



Modern concepts and results of surgery for early stage NSCLC

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Disclosure slide

Nothing to declare



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Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

B Death from Lung Cancer

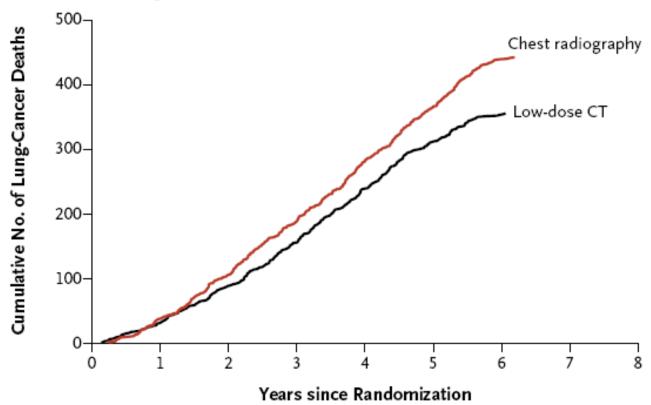




Table 5. Stage and Histo	ologic Type of Lung (Cancers in the Two	Screening Groups, A	ccording to the Resu	lt of Screening.*						
Stage and Histologic Type		Low-D	ose CT		Chest Radiography						
	Positive Screening Test (N = 649)	Negative Screening Test (N=44)†	No Screening Test (N=367)‡	Total (N = 1060)	Positive Screening Test (N = 279)	Negative Screening Test (N=137)†	No Screening Test (N=525)\$	Total (N = 941)			
				number/total n	umber (percent)						
Stage											
IA	329/635 (51.8)	5/44 (11.4)	82/361 (22.7)	416/1040 (40.0)	90/275 (32.7)	16/135 (11.9)	90/519 (17.3)	196/929 (21.1)			
IB	71/635 (11.2)	2/44 (4.5)	31/361 (8.6)	104/1040 (10.0)	41/275 (14.9)	6/135 (4.4)	46/519 (8.9)	93/929 (10.0)			
IIA	26/635 (4.1)	2/44 (4.5)	7/361 (1.9)	35/1040 (3.4)	14/275 (5.1)	2/135 (1.5)	16/519 (3.1)	32/929 (3.4)			
IIB	20/635 (3.1)	3/44 (6.8)	15/361 (4.2)	38/1040 (3.7)	11/275 (4.0)	6/135 (4.4)	25/519 (4.8)	42/929 (4.5)			
IIIA	59/635 (9.3)	3/44 (6.8)	37/361 (10.2)	99/1040 (9.5)	35/275 (12.7)	21/135 (15.6)	53/519 (10.2)	109/929 (11.7)			
IIIB	49/635 (7.7)	15/44 (34.1)	58/361 (16.1)	122/1040 (11.7)	27/275 (9.8)	24/135 (17.8)	71/519 (13.7)	122/929 (13.1)			
IV	81/635 (12.8)	14/44 (31.8)	131/361 (36.3)	226/1040 (21.7)	57/275 (20.7)	60/135 (44.4)	218/519 (42.0)	335/929 (36.1)			
Histologic type											
Bronchioloalveolar carcinoma	95/646 (14.7)	1/44 (2.3)	14/358 (3.9)	110/1048 (10.5)	13/276 (4.7)	1/135 (0.7)	21/520 (4.0)	35/931 (3.8)			
Adenocarcinoma	258/646 (39.9)	8/44 (18.2)	114/358 (31.8)	380/1048 (36.3)	112/276 (40.6)	37/135 (27.4)	179/520 (34.4)	328/931 (35.2)			
Squamous cell carcinoma	136/646 (21.1)	13/44 (29.5)	94/358 (26.3)	243/1048 (23.2)	70/276 (25.4)	24/135 (17.8)	112/520 (21.5)	206/931 (22.1)			
Large-cell carcinoma	28/646 (4.3)	3/44 (6.8)	10/358 (2.8)	41/1048 (3.9)	12/276 (4.3)	10/135 (7.4)	21/520 (4.0)	43/931 (4.6)			
Non–small-cell carci- noma or other§	75/646 (11.6)	4/44 (9.1)	52/358 (14.5)	131/1048 (12.5)	40/276 (14.5)	30/135 (22.2)	88/520 (16.9)	158/931 (17.0)			
Small-cell carcinoma	49/646 (7.6)	15/44 (34.1)	73/358 (20.4)	137/1048 (13.1)	28/276 (10.1)	32/135 (23.7)	99/520 (19.0)	159/931 (17.1)			
Carcinoid	5/646 (0.8)	0	1/358 (0.3)	6/1048 (0.6)	1/276 (0.4)	1/135 (0.7)	0	2/931 (0.2)			

^{*} The denominators represent only cancers with a known stage or known histologic type. The stage was not known in the case of 14 cancers after a positive screening test and 6 after no screening in the low-dose CT group and in the case of 4 cancers after a positive screening test, 2 after a negative screening test, and 6 after no screening in the radiography group. The histologic type was not known for 3 cancers after a positive screening test and 9 after no screening in the low-dose CT group and for 3 cancers after a positive screening test, 2 after a negative screening test, and 5 after no screening in the radiography group.



[†] Negative screening tests included tests that revealed either minor or clinically significant abnormalities that were not suspicious for lung cancer.

The 892 lung cancers in participants with no screening test included 35 in participants who were never screened, 802 that were diagnosed during the post-screening period, and 55 in participants who were due for a screening test.

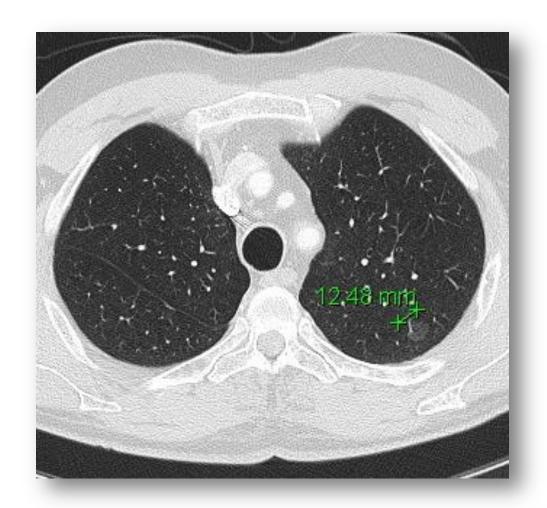
[§] The 289 lung cancers in this category (in the two groups combined) included 28 adenosquamous carcinomas, 6 sarcomatoid carcinomas, 55 unclassified carcinomas, 1 anaplastic-type carcinoma, 1 carcinosarcoma, and 198 coded only as "non-small-cell carcinoma."

Ground Glass Opacity

STAGE I
BAC= 17% (screening group) vs.
6% (control group)



National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409





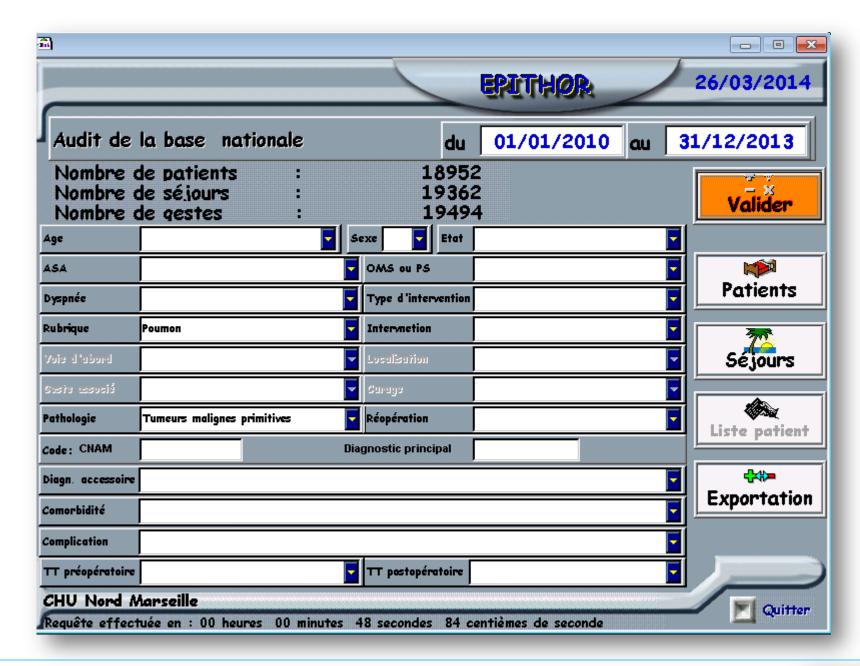
Current surgical risks in the real life

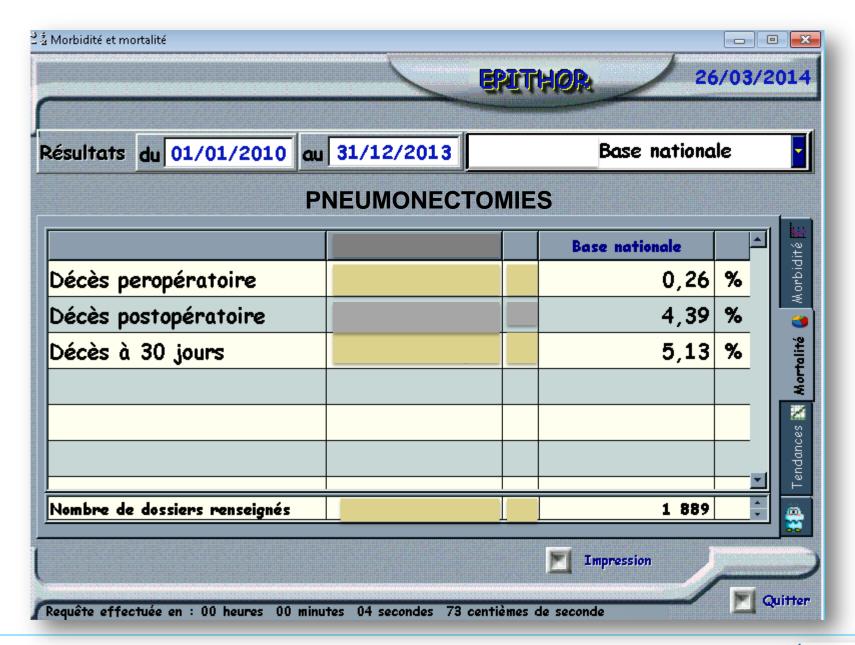


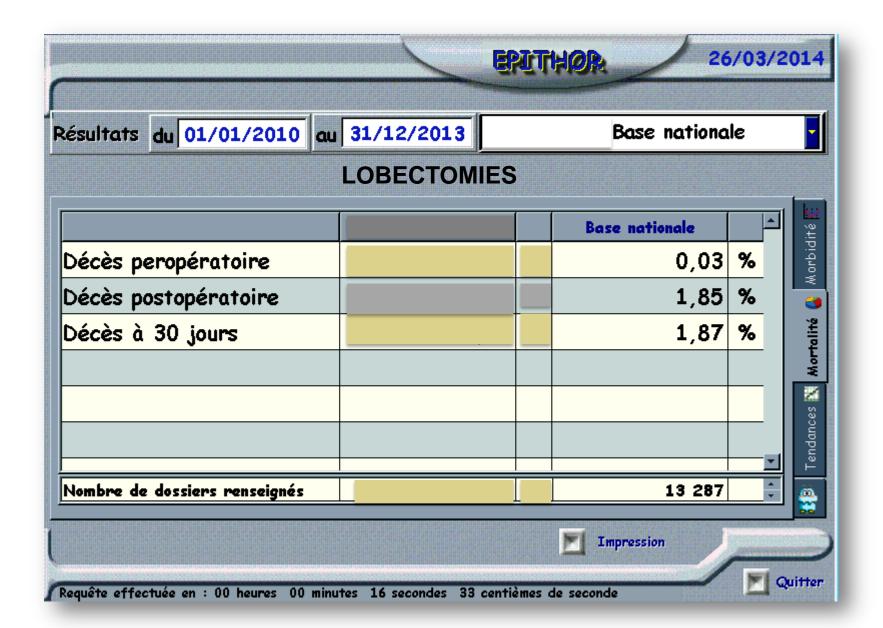


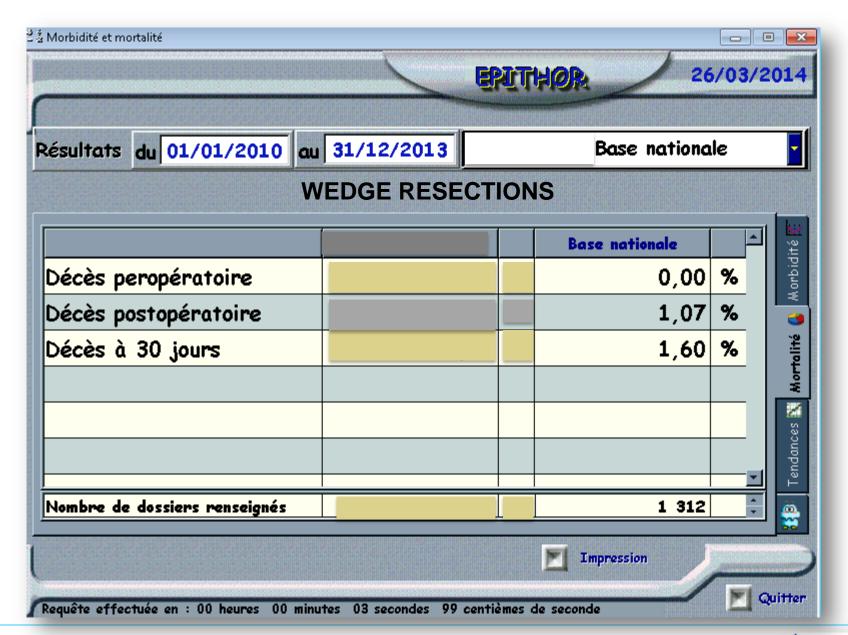


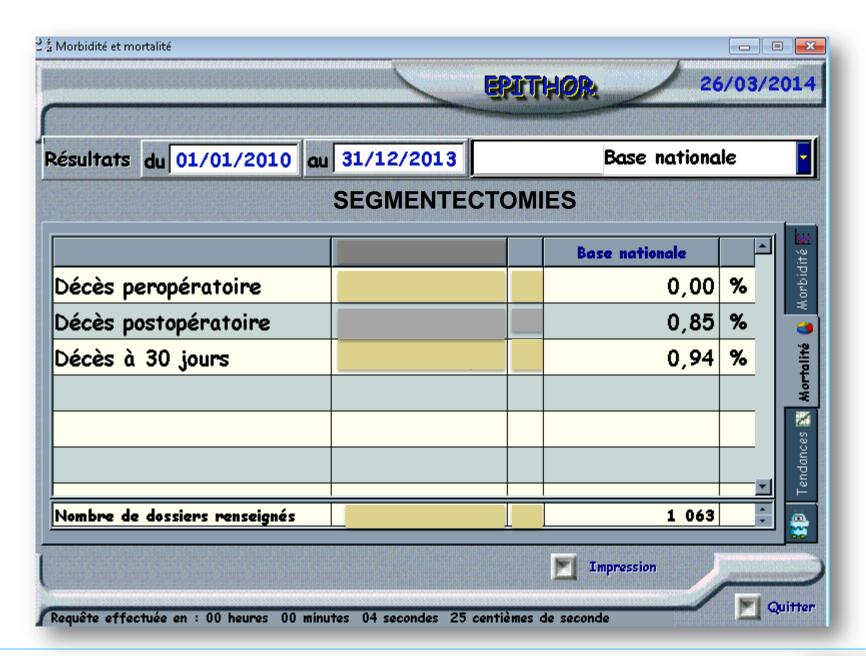












Video-Assisted Thoracic Surgery Lobectomies







Early outcomes

	VAT	S	Thoraco	tomy		Risk ratio		R	isk rati	0	
Study or subgroup Events To		Total	Events Tota		Weight	M-H, random, 95% C	M-H, randon			n, 95% CI	
Ilonen (2011)	3	116	4	116	12.7%	0.75 [0.17, 3.28]		111	•	-	
Park (2011)	1	136	0	136	2.7%	3.00 [0.12, 73.00]		-		-	_
Paul (2010)	12	1281	13	1281	45.5%	0.92 [0.42, 2.02]			-	4	
Villamizar (2009)	8	284	15	284	39.1%	0.53 [0.23, 1.24]			-		
Total (95% CI)		1817		1817	100.0%	0.75 [0.44, 1.27]				Mort	ality
Total events	24		32			73. 2457-27. 1.76					•
Heterogeneity: $T^2 = 0$.	.00; $\chi^2 = 1$.63, df	= 3(P = 0)	.65); /2 =	= 0%		1	-	-	- (+
Test for overall effect:					A		0.01 Fa	0.1 avors \	ATS fa	10 avors ope	100

	VAT	S	Thoraco	tomy		Risk ratio	Risk rat	io
Study or subgroup	Events	Total	Events	Total	Weight	M-H, random, 95% CI	M-H, rando	m, 95% CI
Ilonen (2011)	12	116	30	116	8.4%	0.40 [0.22, 0.74]		
Park (2011)	17	136	22	136	9.2%	0.77 [0.43, 1.39]		-
Paul (2010)	336	1281	444	1281	47.8%	0.76 [0.67, 0.85]		
Villamizar (2009)	88	284	140	284	34.6%	0.63 [0.51, 0.78]	-	
Total (95% CI)		1817		1817	100.0%	0.67 [0.56, 0.82]		Morbidity
Total events	453		636					,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
Heterogeneity: $T^2 = 0$.02; Y2 = 5	5.79, df	= 3 (P = 0)	.12); /2=	48%	-	1 1	1 1
Test for overall effect:							0.2 0.5 1 Favors VATS	favors open



Meta-analysis of propensity score-matched patients

Pulmonary complications

0)	VAT	S	Thoraco	tomy		Risk ratio	Risk ratio	
Study or subgroup	Events	Total	Events	Total	Weight	M-H, random, 95% CI	M-H, random, 95% CI	
llonen (2011)	5	116	5	116	7.1%	1.00 [0.30, 3.36]		
Park (2011)	1	136	2	136	1.8%	0.50 [0.05, 5.45]		
Paul (2010)	38	1281	56	1281	64.1%	0.68 [0.45, 1.02]	-	
Villamizar (2009)	14	284	27	284	26.9%	0.52 [0.28, 0.97]	-	
Total (95% CI)		1817		1817	100.0%	0.65 [0.47, 0.89]	•	
Total events	58		90					
Heterogeneity: $\tau^2 = 0.0$	00; $\chi^2 = 1$.08, df	= 3 (P = 0.	78); /2=	0%		205 00 1	+
Test for overall effect:							0.05 0.2 1 5 Favors VATS favors open	20 n

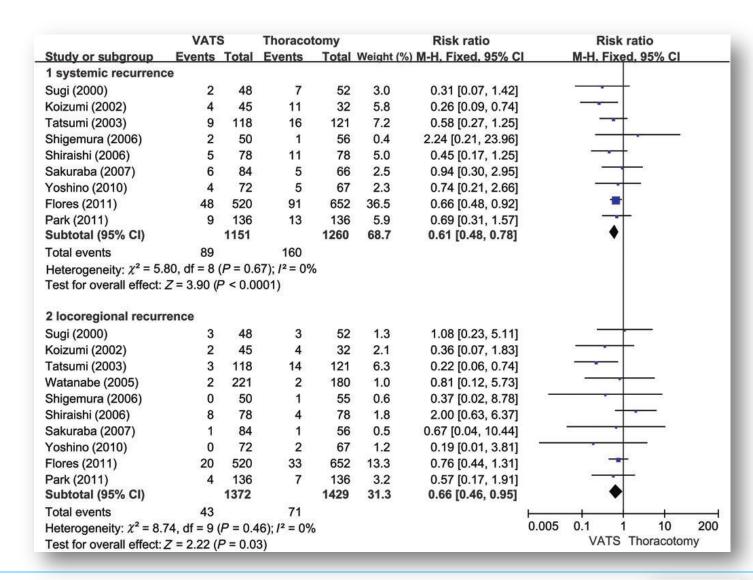




Survival

Metastatic recurrence

Local relapse







Quality of Life

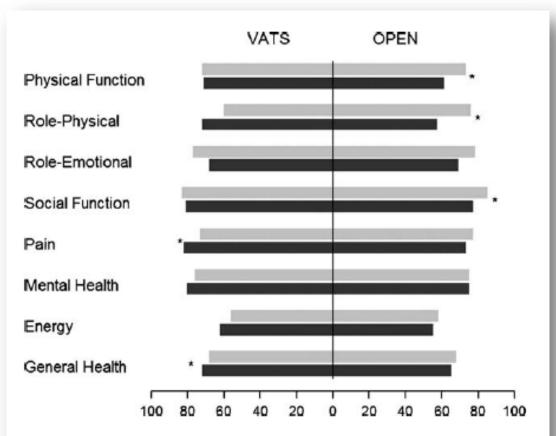


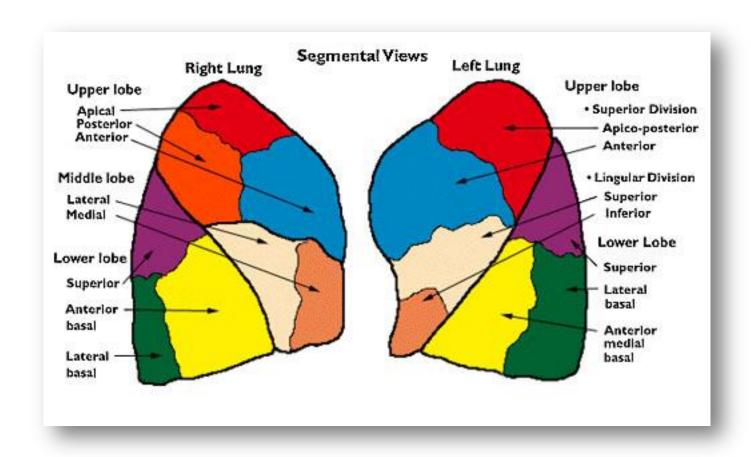
Fig. 1. VATS and OPEN lobectomy SF36 scores (gray = preop, black = postop), 0 = worst; 100 = best, p < 0.05.



Handy JR Jr et al. Does video-assisted thoracoscopic lobectomy for lung cancer provide improved functional outcomes compared with open lobectomy? Eur J Cardio-thorac Surg 2010; 37: 451—455



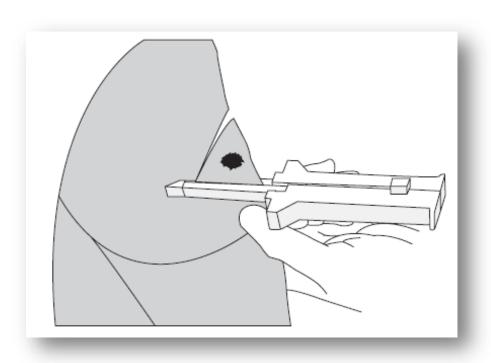
Sublobar resections

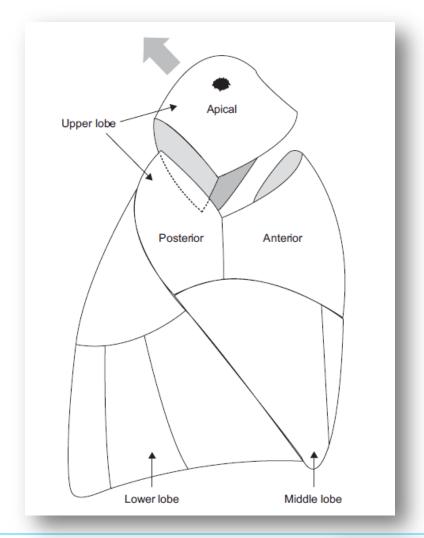




Segmentectomy

Wedge







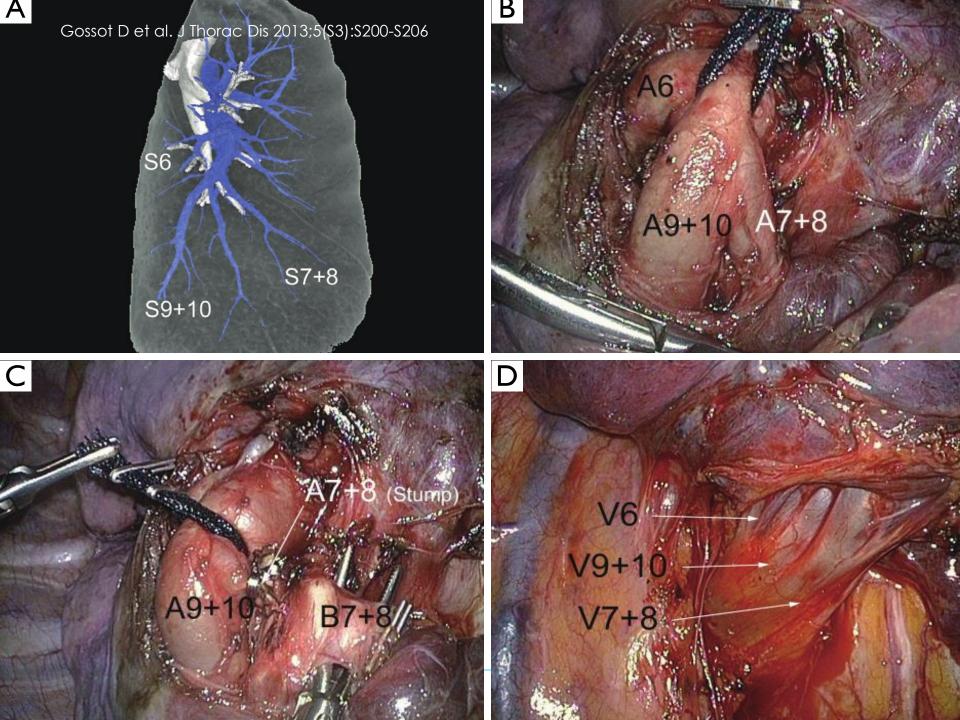
LCSG - 1995

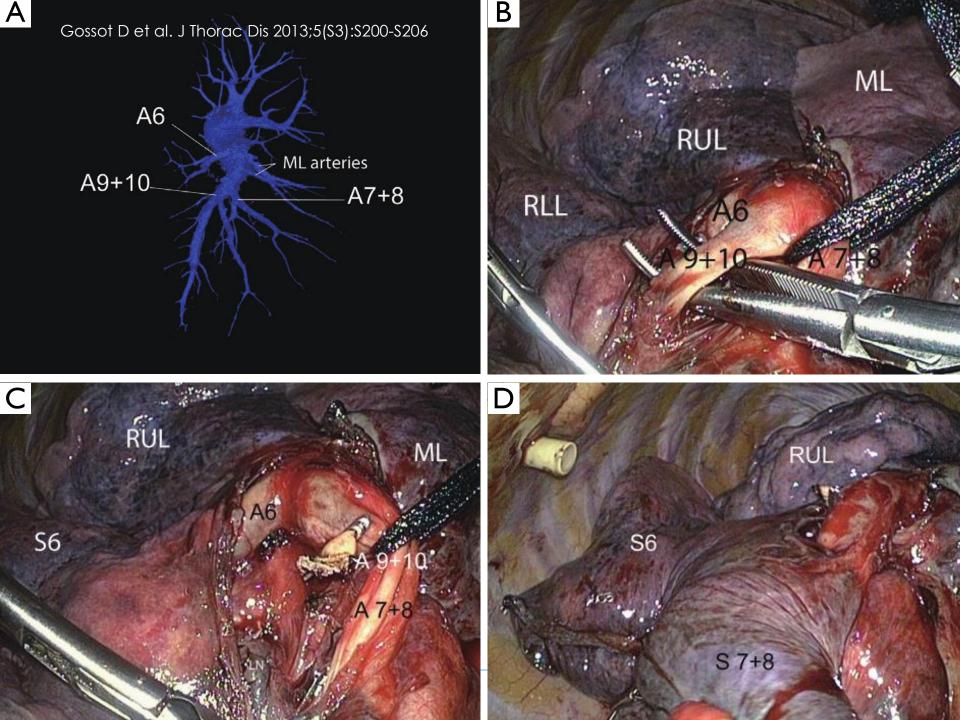
Author, date,	Patient group	Outcomes		Key results	Comments
country, level of evidence		5-year (or specified) survival rate	Locoregional recurrence		
Ginsberg et al.	Lobectomy: 125	Overall death rate	(persons/year)	30% increase in the death ra	te Inconsistent mediastinal
(1995), USA	(Wedge resection +	(persons/year):	Lobectomy: 0.020	with limited resection $(P =$	lymph node sampling
,	Segmentectomy):		Limited resection:	0.08)	, ,
Randomized control	122	Lobectomy: 0.089	0.060	, in the second	
trial				300% increase in locoregion	al /
(level 1b)		Limited resection:		recurrence (<i>P</i> = 0.008)	
(level 15)		0.117		recurrence (i o.ooo)	



Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Ann Thorac Surg 1995;60:615–22.







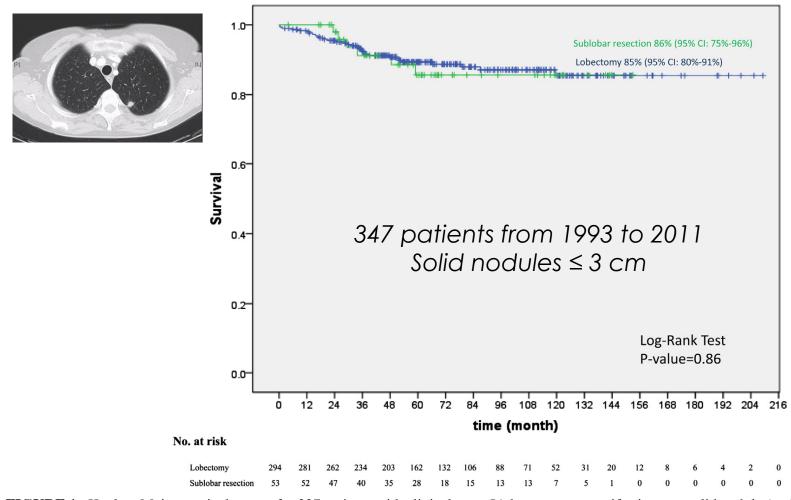


FIGURE 1. Kaplan–Meier survival curves for 337 patients with clinical stage IA lung cancer manifesting as a solid nodule (nodule diameter of \leq 30 mm), separately for those who underwent lobectomy (n = 294) and SLR (n = 53). CI, Confidence interval.

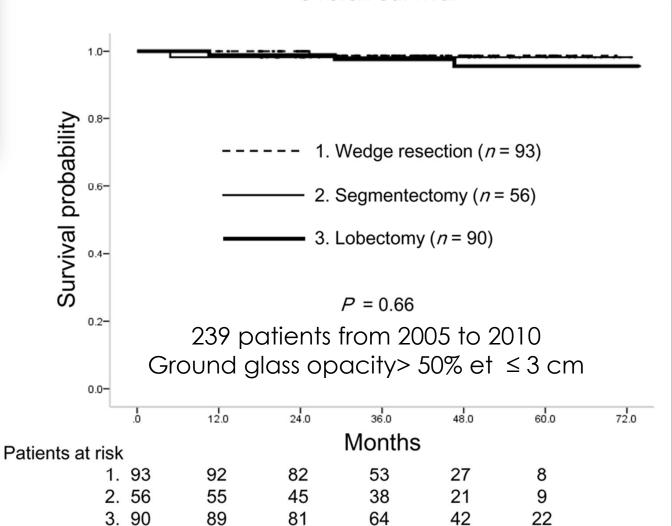


International Early Lung Cancer Action Program (I-ELCAP) database Altorki NK et al. Sublobar resection is equivalent to lobectomy for clinical stage 1A lung cancer in solid nodules. J Thorac Cardiovasc Surg 2014; in press.





Overall survival





Tsutani Y et al. Appropriate sublobar resection choice for ground glass opacity-dominant clinical stage IA lung adenocarcinoma: wedge resection or segmentectomy. Chest 2004, in press





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From: Treatment of Stage I and II Non-small Cell Lung CancerTreatment of Stage I and II Non-small Lung Cancer: Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

		1	1	%	% of W/S patients			tient eteristics	% 5	5-year Sur	vival	% L	ocal Rec	currence
First Author Year	Design	Lobe	W/S	% Wedge	% able to have lobe	% GGO ^a	Stage	Size (cm)	Lobe	W/S	р	Lobe	W/S	р
Sublobar Resection as	s an Electiv	e Altern	<u>ative</u>											
Ginsberg 1995 ^{95,96}	RCT	127	120	32	100	few	Ia	≤3cm	73	56	.06	7	18	0.009
Okada 2006 ⁹⁷	Prosp ^b	260	305	12	100	Many	Ia	≤2cm	89	89	NS	-		-
Koike 2003 ⁹⁸	Prosp ^b	159	74	14	100	-	Ia	≤2cm	90	89	NS	1	3	-
Large Database Com	parisons													
Kates 20119	SEER	1402	688	-	-	-	Ia	≤1cm	HR	1.12	NS	_	-	-
Wisnivesky ^c 2010 ¹⁰⁰	SEER	969	196	-	-	16 ^d	Ia	≤2cm	HR	1.10 ^c	NS	-	-	-
Case-matched and Se	lected Unco	ntrolled	Compa	risons										
Martin-Ucar ^e 2005 ¹⁰¹	Retro	17 ^f	17	0	0	-	Ia,b	-	64	70	NS	12	0	NS
Iwasaki 2004 ¹⁰²	Retro	55	31	0	_	-	Ia	<2cm	73	70	NS	4	3	NS
El Sherif 2006 ¹⁰³	Retro	577	207	59	0	-	I	≤3cm	54	40	0.004	8	15	0.02
Wolf 2011 ¹⁰⁴	Retro	172	66	64	-	Few ^g	Ia	<2cm	80	59	0.003	8	16	NS
Landreneau 1997 ¹⁰⁵	Retro	117	102	100	0	-	I	≤3cm	65	58	NS	9	18	.07
Schuchert 2007 ¹⁰⁶	Retro	246	182	0	most	Few	I	≤3cm	83	82	NS	5	8	NS
Schuchert 2011 ¹⁰⁷	Retro	32	75	71	most	-	I	≤1cm	64	55/73 ^h	NS	3	3	NS
Campione 2004 ¹⁰⁸	Retro	98	22	0	0	-	Ia	≤3cm	65	62	NS	2	19	_
Kilic 2009 ¹⁰⁹	Retro	106	78	0	-	-	Ia,b	-	47	46	NS	4	6	NS
Kodama 1997 ¹¹⁰	Retro	77	64	5	73	-	Ia	≤3cm	88	93/48 ⁱ	NS	1	2/12 ⁱ	NS/0.02i

Comparative outcomes for lobectomy and sublobar resection. Inclusion criteria: Studies reporting comparative outcomes for lobectomy and sublobar resection from RCT, prospective studies, large database comparisons, case-matched studies, and selected uncontrolled cohort studies up through 2012. GGO = ground-glass opacity; HR = hazard ratio of death, with lobectomy as the reference; Prosp = prospective; RCT = randomized controlled trial; Retro = retrospective; W/S = wedge and segmentectomy. See Figure 1 legend for expansion of other abbreviations.

Results for patients able to tolerate a lobectomy/and for those who could not.

aLesions that are > 50% GGO.

bLobectomy "control subjects" refused sublobar resection.

^cPropensity-matched cohorts.

dProportion with BAC histology.

eCase-matched.

fall high risk (fell below standard criteria for lobectomy); case-matched series.

gExcluded pure bronchioloalveolar carcinoma.

hResults for wedge and segmentectomy reported separately.



From: Treatment of Stage I and II Non-small Cell Lung CancerTreatment of Stage I and II Non-small Lung Cancer: Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

	%		n		Patient Characteristics		% 5-year Survival			% Local Recurrence		
First Author Year	Study Design	Comp- romise	Wedge	Segm	Stage	Size (cm)	Wedge	Segm	p	Wedge	Segm	p
Watanabe 2005 ¹¹⁵	Prosp	0	14	20	Ia	≤2	100 ^a	93	NS	0^{a}	0	NS
Nakamura 2011 ¹¹⁶	Retro	-	84	38	I	-	55	87	-	6	5	NS
Schuchert 2011 ¹⁰⁷	Retro	few	35	40	Ia	<1	55	73	NS	3	3	NS
Sienel 2008 ¹¹⁷	Retro	100	31	56	Ia		48	80	0.005	55	16	0.001
El Sherif 2007 ¹¹⁸	Retro	-	55	26	Ia,b	≤3cm	-	_	-	15	4	0.002
Okada 2005 ¹¹⁹	Retro	-	35	123	I	<2	(86) ^b	$(96)^{b}$	NS	-	-	-
Okada 2005 ¹¹⁹	Retro	-	14	64	I	2-3	(39) ^b	$(85)^{b}$	0.0001	-	-	-
Okada 2005 ¹¹⁹	Retro	_	6	34	I	>3	(0) ^b	(63) ^b	.001	-	-	-
Miller 2002 ¹²⁰	Retro	many	13	12	I-III	<1	42	75	-	30	8	-

Figure Legend:

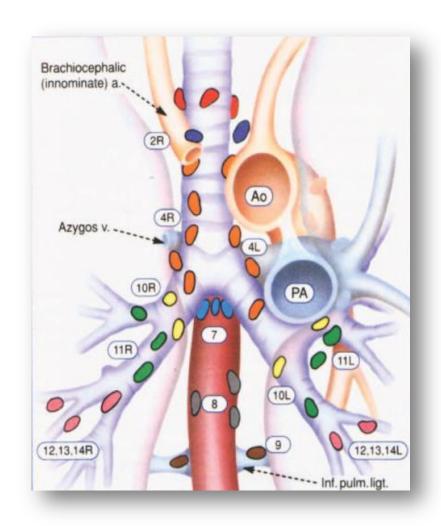
Comparative outcomes for wedge resection and segmentectomy. Inclusion criteria: studies reporting comparative outcomes for wedge vs segmentectomy for non-small cell lung cancer up through 2012. See Figure 1, 2, and 6 legends for expansion of abbreviations.

^aAll patients undergoing wedge resection were required to have a pure ground-glass opacity; others underwent segmentectomy.

^bCancer-specific survival.

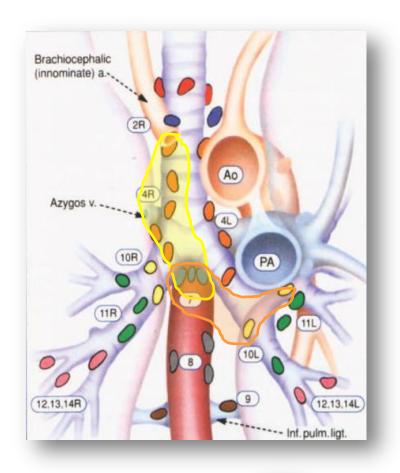


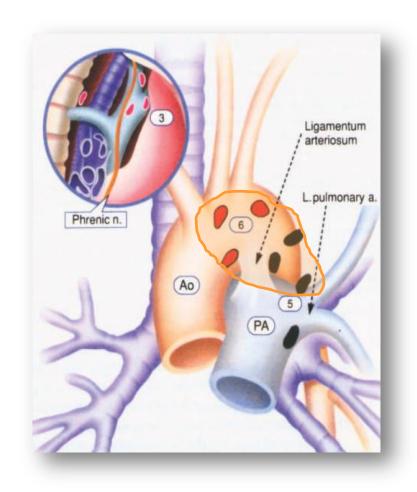
Lymphadenectomy



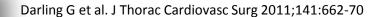


Lymphadenectomy











Lymphadenectomy vs. Sampling Evidence-based Medicine

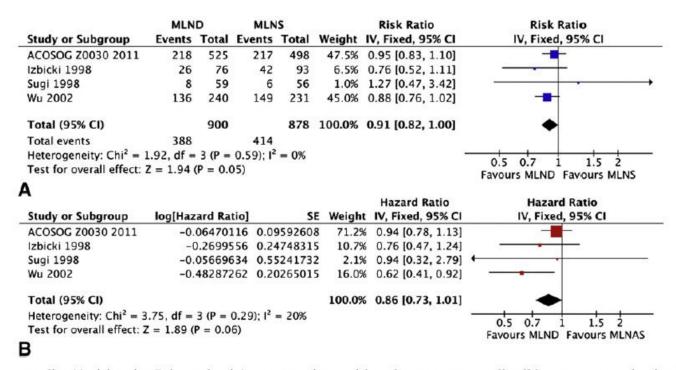


FIGURE 1. All cause mortality (A, risk ratio; B, hazard ratio) among patients with early-stage non-small cell lung cancer randomized to mediastinal lymph node dissection (MLND) versus sampling (MLNS) during pulmonary resection. IV, Inverse variance; CI, confidence interval; ACOSOG, American College of Surgery Oncology Group; SE, standard error.

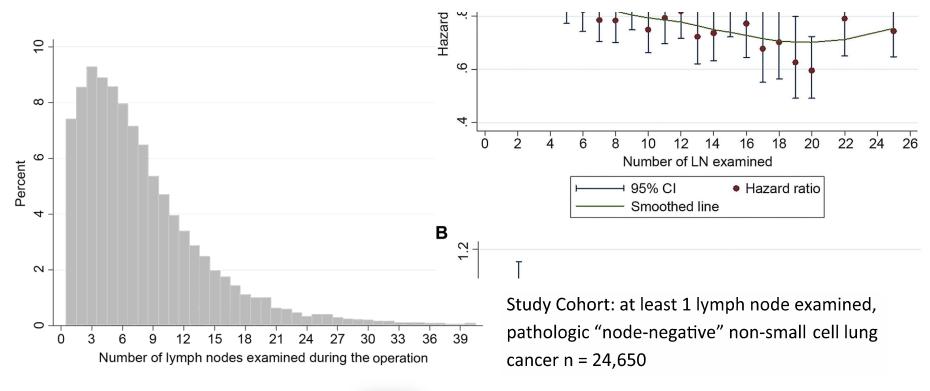




Lymphadenectomy – N0



SEER Database 1998-2009





Osarogiagbon RU et al. Ann Thorac Surg 2014;in press



VATS vs. thoracotomy

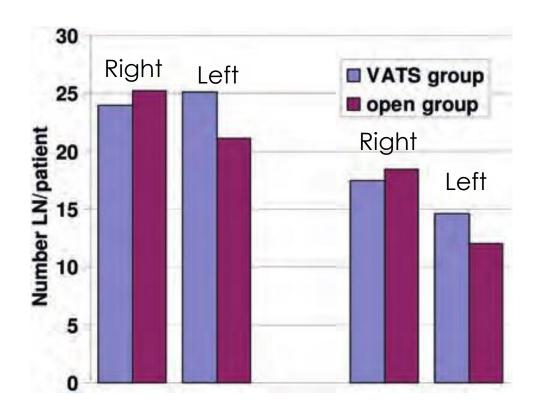
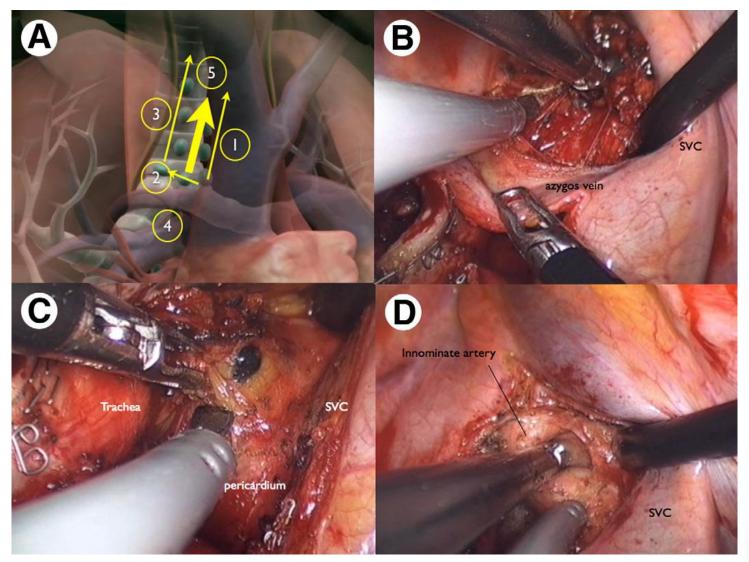


Figure 4: Number of lymph nodes removed per patient, overall (N1 and N2) and mediastinal (N2).

Aix*Marseille



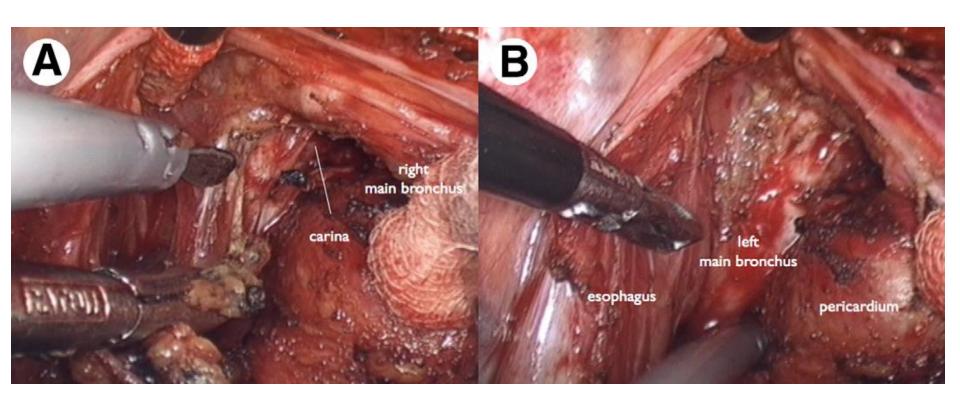
VATS Lymphadenectomy





Lee HS et al. Semin Thoracic Surg 2012;24:131-141.

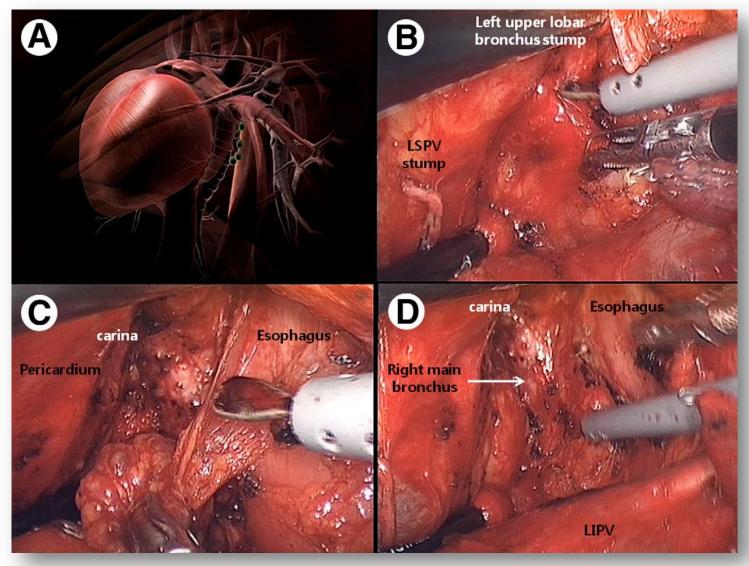




Lee HS et al. Semin Thoracic Surg 2012;24:131-141.







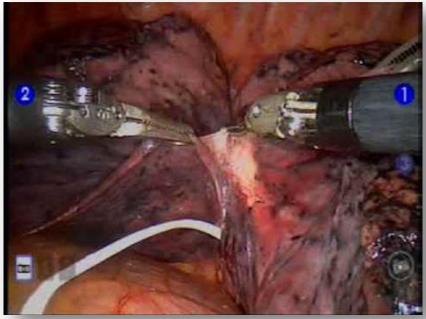
Lee HS et al. Semin Thoracic Surg 2012;24:131-141.





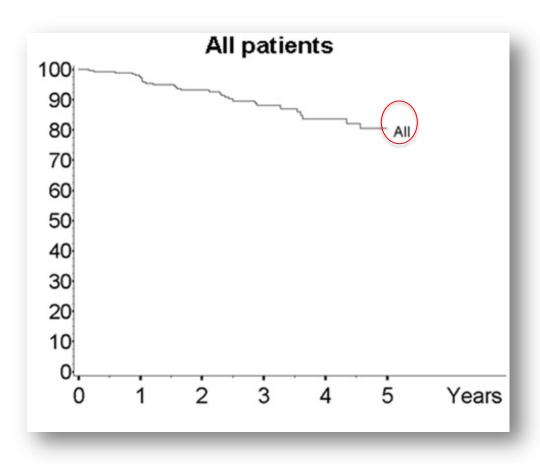
Robot-Assisted Thoracic Surgery





RATS Lobectomies

From 2002 to 2010, 325 consecutive patients with earlystage NSCLC at 3 institutions.





Park BJ et al. Robotic lobectomy for non–small cell lung cancer (NSCLC): Long-term oncologic results. J Thorac Cardiovasc Surg 2012;143:383-9



RATS segmentectomies

Robotic Anatomic Segmentectomy of the Lung: Technical Aspects and Initial Results

Alessandro Pardolesi, MD, Bernard Park, MD, Francesco Petrella, MD, Alessandro Borri, MD, Roberto Gasparri, MD, and Giulia Veronesi, MD

Division of Thoracic Surgery, European Institute of Oncology, Milan, Italy; and Division of Thoracic Surgery, Hackensack University Medical Center, Hackensack, New Jersey

Background. Robotic lobectomy with radical lymph node dissection is a new frontier of minimally invasive thoracic surgery. Series of sublobar anatomic resection for primary initial lung cancers or for metastasis using video-assisted thoracic surgery have been reported but no cases have been so far reported using the robot-assisted approach. We present the technique and surgical outcome of our initial experience.

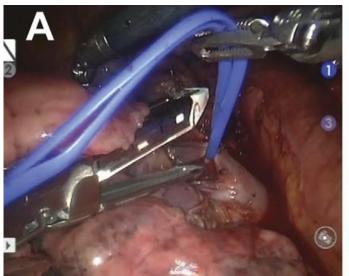
Methods. Clinical data of patients undergoing robotic lung anatomic segmentectomy were retrospectively reviewed. All cases were done using the DaVinci System. A 3- or 4-incision strategy with a 3-cm utility incision in the anterior fourth or fifth intercostal space was performed. Individual ligation and division of the hilar structures was performed using Hem-o-Lok (Teleflex Medical, Research Triangle Park, NC) or endoscopic staplers. The parenchyma was transected with endovascular staplers introduced by the bedside assistant mainly through the utility incision. Systematic mediastinal lymph node dissection or sampling was performed.

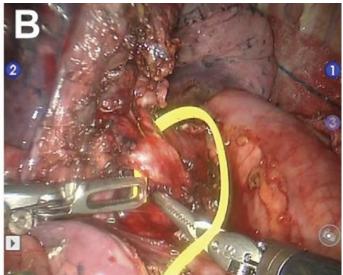
Results. From 2008 to 2010, 17 patients underwent a robot-assisted lung anatomic segmentectomy in two centers. There were 10 women and 7 men with a mean age of 68.2 years (range, 32 to 82). Mean duration of surgery was 189 minutes. There were no major intraoperative complications. Conversion to open procedure was never required. Postoperative morbidity rate was 17.6% with pneumonia in 1 case and prolonged air leaks in 2 patients. Median postoperative stay was 5 days (range, 2 to 14), and postoperative mortality was 0%. Final pathology was non-small cell lung cancer in 8 patient, typical carcinoids in 2, and lung metastases in 7.

Conclusions. Robotic anatomic lung segmentectomy is feasible and safe procedure. Robotic system, by improving ergonomic, surgeon view and precise movements, may make minimally invasive segmentectomy easier to adopt and perform.

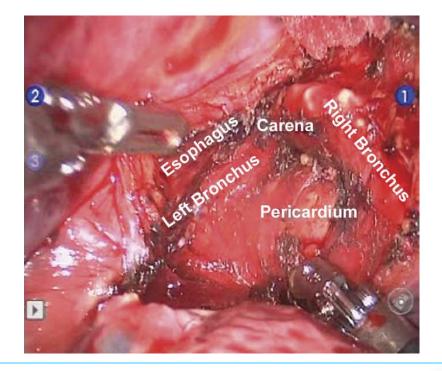
(Ann Thorac Surg 2012;94:929-34) © 2012 by The Society of Thoracic Surgeons







By courtesy of Giulia Veronesi





Marginal surgical candidates





University of Virginia, Charlottesville Retrospective study of 1259 patients 1999-2011 Open lobectomies

ACOSOG Z4099/RTOG

ACCP

FEV1≤ 50% or DLCO ≤ 50%

ppo FEV1< 40% or ppo DLCO < 40%

Age >75 years and FEV1 50%-60%

Age >75 years and DLCO 50%-60%

206 vs. 1053 patients

131 vs. 1128 patients





TABLE 1. Patient demographics

	ACOSOG Z4099/I	RTOG 1021 M-PFT criteria	ACCP M-PFT criteria (n = 1259)				
Variable	M-PFTs (n = 206)	Non-M-PFTs $(n = 1053)$	P	M-PFTs (n = 131)	Non–M-PFTs (n = 1128)	P	
Postoperative complications							
30-d mortality, %	0.5	1.4	.10	0.8	1.3	.09	
Pneumonia, %	10.4	5.6	.002	10.6	5.8	.01	
Re-intubation, %	5.3	1.1	.62	4.6	3.7	.44	
Myocardial infarction, %	2.7	0.7	.008	2.3	0.8	.01	
Acute renal failure, %	2.8	0.7	.01	2.3	0.8	.01	
Supraventricular arrhythmia, %	12.4	9.3	.16	13.7	9.4	.06	





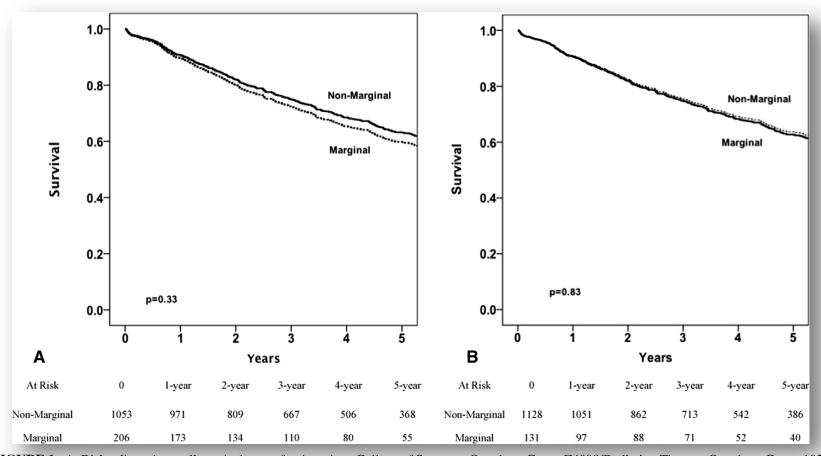


FIGURE 1. A, Risk-adjusted overall survival curve for American College of Surgeons Oncology Group Z4099/Radiation Therapy Oncology Group 1021 trial or American College of Chest Physicians (ACCP) marginal-pulmonary function test (M-PFIT) criteria. B, Risk-adjusted overall survival curve for ACCP M-PFT criteria.





Marginal pulmonary function should not preclude lobectomy in selected patients with non-small cell lung cancer

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Objective: Current clinical trials are investigating the role of stereotactic body radiation therapy (SBRT) versus sublobar resection for patients with non-small cell lung carcinoma (NSCLC) and marginal pulmonary function tests (M-PFTs). We compared the outcomes of patients undergoing lobectomy with M-PFTs characterized by 2 accepted M-PFT criteria.

Methods: A total of 1,259 consecutive patients underwent lobectomy for NSCLC between 1999 and 2011. Patients were stratified into 2 classifications of M-PFT: American College of Surgeons Oncology Group (ACOSOG) Z4099/Radiation Therapy Oncology Group (RTOG) 1021 trial or American College of Chest Physicians (ACCP) criteria. There were 206 patients classified as having M-PFT according to ACOSOG Z4099/RTOG 1021 criteria and 131 patients classified as having M-PFT by ACCP criteria. The primary endpoints of the study were post-operative complications and survival.

Results: Median follow-up was 3.8 years. Cox-proportional survival analysis found that pathologic stage (P < .001), age (P < .001), and higher Zubrod functional status (P < .001) were independent predictors of mortality. Using multivariable analysis for major morbidity, M-PFT status was not associated with the development of a major complication following lobectomy (P = .68). M-PFT classification was not an independent predictor of mortality when controlling for other variables (ACOSOG Z4099/RTOG 1021 [P = .34]; ACCP criteria [P = .83]). A composite major morbidity analysis for major morbidity following lobectomy showed no association between clinicopathologic variables or M-PFTs and the occurrence of a major postoperative morbidity.

Conclusions: In carefully selected patients with M-PFTs, lobectomy for NSCLC can be performed with acceptable morbidity and mortality. These results need to be considered when deciding if a patient should undergo lobectomy or other therapies for resectable NSCLC. (J Thorac Cardiovasc Surg 2014;147:738-46)

« Current trials characterizing patients as nonsurgical candidates based on 2 accepted marginal pulmonary function tests definitions may be excluding patients from undergoing lobectomy, the current gold standard therapy for lung cancer »





Take-home messages

- Lung resection provides tissue for pathological and biological information
- Lymph node dissection provides adequate staging
- Minimally invasive lung resection +
 lymphadenectomy provides the current
 landmarks to which new therapies should be
 compared
- Inoperable patients: do they really exist...?

