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LUNG CANCER SYMPOSIUM

Early Stage NSCLC: When is Sub-Lobar Resection Appropriate?

Onkar Khullar MD, MSc

Emory University School of Medicine, Winship Cancer Institute

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Disclosures

Roche Diagnostics – Advisory Board

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Surgery is Standard Treatment for Early Stage NSCLC

Anatomic resections

Lobectomy

Pneumonectomy

Segmentectomy

Non-anatomic resection

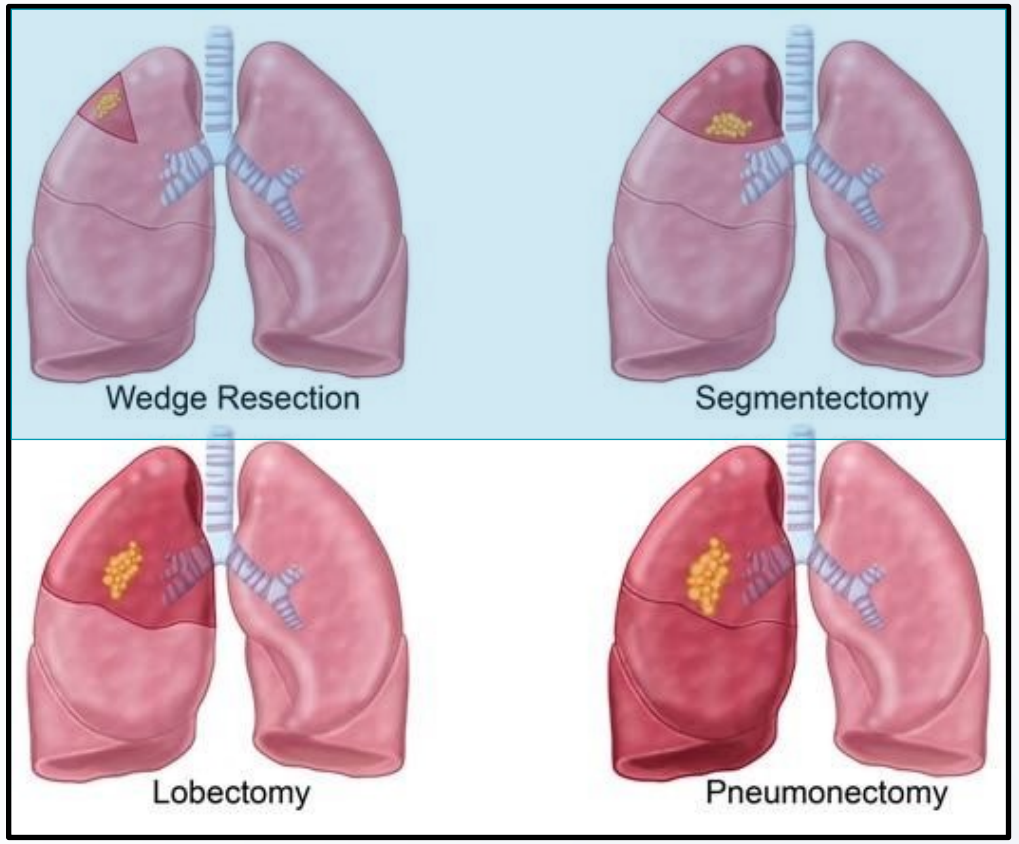
Wedge Resection

Sub-Lobar Resection

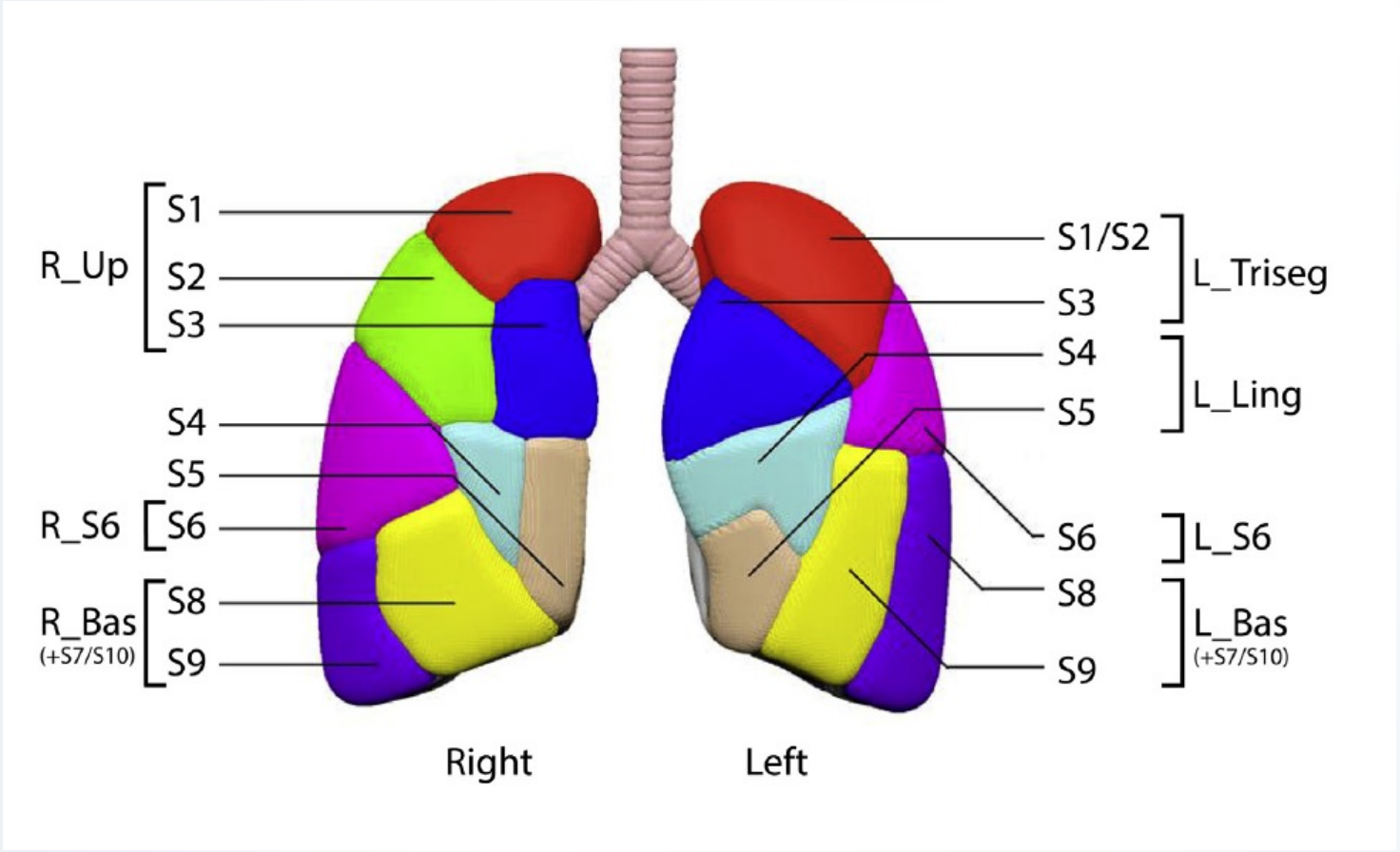
Minimally invasive surgery

Video Assisted Thoracic Surgery (VATS)

Robotic Assisted



Brief Anatomy Lesson – Lung Segments

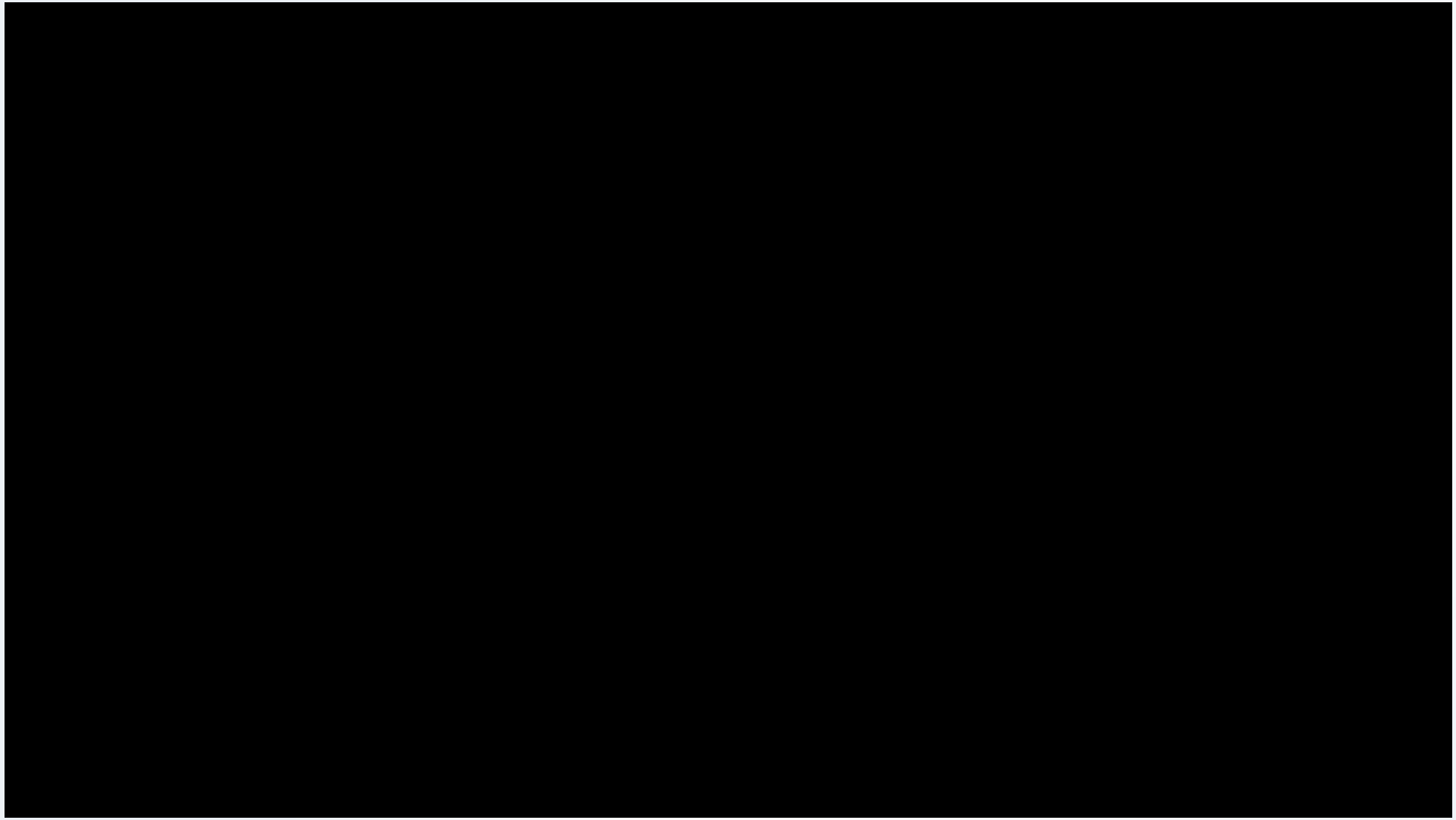


From: Jones GD, et al. Ann Thorac Surg 2021; 111:1028-35

When would we want to consider sublobar resection?

1. Small tumor
2. High risk patient
3. Marginal pulmonary function
4. High risk for future pulmonary disease

Robotic Segmentectomy



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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)

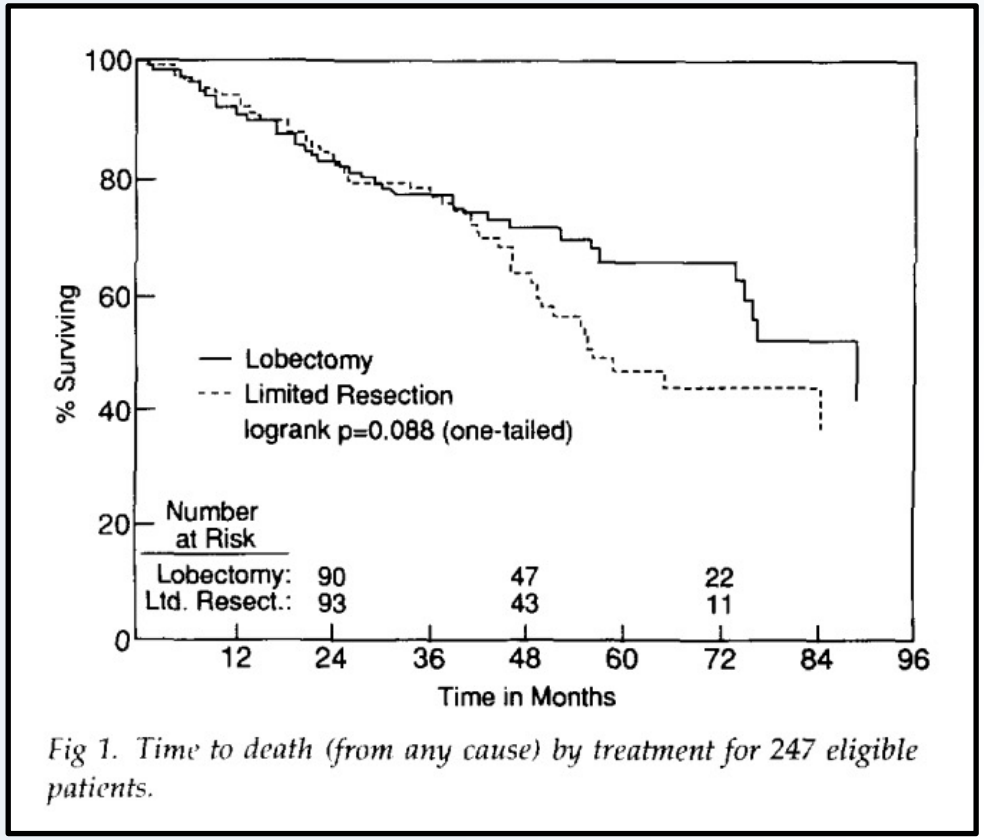


Fig 1. Time to death (from any cause) by treatment for 247 eligible patients.

30% higher incidence of death from any cause
50% higher incidence of death from cancer
Logrank p = 0.088

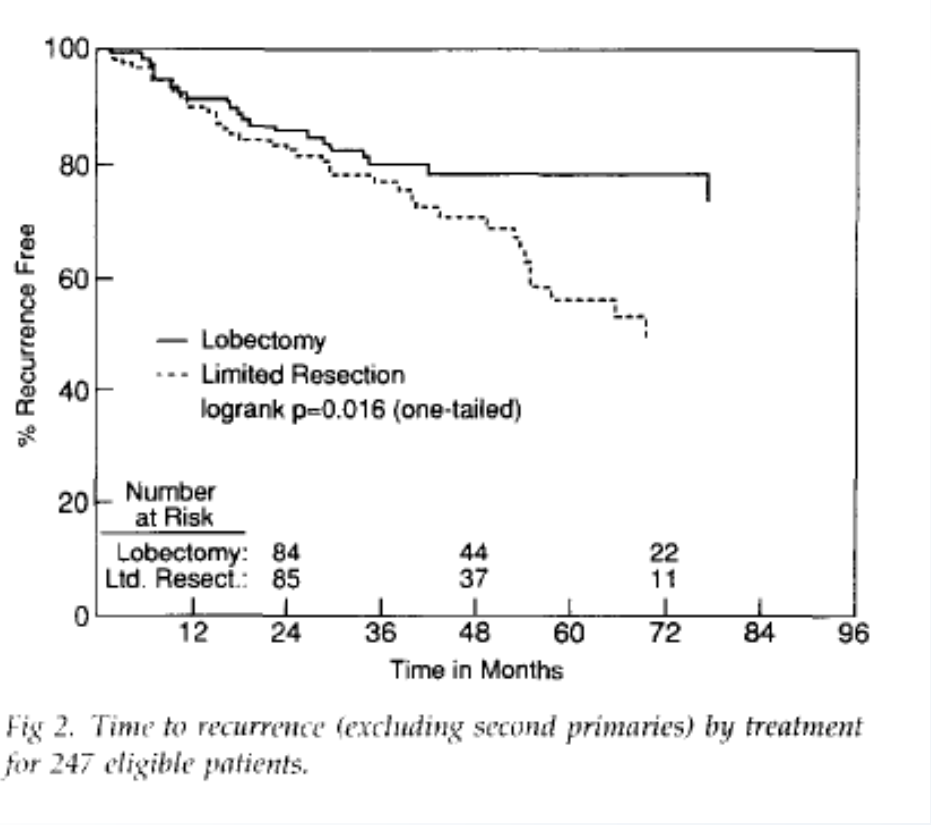


Fig 2. Time to recurrence (excluding second primaries) by treatment for 247 eligible patients.

2x higher incidence of recurrence
Logrank p = 0.016

Survival After Sublobar Resection versus Lobectomy for Clinical Stage IA Lung Cancer

An Analysis from the National Cancer Data Base

Onkar V. Khullar, MD, Yuan Liu, PhD,†‡ Theresa Gillespie, PhD,§‖ Kristin A. Higgins, MD,¶ Suresh Ramalingam, MD,§ Joseph Lipscomb, PhD,‡# and Felix G Fernandez, MD**

(*J Thorac Oncol.* 2015;10: 1625–1633)

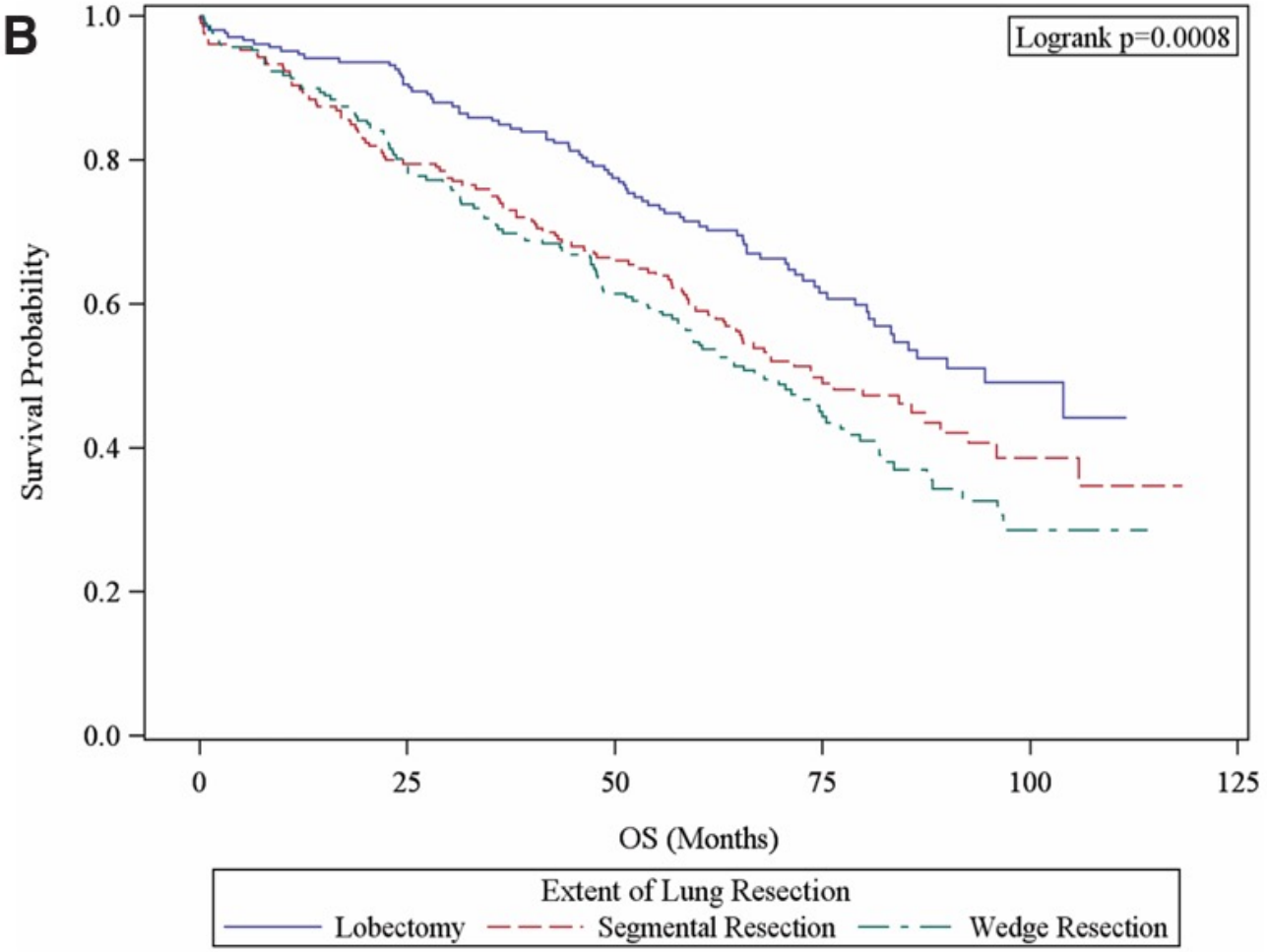
TABLE 5. Comparison of Primary and Secondary Outcomes by Extent of Resection in Propensity Score Matched Samples

	Extent of Surgical Resection		
Outcome	**Wedge Resection, n = 987**	**Segmentectomy, n = 987**	**Lobectomy, n = 987**
30-Day mortality	0.87 (0.41–1.82), $p = 0.706$	1.13 (0.57–2.27). $p = 0.724$	—
Overall survival[a]	1.70 (1.29–2.26), $\mathbf{p < 0.001}$	1.45 (1.10–1.91), $\mathbf{p = 0.009}$	—
Positive surgical margins	2.02 (1.13–3.63), $\mathbf{p = 0.018}$	1.29 (0.69–2.43), $p = 0.426$	—
> 3 LN examined	0.07 (0.05–0.09), $\mathbf{p < 0.001}$	0.18 (0.14–0.22), $\mathbf{p < 0.001}$	—
Positive regional LN	0.39 (0.24–0.63), $\mathbf{p < 0.001}$	0.59 (0.38–0.89), $\mathbf{p = 0.013}$	—

[a]Overall survival analysis limited to patients treated between 2003 and 2006, n = 209 per group. Overall survival reported as hazard ratio. Remaining variables reported as odds ratio with 95% confidence intervals.

LN, lymph nodes.

B



Extent of Lung Resection	No. of Subject	Event	Censored	Median Survival (95% CI)	60 mo Survival
Lobectomy	209	81 (39%)	128 (61%)	94.5 (80.6, NA)	71.4% (64.4%, 77.3%)
Segmental Resection	209	107 (51%)	102 (49%)	73.7 (63.3, 92.6)	59.1% (51.9%, 65.5%)
Wedge Resection	209	121 (58%)	88 (42%)	67.9 (57.7, 77.1)	54.8% (47.6%, 61.3%)

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RICHARD E. CLARK MEMORIAL PAPER FOR GENERAL THORACIC SURGERY

Equivalent Survival Between Lobectomy and Segmentectomy for Clinical Stage IA Lung Cancer

Mark W. Onaitis, MD, Anthony P. Furnary, MD, Andrzej S. Kosinski, PhD, Liqi Feng, MS, Daniel Boffa, MD, Betty C. Tong, MD, Patricia Cowper, PhD, Jeffrey P. Jacobs, MD, Cameron D. Wright, MD, Robert Habib, PhD, Joe B. Putnam, Jr, MD, and Felix G. Fernandez, MD, MSc

Division of Cardiothoracic Surgery, University of California San Diego, La Jolla, California; Starr-Wood Cardiac Group, Portland, Oregon; Duke Clinical Research Institute, Duke University, Durham, North Carolina; Division of Cardiothoracic Surgery, Yale University, New Haven, Connecticut; Division of Cardiothoracic Surgery, Duke University, Durham, North Carolina; Johns Hopkins All Children's Heart Institute, St Petersburg, Florida; Division of Thoracic Surgery, Massachusetts General Hospital, Boston, Massachusetts; The Society of Thoracic Surgeons, Chicago, Illinois; Baptist MD Anderson Cancer Center, Jacksonville, Florida; and Division of Cardiothoracic Surgery, Emory University, Atlanta, Georgia

Background. The oncologic efficacy of segmentectomy is controversial. We compared long-term survival in clinical stage IA (T1N0) Medicare patients undergoing lobectomy and segmentectomy in The Society of Thoracic Surgeons database.

Methods. The Society of Thoracic Surgeons General Thoracic Surgery Database was linked to Medicare data in 14,286 lung cancer patients who underwent segmentectomy (n = 1654) or lobectomy (n = 12,632) for clinical stage IA disease from 2002 to 2015. Cox regression was used to create a long-term survival model. Patients were then propensity matched on demographic and clinical variables to derive matched pairs.

Results. In Cox modeling segmentectomy was associated with survival similar to lobectomy in the entire cohort (hazard ratio, 1.04; 95% confidence interval, 0.89-1.20; P = .64) and in the matched subcohort. A subanalysis restricted to the 2009 to 2015 population (n = 11,811), when T1a tumors were specified and positron emission tomography results and mediastinal staging procedures were accurately recorded in the database, also showed that segmentectomy and lobectomy continue to have similar survival (hazard ratio, 1.00; 95% confidence interval, 0.87-1.16). Subanalysis of the pathologic N0 patients demonstrated the same results.

Conclusions. Lobectomy and segmentectomy for early-stage lung cancer are equally effective treatments with similar survival. Surgeons from The Society of Thoracic Surgeons database appear to be selecting patients appropriately for sublobar procedures.

(Ann Thorac Surg 2020;110:1882-91)
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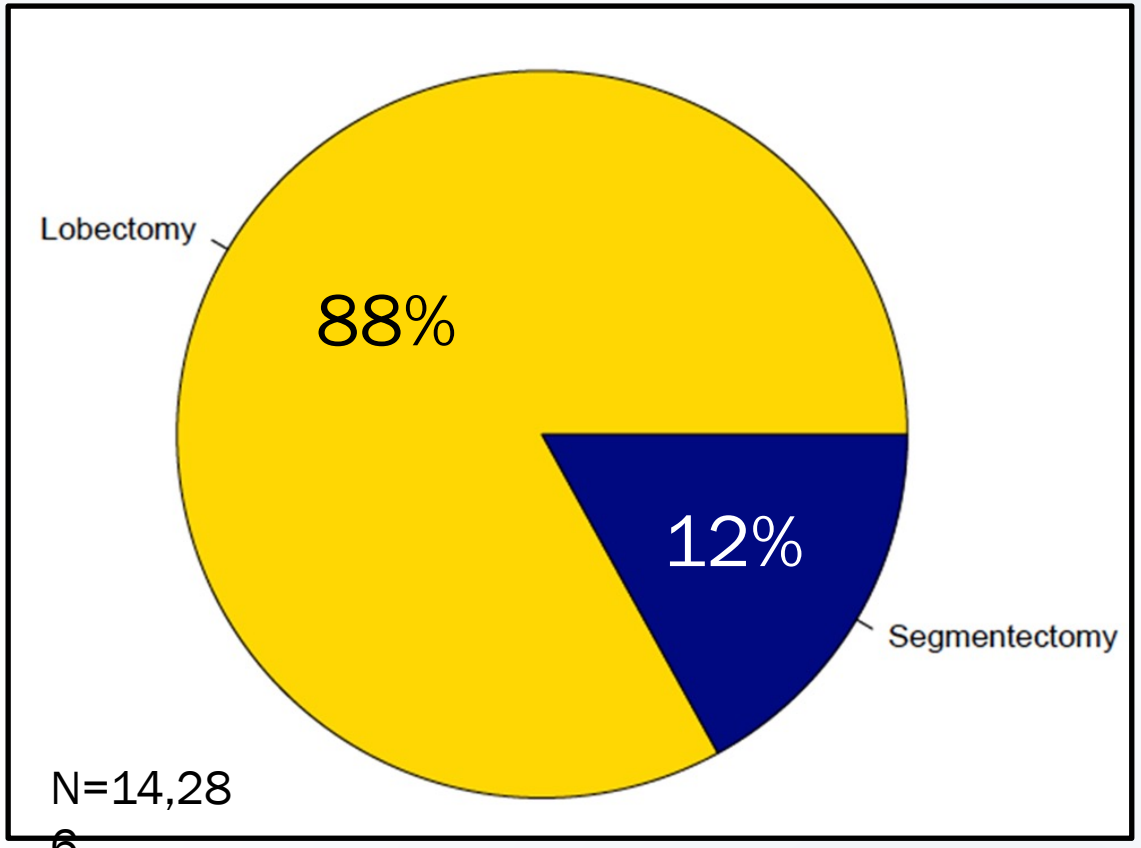
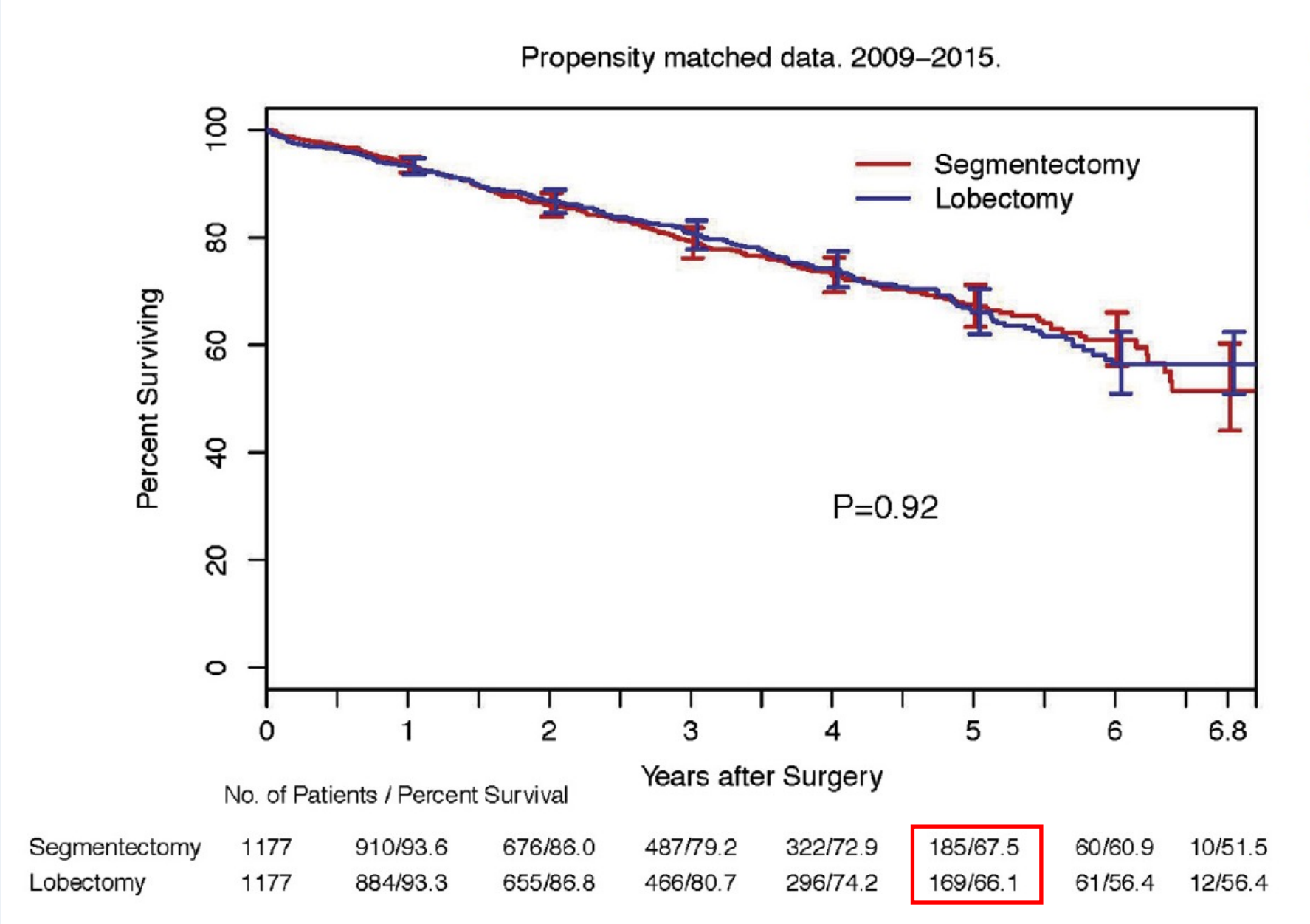


Years 2009-2015
(14% for ≤2cm)



T1a/b (≤2cm): 838 pairs T1c (>2-≤3cm): 339 pairs

Onaitis et al. Annals of Thoracic Surgery. 2020;110: 1882-91.

Predictors of Utilization of Segmentectomy (vs Lobectomy)

Increasing age

Worse pulmonary function

PVD, CAD, CHF

Smaller tumors (cT1a)

VATS approach

No mediastinal staging

Table 2. Predictors of Segmentectomy in the Entire Population

Variable	Category	Odds Ratio (95% Confidence Interval)	*P*
American Society of Anesthesiologists class	I-II	1	.052
	III	1.14 (0.97-1.35)	
	IV-V	0.93 (0.73-1.20)	
Age	65-69	1	<.001
	70-74	0.94 (0.81-1.09)	
	75-79	1.21 (1.04-1.41)	
	>80	1.36 (1.14-1.61)	
Body mass index	18.5-25	1	.286
	<18.5	0.74 (0.50-1.11)	
	15-30	1.02 (0.89-1.16)	
	30-35	0.89 (0.75-1.06)	
	>35	0.91 (0.73-1.14)	
Cardiovascular disease		0.98 (0.83-1.16)	.854
Chronic kidney disease (creatinine > 2 or dialysis)		1.22 (0.83-1.78)	.313
Cigarette use	Never	1	.653
	Past	0.98 (0.83-1.16)	
	Current	0.92 (0.75-1.13)	
Congestive heart failure		1.30 (0.97-1.73)	.074
Coronary artery disease		1.12 (0.98-1.29)	.098
Diabetes mellitus		0.93 (0.80-1.08)	.316
Forced expiratory volume in 1 second predicted	>80%	1	<.001
	<40%	3.78 (2.73-5.24)	
	40-60%	2.59 (2.21-3.03)	
	60-80%	1.26 (1.10-1.43)	
Gender	Male	1	.002
	Female	1.20 (1.07-1.35)	
Hypertension		0.93 (0.82-1.05)	.245
Peripheral vascular disease		0.82 (0.68-1.00)	.047
Race	White	1	.983
	African American	1.02 (0.80-1.29)	
	Other	0.95 (0.37-2.44)	
Steroid use		1.01 (0.74-1.38)	.954
Video-assisted thoracoscopic surgery		1.47 (1.30-1.66)	<.001
Year of surgery		1.00 (0.98-1.02)	.952
Zubrod	0	1	.745
	1	1.04 (0.93-1.16)	
	2-5	0.96 (0.70-1.30)	

Onaitis et al. Annals of Thoracic Surgery. 2020;110: 1882-91.

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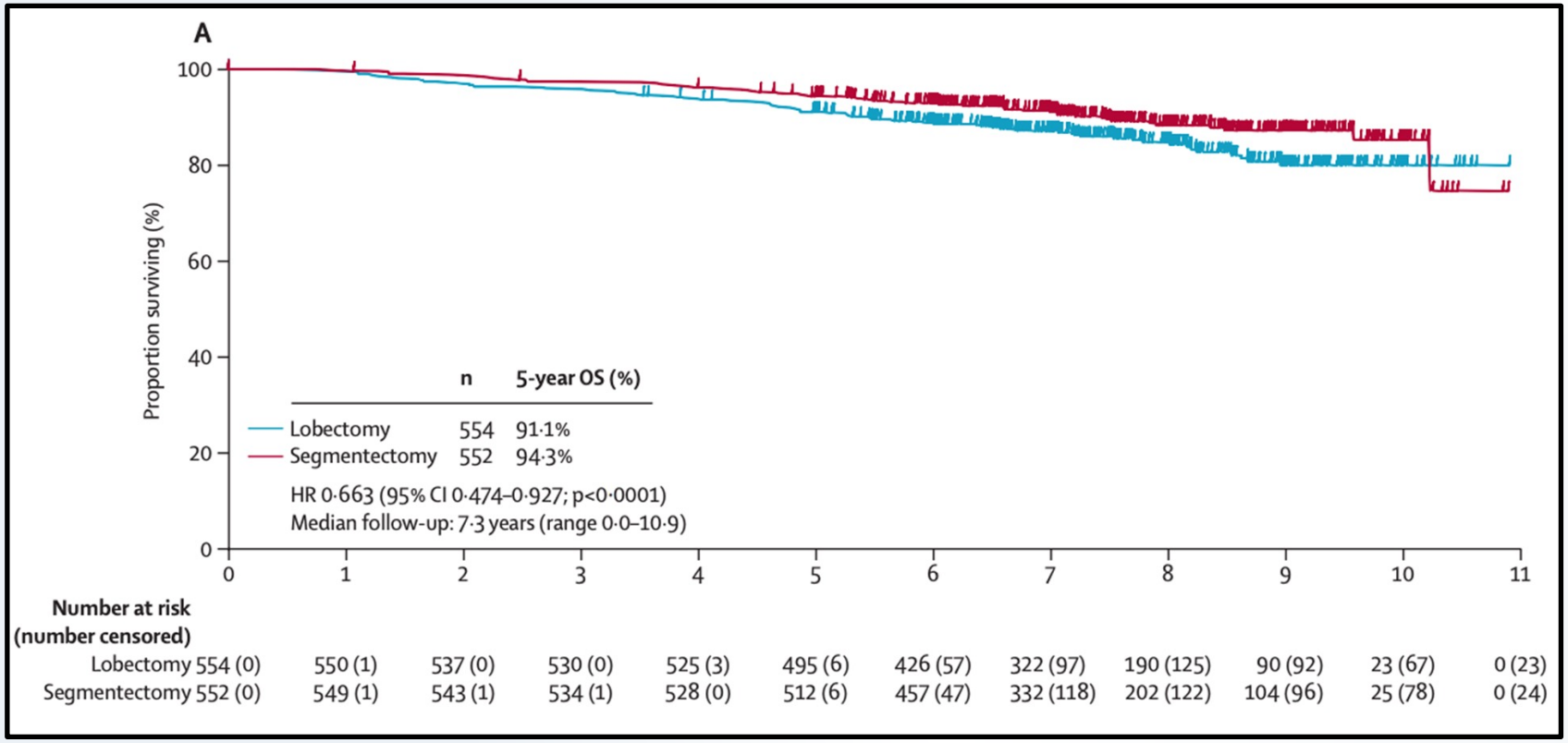
Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial

*Hisashi Saji, Morihito Okada, Masahiro Tsuboi, Ryu Nakajima, Kenji Suzuki, Keiju Aokage, Tadashi Aoki, Jiro Okami, Ichiro Yoshino, Hiroyuki Ito, Norihito Okumura, Masafumi Yamaguchi, Norihiko Ikeda, Masashi Wakabayashi, Kenichi Nakamura, Haruhiko Fukuda, Shinichiro Nakamura, Tetsuya Mitsudomi, Shun-Ichi Watanabe, Hisao Asamura, on behalf of the West Japan Oncology Group and Japan Clinical Oncology Group**

Inclusion:
- **Clinical stage IA NSCLC**
- **Tumor diameter ≤2 cm**
- **Consolidation-to-tumor ratio >0·5**



No statistically significant difference in postoperative PFTs at 1 month – 3% vs 7% decrease (a priori cutoff 10%)

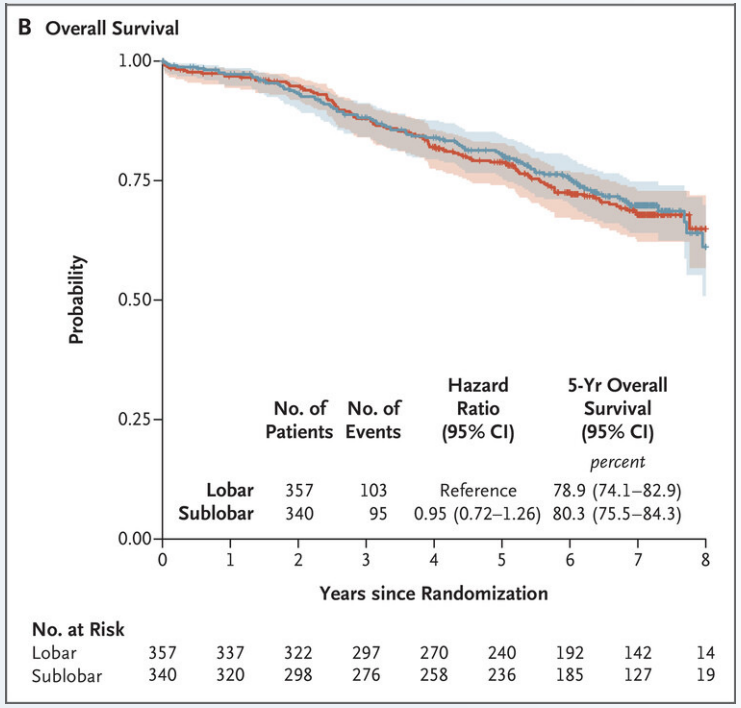
Lancet 2022 Apr 23;399(10335):1607-1617.

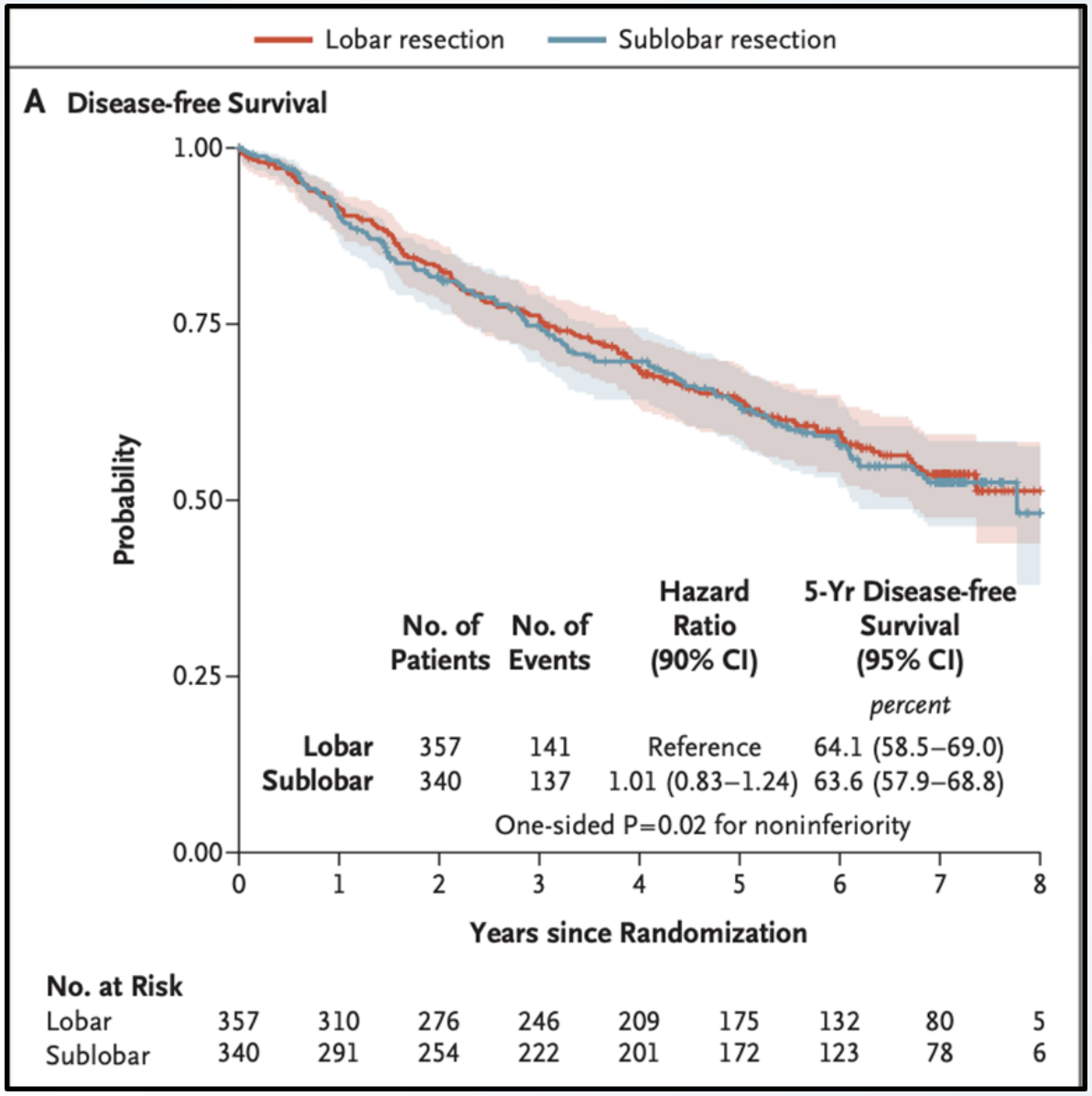
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 9, 2023 VOL. 388 NO. 6

Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

Nasser Altorki, M.D., Xiaofei Wang, Ph.D, David Kozono, M.D., Ph.D., Colleen Watt, B.S., Rodney Landrenau, M.D., Dennis Wigle, M.D., Ph.D., Jeffrey Port, M.D., David R. Jones, M.D., Massimo Conti, M.D., Ahmad S. Ashrafi, M.D., Moishe Liberman, M.D., Ph.D., Kazuhiro Yasufuku, M.D., Ph.D., Stephen Yang, M.D., John D. Mitchell, M.D., Harvey Pass, M.D., Robert Keenan, M.D., Thomas Bauer, M.D., Daniel Miller, M.D., Leslie J. Kohman, M.D., Thomas E. Stinchcombe, M.D., and Everett Vokes, M.D.

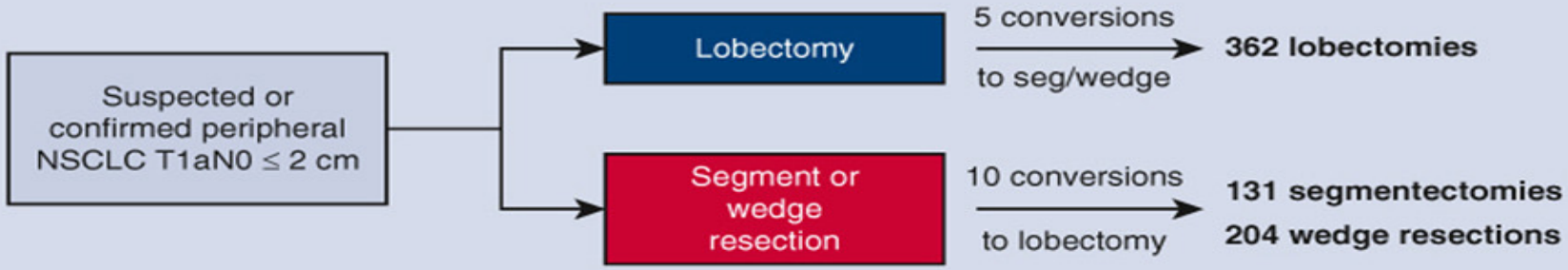


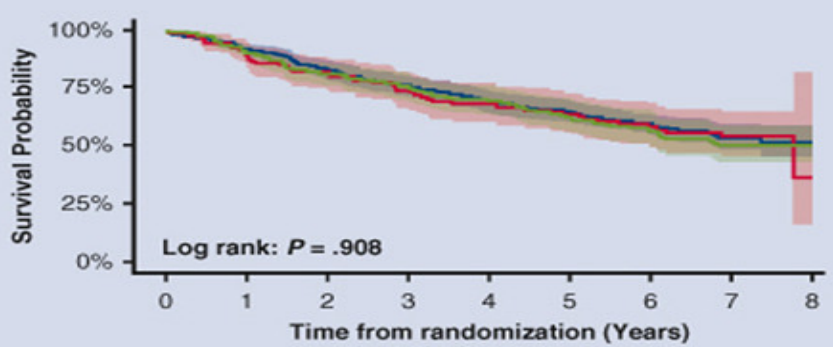


JTCVS

@AATSJournals

Differences between oncologic outcomes between segmentectomy and wedge resection in CALGB 140503



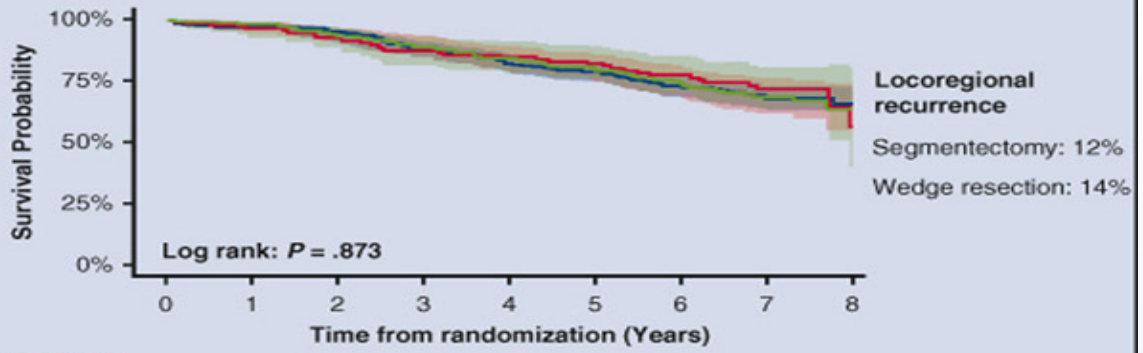


No. at risk									
Lobectomy	362	313	279	248	213	179	134	81	5
Segment	131	112	98	82	74	66	49	30	2
Wedge	204	176	153	138	123	102	72	47	4

	n	nEvents	HR (95% CI)	5-year DFS (95% CI)
Lobectomy	362	141	reference	64.7 (59.6 - 70.1%)
Segment	131	52	1.02 (0.74 - 1.40)	63.8 (55.6 - 73.2%)
Wedge	204	86	1.06 (0.81 - 1.39)	62.5 (55.8 - 69.9%)

Procedure — Lobectomy — Segment — Wedge

Disease-free survival



Locoregional recurrence
Segmentectomy: 12%
Wedge resection: 14%

No. at risk									
Lobectomy	362	339	325	299	271	242	193	141	14
Segment	131	123	114	101	97	93	75	49	6
Wedge	204	195	181	173	160	141	109	79	13

	n	nEvents	HR (95% CI)	5-year OS (95% CI)
Lobectomy	362	103	reference	78.7 (74.5 - 83.2%)
Segment	131	35	0.90 (0.61 - 1.34)	81.9 (75.3 - 89.1%)
Wedge	204	60	0.97 (0.70 - 1.35)	79.7 (74.2 - 85.6%)

Procedure — Lobectomy — Segment — Wedge

Overall survival

In patients with T1aN0 ≤ 2 cm disease-free and overall survival are similar regardless of the extent of pulmonary resection

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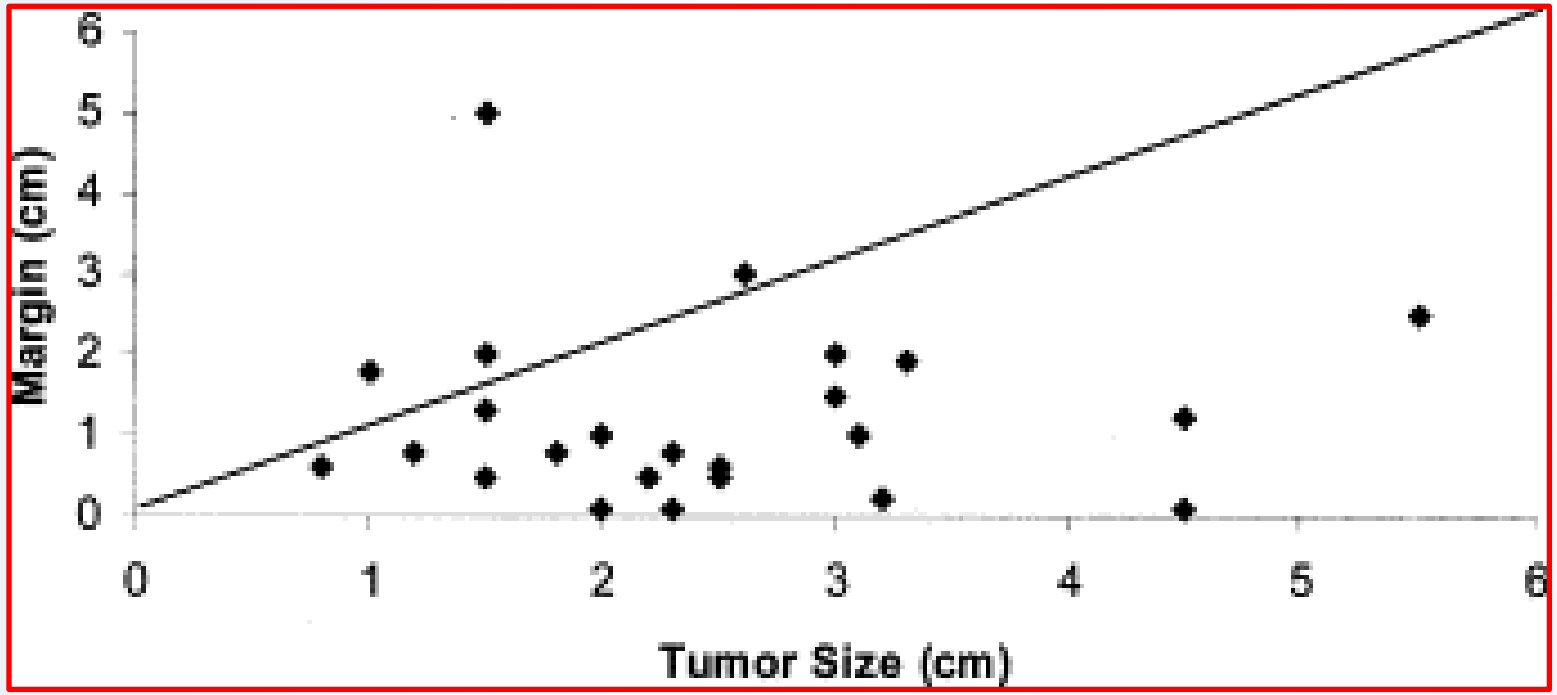
What is an adequate margin for a sub-lobar resection?

Margin:tumor ratio <1cm associated with increased recurrence rate vs. ratio ≥1 (25% vs 6.2%, p=0.0014)

– Schuchert et al. *Ann Thorac Surg* 84:926-933, 2007.



Are all segments are equivalent?

ORIGINAL ARTICLE | GENERAL THORACIC · Volume 111, Issue 3, P1028-1035, March 2021

Intentional Segmentectomy for Clinical T1 No Non-small Cell Lung Cancer: Survival Differs by Segment

Gregory D. Jones, MD [a] · Raul Caso, MD, MSCI [a] · Giye Choe, MD [a] · ... · William D. Travis, MD [c] · David R. Jones, MD [a] · Gaetano Rocco, MD [a] ... Show more

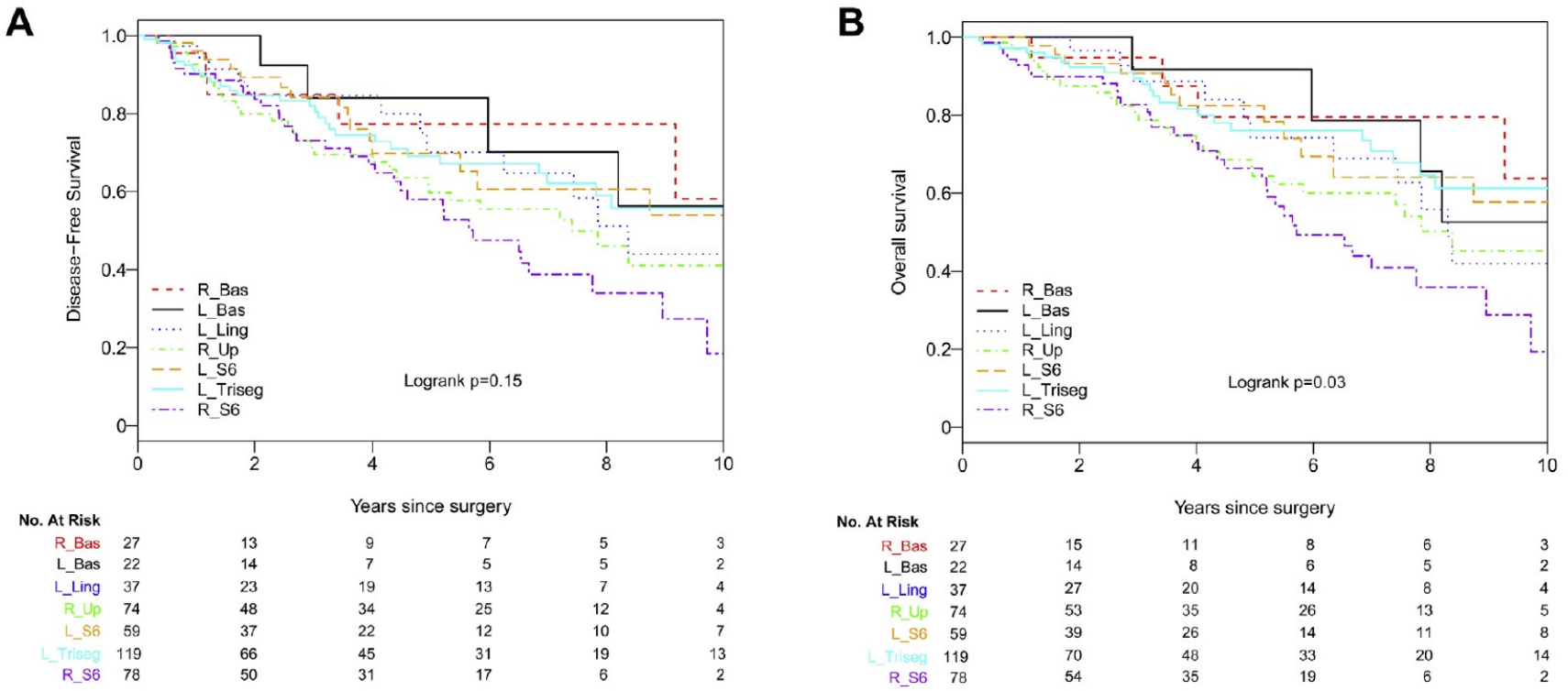
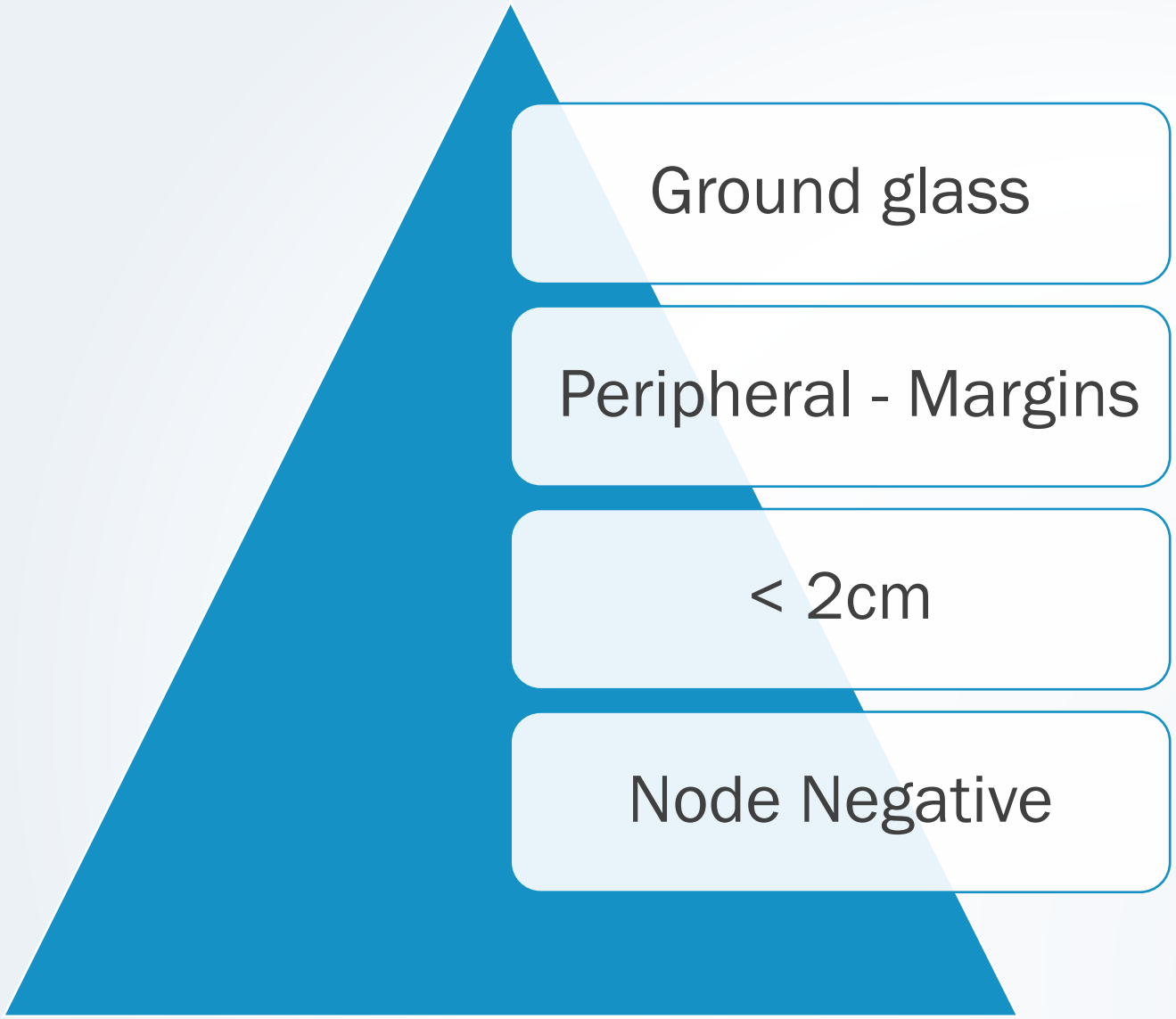


Figure 3. (A) Disease-free and (B) overall survival by segmentectomy location after intentional segmentectomy for clinical T1 N0 M0 non-small cell lung cancer. (L_Bas, left basilar; L_Ling, left lingula; L_S6, left segment 6; L_Triseg, left trisegment; R_Bas, right basilar; R_S6, right segment 6; R_Up, right upper.)

When is sub-lobar resection appropriate?



Remaining Question To Be Answered:

1. In patients with tumors 2-3cm, is sublobar resection equivalent to lobectomy?
2. Does segmentectomy provide greater benefit than wedge resection?
3. Is complex segmentectomy equivalent to simple segmentectomy?
4. Which lung anatomy (ex. peripheral versus central) favors sublobar resection versus lobectomy
5. In patients with high-risk tumor biology (ex. VPI, LVI, histology – small cell and large cell, SAS, ground glass component) is sublobar resection equivalent to lobectomy?
6. In patients with negative nodes on PET and/or EBUS/mediastinoscopy, does intraoperative frozen section analysis of lymph nodes provide a therapeutic benefit?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