Anastomotic Complications after Esophagectomy: Prevention, Management, Outcomes

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Anastomotic Leak

No Relevant Disclosures

Learning Objectives
At the conclusion of this presentation participants will:
1. Will understand the risk of leak
2. Risk factors for anastomotic leak
3. Learn methods for diagnosis of leak
4. Learn strategies for preventing leak
5. Learn the principles of management
Outline

1. Outcomes of Anastomotic Leak
2. Definition
3. Diagnosis
4. Frequency of Anastomotic Leak
5. Risk Factors
6. Prevention
7. Management
Innovative Surgical Practice

Continuous quality improvement
Striving to improve outcomes
Improving technique
Modifying processes

“If you always do what you always do, you get what you always got”
Henry Ford
Defining a successful esophagectomy

↓ Complications
• Leaks
• Pneumonia

↓ Mortality
• in hospital
• 30 day
• 90 day

↑ Oncologic outcomes
• Resection status
  • R0 vs R1/2
• Lymph nodes resected
• Recurrence
• Survival

↑ Quality of Life
Reconstruction
Surgical Outcomes:

What has been the biggest problem in esophagectomy?

⇒ Anastomotic leaks

1. Reduce leaks → reduce strictures
2. Reduce leaks → reduce or eliminate need for feeding jejunostomy
3. Reduce leaks → reduce strictures and reduce need for dilations
4. Reduce leaks → reduce LOS
5. Reduce leaks → reduce mortality
Consequences of Anastomotic Leaks

- ↑ mortality rate
- ↑ readmission rate
- ↑ reoperation rate
- ↑ length of stay
- ↑ hospital costs
- ↑ risk of recurrence
- ↓ quality of life
- Delayed adjuvant therapy
Effect of anastomotic leak on survival

• Decreased survival and increased recurrence rates
  • Multicentre, retrospective review of 2439 patients who underwent esophageal surgery for cancer
  • Decreased median overall survival (35.8 vs. 54.8 months) and disease-free survival (34 vs. 47.9 months)
  • Higher rates of overall (OR 1.35) and locoregional (OR 1.56) recurrences

Anastomotic Leaks

Mortality from 2-12%
Incidence 5-40%
Definition: clinical? Radiographic?

• Lack of consensus on management approach
## Definitions

**International Consensus on Standardization of Data Collection for Complications Associated With Esophagectomy**

<table>
<thead>
<tr>
<th>Conduit Necrosis</th>
<th>Anastomotic Leak</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade I</strong> Conduit necrosis focal</td>
<td><strong>Grade I</strong> Local defect requiring no change in therapy or treated medically or with dietary modification</td>
</tr>
<tr>
<td>Identified endoscopically</td>
<td></td>
</tr>
<tr>
<td>Treatment – Additional monitoring or non-surgical therapy</td>
<td></td>
</tr>
<tr>
<td><strong>Grade II</strong> Conduit necrosis focal</td>
<td><strong>Grade II</strong> Localized defect requiring interventional but not surgical therapy, e.g., IR drain, stent or bedside opening and packing of incision</td>
</tr>
<tr>
<td>Identified endoscopically and not associated with free anastomotic or conduit leak</td>
<td></td>
</tr>
<tr>
<td>Treatment – Surgical therapy not involving esophageal diversion</td>
<td></td>
</tr>
<tr>
<td><strong>Grade III</strong> Conduit necrosis extensive</td>
<td><strong>Grade III</strong> Localized defect requiring surgical therapy</td>
</tr>
<tr>
<td>Treatment – Treated with conduit resection with diversion</td>
<td></td>
</tr>
</tbody>
</table>
Diagnosis of Anastomotic Leak

• High Index of Suspicion
• Patient falling off pathway = leak (until proven otherwise)
• “Pneumonia”, pleural effusion, a fib
• ↑ WBC
• Cough (beware esophago-airway fistula)
Diagnosis of Anastomotic Leak

• Fluoroscopic swallow study
  • Specific, but low sensitivity
  • Barium > water soluble contrast

• CT chest with PO contrast
  • Diagnosis esophageal leak, mediastinal or pleural collections, other causes of sepsis

• Endoscopy
  • Assess viability of conduit, direct visualization of anastomosis
  • Expensive, requires sedation

What is the role of barium swallow?

• 221 patients: Ba Swallow pod 7
• Majority underwent Ivor-Lewis
• Leak rates: cervical anastomoses 23%
  thoracic (10%)
• Barium esophagram in 202/ 221 (91.4%)
• Leak identified in 30 patients (13.6%)

Performance Characteristics

• PPV: 71.4
• NPV: 93.6
• True Positive: 45.5%
• True Negative: 97.8%
• Changed management: 2.5%
Serial Drain Amylase Can Accurately Detect Anastomotic Leak After Esophagectomy and May Facilitate Early Discharge.

- 146 patients
- esophagectomy with gastric conduit, 2007 – 2014
- Daily drain amylase levels collected until POD5
- Barium esophagram obtained routinely as well on POD7
- Sensitivity and specificity calculated at different amylase levels, postoperative days
- Determined day and value at which amylase identified the leak with the highest accuracy, sensitivity, and specificity
Amylase levels POD4 excellent discrimination of leak: AUC = 0.81 for grade II and III leaks

<table>
<thead>
<tr>
<th>Postoperative Day</th>
<th>No.</th>
<th>Mean Drain Amylase</th>
<th>p Value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No Leak+Grade I leak</td>
<td>Grade II/III leak</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(IU/L)</td>
<td>(IU/L)</td>
</tr>
<tr>
<td>1</td>
<td>63</td>
<td>89.9</td>
<td>255.4</td>
</tr>
<tr>
<td>2</td>
<td>97</td>
<td>104.8</td>
<td>2138</td>
</tr>
<tr>
<td>3</td>
<td>109</td>
<td>102.7</td>
<td>313.9</td>
</tr>
<tr>
<td>4</td>
<td>110</td>
<td>91.8</td>
<td>9579</td>
</tr>
<tr>
<td>5</td>
<td>112</td>
<td>295.4</td>
<td>6322.9</td>
</tr>
</tbody>
</table>

Cut-off 38 IU/L 100% sensitive for grade II/III leaks

> 250 IU/L 95.9% specific for significant leak
Anastomotic leak after esophagectomy

- The STS Database from 2001-2011
- 7,595 esophageal resection
- 10.6% total anastomotic leaks
- LOS 13.1 vs 27.4 days
- Mortality 3.1% vs 7.2%
- Increased complication rate with leak
- Cervical anastomotic leak rate 12.3%
- Intrathoracic leak rate 9.3%

<table>
<thead>
<tr>
<th>ECCG Anastomotic Leaks</th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Percent</th>
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</thead>
<tbody>
<tr>
<td>No</td>
<td>1716</td>
<td>88.2%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Yes</td>
<td>224</td>
<td>11.8%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type III: Localized defect requiring surgical therapy</td>
<td>37</td>
<td>3.2</td>
<td>3.2</td>
</tr>
<tr>
<td>Type II: Localized defect requiring interventional but not surgical therapy, (e.g. Interventional radiology drain, stent or bedside opening and packing of incision)</td>
<td>42</td>
<td>3.7</td>
<td>6.9</td>
</tr>
<tr>
<td>Type I: Local defect requiring no change in therapy or treated medically or with dietary modification</td>
<td>44</td>
<td>3.8</td>
<td>10.7</td>
</tr>
<tr>
<td>No leak</td>
<td>1014</td>
<td>88.2%</td>
<td>98.9%</td>
</tr>
<tr>
<td>NA - TBC</td>
<td>13</td>
<td>1.1</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>1150</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>
## Risk Factors for Anastomotic Leak

<table>
<thead>
<tr>
<th></th>
<th>Univariable</th>
<th></th>
<th>Multivariable</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95%CI)</td>
<td>p</td>
<td>OR (95%CI)</td>
<td>p</td>
</tr>
<tr>
<td><strong>CHF</strong></td>
<td></td>
<td>&lt;0.001</td>
<td>1.00</td>
<td>0.005</td>
</tr>
<tr>
<td>N</td>
<td>1.00</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>2.33 (1.56-3.47)</td>
<td></td>
<td>2.77 (1.45-5.31)</td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td>&lt;0.001</td>
<td>1.00</td>
<td>0.20</td>
</tr>
<tr>
<td>N</td>
<td>1.00</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>1.46 (1.23-1.71)</td>
<td></td>
<td>1.33 (1.04-1.69)</td>
<td></td>
</tr>
<tr>
<td><strong>Renal Failure</strong></td>
<td></td>
<td>&lt;0.001</td>
<td>1.00</td>
<td>0.002</td>
</tr>
<tr>
<td>N</td>
<td>1.00</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>2.93 (1.95-4.41)</td>
<td></td>
<td>3.23 (1.66-3.23)</td>
<td></td>
</tr>
<tr>
<td><strong>Cervica</strong></td>
<td>1.00</td>
<td>0.006</td>
<td>1.00</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Thora</strong></td>
<td>0.73 (0.59-0.92)</td>
<td></td>
<td>0.69 (0.55-0.88)</td>
<td></td>
</tr>
</tbody>
</table>
Factors contributing to anastomotic failure

- Ischemia
- Technical Failure
- Radiation
- Tension
- Distension?
Surgical/Apnoesthetic Risk Factors – Optimization

• Technically perfect anastomosis
• Reduce/avoid ischemia
• Minimize conduit edema: minimize intraop IV fluids, ok to use pressors
## Technique and Leak Grade

### Table 5. Relation of Anastomotic Technique and Grade of Leak

<table>
<thead>
<tr>
<th>Anastomotic Technique (n)</th>
<th>Grade I n (%)</th>
<th>Grade II n (%)</th>
<th>Grade III n (%)</th>
<th>Grade IV n (%)</th>
<th>Leak n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS (48)</td>
<td>0</td>
<td>1 (2.1)</td>
<td>2 (4.2)</td>
<td>1 (2.1)</td>
<td>4 (8.3)</td>
</tr>
<tr>
<td>HS (57)</td>
<td>0</td>
<td>7 (12)</td>
<td>3 (5.2)</td>
<td>1 (1.7)</td>
<td>11 (19)</td>
</tr>
<tr>
<td>LS (260)</td>
<td>0</td>
<td>8 (3.1)</td>
<td>11 (4.2)</td>
<td>2 (0.8)</td>
<td>21 (8.0)</td>
</tr>
<tr>
<td>MC (67)</td>
<td>2 (3.0)</td>
<td>11 (16)</td>
<td>1 (1.5)</td>
<td>0</td>
<td>14 (21)</td>
</tr>
<tr>
<td>Total (432)</td>
<td>2 (4.6)</td>
<td>27 (6.2)</td>
<td>17 (3.9)</td>
<td>4 (9.2)</td>
<td>50</td>
</tr>
</tbody>
</table>

CS = circular stapled; HS = hand sewn; LS = linear stapled; MC = modified Collard.
## Technique, Location and Leak

<table>
<thead>
<tr>
<th>Anastomotic Location and Technique</th>
<th>Leak n (%)</th>
<th>Odds Ratio (95% CI)</th>
<th>p Value</th>
<th>Overall p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest, n = 268</td>
<td>16 (6.0)</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>CS, n = 48</td>
<td>4 (8.3)</td>
<td>1.5 (0.5–5.1)</td>
<td>0.50</td>
<td>...</td>
</tr>
<tr>
<td>HS, n = 43</td>
<td>2 (4.6)</td>
<td>0.8 (0.2–3.9)</td>
<td>0.80</td>
<td>0.73</td>
</tr>
<tr>
<td>LS, n = 177</td>
<td>10 (5.6)</td>
<td>1.0 (reference)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>MC, n = 0</td>
<td>0</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Neck, n = 164</td>
<td>34 (20.7)</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>CS, n = 0</td>
<td>0</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>HS, n = 14</td>
<td>9 (64.3)</td>
<td>11.8 (3.3–41.7)</td>
<td>&lt;0.001</td>
<td>...</td>
</tr>
<tr>
<td>LS, n = 83</td>
<td>11 (13.2)</td>
<td>1.0 (reference)</td>
<td>...</td>
<td>0.001</td>
</tr>
<tr>
<td>MC, n = 67</td>
<td>14 (20.9)</td>
<td>1.7 (0.7–4.1)</td>
<td>0.22</td>
<td>...</td>
</tr>
</tbody>
</table>

Technical Factors that Affect Anastomotic Integrity Following Esophagectomy: Systematic Review and Meta-analysis

Sheraz R. Markar, MRCS, MSc, MA¹, Shobhit Arya, MRCS, BSc¹, Alan Karthikesalingam, MRCS, MSc, MA, PhD², and George B. Hanna, FRCS, PhD¹

- Hand-sewn versus stapled (10 studies, 936 pts)
- Cervical versus intrathoracic (9 studies, 1108 pts)
- Minimally invasive vs open (12 studies, 2268 pts)
- Anterior versus posterior mediastinal reconstruction (7 studies, 491 pts)
- Ischemic preconditioning of gastric conduit (12 studies, 1215 pts)
### Hand Sewn vs Stapled

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Law</td>
<td>3.103 (0.239, 165.586)</td>
</tr>
<tr>
<td>Hsu</td>
<td>1.242 (0.332, 4.723)</td>
</tr>
<tr>
<td>Laterza</td>
<td>5.000 (0.422, 258.279)</td>
</tr>
<tr>
<td>Valverde</td>
<td>0.939 (0.356, 2.478)</td>
</tr>
<tr>
<td>Luechakietitisak</td>
<td>0.491 (0.043, 3.608)</td>
</tr>
<tr>
<td>Walther</td>
<td>0.318 (0.000, 38.071)</td>
</tr>
<tr>
<td>Okuyama</td>
<td>0.385 (0.007, 5.641)</td>
</tr>
<tr>
<td>Craig</td>
<td>1.362 (0.217, 9.786)</td>
</tr>
<tr>
<td>George</td>
<td>0.923 (0.011, 75.442)</td>
</tr>
<tr>
<td>Saluja</td>
<td>1.175 (0.496, 2.809)</td>
</tr>
<tr>
<td>Combined [random]</td>
<td>1.094 (0.705, 1.697)</td>
</tr>
</tbody>
</table>

No difference in leaks between hand-sewn and stapled
Visual assessment of perfusion

- Short gastric vessels
- Left gastroepiploic artery
- Right gastroepiploic artery

Kumagai et al.
Fluorescence angiography to assess vascularity
• 82 patients who had gastric perfusion assessment, 14 (17%) post-op anastomotic leak,

<table>
<thead>
<tr>
<th></th>
<th>Leak</th>
<th>No leak</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ingress Rate</strong></td>
<td>14.20 p/s</td>
<td>7.39 p/s</td>
</tr>
<tr>
<td><em>p</em></td>
<td>0.0372</td>
<td></td>
</tr>
<tr>
<td><strong>AUC</strong></td>
<td>0.6970</td>
<td></td>
</tr>
<tr>
<td><strong>Perfusion at tip</strong></td>
<td>18.46 p/s</td>
<td>6.71 p/s</td>
</tr>
<tr>
<td><em>p</em></td>
<td>0.0423</td>
<td></td>
</tr>
<tr>
<td><strong>AUC</strong></td>
<td>0.7207</td>
<td></td>
</tr>
</tbody>
</table>

IR sensitivity of 93%
IR > 11.85 are at very low risk for leak,
IR sensitivity of 100%
IR > 19.65 should not leak.
Perfusion assessment and leak rate

- 150 consecutive patients undergoing esophagectomy
- Major complications 22%
- Anastomotic leak 16.7%

Perfusion assessment and leak rate

- LOS 14 d (20 d if leak vs 13 d if no leak)
- Graft demarcation in 66%
- Major leak in 33% and minor in 67%

Strategies to Reduce Anastomostic Complications

1. Optimize modifiable patient factors
2. Move anastomosis to chest: fewer leaks (mortality is lower than believed)
3. Anastomotic technique: reliable, technically perfect (EEA 2 purse-strings)
4. Place anastomosis on well vascularized portion of stomach: Anastomosis on greater curve as low as possible- just above R gastroepiploic
5. Resect redundant, relatively ischemic fundus
6. Reduce periop fluids: reduce conduit edema → reduce ischemia
7. Leak test prior to closure (r/o technical leak)
How I do it: intrathoracic EEA

1. Circular myotomy
2. divide mucosa
3. 1st purse string
Intrathoracic EEA

7. Insert stapler through anterior port into lesser curve gastrotomy
8. Deploy point out greater curve near pedicle
9. Dock Stapler on anvil and fire
Intrathoracic EEA

Completed anastomosis viewed through gastrotomy

EGD to test for technical failure-submerge anastomosis
### Esophagectomy Perioperative

<table>
<thead>
<tr>
<th></th>
<th>Open N</th>
<th>(%)</th>
<th>MIE N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>193</td>
<td></td>
<td>190</td>
<td></td>
</tr>
<tr>
<td>Thoracic anastomosis</td>
<td>110 (57)</td>
<td></td>
<td>156 (82)</td>
<td></td>
</tr>
<tr>
<td>Leak overall</td>
<td>24 (12)</td>
<td></td>
<td>17 (9)</td>
<td></td>
</tr>
<tr>
<td>Grade III leaks</td>
<td>11 (6)</td>
<td></td>
<td>10 (5)</td>
<td></td>
</tr>
<tr>
<td>Intrathoracic leak</td>
<td>7 (4)</td>
<td></td>
<td>8 (4)</td>
<td></td>
</tr>
<tr>
<td>Cervical leak</td>
<td>17/83 (21)</td>
<td></td>
<td>9/34 (33)</td>
<td></td>
</tr>
</tbody>
</table>

ECCG N= 5252
Overall 12% leaks
Grade III 3%
Management of Anastomotic Leaks

- 19 studies, 273 patients
- Diagnosis by Barium, CT or endoscopy
- Mean time to diagnosis 9 days
- Overall mortality after intra-thoracic anastomotic leak was 11%
  - 14% in conservative group
  - 8% in endoscopic stent, 8% in endoscopic drainage
  - 0% in endoscopic VAC group
  - 50% in surgical treatment group

- Re-intervention rate highest in the endoscopic stent group
  - 37% required at least one re-intervention
  - Mostly stent migration

Management of Anastomotic Leaks

Early < 48-72 hours
- Technical
- Ischemia/Conduit Necrosis
  ➢ Take back to OR
- EGD, re-explore
- repair/revise

Late > 5 days
- drain, antibiotics
- (stent)
Summary

• Use anastomotic technique that works for you-
• It is all about the gastric conduit
• Place anastomosis close to greater curve
• Place anastomosis as close to pedicle as possible (away from most ischemic part of conduit- resect redundant conduit)
• Intrathoracic anastomosis has lower leak rate
• Intraop fluid restriction ↓ conduit edema ↓ conduit failure/leaks: intraop fluid balance <2 litres
• Intraop inotropes (levophed) not a problem
Conclusions

• Preoperative identification of patients at risk and amenable to optimization
• Flawless, standardized and reproducible technique
• Avoid ischemia
• Consider delayed reconstruction or partial anastomosis in high risk patients who cannot be optimized
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Thank you