Radical treatment for early stage NSCLC

Surgery for early stage NSCLC

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Department of Thoracic Surgery
No disclosures
Stage I / II
## Non-Small Cell Lung Cancer - Tumor Stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor Size (cm)</th>
<th>Lymph Node Metastasis</th>
<th>Bone Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>T1a (&lt; 2 cm)</td>
<td>N0 M0</td>
<td></td>
</tr>
<tr>
<td>IB</td>
<td>T2a (2-3 cm)</td>
<td>N0 M0</td>
<td></td>
</tr>
<tr>
<td>IIA</td>
<td>T2b (3-5 cm)</td>
<td>N0 M0</td>
<td></td>
</tr>
<tr>
<td>IIB</td>
<td>T2b (3-5 cm)</td>
<td>N1 M0</td>
<td></td>
</tr>
<tr>
<td>IIIA</td>
<td>T1-2a (2-5 cm)</td>
<td>N2 M0</td>
<td></td>
</tr>
<tr>
<td>IIIB</td>
<td>T4 (4+ cm)</td>
<td>N3 M0</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>T1-4 (4+ cm)</td>
<td>N0-3 M1</td>
<td></td>
</tr>
</tbody>
</table>

### Early Lung Cancer
- IA: T1a, N0, M0
- IB: T2a, N0, M0

### Localized Lung Cancer
- IIA: T2b, N0, M0
- IIB: T2b, N1, M0
- IIIA: T1-2a, N2, M0

### Locally Advanced Lung Cancer
- IIIB: T4, N2, M0

### Disseminated Lung Cancer
- IV: T1-4, N0-3, M1

- **T1a**: < 2 cm
- **T1b**: 2-3 cm
- **T2a**: 3-5 cm

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*University Hospital Zurich*
Treatment of clinical stage I and II NSCLC

- Surgical resection (lobectomy, sublobar resection) with lobar, hilar and mediastinal Lymphadenectomy is the standard treatment

- Inoperable patients
  - Stereotactic Body Radiation Therapy (SBRT)
  - Radiofrequency Ablation (RFA)
Anterolateral Thoracotomy
VATS
NSCLC Stage II

70 year old smoker (20 py)
VATS Lobectomy
Follow-up

First postoperative day: drain removed

Fifth postoperative day: discharged

pT2, pN1(1/23), cM0

X-ray at discharge
Postoperative pain and quality of life after lobectomy via video-assisted thoracoscopic surgery or anterolateral thoracotomy for early stage lung cancer: a randomised controlled trial

Morten Bendixen, Ole Dan Jørgensen, Christian Kronborg, Claus Andersen, Peter Bjørn Licht

Figure 2: Proportion of patients with moderate-to-severe postoperative pain during 52 weeks of follow-up

Moderate-to-severe pain was defined as pain that scored at least 3 on the numeric rating scale. p value is for a between-group comparison of the proportions of patients with moderate-to-severe pain over time as analysed by ordinary regression. VATS = video-assisted thoracoscopic surgery.
Minimal invasive lobectomy
Da Vinci Surgical System
Da Vinci Surgical System
No diagnosis...
Review

Robot-assisted surgery for lung cancer: State of the art and perspectives

Giulia Veronesi (MD), Pierluigi Novellis (MD)*, Emanuele Voulaz (MD), Marco Alloisio (MD) Thoracic Surgery Division, Humanitas Cancer Center, Rozzano, Italy

Highlights

• Robot-assisted surgery has technical advantages over traditional surgery.

• Robotics is a safe and promising alternative to VATS for difficult lobectomies.

• Robotic allows superior lymph node dissection than VATS.

• Costs are bound to fall when new robot producers will enter the market.

• Randomized studies are needed to validate advantages of robotics for the patients.
Sublobar resection in stage I NSCLC

What about Segmentectomy or Wedge Resection?
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)

Ann Thorac Surg 1995
Limited (sublobar) resection

Wedgeresection

Segmentectomiy
### Sublobar resection in stage I NSCLC

Population-based analysis

#### Table 2
Recent population-based analysis comparing lobectomy to sublobar resection for stage I non-small cell lung cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>Source</th>
<th>Population</th>
<th>Lobectomy</th>
<th>Years</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yendamuri et al</td>
<td>SEER</td>
<td>Stage I, ≤2 cm</td>
<td>Segmentectomy and wedge</td>
<td>1988–1998</td>
<td>Overall survival benefit for lobectomy</td>
</tr>
<tr>
<td>Whitson et al</td>
<td>SEER</td>
<td>Stage IA</td>
<td>Segmentectomy</td>
<td>1998–2007</td>
<td></td>
</tr>
<tr>
<td>Shirvani et al</td>
<td>SEER</td>
<td>Stage I</td>
<td>Sublobar resection</td>
<td>2001–2007</td>
<td></td>
</tr>
<tr>
<td>Shirvani et al</td>
<td>SEER</td>
<td>Stage I</td>
<td>Sublobar resection</td>
<td>2003–2009</td>
<td></td>
</tr>
<tr>
<td>Speicher et al</td>
<td>NCDB</td>
<td>Stage IA</td>
<td>Sublobar resection</td>
<td>2003–2011</td>
<td></td>
</tr>
<tr>
<td>Khuller et al</td>
<td>NCDB</td>
<td>Stage IA</td>
<td>Sublobar resection</td>
<td>2003–2011</td>
<td></td>
</tr>
<tr>
<td>Kates et al</td>
<td>SEER</td>
<td>Stage IA, ≤1 cm</td>
<td>Sublobar resection</td>
<td>1988–2005</td>
<td>Equivalent overall survival</td>
</tr>
<tr>
<td>Yendamuri et al</td>
<td>SEER</td>
<td>Stage I, ≤2 cm</td>
<td>Segmentectomy and wedge</td>
<td>1999–2004</td>
<td></td>
</tr>
<tr>
<td>Wisnivesky et al</td>
<td>SEER</td>
<td>Stage I ≤2 cm</td>
<td>Sublobar resection</td>
<td>1998–2002</td>
<td></td>
</tr>
<tr>
<td>Whitson et al</td>
<td>SEER</td>
<td>AIS, MIA, or lepidic</td>
<td>Segmentectomy and wedge</td>
<td>1998–2007</td>
<td></td>
</tr>
<tr>
<td>Razi et al</td>
<td>SEER</td>
<td>Stage IA, ≤2 cm, age ≥75</td>
<td>Segmentectomy and wedge</td>
<td>1998–2007</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviation:** ADC, adenocarcinoma.

- a Segmentectomy and wedge resection analyzed together.
- b Segmentectomy equivalent to lobectomy, wedge resection inferior to lobectomy.
- c Segmentectomy and wedge equivalent to lobectomy.

*Thorac Surg Clin 2016*
Sublobar resection in stage I NSCLC

Retrospective analysis

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Population</th>
<th>Extent of Resection</th>
<th>5-y Survival (%)</th>
<th>Local Recurrence (%)</th>
<th>Systemic Recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martin-Ucar et al, 2005</td>
<td>55</td>
<td>C</td>
<td>100% S</td>
<td>70 64 NS</td>
<td>0 12 NS</td>
<td>18 6 NS</td>
</tr>
<tr>
<td>El-Sherif et al, 2006</td>
<td>784</td>
<td>C</td>
<td>41% S 59% W</td>
<td>40 54 .004</td>
<td>14 8</td>
<td>15 20 28</td>
</tr>
<tr>
<td>Kilic et al, 2009</td>
<td>184</td>
<td>C</td>
<td>100% S</td>
<td>46 47 .28</td>
<td>6 4 .50</td>
<td>10 17 .28</td>
</tr>
<tr>
<td>Koike et al, 2003</td>
<td>74</td>
<td>I</td>
<td>81% S 19% W</td>
<td>89 90 NS</td>
<td>2 1 .42</td>
<td>4 4 .9</td>
</tr>
<tr>
<td>Okada et al, 2006</td>
<td>260</td>
<td>I</td>
<td>88% S 12% W</td>
<td>90 89 .10</td>
<td>5 7 NS</td>
<td>9 10 NS</td>
</tr>
<tr>
<td>Altorki et al, 2014</td>
<td>327</td>
<td>I</td>
<td>30% S 70% W</td>
<td>86 85 .86</td>
<td>19 12 .15</td>
<td>— — —</td>
</tr>
</tbody>
</table>

Abbreviations: S, segmentectomy; W, wedge resection.

Long term survival for clinical stage I NSCLC: Prospective single centre study

- Prospective analysis; 2005-2009
- 245 patients
- Inclusion criteria:
  - peripheral cT1,cN0, cM0 NSCLC
  - neg. PET-CT, brain-MRI
  - resection margin > 2cm
  - Lymph nodes negative by intraoperative frozen section
- Segmentectomy with intralobar lymph node dissection

Long term survival for clinical stage I NSCLC: Prospective single centre study

Local recurrences: 3/179 (2%): resection margin (2x); lung metastases (1x)
Long term survival for clinical stage I NSCLC: Prospective single centre study

Local parenchymal recurrence: 30/1737 (1.7%); Lymph node recurrence: 28/1737 (1.6%)
10-year survival after intentional segmentectomy for T1 (<2cm) NSCLC

Importance of Experienced Centers

NSCLC outcomes are significantly influenced by the type of treatment facility
Dr. Bhagirathbhai Dholaria of the Moffitt Cancer Center in the United States

NSCLC incident cases between 2004 and 2013 from the National Cancer Database
Overall survival (OS) by year of diagnosis and type of treatment facility
more than 1 million NSCLC patients
separated by initial treatment facility type (academic: 31.5%, non-academic: 68.5%)

→ NSCLC treatment at academic centers was associated with reduced risk of death when compared to non-academic centers

4-year OS for academic and non-academic cohorts was 25% and 19%, resp. (p<0.001)
survival difference between academic and community centers was greater among non-metastatic compared to metastatic NSCLC.

These findings highlight the importance of ensuring easier access to facilities with multidisciplinary expertise and training programs to increase survival of NSCLC patients
The role of tumor histology and staging in lung cancer treatment

- Adjuvant therapy depends on the final stage
- Histological subtyping influences prognosis and adjuvant therapy
- Approx. 10% of tumors (SCLC, LCNEC) require adjuvant chemotherapy
- Patients have a right to know if they have cancer
Despite best clinical staging with PET-CT occult $N_1/N_2$ are found in 22 %

- Adjuvant chemotherapy is recommended (survival benefit 5-15%)

- The majority of patients with intralobar $N_1$ are cured with surgery (lobectomy) alone

ESMO guidelines, 2014
Maeshima, Cancer, 2012
In-Hospital Mortality in lung cancer patients (ESTS database)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No of procedures</th>
<th>Hospital mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobectomy</td>
<td>24043</td>
<td>2.3%</td>
</tr>
<tr>
<td>Segmentectomy</td>
<td>1492</td>
<td>1.9%</td>
</tr>
<tr>
<td>Wedge resection</td>
<td>2770</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

2007-2010: 4.6%  →  2011-2013: 2.0%
## Surgical Mortality for clinical stage I-II NSCLC: Current series from specialized centres

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Patients</th>
<th>Stage</th>
<th>Approach</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stephens, 2013</td>
<td>307</td>
<td>Clinical I</td>
<td>VATS</td>
<td>0.3%</td>
</tr>
<tr>
<td>Burt, 2014</td>
<td>6802</td>
<td>Clinical I-IIIA</td>
<td>VATS</td>
<td>0.8%</td>
</tr>
<tr>
<td>Okada, 2014</td>
<td>634</td>
<td>Clinical I</td>
<td>Open</td>
<td>0%</td>
</tr>
<tr>
<td>Nasir, 2014</td>
<td>316</td>
<td>Clinical I-II</td>
<td>Robotic</td>
<td>0.3%</td>
</tr>
<tr>
<td>Weder, 2015</td>
<td>&gt;400</td>
<td>Clinical I-II</td>
<td>VATS</td>
<td>0%</td>
</tr>
</tbody>
</table>
Surgery does not impair lung function with clinical relevance

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Patients (L/SL)</th>
<th>Months follow-up</th>
<th>Postoperative reduction of FEV-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCSG, 1995</td>
<td>58/71</td>
<td>12-18</td>
<td>- 11% - 5%</td>
</tr>
<tr>
<td>Keenan, 2004</td>
<td>147/54</td>
<td>12</td>
<td>- 9% - 3%</td>
</tr>
<tr>
<td>Harada, 2005</td>
<td>45/38</td>
<td>6</td>
<td>- 16% - 11%</td>
</tr>
<tr>
<td>Yoshimoto, 2010</td>
<td>24/65</td>
<td>10</td>
<td>- 18% - 11%</td>
</tr>
<tr>
<td>Total</td>
<td>247/228</td>
<td>10</td>
<td>-13% -7%</td>
</tr>
</tbody>
</table>
Surgery in the elderly

- decreased perioperative morbidity and equivalent overall survival in patients > 75 who underwent sublobar resection as compared with lobectomy
  
  Kilic, Ann Thorac Surg 2009
  Dell’Amore, Interact Cardiovasc Thorac Surg 2013

- no significance difference in 5-y cancer-specific survival for patients > 75 with T1a tumors between wedge, segmentectomy or lobar resections
  

Curative resection for lung cancer in octogenarians is justified

Michaela Tutic-Horn*, Franco Gambazzi*, Gaetano Rocco³, Monique Mosimann³, Didier Schneiter¹, Isabelle Opitz¹, Nono Martucci³, Sven Hillinger¹, Walter Weder¹, Wolfgang Jungraithmayr¹*

88 patients (24 females) aged ≥80 who underwent complete resection for lung cancer up to pneumonectomy between 2000 and 2013 were analysed → 5y survival comparable to younger ages

JTD 2017
SBRT versus lobectomy in stage I NSCLC: knowns, unknowns and its interpretation

Matthias Guckenberger

«Future comparative studies are urgently needed and they need to provide more in-depth information about the patients’ comorbidities and their non-cancer related risk factors.

[...] surgical lobectomy remains the standard of care for appropriately selected patients.»
Cancer resection in «inoperable» patients

Concomitant cancer resection and lung volume reduction surgery

<table>
<thead>
<tr>
<th></th>
<th>FEV1</th>
<th>TLC</th>
<th>RV/TLC</th>
<th>DLCO</th>
</tr>
</thead>
<tbody>
<tr>
<td>pre-operative %</td>
<td>32.5 (27 – 37.25)</td>
<td>117 (109.5 – 135.5)</td>
<td>183 (104.25 – 232.25)</td>
<td>63 (58 – 70.6)</td>
</tr>
<tr>
<td>postoperative %</td>
<td>40.5 (28.8 – 47.75)</td>
<td>115 (108 – 132.5)</td>
<td>203 (147 – 216)</td>
<td>65 (56.5 – 67)</td>
</tr>
<tr>
<td>p value</td>
<td>0.012</td>
<td>0.373</td>
<td>0.173</td>
<td>0.123</td>
</tr>
</tbody>
</table>

14 patients (8 female, 6 male) mean age 64 +/- 7 years

3-year-survival rate 67 %

5-year-survival rate 57 %
Neoadjuvant anti-PD1, Nivolumab, in Early Stage Resectable NSCLC


63yo M, ex-smoker, adeno, PD-L1 2%+, <10% viable tumor at resection

PD-L1 100%, isolated tumor cells in a dense T cell infiltrate at resection

PD-L1 17%, CR in primary tumor at resection

Neoadjuvant immunotherapy prior to surgery is safe and feasible in early lung cancer

ESMO 2016
Screening, Hybrid Theater and VATS ‘one stop shop’

Hybrid Theater and Uniportal Video-Assisted Thoracic Surgery
The Perfect Match for Lung Nodule Localization
Ze-Rui Zhao, MD, Rainbow W.H. Lau, MBChB, FRCS,
Calvin S.H. Ng, MD, FRCS

Thoracic Surgery Clinics 2017
A novel technique for tumor localization and targeted lymphatic mapping in early-stage lung cancer

Krista J. Hachey, MD, Christopher S. Digesu, MD, Katherine W. Armstrong, MPH, Denis M. Gilmore, MD, Onkar V. Khullar, MD, Brian Whang, MD, Hisashi Tsukada, MD, PhD, and Yolonda L. Colson, MD, PhD

Navigational bronchoscopy-guided near-infrared tumor marking is feasible and allows localization and nodal staging of early stage lung cancers

J Thoracic Cardiovasc Surgery 2017
Non-intubated VATS

Non-intubated single-incision video-assisted thoracic surgery: a two-center cohort of 188 patients

Man-Ling Wang1, Carlos Galvez2, Jin-Shing Chen3, Jose Navarro-Martinez4, Sergio Bolufer2, Ming-Hui Hung1, Hsao-Hsung Hsu3, Ya-Jung Cheng1

188 patients undergoing non-intubated single-incision video-assisted thoracic surgery (NI-SI-VATS) procedures between July 2013 to November 2015 in two centers in Taiwan (170 patients) and Spain (18 patients) with two different anesthetic methods.

Non-intubated single-incision procedures can be feasible and safe in expert hands and experienced teams, even for anatomical resections. Strict selection criteria, skill and experience are mandatory. Comparative cohorts and randomized trials are needed.

JTD 2017
Conclusion

- Surgery is (still) the golden standard for early stage NSCLC
- Excellent and proven long term outcome
- Minimal morbidity and mortality (in specialized centers)
- No or little functional impairment
- Provides tumor histology, stage including lymph node resections
- Immunotherapy in combination with surgery will become important
- ‘one stop shop’
- Radiotherapy plays a major role in inoperable +/- elderly patients and once might play a major role in all patients