Faculty Disclosure

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Dr. DeMeester has listed no financial interest/arrangement that would be considered a conflict of interest.
Individualizing Resection for Esophageal Cancer
One Size Does Not Fit All

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Goals of Surgical Therapy for Esophageal Cancer

1. Local Control:
   - Removal of diseased esophagus ± stomach
   - Resection of potentially involved regional nodes

2. Allow comfortable alimentation
   - Reconstruction of the foregut
     - Stomach, colon, jejunum
Considerations

- Location of tumor
- Use of neoadjuvant or definitive therapy
  - Chemotherapy alone
  - Chemoradiotherapy
- Dose of radiotherapy
- Physiologic status of the patient
- Past surgical history
- Extent (stage) of disease
Types of Resection

- Transhiatal
- Ivor-Lewis
- Minimally invasive
- Vagal-sparing (open or laparoscopic)
- En-bloc (2 field)
- En-bloc (3 field)
General Concepts

- Fit the therapy to the patient and the disease to optimize cure and minimize morbidity / mortality
- In reality these principles often conflict, and must be balanced against each other
- The worst situation is to accept higher morbidity without improving outcome
Therapy for Superficial Disease:
High-grade Dysplasia or Intramucosal Cancer

Endoscopic Therapy
versus
Vagal-Sparing Esophagectomy
Treatment Goals

HGD or Intramucosal Esophageal Cancer

- Remove diseased mucosa
- Minimize recurrence
- Maintain or improve function / quality of life

- Lymphadenectomy not necessary
- But, must know that there is no submucosal invasion (ER for any nodules)
Survival By Type of Resection:
Intramucosal Adenocarcinoma (n=85)

EMR as Therapy for Intramucosal Adenocarcinoma

Ell, et al. Gastrointest Endo, 2007

n=100

<table>
<thead>
<tr>
<th>FU [months]</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
<th>72</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pts at risk</td>
<td>99</td>
<td>80</td>
<td>43</td>
<td>21</td>
<td>11</td>
<td>3</td>
</tr>
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</table>
Poor Candidates for Esophageal Preservation

- Severe, poorly controlled GERD symptoms
  - Dysphagia
  - Regurgitation / aspiration
- Difficult to correct pathophysiology
  - Delayed gastric emptying
  - Poor esophageal body motility
  - Very large hiatal hernia
- Anxious personality
- Unable to return for frequent follow-up EGDs
Vagal Sparing Esophagectomy

Esophageal vagal plexus

Right vagal trunk

Invaginated esophagus

Left vagal trunk

Nerves, plexus and trunks remain after esophageal muscle stripped away

No lymph node dissection

Reconstruction After Vagal Sparing Esophagectomy
Rationale for Vagal-Sparing Esophagectomy

- Technically easy, tolerated better than transhiatal
- Vagal division is not necessary during esophagectomy (only for node dissection)
- Avoidance of pyloroplasty and potential for leak or dumping syndrome
- Avoidance of post-vagotomy diarrhea
- Maintain immunologic and cardiovascular functions of vagus nerves
- Improves blood supply to graft
## Improved Morbidity with VSE

<table>
<thead>
<tr>
<th>Condition</th>
<th>Vagal Sparing (n=48)</th>
<th>Transhiatal (n=34)</th>
<th>En Bloc (n=21)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regurgitation</td>
<td>67 %</td>
<td>44 %</td>
<td>67 %</td>
<td>NS</td>
</tr>
<tr>
<td>Pulmonary Aspiration</td>
<td>27 %</td>
<td>24 %</td>
<td>43 %</td>
<td>NS</td>
</tr>
<tr>
<td>Anastomotic Stricture</td>
<td>24 %</td>
<td>47 %</td>
<td>38 %</td>
<td>NS</td>
</tr>
<tr>
<td>Sx Delayed Emptying</td>
<td>15 %</td>
<td>18 %</td>
<td>19 %</td>
<td>NS</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8 %</td>
<td>29 %</td>
<td>48 %</td>
<td>0.00111</td>
</tr>
<tr>
<td>Dumping</td>
<td>4 %</td>
<td>33 %</td>
<td>43 %</td>
<td>0.0004</td>
</tr>
<tr>
<td>Weight Loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 1 year (lbs)</td>
<td>-8</td>
<td>-21</td>
<td>-37</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>At 2 years (lbs)</td>
<td>-8</td>
<td>-21</td>
<td>-32</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

## Improved Morbidity with VSE

<table>
<thead>
<tr>
<th></th>
<th>Vagal Sparing (n=49)</th>
<th>Transhiatal (n=39)</th>
<th>En Bloc (n=21)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of Stay</td>
<td>12</td>
<td>16</td>
<td>18</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>30 day Mortality</td>
<td>2 %</td>
<td>5 %</td>
<td>0 %</td>
<td>NS</td>
</tr>
<tr>
<td>All Complications</td>
<td>35 %</td>
<td>56 %</td>
<td>76 %</td>
<td>0.0041</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4 %</td>
<td>18 %</td>
<td>33 %</td>
<td>0.0051</td>
</tr>
<tr>
<td>Resp. Failure</td>
<td>0 %</td>
<td>15 %</td>
<td>14 %</td>
<td>0.018</td>
</tr>
<tr>
<td>Pleural Effusion</td>
<td>2 %</td>
<td>10 %</td>
<td>24 %</td>
<td>NS</td>
</tr>
<tr>
<td>Abscess</td>
<td>0 %</td>
<td>8 %</td>
<td>19 %</td>
<td>0.011</td>
</tr>
<tr>
<td>Leak</td>
<td>2 %</td>
<td>10 %</td>
<td>19 %</td>
<td>NS</td>
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Esophagectomy for Intermediate Disease:
Submucosal or deeper lesion with limited nodes

En bloc esophagectomy
Versus MIE
Rationale for an En Bloc Esophagectomy

- Minimize local recurrence
- Ensure potentially involved regional nodes are removed
- Better patient staging for prognostication purposes
- Maximize survival potential
Location of Nodal Metastases

Adenocarcinoma

Distal esophagus        GEJ

Leers J, et al.  
*JTCVS*, 2009
Local-Regional Recurrence

- Trans-hiatal
  - Van Sandick (*JACS*, 2002): 34%
  - Urba (*J Clin Oncology*, 2001): 42%
  - Hulscher (*JACS*, 2000): 35%
  - Hulscher (*NEJM*, 2002): 14%
  - Avg: 31%

- En-bloc
  - USC (Hagen; *Ann Surg*, 2001): 1%
  - Swanson (*Ann Thorac Surg*, 2001): 5.6%
  - Hulscher (*NEJM*, 2002): 12%
  - Lerut (*Ann Surg*, 2004): 5.2%
  - Avg: 6%
En-Bloc versus Trans-Hiatal Resection

En bloc resections
1-8 pos nodes (n = 18)

Transhiatal resections
1-8 pos nodes (n = 13)

Survival

En Bloc versus Trans-Hiatal Resection
Randomized Controlled Trial

1-8 nodes involved

> 8 nodes involved

Survival and Number of Resected Nodes

Actuarial overall survival curve for patients with esophageal cancer by various total lymph and separated by N category

Schwarz RE and Smith DD. *J Gastrointest Surg*, 2007
Survival and Number of Resected Nodes

Figure 8  Plots of actuarial overall survival at 5 and 10 years by total lymph node count categories. The shaded areas represent the 95% confidence intervals.

Schwarz RE and Smith DD. J Gastrointest Surg, 2007
Survival and Number of Resected Nodes

Survival for all tumor stages significantly improved when ≥ 23 nodes removed

Pooled data from 9 centers worldwide

### Independent Predictors of Survival

Cox analysis of 2303 patients with esophageal cancer*

<table>
<thead>
<tr>
<th>Factor</th>
<th>$\chi^2$</th>
<th>p value</th>
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<tbody>
<tr>
<td>Number of involved nodes</td>
<td>614</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tumor depth</td>
<td>195</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Number of nodes removed*</td>
<td>65</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Node status</td>
<td>41</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cell type</td>
<td>28</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>20</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender</td>
<td>9</td>
<td>0.0024</td>
</tr>
</tbody>
</table>

*Data from 9 esophageal surgery centers worldwide

*Maximum effect with resection of $\geq$ 23 nodes

MIE at USC

- Compared MIE with En bloc and transhiatal for number and location of nodes removed and morbidity
- 2002-2008: 30 MIE, 49 TH, 108 EB
- Node removal EB>MIE>TH
- % of nodes removed that were mediastinal
  - EB and MIE: 50%
  - TH: 27%
- MIE not associated with reduced morbidity

USC data
Azygos Vein Resection

- 92 patients: 2,778 nodes (30.2/patient)
- 60% of resected nodes were mediastinal
- 13% of mediastinal nodes were along azygos
  - Mean 2.4/patient (range 0-14)
- 7.6% of all patients and 18% of N1 patients had involved azygos nodes
- Must be removed as part of en bloc resection

Local-Regional Advanced Disease

- Multiple involved nodes (4 or more)
- Size and extent of primary tumor less important provided resectable (15% of large transmural tumors are node negative)
- Neoadjuvant therapy
  - Chemoradiotherapy with maximal XRT 45 Gy
Resection After Neoadjuvant Therapy

- Retrospective comparison of patients that had neoadjuvant therapy followed by either transhiatal or en bloc esophagectomy at USC from 1992-2005

- Total of 58 patients

Survival After Neoadjuvant Therapy

Influence of Type of Resection

En bloc (n=40)

Transhiatal (n=18)

Survival (%)

Months

p=0.04

Rizetto C, et al. JTCVS, 2008
Survival in Patients with pCR

Influence of Type of Resection

- En bloc (n=10)
- Transhiatal (n=7)

Survival (%)

Months

Survival (\%)

Survival in Patients with Residual Disease

Influence of Type of Resection

Survival (%)

En bloc (n=30)

Transhiatal (n=11)

p=0.02

Absolute Survival at 5 years

Patients with Residual Disease After Neoadjuvant Therapy

- En bloc: 6/17 = 35%
- Transhiatal: 0/8

Death after Esophagectomy

- Systemic disease is most common cause of cancer death
- Risk can be determined based on number of involved nodes at primary resection
- Those at high risk should be offered adjuvant chemotherapy
Predicting Systemic Disease

Conclusions

- A more thorough understanding of the biology of esophageal adenocarcinoma allows individualization of therapy
- Deadly disease and get 1 chance at therapy
- Strategy of inches
- While systemic disease remains most common cause of death, local-regional control is what we bring to the table as surgeons, and is our contribution to cure