Surgical Approach to Early Esophageal Cancer: What to Do?

Raphael Bueno, MD
Associate Chief, Division of Thoracic Surgery
Brigham and Women’s Hospital
Professor of Surgery
Harvard Medical School
Esophageal Cancer Epidemiology

- Esophageal Cancer is the 8th most common cancer world-wide
- Cases in 2012: 17,460, Deaths: 15,070
- Lifetime chance of developing 1/126
- Risk factors for SCC: smoking and ETOH
- Risk factors for ADC: GERD, Barrett’s Esophagitis, high BMI, age, male gender, Caucasian race
Types of Esophageal Cancer

• By histology
  – Squamous cell, Adenocarcinoma, Small cell
  – In presence or absence of Barrett’s
  – Signet cell

• By location
  – Upper third
  – Middle third
  – Lower third/GE junction
What to Do?

- Depends on the precise stage and histology
  - T and N
- Depends on your colleagues
  - Quality of EUS and interventional
  - Quality of patient follow up
  - Quality of pathology and specimen processing
- Depends on your institution
  - Experience and outcome
- Depends on the patient
  - Medically fit?
It is all about the depth
Distinguishing T1

T Staging Scheme for Squamous Esophageal Cancer

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis High-grade dysplasia
- T1 Tumor invades lamina propria, muscularis mucosae, or submucosa
  - T1a Tumor invades lamina propria or muscularis mucosae
  - T1b Tumor invades submucosa
- T2 Tumor invades muscularis propria
- T3 Tumor invades adventitia
- T4 Tumor invades adjacent structures
  - T4a Resectable tumor invading pleura, pericardium, or diaphragm
  - T4b Unresectable tumor invading other adjacent structures, such as the aorta, vertebral body, and trachea
Regional Lymph Node (N) Staging Scheme for Esophageal Cancer

- NX Regional lymph node(s) cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in 1-2 regional lymph nodes
- N2 Metastasis in 3-6 regional lymph nodes
- N3 Metastasis in 7 or more regional lymph nodes
Histologic Grading

- GX Grade cannot be assessed—stage grouping as G1
- G1 Well differentiated
- G2 Moderately differentiated
- G3 Poorly differentiated
- G4 Undifferentiated—stage grouping as G3 squamous
<table>
<thead>
<tr>
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<th>T</th>
<th>N</th>
<th>M</th>
<th>Grade</th>
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Clinical Staging

- Endoscopy
  - Diagnosis
- PET
  - Mets/lymph nodes
- CT
  - Mets/relationships
- EUS
  - TN
  - Abdominal staging
Sensitivity and Specificity of EUS T staging of Esophageal cancer

<table>
<thead>
<tr>
<th></th>
<th>Pooled sensitivity (%)</th>
<th>Pooled specificity (%)</th>
<th>Pooled LR+</th>
<th>Pooled LR-</th>
<th>Pooled DOR</th>
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<td>44.4</td>
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<td>(77.8-84.9)</td>
<td>(99.0-99.7)</td>
<td>(15.5-127.4)</td>
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<td>(118.5-413.9)</td>
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<td>(77.5-84.8)</td>
<td>(95.4-97.1)</td>
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<td>(89.5-93.0)</td>
<td>(93.1-95.5)</td>
<td>(7.7-20.3)</td>
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<td>(96.6-98.0)</td>
<td>(13.7-47.0)</td>
<td>(0.1-0.2)</td>
<td>(145.2-430.5)</td>
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*Sensitivity* measures the proportion of actual positives which are correctly identified as such.

*Specificity* measures the proportion of negatives which are correctly identified.

Puli SR et al. EUS to stage esophageal cancer: A meta-analysis

*World J Gastroenterol* 2008 March 14; 14(10): 1479-1490
FNA improves EUS diagnosis

<table>
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<td>Pooled sensitivity (%)</td>
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<td>96.7 (92.4-98.9)</td>
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<tr>
<td>Pooled specificity (%)</td>
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<td>95.5 (91.0-98.2)</td>
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<td>Positive likelihood ratio</td>
<td>3.3 (2.6-4.3)</td>
<td>7.3 (0.9-54.3)</td>
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<td>Negative likelihood ratio</td>
<td>0.24 (0.9-0.3)</td>
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<td>Diagnostic odds ratio</td>
<td>19.1 (12.7-28.5)</td>
<td>164.5 (4.5-6027.7)</td>
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Puli SR et al. EUS to stage esophageal cancer: A meta-analysis
*World J Gastroenterol* 2008 March 14; 14(10): 1479-1490
The Problems

• Making sure that a patient with very early T status does not have lymphatic invasion
• Concern about multi-focality
• Concern about recurrence due to GERD
• Assure follow up for these patients if they do not have surgery

• It is all in the definition
Recurrence Associated Mortality Related to tumor invasion

<table>
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<th>Tumor depth</th>
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<th>Recurrence-related mortality, %</th>
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<tr>
<td>SM3</td>
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</tbody>
</table>

SM, submucosa; SM1, superficial third of submucosa; SM2, middle third of submucosa; SM3, deep third of submucosal.

Sepesi et al Nodal Disease in Early Esophageal Adenocarcinoma
JACS Vol. 210, No. 4, April 2010
Studies focusing on N prevalence in early esophageal cancer

<table>
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<tr>
<th>First author</th>
<th>Year</th>
<th>n</th>
<th>Depth of invasion</th>
<th>Nodal metastasis, %</th>
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<td>Riccì</td>
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<td>60</td>
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<td>T1b (n = 24)</td>
<td>21</td>
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<td>Nigro</td>
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<td>Van Sandick</td>
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<td>Stein</td>
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<td>94</td>
<td>M2, M3 (n = 38)</td>
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<td>Liu</td>
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<td>90</td>
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<td>SM (superficial)</td>
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<td>(n = 12)</td>
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<td>Oh</td>
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<td>23</td>
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<td>T1b (n = 29)</td>
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M1, epithelium; M2, lamina propria; M3, muscularis mucosa; SM, submucosa; SM1, superficial third of submucosa; SM2, middle third of submucosa; SM3, deep third of submucosa; T1a, intramucosal carcinoma; T1b, submucosal carcinoma.
Treatment by Stage

• Tis or T1a tumors defined as those involving the mucosa but not the and that are well, or moderately well differentiated
  – multifocal disease
  – Size (2cm)
  – grade

• Therapeutic Options
  – Esophagectomy
  – Vagal sparing esophagectomy
  – EMR
  – Ablation
Early Esophageal Cancer

• T1bN0 is defined as a tumor which invades both the mucosa and submucosa
  – preferred therapy is esophagectomy
  – Required:
    • Expertise of the center and surgeon
    • Medically fit patient
Intermediate Esophageal Cancer

- T1N1
- T2-T4 N0-1
  - Preoperative chemotherapy (ADC GE Junction)
  - Preoperative chemoradiation
  - Followed by restaging and esophagectomy in medically fit patients
Esophageal Cancer

STAGE

Tis or T1a

Medically fit, resectable Tis, T1-T4, N0-1, NX, or Stage IVA

Multi-disciplinary evaluation preferred

T1b, N0, NX

Definitive chemoradiation n, o

Preoperative chemotherapy n

Endoscopic mucosal resection (EMR) or Ablation i, k or Esophagectomy d

Esophagectomy c, d, i, m

(preferred for noncervical T1b disease)

No evidence of disease

- CT scan with contrast
- PET/CT (preferred) or PET scan (category 2B)
- Upper GI endoscopy p (optional)

Persistent local disease without metastatic disease

Unresectable or Metastatic disease

Palliative chemotherapy n and/or Best supportive care q

ADJUNCTIVE/ADJUVANT TREATMENT

Surgery

Observe/palliative surgery (optional)

Esophagectomy d, i (preferred) or Observe (category 2B)

Esophagectomy d, i if fit for surgery (preferred) or Palliative treatment, including chemotherapy n

Follow-up

(See ESOPH-6)

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Note: All recommendations are category 2A unless otherwise indicated.

Guidelines Index
Esophageal Table of Contents
Staging, Diagnosis, References
Esophageal Cancer

Surgical Outcomes After Esophagectomy/Clinical Pathologic Findings

- Adenocarcinoma
  - Node negative:
    - R0 resection:
      - Squamous
        - Tis
          - Observe
        - T1, N0
          - Observe
        - T2, N0
          - Observe
          - Chemoradiation (Fluoropyrimidine-based) for selected patients
        - T3, N0:
          - Chemoradiation (Fluoropyrimidine-based)
  - Node positive:
    - Adenocarcinoma proximal or mid esophagus
      - Chemoradiation (Fluoropyrimidine-based) or ECF if received preoperatively (category 1)
    - Adenocarcinoma distal esophagus, GE junction
      - Chemoradiation (Fluoropyrimidine-based) or Palliative therapy (See ESOPH-6)

- R1 resection:
  - Chemoradiation (Fluoropyrimidine-based)

- R2 resection:
  - Chemoradiation (Fluoropyrimidine-based)

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Follow-up (See ESOPH-5)
Surgical Approaches

• Multiple surgical options
  – Three hole
  – Trans-hiatal (THE)
  – Ivor Lewis
  – Esophagogastrectomy (left thoraco-abdominal)

• Center/operator dependent
  – Approach
  – Open vs Minimally invasive

• Disease dependent (cancer, Barrett’s, etc.)
• Conduit (stomach, colon, jejunum)
Upper third tumor, HGD or achalasia
– Usually stomach to neck via 3 hole or THE
– Definitive chemoradiation if with 5cm of UES

Middle third
– 3-hole, THE, rarely Ivor Lewis

Distal third/GEJ
– Great debate for years
  • Margins, lymph node dissection, safety, functional outcome
  • but in 7th edition TNM manual GEJ= esophageal cancer and thus to be treated as such
Choice of Conduit

- **Stomach** most common
  - One anastomosis
  - Excellent blood supply
  - Less common redundancy
- **Colon** as needed
  - Redundant
  - 3 anastomoses
- **Jejunum** if necessary
  - May need a vascular supercharge
Reasons to use 3-hole approach

• Stomach can almost always get to the neck
• Leak in the neck much easier to manage
• Anastomosis away from radiation field
• Esophagus stays centered in mediastinum
• Avoid recurrence of Barrett’s/cancer
• Sufficient margins on both sides
• 2-3 field lymph node dissection possible
• Reflux better managed
Reasons given for not doing total esophagectomy

- Swallowing problems (risk of nerve palsy)
- Concerns about tension
- Limitations of some conduits
- Ivor Lewis anastomosis can be placed quite high
- Avoiding operating on the chest
- Make sure that there is no metastatic disease in the peritoneum
Known Complications after Esophagectomy

- **Respiratory**
  - ARDS
  - Aspiration/pneumonia
  - effusion
- **Cardiac/vascular**
  - MI
  - AF
  - CVA
- **DVT/PE**
- **Hemorrhage**
- **Dehiscence**
- **Sepsis**

- **Anastomotic leak**
- **Leak from the conduit**
- **Conduit necrosis**
- **Anastomotic stricture**
- **Recurrent nerve palsey**
- **Thoracic duct leak**
- **Airway injury/fistula**
- **Abscess infection**
- **Splenic injury**
- **Bowel injury**
- **Radiation pneumonitis**
Reducing Mortality and Managing Complications

• High volume centers with high volume specialist (mortality 1-5%)
• Team experience with system approach
• Preventative measures
  – Pathway/orders; DVT/PE/CAD prophylaxis
  – Intensive mobilization; Nutrition
• Aggressive search and early management of complications
Minimally Invasive Esophagectomy

- Developed in the 1990s
- Popularized in the 2000s
- Slowly gaining traction
- Good results in expert centers
- Initially developed for 3 hole, now also developed for Ivor Lewis
- Robotic option
Why Should Surgeons Do MIE

• Truly no randomized data
• Rationale given so far:
  – Less pain
  – Faster recovery
  – Reduced blood loss
  – Shorter ICU and hospital stay
  – Immune response and cancer
  – Better visualization
  – Fewer splenectomies
How About the Patients

- Patients want it because they perceive (rightly so) that it hurts less
- It is done well mainly in major centers of expertise and may associated with lower mortality
- Patients will go to centers that offer these cases, even if they have to fly and pay out of pocket
Early UPMC Data

- Luketich early series 222 patients
- Mortality 1.4%
- LOS 7 days
- ICU 1 day
- Anastomotic leak 11.7%

Previous Published Trials

- Single center comparing different types of cases overtime
- 114 open, 309 lap/VATS assisted, 33 MIE
- Findings:
  - Less blood loss
  - Shorter LOS
  - Similar lymph node retrieval
  - Similar survival

Most Recent UPMC Data

- MIE for T1 cancer in 100 patients
- N1 disease in 21 patients
- Assoc HGD in 64
- Angiolymphatic invasion in 19
- 0% mortality 62% five-yr overall survival
- Quality of life at 5 years: excellent in 42/47, satisfactory in 5/47

How to Build an MIE Program
BWH Experience

• Learn independently how to do VATS
  – May need to partner with a VATS surgeon
• Develop expertise in laparoscopic foregut surgery
  (lap nissen, paraesophageal hernias)
• Get buy in from institution and departmental leadership
• Go learn tricks from other programs
• Get outside help
• Start early-makes a learning curve affordable
• Make modifications that retain your comfort
BWH Experience

- 1990-2012 Division of Thoracic Surgery
- 1122 Esophagectomy cases
- 910 three hole esophagectomy cases
- 119 Ivor Lewis
- 93 others (thoracoabdominal, THE)
Breakdown of the cases

- Total 3 hole esophagectomy 910
  - Completely open* 661
  - VATS and laparotomy* 117
  - Thoracotomy and laparoscopy* 14
  - MIE (3 hole) 118

*Some were opened due to complications, adhesions or other diseases
Ivor Lewis

- **Total cases**: 119
  - Thoracotomy and laparotomy: 38
  - VATS and laparotomy: 9
  - Thoracotomy and laparoscopy: 5
  - MIE (Ivor Lewis): 67
3 Hole and Ivor Lewis distribution (MIE vs OPEN)

No. of procedures vs Years:
- 1989:
  - Ivor Lewis Open: 1
  - 3 Hole Open: 1
  - 3 Hole MIE: 1
- 1991:
  - Ivor Lewis Open: 1
  - 3 Hole Open: 1
  - 3 Hole MIE: 1
- 1993:
  - Ivor Lewis Open: 2
  - 3 Hole Open: 2
  - 3 Hole MIE: 2
- 1995:
  - Ivor Lewis Open: 3
  - 3 Hole Open: 3
  - 3 Hole MIE: 3
- 1997:
  - Ivor Lewis Open: 4
  - 3 Hole Open: 4
  - 3 Hole MIE: 4
- 1999:
  - Ivor Lewis Open: 5
  - 3 Hole Open: 5
  - 3 Hole MIE: 5
- 2001:
  - Ivor Lewis Open: 6
  - 3 Hole Open: 6
  - 3 Hole MIE: 6
- 2003:
  - Ivor Lewis Open: 7
  - 3 Hole Open: 7
  - 3 Hole MIE: 7
- 2005:
  - Ivor Lewis Open: 8
  - 3 Hole Open: 8
  - 3 Hole MIE: 8
- 2007:
  - Ivor Lewis Open: 9
  - 3 Hole Open: 9
  - 3 Hole MIE: 9
- 2009:
  - Ivor Lewis Open: 10
  - 3 Hole Open: 10
  - 3 Hole MIE: 10
- 2011:
  - Ivor Lewis Open: 11
  - 3 Hole Open: 11
  - 3 Hole MIE: 11
Patient Demographics

- AGE - average age of patients - 63.18 years (49 patients over 65 y, 69 patients under 65 y)
- GENDER DISTRIBUTION - 27 women, 91 men
Stage Pre-op MIE (3 hole)

<table>
<thead>
<tr>
<th>CRT neo adjuvant</th>
<th>No neo adjuvant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>73</td>
<td>45</td>
<td>118</td>
</tr>
<tr>
<td>61.8%</td>
<td>38.1%</td>
<td></td>
</tr>
</tbody>
</table>

- We treat nearly all T3 or N1 and most of T2N0
- Most patients receive both chemotherapy and radiation therapy
**Stage Post-Op MIE (3 hole)**

<table>
<thead>
<tr>
<th>Stage at resection</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>37</td>
<td>31.6%</td>
</tr>
<tr>
<td>1A</td>
<td>27</td>
<td>23%</td>
</tr>
<tr>
<td>1B</td>
<td>20</td>
<td>17%</td>
</tr>
<tr>
<td>2A</td>
<td>3</td>
<td>2.5%</td>
</tr>
<tr>
<td>2B</td>
<td>16</td>
<td>13.6%</td>
</tr>
<tr>
<td>3A</td>
<td>4</td>
<td>3.4%</td>
</tr>
<tr>
<td>3B</td>
<td>5</td>
<td>4.2%</td>
</tr>
<tr>
<td>3C</td>
<td>2</td>
<td>1.7%</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

Lymph node capture 20.7 on average per case
Mortality at 30 days

- 1/118 MIE
- 0/67 Ivor Lewis MIE
Outcome Post Discharge
MIE (3 hole)

• Median and mean follow up of 118 patients
  – mean 20.04 SD 19.2, median 13 months (0-103)
• Overall death at follow up
  – 32 /118 cases (27.1%)
• mean survival among patients who died
  – 14.83 months, with SD of 10.04
• mean survival of patients still alive
  – 29.84 months, with SD of 22.12
• mean survival of all patients
  – 25.7 months with SD of 20.7, and median of 19 months (0-106).
Highlights

• Be very sure about the exact T stage
  – Only intramucosal carcinoma and HGD should be considered for non surgery and the patients will require lifelong follow up

• Surgery for T1b as long as the lymph nodes are negative

• Upfront therapy for more advanced cancer with restaging and resection

• Work with your colleagues

• Evolve or become extinct!
Opening Remarks
Speakers: Raphael Bueno, MD,
John Byrne, MD,

How to Convince Your Hospital Administrators to Fund a Hybrid OR
Speaker: Joseph E. Bavaria, MD,

Identifying and Analyzing Your Needs
Speaker: Gina Cronin, Administrator, Cleveland Clinic, Cleveland, OH

Building The Consensus With Your Team
Speaker: Stephen Ball, MD, Assistant Professor of Cardiac Surgery,

Negotiating Your Ideas Into Reality (Presented in a business school approach)
Speaker: Ed Bernard, Edwords

What's In It For The Institution?
Understanding What Your Institution Needs -- From Small Hospitals To Large Health Care Systems.
Speaker: Michael J. Mack, MD, Industry Partners
Speaker: Joseph L. Fredi, MD,

The Hybrid OR: How To Implement and Avoid Pitfalls
Speaker: David L. Brown, MD, President and Chairman of the Medical Staff,
Data collection and analysis
Avi Lebenthal
Jon Wee
Urs Von Holzen
David Marchosky
Rona Spector

The Division of Thoracic Surgery
Brigham and Women’s Hospital
Harvard Medical School
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