more detailed Forrest plots in the source article [1]. Dichotomized variables are expressed as an Odds Ratio, with values <1 being in favor of VATS lobectomy. Continuous variables are reported as weighted mean differences. The numbers of studies and patients contributing to a summary endpoint are indicated whenever this data was available.

There were no differences in patient characteristics in the VATS group vs. the open group in the randomized studies. However, because most of the studies were not randomized, there were some significant differences when all patients were examined. The VATS patients were significantly more often women, had smaller and more often earlier stage tumors, and a higher proportion of adenocarcinoma. There was no difference in age (Table 1).

Table 1: Baseline characteristics of patients in controlled trials

Characteristic	VATS	Open	p
Women (%)	45	36	.0001
Tumor size (cm)	2.6	3.1	.0004
Stage I (%)	77	71	.00001
Stage II (%)	10	12	.01
Stage III (%)	9	18	.00001
Adenocarcinoma (%)	66	56	.00001
Age (years)	65	65	NS

Results

Intraoperative outcomes

There is no significant difference in the rates of major bleeding (>500 ml), blood transfusion or re-operation (Figure 1). In fact there was a trend to better outcomes in VATS lobectomy patients (perhaps not statistically significant because only a small number of trials reported this data). Blood loss as a continuous variable was statistically less in VATS lobectomy patients, although the difference of 80 ml is clinically insignificant. Despite obviating the time needed to open and close a thoracotomy incision, the operative time for a VATS lobectomy is statistically longer, but only by 16 minutes. Overall, the rate of conversion from VATS to open among all series reporting this data was 6%. Other large series have reported conversion rates of approximately 2% [5], [6], with bleeding accounting for only a minority of conversions. The need for conversion to an open procedure does not result in inferior outcomes [19].

Short-term postoperative outcomes

VATS lobectomy is associated with a significantly lower rate of complications in general and pulmonary complications in particular compared with open lobectomy (Figure 2). There is a trend to a lower rate of pneumonia and respiratory dysfunction. Other specific complications do not appear to be different between the two techniques. There is a strong trend to a higher proportion of patients with an air leak >7 days among VATS lobectomy patients. This appears to be in contradiction to the significantly shorter hospital stay and duration of chest tube drainage. This can perhaps be explained by the fact that several centers performing many VATS lobectomies occasionally discharge patients to home with a Heimlich valve after 2–3 days if the patient is otherwise ready to go home but there is still an air leak. This may lead to an increased proportion of patients with a chest tube in place at 7 days instead of removal at day 5 or 6.

It is important to remember that the majority of included trials were not randomized, and that there were differences among the patients that may confound an analysis

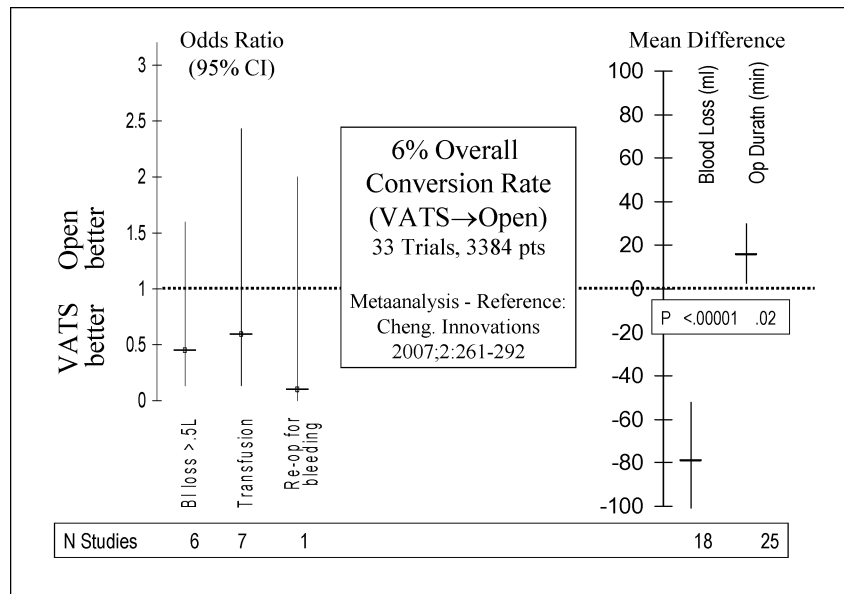


Figure 1: Intraoperative outcomes of VATS vs. open lobectomy

Bl, blood; CI, confidence interval; Op duratn, operative duration; Re-op, re-operation

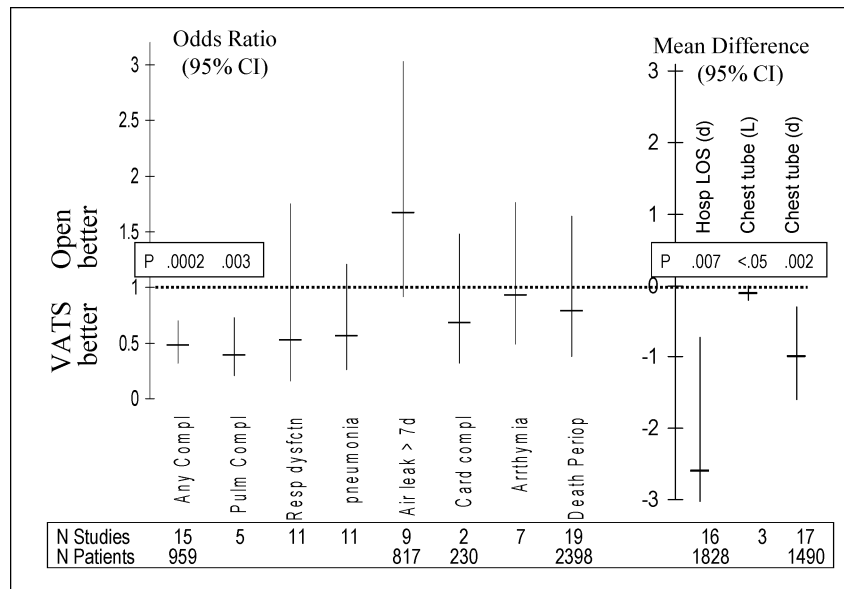


Figure 2: Peri-operative complications of VATS vs. open lobectomy

Card, cardiac; CI, confidence interval; Compl, complications; d, days; Hosp. LOS, hospital length of stay; Periop, peri-operative; Pulm, pulmonary; Resp dysfctn, respiratory dysfunction

of postoperative complications. Exploratory analyses however did not suggest that such confounding was occurring. There was no difference in age between VATS vs. Open lobectomy patients, nor was there a difference in preoperative FEV1. Unfortunately, there was no data was available regarding the relative incidence of comorbidities or on surgeon or center experience.

Postoperative pain is clearly reduced after VATS lobectomy (Figure 3), although the number of controlled studies reporting pain outcomes was somewhat limited. Significantly fewer patients experienced severe pain or had pain at home, and there was a trend to a decreased incidence of any pain. There was a statistically significant lower incidence of pain at 1 year. Postoperative pain was lower by Visual Analog Scale (VAS) assessment despite a lower

dose, frequency and duration of need for narcotics. Less pain was seen at early time points, but by 3 months postoperatively there was no difference.

Functional outcomes are better after VATS lobectomy, although the data is very limited (Figure 4). Overall quality of life is not different for VATS vs. open lobectomy. However, pulmonary function tests at 1 year postoperatively were better after VATS lobectomy – a time at which full recovery would seem to have absolved any differences.

Oncologic aspects

Data from a large number of studies has shown no difference in mediastinal node staging between VATS and open lobectomy (Figure 5). There is no difference in the number

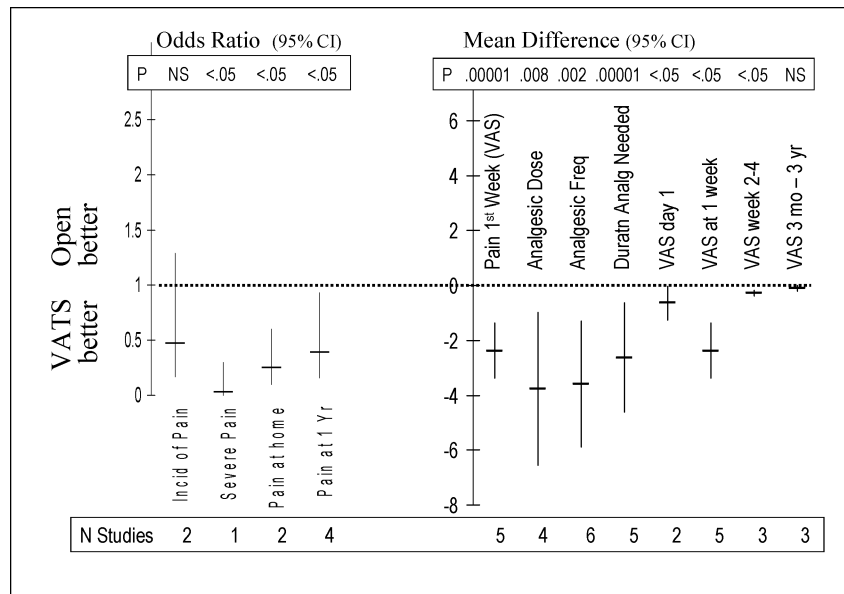


Figure 3: Post-operative pain with VATS vs. open lobectomy

CI, confidence interval; Incid, incidence; Duratn Analg, duration analgesic medication needed; freq, frequency; mo, months; VAS, Visual Analog Scale pain score; yr, year

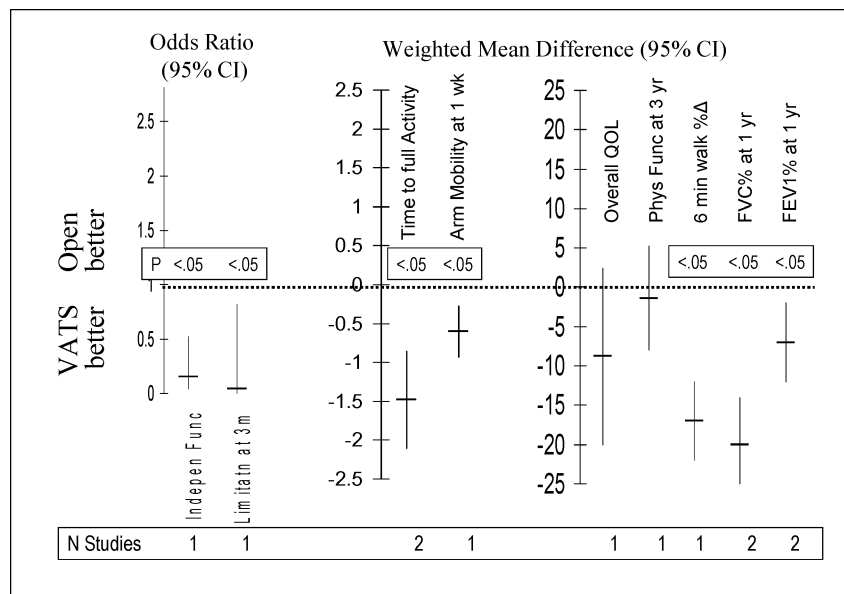


Figure 4: Quality of life and functional outcomes of VATS vs. open lobectomy

CI, confidence interval; FEV1, forced expiratory volume in 1 second (post-operative as compared with pre-operative results as % of normal); FVC, forced vital capacity (post-operative as compared with pre-operative results as % of normal); Indepen func, independent functioning; Limitatn, limitation; m, months; min, minute; Phys func, physical functioning; QOL, Quality of Life; wk, week; yr, year; Δ, change (between pre-operative and post-operative results)

of nodes or the number of node stations sampled. This issue has also been addressed in 2 randomized trials, which found no difference (although the number of patients was limited) [16], [17]. The ability of patients to receive adjuvant chemotherapy is improved following VATS lobectomy as assessed in only one study [20].

Long-term outcomes

There is no difference in survival at 1 and 3 years between VATS vs. open lobectomy for lung cancer (all stages combined). However, there is a significant survival

benefit to VATS lobectomy at 5 years and at maximal follow-up, as demonstrated by a large number of studies (Figure 6). A strong trend is seen to a lower rate of recurrence, consistent with the lower rate of death at maximal follow-up. However, this data is difficult to interpret, given the differences in tumor stage between the 2 groups (Table 1). Stage specific survival, which neutralizes this confounding factor, shows no difference for any stage or subgroup. Furthermore, no survival difference was found in the randomized studies. Examination of the long-term survival curves from the largest series also suggest that there is minimal, if any difference in survival (Figure 7)

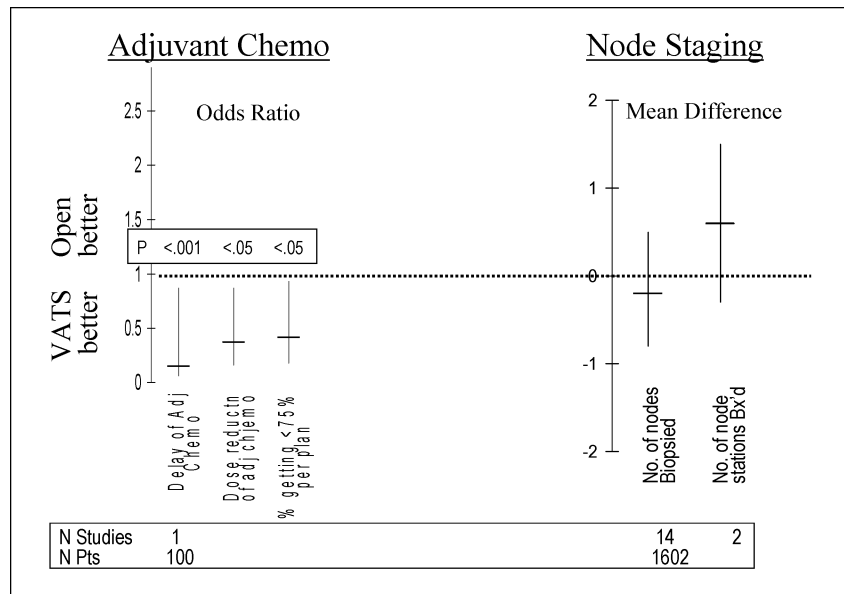


Figure 5: Oncologic aspects of VATS vs. open lobectomy

Adj, adjuvant; Bx'd, biopsied; Chemo, chemotherapy; CI, confidence interval; No., number; reductn, reduction

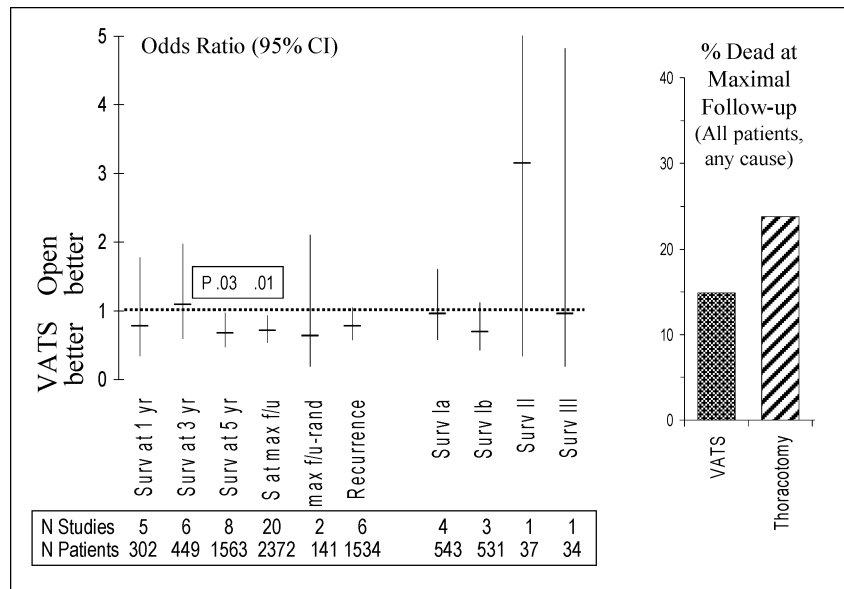


Figure 6: Long-term outcomes of VATS vs. open lobectomy

CI, confidence interval; max f/u, maximal follow-up; rand, randomized studies; S, survival; Surv, survival; yr, year

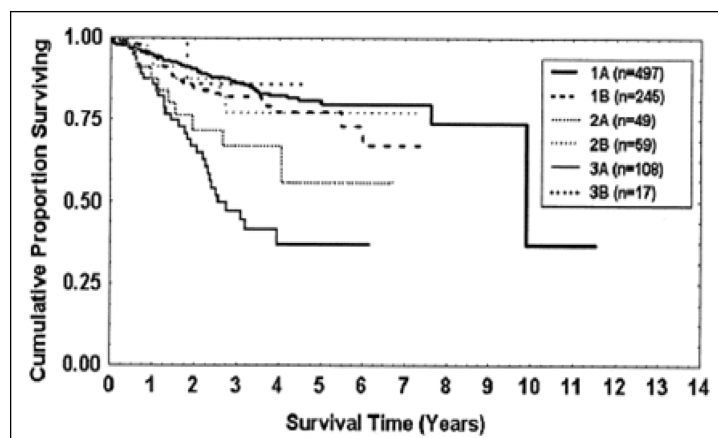


Figure 7: Overall survival after VATS lobectomy for lung cancer in 1100 patients

Reproduced with permission from McKenna et al. [5]

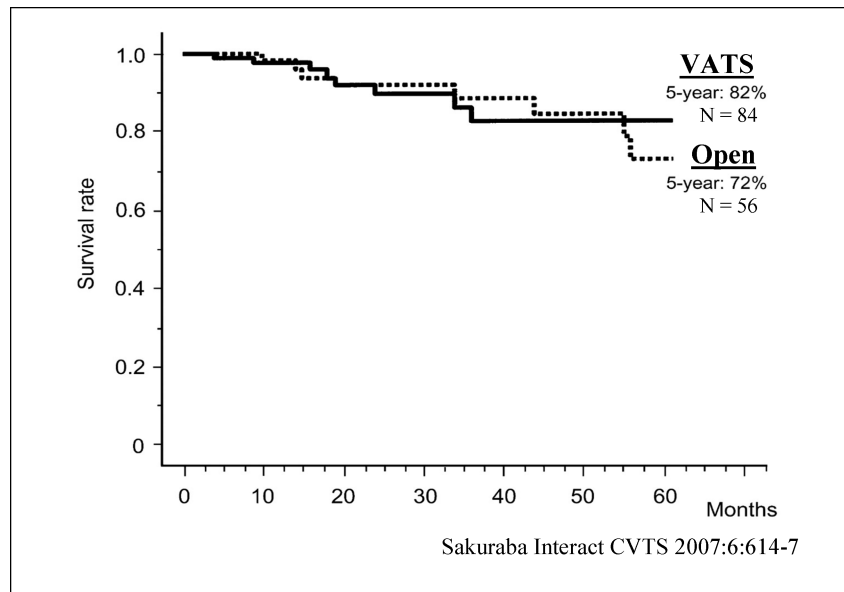


Figure 8: Overall survival after VATS vs. open lobectomy in clinical stage Ia patients
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[5]. This is corroborated by stage specific non-randomized comparisons (Figure 8) [21].

Technical factors of VATS lobectomy

Details of the incision made to accomplish a thoracoscopic lobectomy vary significantly. Probably the biggest aspect is whether the procedure is done purely by looking at the video-image without rib-spreading (complete VATS or c-VATS), or whether a rib spreader is used and the resection is accomplished at least partially by looking directly through this incision (known as assisted VATS or a-VATS). This issue was also addressed in the Metaanalysis by Cheng et al. [1]. A c-VATS approach is associated with a shorter length of hospitalization and less pain compared with a-VATS (Figure 9). There is no difference in nodal staging, but longer operative time with c-VATS (by 27 minutes). Additional analyses suggested that the differences between open thoracotomy and a-VATS were much less pronounced than when thoracotomy is compared with c-VATS (data not shown) [1]. Others have also found benefits to c-VATS, including shorter hospitalization, more rapid return to normal functioning (within days), and reduced inflammatory mediators [22]. In aggregate, this data suggests that the more dramatic benefits of VATS are seen when rib-spreading is avoided.

Discussion

It has been nearly 2 decades that thoracoscopic lobectomy has been performed and perfected, and a large amount of data has been reported. When taken together, the data suggests that VATS lobectomy for NSCLC is safe, results in fewer complications, less pain, and more rapid return of normal functioning. However, after 3 months there is no difference in pain, and overall quality of life

is only marginally improved. There is no difference in the ability to carry out an oncologic operation including removal of mediastinal lymph nodes, and there appears to be either no difference or a slight benefit in long term survival after VATS lobectomy. These conclusions are demonstrated by a comprehensive, rigorous metaanalysis of the controlled clinical trials, but are weakened by the fact that most of the studies were not randomized. However, because a large randomized trial is not likely to ever be conducted, this represents the best assessment of the value of VATS lobectomy that is available.

Several other reviews have arrived at the same conclusions [7], [8], [9]. In addition, European and North American clinical guideline committees have reviewed the data, and come to the conclusion that VATS lobectomy is a reasonable alternative to open resection [23], [24]. Thus thoracoscopic lobectomy must be regarded as established and justified approach, even though it is available in only a minority of centers.

A comparison of the cost of a VATS vs. an open lobectomy is complicated, because it is dependent on many factors, such as whether or not staplers are used extensively during open and during VATS resections, whether the better functional status of the patient actually leads to earlier discharge from the hospital, and different rules for health care reimbursement in different countries. When costs have been compared, it appears that a VATS resection is approximately 5–20% more expensive [1], [25], [26]. This may be worthwhile if one considers earlier return to work from a societal perspective, although this aspect is of limited importance from the perspective of a physician, a hospital or an insurance carrier.

It is always difficult to learn a new technique, and be comfortable that one can perform this safely and with good results. Details of the learning curve have not been well defined, but it has been suggested that around 50 lobectomies are needed [27]. The volume of lobectomy

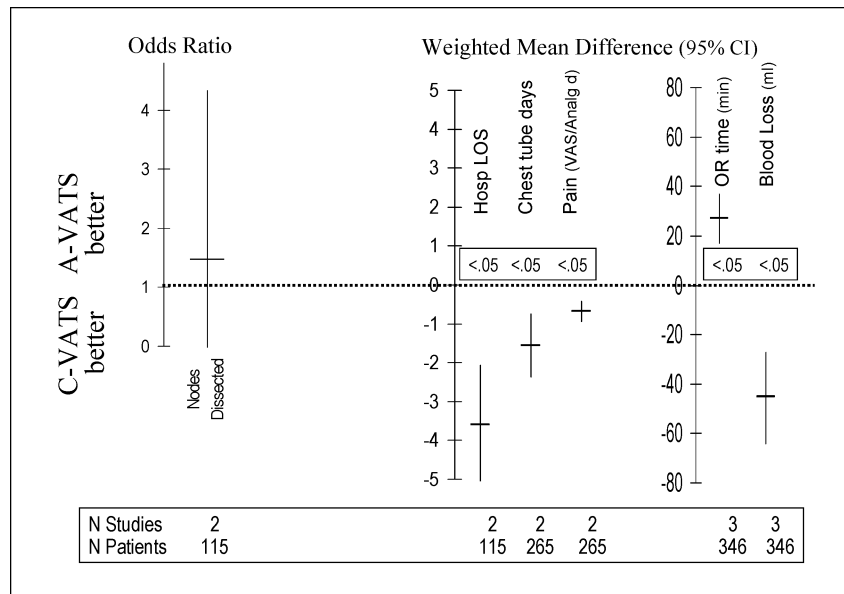


Figure 9: Rib-spreading vs. non-rib-spreading VATS approaches

a-VATS, assisted VATS (rib-spreading, with dissection done by direct vision through an incision as well as on a video monitor); CI, confidence interval; c-VATS, complete VATS (no rib-spreading, dissection done entirely by viewing structures on a video monitor); Hosp. LOS, hospital length of stay; OR, operating room; VAS/Analg d, Visual Analog Scale pain scores or analgesic days

in a particular surgeon's practice may not be sufficient to make it worthwhile to develop these skills, especially given that most of the benefits are transient (gone after 3 months), and data regarding superior long-term outcomes with VATS lobectomy must be regarded as suggestive but not conclusive. However, the data indicates that condemnation of VATS lobectomy as an unsafe or oncologically unsound procedure is not justified.

An approach to learning VATS lobectomy is to use an anterolateral thoracotomy approach, and then gradually decrease the size of the incision and the amount of rib spreading. Although it appears that the benefits of VATS lobectomy are much more marked with a non-rib spreading approach, period of limited rib spreading in order to achieve the skills and comfort needed can certainly be justified [28]. However, patience and a true commitment to learning a new technique are required. Abandonment of VATS lobectomy after 5–10 attempts in which one does not feel equally comfortable as with an open approach does not constitute a serious effort at learning a new technique.

In conclusion, VATS lobectomy has been shown to be safe, result in fewer complications, less postoperative pain and more rapid recovery compared with lobectomy via thoracotomy. There is no difference in the ability to carry out mediastinal node dissection, and a suggestion that the ability to administer adjuvant chemotherapy is improved. Long-term outcomes are at least as good, if not better after VATS lobectomy as compared with thoracotomy. The data demonstrates that the VATS approach is an appropriate alternative to open thoracotomy in patients undergoing lobectomy for lung cancer.

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