Lungebevarende resektioner ved lungecancer – metode og resultater

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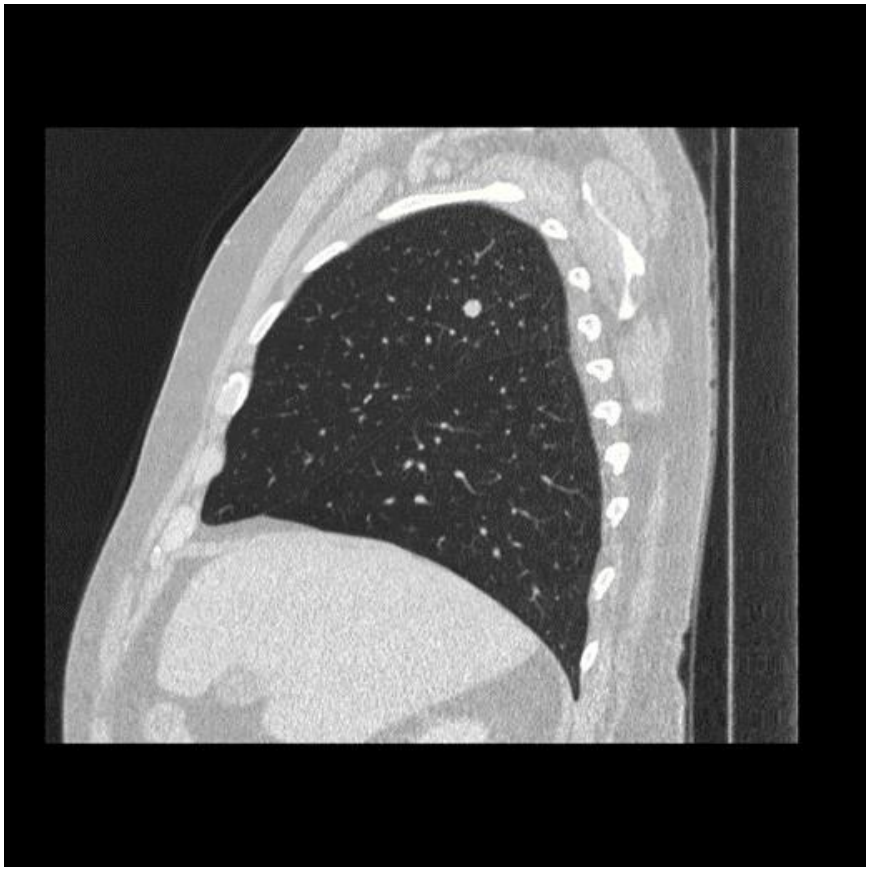
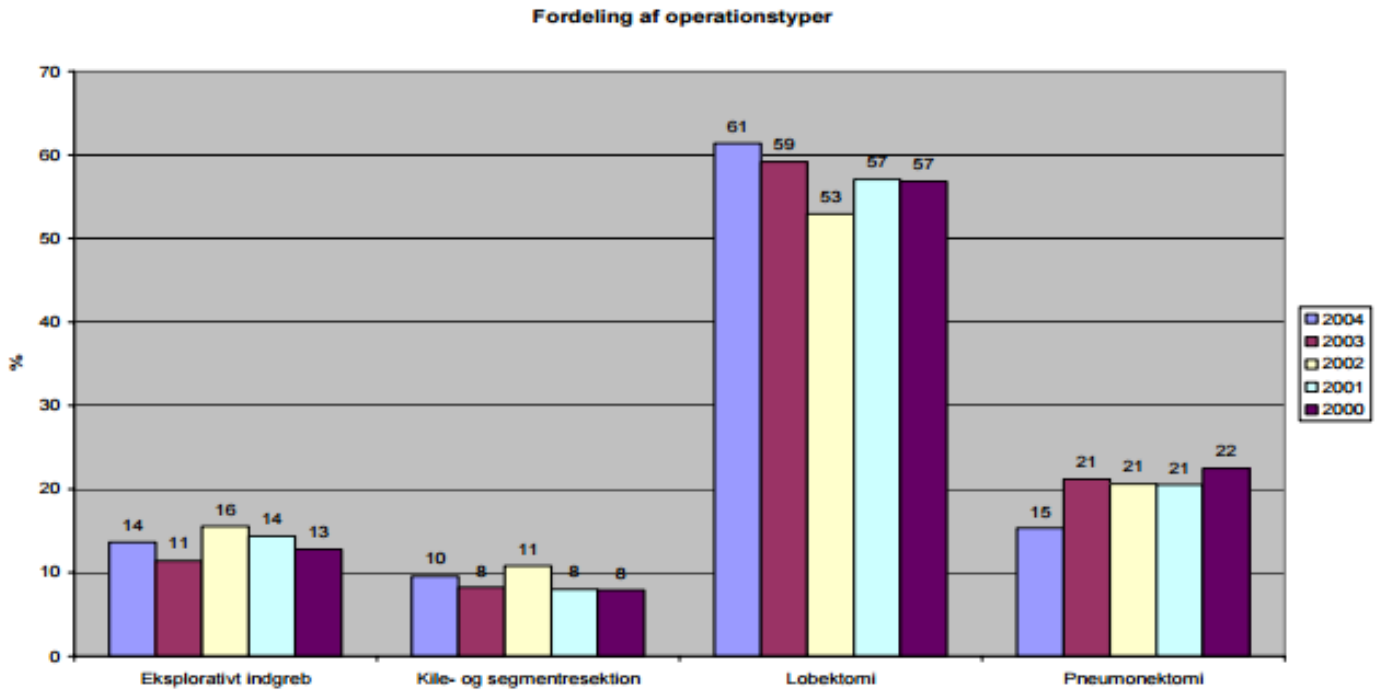
Does this really need a lobectomy



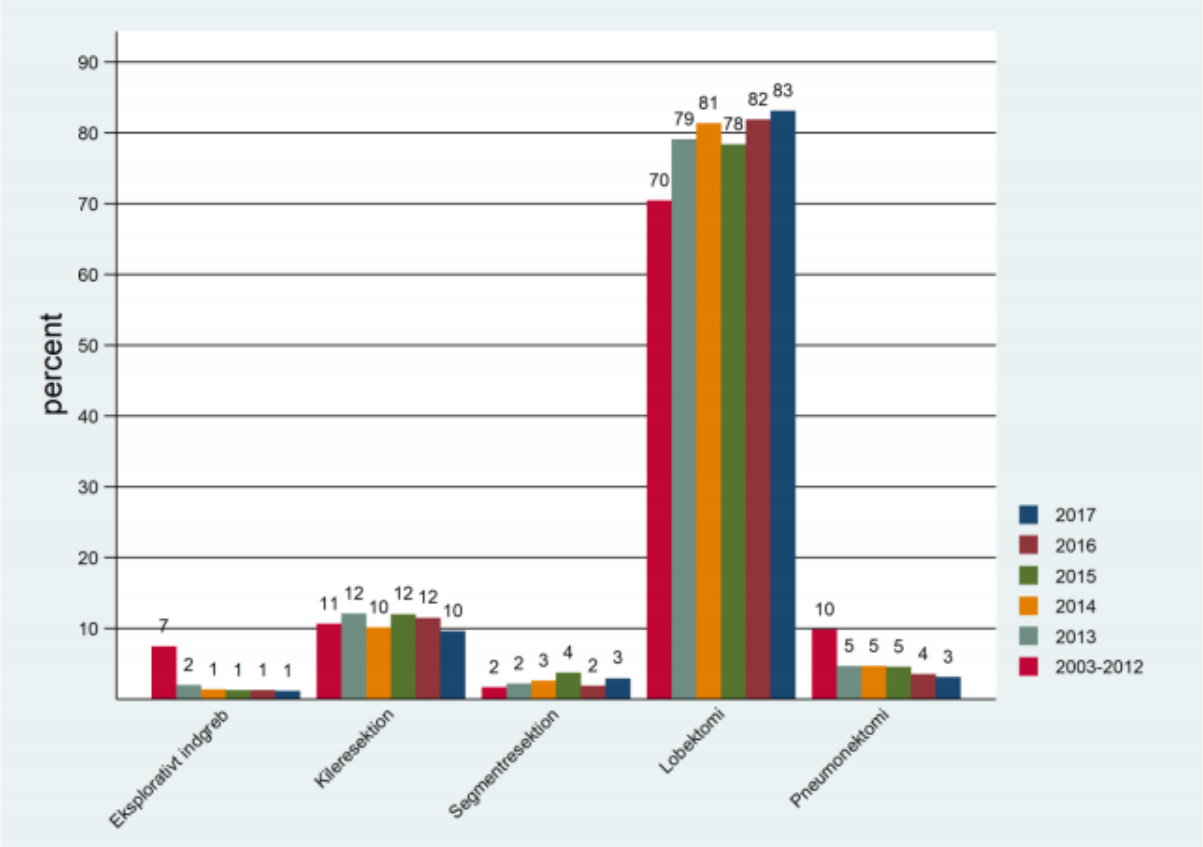
Årsrapporten 2004

Figur 20:



Årsrapporten 2017

7.2.3.2 Figur Operationer fordeling grafisk

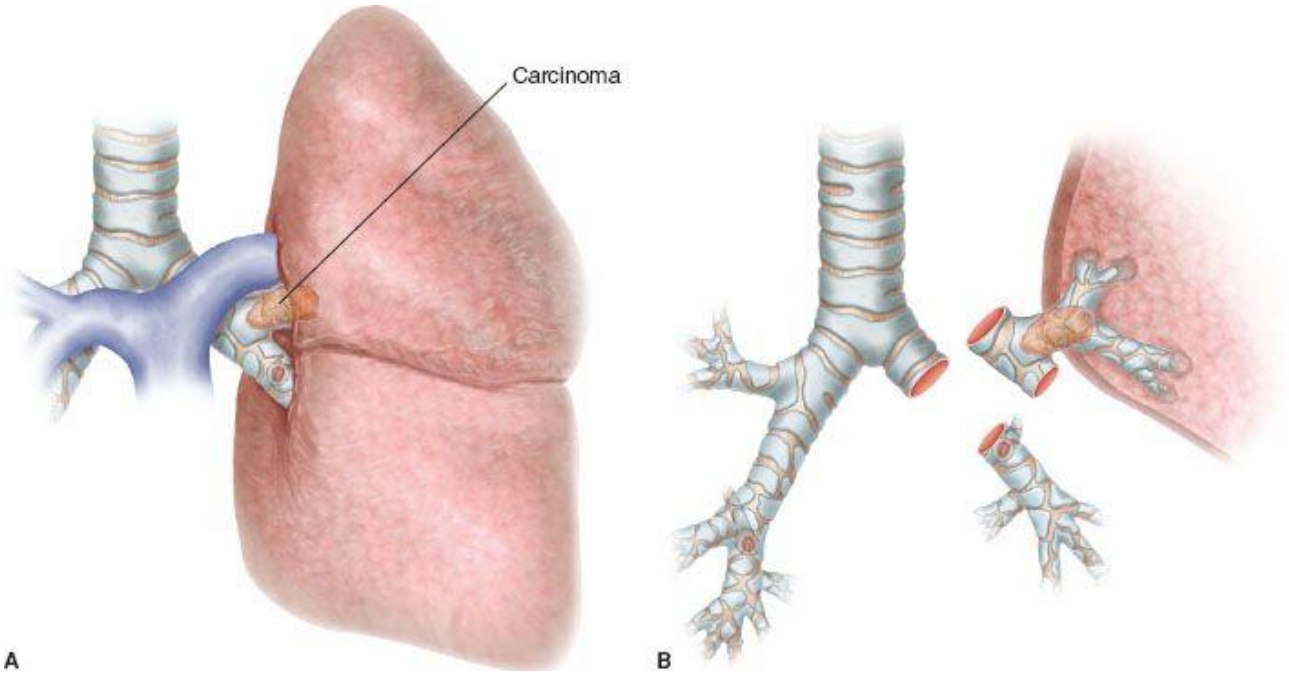


30 dages dødelighed ved forskellige kirurgi typer

8.2.1.4 Tabel 30 dages postoperativ mortalitet DK og fordelt på afdelinger

Afdeling	Type	2017	2016	2015	2014	2013	2003-2012*
Danmark	Total	1,2	0,9	2,0	1,9	1,4	2,9
	Eksplorativt	7,1	0,0	0,0	0,0	4,8	5,8
	Kile	0,9	0,0	0,0	0,0	1,9	1,5
	Segment	0,0	0,0	7,7	0,0	5,9	3,4
	Lobektomi	1,0	0,6	1,6	2,2	0,9	2,2
	Pneumonektomi	6,7	11,4	10,0	2,7	2,9	7,6

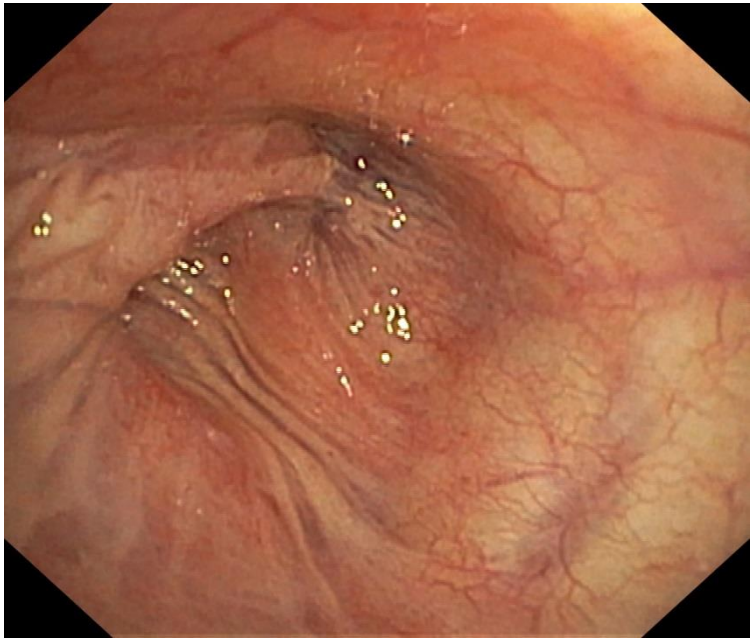
Sleeve lobectomy

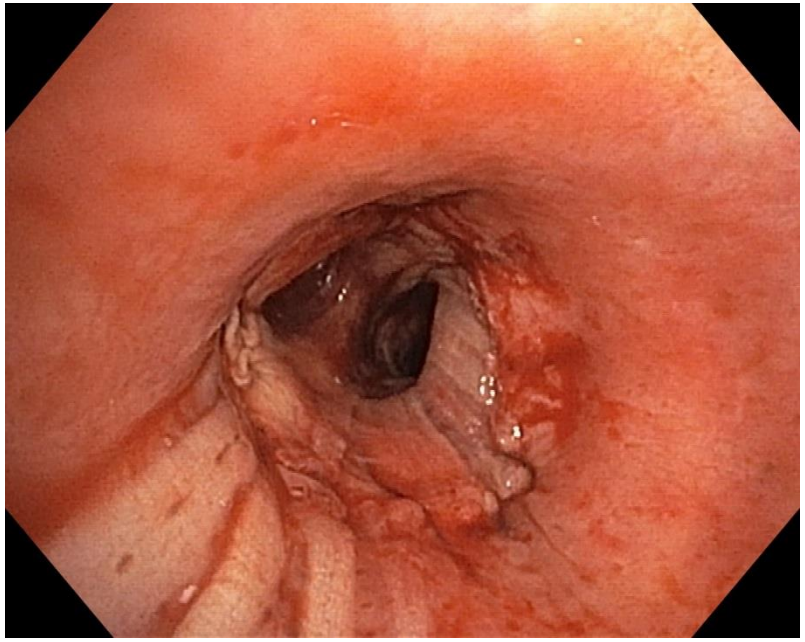


7.2.3.6 Tabel Lobektomitype

Afdeling	Antal	Lobektomi	Bilobektomi	Lobektomi_sleeve	Lobektomi_resek
Rigshospitalet	259	92,7	3,5	3,5	0,4
Odense	306	93,8	2,6	0,3	3,3
Aarhus	184	92,4	2,2	1,1	4,3
Aalborg	150	93,3	4,0	2,0	0,7
Danmark	**899**	**93,1**	**3,0**	**1,7**	**2,2**

Bronkial sleeve af ve. hovedbronkus

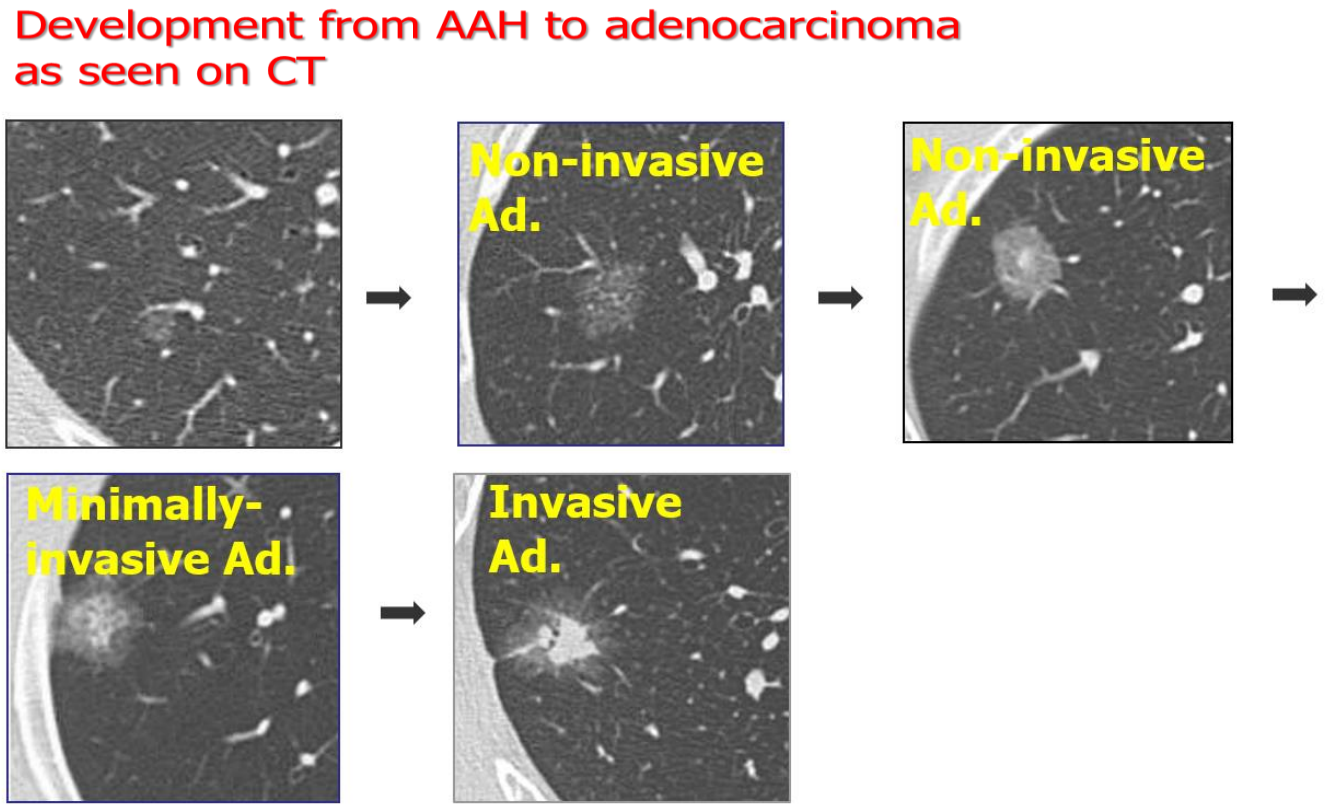




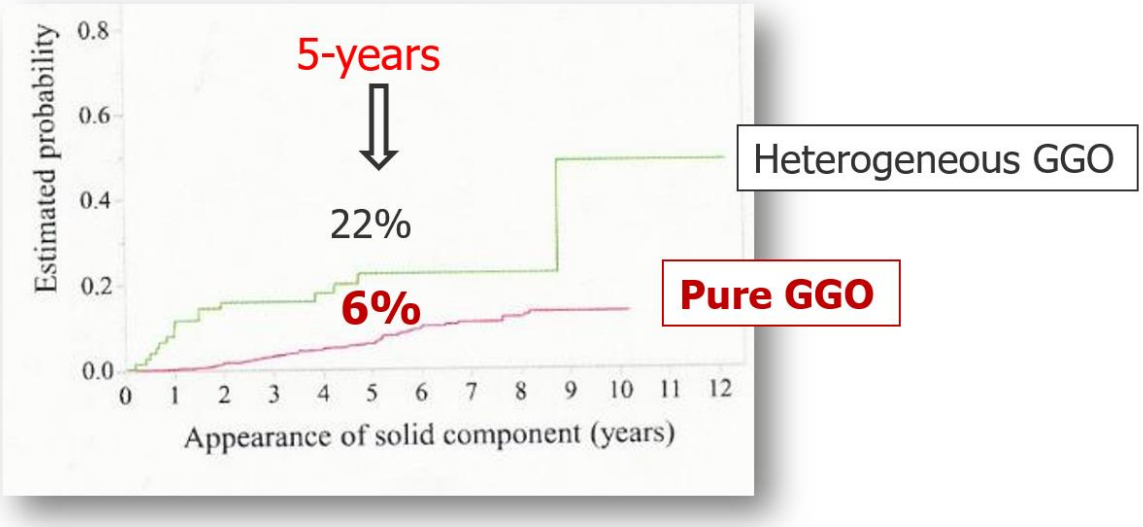
Current status

- Lobectomy is “the golden standard”
- Pneumonectomy is associated with high mortality and morbidity
- “Sleeve lobectomy” is an attractive alternative in central tumors
- Much interest about sublobar resections

Resections in the age of screening

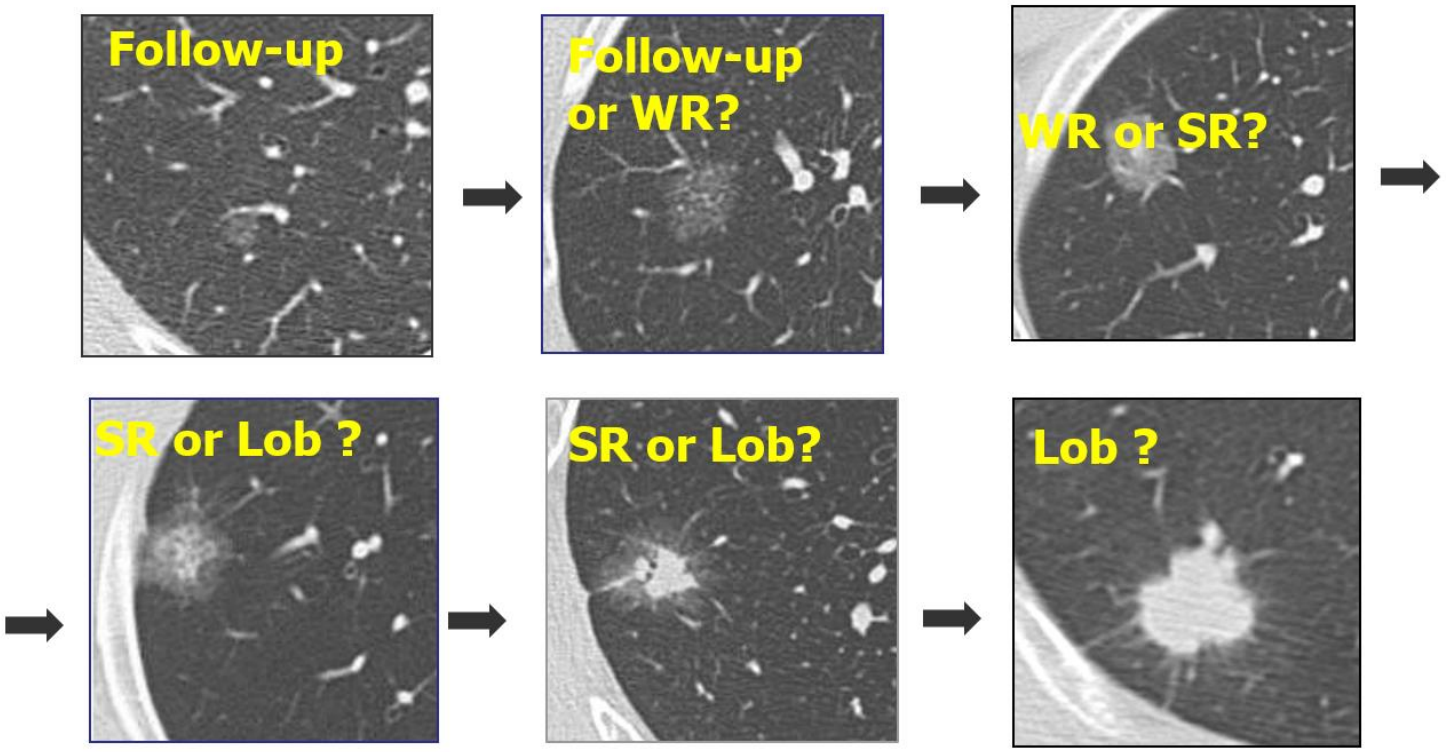


What is the natural history of subsolid nodules ?



Kakinuma R, et al. *JTO* 2016;11:1012-1028

What management ?



WR = wedge resection, Seg= Segmental Resection,
Lob = Lobectomy

Questions to sublobar resection

- The type of resection
- Is it oncologically equel
- Is there a patient benefit in parenchyma sparring resections

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)

RCT LOBECTOMY VS SUBLOBAR RESECTION LUNG CANCER STUDY GROUP TRIAL (1995)

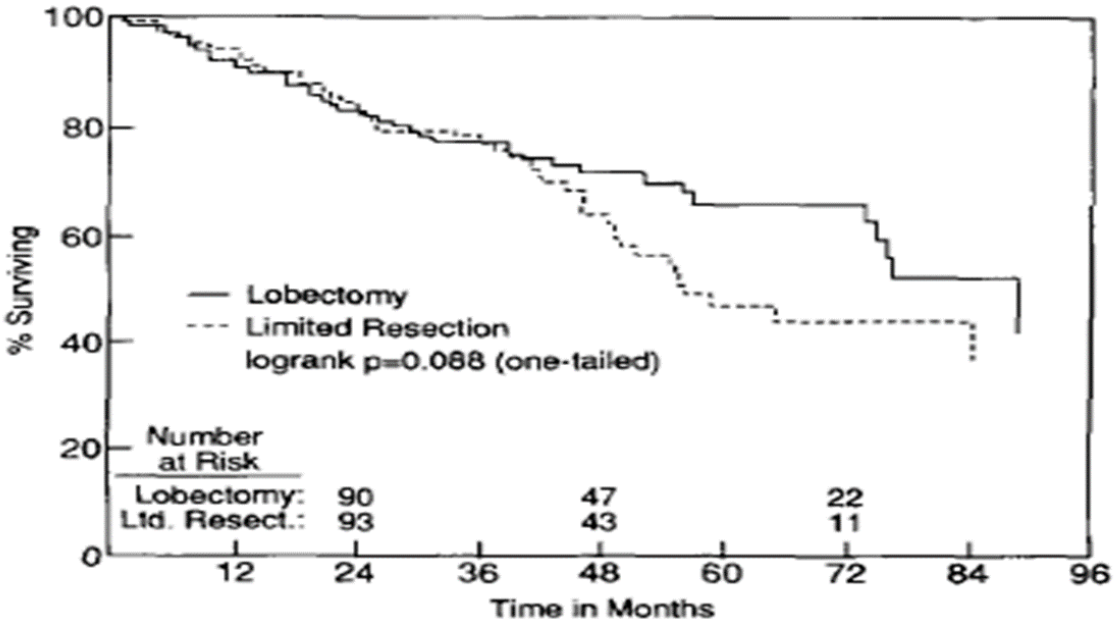


Fig 1. Time to death (from any cause) by treatment for 247 eligible patients.

Ginsberg et al, Ann Thorac Surg 1995;60:615-623

RCT LOBECTOMY VS SUBLOBAR RESECTION LUNG CANCER STUDY GROUP TRIAL (1995)

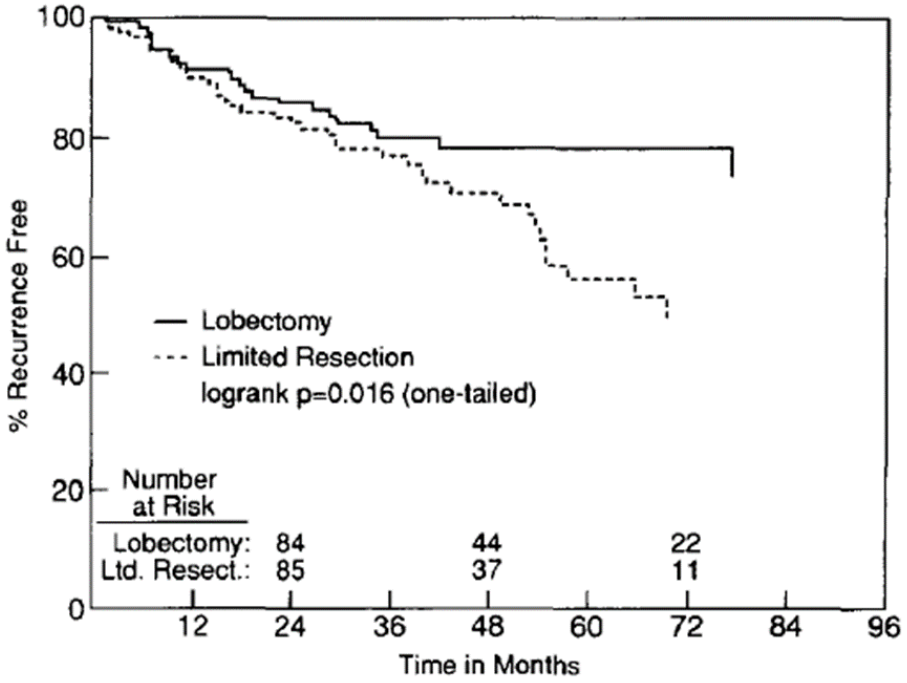


Fig 2. Time to recurrence (excluding second primaries) by treatment for 247 eligible patients.

Ginsberg et al, Ann Thorac Surg 1995;60:615-623

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

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(*Ann Thorac Surg* 1995;60:615–23)

Sublobar resections for lung cancer?

- We do have a good and well documented procedure – VATS Lobectomy
- Sublobar resections a bad idea – end of show
- But
- Let us have a look at the paper

Ginsberg et al 1995 paper

chest roentgenogram. Patients were screened preoperatively and "registered" for entry into the study if they had a clinical T1 N0 peripheral tumor (3 cm or less in all dimensions on posteroanterior and lateral chest roentgenogram), suspected or proven to be a lung cancer that was not visible on flexible bronchoscopy. All patients

30 % larger than 2 cm
Now better selection due to CT, PET, PET-CT, EBUS and EUS

The revised TNM staging system for lung cancer. Rami-Porta R, Crowley JJ, Goldstraw P.

Ann Thorac Cardiovasc Surg. 2009 Feb;15(1):4-9. Review.

- 5 year survival dependent on T-status:
  - pT1 < 2 cm 77% *(new T1a)*
  - pT1 > 2 cm but < 3 cm 71% *(new T1b)*
  - pT2 > 3 cm but < 5 cm 58% *(new T2a)*
- Same tendency in all scenarios also with nodal involvement.

8th edition – Every cm counts

T-descriptor

Every cm counts…

Proposed (TNM 8th)	*Previous (TNM 7th)*
Up to 1 cm: T1a	T1a
>1-2 cm: T1b	T1a
>2-3 cm: T1c	T1b
>3-4 cm: T2a	T2a
>4-5 cm: T2b	T2a
>5-7 cm: T3	T2b
>7 cm: T4	T3

Rami Porta R, J Thoracic Oncol, 2013
International Association for the Study of Lung Cancer, 2015

Table 2 Five-year survival per T stage of the 8th Tumor, Node, Metastasis staging system

	5-yr survival
T1a	92%
T1b	83%-86%
T1c	76%-81%
T2a	67%-74%
T2b	60%-65%
T3	52%-57%
T4	38%-47%

Ginsberg et al 1995 paper

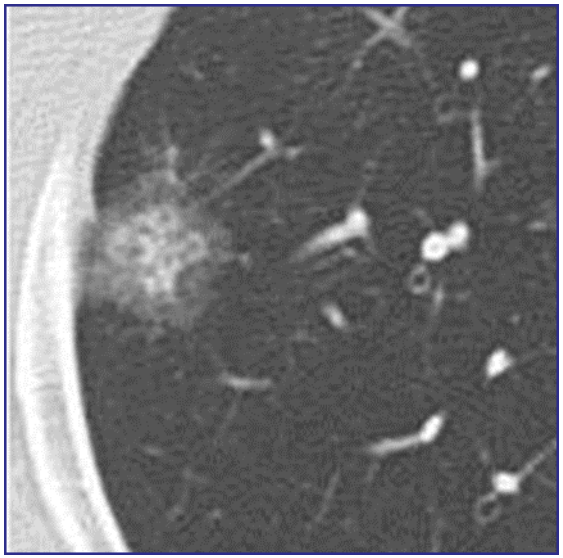
Surgical Technique

The technique of segmental resection required isolation, division, and suture of the appropriate segmental bronchus, artery, and vein. In this protocol, portions of up to two adjacent segments could be removed as part of a limited resection. Surgeons were allowed latitude of technique in methods of division of pulmonary tissue. This included segmental stripping, "cut-and-sew" technique, or the use of surgical staplers.

Large adequate wedge resections could also be used as a limited resection treatment when considered appropriate. At least 2 cm of normal lung tissue was required to be resected beyond the tumor. As with segmental resection, surgeons were allowed latitude in surgical technique for division of pulmonary tissue.

32.8 % were wedge resections = non anatomical resections
Inconsistent lymph node sampling
No thoracoscopic procedures

Subsolid nodules: Lobectomy or sublobar resection?



JAPANESE CLASSIFICATION OF SUBSOLID NODULES: 3 CATEGORIES

Pure GGO

Heterogeneous GGO
(= solid component disappearing in the mediastinal window)

Part-solid GGO

Table. Japan Clinical Oncology Group Strategy for Small Lung Cancers With GGO Characteristics

Tumor Size	C/T Ratio: 0–0.25	C/T Ratio: 0.25–0.5	C/T Ratio: 0.5–1.0
0–2.0 cm	Wide wedge resection (Study ID: JCOG0804)	Segmentectomy (Study ID: JCOG1211)	Lobectomy vs segmentectomy (Study ID: JCOG0802)
2.0–3.0 cm	Segmentectomy (Study ID: JCOG1211)	Segmentectomy (Study ID: JCOG1211)	Standard lobectomy
> 3.0 cm	Standard lobectomy	Standard lobectomy	Standard lobectomy

C/T = consolidation/tumor; GGO = ground-glass opacity.
Data from: Asamura H. Presentation at 16th World Conference on Lung Cancer.[70]

Lymph node metastasis in clinical stage IA peripheral lung cancer

CONCLUSIONS:

The rate of metastasis to the lymph nodes is very low in clinical stage IA peripheral lung cancer patients.

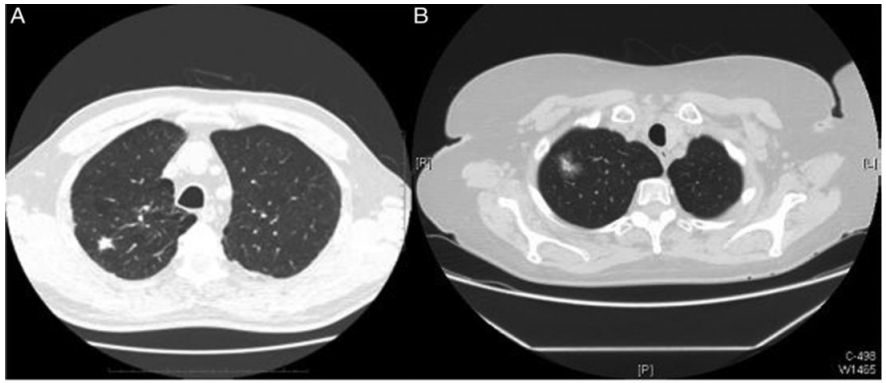
Patients with a dominant GGO component on CT might be the suitable candidates for lung segmentectomy because of almost no lymph node metastasis.

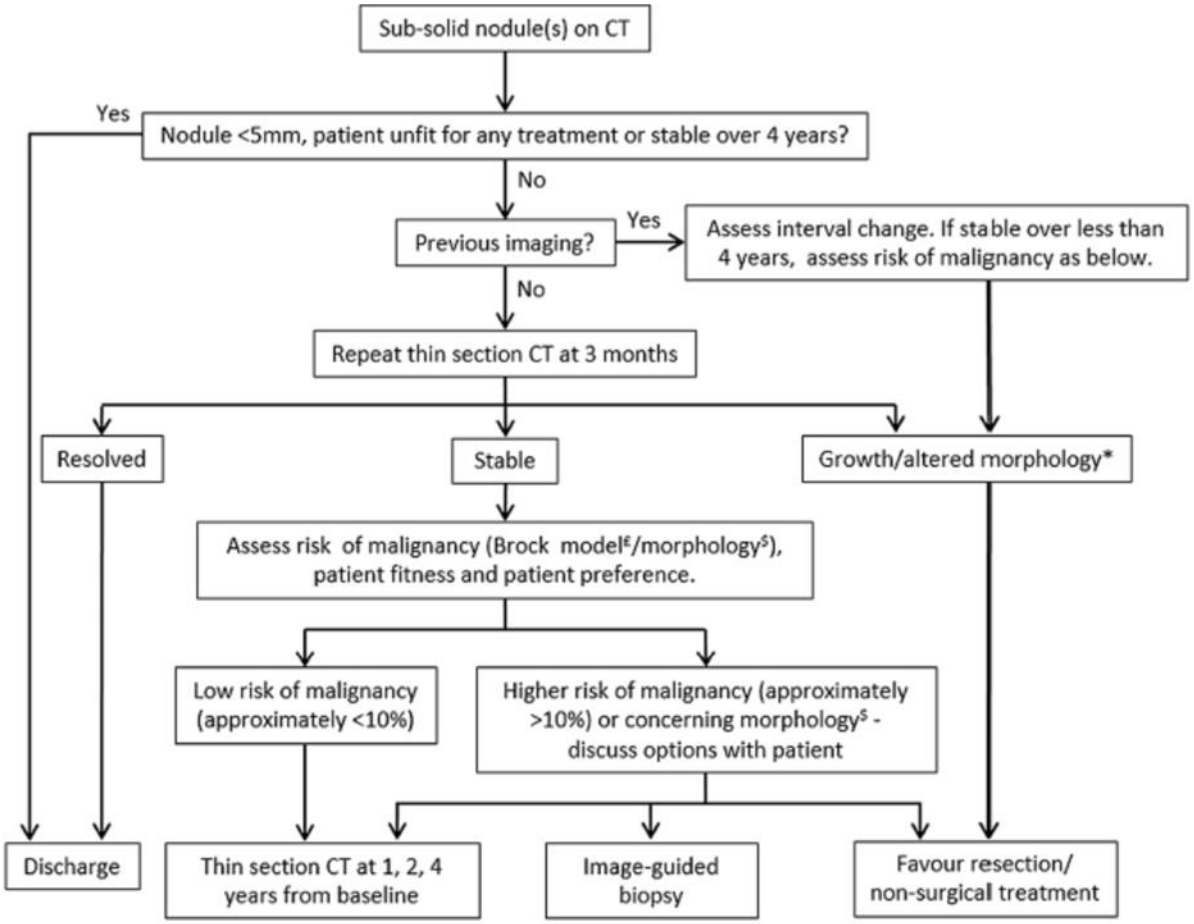
Careful selection should be made for the patients with tumor size ≤2cm who had metastasized nodes in non-tumor bearing segment when considering segmentectomy.

If the resected tumor had micropapillary or solid component, the lobectomy might be considered.

Wang L et al. Lung Cancer. 2015 Oct;90(1):41-6.

Early/small adeno-carcinoma and sublobar resections

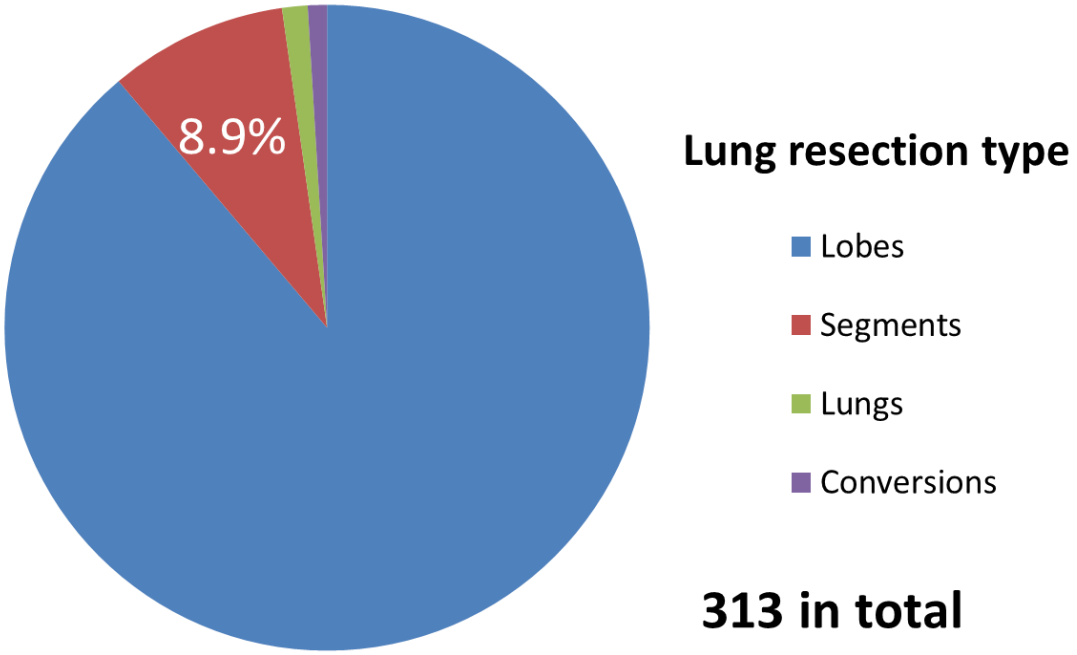




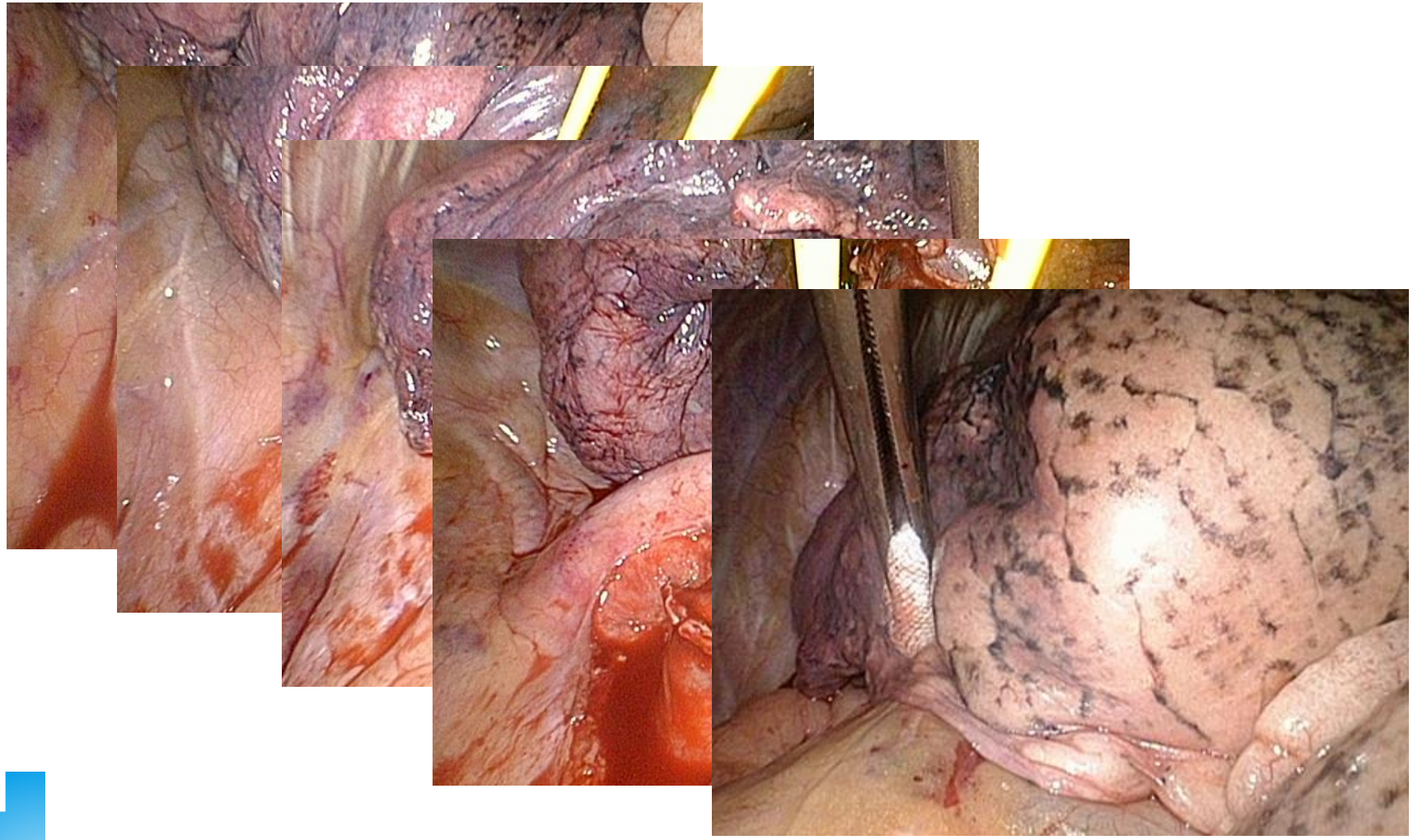
* Change in mass/new solid component
£ Brock model may underestimate risk of malignancy in SSN that persist at 3 months
$ Size of the solid component in PSN, pleural indentation and bubble-like appearance

Figure 3 Sub-solid pulmonary nodules algorithm. PSNs, part solid nodules; SSN, sub-solid nodules.

2015 VATS anatomical lung resection profile - Copenhagen



Lingula sparring lobectomy



Histology 2010-18

- NSCLC 55
- NSCLC + former lobe 18
- Carcinoid 6
- Metastatic 95
- Benign 13

Is limited pulmonary resection equivalent to lobectomy for surgical management of stage I non-small-cell lung cancer?

Maya K. De Zoysa[a,*], Dima Hamed[b], Tom Routledge[b] and Marco Scarci[a]

Abstract

A best evidence topic in thoracic surgery was written according to a structured protocol. The question addressed was: is limited pulmonary resection equivalent to lobectomy in terms of morbidity, long-term survival and locoregional recurrence in patients with stage I non-small-cell lung cancer (NSCLC)? A total of 166 papers were found using the reported search; of which, 16 papers, including one meta-analysis and one randomized control trial (RCT), represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. With regards to 5-year survival rates, the evidence is conflicting: a 2005 meta-analysis and six other retrospective or prospective non-randomized analyses did not find any statistically significant difference when comparing lobectomy with limited resection. However, three studies found evidence of a decreased overall survival with limited resection, including the only randomized control trial, which showed a 50% increase in the cancer-related death rate ($P = 0.09$), and a 30% increase in the overall death rate in patients undergoing limited resection ($P = 0.08$). Age, tumour size and specific type of limited resection were also factors influencing the survival rates. Four studies, including the RCT, found increased locoregional recurrence rates with limited resection. There is also evidence that wedge resections, compared with segmentectomies, lead to lower survival and higher recurrence rates. In conclusion, lobectomy is still recommended for younger patients with adequate cardiopulmonary function. Although limited resection carries a decreased rate of complications and shorter hospital stays, it may also carry a higher rate of loco-regional recurrences. However, limited resection may be comparable for patients >71 years of age, and those with small peripheral tumours.

Interactive CardioVascular and Thoracic Surgery 14 (2012) 816–820
doi:10.1093/icvts/ivs031 Advance Access publication 27 February 2012

Survival After Segmentectomy and Wedge Resection in Stage I Non–Small-Cell Lung Cancer

Cardinale B. Smith, MD, MSCR,† Scott J. Swanson, MD,‡ Grace Mhango, MPH,§ and Juan P. Wisnivesky, MD, DrPH§‖*

(*J Thorac Oncol.* 2013;8: 73–78)

Introduction: Although lobectomy is considered the standard surgical treatment for stage IA non–small-cell lung cancer (NSCLC), wedge resection or segmentectomy are frequently performed on patients who are not lobectomy candidates. The objective of this study was to compare survival among patients with stage IA NSCLC, who are undergoing these procedures.

Methods: Using the Surveillance, Epidemiology and End Results registry, we identified 3525 patients. We used logistic regression to determine propensity scores for patients undergoing segmentectomy, based on the patient's preoperative characteristics. Overall and lung cancer-specific survival of patients treated with wedge resection versus segmentectomy was compared after adjusting, stratifying, or matching patients based on propensity score.

DATABASE STUDY

REGION

Survival After Segmentectomy and Wedge Resection in Stage I Non–Small-Cell Lung Cancer

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(*J Thorac Oncol.* 2013;8: 73–78)

Results: Overall, 704 patients (20%) underwent segmentectomy. Analyses, adjusting for propensity scores, showed that segmentectomy was associated with significant improvement in overall (hazard ratio: 0.80, 95% confidence interval: 0.69–0.93) and lung cancer-specific survival (hazard ratio: 0.72, 95% confidence interval: 0.59–0.88) compared with wedge resection. Similar results were obtained when stratifying and matching by propensity score and when limiting analysis to patients with tumors sized less than or equal to 2 cm, or aged 70 years or younger.

Conclusions: These results suggest that segmentectomy should be the preferred technique for limited resection of patients with stage IA NSCLC. The study findings should be confirmed in prospective studies.

REGION

Ungoing studies

- CALGB 140503

- JCOG0802/WJOG4607L

Lung segmentectomy: does it offer a real functional benefit over lobectomy?

- Anatomical segmentectomy has been implemented to offer better pulmonary function preservation than lobectomy.
- … the assumption that reducing the resected lung volume may enhance the possibility of further resections in the case of a second primary lung cancer has provided an additional substantial incentive to perform segmentectomy.
- … the development of this procedure was the intent to propose surgical treatment to patients with impaired lung function.
- Indeed, based on early published studies, the use of segmentectomy in these patients was recommended as an alternative to lobectomy by several task forces

Cite this article as: Charloux A, Quoix E. Lung segmentectomy: does it offer a real functional benefit over lobectomy? *Eur Respir Rev* 2017; 26: 170079 [https://doi.org/10.1183/16000617.0079-2017].

Lung segmentectomy: does it offer a real functional benefit over lobectomy?

Questions:

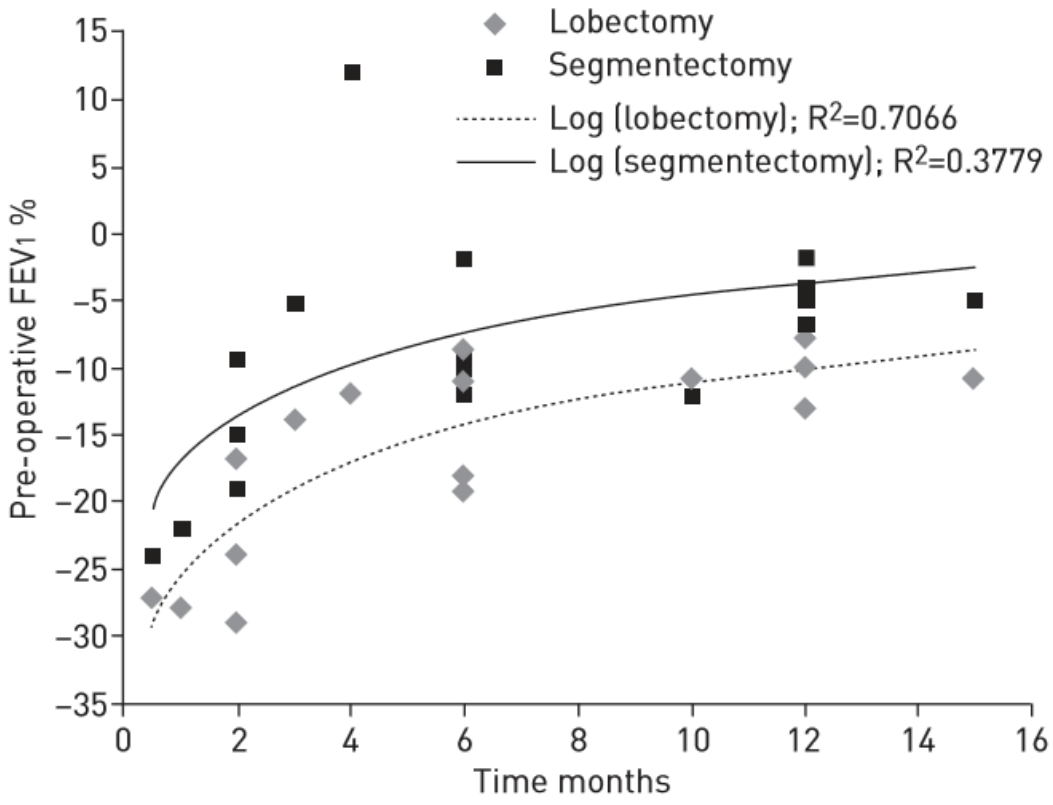
- How big is the loss of function in reality - both postoperatively and over time
- Improvement over time
- Method of surgery: Open or VATS
- Number of segments to be resected
- What about patients with poor preoperative lung function
- Does the differences have any clinical impact

Cite this article as: Charloux A, Quoix E. Lung segmentectomy: does it offer a real functional benefit over lobectomy? *Eur Respir Rev* 2017; 26: 170079 [https://doi.org/10.1183/16000617.0079-2017].

TABLE 1 Studies providing pre- and post-segmentectomy pulmonary function tests (PFTs)

First author [ref.]	Year	Patients n	Open/VATS	PFT delay months	Initial FEV_1 % pred	FEV_1 variation %	Initial D_{LCO} % pred	D_{LCO} variation %	Initial FVC % pred	FVC variation %
Ginsberg [4]	1995	71	Open	6 12–18		−1.76±15.3 −5.18±16.1				+1.93±19.4 +0.52±22.1
Takizawa [16]	1999	40	Open	0.5 12	105.0±23.6	−26.7±16.4 −6.7±10.3			101.4±16.5	−27.3±12.5 −5.1±10.6
Yoshikawa [18]	2002	55	Open	12		−13.4±10.4				−11.3±9.8
Keenan [8]	2004	54	Open	12	55.3±3.0	−5#	67.5±3.0	−17#	72.8±2.5	−5#
Martin-Ucar [11]	2005	34	Both	4 (3–6)	45 (19–54)	+12 (−2 to +47)				
Harada [5]	2005	38	Mini-thoracotomy	2 6	75.0±3.8	−15# −12#			3.13±0.67 L¶	−15# −10#
Okada [13]	2006	168	Open	2	2.32±0.64 L¶	−9.4#			3.16±0.84 L¶	−10.4#
Yoshimoto [19]	2009	56	NA	12 (6–24)	2.2±0.6 L¶	−12±9			109±14	
Watanabe [17]	2009	41	VATS	6	74.2±10.4	−3#			110.4±25.6	−7#
Kashiwabara [7]	2009	71	Open	6	109.4±20.8	Normal FEV_1: −12.9±8.7; FEV_1 <70%: −13.8±9.9			111.15±12.3	Normal FEV_1: −13.4±8.6; FEV_1 <70%: −16.0±11.8
Saito [14]	2014	52	Open	1 6	77.6±7.7	−28±7 −19±7			107.1±19.9	−14±6 −10±5
Hwang [6]	2015	94	VATS	NA	101.6±24.0	−8.9±10.8	92.7±17.4		100.8±16.3	
Kim [9]	2015	73	VATS	3 12	100.1±18.9	−4.83±8.74 −2.75±8.10	104.2±20.7	−3.44±11.49 −0.38±22.11	99.7±13.8	−4.45±7.30 −2.01±8.33
Macke [10]	2015	89	Both	6–36	79±22	−4.3±17.4	63±22	−3.6±15.8		
Suzuki [15]	2016	37	Both	2 7–12	73.3±9	−18.6# −12.2#			3.06±0.68 L¶	−18.2# −6.6#
Nomori [12]+	2016	117	Open	7 (6–13)	<2 seg: 105±23; ⩾2 seg: 114±23; LUD: 117±27	<2 seg: −3±10; ⩾2 seg: −10±9; LUD: −16±7				

Data are expressed as mean±SD or mean (range). Variation data are relative to the initial values. VATS: video-assisted thoracic surgery; FEV_1: forced expiratory volume in 1 s; D_{LCO}: diffusing capacity of the lung for carbon monoxide; FVC: forced vital capacity; Open: thoracotomy; Both: VATS and thoracotomy; NA: not available. #: calculated from data or extracted from figures; ¶: absolute values in L given where no % pred values available; +: compared resections <2 segments (<2 seg), ⩾2 segments (⩾2 seg), and of the left upper division (LUD).


Lobectomy
Segmentectomy
Log (lobectomy); R2=0.7066
Log (segmentectomy); R2=0.3779
Pre-operative FEV1 %
15
10
5
0
−5
−10
−15
−20
−25
−30
−35
0
2
4
6
8
10
12
14
16
Time months

…when evaluating the difference between lobectomy and segmentectomy, the delay after surgery should be considered.

Within 2 months after surgery, the mean loss of FEV1 ranged from −17% to −29% of initial value after lobectomy (mean −25%) and from −9% to −24% after segmentectomy (mean −18%)

Beyond 12 months, the mean FEV1 loss ranged from −8% to −13% of initial value after lobectomy (mean −11%) and from −2% to −7% after segmentectomy (mean −5%)

Within 2 months after surgery, the difference between lobectomy and segmentectomy was 3–10% of initial FEV1, whereas after 12 months, this difference ranged from 4% to 7% of initial FEV1

Lung segmentectomy: does it offer a real functional benefit over lobectomy?

- Conclusions The published studies show that the long-term reduction (⩾12 months) in lung function induced by segmentectomy is very small, and a little smaller than that induced by lobectomy.
- However, this tiny difference may benefit lung cancer patients who may need subsequent lung resections. Within the 2 months after surgery, lung function reduction is mild to moderate, but also a little smaller than that induced by lobectomy.
- However, PFT monitoring within the early days after VATS segmentectomy, days that are critical determinants of post-operative morbidity, needs to be assessed.
- Two issues remain to be addressed: whether VATS segmentectomy may preserve lung function better than VATS lobectomy in patients with poor lung function, and whether this may translate into a lowering of the functional limit for surgery

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Conclusions:

- Avoid pneumonectomies if possible
- Use sleeve resections
- VATS lobectomy should be the surgery of choice by early stage NSCLC and sufficient lung function
- Wait to the randomized studies are published on segments
- Wedge resection is a NO GO

Conclusions:

- VATS segmentectomies is a acceptable option in patients with NSCLC and:
- poor lung function
- older than 70
- with several small lesions in different lobes
- GGO
- The lesion has to be < 2cm and the free margin > than the lesion
- Both N1 and N2 lymph nodes has to be removed according to guidelines.