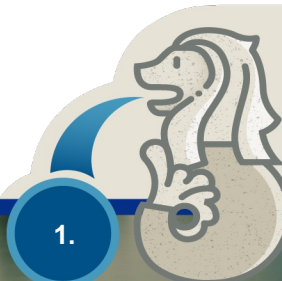




Surgery for Early-Stage NSCLC

Best of WCLC 2023

Luis A. Godoy, MD
Thoracic Surgery
University of California, Davis





Overview

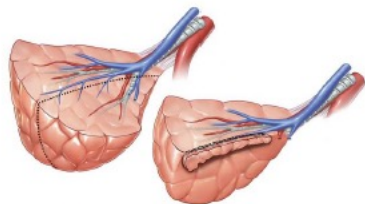
- Surgical resection types
- Sublobar resection vs Lobectomy
- Wedge resection
- Surgical techniques
- New technologies



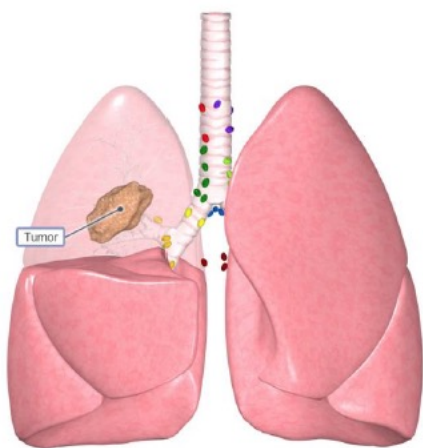


PULMONARY RESECTION in EARLY STAGE:

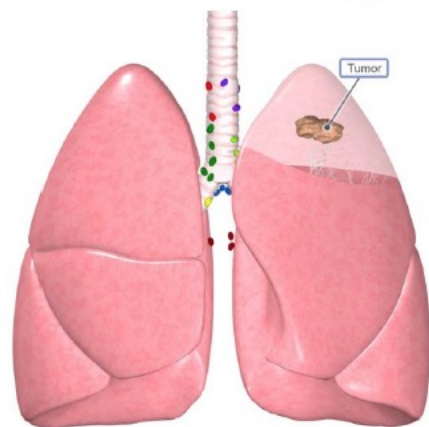
ANATOMIC



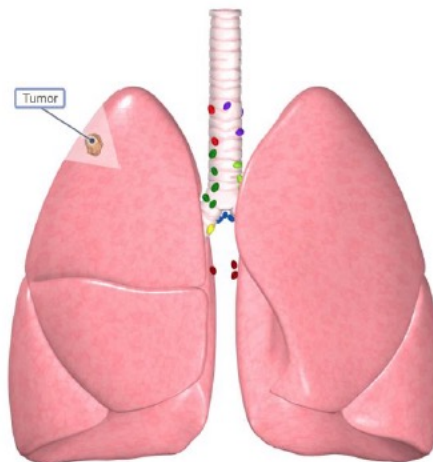
NON-ANATOMIC



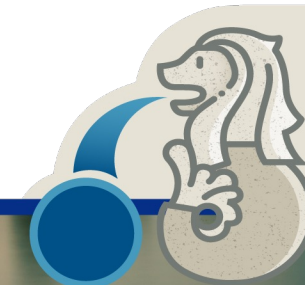
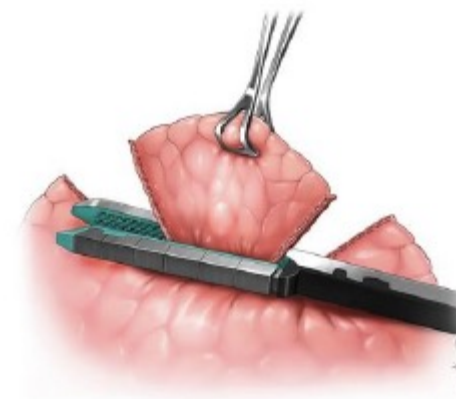
LOBECTOMY



SEGMENTECTOMY



WEDGE RESECTION





**2023 World Conference
on Lung Cancer**

SEPTEMBER 9-12, 2023 | SINGAPORE



Lobectomy reigns supreme!

Professor Eric Lim

MB ChB, MSc (Biostatistics), MD, FRCS (C-Th)

Consultant Thoracic Surgeon
Academic Division of Thoracic Surgery
Royal Brompton Hospital, London, United Kingdom

Professor of Thoracic Surgery
National Heart and Lung Institute
Imperial College, London, United Kingdom

Eric Lim, Royal Brompton Hospital





Evidence base and timeline



Eric Lim, Royal Brompton Hospital





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

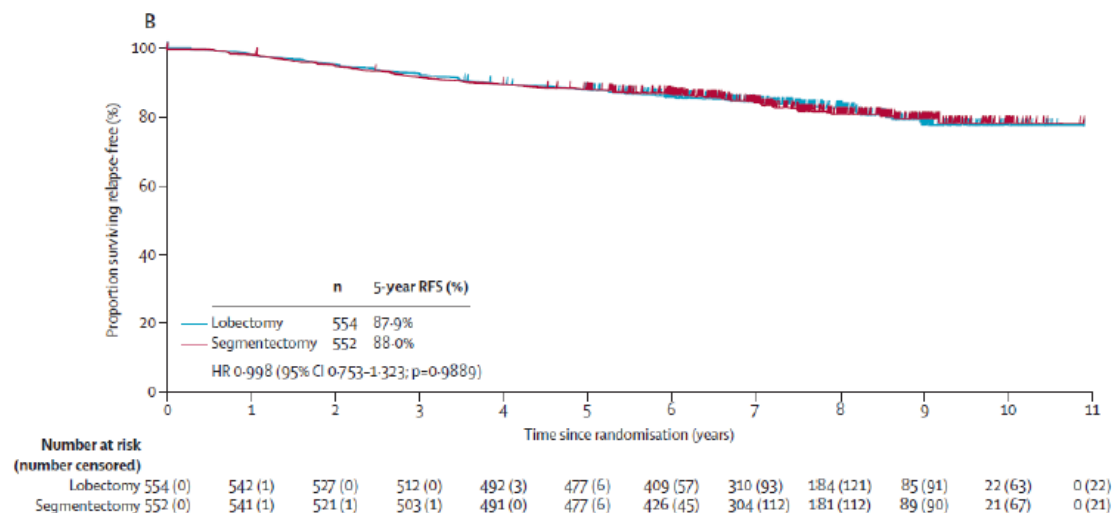
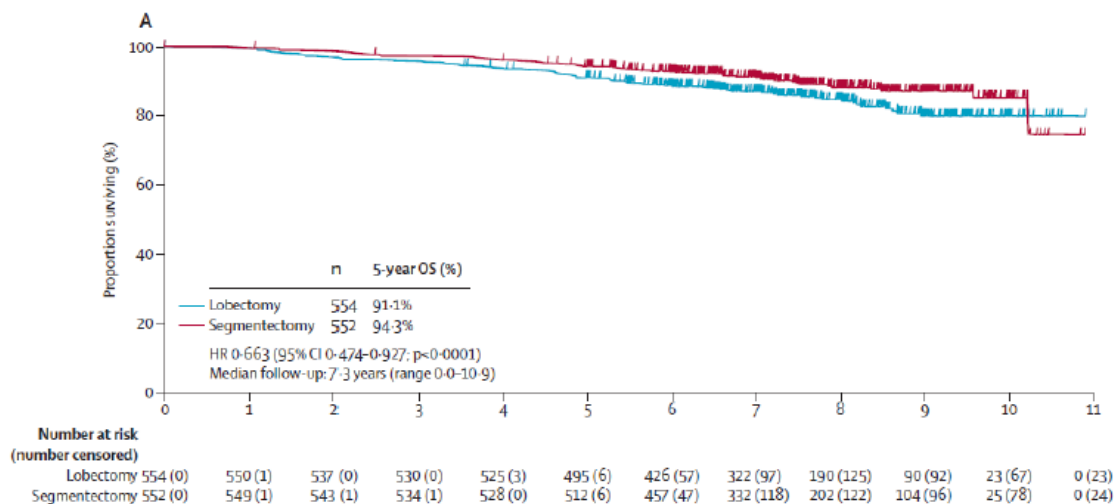
*Hisashi Saji, Morihito Okada, Masahiro Tsuboi, Ryu Nakajima, Kenji Suzuki, Keiju Aokage, Tadashi Aoki, Jiro Okami, Ichiro Yoshino, Hiroyuki Ito, Norihito Okumura, Masafumi Yamaguchi, Norihiko Ikeda, Masashi Wakabayashi, Kenichi Nakamura, Haruhiko Fukuda, Shinichiro Nakamura, Tetsuya Mitsudomi, Shun-Ichi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

Interpretation To our knowledge, this study was the first phase 3 trial to show the benefits of segmentectomy versus lobectomy in overall survival of patients with small-peripheral NSCLC. The findings suggest that segmentectomy should be the standard surgical procedure for this population of patients.





Does segmentectomy compromise overall survival?



Interpretation To our knowledge, this study was the first phase 3 trial to show the benefits of segmentectomy versus lobectomy in overall survival of patients with small-peripheral NSCLC. The findings suggest that segmentectomy should be the standard surgical procedure for this population of patients.

Similar overall and disease free survival

Lancet 2022; 399: 1607-17





Causes of death	Arm A: Lobectomy (N=554)	V.S.	Arm B: Segmentectomy (N=552)
Total	83 (14.9%)	>	
Lung cancer-related death	28 (5.1%)	=	26 (4.7%)
Other death	52 (9.4%)	>	27 (4.9%)
Other cancer incl. second lung cancer	31 (5.6%)	>	12 (2.2%)
Non-malignant disease	21 (3.8%)	>	15 (2.7%)
Respiratory disease	8		4
Cerebrovascular disease	7		2
Cardiovascular disease	4		4
Others	2		5
Unknown	3		5

Recurrence location	Arm A: Lobectomy (N=554)	Arm B: Segmentectomy (N=552)	P value
Total events of recurrence	44 (7.9%)	67 (12.1%)	
Loco-regional	17 (3.1%)	38 (6.9%)	
Distant	14 (2.5%)	7 (1.3%)	
Loco-regional + distant (both)	13 (2.3%)	20 (3.6%)	
Unclassified*	0	2	
Proportion of local recurrence	30 (5.4%)	58 (10.5%)	0.0018

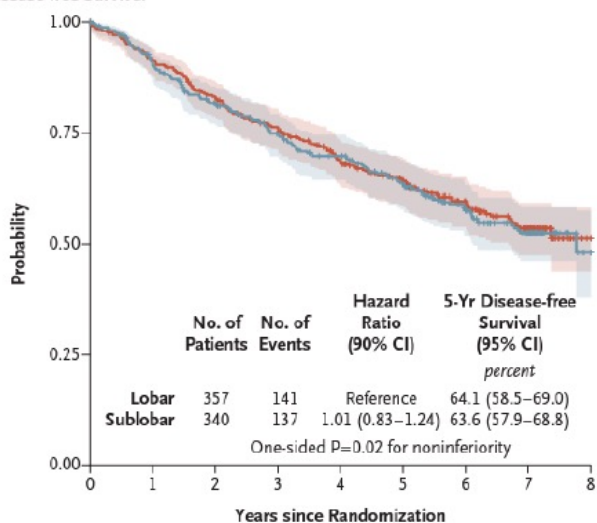




Lobar or Sublobar Resection for Peripheral Stage IA Non-Small-Cell Lung Cancer

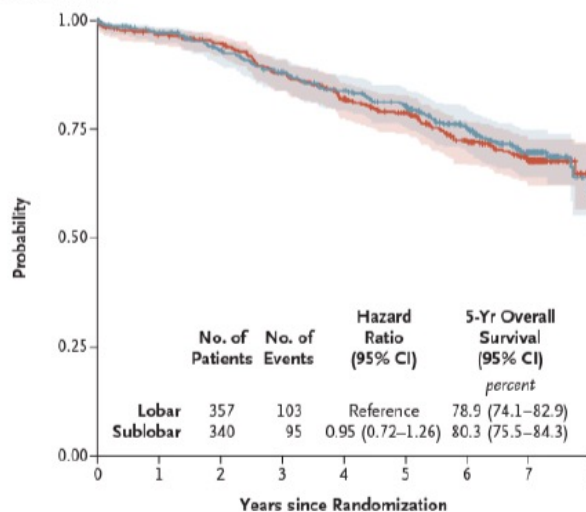
Nasser Altorki, M.D., Xiaofei Wang, Ph.D, David Kozono, M.D., Ph.D., Colleen Watt, B.S., Rodney Landrenau, M.D., Dennis Wigle, M.D., Ph.D., Jeffrey Port, M.D., David R. Jones, M.D., Massimo Conti, M.D., Ahmad S. Ashrafi, M.D., Moisha Liberman, M.D., Ph.D., Kazuhiro Yasufuku, M.D., Ph.D., Stephen Yang, 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.

A Disease-free Survival



No. at Risk	0	1	2	3	4	5	6	7	8
Lobar	357	310	276	246	209	175	132	80	5
Sublobar	340	291	254	222	201	172	123	78	6

B Overall Survival



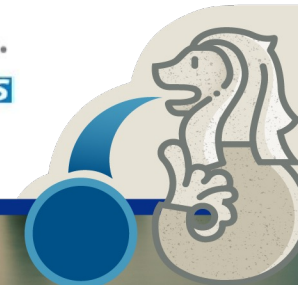
No. at Risk	0	1	2	3	4	5	6	7	8
Lobar	357	337	322	297	270	240	192	142	14
Sublobar	340	320	298	276	258	236	185	127	19

Local regional recurrence

- Lobectomy (N=351): 35 (10%)
- Sublobar (N=336): 45 (13.4%)

N Engl J Med 2023;388:489-98.

Royal Brompton & Harefield NHS Foundation Trust





Conclusions

- For segmentectomy
 - clinical and oncologic “safety” not preserved
 - not inferior in survival (was it superior?)
- For wedge
 - clinical, oncologic safety comparable
 - not inferior in survival
- Neither trial demonstrated less lung function lost with sub-lobar resection
- Lobectomy has lowest locoregional recurrence rate

Eric Lim, Royal Brompton Hospital: Lobectomy reigns supreme!





WHEN AND WHY WEDGE RESECTION IS GOOD ENOUGH

Alejandra Romero
Puerta de Hierro University Hospital
Spain





ELECTIVE SLR - Radiologic invasive tumor: Solid tumors \leq 2cm

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

FEBRUARY 9, 2023

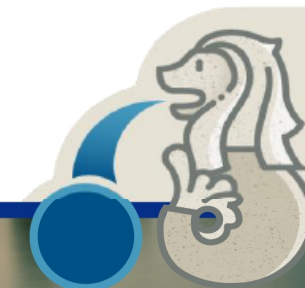
VOL. 388 NO. 6

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



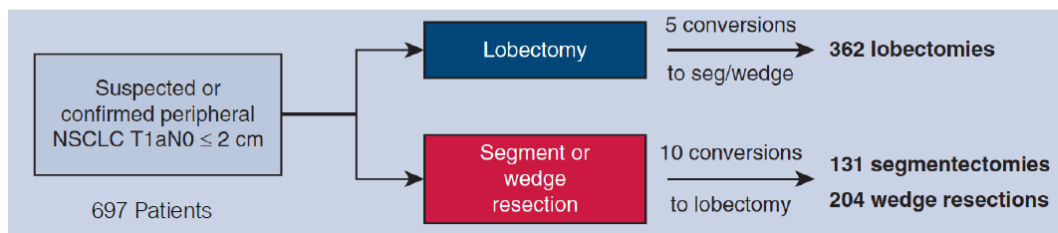
Lobectomy, segmentectomy, or wedge resection for
peripheral clinical T1aN0 non-small cell lung cancer: A
post hoc analysis of CALGB 140503 (Alliance)

- Peripheral Tumor
- Confirmation of N0 by FS
- Margins: 2 cm or equivalent to the greatest diameter of the tumor. FS recommended.
- SLR not randomly assigned





ELECTIVE SLR: CALGB 140505 post-hoc analysis lobectomy, segmentectomy or wedge



38%
59%

	n	nEvents	HR (95% CI)	5-year LRF5 (95% CI)
Segment	131	16	reference	87.6 (81.4 - 94.2%)
Wedge	204	29	1.06 (0.57 - 1.97)	84.7 (79.2 - 90.5%)

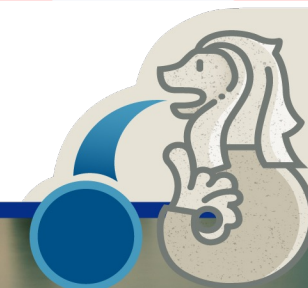
Procedure ■ Segment ■ Wedge

Locoregional recurrence (NS, p=0.295):

- 12.3% SR
- 14.4% WR
- 10% LR

LYMPH NODE RESECTION

Characteristic	Lobectomy (N = 362)	Wedge resection (N = 204)	Segmentectomy (N = 131)	Total (N = 697)	P value
Mediastinal node staging, n (%)					.02201
Complete dissection	96 (26.7)	58 (28.7)	28 (21.4)	182 (26.3)	
Systematic sampling	185 (51.4)	84 (41.6)	80 (61.1)	349 (50.4)	
Simple sampling	79 (21.9)	60 (29.7)	23 (17.6)	158 (22.8)	
Patients with positive nodes, n (%)					.04831
0	338 (93.4)	199 (97.5)	127 (96.9)	664 (95.3)	
1+	24 (6.6)	5 (2.5)	4 (3.1)	33 (4.7)	
Nodes sampled, mean (SD)	4.7 (1.45)	4.0 (1.30)	4.9 (1.46)	4.6 (1.46)	<.0001





ELECTIVE SLR: CALGB 140505 post-hoc analysis lobectomy, segmentectomy or wedge

- Limitations of post-hoc analysis but best evidence to date
- DFS and OS were similar regardless the extent of pulmonary resection
- Wedge and segmentectomy are acceptable options for patients with peripheral NSCLC ≤ 2 cm
- MAIN LIMITATIONS:
 - Patients not randomly assigned to modalities of SLR
 - **The trial was not powered to determine noninferiority between the SLR modalities**
 - Hypothesis generating rather than result of hypothesis testing





COMPROMISE SLR: Segmentectomy vs. wedge

- Lack of strong evidence (Retrospective analysis, selection bias and confounders)
- Wedge: Similar long-term outcomes, more LRR, lower toxicity
- Balancing oncologic benefit and technical difficulty
- Reduce surgical time, risk of postoperative complications, preserve lung function
- Quality of wedge (margins and lymphadenectomy)
- Two ongoing RCT:
 - AWESOME Trial/JCOG2109 (> 80 years)
 - ANSWER Trial/JCOG1909 (high risk patients)





Take Home Message

WHEN AND WHY WEDGE RESECTION IS GOOD ENOUGH?

- GGO-predominant peripheral LC
- Peripheral solid tumors ≤ 2 cm \rightarrow Further studies are necessary to confirm this hypothesis
- High risk patients \rightarrow Additional evidence is forthcoming
- Personalized treatment: tumor location and radiologic characteristics, patient comorbidities...
- Quality of wedge resection: Surgical margins and lymphadenectomy





Prognostic Impact of Ground Glass Opacity Component and Consolidation Size after Sublobar Resection : A Quantitative Analysis

Ji Yong Kim
Asan Medical Center, Seoul
Korea





Clinical trials of the Japan Clinical Oncology Group (JCOG)

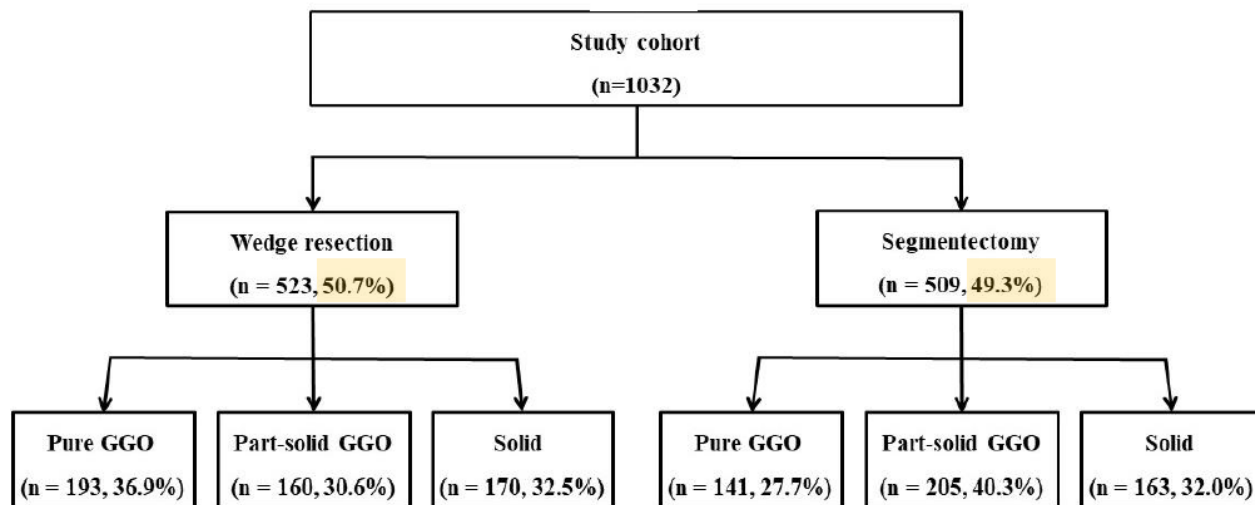
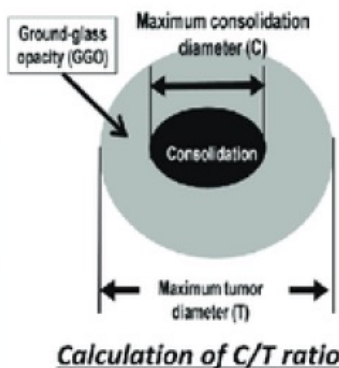
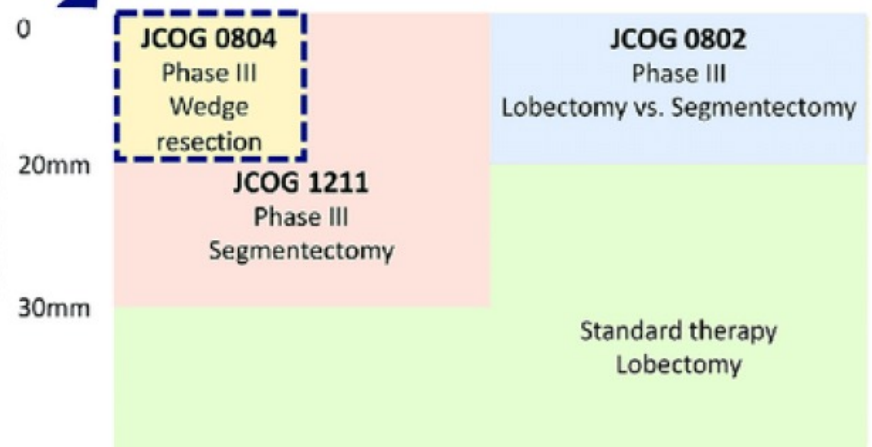
JCOG 1906

Phase III
Follow-up

C/T ratio

0 0.25 0.5 1.0
 +--- GGO dominant ---+ +--- Solid dominant ---+

Tumor size



A quantitative analysis of maximal consolidation size and GGO component for the risk of cancer recurrence after sublobar resection in patients with clinical stage IA lung adenocarcinoma.





Conclusion

- Risks of cancer recurrence after sublobar resection are consistently increased according to the increase of **C/T ratio** and **consolidation tumor size** in stage IA adenocarcinoma.
- The risk of cancer recurrence was **synergistically affected** by these two variables
- A positive correlation between these two variables
- It is reasonable to perform sublobar resection according to the cutoff values of tumor size $\leq 2\text{cm}$ (consolidation size $\leq 1\text{ cm}$) and C/T ratio $\leq 50\%$.





2023 World Conference on Lung Cancer

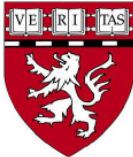
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Sublobar Resection for Non-Small-Cell Lung Cancers ≤2cm with High-Risk Features is Associated with Similar Survival as Lobectomy

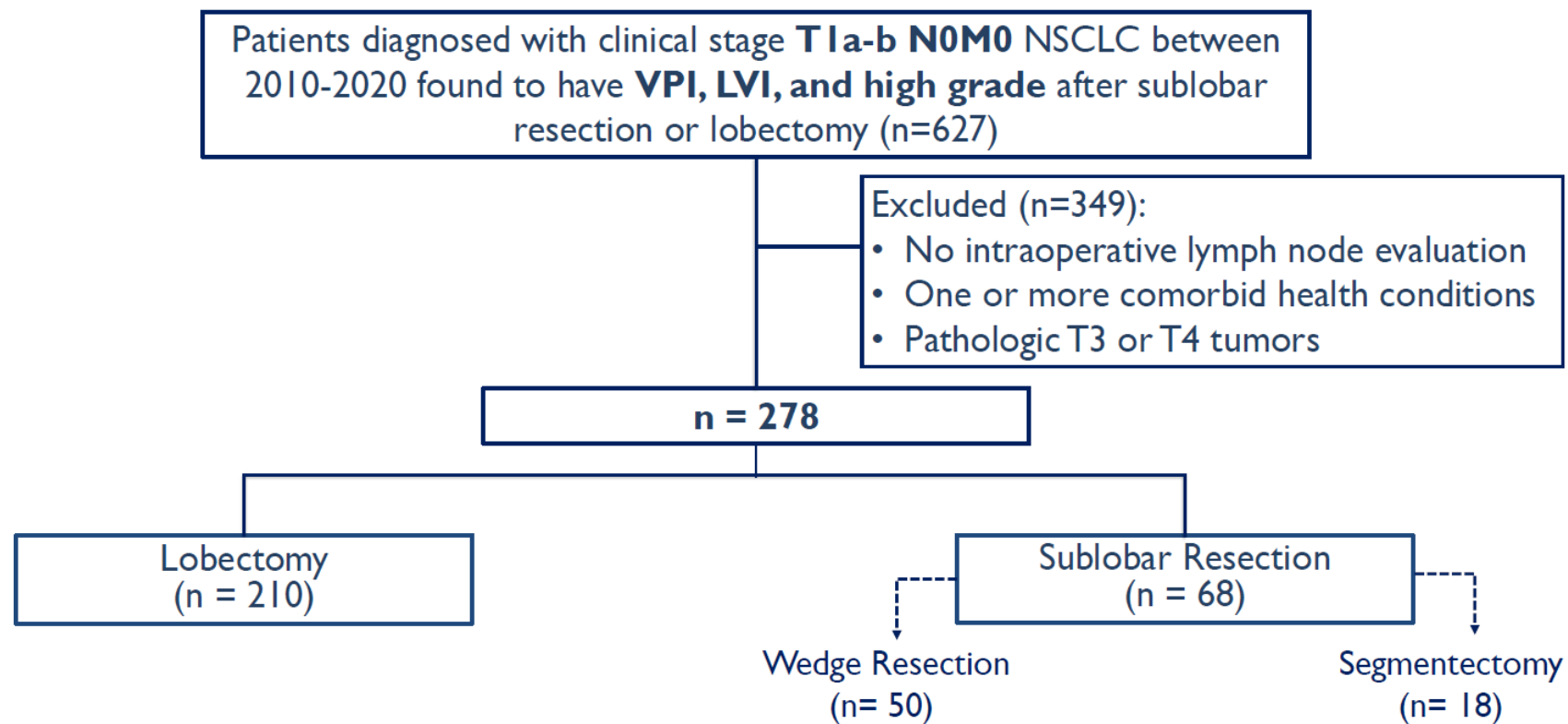
Camille Mathey-Andrews MD¹, Annie Abruzzo BA¹, Shivaek Venkateswaran¹, Alexandra Potter¹,
Chi-Fu Jeffrey Yang MD¹

¹Department of Surgery, Division of Thoracic Surgery, Massachusetts General Hospital, Boston, MA





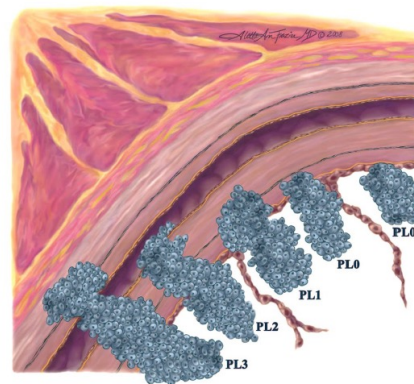
Study Cohort





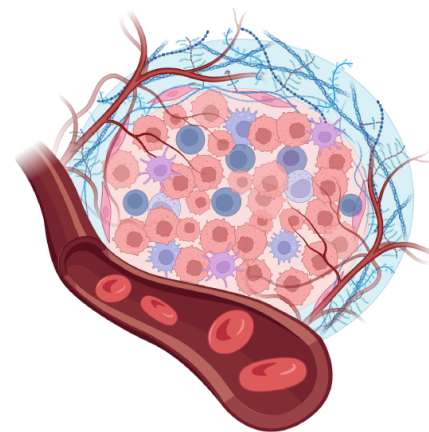
VPI as an adverse prognostic factor

- ▶ VPI is detected in 10-14% of tumors ≤ 2 cm in size and is associated with increased likelihood of lymph node metastasis, aggressive disease biology, and reduced survival.¹
- ▶ The positive predictive value of preoperative CT in diagnosing VPI is low and accurate diagnosis generally requires the use of elastin stains.^{2,3}
- ▶ We previously found no difference in survival between patients undergoing segmentectomy vs. lobectomy for stage IA NSCLC and VPI on final pathology.⁴



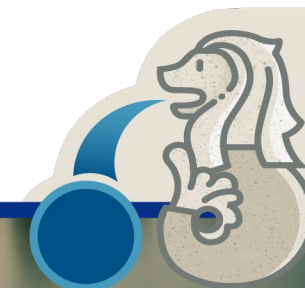
1. Takizawa et al. *Eur J Cardiothorac Surg.* 2018; 53:987-992
2. Snoeckx. *Quant Imaging Med Surg* 2019;9(12):2019-2022
3. Travis et al. *J Thorac Oncol.* 2008;3:1384-1390.
4. Mathey-Andrews et al. *Ann Thorac Surg.* 2023.

LVI and grade as additional high-risk features



- ▶ Although not included in AJCC T stage cataloguing, LVI and high grade have been demonstrated to increase the risk of locoregional recurrence after surgery.¹
- ▶ In 2020, Yun et al. found that LVI was associated with worse survival among patients with stage IA NSCLC undergoing sublobar resection and lobectomy.²
 - ▶ This prognostic impact was more pronounced for those undergoing sublobar resection.²

1. Kelsey et al. *Cancer.* 2009; 115:5129-5351
2. Yun et al. *Lung Cancer.* 2020; 146: 105-111

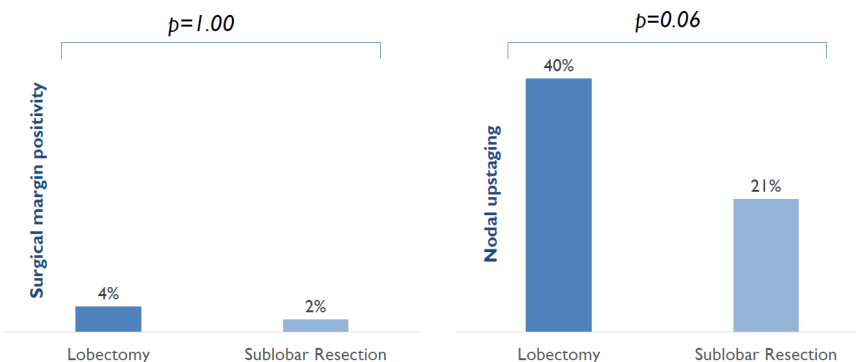




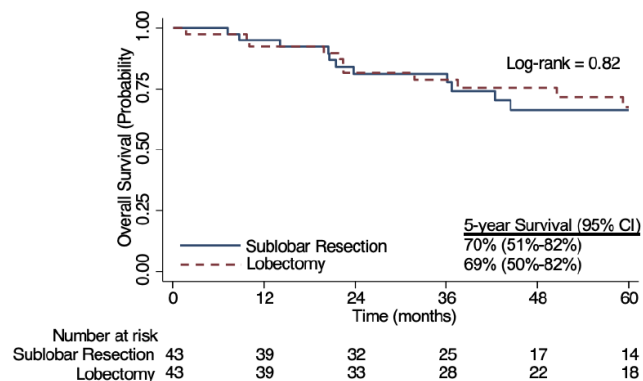
Pathologic Outcomes of Matched Cohort

Characteristics	Lobectomy (n = 43)	Sublobar Resection (n = 43)	p-value
Pathologic T2, %	100%	100%	1.00
Pathologic N stage, %			0.19
N0	60%	79%	
N1	14%	7%	
N2	26%	14%	
Number of lymph nodes evaluated (median)	11	5	<0.01

Pathologic outcomes: matched analysis of patients with stage IA NSCLC and high-risk features



Survival of patients in the propensity-score matched cohort



5-year overall survival of patients in the NCDB undergoing sublobar resection vs. lobectomy for NSCLC tumors ≤2cm with high-risk features (VPI, LVI, high grade): propensity-score matched analysis





Conclusions

- For patients with clinical T1a-bN0M0 NSCLC with highest risk features (i.e., visceral pleural invasion + lymphovascular invasion + high grade) there were **no significant differences** in five-year overall survival between patients undergoing sublobar resection or lobectomy.
- There were also **no differences** in perioperative outcomes between patients who received either type of operation.
- If patients with clinical stage IA NSCLC are found to have high-risk features after sublobar resection, a **completion lobectomy may not be of benefit.**





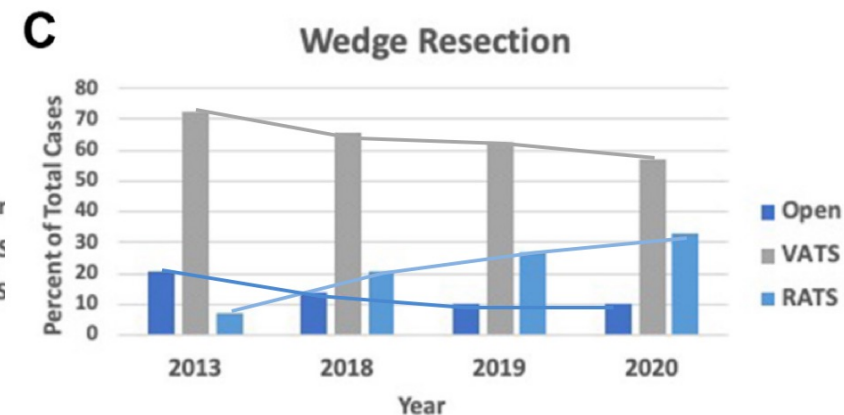
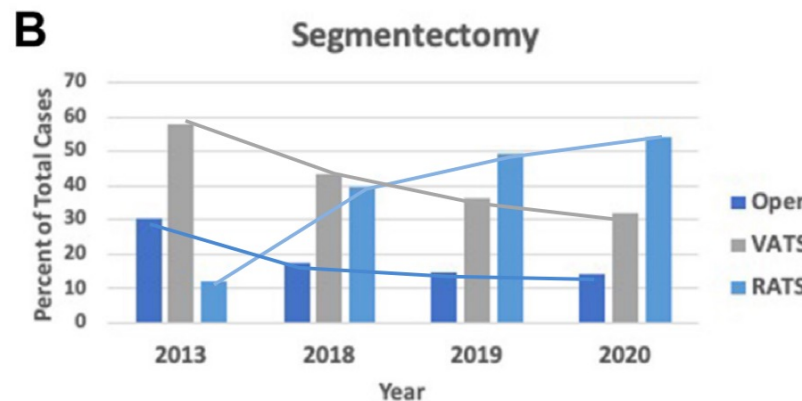
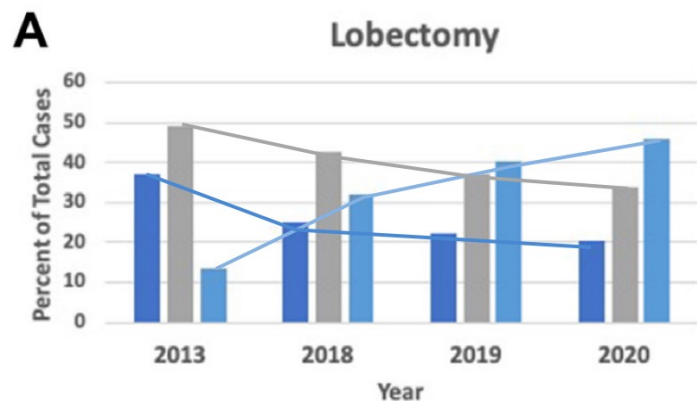
Trends in Surgical Resection

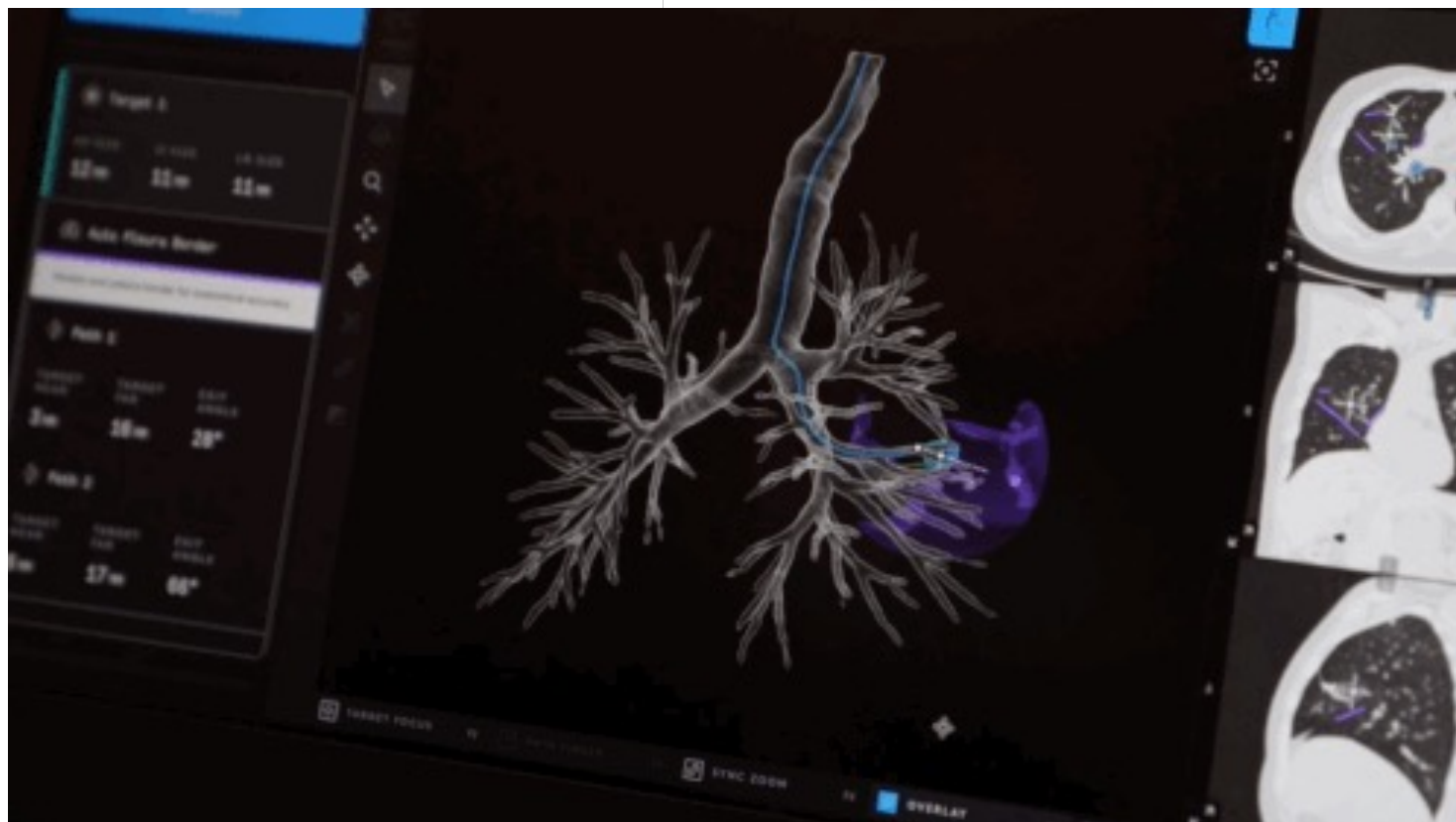
THE SOCIETY OF THORACIC SURGEONS GENERAL THORACIC SURGERY DATABASE: UPDATE ON OUTCOMES AND RESEARCH

The Society of Thoracic Surgeons General Thoracic Surgery Database: 2022 Update on Outcomes and Research

Check for updates

Elliot L. Servais, MD,¹ Justin D. Blasberg, MD,² Lisa M. Brown, MD, MAS,³ Christopher W. Towe, MD,⁴ Christopher W. Seder, MD,⁵ Mark W. Onaitis, MD,⁶ Mark I. Block, MD,⁷ and Elizabeth A. David, MD, MAS⁸





“The era of precision lung cancer surgery is here”

-Valerie Rusch





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