Surgical Approaches to Early Stage Lung Cancer

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The North American Experience

- Surgical resection remains the single most consistent and successful option for cure for Stage I and II NSCLC
- Surgical treatment for potential cure remains predicated on R0 resection
- Lobectomy—the gold standard
- Mediastinal lymph node dissection confers OS advantage as well as LCSS

Fact is…

- Overall survival less than 15%
- Only 20% of cases are diagnosed in Stages 1 or 2
- Survival for Stage 1 and 2 is 70% and 45% respectively

Why Stage?

1. First, the staging system provides a standardized description of the disease
2. Second, stage dictates treatment and the treatment regimens vary considerably by stage
3. Third, stage predicts survival
4. And fourth, the staging system allows us to facilitate research and compare results of different clinical trials
Historical Perspective

Table 1. Evolution of TNM staging system (EUSC)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td>T4</td>
</tr>
<tr>
<td>N1</td>
<td>N2</td>
<td>N3</td>
<td>N4</td>
</tr>
<tr>
<td>M1</td>
<td>M0</td>
<td>M0</td>
<td>M0</td>
</tr>
</tbody>
</table>


7th Edition Lung Cancer Staging System

Table 4. Descriptors, Proposed T and M Categories, and Proposed Stage Groupings

<table>
<thead>
<tr>
<th>Prognosed T/M Descriptor</th>
<th>Proposed T/M</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 (≤ 2 cm)</td>
<td>T1a</td>
<td>IA</td>
<td>IA</td>
<td>IA</td>
<td>IB</td>
</tr>
<tr>
<td>T1 (&gt; 2-3 cm)</td>
<td>T1b</td>
<td>IA</td>
<td>IA</td>
<td>IA</td>
<td>IB</td>
</tr>
<tr>
<td>T2 (≥ 5 cm)</td>
<td>T2a</td>
<td>IB</td>
<td>IA</td>
<td>IA</td>
<td>IA</td>
</tr>
<tr>
<td>T2 (&gt; 5-7 cm)</td>
<td>T2b</td>
<td>IA</td>
<td>IB</td>
<td>IA</td>
<td>IB</td>
</tr>
<tr>
<td>T3</td>
<td>T3</td>
<td>HB</td>
<td>IA</td>
<td>IA</td>
<td>IB</td>
</tr>
<tr>
<td>T4 (same lobe nodules)</td>
<td>T4</td>
<td>HB</td>
<td>IA</td>
<td>IA</td>
<td>HB</td>
</tr>
<tr>
<td>T4 (extension)</td>
<td>T4</td>
<td>HB</td>
<td>IA</td>
<td>IA</td>
<td>HB</td>
</tr>
<tr>
<td>M1 (ipsilateral lung)</td>
<td>M1a</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
</tr>
<tr>
<td>T4 (pleural effusion)</td>
<td>M1b</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
</tr>
</tbody>
</table>

Cells in bold indicate a change from the sixth edition for a particular TNM category.

11/8/2008

T“N”M Descriptor
The Japanese-American Connection

- Naruke first proposed the lymph node map for lung cancer in 1967 and was adopted by AJCC in 1976
- Mountain modified the American Thoracic Society map which was adopted by the North American Lung Cancer Study Group in 1997

Yes We Can!

- Change the stage distribution at presentation so that surgery is feasible
- Do CT screening to shift this stage distribution
- ELCAP early detection CT scan detected 85% tumors in early stage
- 75% underwent resection within 1 month
- 92% Stage I 5-year survival


Extent Of Surgery

- Increase life span leading to elderly lung cancer patients with increased comorbidities
- More post-operative problems
- Therefore, the extent of surgery is certainly in question
- CALGB 140503 trial: A Phase III randomized trial of lobectomy vs sublobar resections for small (≤ 2cm) peripheral NSCLC

Evolution in Surgical Technique

- Minimally invasive surgical techniques such as video-assisted thoracic surgery (VATS) or robotic surgery
- Less morbidity and mortality when compared with thoracotomy
- Lesser cost compared with thoracotomy
NEW SURGICAL TECHNIQUES

- VATS Approach - advantages over open include: comparable if not better survival, shorter LOS, reduced pain, better pulmonary function
- Robotic Surgery – advantages over VATS include: binocular vision, 3-D depth perception, increased manual dexterity

VATS

- A major advance for surgery in the chest
- For an experienced surgeon, the learning curve is usually very steep
- A new set of manual skills and hand-eye coordination
- <10% lobectomies are performed via VATS

Definition of VATS Lobe

- No rib spreading
- Individual hilar dissection
- Standard mediastinal lymph node sampling/dissection
- ?VATS credentialing in anatomic resection
Indications for VATS Lobectomy

Stage I
- Tumor size < 6 cm
- Negative mediastinum by either cervical mediastinoscopy or chest CT or PET/CT

Contraindications to VATS Lobectomy

- T3 tumors
- Endobronchial tumors at bronchoscopy
- Positive cervical mediastinoscopy
- Neoadjuvant chemotherapy and/or radiation therapy
- Centrally located tumors
- Nodes adherent to pulmonary vessels
- Need for a sleeve resection (relative)

Video-assisted thoracic surgery lobectomy: experience with 1,100 cases.

- McKenna RJ Jr, Houck W, Fuller CB.
  Cedars Sinai Medical Center
  Los Angeles, California, USA.

VATS Lobe-Data

- 1100 VATS lobes between 1993-2004:
  - 53 benign versus 1,047 malignant causes
  - Morbidity 0.8% (9/1100)
  - Morbidity 15%
  - Bronchopleural fistula ~0.3% (3/1100)
  - Conversion rate 2.5% (28/1100)
  - LOS median 3 days (mean 4.78 d)


VATS Lobectomy-Controversies

- Surgical Technique
- Overall Survival (OS)
- Pain
- Mediastinal lymph node dissection/sampling (MLND/S)

VATS Lobectomy: The Evidence Base

Table 1: Bronchoscopic Control Trials of VATS Major Lung Resections

<table>
<thead>
<tr>
<th>Study</th>
<th>Lobes</th>
<th>Recons.</th>
<th>Complications</th>
<th>Results</th>
<th>Concl.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattey 3X09</td>
<td>28 VATS</td>
<td>80 Open</td>
<td></td>
<td>Loss complications at VATS, no other differences</td>
<td>VATS preferred</td>
</tr>
<tr>
<td>Segal 3X00</td>
<td>48 VATS</td>
<td>32 Open</td>
<td></td>
<td>Survival, no recurrence</td>
<td>All periop MDRD</td>
</tr>
<tr>
<td>Gatto 2X00</td>
<td>21 VATS</td>
<td>10 Open</td>
<td></td>
<td>Sputum, no fevers</td>
<td>VATS better</td>
</tr>
<tr>
<td>Almog 3(6)</td>
<td>10 Complete VATS</td>
<td>8 Assisted VATS</td>
<td>Off time, 3/3, pain, complications, infection</td>
<td>Complete VATS - no soapaking</td>
<td></td>
</tr>
</tbody>
</table>
Survival Controversy: VATS vs Open Lobectomy

- Sakuraba et al. reported 5-yr OS for VATS 82% vs 72%, \( p = 0.93 \)
- Sugi et al. found the 5-yr survival for VATS 90% vs 85%, \( p = 0.74 \)
- Kaseda and Aoki reported a 94.4% survival at 4 years

CALGB 140501 trial: VATS lobectomy vs open lobectomy:
A registry study to examine outcomes for patients with Stage I NSCLC

MLND/S Controversy

- Sagawa et al. VATS lobectomy and MLND f/b thoracotomy at same operation found <3% missed lymphatic tissue at VATS
- Watanabe et al. compared 191 VATS lobe with 159 thoracotomies and found similar number of nodes removed

Stage I Recurrence…When/Why?

- 40% relapse rate within 24 months following an R0 resection with complete lymphadenectomy
- Recurrence due to:
  - Incomplete lymphadenectomy
  - Unpredictable lymphatic patterns
  - Inadequacy of pathologic examination
SLN Mapping

- Isosulfan blue dye injection
- Technetium 99m–labeled sulfur colloid
- Technetium 99m–labeled tin colloid
- Intraoperative 18-FDG (ID mets rather than SLN)
- Non-radioactive tracers (Quantum dots, HSV containing fluorescent protein transgene)

Radio injection (99mTc-nanocolloid®) by bronchoscopy

Comparing 3 Detection Techniques For Micrometastases in SLN

Radio injection (99mTc-nanocolloid®) under CT-guidance/thoracoscopy

SLN Map—"The Holy Grail?"

- Mapping and RT-PCR may help determine which early stage cancer have micrometastatic disease
- May help direct adjuvant therapy in this cohort
- May enable development of molecular biomarkers to discern those at increased risk of recurrence
- A molecular staging system may supersede TNM staging

Conclusion

- Future innovation in the surgical sciences will rely on tumour biology, enabling early detection with molecular diagnostic and new imaging techniques, allowing molecularly targeting any residual disease following minimally invasive resection