Determining the Optimal Surgical Approach to Esophageal Cancer

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Open Esophagectomy versus Minimally Invasive Esophagectomy
### Open Esophagectomy

<table>
<thead>
<tr>
<th>Techniques</th>
<th>Transhiatal</th>
<th>Ivor Lewis</th>
<th>Three hole</th>
<th>L Thoracoabdominal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td>Shorter operation</td>
<td>↓ Neck Morbidity</td>
<td>↓ Chest Leaks</td>
<td>One Incision</td>
</tr>
<tr>
<td></td>
<td>↓ Pulm Comps</td>
<td>↑ LNs</td>
<td>↑ LNs</td>
<td>↑ LNs</td>
</tr>
<tr>
<td></td>
<td>↓ Pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>↓ LNs</td>
<td>↑ Pulm Comps</td>
<td>↑ Pulm Comps</td>
<td>↑ Pulm Comps</td>
</tr>
<tr>
<td></td>
<td>Inability to achieve extended en bloc resection</td>
<td>↑ Pain</td>
<td>↑ Pain</td>
<td>Upper esophageal mobilization difficult</td>
</tr>
<tr>
<td></td>
<td>Risk of injury to thoracic structures</td>
<td>Chest Leaks</td>
<td>Longer Operation</td>
<td></td>
</tr>
</tbody>
</table>

- **Visualization**
  - ↑}
- **Completeness of Resection?**
  - ↑
Outcomes - Mortality

- Ochsner and Debakey (1941): 191 patients; 72% mortality
- 1970’s: 25-30%
- 1980’s: 10-15%
- 1990’s: 5-10%
- 2000-Present: <5% (High-Volume Centers)
Results of Open Transhiatal Esophagectomy

- Operative mortality of 5% or less in experienced hands
- 5-year survival rates:
  - Overall 20-25%
  - Stage I: 60-70%
  - Stage III 5-10%
- 40% local recurrence rate

Altorki Review 2006
Extended Transthoracic Resection versus Limited Transhiatal Resection for Esophageal Adenocarcinoma

- Randomized trial of transhiatal v. transthoracic with en bloc lymphadenectomy for adenocarcinoma of the mid to distal esophagus or GE junction
- Transhiatal 106 pts, Transthoracic en bloc 114 pts
- Morbidity increased after transthoracic en bloc (Operative deaths 5 vs 2, ICU 6 days vs 2, LOS 19 days vs 15)
- Trend to lower local recurrences
- 5-year survival: Transthoracic en bloc 36% vs Transhiatal 34% (p=0.71)
- Median survival: Transthoracic en bloc 2.0 years vs 1.8 years after transhiatal (p=0.38)

Hulscher NEJM 2002; 347: 1662-9
Omloo Ann Surg, 2007; 246: 992-1000
Transthoracic vs. Transhiatal Resection for Adenocarcinoma of the Esophagus

- Trend towards higher survival in the transthoracic approach with 2-field LN dissection for tumors of the mid to distal esophagus
- No advantage of extended approach seen in tumors of the GE junction with cardia involvement, thus either approach may be acceptable
Three Field Esophagectomy: Randomized Trial For Squamous Cell Carcinoma of the Thoracic Esophagus

- Randomized trial of Extended (Cervical and superior mediastinal) vs Conventional lymph node dissection
- 62 patients randomized
- 32 in extended LND group, 30 in conventional group
- Mean duration of surgery 487 mins vs 396 mins

Three Field Esophagectomy: Randomized Trial - Results

- Increase in complications in extended LN dissection group
- RLN injury 56% vs 30%
- Tracheostomy 53% vs 10%
- Phrenic nerve palsy 13% vs 0%
- One death in extended resection group, 2 deaths in conventional (p=ns)
- 5-year survival: No significant difference (p=0.192)
  - 66% in extended resection group
  - 48% in conventional group

Does More Radical Esophagectomy Improve Staging of Esophageal Cancer?

- Compared to transhiatal with no lymph node dissection? Yes
- 2 Radical series can’t agree on cervical LN importance
  - Lerut 2004: 12% incidence of occult metastases to cervical lymph nodes
    - 5-year survival in these patients was 27%, thus argues for three-field lymphadenectomy for improved staging and survival
    - T1b: 22% lymph node positive rate, with over half of these found in the cervical region
  - USC: 100 en bloc resections, 19% of T1b had positive lymph nodes, all but one lymph node in the periesophageal tissues
- Rizk 2006: Analysis of all stages, found if 18 or more lymph nodes are harvested, accurate loco regional staging can be achieved
Why MIE?

• Improve referral pattern
• Better ability to compete with other relatively low risk procedures (EMR, PDT, Chemo/RT)
• Change the perception that surgical options for esophageal cancer are “bad”
Minimal Standards for MIE as Compared to Open Surgery

- Less morbidity
- Less mortality
- Improved quality of life
- Same oncologic surgical principles
- Same long term survival
What constitutes MIE?

- VATS+Open
  - MiniThorac+Open
- Lap+Inversion
- VATS+Hand assist
- Prone VATS
  - Ivor Lewis
- LAP+THE
- VATS+Lap
- Neck Anastomosis
UPMC experience

• McKeown type MIE (n=481)
  – Access chest, abdomen and neck
  – Neck anastomosis

• Ivor-Lewis type MIE (n=530)
  – Access abdomen and neck
  – Chest anastomosis

Operative Data

• Median operative time: 7.5 hours (4-13.6)
• Median ICU stay: 1.0 days (range 0-60)
• Median number lymph nodes dissected: 16 (10-51)

TABLE 2. Technical and Perioperative Aspects of Elective MIE With Either a Cervical (MIE-Neck) or Intrathoracic (MIE-Chest) Anastomosis

<table>
<thead>
<tr>
<th></th>
<th>MIE-Neck, n = 481 (48%)</th>
<th>MIE-Chest, n = 530 (52%)</th>
<th>Total, n = 1011</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric conduit, n (%)</td>
<td>480 (99.8)</td>
<td>530 (100)</td>
<td>1010 (99.9)</td>
<td>0.294</td>
</tr>
<tr>
<td>Pyloric drainage procedure, n (%)</td>
<td>410 (86)</td>
<td>459 (87)</td>
<td>869 (86)</td>
<td>0.59</td>
</tr>
<tr>
<td>Feeding jejunostomy, n (%)</td>
<td>454 (95)</td>
<td>498 (95)</td>
<td>952 (95)</td>
<td>0.829</td>
</tr>
<tr>
<td>Stapled anastomosis, n (%)</td>
<td>375 (79)</td>
<td>526 (99)</td>
<td>901 (89)</td>
<td>-0.001</td>
</tr>
<tr>
<td>Conversion to open, n (%)</td>
<td>25 (5)</td>
<td>20 (4)</td>
<td>45 (5)</td>
<td>0.272</td>
</tr>
<tr>
<td>Abdomen</td>
<td>13 (3)</td>
<td>7 (1)</td>
<td>20 (2)</td>
<td>0.528</td>
</tr>
<tr>
<td>Chest</td>
<td>9 (2)</td>
<td>13 (3)</td>
<td>22 (2)</td>
<td>0.115</td>
</tr>
<tr>
<td>Both</td>
<td>3 (0.6)</td>
<td>0 (0)</td>
<td>3 (0.3)</td>
<td>0.069</td>
</tr>
<tr>
<td>Postoperative length of stay, days, median (IQR)</td>
<td>8 (6-14)</td>
<td>7 (6-14)</td>
<td>8 (6-14)</td>
<td>0.069</td>
</tr>
<tr>
<td>ICU length of stay, days, median (IQR)</td>
<td>1 (1-3)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>0.877</td>
</tr>
</tbody>
</table>
Outcomes after MIE - UPMC

- Decreased RLN injury, ARDS in Ivor Lewis
- Decreased CHF in 3-hole

**FIGURE 3.** Kaplan–Meier plot of the estimated overall survival of patients who did not receive induction therapy, stratified by stage.
Long-Term Results: Local Recurrence Rates After MIE in Pittsburgh

- 70 patients with esophageal cancer with documented N disease by lap staging
- Three cycles of chemotherapy followed by MIE with 2-filed lymph node dissection
- Oncologic outcomes:
  - 5-year survival 35%
  - At a median follow-up of over 40 months, local recurrence only in less than 5%
  - Distant recurrence, primarily liver in 60%
- Lerut: 5% local recurrence rate after en bloc resection

Laparoscopic Port Placement

- 4 5-mm ports
- One 10-mm port

Self-retaining liver retractor
Laparoscopic Steps: Gastric Tubularization, Celiac node dissection, stapling of left gastric vessels
Pyloroplasty
Laparoscopic Gastric Tubularization
Tack Gastric Tube to Mobilized GE-Junction Tumor For Neck Retrieval
Laparoscopic Needle Catheter J-Tube
Laparoscopic Needle Catheter J-Tube
Lateral Decubitus Position and VATS Port Sites
Quality of Life Results

• SF-36 Global QOL
  – Physical Component Score: 44 post-op, no significant difference compared to pre-op values or age-matched norms
  – Mental Component score: 51 post-op, no significant difference compared to pre-op values or age-matched norms

• Heartburn-Related QOL
  – Post-op score 4.6 consistent with normal population score
  – Only 4% of patients had a post-op score in the severe reflux range (>15)
There is growing evidence that MIE can decrease morbidity and mortality without compromising long term survival.
Comparing MIE and Open Surgery

- Studies are small and retrospective
- Usually single institution
- Hard to assess real MIE experience of the publishing center
Comparing MIE to Open Surgery

- 7 retrospective studies comparing MIE to open surgery
  - 6 reported less blood loss with MIE
  - 4 reported shorter hospital LOS
  - 3 reported shorter ICU LOS
  - 1 reported less complications
  - 1 reported less mortality
Nguyen et al

<table>
<thead>
<tr>
<th></th>
<th>MIE (n=18)</th>
<th>TT (n=16)</th>
<th>THE (n=20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oper. Time (min)</td>
<td>364 ± 73</td>
<td>437 ± 65</td>
<td>391 ± 144</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Blood loss</td>
<td>297 ± 233</td>
<td>1046 ± 792</td>
<td>1142 ± 785</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hospital Stay</td>
<td>11.3 ± 14.2</td>
<td>23.0 ± 22.3</td>
<td>22.3 ± 16.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td># nodes</td>
<td>10.8 ± 8.4</td>
<td>6.3 ± 6.0</td>
<td>6.9 ± 5.4</td>
<td></td>
</tr>
</tbody>
</table>

MIE
- VATS
- Laparoscopy
- Neck anastomosis

Arch Surg 135:920-925, 2000
<table>
<thead>
<tr>
<th></th>
<th>TT/HE (n=119)</th>
<th>MIE (n=47)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Major complic</td>
<td>37.8%</td>
<td>21.3%</td>
<td>0.06</td>
</tr>
<tr>
<td>Total complic</td>
<td>60.5%</td>
<td>38.3%</td>
<td>0.015</td>
</tr>
<tr>
<td>Mortality</td>
<td>10.9%</td>
<td>6.3%</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

- MIE
  - VATS
  - Laparoscopy
  - Neck anastomosis

Shiraishi et al

<table>
<thead>
<tr>
<th></th>
<th>Open (n=37)</th>
<th>VATS assist (n=38)</th>
<th>VATS (n=78)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss</td>
<td>882 ± 42 9.7</td>
<td>640.1 ± 3 77.2</td>
<td>670.2 ± 561.1</td>
<td>0.06</td>
</tr>
<tr>
<td>Mortality</td>
<td>13.5%</td>
<td>10.5%</td>
<td>2.6%</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

- MIE
  - VATS (+/- mini thoracotomy)
  - Laparotomy
  - Substernal reconstruction
  - Neck anastomosis

• Multivariate analysis – type of thoracic procedure
• correlates with mortality (odds ratio 0.423, p=0.50)

Smithers et al

<table>
<thead>
<tr>
<th></th>
<th>Open (n=114)</th>
<th>VATS Assist (n=309)</th>
<th>Total MIE (n=23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss</td>
<td>600</td>
<td>400</td>
<td>300</td>
<td>0.02</td>
</tr>
<tr>
<td>ICU LOS (hr)</td>
<td>23</td>
<td>24</td>
<td>19</td>
<td>0.03</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>14</td>
<td>13</td>
<td>11</td>
<td>0.03</td>
</tr>
<tr>
<td>Mortality</td>
<td>2.6%</td>
<td>2.3%</td>
<td>0</td>
<td>n.s.</td>
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</table>

- MIE
  - VATS
  - Laparoscopy (n=23)
  - Laparotomy (n=309)
  - Neck anastomosis

### Perry et al

<table>
<thead>
<tr>
<th></th>
<th>MIE (n=21)</th>
<th>THE (n=21)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Blood loss</td>
<td>168</td>
<td>526</td>
<td>0.001</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>10</td>
<td>14</td>
<td>0.03</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>19%</td>
<td>29%</td>
<td>n.s.</td>
</tr>
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</table>

Arch Surg 144:679-684, 2009

- **MIE**
  - Laparoscopic
  - Inversion
  - Neck anastomosis
Zingg et al
Matched Study

<table>
<thead>
<tr>
<th></th>
<th>Open (n=98)</th>
<th>MIE (n=56)</th>
<th>p</th>
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<tbody>
<tr>
<td>Blood loss</td>
<td>857</td>
<td>320</td>
<td>0.001</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>6.8</td>
<td>3.0</td>
<td>0.022</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>21.9</td>
<td>19.7</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mortality</td>
<td>6.1%</td>
<td>3.6%</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

- **MIE**
  - VATS
  - Laparoscopy (n=30)
  - Laparotomy (n=26)
  - Neck anastomosis

MIE-Prospective Trial: Eastern Cooperative Oncology Group (ECOG 2202)

- Prospective study to assess short and long term outcomes following minimally invasive esophagectomy in a multi-center trial
  - N=106
- Methods: Resectable esophageal cancer, laparoscopic-thoracoscopic esophagectomy
- Centers: University of Pittsburgh, University of Minnesota, Emory, Geisinger, U Mass, Northwestern, Univ of Wisconsin

JCO 2009, 27; (155): 4516
ECOG 2202

• Neoadjuvant therapy
  – Chemo 33%, Radiation 25%
• 99 underwent MIE
  – 11 HGD, rest adenocarcinoma
• 30 day mortality 2%

JCO 2009, 27; (155): 4516
ECOG 2202

• Morbidities
  – Anastomotic leak 7.8%
  – Pneumonia 4.9%

• Mean ICU stay 2 days

• Median LN harvest: 20

JCO 2009, 27; (155): 4516
Summary

• Minimally invasive esophagectomy is comparable from an oncologic perspective when compared to open esophagectomy

• Open and minimally invasive esophagectomy techniques yield similar survival rates when performed regularly