Esophageal Cancer

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The Esophagus

- A muscular pump bordered by 2 sphincters
- One function: Transport

  The unidirectional (aboral) movement of food/saliva

- No endocrine, exocrine, immunologic, digestive, absorptive or secretory functions
Presenting Symptoms

- Dysphagia
- Odynophagia / chest pain
- Weight loss
- Hematemesis
- Others
### Overview

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Demo-graphics</th>
<th>Risk Factors</th>
<th>Location</th>
<th>Incidence</th>
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<tbody>
<tr>
<td>Squamous carcinoma</td>
<td>Black Males</td>
<td>Etoh Smoking Diet-nitrosamines</td>
<td>Proximal and Mid Esophagus</td>
<td>Declining</td>
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<tr>
<td>Adenocarcinoma</td>
<td>White Males</td>
<td>Barrett’s</td>
<td>Lower esophagus</td>
<td>Increasing</td>
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</table>
Squamous Cell Carcinoma

Incidence by Geographic Location

Cases per 100,000

- US and Britain
- South Africa and China
- Kazakhstan
Histology and Esophageal Cancer Incidence (1975–2001)

Relative Change in Incidence of Esophageal Adenocarcinoma and Other Malignancies (1975–2001)

Evolution of Esophageal Cancer

- In the U.S. and western Europe, the incidence of adenocarcinoma of the distal esophagus, GE junction and gastric cardia has increased by approximately 10% / yr over the past 30 years (now 10x incidence compared to 1976.)
- 70-75% of all esophageal CA in the U.S. is now adenocarcinoma.
Esophageal Cancer

2010 Estimates

- 16,640 new cases diagnosed in the U.S.
  ~ 70% adenocarcinoma (~11,000+ cases)
- 14,500 deaths
- 5-year relative survival (2001-2007) = 16.8%
- Median age (2004-2008) = 68 years

NCI SEER Database, 2010
Estimated US Cancer Deaths

Men 290,890
- Lung & bronchus 32%
- Prostate 10%
- Colon & rectum 10%
- Pancreas 5%
- Leukemia 5%
- Non-Hodgkin lymphoma 4%
- Esophagus 4%
- Liver & intrahepatic bile duct 3%
- Urinary bladder 3%
- Kidney 3%
- All other sites 21%

Women 272,810
- Lung & bronchus 25%
- Breast 15%
- Colon & rectum 10%
- Ovary 6%
- Pancreas 6%
- Leukemia 4%
- Non-Hodgkin lymphoma 3%
- Uterine corpus 3%
- Multiple myeloma 2%
- Brain/ONS 2%
- All other sites 24%
Why the Increase in Esophageal Adenocarcinoma?

- GERD?
- Acid suppression therapy?
- Obesity/diet?
- *Helicobacter pylori* eradication?
Persons with recurrent GERD symptoms have an 8-fold increase in the risk of developing esophageal adenocarcinoma


Carcinogenesis Sequence

GERD
(Reflux of gastric/duodenal contents)

Squamous epithelial injury

Intestinal metaplasia of mucosa
(Barrett’s)

Low-grade dysplasia

High-grade dysplasia

Invasive carcinoma
Barrett’s Esophagus

Definition

- Defined as any length of endoscopically visible columnar mucosa extending onto the esophagus
- PLUS *intestinal metaplasia* on histologic examination
  - Short-segment: < 3cm
  - Long-segment: ≥ 3cm
Barrett’s Esophagus
Barrett’s Esophagus

Carcinogenesis Sequence

No dysplasia

→ Low-grade dysplasia

→ High-grade dysplasia

→ Invasive carcinoma
Barrett’s Esophagus
Surgical Considerations

- No dysplasia
  - Anti-reflux Surgery
  - Low-grade dysplasia
    - High-grade dysplasia
      - Esophagectomy
    - Invasive carcinoma
Barrett’s Esophagus
Management Controversies

- **Screening**
  - Baseline endoscopy on patients with GERD
    - When?
    - How often?

- **Surveillance**
  - Serial endoscopies on patients with known BE to R/O progression to dysplasia/CA
    - How often?
    - Are lives saved?

- **Ablation**
Pre-Operative Investigations for Esophageal Carcinoma

- Flexible upper endoscopy with biopsies
- Barium UGI
- Computed tomography (CT)
- Endoscopic ultrasound (EUS)
- PET
Diagnosis & Staging

- 50 y/o male
- Dysphagia
EGD with biopsy
Chest/Abdominal CT

- Evaluate for T4 disease and metastasis
PET/CT Scan

- Radioactive sugar – (fluorodeoxyglucose) is injected into the blood.
- Uptaken by rapidly growing and active cells absorb large.
PET Scan

Liver Metastasis

Primary tumor
**T-stage/Depth of invasion**

- **Tis**: Intraepithelial
- **T₁**: Invades submucosa
- **T₂**: Invades muscularis propria
- **T₃**: Invades paraesophageal tissue
- **T₄**: Invades adjacent organ
Endoscopic Ultrasonography (EUS)
EUS
EUS
Comparison EUS vs Pathology
Proportion Correctly Predicted by EUS

76.5% 82.4%
**Critical Barriers**

**Basement Membrane Barrier**
- Invasive cancer
- Node rarely involved
- Systemic disease rare (< 2%)
- 5yr. Survival = 90%

**Muscularis Mucosa Barrier**
- Nodes likely involved (25%)
- Few in number (0-5)
- Systemic disease possible (17-25%)
- 5yr. Survival = 75%

**Adventitial Barrier**
- Nodes commonly involved (85%)
- Many in number (3-14)
- Systemic disease common (60-75%)
- 5yr. Survival = 30%
**N Stage**

N0 no lymph nodes

N1 1-2 lymph nodes

N2 3-6 lymph nodes

N3 7 or more lymph nodes
Progression of Carcinoma

Implications for Therapy

- Local → Regional → Systemic
- Surgery → ChemoTx + Surgery → ChemoRadTx
  (+/- XRT)
1913 1st Successful Esophagectomy
by Franz John A. Torek

- Transthoracic esophagectomy
- 67-year-old woman who presented with progressive dysphagia and weight loss.
1913 1st Successful Esophagectomy

- Patient was fed through the gastrostomy tube for the first 8 post-op days

- Later received nutrition orally.

- Meal passed from the proximal esophageal stoma through an external tube to the gastrostomy

- Patient survived for 12 years
Surgical Resection

- Prepare conduit - stomach
- Mobilize esophagus
- Divide esophagus proximally and stomach distally
- 5cm margins
- Anastomosis between esophagus and stomach
- Pyloroplasty
## Esophagectomy Options

<table>
<thead>
<tr>
<th>Less Invasive</th>
<th>More Invasive</th>
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</thead>
<tbody>
<tr>
<td>- “Minimally invasive” esophagectomy</td>
<td>- Radical (en bloc) esophagectomy</td>
</tr>
<tr>
<td>- Transhiatal esophagectomy</td>
<td>- with 2-field lymphadenectomy</td>
</tr>
<tr>
<td>- Ivor Lewis Esophagectomy</td>
<td>- with 3-field lymphadenectomy</td>
</tr>
<tr>
<td>Right thoracotomy, laparotomy, intrathoracic esophagogastrostomy</td>
<td></td>
</tr>
<tr>
<td>- 3 hole esophagectomy</td>
<td></td>
</tr>
<tr>
<td>Right thoracotomy, laparotomy, cervical esophagogastrostomy</td>
<td></td>
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</tbody>
</table>

*en bloc* refers to the removal of the affected esophagus as a single unit, including all associated lymph nodes.
Transhiatal Esophagectomy
Transhiatal Esophagectomy
Gastric conduit
Transhiatal Esophagectomy

**Advantages**
- Avoid thoracotomy
- Cervical anastomosis

**Disadvantages**
- Blind mediastinal dissection
- Less accurate staging
- Inferior treatment/less lymphadenectomy
Transthoracic (Ivor Lewis)

**Advantages**
- Complete 2 – field lymphadenectomy
- Less risk of blind mediastinal dissection

**Disadvantages**
- Increased morbidity of thoracotomy
- Intrathoracic leak has higher morbidity
3-hole Esophagectomy
Colon interposition
Surgical Resection Complications

- Anastomotic leak
- Pulmonary complications
- Chylothorax
- Recurrent laryngeal nerve injury
- Airway injury
<table>
<thead>
<tr>
<th>Esophagectomies per year</th>
<th>Operative Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>24</td>
</tr>
<tr>
<td>2-4</td>
<td>20</td>
</tr>
<tr>
<td>5-7</td>
<td>16</td>
</tr>
<tr>
<td>8-19</td>
<td>12</td>
</tr>
<tr>
<td>&gt;19</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Institution</th>
<th>Resection Type*</th>
<th>Year</th>
<th>N</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brigham</td>
<td>TTE</td>
<td>2001</td>
<td>250</td>
<td>3.6</td>
</tr>
<tr>
<td>Cornell</td>
<td>3-field en bloc</td>
<td>2002</td>
<td>80</td>
<td>5</td>
</tr>
<tr>
<td>University of Rochester</td>
<td>THE/TTE</td>
<td>2008</td>
<td>258</td>
<td>2.7</td>
</tr>
</tbody>
</table>

*THE-Transhiatal esophagectomy; TTE-Transsthoracic esophagectomy;
Mortality following esophagectomy

- The perception: High
- The reality: Not in experienced hands
  Not in the right patient population
Evolution in Resection for Early Esophageal Neoplasia

Emphasis on Decreased Morbidity and Improved Quality of Life

- Transthoracic esophagectomy (TTE)
- Transhiatal esophagectomy (THE)
- Minimally invasive esophagectomy (MIE)
- Endoscopic resection (ER) (and ablation)
Methods to Eliminate Esophageal Mucosa

“Burn it”
- Thermal
  - MPEC
  - APC
  - Nd:YAG laser
  - RF ablation (BarrX)

“Freeze it”
- Cryotherapy

“Laser it”
- PDT (photodynamic therapy)
- Mucosectomy

“Resect it”
- Endoscopic
- Surgical
I. Endoscopic Mucosal Resection (EMR)
Techniques of EMR

Risks of EMR

1) Procedural Complications
   - Perforation
   - Stricture
   - Bleeding

2) Inadequate Treatment
   - Positive margins (deep or lateral)
   - Untreated synchronous lesions
   - Associated nodal disease
II. Radiofrequency Ablation of Barrett’s Esophagus

- HALO$^{360}$ and HALO$^{90}$ systems
  (BÂRRX Medical)
HALO RF Energy Generator
HALO$^{360}$ Ablation Catheter
Muscularis mucosae (Ablation Target Depth)

Submucosa with esophageal glands

Muscularis propria

RF ablation depth (avoids stricture)

EMR and PDT Depth

Surgical Depth
Endoscopic Appearance

Baseline, 4 cm IM

Immediate Slough
Effect of RF Ablation

Barrett’s with LGD (Pretreatment)

12 Months Post-Treatment
Potentially Curative Endoscopic Therapies for Early Esophageal Neoplasia

III. Cryotherapy
CryoSpray Ablation™
Surgery For Esophageal Cancer

- The incidence of esophageal adenocarcinoma continues to rise at an alarming rate!
- Esophageal adenocarcinoma is related to Barrett’s esophagus which, in turn, is related to GERD.
- “Improvements” in the medical therapy for GERD have done nothing to halt the progression of esophageal CA.
Surgery For Esophageal Cancer

- In experienced hands, esophagectomy can be performed safely and with good quality of life.
- Esophagectomy, alone or in combination with chemoTx/XRT, remains the gold standard of treatment for potentially curable disease.
- Endoscopic therapies are evolving as curative therapy for early esophageal cancer when the potential for nodal metastasis is low.
Treatment of Esophageal Cancer

The Future

- Improved prognosis will depend upon:
  - Improved prevention (control of GERD)
  - Improved screening, earlier detection
  - Improved systemic therapies!
Treatment of Esophageal Cancer

The Future

- Improved chemotherapy, immunotherapy or cytologic regimens
- Tumor markers to predict potential for nodal/systemic spread, prognosis and the response to chemotherapy
The End