Optimizing NSCLC staging: EBUS vs mediastinoscopy

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no disclosures – no conflict of interest

presentation by thoracic surgeon
not pulmonary physician

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Optimizing NSCLC staging:
EBUS vs mediastinoscopy

• lymph node mapping
• (minimally) invasive techniques
  endosonography (EBUS, EUS)
  mediastinoscopy
  thoracoscopy
• staging - restaging
• conclusion
Lymph node mapping

• prognosis of non-small cell lung cancer (NSCLC)
  complete resectability (T)
  nodal metastases (N)

• stage IIIA / N2
  histological proof of N2
  combined modality therapy
  N2 versus N3

Lymph node mapping

5-year survival

<table>
<thead>
<tr>
<th>pN0</th>
<th>56%</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN1 single</td>
<td>45%</td>
</tr>
<tr>
<td>pN1 multiple</td>
<td>31%</td>
</tr>
<tr>
<td>pN2 found at mediastinoscopy</td>
<td>9 - 15%</td>
</tr>
<tr>
<td>thoracotomy after MS</td>
<td>24 - 33%</td>
</tr>
<tr>
<td>pN3</td>
<td>6%</td>
</tr>
</tbody>
</table>
N factor: 7 zones

Rusch V. J Thorac Oncol 2009; 4:568-77

N staging to be optimized!
Optimizing NSCLC staging:
EBUS vs mediastinoscopy

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EBUS - EUS

bronchus

oesophagus
Minimally invasive tests

Tertiary staging

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Sensitivity</th>
<th>PPV</th>
<th>FN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transbronchial needle aspiration (TBNA)</td>
<td>76 %</td>
<td>100%</td>
<td>29%</td>
</tr>
<tr>
<td>Endoscopic ultrasound (EUS-NA)</td>
<td>88 %</td>
<td>98%</td>
<td>23%</td>
</tr>
<tr>
<td>Transthoracic needle aspiration (TTNA)</td>
<td>91 %</td>
<td>100%</td>
<td>22%</td>
</tr>
</tbody>
</table>

- selected population
- high prevalence of LN involvement
- confirmation mediastinal involvement but ↑ FN rate

Urschel J. Lung Cancer 2003; vol 41 suppl 3: S105
Detterbeck FC. Chest 2003; 123 (suppl 1): S167-S175

EBUS

- 1299 patients – 11 studies
- pooled sensitivity 0.93 (95% CI 0.91-0.94)
  specificity 1.00 (95% CI 0.99-1.00)
- selection + CT or PET sensitivity 0.94 (95% CI 0.93-0.96)
  without selection 0.76 (95% CI 0.65-0.85) p < 0.05
- complications ↓↓ 0.15%

but:
- ↑ prevalence of involved mediastinal LN (63% ↔ 20-40%)
- experienced pulmonary physician!

Gu P. Eur J Cancer 2009; 45:1389-96
EUS

Meta-analysis

- 18 eligible studies
- pooled sensitivity 0.83 (95% CI 0.78-0.87)
  specificity 0.97 (95% CI 0.96-0.98)
- + LN CT sensitivity 0.90 (95% CI 0.84-0.94)
  - LN CT 0.58 (95% CI 0.39-0.75)
- minor complications 0.8%

- complete staging mediastinum?
- ↑ sensitivity: “medical” mediastinoscopy: EBUS + EUS

ASTER study

Micames CG. Chest 2007; 131:539-48

Cervical mediastinoscopy

DISEASES of the CHEST

VOLUME XXXVI october, 1959 Number 4

Mediastinoscopy: * A Method for Inspection and Tissue Biopsy in the Superior Mediastinum

ERIC CARLENS, M.D.
Stockholm, Sweden
Cervical mediastinoscopy

- 25 – 30 % abnormal lymph nodes
- exploratory thoracotomy : 50  ➔ 15 %
- LN stations  1, 2, 4 R+L
  7 ant.
- bilateral exploration (N3 disease)
- mediastinal invasion primary tumor
- general anaesthesia
- large biopsy samples:
  molecular genetic analysis
Cervical mediastinoscopy

- **hot spots**
  - low cervical, supraclavicular + sternal notch nodes (1)
  - upper paratracheal (2 R-L)
  - lower paratracheal (4R-L)
  - ant. subcarinal (7A)
- **blind spots**
  - aortopulmonary (5,6)
  - post. subcarinal (7P)
  - oesophageal (8)
  - inf. pulmonary ligament (9)
  - scalene lymph nodes [N3]

Cervical mediastinoscopy

**REVIEW 20 000 CASES**

- **mortality** < 0.5%
- **morbidity** 2.5%
  - haemorrhage
  - L recurrent nerve paralysis
  - pneumothorax
  - rare: tear tracheobronchial wall
  - perforation of oesophagus
  - stroke, chylous leak, air embolus

Cervical mediastinoscopy

video-assisted

• advantages:
  - magnification
  - ergonomic position of operator
  - teaching possibility

• disadvantages:
  - 2-dimensional view
  - cost
Cervical mediastinoscopy

- 6505 pts NSCLC
- pooled sensitivity 78% specificity 100%
- NPV 91% FN rate 11% prevalence 39%
  Detterbeck F. Chest 2007; 132: 202S-220S

- videomediastinoscopy after induction therapy
  sensitivity 0.81 specificity 1.0 accuracy 0.91

Cervical mediastinoscopy

- VAMLA video-assisted mediastinal lymphadenectomy
  sensitivity 0.94 specificity 1.0 FN rate 0.9%

- TEMLA transcervical extended mediastinal lymphadenectomy
  all mediastinal LN stations except 9 (inf. pulmonary vein)
  staging – restaging of lung cancer
  sensitivity 0.96 NPV 0.98
Invasive staging

- cervical mediastinoscopy
- anterior - aortopulmonary LN 5,6
- combination: extended
- VAMLA - TEMLA

- VATS, thoracoscopy (video-assisted)
  - LN aortopulmonary (5,6)
  - inferior mediastinal (7 post., 8, 9)
  - hilar (10)
  - pleural space, nodules

VATS
Staging N2 disease

- 53-year-old ♀
- 1994 breast cancer conservative resection + adjuvant chemoradiotherapy
- 1999 cervix cancer vaginal hysterectomy
- Sjögren’s disease (ocular manifestations)

- follow-up chest CT: nodule L lung
  - ↑ hilar and mediastinal LN
VATS
Staging N2 disease

- + N2 NSCLC – squamous cell ca.
- induction chemotherapy
- PET – mediastinum
- 06/07 lobectomy LUL
- ypTxN1M0

Mediastinal Staging

<table>
<thead>
<tr>
<th>LN</th>
<th>EBUS</th>
<th>EUS</th>
<th>cervical mediastinoscopy</th>
<th>VAMLA</th>
<th>TEMLA</th>
<th>VATS L</th>
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Mediastinoscopy vs. endosonography
ASTER randomized trial

• 2 staging strategies lung cancer
• 2007-09 241 pts randomized

EBUS + EUS 123 pts + 56 pts 46% *
  — surgical staging 65 pts + 62 pts 50% **

surgical staging 118 pts + 41 pts 35%

* p = 0.11  ** p = 0.02

Annema JT. JAMA 2010; 304: 2245-52

Mediastinoscopy vs. endosonography
ASTER randomized trial

<table>
<thead>
<tr>
<th></th>
<th>surgical staging</th>
<th>EBUS + EUS</th>
<th>combined</th>
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<tbody>
<tr>
<td>sensitivity</td>
<td>79%</td>
<td>85% p = 0.47</td>
<td>94% p = 0.02</td>
</tr>
<tr>
<td>NPV</td>
<td>86%</td>
<td>85% p &gt; 0.99</td>
<td>93% p = 0.18</td>
</tr>
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• complication rate =
• unnecessary thoracotomies 9 endosonography group
  21 mediastinoscopy group p = 0.02
• endosonography + surgical staging ↑ sensitivity

Annema JT. JAMA 2010; 304: 2245-52
**EBUS compared to mediastinoscopy**

**Prospective study**

- 2006-2010 153 eligible pts NSCLC
- EBUS-TBNA → mediastinoscopy; both negative → resection

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<th></th>
<th>sensitivity</th>
<th>NPV</th>
<th>accuracy</th>
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<tr>
<td>EBUS</td>
<td>81%</td>
<td>91%</td>
<td>93%</td>
</tr>
<tr>
<td>mediastinoscopy</td>
<td>79%</td>
<td>90%</td>
<td>93%</td>
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- prevalence N2/N3 35%
- ROSE: rapid on site examination
- EBUS no complications, mediastinoscopy minor (2.6%) may replace mediastinoscopy

*Yasufuku K. J Thorac Cardiovasc Surg 2011; 142: 1393-1400*

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**EBUS N0 – N1 disease**

**Retrospective study**

- 2003-2008 163 pts cN0-1 NSCLC CT or PET-CT
- 94 cN0  69 cN1
  - 123 pN0  24 pN1  16 pN2
- EBUS upstaged 9 pts N2 but FN 7 pts

- EBUS N0-1 sensitivity 76%  accuracy 97%  NPV 96%

*Yasufuku K. Society of Thoracic Surgeons (STS) meeting, Los Angeles 2013*
Accuracy PET - CT scanning anno 2009

- 200 patients operated lung cancer
- PET-CT followed by staging mediastinoscopy and resection, if appropriate
- PET-CT correct staging 99 pts 49.5 %
  under-staged 59 29.5 %
  over-staged 42 21 %
- superior mediastinal nodes not correctly staged in 19 %


True FN rate EUS and EBUS anno 2010

- 352 patients with lung cancer over 1.5 years
- FN rate EBUS 29.4 %
  EUS 14.3 %
  mediastinoscopy 5.8 %
- EBUS and EUS useful initial tests
- EBUS ↑ FN rate 4R,7: mediastinoscopy
- EUS ↑ FN rate 5, 6: VATS

Cerfolio RJ. Ann Thorac Surg 2010; 90:427-34
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Staging NSCLC:
which false negative rate do you accept?

Sensitivity in unselected population NSCLC

- PET-CT 70%
- EBUS-EUS 80%
- Mediastinoscopy 90%
- EBUS/EUS + mediastinoscopy 95%
- TEMPLA – VAMLA 99%

Cost - experience (ASTER) – ROSE
Staging versus restaging?
Mediastinal staging NSCLC

Staging
- PET-CT -
- ES -
- ES +
- PET-CT +

Surgery
- MS -
- MS +
- MMT

Restaging

ES endosonography (EBUS-EUS)
MS mediastinoscopy
MMT multimodality treatment

Restaging after initial ES

Restaging after initial ES
- PET-CT -
- MS -
- MS +
- PET-CT +

Surgery
- RT

ES endosonography (EBUS-EUS)
MS mediastinoscopy
RT radiotherapy
Restaging after initial mediastinoscopy

- PET-CT - → Surgery
- PET-CT +
  - ES - → ReMS - → Surgery
  - ES + → ReMS +
    - RT

ES: endosonography (EBUS-EUS)
MS: mediastinoscopy
RT: radiotherapy