



Surgery for lung cancer - a review



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Lung cancer

- Over 1.6 million cases worldwide
- Almost 90% present in advanced stages
- Over 1.4 million deaths annually
- Commonest cause of cancer deaths
- Exceeds combined mortality of the next four common cancers
- Major public health problem



Outline of today's talk

- Mediastinal lymph node staging
- Optimum treatment for early NSCLC
- Extent of surgery
 - Lobar vs sublobar resections
 - Extent of lymphadenectomy
- VATS vs open surgery
- The Tata Memorial Centre experience
- Summary



Early stage NSCLC

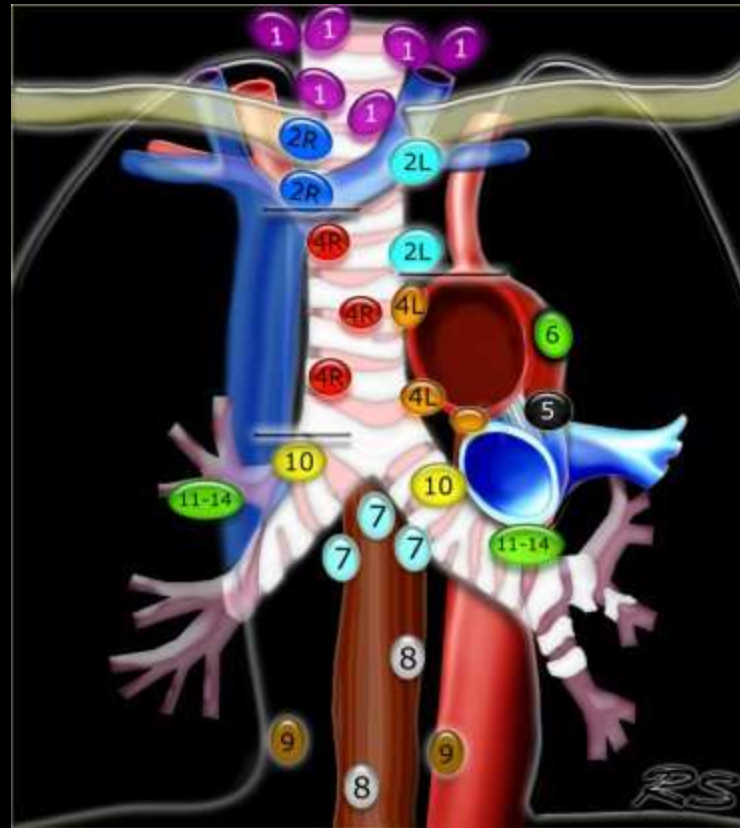
- Stages IA, IB, IIA, IIB and some IIIA
- T1-3, N0-1
- Excludes involvement of
 - Mediastinal vital structures
 - Vertebrae
 - Pleural / pericardial effusion
 - Mediastinal / supraclavicular nodes
 - Distant metastases
- **Note: Chest wall involvement is not T4!**



Why do we need accurate mediastinal staging

- Mediastinal nodal status changes treatment decisions
- Standard of care for metastatic mediastinal nodes is
 - No nodes: Surgery \pm postop chemo
 - Ipsilateral: NACT and surgery
 - Contralateral: CT-RT or pall chemo
- Level I evidence

Mediastinal nodal stations



Diagnostic options for MLN staging



- CECT thorax
- PET-CT scan
- Mediastinoscopy
- EUS-FNAC
- EBUS-FNAC

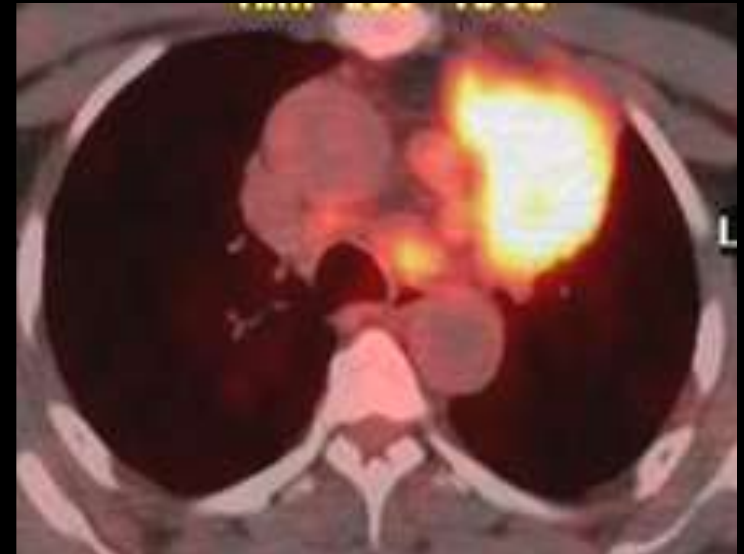
CT scan

- Advantages: Non-invasive
- No added cost or procedure
- 4793 patients analysed
- Sensitivity 60%
- Specificity 81%
- PPV 53%
- NPV 82%



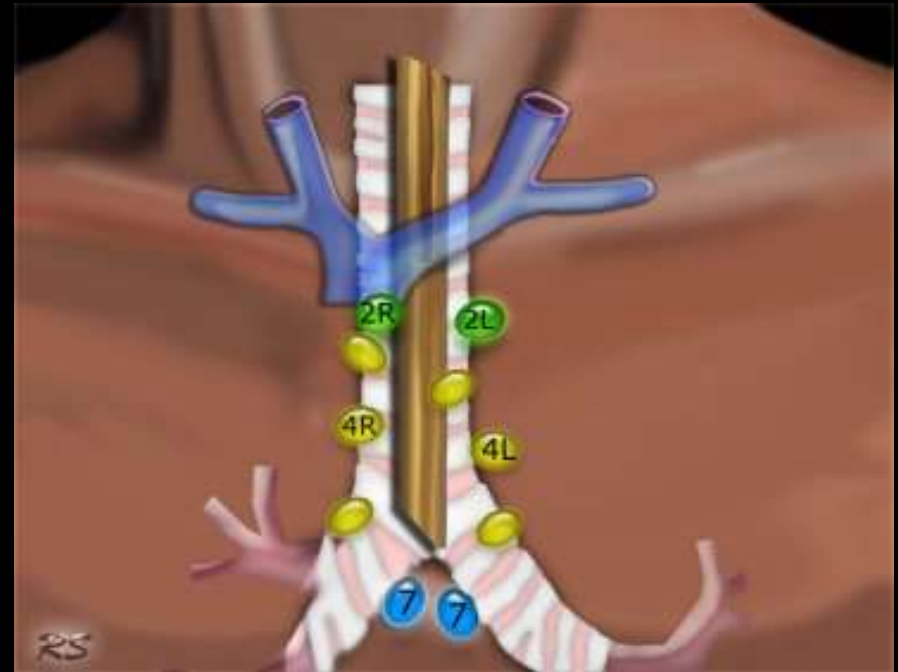
18F FDG-PET-CT scan

- Advantages: Non invasive
Combines metabolic with anatomic imaging
- 1111 patients analysed
- Sensitivity 85%
- Specificity 88%
- PPV 78%
- NPV 93%



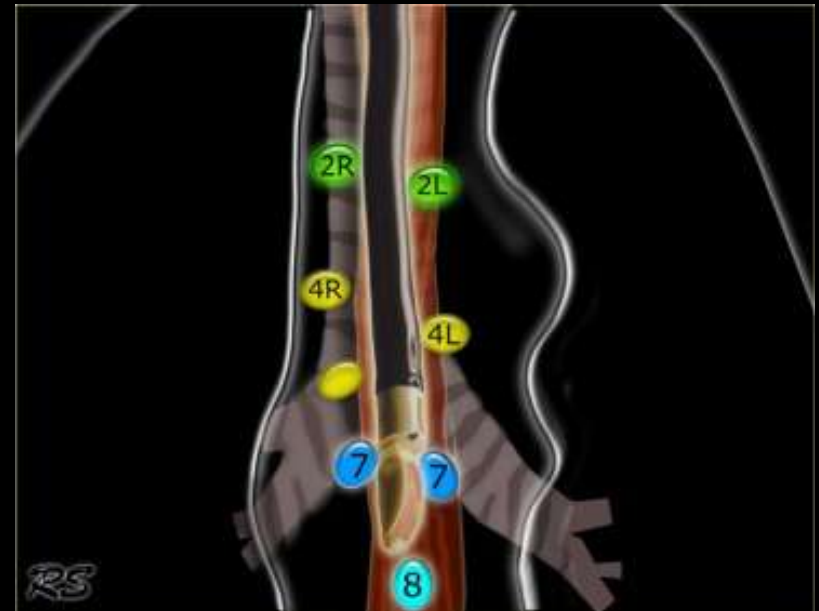
Mediastinoscopy

- Traditionally accepted as gold standard
- Highest accuracy, sensitivity and NPV
- Invasive
- Requires GA
- Expertise
- Morbidity
 - RLN paresis
 - Haemorrhage



EUS and EBUS with FNAC

- Less invasive
- Less morbid
- Provides cyto confirmation
- Operator dependent
- Expensive





What is the evidence?

Mediastinoscopy vs Endosonography for Mediastinal Nodal Staging of Lung Cancer

A Randomized Trial

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Context Mediastinal nodal staging is recommended for patients with resectable non-small cell lung cancer (NSCLC). Surgical staging has limitations, which results in the performance of unnecessary thoracotomies. Current guidelines acknowledge minimally invasive endosonography followed by surgical staging (if no nodal metastases are found by endosonography) as an alternative to immediate surgical staging.

Objective To compare the 2 recommended lung cancer staging strategies.

Design, Setting, and Patients Randomized controlled multicenter trial (Ghent, Leiden, Leuven, Papworth) conducted between February 2007 and April 2009 in 241 patients with resectable (suspected) NSCLC in whom mediastinal staging was indicated based on computed or positron emission tomography.

Intervention Either surgical staging or endosonography (combined transesophageal and endobronchial ultrasound [EUS-FNA and EBUS-TBNA]) followed by surgical staging in case no nodal metastases were found at endosonography. Thoracotomy with lymph node dissection was performed when there was no evidence of mediastinal tumor spread.

Main Outcome Measures The primary outcome was sensitivity for mediastinal nodal (N2/N3) metastases. The reference standard was surgical pathological staging. Secondary outcomes were rates of unnecessary thoracotomy and complications.

Results Two hundred forty-one patients were randomized, 118 to surgical staging and 123 to endosonography, of whom 65 also underwent surgical staging. Nodal metastases were found in 41 patients (35%; 95% confidence interval [CI], 27%-44%) by surgical staging vs 56 patients (46%; 95% CI, 37%-54%) by endosonography ($P = .11$) and in 62 patients (50%; 95% CI, 42%-59%) by endosonography followed by surgical staging ($P = .02$). This corresponded to sensitivities of 79% (41/52; 95% CI, 66%-88%) vs 85% (56/66; 95% CI, 74%-92%) ($P = .47$) and 94% (62/66; 95% CI,



Study design

- Randomized trial
- Mediastinoscopy (surgical staging) – 118 patients vs
- Endoscopic (EUS and EBUS-FNAC) plus surgical staging – 123 patients
- Primary endpoint – sensitivity of detection of N2/N3 nodes
- Intention to treat



Results

	Surgical	Endoscopic + surgical
MLN metastases	44%	50%
Sensitivity	79%	94%
Negative predictive value	86%	93%
Futile thoracotomies	18%	9%

- Mediastinoscopy identified positive MLN in 9% of patients after a negative EUS/EBUS
- Mediastinoscopy can be avoided in approx 50% patients by EUS/EBUS FNAC



Mediastinal staging in NSCLC

- Tissue diagnosis is a must in most situations (Exceptions: Squamous, T1 and PET-CT showing no MLN uptake)
- EBUS and EUS FNAC may avoid mediastinoscopy in half the patients
- EBUS and EUS heavily operator dependent
- Mediastinoscopy still the gold standard



Treatment of early NSCLC

- Surgery is the treatment of choice
- No randomized evidence
- Randomized evidence unlikely
 - Surgery established
 - Clinical staging is inaccurate
- Chemoradiation / radical radiotherapy
- SBRT / Radio Frequency Ablation



Surgery vs radiotherapy

Surgery

- | | 5 yr surv |
|---------|-----------|
| • T1 N0 | 70-90% |
| • T2 N0 | 45-68% |
| • T1 N1 | 40-57% |
| • T2 N1 | 33-45% |

Radiotherapy

- | | 5 yr surv |
|----------------|-----------|
| • Stages I, II | 6-42% |

This is an unfair comparison, but it's the best we have!



What are the results of SBRT?



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Meta-analysis

Comparison of the effectiveness of radiotherapy with photons, protons and carbon-ions for non-small cell lung cancer: A meta-analysis

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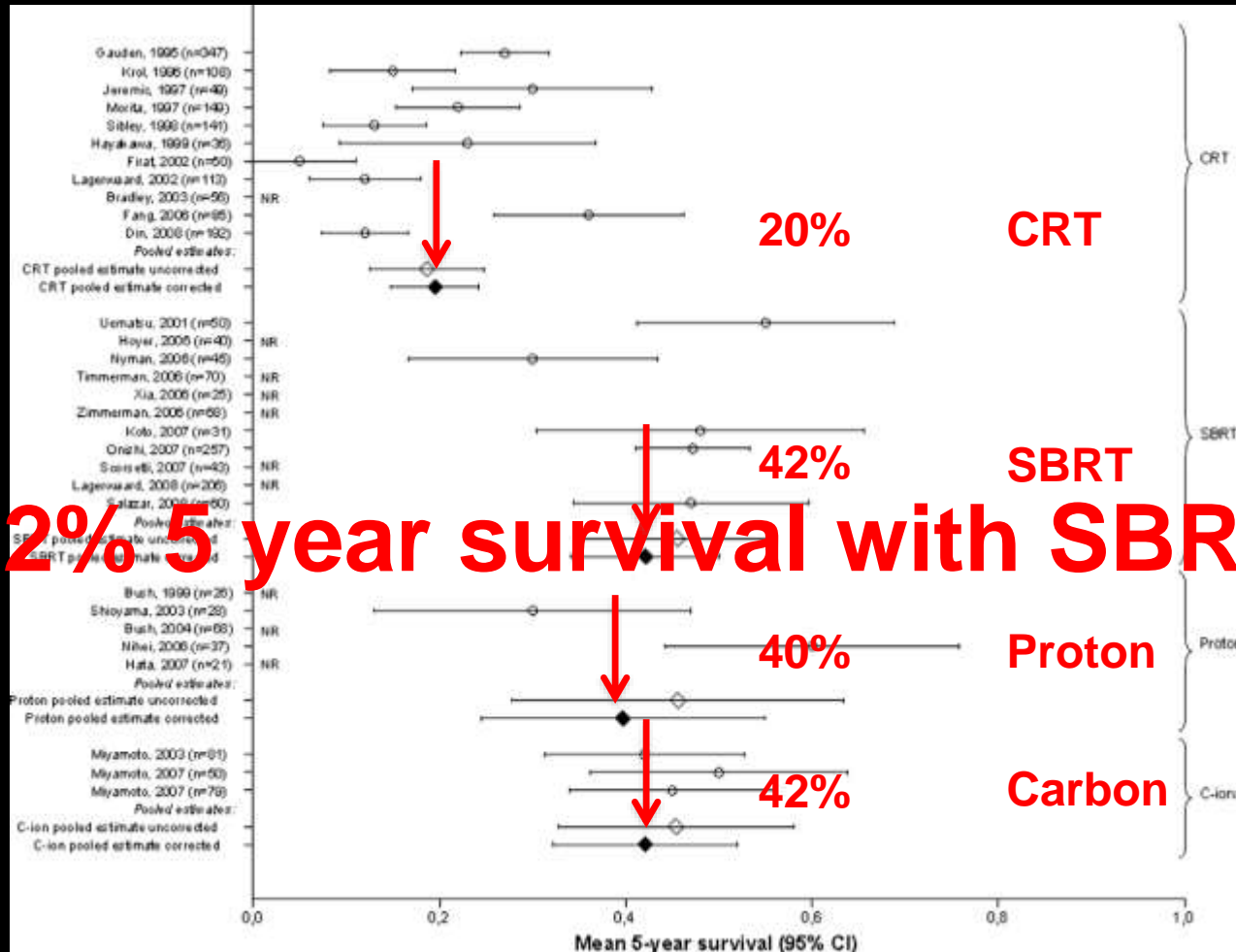
Particle therapy

Evidence synthesis

ABSTRACT

Purpose: To provide a comparison between radiotherapy with photons, protons and carbon-ions in the treatment of Non-Small-Cell Lung Cancer (NSCLC), performing a meta-analysis of observational studies. **Methods:** Eligible studies on conventional radiotherapy (CRT), stereotactic radiotherapy (SBRT), concurrent chemoradiation (CCR), proton therapy and carbon-ion therapy were searched through a systematic review. To obtain pooled estimates of 2- and 5-year disease-specific and overall survival and the occurrence of severe adverse events for each treatment modality, a random effects meta-analysis was carried out. Pooled estimates were corrected for effect modifiers. **Results:** Corrected pooled estimates for 2-year overall survival in stage I inoperable NSCLC ranged from 53% for CRT to 74% for carbon-ion therapy. Five-year overall survival for CRT (20%) was statistically significantly lower than that for SBRT (42%), proton therapy (40%) and carbon-ion therapy (42%). However, caution is warranted due to the limited number

Five year survival





Comparative studies – Puri

General Thoracic Surgery

Puri et al

A comparison of surgical intervention and stereotactic body radiation therapy for stage I lung cancer in high-risk patients: A decision analysis

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Objective: We sought to compare the relative cost-effectiveness of surgical intervention and stereotactic body radiation therapy in high risk patients with clinical stage I lung cancer (non-small cell lung cancer).

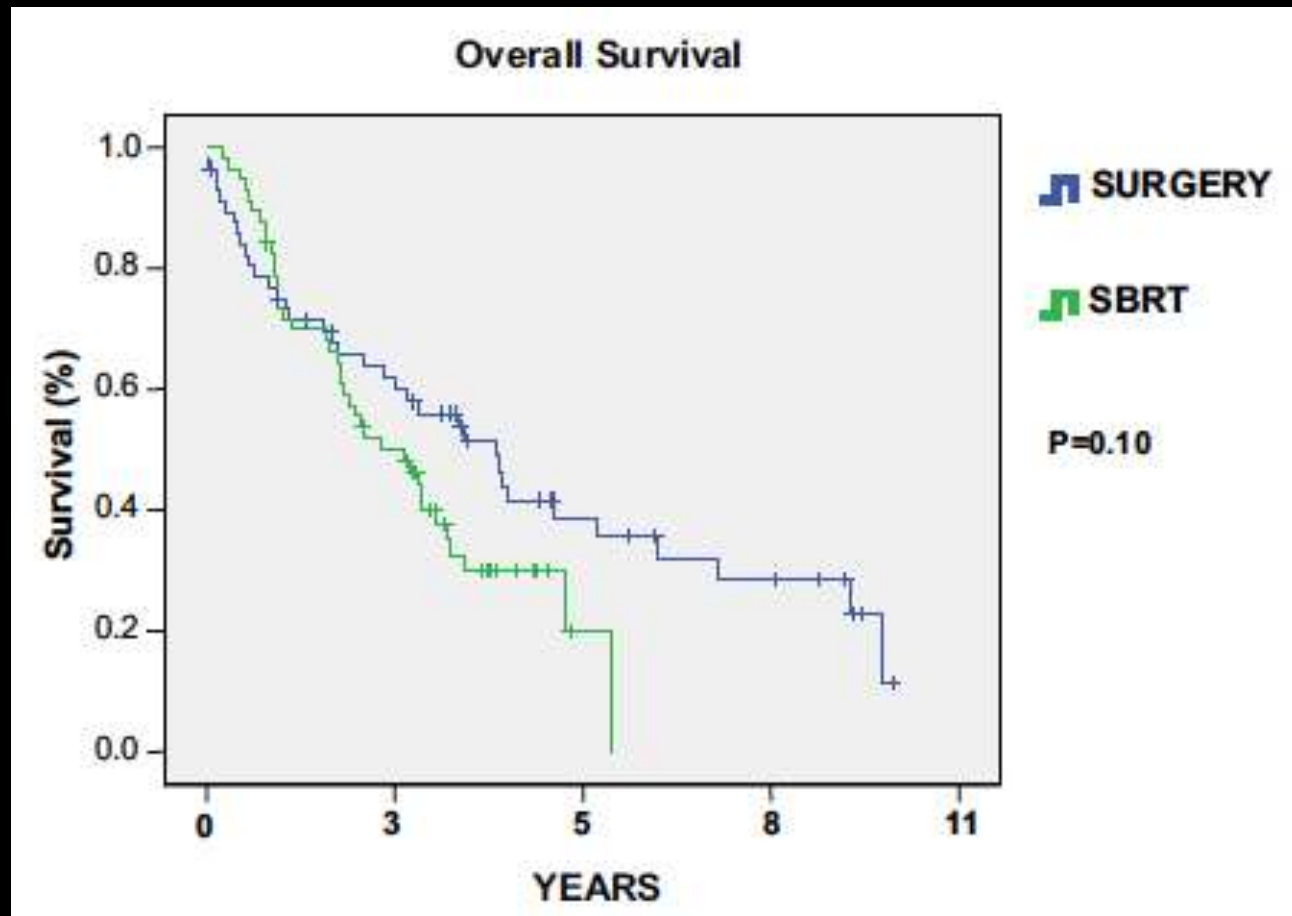
Methods: We compared patients chosen for surgical intervention or SBRT for clinical stage I non-small cell lung cancer. Propensity score matching was used to adjust estimated treatment hazard ratios for the confounding effects of age, comorbidity index, and clinical stage. We assumed that Medicare-allowable charges were \$15,034 for surgical intervention and \$13,964 for stereotactic body radiation therapy. The incremental cost-effectiveness ratio was estimated as the cost per life year gained over the patient's remaining lifetime by using a decision model.

Results: Fifty-seven patients in each arm were selected by means of propensity score matching. Median survival with surgical intervention was 4.1 years, and 4-year survival was 51.4%. With stereotactic body radiation therapy, median survival was 2.9 years, and 4-year survival was 30.1%. Cause-specific survival was identical between the 2 groups, and the difference in overall survival was not statistically significant. For decision modeling, stereotactic body radiation therapy was estimated to have a mean expected survival of 2.94 years at a cost of \$14,153 and mean expected survival with surgical intervention was 3.39 years at a cost of \$17,629, for an incremental cost-effectiveness ratio of \$7753.

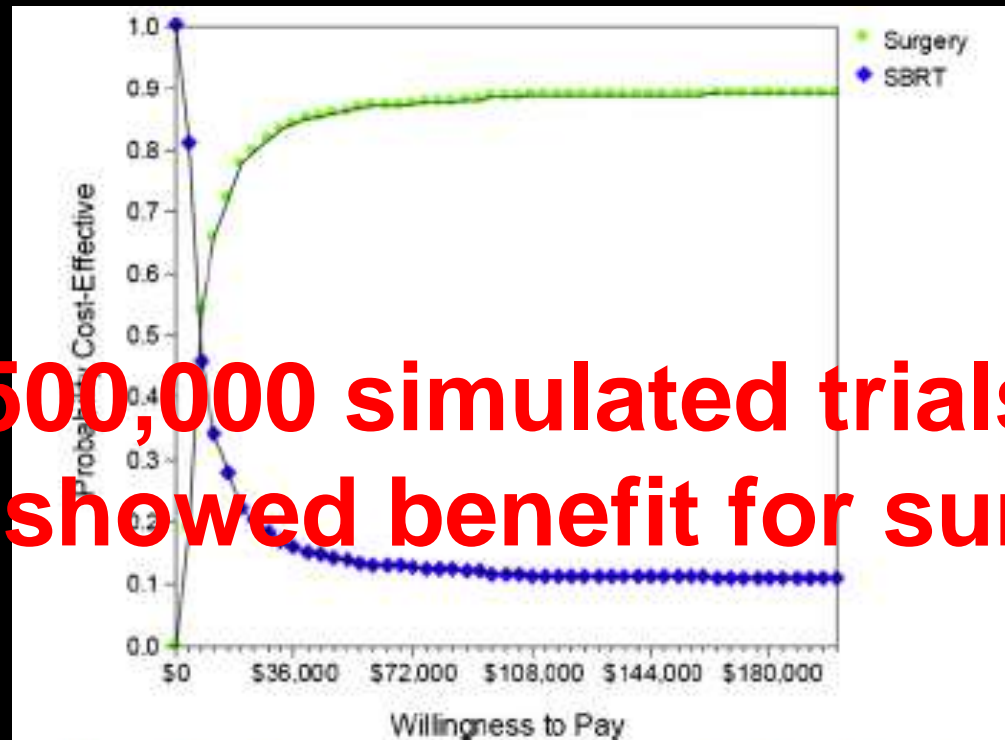
Conclusions: In our analysis stereotactic body radiation therapy appears to be less costly than surgical intervention in high-risk patients with early stage non-small cell lung cancer. However, surgical intervention appears to meet the standards for cost-effectiveness because of a longer expected overall survival. Should this advantage not be confirmed in other studies, the cost-effectiveness decision would be likely to change. Prospective randomized studies are necessary to strengthen confidence in these results. (J Thorac Cardiovasc Surg 2012;143:428-36)



Overall survival



Monte Carlo simulation



500,000 simulated trials
85% showed benefit for surgery

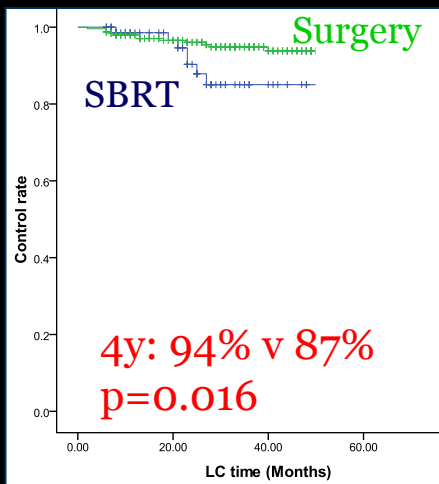
FIGURE 4. Cost-effectiveness acceptability curve based on the results of Monte Carlo simulation. At a willingness to pay of \$72,000 per life year gained, approximately 85% of the trials resulted in greater net benefit for surgical intervention than for stereotactic body radiation therapy (SBRT).

Comparisons of SBRT and Surgery

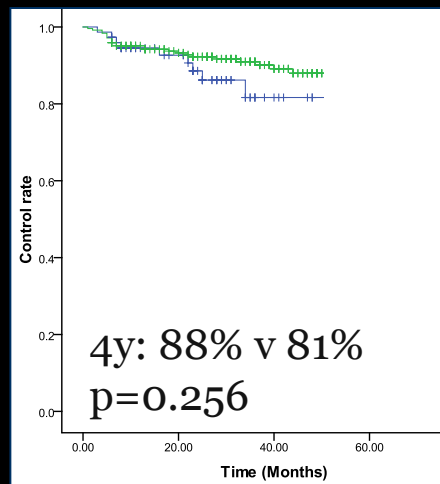


Un-matched SBRT vs. Surgery

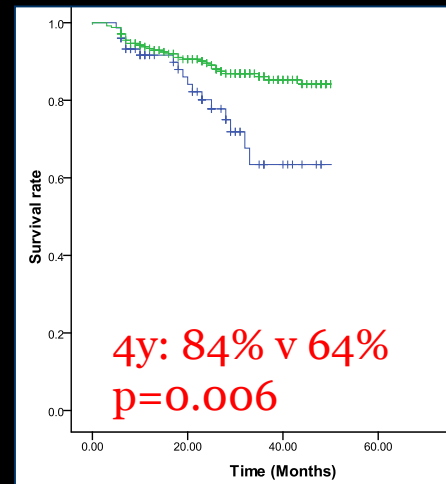
LC



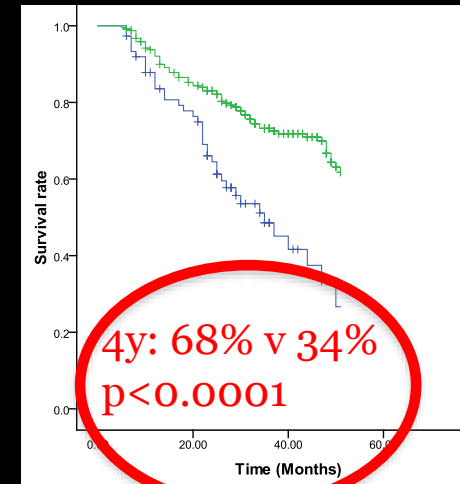
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DMFS



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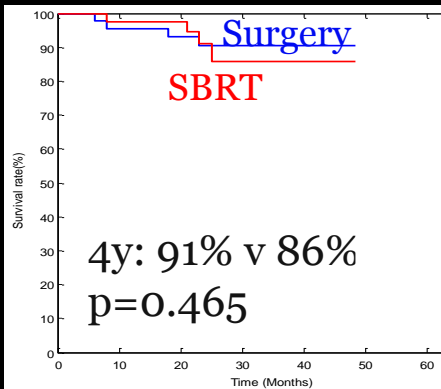


Comparisons of SBRT and Surgery

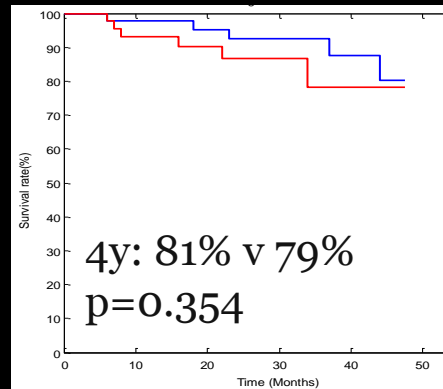


Matched SBRT vs. Surgery

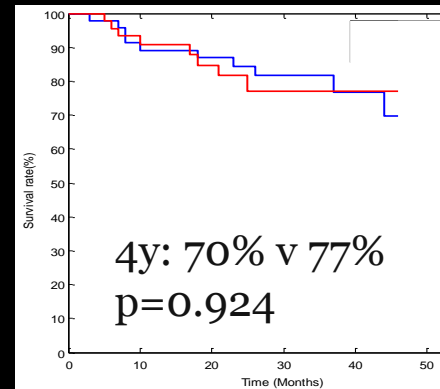
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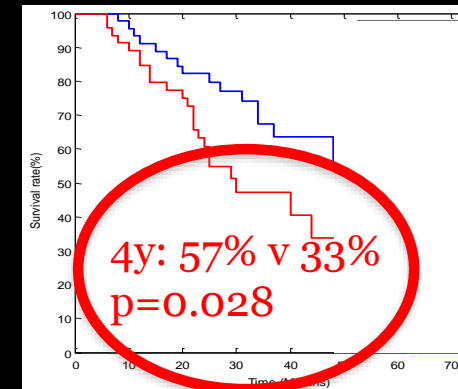
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**Surgery is the treatment of choice
in early stage NSCLC**



What is the minimum surgery
for lung cancer?



Lung cancer • 6: The case for limited surgical resection in non-small cell lung cancer

Segmental Resection for Lung Cancer in Non-Small Cell Lung Cancer Patients With Limited Lung Function

Sublobar resection for lung cancer[☆]

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Abstract

The role of limited lung resection 'segmentectomy and wedge resection' in the treatment of lung cancer has been reviewed. Survival for patients with stage I lung cancer and lesions less than 2 cm is comparable to that of major resections such as lobectomy. The theoretical advantage of limited resection is the simplicity of the procedure and the potential for performing it through lesser invasive techniques. The major drawback at this time which should render it a compromise rather than a choice operation is the increased risk of locoregional recurrence. Until properly conducted clinical trials validate its efficacy in peripheral T1 lung cancer with or without adjuvant therapy, sublobar resection should be limited to patients that are at poor risk of tolerating major lung resection. Sublobar resections however may also play a useful role in treatment of metachronous or synchronous lung cancer. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Limited lung resection; Survival; Stage I lung cancer

Background. Segmental resection for lung cancer remains controversial because that segmentectomy confers lung function and compromise. We undertook a retrospective study to assess the value of segmentectomy.

Methods. We retrospectively reviewed 147 patients who underwent lobectomy (n = 147) or segmentectomy (n = 32) for stage I non-small cell lung cancer between January 1990 and June 2001. All patients underwent pulmonary function testing preoperatively and at 1 year postoperatively. Pulmonary function was compared with lobectomy patients. Complications, forced expiratory volume in 1 second, and diffusing capacity were compared. Stepper exercise was performed. Patients who underwent segmentectomy had better pulmonary function than lobectomy patients. Confounding variables of tobacco use, age, and sex were controlled.

Results. Preoperative pulmonary function was compared with lobectomy patients. Postoperative pulmonary function was compared with lobectomy patients. There was no significant difference in pulmonary function between the two groups.

1. Introduction

It is agreed upon that lung resection when possible is the best therapeutic option for stage I lung cancer. Approximately 40 years ago, the debate on the appropriateness of lobectomy as opposed to a pneumonectomy as the resection of choice for lung cancer raged and settled on the conclusion that a more limited resection at that time (lobectomy) was adequate and more preserving of lung function. Approximately 15 years ago, several retrospective reviews of a vari-

2. The evidence that limited resection works

There is no question that the surgical team at the Rush Presbyterian St. Luke's Medical Centre were the champions of conservative lung resection [1,4,5,10-12]. Jensik and co-workers repeatedly presented evidence that sparing the whole lung by performing a sleeve lobectomy was advantageous to the patients and did not compromise long-term survival [10]. Similarly his 15-year experience on the outcome of segmental resection for lung cancer was the



Sublobar vs lobar resection

Randomized Trial of Lobectomy Versus Limited Resection for T1 N0 Non-Small Cell Lung Cancer

Lung Cancer Study Group (Prepared by Robert J. Ginsberg, MD, and Lawrence V. Rubinstein, PhD)

Background. It has been reported that limited resection (segment or wedge) is equivalent to lobectomy in the management of early stage (T1-2 N0) non-small cell lung cancer.

Methods. A prospective, multiinstitutional randomized trial was instituted comparing limited resection with lobectomy for patients with peripheral T1 N0 non-small cell lung cancer documented at operation. Analysis included locoregional and distant recurrence rates, 5-year survival rates, perioperative morbidity and mortality, and late pulmonary function assessment.

Results. There were 276 patients randomized, with 247 patients eligible for analysis. There were no significant differences for all stratification variables, selected prognostic factors, perioperative morbidity, mortality, or late pulmonary function. In patients undergoing limited resection, there was an observed 75% increase in recurrence

rates ($p = 0.02$, one-sided) attributable to an observed tripling of the local recurrence rate ($p = 0.008$ two-sided), an observed 30% increase in overall death rate ($p = 0.08$, one-sided), and an observed 50% increase in death with cancer rate ($p = 0.09$, one-sided) compared to patients undergoing lobectomy ($p = 0.10$, one-sided was the predefined threshold for statistical significance for this equivalency study).

Conclusions. Compared with lobectomy, limited pulmonary resection does not confer improved perioperative morbidity, mortality, or late postoperative pulmonary function. Because of the higher death rate and locoregional recurrence rate associated with limited resection, lobectomy still must be considered the surgical procedure of choice for patients with peripheral T1 N0 non-small cell lung cancer.

(*Ann Thorac Surg* 1995;60:615-23)

Non-small cell lung cancer (NSCLC) affects more than 140,000 people in the United States annually.

potential for an increased local recurrence rate and, ultimately, a poorer cure rate for this deadly disease.



Limited resections in T1 N0

- Randomised trial
- Lung Cancer Study Group
- 276 patients
- Patients undergoing limited resections had
 - 75% increased recurrence
 - Local recurrence tripled
 - 30% increased overall deaths
 - 50% increased cancer deaths



Survival After Lobectomy Versus Segmentectomy for Stage I Non-Small Cell Lung Cancer: A Population-Based Analysis

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Background: Data comparing survival after lobectomy versus that after segmentectomy for stage I non-small cell lung cancer (NSCLC) are limited to single-institution observational studies and 1 clinical trial. We sought to determine if lobectomy offers a survival advantage over segmentectomy for stage I NSCLC based on population-based data.

Methods: Using the Surveillance Epidemiology and End Results (SEER) database (1998 to 2007), we identified patients who underwent either anatomic segmentectomy or lobectomy. Wedge resections were excluded. Analysis was limited to patients with stage I adenocarcinoma or squamous cell carcinoma. After stratifying patients based on tumor size (less than or equal to 2.0 cm, 2.1 to 3.0 cm, and 3.1 to 7.0 cm), we assessed for association between extent of resection and survival using the Kaplan-Meier method. To adjust for potential confounding variables, we used Cox proportional hazards regression models.

Results: There were 14,473 patients who met our inclusion criteria. Lobectomy conferred superior unadjusted overall ($p < 0.0001$) and cancer-specific ($p = 0.0053$) 5-year survival compared with segmentectomy. Even after adjusting for patient factors, tumor characteristics, and geographic location, we noted that patients who underwent lobectomy had superior overall and cancer-specific survival rates, regardless of tumor size. Squamous cell histologic type, male sex, low lymph node counts, and increasing age, tumor size, and grade were all independent negative prognostic factors.

Conclusions: Using a population-based data set, we found that lobectomy confers a significant survival advantage compared with segmentectomy. Our results provide additional evidence supporting the role of lobectomy as the standard of care for resection of stage I NSCLC regardless of tumor size.

(Ann Thorac Surg 2011;xx:xxx)

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Sublobectomy Versus Lobectomy for Stage I Non-Small-Cell Lung Cancer, A Meta-Analysis of Published Studies

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ABSTRACT

Background. The selection of surgeries for patients with stage I NSCLC remains controversial. We evaluated the effectiveness of different surgeries for stage I NSCLC through a meta-analysis of studies that compared sublobectomy with lobectomy.

Methods. The overall survival/cancer-specific survival (OS/CSS) of stage I NSCLC after sublobectomy or lobectomy was compared. The log (hazard ratio) [ln (HR)] and its standard error (SE) were used as the outcome measure for data combining.

Results. There were 24 eligible studies, published from 1990 to 2010, enrolled (11,360 patients). Compared with sublobectomy, there was a significant benefit of lobectomy

stage Ia patients with tumor ≤ 2 cm, sublobectomy produces similar survival to lobectomy.

Lobectomy remains the standard treatment for patients with resectable non-small-cell lung cancer (NSCLC).¹ However, there are more complications followed by lobectomy. Furthermore, patients with stage I NSCLC, with tumor less than 2 cm, might be overtreated by lobectomy. With the wide use of high-resolution computed tomography (CT) and low-dose helical CT in lung cancer screening, more and more NSCLCs were diagnosed at early T1 stage. Considering the relatively good prognosis of T1 stage NSCLC, many sur-



Lobectomy is the minimum surgery for operable NSCLC
There may be a role for anatomical segmentectomy in tumors <2 cm



What should be the extent of lymphadenectomy?



Extent of lymphadenectomy

Mediastinal lymphadenectomy in non-small cell lung cancer: effectiveness in patients with or without nodal micrometastases — results of a preliminary study[☆]

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Abstract

Objectives: So far it has not clearly been demonstrated that systematic mediastinal lymphadenectomy improves survival in patients with non-small cell lung cancer. One explanation might be that in some patients an early spread of tumor cells has occurred which might not be curable by surgical means. To test this hypothesis lymph nodes of patients which were treated either by lymph node sampling or systematic lymphadenectomy were screened for micrometastatic spread of tumor cells and the influence of nodal micrometastases on the efficacy of lymphadenectomy was analyzed. **Methods:** Lymph nodes from patients ($n = 94$) which were included in a randomized trial of lymph node sampling (LS, $n = 41$) versus radical systematic lymphadenectomy (LA, $n = 53$) were screened by immunohistochemistry for disseminated tumor cells using the antibody Ber-Ep4. The median observation time was longer than 5 years and follow-up data were available from all 94 patients. Kaplan–Meier curves were calculated and tested for statistical significance using the log-rank test. **Results:** Standard histopathological analysis revealed no lymph node involvement (pN0) in 61 patients, pN1 disease in 13 patients and pN2 disease in 20 patients without significant differences between LA and LS with respect to T-stage, N-stage or age and sex of the patients. By immunohistochemistry a minimal nodal spread of tumor cells was detected in 21 out of 94 patients (LS, $n = 10$ (24%); LA, $n = 11$ (21%)). Similar to the entire group of patients also in the subset of patients with nodal micrometastases the type of lymphadenectomy did not significantly influence the long-term survival ($P = 0.27$ and $P = 0.39$, respectively). In contrast, in patients with a negative immunohistochemical analysis systematic lymphadenectomy resulted in an improved overall survival ($P = 0.044$). **Conclusions:** Our data provide some evidence that systematic lymphadenectomy improves survival in patients without an early locoregional spread of cancer cells. As long as these patients can not be

The role of mediastinal lymphadenectomy in the staging and treatment of non-small cell lung cancer

moved. “Systematic sampling” refers to routine biopsy of lymph nodes at levels specified by the author. “Complete

who underwent c
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for those patients
and 29.2 months
0.004). However,
patients with rig
months, $p < 0.001$
Conclusions. In
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Extent of lymphadenectomy



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Lung Cancer 36 (2002) 1–6



www.elsevier.com/locate/lungcan

A randomized trial of systematic nodal dissection in resectable non-small cell lung cancer[☆]

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Abstract

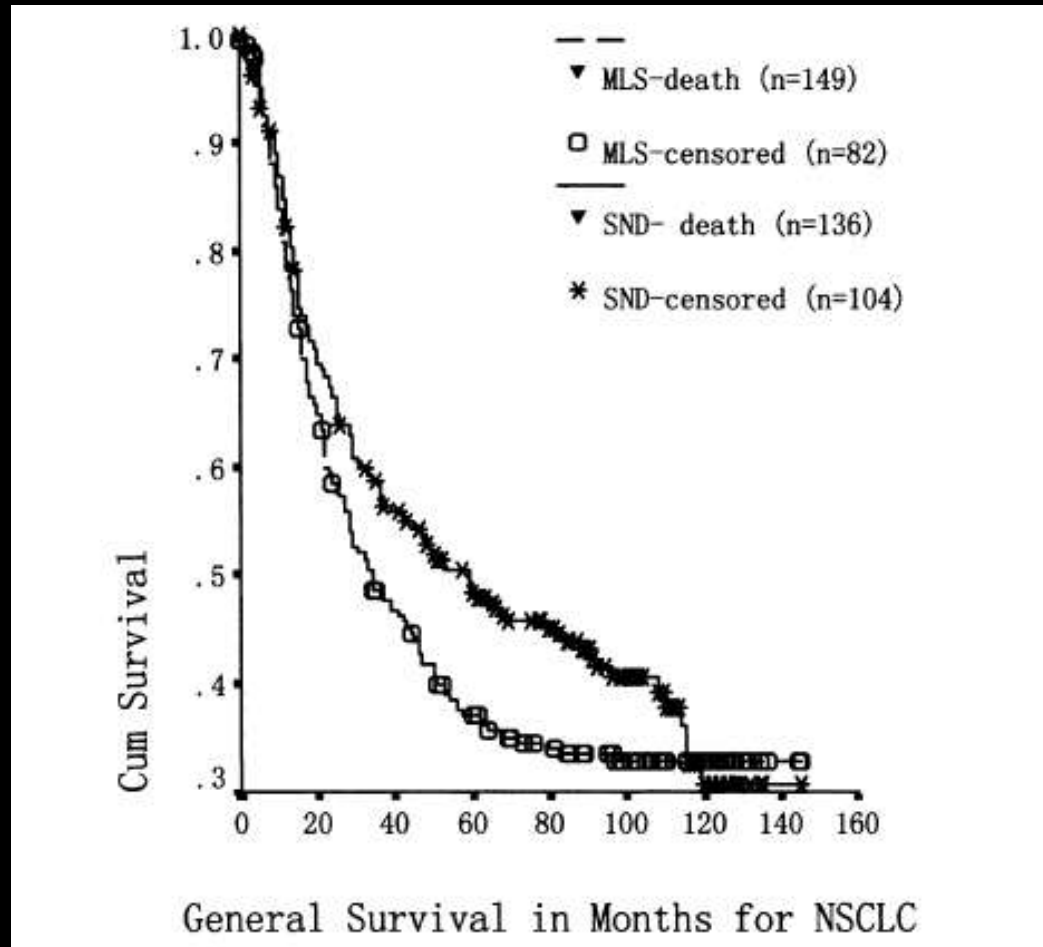
Purpose: We conducted a randomized trial to investigate whether systematic nodal dissection (SND) is superior to mediastinal lymph nodal sampling (MLS) in surgical treatment of non-small cell lung cancer (NSCLC). **Methods:** The patients resectable clinical Stage I–IIIA NSCLC were randomly assigned to lung resection combined with SND or lung resection combined with MLS. After postoperative pathological re-staging, eligible cases were followed up until 30 November 2000. The Kaplan–Meier method was used for survival analysis, COX proportional hazards model was used for prognostic analysis. **Results:** Of the 532 patients who were enrolled in the study, 268 patients were assigned to lung resection combined with SND and 264 were assigned to lung resection combined with MLS. After surgical restaging only 471 cases were eligible for follow-up. The median survival was 59 months in the group given SND and 34 months in the group given MLS ($P = 0.0000$ by the log rank test). There was significant difference in survival in Stage I (5-year survival 82.16 vs. 57.49%) and Stage IIIA (26.98 vs. 6.18%) by the log rank test and Breslow test. There was no significant yet marginal difference in survival by log rank test (10-year survival 32.04 vs. 26.92%, $P = 0.0523$) but significant difference in survival by Breslow test (5-year survival 50.42 vs. 34.05%, $P = 0.0284$) in Stage II. Types



Extent of lymphadenectomy

- Randomized trial – stage I-IIIa NSCLC
- 532 patients
- Median survival – 59 months vs 34 months (p=0.0000)
- “...SMLND can improve survival in resectable NSCLC...”

Extent of lymphadenectomy



48% vs 37% 5 year survival

Extent of lymphadenectomy – the ACOSOG Z0030



Randomized trial of mediastinal lymph node sampling versus complete lymphadenectomy during pulmonary resection in the patient with N0 or N1 (less than hilar) non–small cell carcinoma: Results of the American College of Surgery Oncology Group Z0030 Trial

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Objective: To determine whether mediastinal lymph node dissection improves survival compared with mediastinal lymph node sampling in patients undergoing resection for N0 or nonhilar N1, T1, or T2 non–small cell lung cancer.

Methods: Patients with non–small cell lung cancer underwent sampling of 2R, 4R, 7, and 10R for right-sided tumors and 5, 6, 7, and 10L for left-sided tumors. If all tumors were negative for malignancy, patients were randomized to no further lymph node sampling (mediastinal lymph node sampling) or complete mediastinal lymph node dissection.

Results: Of 1111 patients randomized, 1023 (mediastinal lymph node sampling in 498, mediastinal lymph node dissection in 525) were eligible and evaluable. There were no significant differences between the 2 groups in terms of demographics, Eastern Cooperative Oncology Group status, histology, cancer location, type or extent of resection, and pathologic stage. Occult N2 disease was found in 21 patients in the mediastinal lymph node dissection group. At a median follow-up of 6.5 years, 435 patients (43%) have died: mediastinal lymph node sampling in 217 (44%) and mediastinal lymph node dissection in 218 (42%). The median survival is 8.1 years for mediastinal lymph node sampling and 8.5 years for mediastinal lymph node dissection ($P = .25$). The 5-year disease-free survival was 69% (95% confidence interval, 64–74) in the mediastinal lymph node sampling group and 68% (95% confidence interval, 64–73) years in the mediastinal lymph node dissection group ($P = .92$). There was no difference in local ($P = .52$), regional ($P = .10$), or distant ($P = .76$) recurrence between the 2 groups.

Conclusions: If systematic and thorough presection sampling of the mediastinal and hilar lymph nodes is negative, mediastinal lymph node dissection does not improve survival in patients with early stage non–small cell lung cancer, but these results are not generalizable to patients staged radiographically or those with higher stage tumors. (J Thorac Cardiovasc Surg 2011;141:662-70)

Overall survival

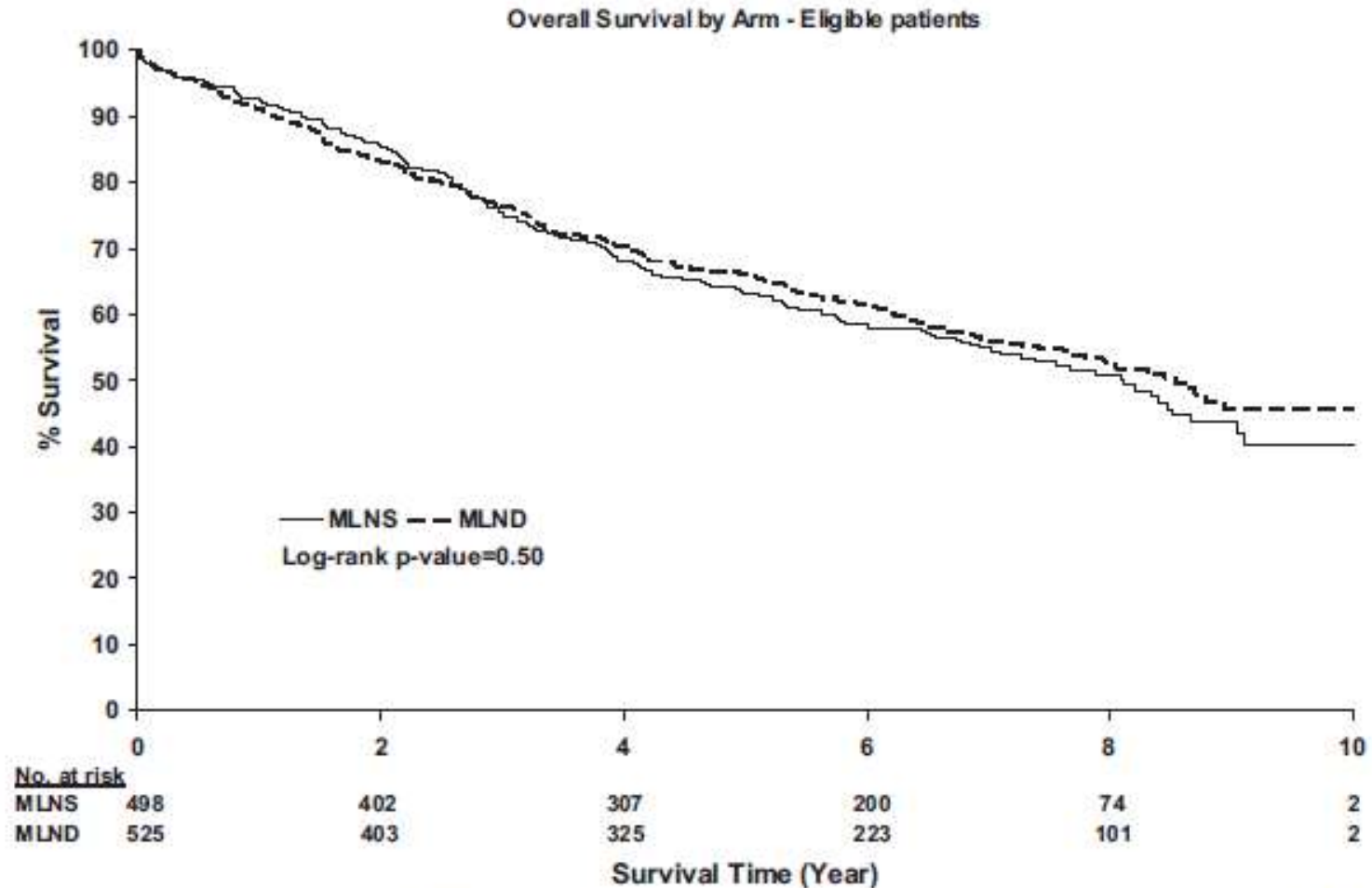
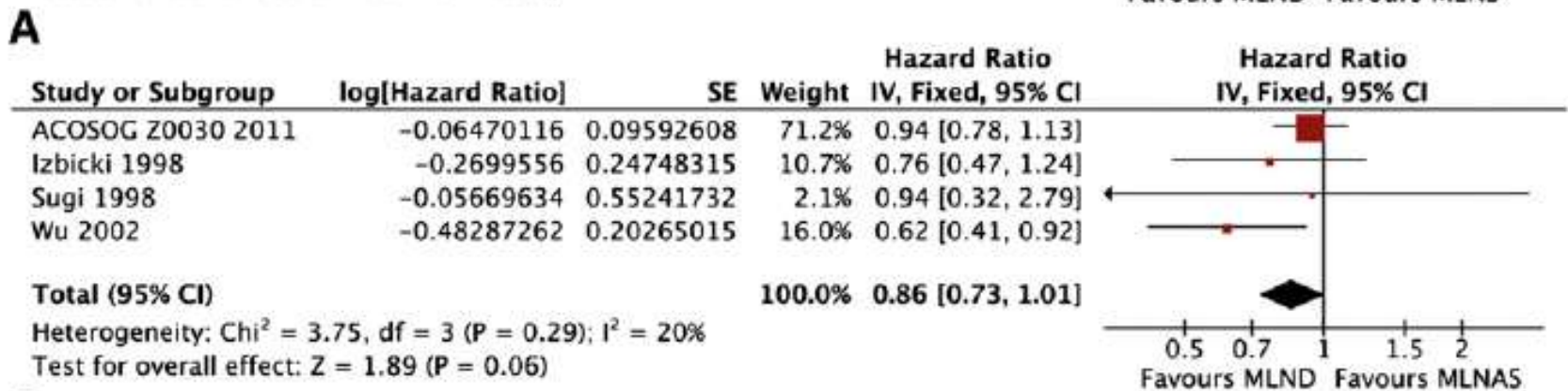
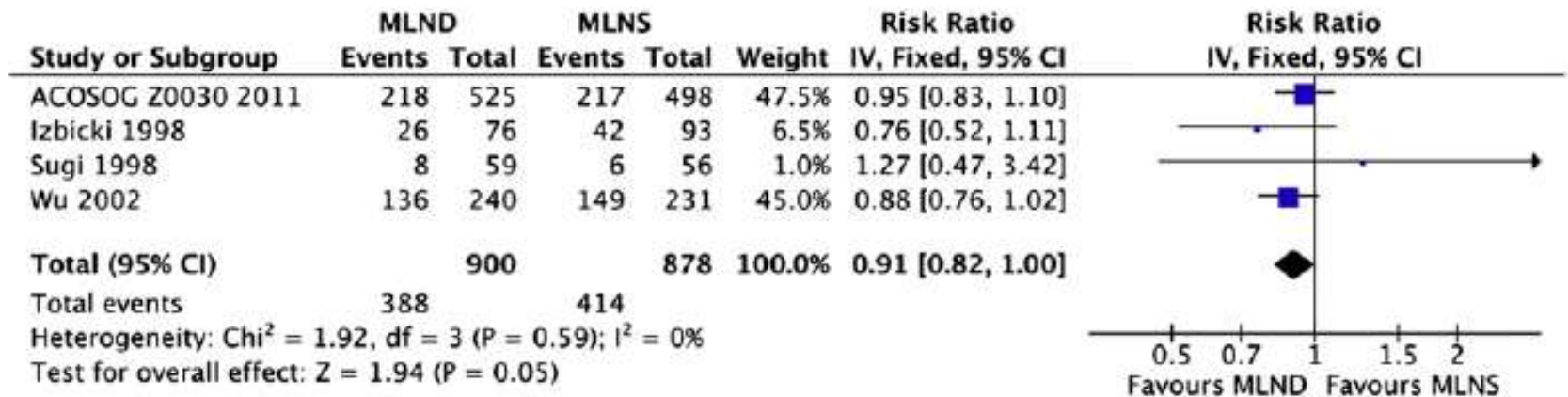


FIGURE 2. Overall survival. *MLNS*, Mediastinal lymph node sampling; *MLND*, mediastinal lymph node dissection.

Mediastinal LND – meta analysis



B



**Systematic mediastinal
lymphadenectomy should be done
in operable NSCLC**



VATS vs open lung resections

Posterolateral thoracotomy



Video assisted thoracoscopic surgery (VATS)





VATS - caveats

- Learning curve
- Should be a competent open thoracic surgeon
- No compromise on oncological safety
- Reduced complications usually after learning curve
- Pulmonary adhesions – specific problem in India



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

Tristan D. Yan, Deborah Black, Paul G. Bannon, and Brian C. McCaughan

A B S T R A C T

Purpose

The current randomized trials comparing video-assisted thoracic surgery (VATS) lobectomy with open lobectomy for patients with early-stage non–small-cell lung cancer (NSCLC) have been of small size. We performed the present meta-analysis of the randomized and nonrandomized comparative studies in an attempt to assess the safety and efficacy of VATS lobectomy.

Methods

Electronic searches identified 21 eligible comparative studies (two randomized and 19 nonrandomized) for inclusion. Two reviewers independently appraised each study. Meta-analysis was performed by combining the results of reported incidence of morbidity and mortality, recurrence, and 5-year mortality rates. The relative risk (RR) was used as a summary statistic.

Results

There were no significant statistical differences between VATS and open lobectomy in terms of postoperative prolonged air leak ($P = .71$), arrhythmia ($P = .86$), pneumonia ($P = .09$), and mortality ($P = .49$). VATS did not demonstrate any significant difference in locoregional recurrence ($P = .24$), as compared with the open lobectomy arm, but the data suggested a reduced systemic recurrence rate ($P = .03$) and an improved 5-year mortality rate of VATS ($P = .04$). There was no evidence to suggest heterogeneity of trial results. Fourteen studies reported VATS to open lobectomy conversion rate ranging from 0% to 15.7% (median = 8.1%).

Conclusion

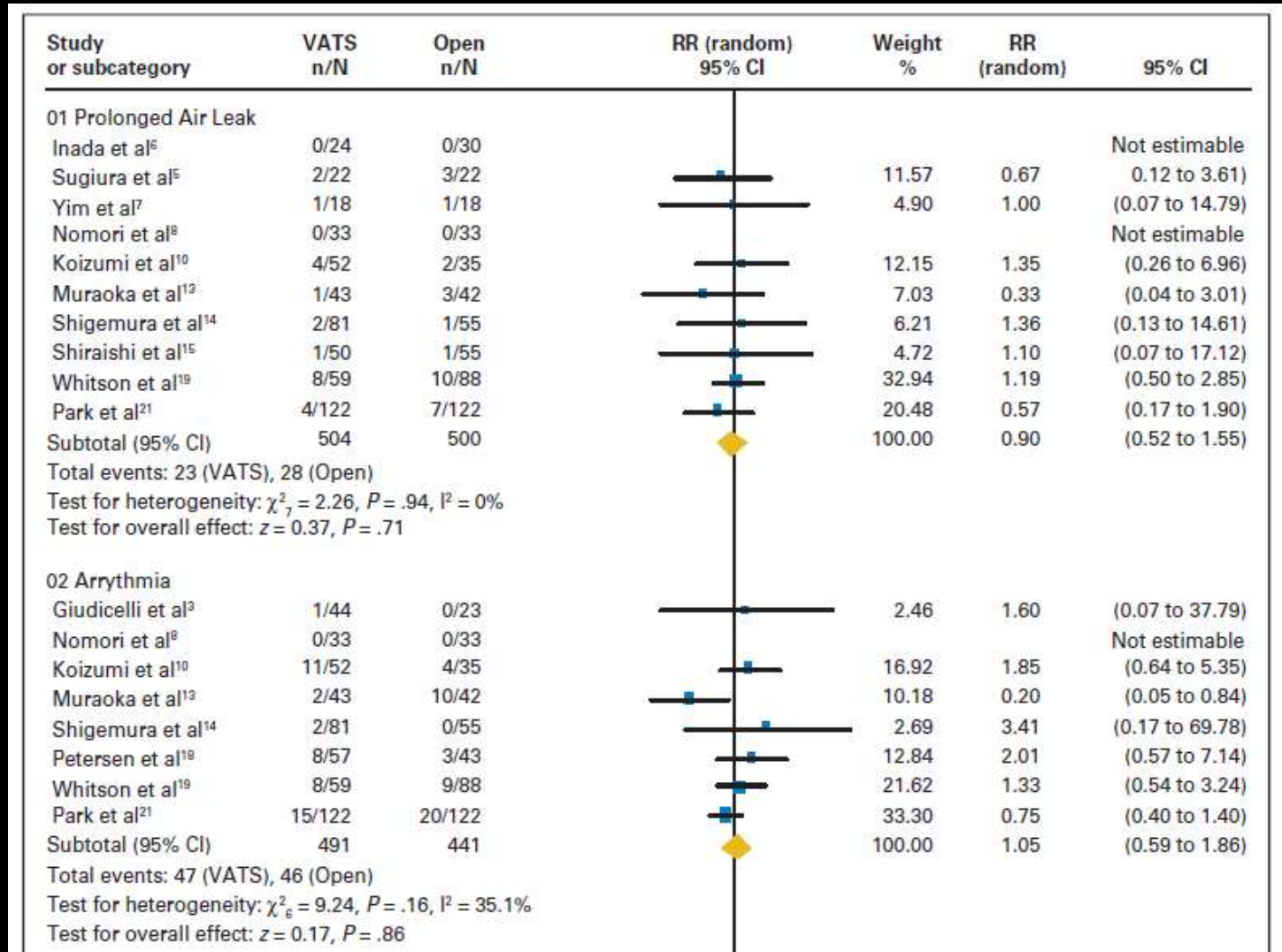
Both randomized and nonrandomized trials suggest that VATS lobectomy is an appropriate procedure for selected patients with early-stage NSCLC when compared with open surgery.



VATS vs open meta analysis

- 21 studies; 2641 patients
- Two randomized trials
- 1391 VATS resections
- 1250 open resections

Air leak and arrhythmia



Pneumonia and mortality

Study	VATS	Open	OR	95% CI	95% CI
Sugiura et al ⁵	2/22	0/22	11.36	5.00	(0.25 to 98.52)
Nomori et al ⁹	0/33	0/33			Not estimable
Koizumi et al ¹⁰	0/52	4/35	12.05	0.08	(0.00 to 1.36)
Muraoka et al ¹³	1/43	1/42	13.36	0.98	(0.06 to 15.11)
Petersen et al ¹⁸	1/57	3/43	19.69	0.25	(0.03 to 2.33)
Whitson et al ¹⁹	2/59	17/88	43.54	0.18	(0.04 to 0.73)
Subtotal (95% CI)	266	263	100.00	0.34	(0.10 to 1.16)

Total events: 6 (VATS), 25 (Open)

Test for heterogeneity: $\chi^2_4 = 5.58$, $P = .23$, $I^2 = 28.3\%$

Test for overall effect: $z = 1.72$, $P = .09$

Study	VATS	Open	OR	95% CI	95% CI
Giudicelli et al ³	3/44	0/23	34.31	3.73	(0.20 to 69.32)
Kirby et al ¹	0/25	0/30			Not estimable
Sugiura et al ⁵	0/22	0/22			Not estimable
Yim et al ⁷	0/18	0/18			Not estimable
Nomori et al ⁹	0/33	0/33			Not estimable
Koizumi et al ¹⁰	0/52	0/35			Not estimable
Tatsumi et al ¹¹	0/118	2/121	32.07	0.21	(0.01 to 4.23)
Muraoka et al ¹³	0/43	0/42			Not estimable
Shigemura et al ¹⁴	0/50	0/55			Not estimable
Shiraishi et al ¹⁵	0/81	0/79			Not estimable
Sakuraba et al ¹⁷	0/84	0/56			Not estimable
Petersen et al ¹⁸	0/57	0/43			Not estimable
Park et al ²¹	0/122	3/122	33.62	0.14	(0.01 to 2.74)
Subtotal (95% CI)	749	679	100.00	0.49	(0.06 to 3.76)

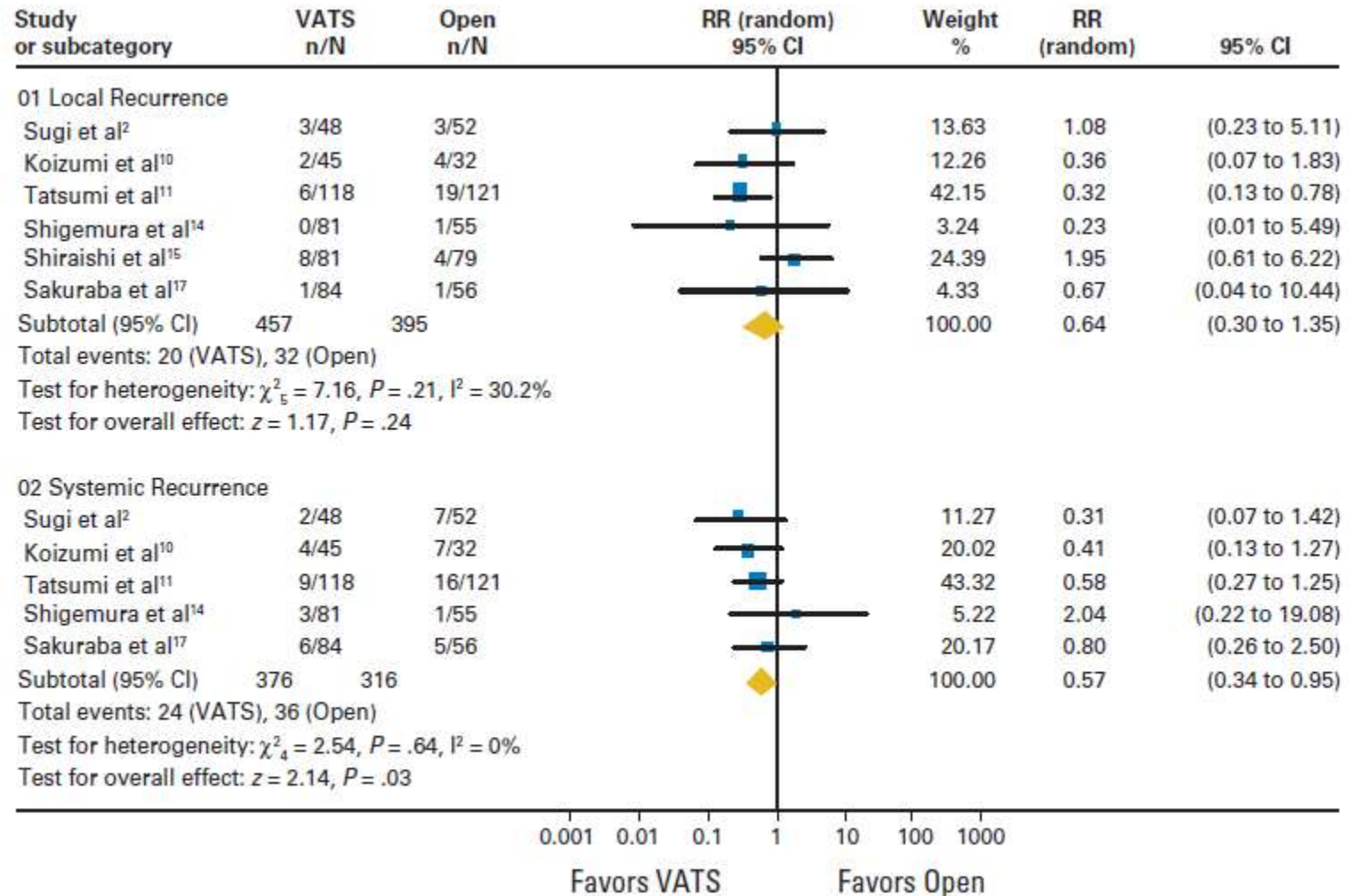
Total events: 3 (VATS), 5 (Open)

Test for heterogeneity: $\chi^2_2 = 2.85$, $P = .24$, $I^2 = 29.8\%$

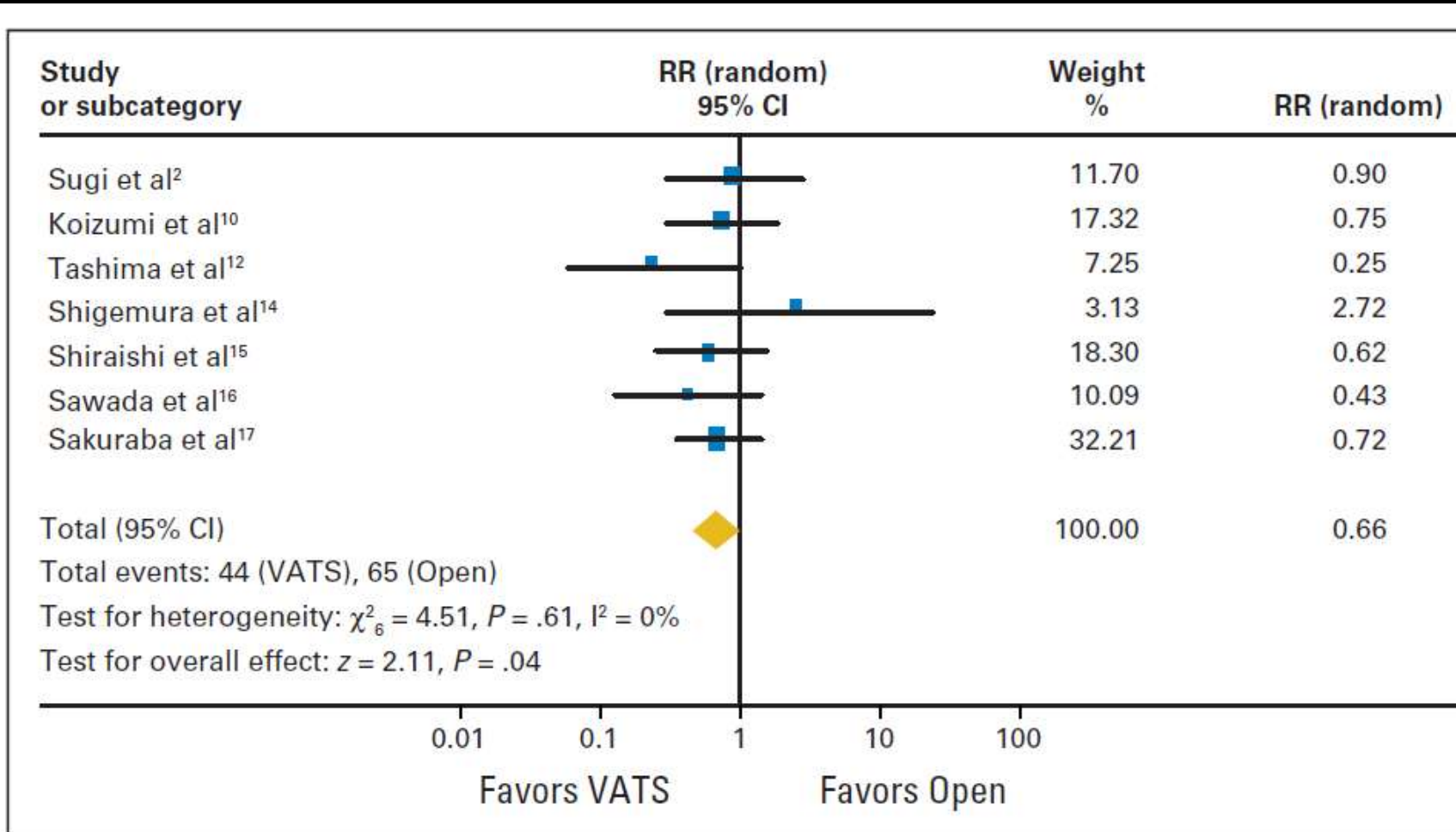
Test for overall effect: $z = 0.69$, $P = .49$

0.001 0.01 0.1 1 10 100 1000
Favors VATS Favors Open

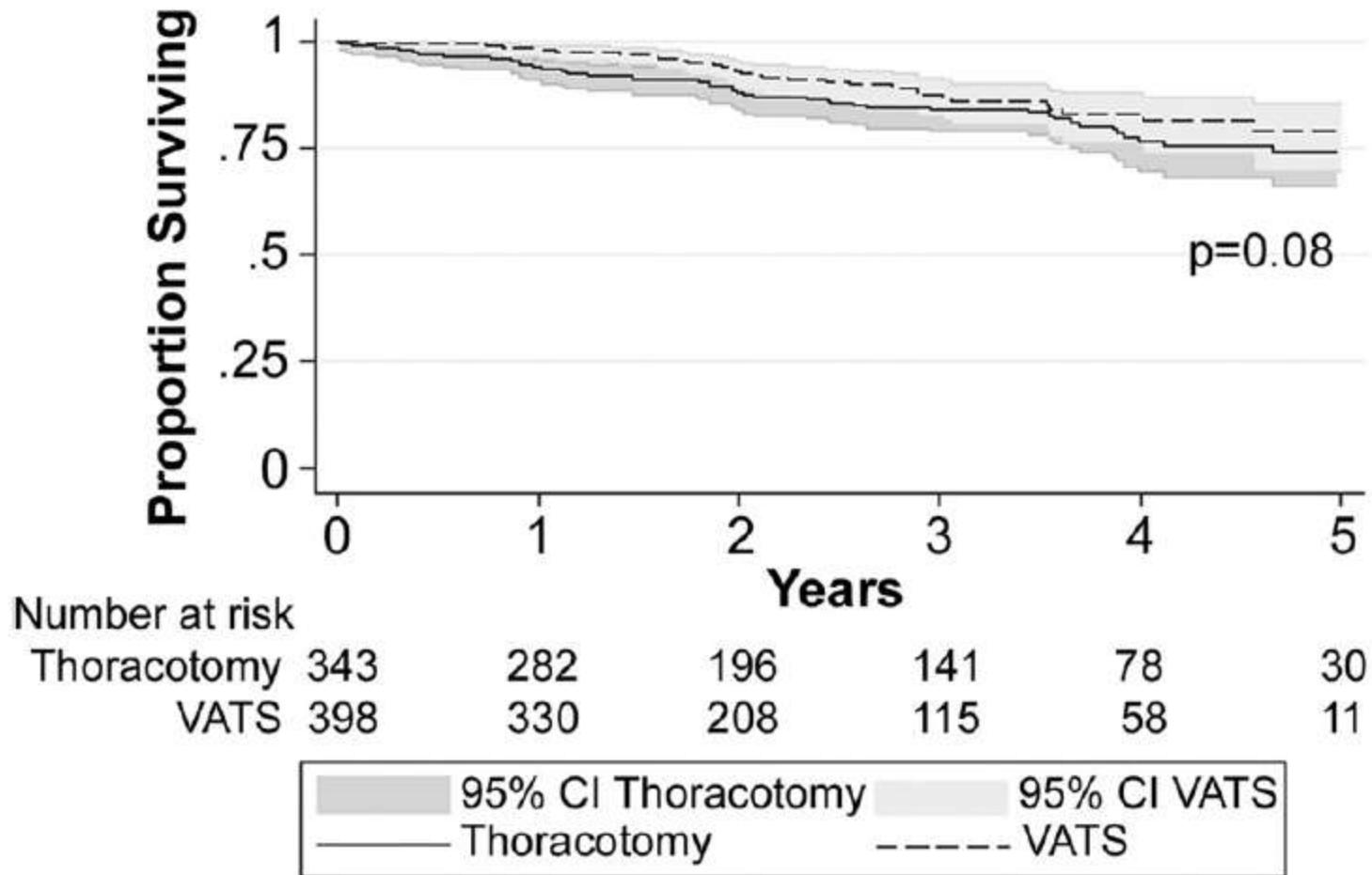
Oncologic control



All cause mortality



Five year survival





VATS lung resections have promise in reducing immediate postoperative complications without compromising overall survival



Outcomes

Immediate perioperative

Long term survival



Postoperative morbidity and mortality – the new standard

J. MAXWELL CHAMBERLAIN MEMORIAL PAPER

Morbidity and Mortality of Major Pulmonary Resections in Patients With Early-Stage Lung Cancer: Initial Results of the Randomized, Prospective ACOSOG Z0030 Trial

Mark S. Allen, MD, Gail E. Darling, MD, Taine T. V. Pechet, MD, John D. Mitchell, MD, James E. Herndon II, PhD, Rodney J. Landreneau, MD, Richard I. Inculet, MD, David R. Jones, MD, Bryan F. Meyers, MD, David H. Harpole, MD, Joe B. Putnam, Jr, MD, Valerie W. Rusch, MD, and the ACOSOG Z0030 Study Group*

GENERAL THORACIC

Background. Little prospective, multiinstitutional data exist regarding the morbidity and mortality after major pulmonary resections for lung cancer or whether a mediastinal lymph node dissection increases morbidity and mortality.

Methods. Prospectively collected 30-day postoperative data was analyzed from 1,111 patients undergoing pulmonary resection who were enrolled from July 1999 to February 2004 in a randomized trial comparing lymph node sampling versus mediastinal lymph node dissection for early stage lung cancer.

Results. Of the 1,111 patients randomized, 1,023 were included in the analysis. Median age was 68 years (range, 23 to 89 years); 52% were men. Lobectomy was performed in 766 (75%) and pneumonectomy in 42 (4%). Pathologic stage was IA in 424 (42%), IB in 418 (41%), IIA in 37 (4%),

was performed in 498 patients and lymph node dissection in 525. Operative mortality was 2.0% (10 of 498) for lymph node sampling and 0.76% (4 of 525) for lymph node dissection. Complications occurred in 38% of patients in each group. Lymph node dissection had a longer median operative time and greater total chest tube drainage (15 minutes, 121 mL, respectively). There was no difference in the median hospitalization, which was 6 days in each group ($p = 0.404$).

Conclusions. Complete mediastinal lymphadenectomy adds little morbidity to a pulmonary resection for lung cancer. These data from a current, multiinstitutional cohort of patients who underwent a major pulmonary resection constitute a new baseline with which to compare results in the future.

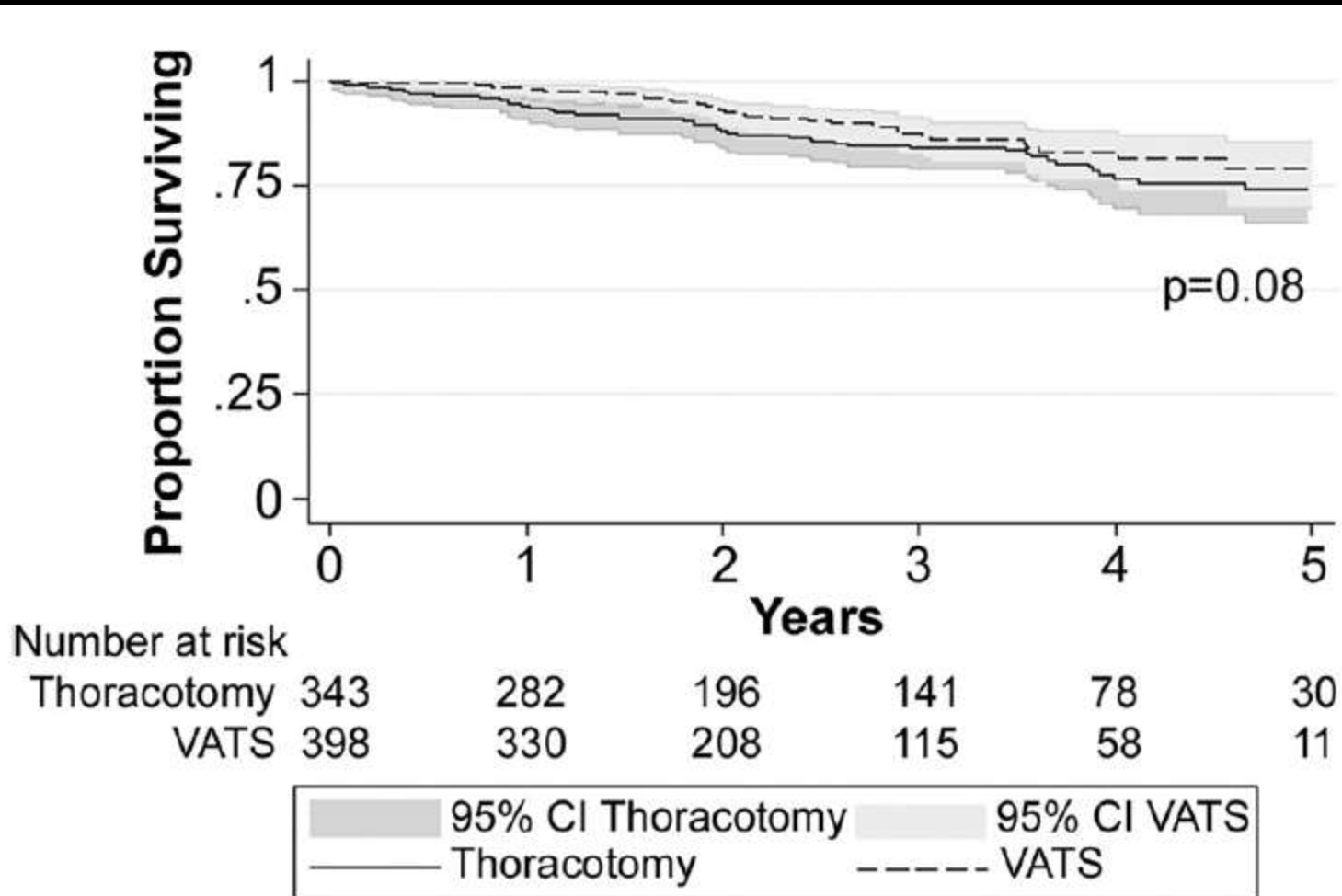
(Ann Thorac Surg 2006;81:1013–20)



Postoperative morbidity and mortality – the new standard

- Overall morbidity – 38% (any complication)
- Operative mortality
 - Lobectomy 1%
 - Pneumonectomy 0%

Five year survival



I-ELCAP survival curve

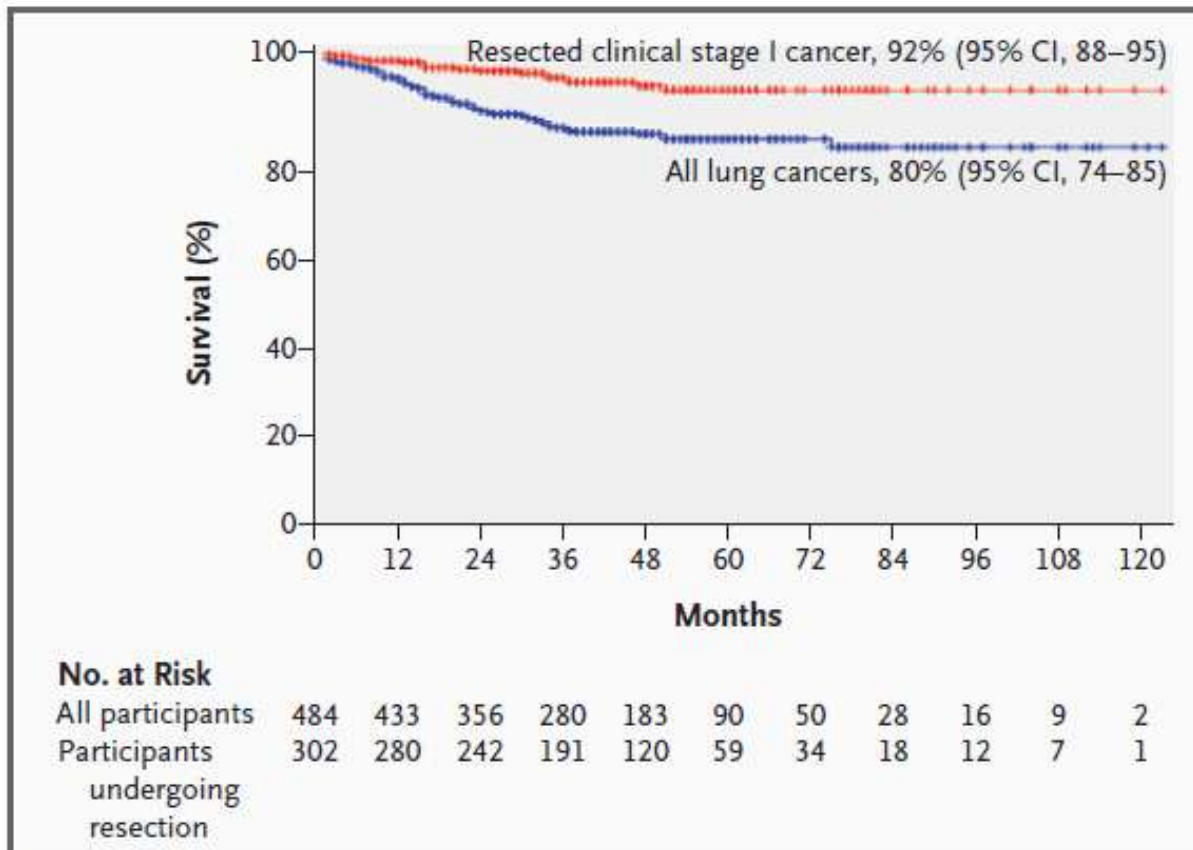


Figure 2. Kaplan–Meier Survival Curves for 484 Participants with Lung Cancer and 302 Participants with Clinical Stage I Cancer Resected within 1 Month after Diagnosis.



Short and long term outcomes after surgery for NSCLC have improved

The Tata Memorial Centre experience





2012 – a snapshot

- Lung cancer 1365
- Esophageal cancer 1234
- Mediastinal tumors 211

Surgery

- Esophageal cancer 187
- Lung cancer 97
- Lung metastasectomy 109

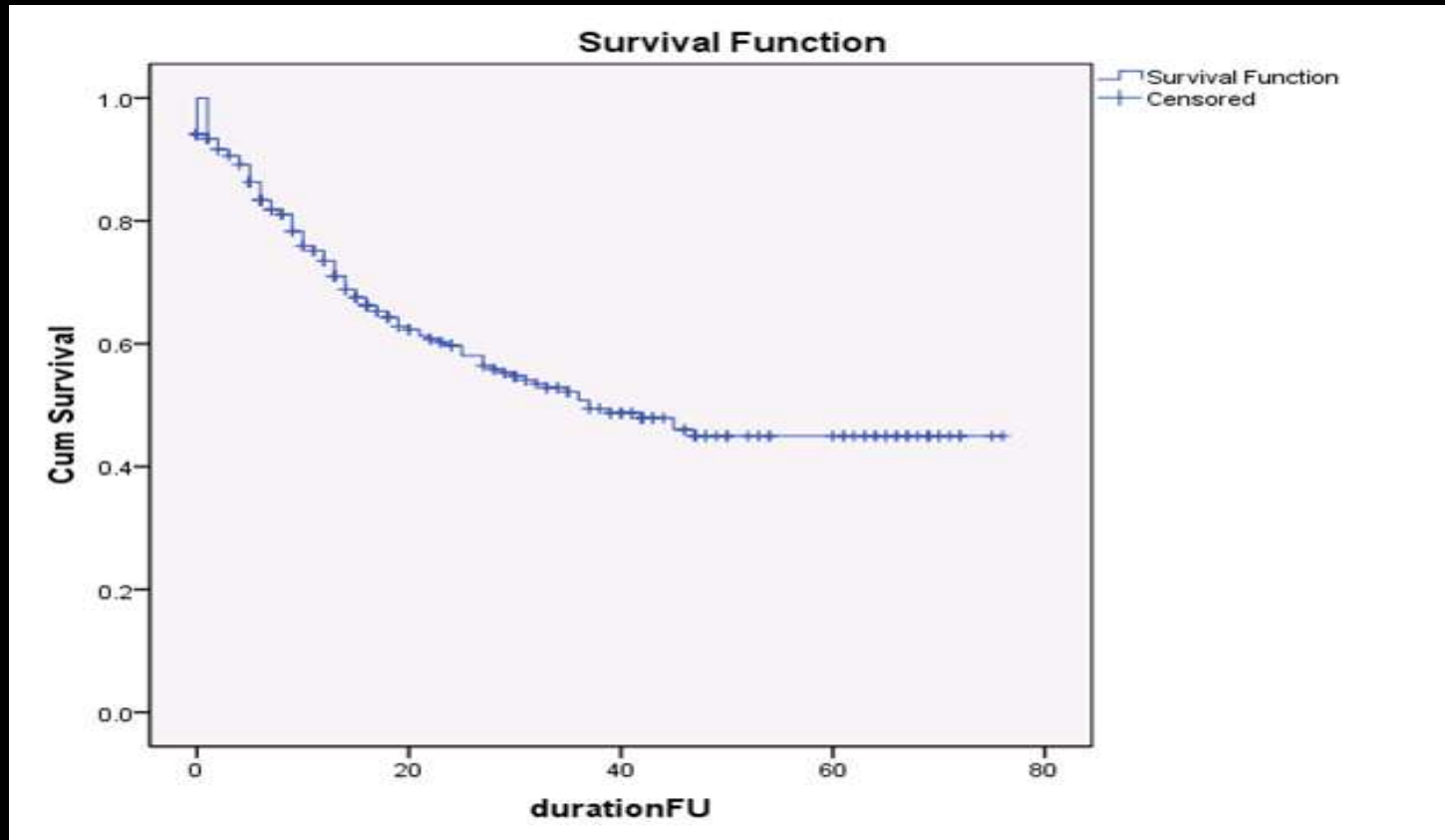


Lung surgery (666) – M&M

Pulmonary compl	61	9.2%
Major morbidity	70	10.5%
Mortality	11	1.7%
Median ICU stay	0 day	
Median hospital stay	4 days	



Overall survival



Median survival – 37 months
5 year survival – 42%



Summary

- Lung cancer surgery has evolved over the last two decades
- VATS lung resection is here to stay and has promise
- Outcomes – both short and long term have improved
- The Tata Memorial Hospital experience



Lung cancer

- Over 1.6 million cases worldwide
- Almost 90% present in advanced stages
- Over 1.4 million deaths annually
- Commonest cause of cancer deaths
- Exceeds combined mortality of the next four common cancers
- Major public health problem





Thank you