Surgery for the High-Risk Lung Cancer Patient

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Disclosures
Lung Cancer: 5-Year Survival Rates by Stage of Diagnosis

25% of cases

Local
70%

Regional
35%

Advanced
17%

Distant
1%
Introduction

- 10-15% patients who have early stage NSCLC are medically inoperable because of coexisting comorbidities
- Improvements in preop assessment, anesthesia, surgical techniques and postop care have allowed surgery in these patients
- Experience with other high risk cases (e.g. lung transplant) have led to novel thinking
Overview

- Definition of high risk patient
- Discuss controversies of lobectomy versus sublobar resection
- Review of ongoing trials and emerging technologies
In other words…

- Do we really need to do a lobectomy?
- Do we really need to do surgery at all for Stage I NSCLC?
CASE 1

- A 65-year-old white male former smoker (40 pack/year history) presents with a new spiculated mass measuring 2 cm near the apex of the right upper lobe (RUL). He has no other symptoms.

- He has an FEV1 of 1.20 (40% predicted) and DLCO of 19.3 (75% of predicted).

- A PET/CT scan shows FDG uptake only in the RUL mass. There is no evidence of activity elsewhere, and hilar/mediastinal nodes on the CT scan are normal in size.
Question: What is your next recommendation?

1. Continued observation with CT scans every 3 months
2. Surgical resection (sublobar resection)
3. Needle biopsy confirmation of cancer and radiofrequency ablation
4. Needle biopsy confirmation of cancer and external beam radiation
5. Needle biopsy confirmation of cancer and stereotactic body radiotherapy (SBRT)
Evarts Graham, M.D.
Lesser Resection

A. Upper lobe retracted downward and backward; hilar pleura incised. Anterior and apical-posterior segmental arteries ligated, suture ligated and divided

B. Upper lobe retracted anteriorly and downward, opening fissure. Segmental arteries successively ligated and divided from above downward with care to preserve superior segmental artery of lower lobe

C. Lung again drawn downward and superior pulmonary vein doubly ligated and divided

D. Upper lobe bronchus clamped preparatory to division and stapling close to its origin (as indicated by broken line), thus freeing upper lobe for removal
The Gold Standard

- Standard surgical care for early stage NSCLC is lobectomy with mediastinal LN staging
- 1995 LCSG: randomized trial lobectomy vs limited resection (wedge and segment)
- Lobectomy group had significantly lower loco-regional recurrence rate, but no difference between overall survival (p = 0.08) and disease free survival (p=0.09)
Advantages Lesser Resection

- Preservation of pulmonary function
- Wider applicability of minimally invasive techniques and thus improvement in QOL
- In the event of a second primary, enhancing curative surgical intervention
Challenges to Lobectomy

- Flaws in LCSG (small size, design, tumors up to 3 cm)
- Newer evidence that survival better ≤ 2 cm
- Retrospective trials in US and Japan showing equivalent survival in patients undergoing lobectomy and sublobar resection (especially age ≥ 75)
- Increasingly important given widespread CT screening, more higher risk surgical patients, and growing older population
The Ideal VATS Patient

- peripheral
- size <3 cm
- no deeper than 1 cm
- minimal adenopathy
Decision Factors in Choosing Surgical Therapies

- Tumor size
- Patient age
- Location (peripheral vs central)
- Stage of disease
- Medical co-morbidities
- Experience of team/treating physician
- Available modalities
Lung Cancer: Operative Criteria for Complete Resection

- can the patient tolerate a thoracotomy
- is there sufficient pulmonary reserve
- can the tumor be completely resected (primary, margins, LN basins)
Lung Cancer: Standard Criteria for Complete Resection

- FEV1 > 2 l
- MVV > 50% predicted
- DLCO > 40%
- Predicted postop FEV1 > 0.8 l or 40% predicted
- Absence of major cardiac disease
Lung Cancer:  
“Formula” for Operative Resection

- Eye-Ball: 20%
- Cardiac: 15%
- Stair Climbing: 15%
- PFTs: 50%
Morbidity and Mortality of Major Pulmonary Resections in Patients With Early-Stage Lung Cancer: Initial Results of the Randomized, Prospective ACOSOG Z0030 Trial

Mark S. Allen, MD, Gail E. Darling, MD, Taine T. V. Pechet, MD, John D. Mitchell, MD, James E. Herndon II, PhD, Rodney J. Landreneau, MD, Richard I. Inculet, MD, David R. Jones, MD, Bryan F. Meyers, MD, David H. Harpole, MD, Joe B. Putnam, Jr, MD, Valerie W. Rusch, MD, and the ACOSOG Z0030 Study Group*

Background. Little prospective, multiinstitutional data exist regarding the morbidity and mortality after major pulmonary resections for lung cancer or whether a mediastinal lymph node dissection increases morbidity and mortality.

Methods. prospectively collected 30-day postoperative data was analyzed from 1,111 patients undergoing pulmonary resection who were included in the analysis. Median age was 68 years (range, 23 to 89 years); 52% were men. Lobectomy was performed in 766 (75%) and pneumonectomy in 42 (4%). Pathologic stage was IA in 424 (42%), IB in 418 (41%), IIA in 76 (7%), IIIB in 97 (9%), and III in 45 (5%). Lymph node sampling was performed in 498 patients and lymph node dissection in 525. Operative mortality was 2.0% (10 of 498) for lymph node sampling and 0.76% (4 of 525) for lymph node dissection. Complications occurred in 38% of patients in each group. Lymph node dissection had a longer median operative time and greater total chest tube drainage (15 minutes, 121 mL, respectively). There was no difference in the median hospitalization, which was 6 days in each group (p = 0.490).

Conclusions. Complete mediastinal lymphadenectomy adds little morbidity to a pulmonary resection for lung cancer. These data from a current, multiinstitutional cohort of patients who underwent a major pulmonary resection constitute a new baseline with which to compare results in the future. (Ann Thorac Surg 2006;81:1013–20) © 2006 by The Society of Thoracic Surgeons
Lung Cancer: Surgical Mortality
(LCSG 1979, n=2220 vs ACOSOG 2006, n = 1026)

<table>
<thead>
<tr>
<th></th>
<th>1979</th>
<th>2006</th>
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<tbody>
<tr>
<td><strong>OVERALL</strong></td>
<td>4%</td>
<td>3%</td>
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<tr>
<td>Lesser resection</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>6%</td>
<td>0%</td>
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<tr>
<td>&lt;60 yo</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td>60-69 yo</td>
<td>4%</td>
<td>1%</td>
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<tr>
<td>&gt;70</td>
<td>7%</td>
<td>2%</td>
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Lung Volume Reduction Surgery

- 10-15% suspicious nodules found in LVRS candidates
- Most are Stage I tumors
- Allows lung cancer surgery in patients historically were inoperable because of bad lung function
Smoking  Alpha 1 antitrypsin
Lung Cancer: *Operating on the “High Risk Surgical Patient*

- 5%/segment
- Predicted postop PFT overestimated by 25% (Lanza, 1994)
- Quantitative V/Q scans data inexact
- LVRS experience
- FEV1 < 1l: improvement in pulmonary function
- COPD patient – relative sparing of lower lobes
- Improvements in anesthesia and postop care
  - Pain control
  - Pulmonary physiotherapy
Lung Cancer: “High Risk” Surgical Patient

- \( pCO_2 > 45 \text{ mm Hg} \)
- \( pO_2 < 50 \text{ mm Hg} \)
- Predicted postop FEV1 < 0.7 l or 40% predicted
- Age > 70
- MVO2 max < 10 ml/kg/min
- Poor exercise performance
Lung Cancer: Preop Strategies for the “High Risk Surgical Patient

- Smoking cessation
Lung Cancer: Preop Strategies for the “High Risk Surgical Patient

- Smoking cessation
- Optimize medical therapy (inhalers, steroids)

“My doctor says this little baby will open up just about anything”
Lung Cancer: Preop Strategies for the “High Risk Surgical Patient

- Smoking cessation
- Optimize medical therapy (inhalers, steroids)
- Pulmonary rehabilitation
Case 2

- An 85-yo female current smoker presents with a new 2 cm mass in the LLL. She has no other symptoms.
- PFTs: FEV1 of 0.90 l (32% predicted) and DLCO 16.9 (45% of predicted).
- PET-CT scan shows FDG uptake only in the LLL mass (no activity elsewhere, LN on the CT scan are normal in size).
- Bx: positive for adenocarcinoma.
Question: What is your recommendation? (she trusts you....)

1. Oral biologic therapy
2. Surgical resection (sublobar resection)
3. Radiofrequency ablation
4. Radiation therapy/ SBRT
5. Do nothing; she will die before the cancer becomes significant.
ACOSOG Clinical Trials

• High risk patient
• Less than lobectomy
• Other studies needing radiology expertise
Radiofrequency Ablation of Lung Cancers: 
*Ablate and Resect Trial (1997)*

- Steep learning curve
- 80-100% tumor kill – mean 90%
- 1 cm rim of cell death
- Does not address lymph node drainage basin
ACOSOG Z4033: A Pilot Study of Radiofrequency Ablation in High-risk Patients with Stage 1A Non-Small Cell Lung Cancer

Study Closed: 55 accrued
Study Closed:
226 accrued
Lobectomy vs Sub-Lobar Resection

• **1995**: Lung Cancer Study Group established lobectomy as the standard of care for T1N0

• 30% local recurrence rate for sub-lobar resection (1-2% for lobectomy)

• Within T1 stage, size did not influence recurrence but small numbers with ≤ 2 cm

• Coupled with increasing incidence of small nodules with CT screening has reopened the debate especially for BAC
Figure 3. Actuarial survival of patients undergoing anatomic segmentectomy (n = 239, blue) or lobectomy (n = 285, green) for NSCLC. (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)
Do we really need to do a lobectomy?

- CALGB 140503: A Phase III Randomized Trial of Lobectomy versus Sublobar Resection for Small (≤ 2 cm) Peripheral Non-Small Cell Lung Cancer

- RTOG 0618: SBRT for Operable Stage I NSCLC
CALGB 140503

**Schema**

**Pre-registration**

- **Surgery:** Confirm path diagnosis of NSCLC and N0 status by frozen exam of levels 4, 7, and 10 on the right side and 5 OR 6, 7, and 10 on the left side.

**Randomization**

- **Lobectomy** (if VATS lobectomy is planned, surgeons must be credentialed per Section 9.0)

- **Limited resection** (segmentectomy or wedge resection)

**Follow-up**

*Randomization is done intra-operatively after determining patient eligibility. CALGB CRAs must be able to access the web-based CALGB registration system during surgery to obtain treatment assignment and inform the surgeon of the assignment at the site. Patients who are not randomized intraoperatively will not be considered “on-study” and should follow the instructions in Section 6.1.*
A Randomized Phase III Study of Sublobar Resection versus Stereotactic Body Radiation Therapy in High Risk Operable Patients with Non-Small Cell Lung Cancer (NSCLC), 3 cm or Smaller

PI: Chris Fernando & Robert Timmerman

Awaiting approval

Endpoints: (primary) 3 year survival, (secondary) failure patterns and toxicity
Other ACOSOG Clinical Trials


- Z409X: Phase II Trial of Surgery for Resectable Early Stage (IA-IIB) Small Cell Lung Cancer Followed by Adjuvant Chemo

- Phase II study evaluating post-op radiotherapy in pts with completely resected NSCLC and N2 involvement
Surgical Treatment Summary

- Optimal: lobectomy (open or VATS)
- Marginal patient: sublobar resection
- Central lesions: lobectomy or segmentectomy
- Older patient/co-morbidities: VATS wedge
- Very poor PFTs and/or medically inoperable……..?
“All tumors should be in the bucket!”

-Halsted-
Case 2

- A very active 79-year-old white female former remote smoker (more than 30 years) is found to have a new ground glass opacity measuring 2 cm in the superior segment of the right lower lobe (RLL) during a screening cardiac scan.
- A PET/CT scan shows mild activity in the nodule.
- Transbronchial biopsies are suggestive of adenocarcinoma with BAC features.
- Her FEV1 is 2.2 l (75% predicted) and DLCO 18.3 (70% predicted).
- She has no significant medical issues.
Question: What is your recommendation?

1. Oral gefitinib
2. Surgical resection (sublobar resection)
3. Radiofrequency ablation
4. Radiation therapy/ SBRT
5. Do nothing; she will die before the cancer becomes significant.