Pretreatment Assessment of the Lung Resection Candidate

Peter Mazzone
Disclosures

- None related to the content of this talk.
Case 1

- 50 year old man diagnosed with a stage IIIA squamous cell cancer of the right upper lobe (N2 involvement) was treated with definitive chemoradiation.

- Cancer has persisted at the tumor site. Restaging suggests no nodal involvement. He has received maximal doses of radiation.

- He feels he could walk at least 1/2 mile. He rides a bicycle with his 11 year old grandson, perhaps 10-12 city blocks. He has a chronic cough and recently an episode of frank hemoptysis.

- He is a former smoker with known COPD receiving an ICS/LABA and LAMA for maintenance therapy. He does not have known cardiac risks.
Case 1

- PFTs - FEV$_1$ 1.38L, 39% predicted; DLCO 20.6, 70% predicted
Which statement is most correct about his preoperative evaluation?

A. He should have a cardiac stress test.
B. Segment methods for calculating predicted post-operative values will be more accurate than perfusion methods.
C. He should have some form of exercise test.
D. He should participate in pulmonary rehab prior to surgery.
Case 2

- A 70 year old smoker is seen with a localized adenocarcinoma of the lung. She currently feels well, exercising regularly without limitation from excessive dyspnea.

- She is an active smoker, down to 1 cigarette per week.

- She has been diagnosed with emphysema and started using maintenance tiotropium within the year.

- She developed a severe influenza infection 8 months ago. She required hospitalization and was discharged with home oxygen for 3 weeks.
Pulmonary function tests show severe obstruction (FEV₁ 0.95L, 45% predicted) and a reduced diffusing capacity (42% predicted). Thoracic surgery does not feel that a wedge resection is feasible.
Which statement is most correct about her preoperative evaluation?

A. Her surgery should be delayed until she has been abstinent from smoking for 2 months.

B. Her FEV₁ suggests the risk of complications from lung resection is low.

C. Her DLCO suggests the risk of complications from lung resection is moderate.

D. The location of her cancer increases the risk of complications from lung resection.
Overview

- Striking the Best Balance
- Comparison of Benefits and Harms
  - Considerations
- Making the Decision
Striking the Best Balance

**Benefits:** surgery (traditional anatomic, sublobar) vs. SBRT
- Overall survival
- Disease free survival
- Recurrence

**Harms:** surgery (traditional anatomic, sublobar) vs. SBRT
- Mortality
- Morbidity
- Long-term QOL

**Considerations:**
- Size
- Location
- Stage
- Availability

**Considerations:**
- Cardiopulmonary fitness
- Modifying interventions
- Experience
- Surgical approach
Lobe vs. Sub-lobar

# Lobe vs. Sublobar

<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Lobe (N)</th>
<th>W/S (N)</th>
<th>Lobe (5 YS; %)</th>
<th>W/S (5 YS; %)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginsberg</td>
<td>RCT</td>
<td>127</td>
<td>120</td>
<td>73</td>
<td>56</td>
<td>.06</td>
</tr>
<tr>
<td>Okada</td>
<td>Prospective</td>
<td>260</td>
<td>305</td>
<td>89</td>
<td>89</td>
<td>NS</td>
</tr>
<tr>
<td>Koike</td>
<td>Prospective</td>
<td>159</td>
<td>74</td>
<td>90</td>
<td>89</td>
<td>NS</td>
</tr>
<tr>
<td>Kates</td>
<td>SEER</td>
<td>1402</td>
<td>688</td>
<td>HR 1.12</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Wisnivesky</td>
<td>SEER</td>
<td>969</td>
<td>196</td>
<td>HR 1.10</td>
<td></td>
<td>NS</td>
</tr>
</tbody>
</table>

Howington, Chest 2013.
## Wedge vs. SBRT

<table>
<thead>
<tr>
<th></th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LR</td>
</tr>
<tr>
<td>SBRT</td>
<td>4</td>
</tr>
<tr>
<td>Wedge</td>
<td>20</td>
</tr>
<tr>
<td>P-value</td>
<td>.07</td>
</tr>
</tbody>
</table>

Lobe vs. SBRT - Propensity Matched

- VATS lobectomy from 6 hospitals, SBRT from one
- Propensity score matching based on cTNM stage, age, gender, Charlson comorbidity score, lung function, and performance status.
- 64 SBRT and 64 VATS lobectomy patients matched from 527 SBRT and 86 VATS
- Locoregional control better in SBRT group at 1 and 3 years
- Distant recurrences and overall survival not significantly different
Lobe vs. SBRT - Propensity Matched

Comparative Efficacy

3-year overall survival (95% CI):
SABR 95% (85-100); surgery 79% (64-97)
HR (95% CI): 0.14 (0.017-1.190)
log-rank p=0.037

3 year recurrence-free survival (95% CI):
SABR 86% (74-100); surgery 80% (65-97)
HR (95% CI): 0.69 (0.21-2.29)
log-rank p=0.5379

Surgical Mortality

## Surgical Morbidity

<table>
<thead>
<tr>
<th>Complication</th>
<th>Actual Rate (%)</th>
<th>NSQIP Predicted (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious</td>
<td>16.6</td>
<td>8.8</td>
</tr>
<tr>
<td>Any</td>
<td>17.3</td>
<td>13.0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>6.0</td>
<td>3.2</td>
</tr>
<tr>
<td>Cardiac</td>
<td>1.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Site infection</td>
<td>1.8</td>
<td>1.6</td>
</tr>
<tr>
<td>UTI</td>
<td>4.0</td>
<td>1.8</td>
</tr>
<tr>
<td>VTE</td>
<td>4.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Renal failure</td>
<td>1.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Return to OR</td>
<td>4.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Death</td>
<td>1.0</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Impact on Pulmonary Function

- **FEV₁**: 84-91% of pre-operative values when measured up to 6 months after lobectomy, and 64-66% after pneumonectomy.¹⁻³
- **DLCO**: 89-96% of pre-operative values when measured up to 6 months after lobectomy, and 72-80% after pneumonectomy.¹⁻³
- **VO₂ peak**: 87-100% of pre-operative values after lobectomy, and 71-89% after pneumonectomy.¹⁻³ 70% of baseline 3 years after pneumonectomy.⁴

Impact on Pulmonary Function

Sub-lobar Resection

- 12-month post-operative FEV₁ of 93.3% of the pre-operative value in patients with normal lung function who underwent segmentectomy.[1] 87.3% of the pre-operative value in those who had a lobectomy.

- FVC, FEV₁, maximum voluntary ventilation (MVV), and DLCO all decreased after lobectomy for stage I lung cancer.[2] Only the DLCO was decreased in those who had a segmentectomy.

- 40 patients who had a thoracotomy, 13 wedge resections, 14 lobectomies, and 13 a thoracotomy alone (inoperable tumor).[3] No decline in measures of pulmonary function or exercise capacity in the wedge resection group. Similar declines were seen in the lobectomy and thoracotomy alone groups.

# Impact on Pulmonary Function

<table>
<thead>
<tr>
<th></th>
<th>1-2 Segments</th>
<th>3-5 Segments</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; (L)</td>
<td>0.1</td>
<td>0.3</td>
<td>0.003</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; (%) predicted</td>
<td>4.3</td>
<td>8.2</td>
<td>0.055</td>
</tr>
<tr>
<td>DLCO (ml/min/mmHg)</td>
<td>1.3</td>
<td>2.4</td>
<td>0.015</td>
</tr>
<tr>
<td>DLCO (%) predicted</td>
<td>3.6</td>
<td>5.9</td>
<td>0.280</td>
</tr>
</tbody>
</table>

Quality of Life

- Lower than the general population.
- Physical measures decline at the 1 month post-op time but return to baseline by 3 months post-op.
- Mental measures may not decline throughout.
- Poor correlation with measures of pulmonary function or other high-risk patient features.

# SBRT Toxicities

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central airway toxicity</td>
<td>Tumors close to the bronchial tree</td>
</tr>
<tr>
<td>Esophageal toxicity</td>
<td>Volume of esophagus exposed to higher doses of radiation</td>
</tr>
<tr>
<td>Vascular injury including hemoptysis</td>
<td>Central location, squamous cell, cavitation, endobronchial involvement</td>
</tr>
<tr>
<td>Radiation pneumonitis</td>
<td>0-29%, grade 3-5 uncommon, mean dose, V5, V20, lower zone, ILD</td>
</tr>
<tr>
<td>Other pulmonary toxicities</td>
<td>Rare</td>
</tr>
<tr>
<td>Chest wall and skin toxicities</td>
<td>Peripheral lesions, younger age, smoking, obesity</td>
</tr>
<tr>
<td>Brachial plexopathy</td>
<td>Apical tumors, dose threshold</td>
</tr>
<tr>
<td>Vagus nerve injury</td>
<td>Central tumor</td>
</tr>
</tbody>
</table>

Kang, Cancers 2015.
# SBRT Toxicities

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of Patients by Grade (N=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Blood or bone marrow</td>
<td>2</td>
</tr>
<tr>
<td>Coagulation</td>
<td>1</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>1</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>2</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1</td>
</tr>
<tr>
<td>Infection</td>
<td>2</td>
</tr>
<tr>
<td>Metabolic</td>
<td>1</td>
</tr>
<tr>
<td>Muskuloskeletal</td>
<td>3</td>
</tr>
<tr>
<td>Neurology</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>8</td>
</tr>
<tr>
<td><strong>Most severe</strong></td>
<td>13 (24%)</td>
</tr>
</tbody>
</table>

Timmerman, JAMA 2010.
## Impact on Pulmonary Function

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>GOLD I-II</th>
<th>GOLD III-IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, L</td>
<td>0.14</td>
<td>0.13</td>
<td>0.06</td>
</tr>
<tr>
<td>FEV₁, %</td>
<td>2.6</td>
<td>3.6</td>
<td>0.0</td>
</tr>
<tr>
<td>FVC, L</td>
<td>0.19</td>
<td>0.07</td>
<td>0.08</td>
</tr>
<tr>
<td>FVC, %</td>
<td>4.8</td>
<td>2.4</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Takeda, Chest 2013.
Impact on QOL

Lagerwaard, J Thorac Oncol 2012.
Comparative Early Mortality

Comparative Morbidity

- **SBRT** – 3 treatment related grade 3 adverse events (2 – dyspnea/cough, 3 – chest pain, 1 – fatigue)

- **Surgical resection** – 1 died of surgical complications, 12 with grade 3-4 adverse events (1 – grade 4 dyspnea, 4 – grade 3 dyspnea, 2 – lung infections, 4 – chest pain, 1 each – bleeding, fistula, hernia, anemia, fatigue, nausea, weight loss, arrhythmia)

## Cardiac Risk

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coefficients</th>
<th>SEM</th>
<th>p Value</th>
<th>Bootstrap %b</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHD</td>
<td>1.4</td>
<td>0.3</td>
<td>&lt;0.0001</td>
<td>98%</td>
</tr>
<tr>
<td>Creatinine &gt; 2 mg/dL</td>
<td>0.97</td>
<td>0.5</td>
<td>0.06</td>
<td>54%</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.32</td>
<td>0.4</td>
<td>0.003</td>
<td>82%</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>1.46</td>
<td>0.3</td>
<td>&lt;0.0001</td>
<td>99%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ThRCRI Score</th>
<th>Risk Class</th>
<th>Number of Cases</th>
<th>Major Cardiac Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>A</td>
<td>1,173</td>
<td>18 (1.5%)</td>
</tr>
<tr>
<td>1–1.5</td>
<td>B</td>
<td>468</td>
<td>27 (5.8%)</td>
</tr>
<tr>
<td>2–2.5</td>
<td>C</td>
<td>16</td>
<td>3 (19%)</td>
</tr>
<tr>
<td>&gt;2.5</td>
<td>D</td>
<td>39</td>
<td>9 (23%)</td>
</tr>
</tbody>
</table>

Standard Lung Function Testing

Absolute and percent predicted FEV₁:

- Pre-operative values of **2L for pneumonectomy and 1.5L for lobectomy** have been suggested. FEV₁ above these thresholds = low risk of mortality.¹⁻³

- Pre-operative **FEV₁ < 60% predicted** - OR of 2.7 for respiratory complications and 1.9 for 30-day mortality.⁴

- The mean FEV₁ was 75% predicted in uncomplicated resections and 66% in complicated resections.⁵

- A value of 80% predicted or higher has been suggested in a reported algorithm as a cutoff.⁶

Diffusing capacity

- The DLCO is a **predictor of post-operative complications including death, length of hospital stay and hospital costs**.\(^1\)-\(^3\)

- Individuals with a **pre-operative DLCO less than 60% predicted** had a higher risk of respiratory complications, hospitalizations for respiratory compromise, and lower median dyspnea scores.\(^4\)

- The mean DLCO was 77% predicted in those without complications and 67% in those with.\(^5\)

---

The FEV$_1$ and DLCO have only a modest correlation. 43% of patients with an FEV$_1$ > 80% predicted had a DLCO < 80% predicted.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Number of patients</th>
<th>FEV$_1$–DLCO correlation coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire dataset</td>
<td>872</td>
<td>0.38</td>
</tr>
<tr>
<td>Elderly (&gt;70 years old)</td>
<td>330</td>
<td>0.38</td>
</tr>
<tr>
<td>Young (&lt;70 years old)</td>
<td>542</td>
<td>0.39</td>
</tr>
<tr>
<td>FEV$_1$ &gt; 80%</td>
<td>508</td>
<td>0.20</td>
</tr>
<tr>
<td>FEV$_1$ &lt; 80%</td>
<td>364</td>
<td>0.23</td>
</tr>
<tr>
<td>ppoFEV$_1$ &lt; 40%</td>
<td>50</td>
<td>0.19</td>
</tr>
<tr>
<td>ppoFEV$_1$ &gt; 40%</td>
<td>822</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Predicted Post-Operative Values

Comparison

- A study of 44 subjects comparing radionuclide perfusion scan, quantitative CT, and 3 segment methods.
  - **Perfusion imaging outperformed other methods** for all measures.
  - **All other methods performed well in those who had a lobectomy**. Segment methods did not perform well in those who had a pneumonectomy.\(^1\)

- Perfusion imaging prediction outperformed the segment method in 32 patients who underwent pneumonectomy.\(^2\)

Predicted Post-Operative Values

- The ppoFEV$_1$ is an independent predictor of complications, including mortality.$^{1-3}$
- All with ppoFEV$_1$ less than 30% developed respiratory failure or died.$^4$
- 70% with a ppoFEV$_1$ less than 35% experience complications.$^5$
- Individuals with a ppoFEV$_1$ greater than 34% or greater than 58% of the pre-operative value have a decreased post-operative mortality.$^6,7$
- No deaths if ppoFEV$_1$ greater than 40% and a 50% mortality rate in those less than 40%.$^8$

Predicted Post-Operative Values

- The ppoDLCO was a **predictor of mortality**.¹
- Others determined it to be an **independent predictor of pulmonary complications, morbidity, and death**.²⁻⁴
- A **ppoDLCO < 40%** was a predictor of post-operative complications in patients with a normal FEV₁.⁵
- The predicted postoperative product (PPP) was found to be the best predictor of surgical mortality.
  - A PPP less than 1650 was found in 75% of those who died and 11% of those who survived surgery.⁶

CHEST Guidelines

- In patients with lung cancer being considered for surgery, it is recommended that both FEV\textsubscript{1} and DLCO be measured in all patients and that both ppoFEV\textsubscript{1} and ppoDLCO are calculated.
  - For pneumonectomy candidates, we suggest to use Q scan to calculate predicted postoperative values of FEV\textsubscript{1} or DLCO.
  - For lobectomy patients, segmental counting is indicated to calculate predicted postoperative values of FEV\textsubscript{1} or DLCO.

Brunelli, Chest 2013.
In patients with lung cancer being considered for surgery, if both ppoFEV$_1$ and ppoDLCO > 60% predicted, no further tests are recommended.

Values of both ppoFEV$_1$ and ppoDLCO > 60% indicate low risk for perioperative death and cardiopulmonary complications following resection including pneumonectomy.
Exercise Testing

- The altitude reached on a stair climbing test was associated with cardiopulmonary complications, mortality, and costs. A cutoff of 12 m altitude had a PPV of 40% for morbidity and 13% for mortality with a NPV of 78% for morbidity and 97% for mortality.\(^1\)

- Those unable to perform a stair climbing test due to underlying co-morbidities have an increased risk of mortality after major lung resection.\(^2\)

- A cutoff of 18 m was found to be an independent predictor of 5-year survival, both cancer and non-cancer related in a cohort with resected stage I NSCCa.\(^3\)

## Exercise Testing

<table>
<thead>
<tr>
<th>Stair-Climbing Cutoff, m</th>
<th>Morbidity</th>
<th></th>
<th>Mortality</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PPV</td>
<td>NPV</td>
<td>PPV</td>
<td>NPV</td>
</tr>
<tr>
<td>12</td>
<td>40%</td>
<td>78%</td>
<td>13%</td>
<td>97%</td>
</tr>
<tr>
<td>14</td>
<td>31%</td>
<td>78%</td>
<td>6%</td>
<td>97%</td>
</tr>
<tr>
<td>18</td>
<td>28%</td>
<td>80%</td>
<td>5%</td>
<td>98%</td>
</tr>
<tr>
<td>22</td>
<td>28%</td>
<td>83%</td>
<td>5%</td>
<td>99%</td>
</tr>
</tbody>
</table>

Exercise Testing

Relationship between shuttle walk distance and surgical outcome in all patients undergoing surgical resection ($n=103$)

<table>
<thead>
<tr>
<th>Shuttle distance (m)</th>
<th>Poor outcome</th>
<th>Good outcome</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>$&lt;250$</td>
<td>8 (66%)</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>$&lt;300$</td>
<td>10 (44%)</td>
<td>13</td>
<td>23</td>
</tr>
<tr>
<td>$&lt;400$</td>
<td>19 (37%)</td>
<td>33</td>
<td>52</td>
</tr>
<tr>
<td>$&gt;400$</td>
<td>15 (29%)</td>
<td>36</td>
<td>51</td>
</tr>
<tr>
<td>140–780</td>
<td>34 (33%)</td>
<td>69</td>
<td>103</td>
</tr>
</tbody>
</table>
Exercise Testing

- A 6-minute walk test distance of 1000 feet or greater has been found to predict positive outcome.¹

- The 6-minute walk test distance was the best predictor of post-operative respiratory failure.²

- HRR <12 1 minute after 6-minute walk test was an independent predictor of cardiopulmonary complications with an OR of 4.3.³

- A distance of 500 m and 100% predicted used to predict risk of postoperative complications (OR 2.6) and prolonged hospitalization.⁴

Exercise Testing

- VO₂ peak has been reported to be a predictor of post-operative complications including post-operative and long-term mortality.¹,²

## Exercise Testing

<table>
<thead>
<tr>
<th>Author</th>
<th>Findings (VO₂ peak in ml/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olsen</td>
<td>Mean VO₂ peak 11.3 in those without complications and 7.8 in those with</td>
</tr>
<tr>
<td>Bolliger</td>
<td><strong>ppoVO₂ peak &lt; 10 – 100% mortality</strong></td>
</tr>
<tr>
<td>Bolliger</td>
<td>Mean VO₂ peak 84% predicted in those without complications and 61% in those with</td>
</tr>
<tr>
<td>Larsen</td>
<td>VO₂ peak &lt; 50% predicted – high mortality</td>
</tr>
<tr>
<td>Smith</td>
<td><strong>All with VO₂ peak &lt; 15 had complications</strong></td>
</tr>
<tr>
<td>Bechard</td>
<td>VO₂ peak &lt; 10 – 29% mortality; &gt; 20 – 0%</td>
</tr>
<tr>
<td>Win</td>
<td>Mean VO₂ peak 92% predicted in those with a satisfactory outcome and 66% in others</td>
</tr>
<tr>
<td>Brutsche</td>
<td>VO₂ peak and extent of resection independent predictors of complications</td>
</tr>
<tr>
<td>Loewen</td>
<td>VO₂ peak &lt; 65% or 16 more likely to have complications; &lt;15 – resp failure or death</td>
</tr>
<tr>
<td>Win</td>
<td>VO₂ peak 91.7% predicted - satisfactory outcome, 65.9% in those with a poor outcome</td>
</tr>
<tr>
<td>Brunelli</td>
<td><strong>No deaths if VO₂ peak &gt; 20, 13% mortality if VO₂ peak was &lt; 12</strong></td>
</tr>
</tbody>
</table>
### Table 5—Positive and Negative Predictive Probabilities of Poor Outcome (\( \text{VO}_2 \text{peak \% Predicted} \))

<table>
<thead>
<tr>
<th>Threshold, %</th>
<th>Good Outcome if ( \text{VO}_2 ) Is Greater Than Threshold</th>
<th>Poor Outcome if ( \text{VO}_2 ) Is Less Than or Equal to Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>85/96 (89)</td>
<td>2/3 (67)</td>
</tr>
<tr>
<td>60</td>
<td>77/85 (91)</td>
<td>5/14 (36)</td>
</tr>
<tr>
<td>65</td>
<td>71/76 (93)</td>
<td>8/23 (35)</td>
</tr>
<tr>
<td>70</td>
<td>65/70 (93)</td>
<td>8/29 (28)</td>
</tr>
<tr>
<td>75</td>
<td>57/61 (93)</td>
<td>9/38 (24)</td>
</tr>
</tbody>
</table>

*Data are presented as No. of patients/total patients (%).*
204 patients had a CPET regardless of their standard lung function parameters:

- CPET did not add to risk stratification if the FEV$_1$ and DLCO were > 80%.

- Either FEV$_1$ or DLCO < 80%, but both ppoFEV$_1$ and ppoDLCO > 40%, there were 5 deaths, 3 of which occurred in patients with a peak VO$_2$ < 12 ml/kg/min.

- ppoFEV$_1$, ppoDLCO, or both < 40% tolerated resection if their peak VO$_2$ was > 10 ml/kg/min.

- ppoFEV$_1$ < 30% or PPP < 1650 tolerated resection reasonably well if the peak VO$_2$ was > 10 ml/kg/min.

Brunelli, Chest 2009.
CHEST Guidelines

- In patients with lung cancer being considered for surgery, if either the ppoFEV$_1$ or ppoDLCO are < 60% predicted and both are above 30% predicted, it is recommended that a low technology exercise test (stair climb or shuttle walk test) is performed.

Brunelli, Chest 2013.
In patients with lung cancer being considered for surgery, with either a ppoFEV$_1$ < 30% predicted or a ppoDLCO < 30% predicted performance of a formal cardiopulmonary exercise test (CPET) with measurement of maximal oxygen consumption (VO$_2$ max) is recommended.

- Either ppoFEV$_1$ < 30% predicted or a ppoDLCO < 30% predicted indicate an increased risk for perioperative death and cardiopulmonary complications with anatomic lung resection.
In patients with lung cancer being considered for surgery who walk < 40 shuttles (or < 400 m) on the shuttle walk test or climb < 22 m at symptom limited stair climbing test performance of a formal cardiopulmonary exercise test (CPET) with measurement of maximal oxygen consumption (VO₂ max) is recommended.

- Walking < 40 shuttles (or < 400 m) on the SWT or climbing < 22 m at symptom limited stair climbing test suggests an increased risk for perioperative death and cardiopulmonary complications with anatomic lung resection.
In patients with lung cancer being considered for surgery, with a $\text{VO}_2\text{max} < 10\text{ ml/kg/min or < 35\% predicted}$, it is recommended that they are counseled about minimally invasive surgery, sublobar resections or nonoperative treatment.

For values of $\text{VO}_2\text{max}$ in the range of 10 to 15 mL/kg/min an increased risk of mortality is expected. However, data are less definitive for making decisions based solely on those values without taking into account other factors like ppoFEV$_1$ and DLCO as well as patient comorbidities.
Considerations
Considerations

- **COPD**: smaller decline in FEV$_1$ after lobectomy (0-8%) compared to those without COPD (16-20%).$^{1-3}$ The fall in DLCO and VO$_2$ max was more variable (3-20% for DLCO, 0-21% for VO$_2$ max).$^{2-3}$

- **Location**: can influence the degree of loss of lung function.$^3$

- **Recovery**: pulmonary function and exercise capacity increased from the time of surgery through 6 months after lobectomy. Not beyond 3 months post pneumonectomy.$^{3-5}$

Considerations

LVRSx

- In select patients with severe emphysema, removal of the most emphysematous portion of their lung can lead to improvements in lung function.[1-3]

- Localized lung cancer has been found in approximately 5% of those undergoing lung volume reduction surgery.[4]

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Cancer</th>
<th>Preop FEV₁ (%)</th>
<th>Postop FEV₁ (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choong</td>
<td>21</td>
<td>21</td>
<td>29</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>Edwards</td>
<td>14</td>
<td>14</td>
<td>40.7</td>
<td>41.5</td>
<td>14</td>
</tr>
<tr>
<td>DeRose</td>
<td>14</td>
<td>9</td>
<td>27</td>
<td>35</td>
<td>7</td>
</tr>
<tr>
<td>DeMeester</td>
<td>5</td>
<td>5</td>
<td>29.6</td>
<td>42.3</td>
<td>0</td>
</tr>
<tr>
<td>Ojo</td>
<td>11</td>
<td>3</td>
<td>26.2</td>
<td>38.5</td>
<td>0</td>
</tr>
<tr>
<td>McKenna</td>
<td>51</td>
<td>11</td>
<td>21.7</td>
<td>49</td>
<td>0</td>
</tr>
<tr>
<td>Pompeo</td>
<td>16</td>
<td>16</td>
<td>0.92*</td>
<td>1.20*</td>
<td>0</td>
</tr>
</tbody>
</table>

Considerations

- Patients who undergo resection for lung cancer at hospitals performing large numbers of such procedures have fewer peri-operative deaths and survive longer than those whose surgery is performed at hospitals with a low volume.¹ ²

Considerations

- Patients who see physicians with a higher volume are more likely to have their cancers histologically confirmed, and to receive active treatment for their cancer.\(^1\)

- Patients who are diagnosed by or referred to a specialist within 6 months of diagnosis have been shown to have a lower risk of death.\(^2\)

- In-hospital mortality post lung resection is lower at teaching hospitals than non-teaching hospitals independent of patient volume.\(^3\)

### Open Thoractomy vs. VATS

<table>
<thead>
<tr>
<th></th>
<th>Open (%)</th>
<th>VATS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory complications</td>
<td>32</td>
<td>27</td>
</tr>
<tr>
<td>Extended length of stay</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>Mortality</td>
<td>4</td>
<td>2</td>
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</tbody>
</table>

### Surgical Approach – VATS in the Elderly

<table>
<thead>
<tr>
<th></th>
<th>VATS</th>
<th>Thoracotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay (days)</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>ICU admission (%)</td>
<td>2.5</td>
<td>14.8</td>
</tr>
<tr>
<td>Discharge to rehab (%)</td>
<td>5.0</td>
<td>22.5</td>
</tr>
<tr>
<td>30 day readmission (%)</td>
<td>0</td>
<td>8.6</td>
</tr>
</tbody>
</table>

*Port, Ann Thorac Surg 2011.*
VATS vs. Thoracotomy Survival

Survival Rate (%)

Time After Surgery (years)

HR, 0.91; 95% CI, 0.78 to 1.05; P = .18

Boffa, J Clin Oncol 2018.
Surgical Approach – Sublobar Resection in LPA

Cox, J Thorac Oncol 2017.
Considerations

- Those who continue to smoke within one month of a pneumonectomy are at increased risk for developing major pulmonary events.\(^1\)
- Unable to find a paradoxical increase in pulmonary complications among those who **quit smoking** within two months.\(^2\)
- Review found **smoking abstinence led to fewer PPCs**, though the optimal timing of cessation not identified.\(^3\)
- The sooner one is able to quit, the more likely it is that he or she will remain abstinent after surgery.\(^4\)

Peri-Operative Considerations - Rehab

In patients with lung cancer it is recommended that they be assessed for curative surgical resection by a multidisciplinary team, which includes a thoracic surgeon specializing in lung cancer, medical oncologist, radiation oncologist and pulmonologist.
CHEST Guidelines

- In all patients with lung cancer being considered for surgery who are actively smoking, **tobacco dependence treatment** is recommended.

- In patients with lung cancer being considered for surgery and deemed at **high risk** (as defined by the proposed functional algorithm, ie, ppoFEV$_1$ or ppoDLCO < 60% and VO$_2$ max < 10 mL/kg/min or < 35%), **preoperative or postoperative pulmonary rehabilitation** is recommended.
Ability to Select

## Ability to Select

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pulmonologist</th>
<th>Thoracic Surgeon</th>
<th>Radiation Oncologist</th>
</tr>
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<tbody>
<tr>
<td>CCI</td>
<td>32</td>
<td>66</td>
<td>43</td>
</tr>
<tr>
<td>WHO-PS</td>
<td>33</td>
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<td>21</td>
</tr>
<tr>
<td>Age</td>
<td>17</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Patient preference</td>
<td>16</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>COPD GOLD</td>
<td>2</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

Hopman, Radiother Oncol 2015.
Case 1

- 50 year old man diagnosed with a stage IIIA squamous cell cancer of the right upper lobe (N2 involvement) was treated with definitive chemoradiation.

- Cancer has persisted at the tumor site. Restaging suggests no nodal involvement. He has received maximal doses of radiation.

- He feels he could walk at least 1/2 mile. He rides a bicycle with his 11 year old grandson, perhaps 10-12 city blocks. He has a chronic cough and recently an episode of frank hemoptysis.

- He is a former smoker with known COPD receiving an ICS/LABA and LAMA for maintenance therapy. He does not have known cardiac risks.
Case 1

- PFTs - FEV₁ 1.38L, 39% predicted; DLCO 20.6, 70% predicted
Which statement is most correct about his preoperative evaluation?

A. He should have a cardiac stress test.
B. Segment methods for calculating predicted post-operative values will be more accurate than perfusion methods.
C. He should have some form of exercise test.
D. He should participate in pulmonary rehab prior to surgery.
Case 1

- Quantitative perfusion scan - 16% to right upper and 16% to right lower.
- $\text{ppoFEV}_1$ - 33% predicted; $\text{ppoDLCO}$ 59% predicted
- Walk 6 – 330m, 63% predicted, SpO2 95% on RA at rest and 91% during the walk, HRR 16
- CPET - peak VO$_2$ 21.4 ml/kg/min, 67% predicted, MVV 34% predicted, breathing reserve depleted at 1.5%, pO$_2$ at baseline 68 mmHg.
This patient would be considered:

A. Low risk
B. Moderate risk
C. High risk
D. Prohibitive risk
Algorithm for Thoracotomy and Major Anatomic Resection (Lobectomy or greater)

- Positive high-risk cardiac evaluation

- ppoFEV1 or ppoDLCO <30%

- VO2max <10 ml/kg/min or < 35%
  - High Risk

- VO2max 10-20 ml/kg/min or 35%-75%
  - Moderate Risk

- ppoFEV1 or ppoDLCO < 60% AND both > 30%

- Stair climb or Shuttle walk

- VO2max >20 ml/kg/min or > 75%
  - Low Risk

- ppoFEV1 and ppoDLCO > 60%

- SCT <22m OR SWT < 400m

- >22m OR >400m

- ppoFEV1% ppoDLCO%
Case 1: Nuances

- No other treatment option
- Young age
- Upper lobe location
- Ventilatory limitation
- Prior treatment
Case 2

- A 70 year old smoker is seen with a localized adenocarcinoma of the lung. She currently feels well, exercising regularly without limitation from excessive dyspnea.
- She is an active smoker, down to 1 cigarette per week. She has been diagnosed with emphysema and started using maintenance tiotropium within the year. She developed a severe influenza infection 8 months ago. She required hospitalization and was discharged with home oxygen for 3 weeks.
Case 2

- Pulmonary function tests show severe obstruction (FEV₁ 0.95L, 45% predicted) and a reduced diffusing capacity (42% predicted). Thoracic surgery does not feel that a wedge resection is feasible.
Which statement is most correct about her preoperative evaluation?

A. Her surgery should be delayed until she has been abstinent from smoking for 2 months.

B. Her FEV$_1$ suggests the risk of complications from lung resection is low.

C. Her DLCO suggests the risk of complications from lung resection is moderate.

D. The location of her cancer increases the risk of complications from lung resection.
Case 2

- Pulmonary function tests show severe obstruction (FEV$_1$ 0.95L, 45% predicted) and a reduced diffusing capacity (42% predicted).
  - ppoFEV1 – 33%, ppoDLCO – 31%
- A cardiopulmonary exercise test showed a peak VO$_2$ of 17 ml/kg/min (80% predicted).
  - There was ventilatory limitation (no breathing reserve at peak exercise) and her SpO$_2$ fell from 96% on RA at rest to 92% during the test.
This patient would be considered:

A. Low risk
B. Moderate risk
C. High risk
D. Prohibitive risk
Algorithm for Thoracotomy and Major Anatomic Resection (Lobectomy or greater)

- Positive high-risk cardiac evaluation
- ppoFEV1 or ppoDLCO <30%
- ppoFEV1 or ppoDLCO <60% AND both >30%
- ppoFEV1 and ppoDLCO >60%

Algorithm:

- Positive low-risk or Negative cardiac evaluation
- ppoFEV1% ppoDLCO%

CPET:

- SCT <22m OR SWT < 400m
- Stair climb or Shuttle walk

High Risk:
- VO2max <10 ml/kg/min Or < 35%

Moderate Risk:
- VO2max 10-20 ml/kg/min Or 35%-75%

Low Risk:
- VO2max >20 ml/kg/min Or >75%
- >22m OR >400m
Case 2: Nuances

- Other reasonable treatment option
- Upper lobe predominant emphysema, lower lobe resection
- Ventilatory limitation
- Patient values
Striking the Best Balance

**Benefits:** surgery (traditional anatomic, sublobar) vs. SBRT
- Overall survival
- Disease free survival
- Recurrence

**Harms:** surgery (traditional anatomic, sublobar) vs. SBRT
- Mortality
- Morbidity
- Long-term QOL

**Considerations:**
- Size
- Location
- Stage
- Availability

**Considerations:**
- Cardiopulmonary fitness
- Modifying interventions
- Experience
- Surgical approach
Summary

- Striking the best balance
- Comparison of Benefits and Harms
  - Considerations
- Making the Decision