VATS after induction therapy: Effective and Beneficial Tips on Strategy

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Scott J. Swanson, M.D.
Professor of Surgery, Harvard Medical School
Director of Minimally Invasive Thoracic Surgery, BWH
Associate Chief of Surgery, Dana Farber Cancer Institute
Disclosures

• Teach learning sessions for ethicon and covidien
Lung surgery after chemotherapy +/- radiation

- Higher morbidity and possibly mortality
- Efficacy is thought to be controversial
- Wide variation as to how well this is incorporated around the United States
- Indication for induction therapy
  - N2 and in some situations N3 disease
  - Locally advanced tumors (T3 or T4)
Significant mortality from surgery after induction therapy

Radiotherapy and chemotherapy with or without surgical resection for stage III NSCLC. Albain et al Lancet 2009
Safety and feasibility of lobectomy following concurrent chemotherapy and high dose radiation for stage IIIa NSCLC: pooled surgical results of NRG oncology RTOG 0229 and 0839

Donnington et al AATS Boston 2017

- 2 prospective trials, resectable N2 Stage IIIa NSCLC treated with concurrent chemo/full dose XRT, primary endpoint mediastinal LN sterilization
- Weekly carbo/taxol and RT 60G
- N=118, >87% xrt and chemo, 91 (77%) to OR
- Lobectomy 81, px-6, bilobe-3, sleeve lobe – 1
- R0 in 81% (74), 10/12 lobes completed by VATS
- 30d mortality = 4 (4%), lobectomy = 1 (1.4%)
- Surgery is safe after chemo/xrt for stage IIIa
Thoracoscopic (VATS) Lobectomy

- Now done in >50% of lobectomies in U.S.
- Outcome data shows superiority of VATS Lobe
  - Complication rate
  - Peri-operative mortality
  - Hospital LOS
  - Discharge independence
  - Functional recovery
  - Pain assessment/tolerance
  - Chemotherapy tolerance

Nicastri D, Wisnivesky J, Dembitzer F, Litle V, Yun J, Chin C and Swanson S. JTCS March 2008
Locally Advanced Disease

- Chest wall invasion
- Following neoadjuvant treatment for T4 and/or N2 disease
- Invasion of other structures such as diaphragm, SVC, pericardium
Advances in Technology

- Stapler
- Energy devices
- Sealants
Important Technology - Energy

• Test ultrasonic energy source to control pulmonary vessels in 9 pigs followed 1-6 wks
• 76% pulmonary arteries, 92% veins – controlled
• When PA $\leq$ 5 mm, veins $\leq$ 7 mm, all worked
• Histopath showed acute coagulation necrosis at 1 wk and normal healing at 6 wks
• Fast speed worked better than slow speed

Energy-Based Ligation of Pulmonary Vessels: A Six-Year Experience With Ultrasonic Shears in Video-Assisted Thoracoscopic Lobectomy and Segmentectomy

Abby White, DO, Suden Kucukak, MD, Daniel N. Lee, BS, and Scott J. Swanson, MD

Department of Surgery, Division of Thoracic Surgery, Brigham and Women’s Hospital, Boston, Massachusetts

Conclusions. Energy-based ligation of small-diameter pulmonary vessels is a safe and useful adjunct in anatomic VATS resection and a viable alternative to mechanical stapling. Its narrow profile and thin blades make it ideal for ligation of pulmonary vasculature, particularly where the size and necessary clearance of mechanical staplers prohibit safe dissection.
Rationale for VATS following induction therapy

• Can re-assess chest
  – Any sign of disseminated disease?
  – Status of lymph nodes
  – Difficult areas for resection

• Most cases can accomplish compete resection by VATS and confer all the advantages of VATS – mortality, morbidity, pain, function, marginal patient
Personal Observations

38 vats lobe after chemoxrt for N2(+) NSCLC over 7yrs
no mortality and overall 40% conversion (65 total N2)

- Imaging often cannot determine areas of technical concern
- Tissue planes are not always easily identifiable
- More sharp dissection is needed
- Conversion is more likely but still less than half and improves with time
- May need more alternative approaches such as:
  - posterior approach to bronchus for right upper lobe
  - PA last for lower lobes
  - cutting bronchus sharply prior to PA division for LUL
- Use tapes around the main PA if any concern about lobar PA dissection
VATS lobectomy after induction chemotherapy


- Propensity-matched comparison (1:2)
- VATS, n = 40; thoracotomy, n = 74
- No difference in LNs (12 vs 15), LN stations (4 for each) or in rate of R0 resection (95% vs 96%)
- 5 cases converted due to adhesions
- VATS – less blood loss, less LOS and trend towards fewer complications
- No difference in 5 yr DFS (73% vs 48%, p =0.09)
- No difference DFS pts who presented with cN2
- MVA – only cN1/2 predicted poor DFS
Lobectomy after induction Rx
Series Details from Duke U

Table 2: Treatment and tumour details

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Video-assisted thoracoscopic surgery</td>
<td>37 (33%)</td>
</tr>
<tr>
<td>Induction chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Epidermal growth factor receptor inhibitor</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Taxane only</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Platinum-doublet therapy</td>
<td>98 (88%)</td>
</tr>
<tr>
<td>Multistation N2 disease prior to induction therapy</td>
<td>27 (24%)</td>
</tr>
<tr>
<td>Pre-induction therapy histology</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>54 (49%)</td>
</tr>
<tr>
<td>Squamous</td>
<td>27 (24%)</td>
</tr>
<tr>
<td>Large cell</td>
<td>8 (7%)</td>
</tr>
<tr>
<td>Non-small cell, not otherwise specified</td>
<td>22 (20%)</td>
</tr>
<tr>
<td>Pre-induction therapy tumour size³, mean (SD)</td>
<td>3.8 ± 2.3</td>
</tr>
<tr>
<td>Post-induction therapy tumour size (n, %), mean (SD)</td>
<td>2.4 ± 2.3</td>
</tr>
<tr>
<td>Down-staged from pN2 to pN1/N0 (n, %)</td>
<td>71 (64%)</td>
</tr>
<tr>
<td>Down-staged from pN2 to pN0 (n, %)</td>
<td>57 (51%)</td>
</tr>
<tr>
<td>Complete pathologic response (ypT0N0) (n, %)</td>
<td>23 (21%)</td>
</tr>
<tr>
<td>Received induction chemoradiation</td>
<td>17 (30%)</td>
</tr>
<tr>
<td>Received induction chemotherapy</td>
<td>6 (11%)</td>
</tr>
</tbody>
</table>

Peri-operative Outcomes

N = 112

- Mortality, 30d 4 (4%)
- Complications 53 (48%)
  - Afib 23 (21%)
  - Prolonged air leak 15 (14%)
  - Postop bleeding, tx 10 (9%)
  - Resp failure 2 (2%)
  - Other major 10 (9%)
- Hospital LOS (25-75%) 5 days (4-6d)

Increasing VATS and decreasing XRT for induction over time for stage IIIa

Overall Survival: lobectomy after induction therapy

Figure 2: Overall survival of patients with stage IIIA-pN2 who underwent induction therapy followed by lobectomy.

Feasibility of VATS after neoadjuvant therapy for locally advanced NSCLC

Huang, Xu, Chen, Yin, Shao, Xiong and He. JTD 2013

- N=43, 2006-2012, stage IIa-IIIb
  - IIIa-27 (63%) IIIb-11 (26%)
- 42/43 surgery hybrid vats-7 (16.7%)
  - lobes-28 bronchial sleeve-9
  - bilobes-5 pneumonectomy-4
- OR time- 160 min, LN’s-16.88, LOS-5.4d
- Mortality-2.4% Morbidity -9.5%
- Survival- mean f/u 21 months, median OS 33 mos
  - 1 yr 94%
  - 2 yr 79%
  - 3 yr 65%
**Induction therapy**

- Preoperative chemo only 22
- Concurrent radiochemotherapy 13
- Sequential radiochemotherapy 3
- XRT dose = 40 Gy

- 4 weeks after induction, repeat ct scan
  - If disease progression, no surgery
- Time: end of induction-surgery 31d (3-79)

Huang, Xu, Chen, Yin, Shao, Xiong and He. JTD 2013
Clinical Staging

- PET-CT 13 (30.2%)
- CT 37 (86%)
- EBUS 11 (25.6%)
- Mediastinoscopy 3 (7%)

Huang, Xu, Chen, Yin, Shao, Xiong and He. JTD 2013
Surgical outcomes - VATS IIIa after induction therapy

Table 3. Surgical outcomes of 42 patients undergoing c-VATS.

<table>
<thead>
<tr>
<th>Item</th>
<th>No.</th>
<th>Operation time (min)</th>
<th>No. of lymph nodes dissected</th>
<th>Intraoperative blood loss (mL)</th>
<th>Postoperative drainage days (days)</th>
<th>Postoperative hospital stay (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobectomy</td>
<td>19</td>
<td>156.32 ± 13.83</td>
<td>18.32 ± 13.18</td>
<td>247.37 ± 88.94</td>
<td>2.79 ± 0.71</td>
<td>5.26 ± 1.15</td>
</tr>
<tr>
<td>Double lobectomy</td>
<td>5</td>
<td>162.00 ± 20.49</td>
<td>19.40 ± 6.12</td>
<td>280.00 ± 164.31</td>
<td>2.60 ± 1.14</td>
<td>5.40 ± 1.52</td>
</tr>
<tr>
<td>Wedge resection</td>
<td>5</td>
<td>158.00 ± 14.83</td>
<td>16.60 ± 12.32</td>
<td>190.00 ± 22.36</td>
<td>2.20 ± 1.10</td>
<td>5.80 ± 1.10</td>
</tr>
<tr>
<td>Total pneumonectomy</td>
<td>4</td>
<td>165.00 ± 19.15</td>
<td>16.25 ± 9.85</td>
<td>200.00 ± 70.71</td>
<td>2.75 ± 0.50</td>
<td>5.50 ± 1.00</td>
</tr>
<tr>
<td>Sleeve resection</td>
<td>9</td>
<td>167.78 ± 19.86</td>
<td>12.89 ± 7.96</td>
<td>311.11 ± 169.15</td>
<td>2.33 ± 1.09</td>
<td>5.67 ± 0.87</td>
</tr>
<tr>
<td>Surgical results</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>40</td>
<td>160.50 ± 16.94</td>
<td>16.80 ± 11.20</td>
<td>258.75 ± 117.06</td>
<td>2.68 ± 0.86</td>
<td>5.10 ± 1.17</td>
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<tr>
<td>R1</td>
<td>1</td>
<td>160.00</td>
<td>20.00</td>
<td>200.00</td>
<td>3.00</td>
<td>5.00</td>
</tr>
<tr>
<td>R2</td>
<td>1</td>
<td>160.00</td>
<td>17.00</td>
<td>100.00</td>
<td>3.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Resection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right upper lobe</td>
<td>14</td>
<td>163.57 ± 14.47</td>
<td>17.14 ± 9.33</td>
<td>292.86 ± 139.86</td>
<td>2.36 ± 1.01</td>
<td>4.50 ± 1.40</td>
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<tr>
<td>Right middle lobe</td>
<td>4</td>
<td>162.50 ± 12.58</td>
<td>18.50 ± 6.56</td>
<td>237.50 ± 47.87</td>
<td>2.00 ± 0.82</td>
<td>4.75 ± 0.50</td>
</tr>
<tr>
<td>Right lower lobe</td>
<td>4</td>
<td>165.00 ± 10.00</td>
<td>24.00 ± 23.71</td>
<td>175.00 ± 50.00</td>
<td>3.50 ± 0.38</td>
<td>5.75 ± 1.26</td>
</tr>
<tr>
<td>Left upper lobe</td>
<td>7</td>
<td>157.14 ± 22.15</td>
<td>9.43 ± 4.20</td>
<td>271.43 ± 111.27</td>
<td>2.29 ± 0.95</td>
<td>4.86 ± 1.46</td>
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<tr>
<td>Left lower lobe</td>
<td>4</td>
<td>142.50 ± 15.00</td>
<td>21.25 ± 15.22</td>
<td>200.00 ± 81.65</td>
<td>3.25 ± 0.96</td>
<td>5.50 ± 1.00</td>
</tr>
<tr>
<td>Left whole lung</td>
<td>3</td>
<td>167.67 ± 23.09</td>
<td>13.67 ± 10.26</td>
<td>200.00 ± 86.60</td>
<td>3.00 ± 0.00</td>
<td>5.67 ± 1.16</td>
</tr>
<tr>
<td>Double lobectomy</td>
<td>6</td>
<td>161.67 ± 14.83</td>
<td>17.83 ± 6.20</td>
<td>266.67 ± 164.32</td>
<td>2.67 ± 1.14</td>
<td>5.50 ± 1.52</td>
</tr>
<tr>
<td>Postoperative TNM staging</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No tumor</td>
<td>1</td>
<td>140.00</td>
<td>14.00</td>
<td>200.00</td>
<td>3.00</td>
<td>5.00</td>
</tr>
<tr>
<td>Ia</td>
<td>3</td>
<td>156.67 ± 5.77</td>
<td>15.67 ± 7.10</td>
<td>233.33 ± 15.47</td>
<td>3.60 ± 1.00</td>
<td>5.33 ± 2.08</td>
</tr>
<tr>
<td>Ib</td>
<td>6</td>
<td>161.67 ± 22.29</td>
<td>10.50 ± 3.78</td>
<td>325.00 ± 204.33</td>
<td>2.17 ± 0.98</td>
<td>4.83 ± 1.72</td>
</tr>
<tr>
<td>Ila</td>
<td>9</td>
<td>156.67 ± 18.03</td>
<td>18.00 ± 10.71</td>
<td>227.78 ± 66.67</td>
<td>2.78 ± 0.97</td>
<td>5.78 ± 1.09</td>
</tr>
<tr>
<td>IIb</td>
<td>6</td>
<td>170.00 ± 16.73</td>
<td>14.83 ± 9.64</td>
<td>241.67 ± 102.06</td>
<td>2.50 ± 1.38</td>
<td>4.50 ± 1.22</td>
</tr>
<tr>
<td>IIIa</td>
<td>12</td>
<td>156.67 ± 13.71</td>
<td>19.67 ± 14.26</td>
<td>233.33 ± 65.13</td>
<td>2.50 ± 1.00</td>
<td>4.67 ± 1.30</td>
</tr>
<tr>
<td>IIIb</td>
<td>5</td>
<td>170.00 ± 14.14</td>
<td>19.60 ± 13.10</td>
<td>300.00 ± 183.71</td>
<td>2.80 ± 0.45</td>
<td>5.20 ± 0.45</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
<td>160.48 ± 16.52</td>
<td>16.88 ± 10.93</td>
<td>253.57 ± 117.08</td>
<td>2.62 ± 0.96</td>
<td>5.45 ± 1.30</td>
</tr>
</tbody>
</table>

Huang, Xu, Chen, Yin, Shao, Xiong and He. JTD 2013
Safety and feasibility of VATS for stage IIIa NSCLC

- N=51, 2009-2010, Median f/u 50.5m
- 41/51 (80%) had N2 disease
- All had vats, LN -22, stations-5
  - Lobe and LND via scope- 98%
  - incisions up to 6cm – 6 12%
  - 12cm incision- 1
  - No open thoracotomy
- No death, complications- 12%
- VATS is safe and feasible for stage IIIa
Survival for Stage IIIa surgery + postop chemotherpay

Figure 1 The survival curves of VATS for clinical resectable stage IIIA lung cancer. VATS, video-assisted thoracoscopic surgery.

Shao, Liu, Liang, Chen, Li, Yin, Zhang and He. Chin J Can Res 2014
VATS strategy after induction therapy

• Two main issues
  – Securing the blood vessels safely
  – Performing a radical node dissection

• Choose patient based on anatomy of tumor and surgical planes

• Assess chest for metastatic or unresectable disease, unusual but not rare

• Have carefully developed plan for dealing with intra-operative problems
Scans before and after CRT
Right VATS lower lobectomy and lymph node dissection following chemo/xrt for N2 (+) NSCLC
Stage IIIa LLL post chemo/xrt
Bleeding during left vats lower lobectomy after chemo/xrt
Summary – Lung surgery after induction therapy

• Lung resection after induction chemotherapy or chemoradiation is safe and effective including in cases of pneumonectomy

• VATS resection following induction therapy is feasible and safe though technically challenging

• VATS confers all of the value and perhaps moreso in patients after induction

• Allows thorough assessment prior to resection