Evolution of Surgery for Early Stage Lung Cancer

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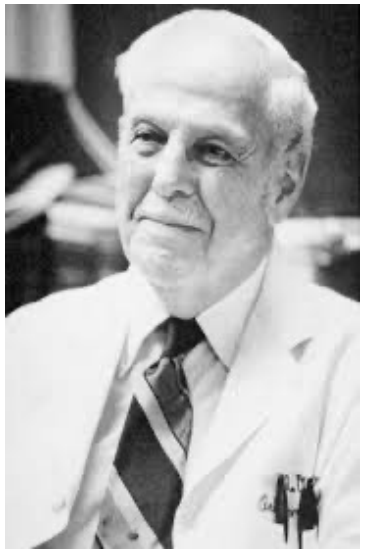
Alton Ochsner 1891-1981



- Published landmark paper on tobacco and lung cancer in 1939 Ochsner A, Debakey M. Surg Gynecol Obstet (JACS)
  - 1919 as 3rd year medical student (Washington University) saw autopsy on lung cancer patient by noted anatomy professor George Dock “None of you will ever see another case again”
  - 1927 Complete residency training in Thoracic Surgery under Dr. Graham at Washington University and joined faculty at Tulane/Charity Hospital as chief of Surgery
  - 1936: After being chief for 9 years, he began to see many cases each year in Veterans from WWI who had become heavy smokers
- Credited with initial creation of systematic treatment plan for lung cancer including outcomes database

Hospital	(n)	Explored	Resected	Discharged
Tulane 1935-1951	948	380 (34%)	205 (21%)	160 (17%)

DeBakey M, Ochsner A. Surgery 1952

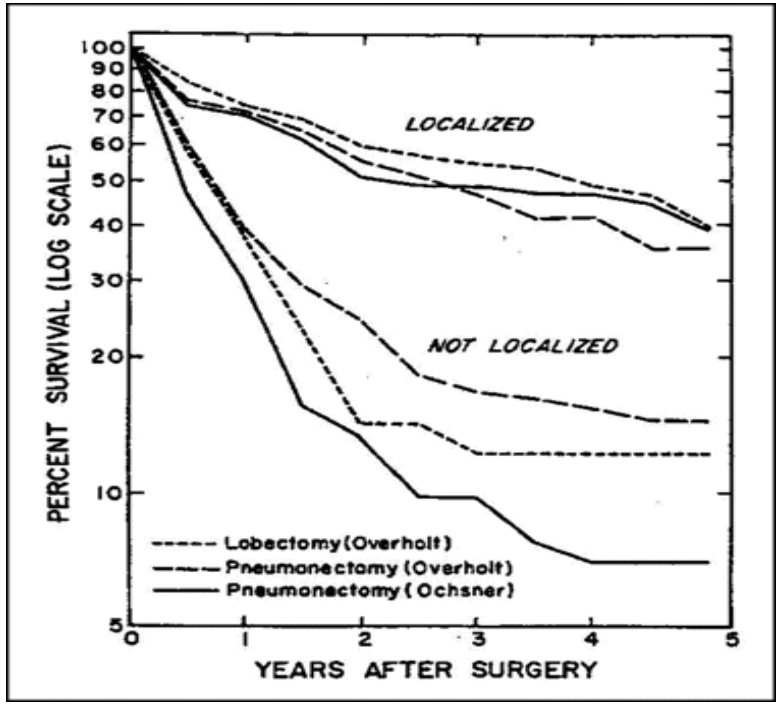
Lung Cancer 1960s

High mortality from pneumonectomy: Should standard of care be changed? Landmark Presentation AATS 1962

Clinic	Overholt	5-year survival	Ochsner	5-year survival
Pneumonectomy	211	40%	191	39%
Lobectomy	116	35%	0	

Statistical analyses showed no survival difference for: histology, age, gender, location and size of lesion comparing lobectomy and pneumonectomy

Conclusion: Ochsner and Overholt recommended lobectomy as new standard of care when feasible



Shimkin MB et al, J Thorac Cardiovasc Surg 1962

LCSG 821

Randomized phase III Lobectomy vs. Limited resection

(Rationale: Is a lobectomy needed for small T1 cancers)

Clinical T1N0 (<3cm) n=771

Confirm NSCLC; n=587

Confirm wedge feasibility

Negative nodes T1N0

Randomize; n=247

Lobectomy; n=125

Segment; n=82; We

Overall Survival

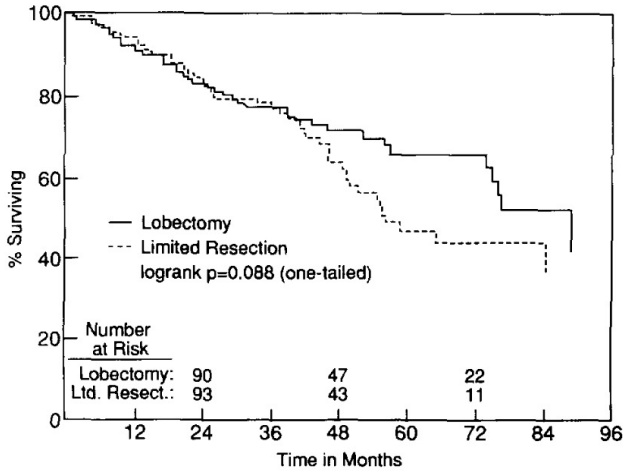


Fig 1. Time to death (from any cause) by treatment for 247 eligible patients.

Relapse-free Survival

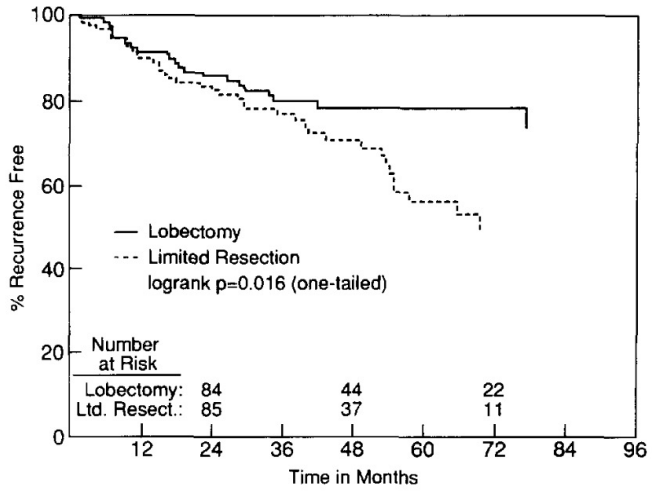


Fig 2. Time to recurrence (excluding second primaries) by treatment for 247 eligible patients.

- No difference in morbidity or mortality
- Complete follow-up: Median 60 months
  - 74 recurrences; 86 deaths
  - Non-significant survival difference (p=0.08)
  - Significant difference in local recurrence (p=0.008)

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)

Transformative: Standard of care is lobectomy NOT limited resection

Ginsberg et al., Ann Thorac Surg 1995

ACOSOG Z030

Randomized Phase III Trial of Mediastinal Lymph Node Sampling vs. Dissection for Patients with N0 or N1 NSCLC Allen, PI

T1-2N0-1; n=1111

Lobectomy

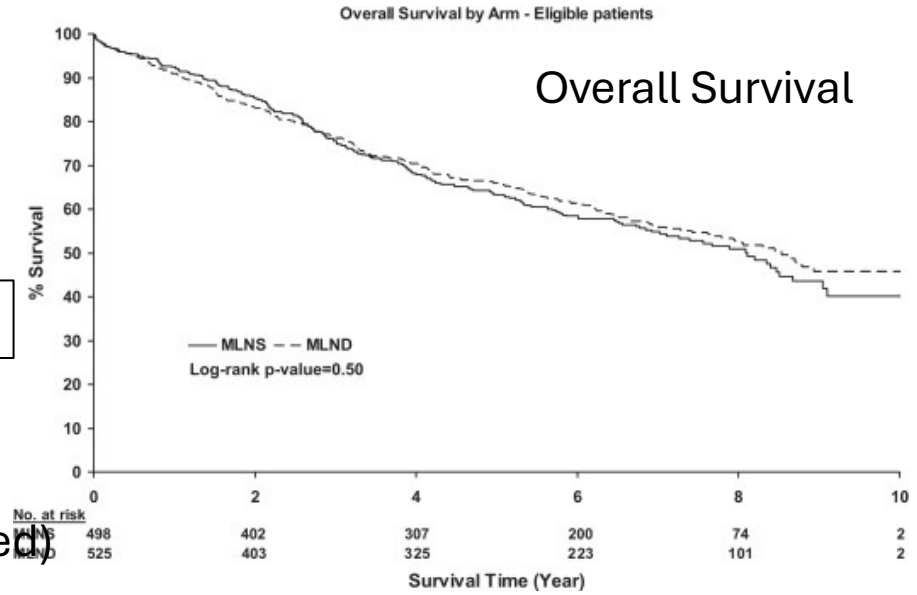
Lymph node sampling (LNS)
Confirm N2(-)

Randomize

Complete dissection
N=525 (LND)

Observation; n=498

Rationale: Japanese data suggested a survival advantage for LND but with morbidity (chyle leak, recurrent nerve injury)



- No morbidity difference or hospital LOS
- Median follow-up 78 months
- 21 patients with LND had occult N2 (upstaged)
- No difference Survival:
  - Median survival (8.1 LNS vs 8.5 years LND)
  - Similar 5-year survival (69%), No difference in local/regional/distant relapse

Transformative: Standard of care at least LNS for all stage I resections

Darling at al., J Thorac Cardiovasc Surg, 2010

ACOSOG Z4032

Randomized Phase III Trial of Brachytherapy on Local Recurrence In High-risk Operative Patient with NSCLC; Fernando, PI

Rationale: Promising data from UPMC and Boston; U *Note: CALGB 9335*

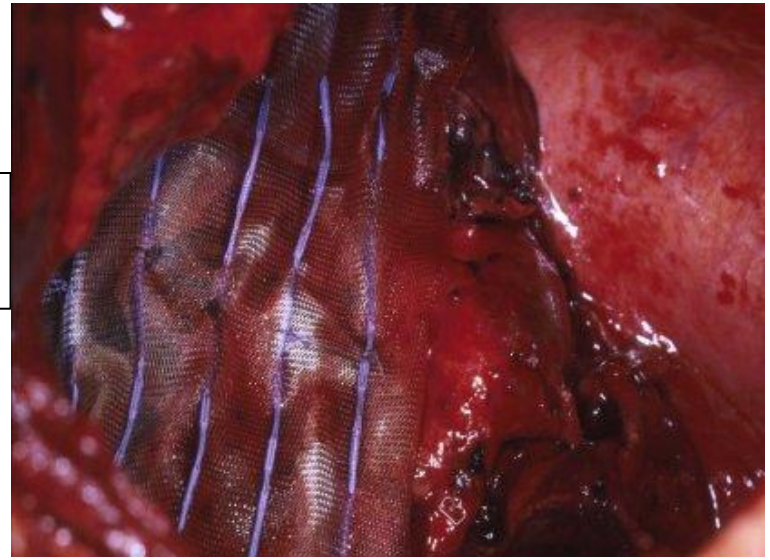
High risk T1N0 Wedge Resection with nodes; n=224

Randomize; n=222

Observation
N=110

Intraop Brachytherapy (BT)
seeds to staple line; n=112

Endpoints: Local relapse (LR)



- Median follow-up 54 months
- No difference in LR; occurring in only 17 (7.7%)
- In patients with <1 cm tumor margin or T-size>2.0 cm there was a slight advantage for BT
- Overall 3-years survival was identical in both arms; 71%

Conclusion: Brachytherapy did not decrease the LR after adequate wedge resection

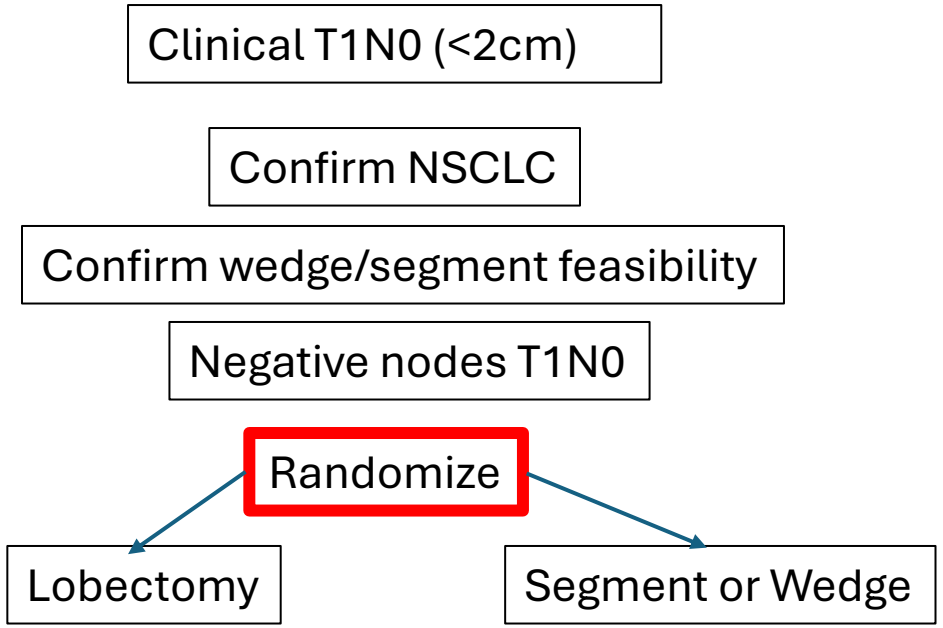
Transformative: No role for adjuvant brachytherapy for high-risk wedge resection

Fernando et al.,J Clin Oncol 2014

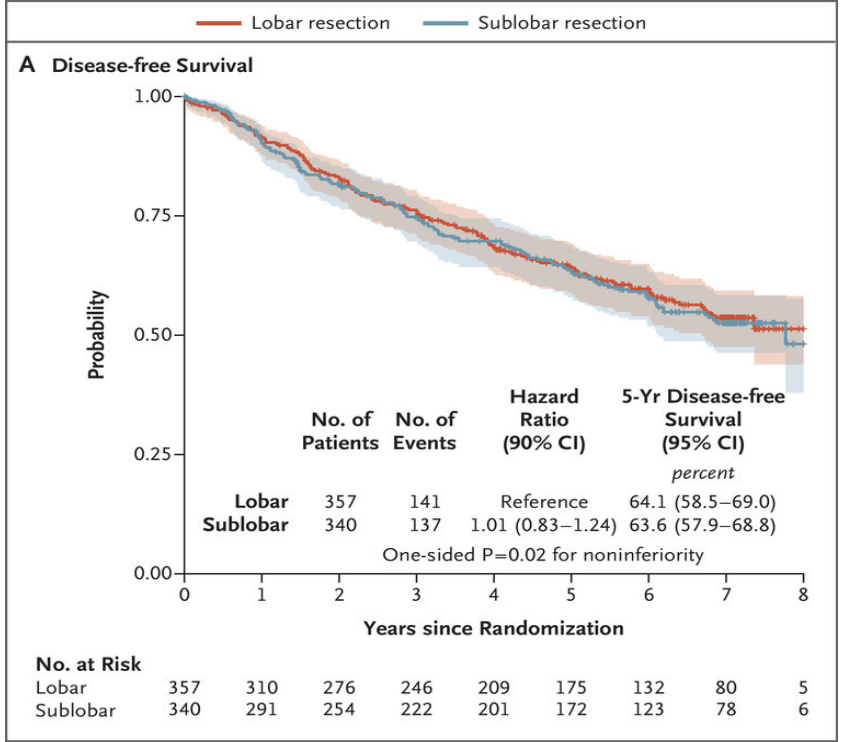
CALGB-Alliance Thoracic Surgery Trial 140503

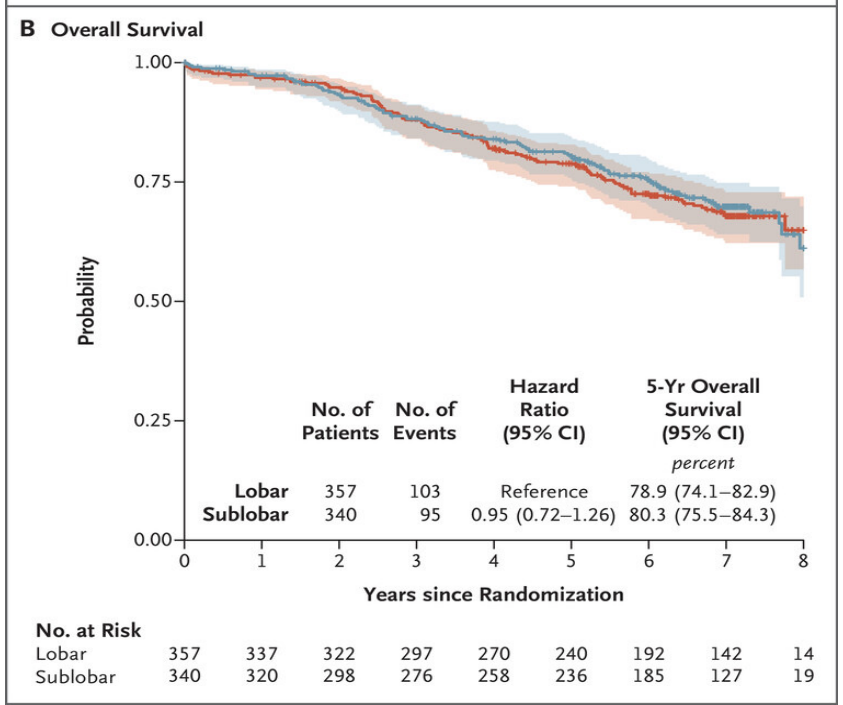
Randomized Phase III Trial of Lobectomy vs. Limited resection for T1N0 NSCLC; Altorki PI

(Rationale: underpowered LCSG 821, improved staging available)



- Overall survival endpoint
- Slow but steady accrual 14-18 per month
- At 70% of accrual, to close in 2 years





No difference
Lobe or sub-lobe

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

Authors: 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., +13, and Everett Vokes, M.D. Author Info & Affiliations

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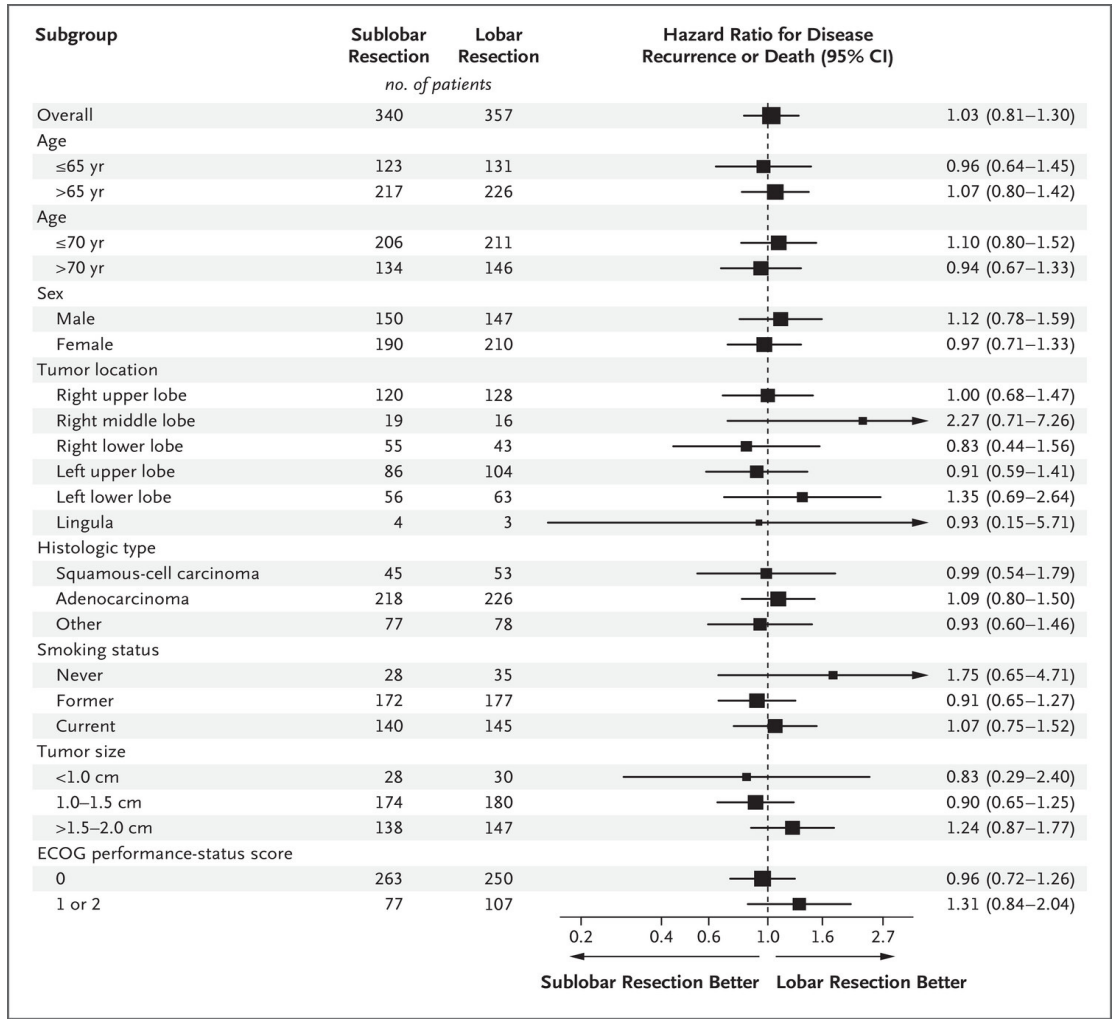
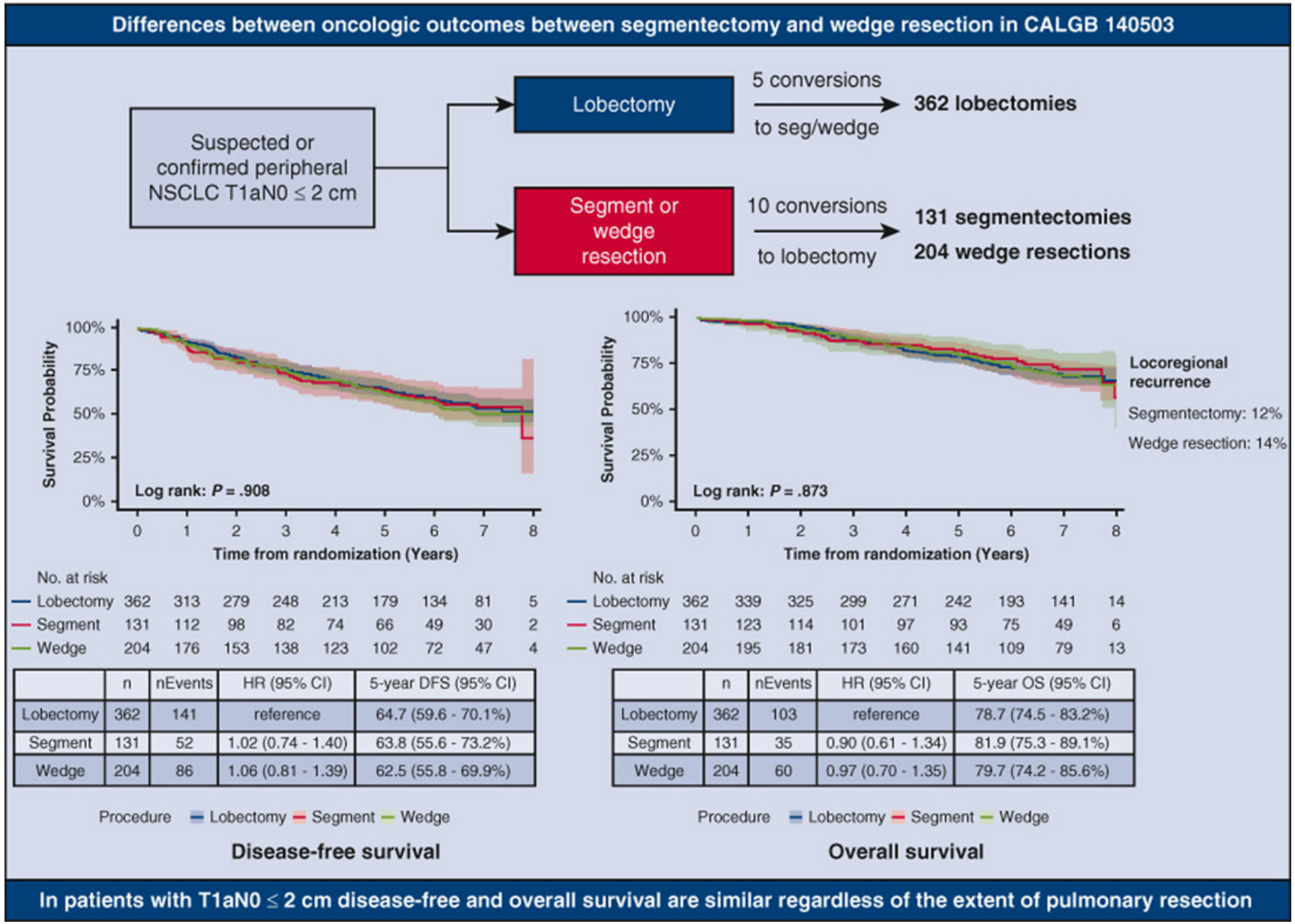




	n	nEvents	HR (95% CI)	5-year DFS (95% CI)
Lobectomy	362	141	reference	64.7 (59.6 - 70.1%)
Segment	131	52	1.02 (0.74 - 1.40)	63.8 (55.6 - 73.2%)
Wedge	204	86	1.06 (0.81 - 1.39)	62.5 (55.8 - 69.9%)

	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%)

No difference for lobe and wedge: *not Powered*

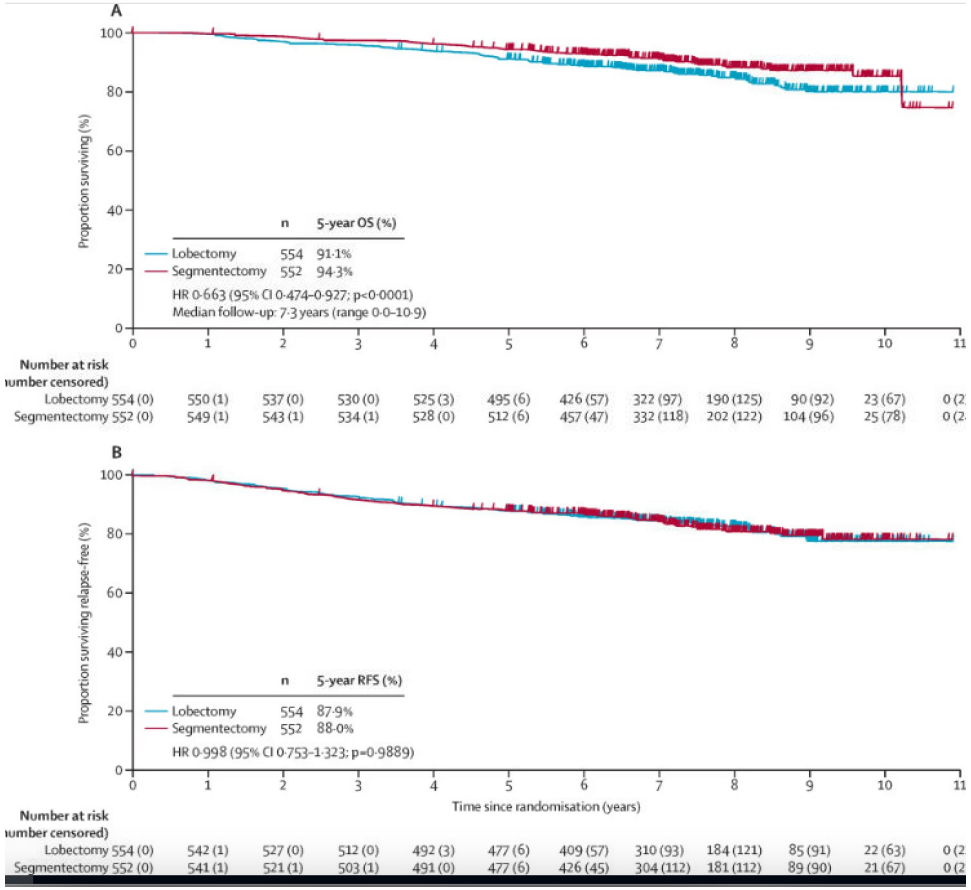
Altorki et al, J Thorac Cardiovasc Surg 2024

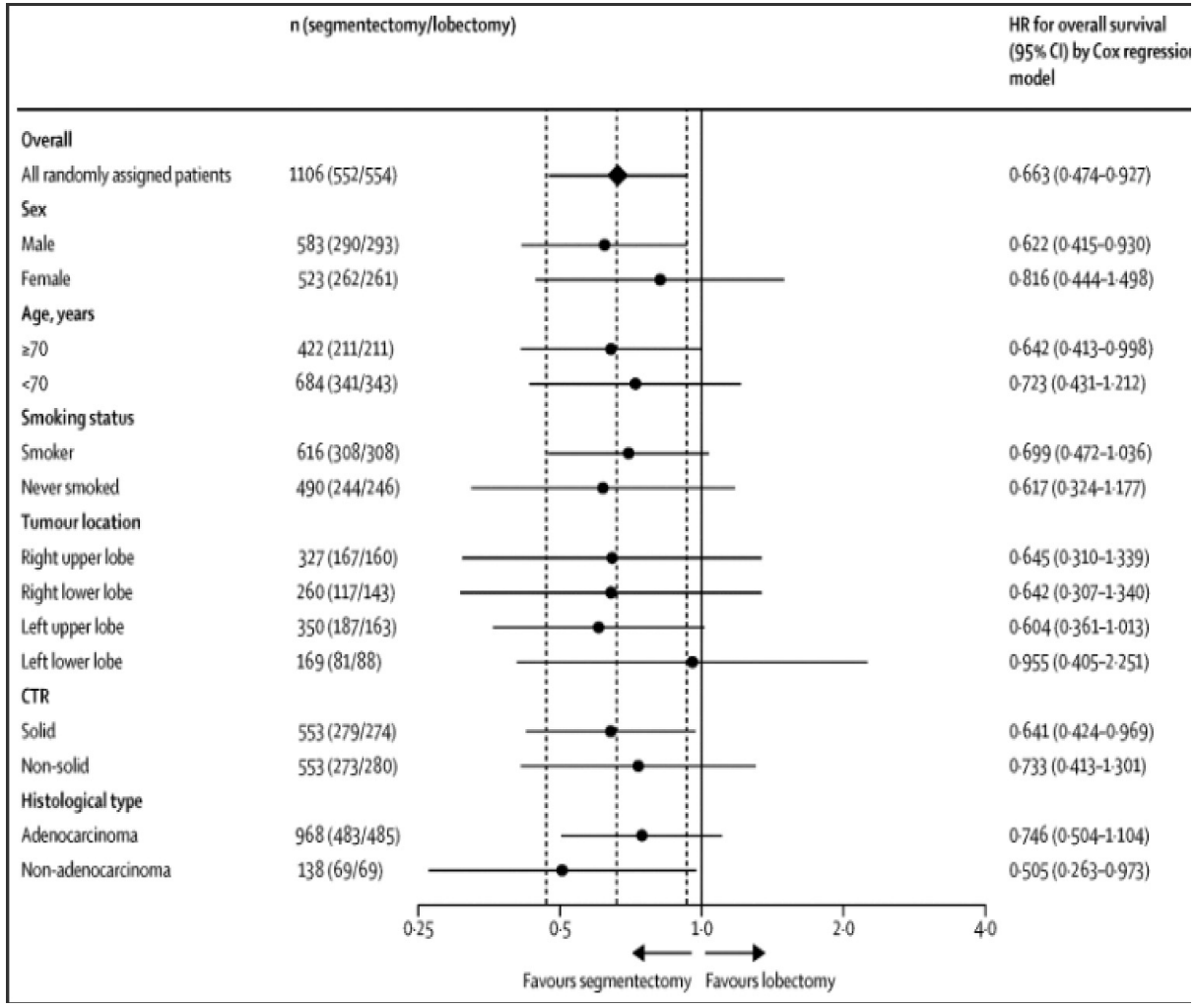
ARTICLES | VOLUME 399, ISSUE 10335, P1607-1617, APRIL 23, 2022 Download Full Issue

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

Prof Hisashi Saji, MD • Morihito Okada, MD • Masahiro Tsuboi, MD • Ryu Nakajima, MD • Kenji Suzuki, MD • Keiju Aokage, MD • et al. Show all authors • Show footnotes

Published: April 23, 2022 • DOI: https://doi.org/10.1016/S0140-6736(21)02333-3 • Check for updates





Favors segment over lobectomy

New Orleans Summer Cancer Meeting 2024

Lancet 2024 JOCO 08002 Update for solid tumors only

			Lobectomy group (n=274)	Segmentectomy group (n=279)	p value*
Cause of death					
	Lung cancer death		20 (7%)	19 (7%)	0·19
	Other cause of death		35 (13%)	19 (7%)	..
		Other cancer including second lung cancer	20 (7%)	8 (3%)	..
		Respiratory disease	4 (1%)	2 (1%)	..
		Cerebrovascular disease	5 (2%)	1 (<1%)	..
		Cardiovascular disease	2 (1%)	3 (1%)	..
		Other	3 (1%)	2 (1%)	..
		Unknown	1 (<1%)	3 (1%)	..
Postoperative recurrence			34 (12%)	52 (19%)	0·043
	Locoregional recurrence		21 (8%)	45 (16%)	0·0021

Higher local and regional recurrence in segment not seen in GGOs

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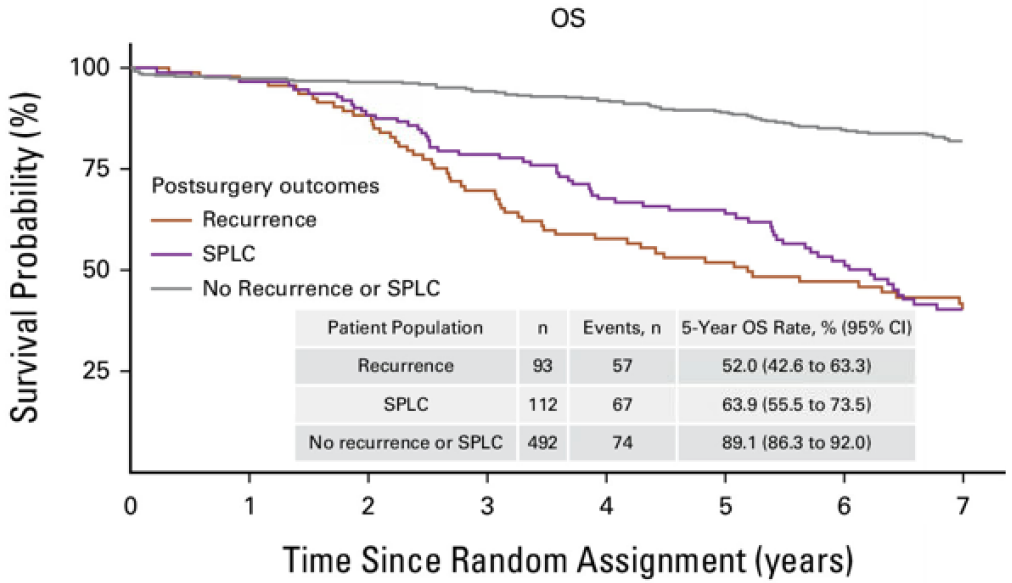
CURRENT

CLINICAL TRIAL UPDATES | January 12, 2024

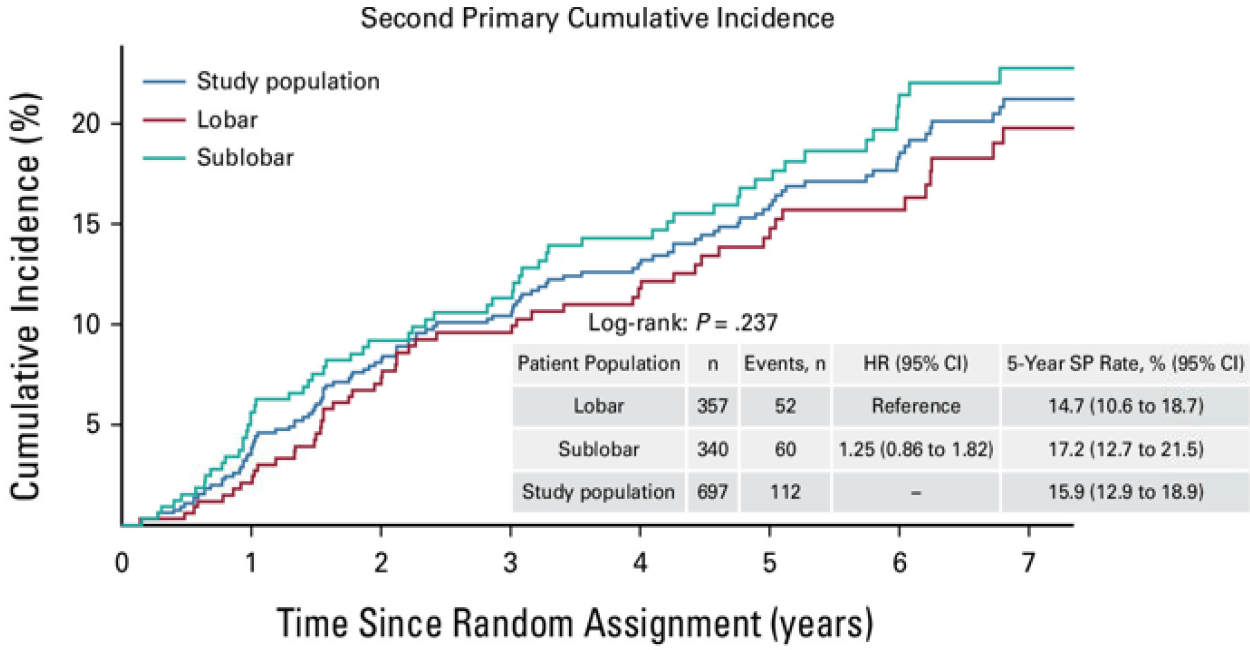
Secondary Analysis of the Rate of Second Primary Lung Cancer From Cancer and Leukemia Group B 140503 (Alliance) Trial of Lobar Versus Sublobar Resection for T1aN0 Non–Small-Cell Lung Cancer

Authors: Thomas E. Stinchcombe, MD, Xiaofei Wang, PhD, Bryce Damman, MS, Jennifer Mentlick, HS, Rodney Landreneau, MD, Dennis Wigle, MD, PhD, David R. Jones, MD, ... SHOW ALL ..., and Nasser Altorki, MD | AUTHORS INFO & AFFILIATIONS



No. at risk:

Recurrence	93	90	82	64	52	45	36	27
SPLC	112	108	99	87	74	66	47	29
No recurrence or SPLC	492	459	439	422	402	365	294	213



No. at risk:

Study population	697	621	565	504	445	375	275	172
Lobar	357	322	296	264	227	186	140	86
Sublobar	340	299	269	240	218	189	135	86

3.8 % per year cumulative!
>18% at 6 years

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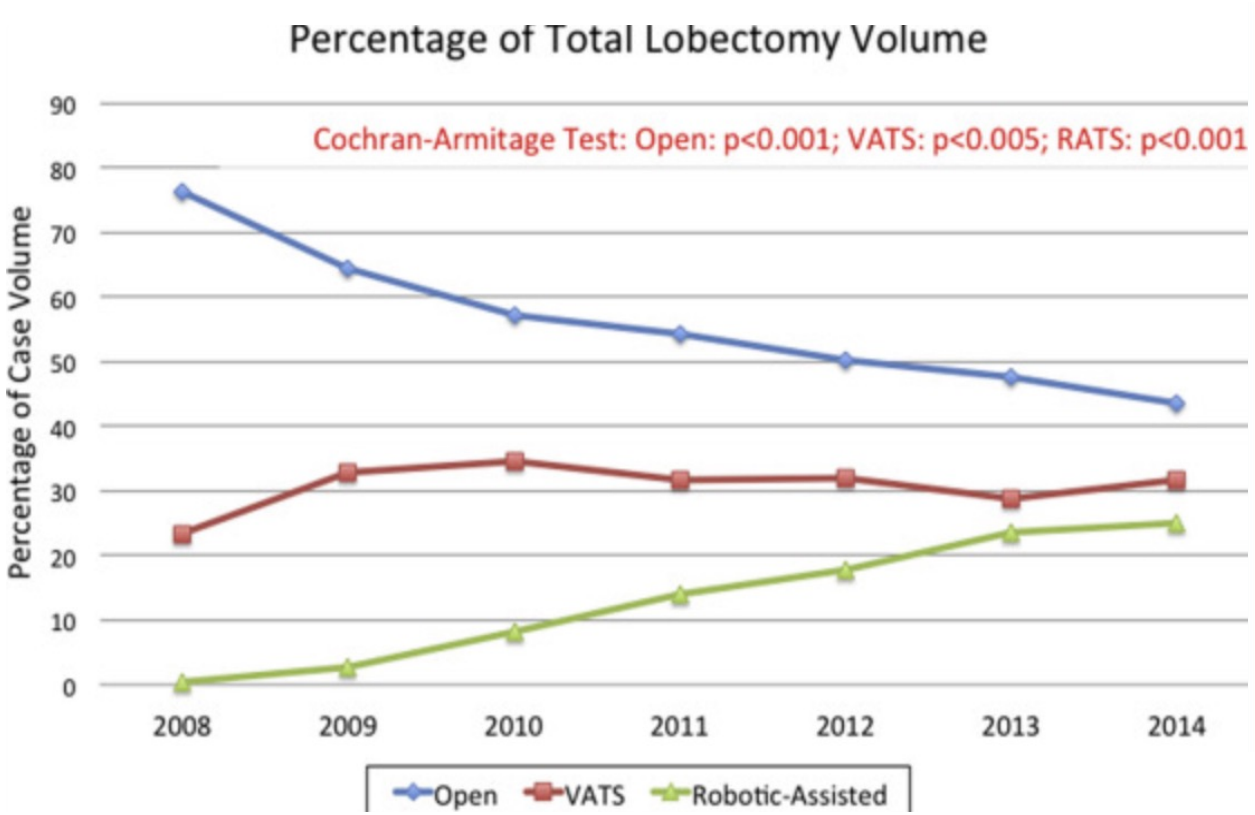
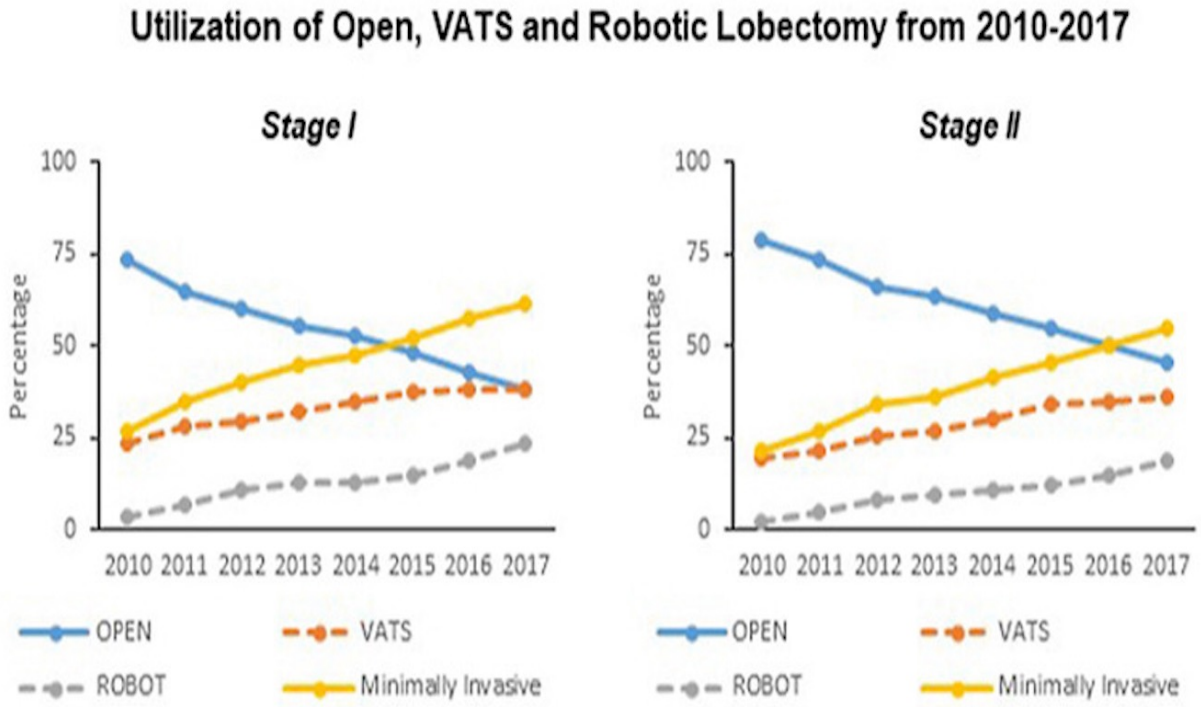
Trends in Minimally-Invasive Lobectomy in US



Subramanian et al, Ann Thorac Surgery 2019



Raman et al, Ann Thorac Surgery 2022

Summary

- There is a long history of evidence-based thoracic surgery trials for early stage lung cancer
- For lesions <2 cm, sub-lobar resection is recommended
  - Resection must include at least sampling of 3 N2 and 1 N1 station
  - Exceptions: larger tumors and central T1 tumors - lobectomy
  - Data are inconclusive for complex segmentectomies
- The majority of lobectomies and sub-lobar resections are minimally invasive, with robotic now dominating
- The alarming rate of second primaries supports sub-lobar resection that saves parenchyma