Session 1: Innovations in The Surgical Treatment of Lung Cancer

Speaker: Scott J. Swanson, MD

7:30 AM - 8:15 AM

History of Surgery for Lung Cancer

• Evarts Graham (St Louis) reported the first successful pneumonectomy for lung cancer using a tourniquet technique in 1933.
• Churchill (Boston, 1950) suggested lobectomy was a good option for surgical treatment of lung cancer.

History of Surgery for Lung Cancer

• Bonfil-Roberts and Claggett (NY, Minneapolis, 1972) reported that segmentectomy was reasonable for small lung cancers.
• 1992, VATS lobectomy
• Currently, lobectomy with lymph node dissection is the gold standard for surgical treatment of lung cancer.

Innovations in the Surgical Treatment of Lung Cancer

• Thoracoscopic technique
• Size of the resection: segmentectomy/wedge vs lobectomy
• Integrating chemotherapy, radiation therapy, and surgery
• Surgery for special populations
  – Elderly
  – Severe emphysema
• Alternatives to surgery
  – Stereotactic radiation – “Cyberknife”
  – Radiofrequency ablation
What are reported advantages of a VATS lobectomy over a thoracotomy and lobectomy?

1. Lower cost, decreased need for general anesthesia, technically easier
2. Shorter anesthetic, simpler to learn, less manipulation of lung during surgery
3. Less need for operative equipment, more lymph nodes removed, shorter operative time
4. Decreased pain, decreased length of hospital stay and lower peri-operative complications

Video-Assisted Thoracic Surgery (VATS)

- Definition-
  - Via several small incisions (1-2 cm)
  - Videoscopic camera
  - Watching a TV monitor
  - No rib spreading is permitted
- Lewis (NJ) reported the first lobectomy using this technique in 1992.

Video-Assisted Thoracic Surgery or VATS

- The Hope
  - Reduced morbidity
  - Reduced mortality
  - Reduced length of stay
  - Earlier return to regular activities
  - WITHOUT compromise of the cancer operation morbidity

VATS Example – Initial View Right Upper Lobectomy

- Exposure

VATS Lobectomy Specimen Removal

VATS Example – Chest View after Specimen Removal
Survival Following Surgery for Stage I NSCLC

<table>
<thead>
<tr>
<th>Author</th>
<th># Patients</th>
<th>5-year Survival</th>
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<tbody>
<tr>
<td>Martini</td>
<td>128</td>
<td>72%</td>
</tr>
<tr>
<td>Williams</td>
<td>461</td>
<td>71%</td>
</tr>
<tr>
<td>Teramachi</td>
<td>121</td>
<td>71%</td>
</tr>
<tr>
<td>Mountain</td>
<td>725</td>
<td>68%</td>
</tr>
<tr>
<td>Naruke</td>
<td>536</td>
<td>65%</td>
</tr>
</tbody>
</table>

Video-Assisted Thoracic Surgery (VATS) Lobectomy Results in 1100 Patients

- 6 intergroup centers, 11 surgeons, 127 pts
- Peripheral, clinical stage 1A NSCLC
- 106/127 (83%) had stage I lung cancer
- Median procedure length: 130 min (47-428)
  - 60% had biopsy at time of procedure
- Median chest tube duration: 3 d (1-14)

Failure-Free Survival

CALGB 39802

Video-Assisted Thoracic Surgery (VATS) Lobectomy Results in 1100 Patients

- None 932 (84.7%)
- Air leak > 7d 56 (5.1%)
- AF 32 (2.9%)
- Serous drainage 14 (1.3%)
- Readmit 13 (1.2%)
- Pneumonia 13 (1.2%)
- SQ 12 (1.1%)
- MI 10 (0.9%)
- Empyema 4 (0.03%)
- Other 14

VATS Lobectomy – Outcomes

CALGB 39802

- Conversion 14/111 13%
- Mortality 3/97 3.1%
- Morbidity 8/97 8.2%
  - SVT: 5/97 (5.2%)
  - Bleeding: 2/97 (2.1%)
  - Prolonged air leak: 1/97 (1%)

**Video-Assisted Thoracic Surgery or VATS**

**VATS vs Thoracotomy**

- Fewer complications: Hoksch\(^1\)
- Less pain: Walker\(^2\)
- Better quality of life: Sugiuira\(^3\)
- Better PFTs: Nakata\(^4\)
- Less pneumonia: Whitson\(^5\)
- Earlier recovery: Demmy\(^6\)
- Easier for octogenarians: McVay\(^7\)

**Video-Assisted Thoracic Surgery or VATS**

**VATS vs Thoracotomy**

- Reduced stress response
- Reduced post-op C-reactive protein
- Reduced IL-6 levels
- Enhanced cellular immune function (better neutrophil and monocyte function)

**Video-Assisted Thoracic Surgery or VATS**

**VATS vs Thoracotomy**

- Less lab charges
- Less anesthesia charges
- Less disposable equipment charges
- Less hospital charges
- Less complications

**Adjuvant Chemotherapy for Stages IB-IIIa**

**ANITA Trial**

- N 0
- N 1
- N 2

**Video-Assisted Thoracic Surgery or VATS**

**VATS vs Thoracotomy**

**VATS Lobectomy – Improved Chemotherapy Tolerance**

- LOS: 4 d
- Morbidity: 6/14, 11%, prolonged leak, 7%, pneumonia, 2%
- Pain at 2 weeks:
  - No pain med: 50%
  - Ibuprofen: 40%
  - Codeine type rx: 10%
- **Chemotherapy:**
  - Completed full course on time: 73%
  - All 4 intended cycles: 85%
- Discharge:
  - 34% home within 3 d
  - 96/144 home without assistance
  - 40/144 home with nursing assistance; 36/40 brief VNA visit
  - 3x/wk for 2 wk
  - 8/144 (5.6%) discharged to rehab

**VATS Lobectomy**

**Summary**

- Current evidence would suggest that a lobectomy done using thoracoscopic or VATS approach is preferred for stage I and possibly stage II NSCLC.
- Long term survival is at least as good as with an open approach.
- The operation does require technical competence.
What are reported advantages of a video-assisted thoracic surgery lobectomy over a thoracotomy and lobectomy?

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What is the current standard of care for treatment of a 2.0 cm non-small cell lung cancer, specifically what operation is best?

1. Lobectomy
2. Segmentectomy
3. Wedge resection
4. Radiofrequency ablation
5. Stereotactic radiation

Lobectomy vs Wedge Resection

- Lung Cancer Study Group: lobectomy vs wedge or segment:
  - 3-5 times local recurrence
  - 20% worse survival (for less than lobectomy)
- Therefore, lobectomy = gold standard

Size of Resection for Lung Cancer

- Data are equivocal and screening finds small masses that might be treated as well with a lesser resection.
- Therefore, revisit question of lobectomy or a sublobar resection (wedge or segmentectomy).
A phase III randomized trial of lobectomy vs sublobar resection for small (≤2 cm) peripheral NSCLC – Nasser Altorki PI

- CALGB, ACOSOG, SWOG, NCIC, RTOG
- Objectives
  - Primary: determine disease-free survival
  - Secondary
    - Determine overall survival
    - Pulmonary function at 6 months
    - Radiologic endpoints: PET predictors of outcome, CT f/u

- Standard of care for stage I NSCLC is a lobectomy.
- However, for tumors ≤2 cm consideration should be given for a segmentectomy (preferred) or wedge resection.

- Segment vs Lobe
  - Better pulmonary function
  - Metachronous cancers
  - Synchronous cancers
  - Without compromising survival
- The best way to consider this option is in the setting of a clinical trial (CALGB 140503).

What is the current standard of care for treatment of a 2.0 cm non-small cell lung cancer, specifically what operation is best?

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- Segmentectomy
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Lung Cancer: Stage At Diagnosis

SEER, 1998

Multi-Modal Therapy for Stage IIIa Disease

Lung Intergroup Trial 0139 Study Design

<table>
<thead>
<tr>
<th>STRATIFY</th>
<th>KPS 70-80 vs 90-100</th>
<th>T1 vs T2 vs T3</th>
</tr>
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<tbody>
<tr>
<td>RANDOMIZE</td>
<td>Induction CT/RT</td>
<td></td>
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</tbody>
</table>

- Cisplatin, 50 mg/m² IV d1, 8, 14, 21
- Etoposide, 50 mg/m² IV d1-5, 22-28
- Thoracic RT, 45 Gy (1.8 Gy/d), begin d1

RE-EVALUATE

- 2-4 weeks after completion of RT
- 7 days before completion of RT
Multi-Modal Therapy for Stage IIIa Disease
CT-RT vs CT-RT-S

Lung Intergroup Trial 0139 Study Design
No progression at re-evaluation
Surgical Resection
Continue RT to 61 Gy without interruption
CONsolidation
cisplatin plus etoposide X 2 cycles

Lung Intergroup Trial 0139/RTOG 9309 Overall Survival by Treatment Arms

Intergroup 0139/RTOG 9309 Overall Survival of the Lobectomy Subset versus Matched CT/RT Subset

Lobectomy Following Induction Therapy is Significantly Superior to Chemoradiation Only

Lung Intergroup Trial 0139/RTOG 9309
Conclusions
- N0 status at surgery significantly predicts greater 5-year survival
- The trimodality approach is not optimal when a pneumonectomy is required due to high mortality risk
- Surgical resection after CT/RT can be considered for fit patients if lobectomy is feasible
Resolution of Histologic Involvement Predicts Improved Survival Following Induction Therapy for Stage III disease

ACCP Guidelines for Stage IIIa (N2) NSCLC

- If N2 disease is found at surgery and complete resection is possible:
  - Resection followed by chemotherapy and possibly RT
- If N2 disease is found prior to resection refer for multimodality therapy:
  - Induction therapy followed by surgery should only be done as part of a clinical trial
- Pt should not have pneumonectomy following chemoradiation.
- Surgery or radiation only is not recommended.
- Primary treatment should be chemoradiation.

Treatment of Stage IIIa NSCLC Summary

- Controversial
- ACCP guideline: definitive chemoradiotherapy is primary treatment choice. Surgical resection is not recommended
- However, induction therapy followed by lobectomy may give the best outcome

Surgery for Special Populations

What about...

- Limited pulmonary reserve
- Elderly: patients > 70

Limited Pulmonary Reserve

- High risk is variable definition
  - Pre-operative FEV1 < 50% predicted
  - Predicted post-operative FEV1 < 800 ml following lobectomy
  - Pre-operative DLCO < 50% predicted
  - VO2 max < 15 ml/m²
- Conventional = best supportive care

Anatomic Pattern of Emphysema

Heterogeneous
Innovative Treatment for High Risk Patients

• Evidence basis for treatment decisions in this setting is limited.
• Video-assisted thoracic surgery (VATS) lobectomy or segmentectomy is preferable particularly if ventilation/perfusion scan suggests minimal function in target lung (≤ 10%).


Combined LVRS and lung cancer surgery:
• 11 patients with NSCLC
• Preop mean FEV1 < 35%
• No deaths
• Median LOS = 5 days


U Pitt Brachytherapy

• I 125 sewn into Vicryl mesh
• 10,000- 12,000 cG to a depth – of 0.5 cm depth

Radiofrequency Ablation (RFA)

“The application of high frequency electric currents to heat and coagulate target tissue”

“Thermal lesion 7 Days Post-RFA”

• Wedge + brachytherapy does appear to decrease local recurrence rates relative to wedge alone.

Landreneau Ann Thorac Surg Feb 2006

—Current American College of Surgeon’s Oncology Group (ACOSOG) trial is ongoing to confirm this.
**PET Assessment of RFA**

Assessment of region of RFA with PET scanning.

RFA lesion did not take up the radiolabeled glucose (18-FDG); inflammatory response to RFA surrounding the thermal lesion did take up the FDG.

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**Innovative Treatment for Elderly Patients**

- Data are limited in this setting.
- Surveillance Epidemiology and End Results (SEER) data suggest if patient is over 72 then wedge and lobectomy have similar survival outcomes.
  

- Video-assisted thoracic surgery (VATS) lobectomy is feasible and has excellent outcomes.
  
  Shaw, Swanson et al Ann Thor Surg March 2007
  McKechnie Am Surg Sept 2005

- Alternative treatment in this population has not been examined.

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**Audience Response Question**

What is the best treatment option for an otherwise fit 80 year-old patient with a 3.5 cm non-small cell lung cancer?

1. Best supportive care
2. External beam radiation
3. Stereotactic radiation
4. VATS lobectomy
5. Radiofrequency ablation

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**Innovative Treatment in Special Populations**

Summary

- Surgical treatment appears feasible and relatively safe although careful diagnostic work-up and surgical expertise is important.
- Minimally invasive options may be particularly useful.
- Alternative treatment may be of benefit but adequate data are currently not available to make informed decisions.

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**Innovative Treatment for Elderly Patients**

Video-assisted thoracic surgery (VATS) lobectomy in octogenarians:

- 159 patients
- Mortality, 2.5%
- Mean LOS, 5.6 days
Questions & Answers