Esophageal Cancer

- Epidemiology and Risk Factors
- Diagnosis — signs, symptoms, and tests
- Work-up
- Treatment Overview
- Future Directions
Epidemiology

• Over 15,000 patients per year in the United States and 7th leading cause of cancer death in men.

• 8th most common cancer worldwide.

• Most cases are squamous cell, related to tobacco and alcohol exposure.

• In Western countries, adenocarcinoma increasing thought due to Barrett’s esophagus.

• Approximately 50% present with advanced disease, which is incurable.
Incidences of Esophageal Cancer

Adenocarcinoma: Barrett’s Esophagus

- Likely related to chronic GERD, obesity.
- Pathway of malignant progression.
- 40 to 125 times relative risk of adenocarcinoma.
- Incidence of cancer is approximately 0.5% per year in patients with BE.
- No known effective screening tool.
- Usually Lower esophagus/GE junction.
Barrett’s Esophagus and Esophageal Cancer

Endoscopic image of Barrett’s esophagus with permission to place in public domain taken from patient.

Endoscopic image of patient with esophageal adenocarcinoma seen at gastro-esophageal junction. Released into public domain on permission of patient.
Adenocarcinoma

From Grading Dysplasia in Barrett's Esophagus. Used with permission. Available at: http://pathology2.jhu.edu/beweb/study.cfm.
Malignant Progression

Squamous Cell Carcinoma

- Usually upper and middle esophagus.
- Tends to be a local problem—less metastases.
- Most common worldwide histology.
- Carcinogens present in tobacco and alcohol.
Squamous Cell Carcinoma

Anatomy

- Esophagus
- Trachea
- Tracheal nodes
- Tracheobronchial node
- Bronchus
- Aorta
- Posterior mediastinal nodes
- Diaphragmatic node
- Celiac axis nodes
- Cardiac nodes
Clinical Presentation

• Signs: weight loss, palpable lymph nodes, usually non-specific.
• Symptoms: dysphagia, loss of appetite, pain with swallowing, fatigue, cough, retrosternal and abdominal pain.
• Lab Data: no tumor markers.
Endoscopic image of patient with esophageal adenocarcinoma seen at gastro-esophageal junction. Released into public domain on permission of patient.

Endoscopic image of Barrett's esophagus with permission to place in public domain taken from patient.
Endoscopic Ultrasound

This image has been deleted because JHSPH OpenCourseWare was unable to secure permission for its use.
Tomographic Imaging (CT)
Positron Emission Tomography

Staging

• Two basic groups
  – Locally Advanced (primary tumor and regional lymph nodes): potentially curable
  – Metastatic (distant spread)
    • Incurable
    • survival increased with chemotherapy
Locally Advanced Stage

• “Best” treatment approach is controversial and continually evolving.
• Concepts to consider:
  – Local control (primary tumor)
  – Distant disease (“micrometastases”)
• Modes of treatment include surgery, radiation and chemotherapy in various sequences and combinations
Surgery Alone


This image has been deleted because JHSPH OpenCourseWare was unable to secure permission for its use.
The distribution curves represent the results of an intention-to-treat survival analysis involving all registered patients. Patients who received chemotherapy before surgery had a median survival of 14.9 months; in comparison, patients who had only surgery had a median survival of 16.1 months (P=0.53 by the log-rank test). Of the 233 patients receiving preoperative chemotherapy, 180 died; of the 234 not receiving it, 173 died.

Chemotherapy plus Surgery

Kaplan-Meier curve showing survival from date of randomisation. Two CS patients died after 5 years. From Medical Research Council Oesophageal Cancer Working Party. Surgical resection with or without preoperative chemotherapy in oesophageal cancer: a randomised controlled trial.

Adapted by CTLT from Lancet 2002;359:1727-1733.
### Chemotherapy & Radiation Without Surgery

<table>
<thead>
<tr>
<th>Time</th>
<th>No. (%) alive after radiation therapy only (randomized)</th>
<th>No. (%) alive after combined modality therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomized</td>
<td>Nonrandomized</td>
</tr>
<tr>
<td>0 years</td>
<td>62 (100)</td>
<td>61 (100)</td>
</tr>
<tr>
<td></td>
<td>69 (100)</td>
<td></td>
</tr>
<tr>
<td>1 years</td>
<td>21 (34)</td>
<td>32 (52)</td>
</tr>
<tr>
<td></td>
<td>43 (62)</td>
<td></td>
</tr>
<tr>
<td>2 years</td>
<td>6 (10)</td>
<td>22 (36)</td>
</tr>
<tr>
<td></td>
<td>24 (35)</td>
<td></td>
</tr>
<tr>
<td>3 years</td>
<td>0 (0)</td>
<td>18 (30)</td>
</tr>
<tr>
<td></td>
<td>18 (26)</td>
<td></td>
</tr>
<tr>
<td>4 years</td>
<td>0 (0)</td>
<td>17 (30)</td>
</tr>
<tr>
<td></td>
<td>13 (19)</td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td>0 (0)</td>
<td>14 (26)</td>
</tr>
<tr>
<td></td>
<td>10 (14)</td>
<td></td>
</tr>
<tr>
<td>6 years</td>
<td>0 (0)</td>
<td>12 (22)</td>
</tr>
<tr>
<td></td>
<td>6 (10)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>7 years</td>
<td>0 (0)</td>
<td>12 (22)</td>
</tr>
<tr>
<td></td>
<td>2 (6)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>8 years</td>
<td>0 (0)</td>
<td>10 (22)</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>9 years</td>
<td>0 (0)</td>
<td>4 (20)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>10 years</td>
<td>0 (0)</td>
<td>3 (20)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Total dead (median, mo)</td>
<td>62/62 (9.3)</td>
<td>48/61 (14.1)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Percentages are unreliable because of the small number of people at risk.

Adapted by CTLT from Cooper JS, et al. JAMA 1999;281:1623-1627
Overall Survival With Surgery Followed by Adjuvant Paclitaxel and Cisplatin (E8296)

- No pre-op therapy
- R0 resection
- T2N1 or greater/T3Nx
- 41% three yr survival

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## Concomitant Chemoradiotherapy Followed by Surgery

<table>
<thead>
<tr>
<th>Study</th>
<th>RO Resection Surgery Only Arm</th>
<th>3 year Surv., Surg.</th>
<th>3 year Surv., CMT*</th>
<th>Median Follow-Up for Survivors</th>
<th>Histology</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preoperative Chemoradiotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Le Prise</td>
<td>Not available (total n = 86)</td>
<td>47%+</td>
<td>47%+</td>
<td>Not available</td>
<td>Squamous</td>
<td>Sequential to 20 Gy</td>
</tr>
<tr>
<td>Bosset</td>
<td>69% (94/137)</td>
<td>34%</td>
<td>36%</td>
<td>55.2 months</td>
<td>Squamous</td>
<td>Sequential, Interrupted (no 5-FU) to 37 Gy</td>
</tr>
<tr>
<td>Urba</td>
<td>88% (44/50)</td>
<td>16%</td>
<td>30%</td>
<td>8.2 years</td>
<td>Both</td>
<td>Concurrent to 45 Gy</td>
</tr>
<tr>
<td>Walsh</td>
<td>Not available (total n = 113)</td>
<td>6%</td>
<td>32%</td>
<td>&gt;5 years</td>
<td>Adeno</td>
<td>Concurrent to 40 Gy</td>
</tr>
<tr>
<td><strong>Preoperative Chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kelsen</td>
<td>59% (135/227)</td>
<td>26%</td>
<td>23%</td>
<td>46.5 months</td>
<td>Both</td>
<td>N/A</td>
</tr>
<tr>
<td>MRC</td>
<td>54% (215/402)</td>
<td>25%</td>
<td>32%</td>
<td>37.9 months</td>
<td>Both</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Primary Chemoradiotherapy (CRT), 5-year Survival</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herskovic</td>
<td>N/A</td>
<td>CRT 27%</td>
<td>R only 0%</td>
<td>12.5 months</td>
<td>Both</td>
<td>CRT, 64 Gy R, 50 Gy</td>
</tr>
</tbody>
</table>
Overall Survival With Pre-operative Chemoradiotherapy Followed by Surgery
Survival by Pathologic Response

Proportion of Patients Surviving

Analysis Time in Days

Complete Response
Partial Response
Progressive Disease
Pattern of Recurrence

- Almost always at a distant site.
- Approaches to this problem.
  - Adjuvant chemotherapy
  - Newer chemotherapy
  - Induction chemotherapy
  - Intensified chemotherapy
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Result: nothing is much better...
Treatment of Metastatic Disease

- Palliative
- No standard chemotherapy approach
- Combination of two drugs based on 5-FU, platins, taxanes.
- Cisplatin/CPT-11, FOLFOX
- Median survival ~ 9 months
- Clinical trial
Palliation

- For swallowing trouble: stent most common
- For pain: narcotics, radiation
- For Cachexia: appetite stimulants, feeding tubes