ROLE OF SURGERY IN OESOPHAGEAL CANCER

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Thiruvananandapram
Percent of Cases by Stage
Esophageal Cancer

- **Localized (21%)**
  Confined to Primary Site
- **Regional (30%)**
  Spread to Regional Lymph Nodes
- **Distant (37%)**
  Cancer Has Metastasized
- **Unknown (11%)**
  Unstaged

SEER 18 2004-2010, All Races, Both Sexes by SEER Summary Stage 2000
5-Year Relative Survival

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>39.6%</td>
</tr>
<tr>
<td>Regional</td>
<td>21.1%</td>
</tr>
<tr>
<td>Distant</td>
<td>3.8%</td>
</tr>
<tr>
<td>Unstaged</td>
<td>11.5%</td>
</tr>
</tbody>
</table>
How Many People Survive 5 Years Or More after Being Diagnosed with Esophageal Cancer?

- Percent Surviving: 17.5%
  - 5 Years

- Based on data from SEER 18 2004-2010
Surgical Objectives

• Potentially curative R0 resection
• No role of resection in metastatic disease
• Survival related to stage of disease
Anatomical Regions
SCC Vs ADENOCARCINOMA-
Two Different tumors at one location?

• The patient of SCC is usually emaciated alcoholic and smoker, Poor GC

• Precursor lesion of SCC is epithelial dysplasia, while for adenocarcinoma it is barretts

• 65 percent of SCCs are located above carina while 94 percent of adenocarcinoma occur below carina

• SCCs tend to arise 10 years earlier, on average, than adenocarcinomas

• SCC Skip lesions and LN spread are more with SCC

• SCCs tend to recur locoregionally first, while distal esophageal adenocarcinomas more commonly recur with distant dissemination.
Pre treatment work up

**NCCN guidelines**
- H&P
- Upper GI scopy and biopsy
- CT –abdomen/chest with oral and IV contrast ( pelvis as indicated )
- EUS (if no suspicion of M1)
- PET CT (if no suspicion of M1)
- Her 2 neu testing (M1 suspicion )
- Nutritional counseling
- CBC and chemistries
- Biopsy of metastasis as indicated
- Assign Sievert category
- EMR- if done for early lesions
- Diagnostic laparoscopy (if no M1,EGJ lesions)
Staging

- CT scan for metastatic disease
- Endoscopic ultrasonography (EUS)
- Integrated PET/CT scans
  - Suspicious PET findings should be confirmed before excluding a patient from surgical consideration.
- Staging laparoscopy is controversial
  - NCCN guidelines suggest that diagnostic laparoscopy is optional - EGJ tumours
- Preoperative bronchoscopy - tumors that are located at or above the level of the carina.
<table>
<thead>
<tr>
<th>PRIMARY TUMOR (T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
</tr>
<tr>
<td>T0</td>
</tr>
<tr>
<td>Tis</td>
</tr>
<tr>
<td>T1</td>
</tr>
<tr>
<td>T1a</td>
</tr>
<tr>
<td>T1b</td>
</tr>
<tr>
<td>T2</td>
</tr>
<tr>
<td>T3</td>
</tr>
<tr>
<td>T4</td>
</tr>
<tr>
<td>T4a</td>
</tr>
</tbody>
</table>
| T4b               | Unresectable tumor invading other adjacent structures, such as aorta, vertebral body, trachea, etc. *

*High-grade dysplasia includes all noninvasive neoplastic epithelium that was formerly called carcinoma in situ, a diagnosis that is no longer used for columnar mucosae anywhere in the gastrointestinal tract

<table>
<thead>
<tr>
<th>REGIONAL LYMPH NODES (N)</th>
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<tbody>
<tr>
<td>NX</td>
</tr>
<tr>
<td>N0</td>
</tr>
<tr>
<td>N1</td>
</tr>
<tr>
<td>N2</td>
</tr>
<tr>
<td>N3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DISTANT METASTASIS (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
</tr>
<tr>
<td>M1</td>
</tr>
<tr>
<td>Anatomic Stage/Prognostic Groups</td>
</tr>
<tr>
<td>----------------------------------</td>
</tr>
<tr>
<td><strong>Stage</strong></td>
</tr>
<tr>
<td>Stage 0</td>
</tr>
<tr>
<td>Stage IA</td>
</tr>
<tr>
<td>Stage IB</td>
</tr>
<tr>
<td>Stage II A</td>
</tr>
<tr>
<td>Stage II B</td>
</tr>
<tr>
<td>Stage III A</td>
</tr>
<tr>
<td>Stage III B</td>
</tr>
<tr>
<td>Stage III C</td>
</tr>
<tr>
<td>Stage IV</td>
</tr>
</tbody>
</table>

* TNM-7 staging system for squamous cell carcinoma.

** TNM-7 staging system for adenocarcinoma.
AJCC-7

- Major changes have been made in this edition

- Separate staging for Adeno/squamous (SCC-poor prog)

- Grade and site have been incorporated

- LN numbers are more important than location

- Regional LN defined as periesophageal from cervical to Coeliac

- LN ratio has not found any role in staging
Treatment Overview
Esophageal Cancer

• Treatment Overview
  – Proximal
    • Definitive Chemoradiation therapy
  – Metastatic
    • Definitive Chemoradiation therapy
    • No role for palliative resection
  – HGD, T1, maybe T2
    • Primary Treatment is Surgical
  – All others
    • Multimodality approach
Esophageal Cancer

Treatment Overview

Proximal

Definitive Chemoradiation therapy
CERVICAL ESOPHAGEAL CANCER

• 6 to 8 cm long
• Cricopharyngeus to the thoracic inlet

• Locally advanced disease at diagnosis.
  • tracheal invasion 35%
  • vocal cord paralysis 24%
• ChemoRT preferred over surgery
  • survival comparable and
  • major morbidity is avoided
Limited disease

Tis-T2 N0-1 M0

SCC

Fit
- Surgery
  - Tis-T1a: Endoscopic resection
  - T1-2 N0-1: surgical resection

Unfit
- CT-RT or palliation
  - Cisplatin / 5-fluorouracil x 4
  - Radiotherapy (50.4 Gy in USA versus >60 Gy in Japan and Europe)

Adenocarc

Fit
- Perioperative CT (or preop. CT-RT)
  - CF(+E) x 3
    - Surgery
    - CF(+E) x 3

Unfit
- Palliative therapy
  - Chemotherapy +/- Radiotherapy
  - Local palliation
Guidelines-ESMO2010

Locally advanced disease

- T3-4 N0-1 M0
  - SCC
    - Fit: Preoperative Chemoradiation (40-50 Gy)
      - Surgery
        - R0: No further treatment
        - R1-2: SFU based postoperative CT-RT for selected patients
    - Unfit: Definitive Chemoradiation (>60 Gy)
  - Adenocarc
    - Fit: Preoperative CRT or perioperative CT
      - CF(+E) x 3
      - Surgery
      - CF(+E) x 3
    - Unfit: Palliative therapy
      - Chemotherapy +/- Radiotherapy
      - Local palliation
• Early stage-
  1. Surgery alone

• Locally advanced-
  1. Neoadjuvant chemo → surgery (± post-op chemo)
  2. Neoadjuvant chemoradiation → surgery
Treatment - Early stage disease

- No role of Trimodality treatment in early stage
- Surgery alone adequate in the majority of these patients.

195 patients T1,2,3 N0

- Surgery
- 69 months follow up
- Preop NA CTRT

Survival | Adverse events | Mortality
---------|---------------|--------
44 months | 35%           | 1%     |

32 months | 65%           | 7.3%   |

French FFD Trial, J Clin Oncol 2010; 28:302s.
Principles of Oesophagectomy

• Spreads longitudinally in submucosal lymphatics
• Crucial to achieve longitudinal resection margin
• Debate on optimum surgical margin
• What surgical approach?
Margins

• Proximal, distal and lateral margin
• Axial margin
  – Propensity for intramural spread, multicentric, skip mets.
  – Taking to account shrinkage of specimen after resection, in situ margin of 10 cm [fresh contracted specimen – 5 cm /SCC]
  – This allows < 5 % of recurrence.
Extent of surgery

• Controversial/Surgeons choice
• Conventional view margin-
  – Adenocarcinoma-5cm – Partial esophagectomy
  – SCC-10-12 cm - Total esophagectomy
CRM

• The College of American Pathologists (CAP) defines a positive CRM as the presence of esophageal cancer at the resection margin.

• United Kingdom Royal College of Pathologists (RCP) defines a positive CRM as the presence of esophageal cancer within 1 mm of the resection margin.

• Negative CRM-independent predictor of survival
Lateral margin

- Concept of *En bloc* resection
- Less suitable for upper and middle esophageal cancers – close proximity to trachea and bronchi
- Applicable to adeno ca – lower esophagus
Surgery

- Perioperative mortality is <5%

- Local recurrence has decreased further

- Surgery after Neoadjuvant CT/CRT is a very promising option

- Surgery restores the nutritional intake and restore QOL
Reasons for Improved results for resection

- Increase in specialist units
- Multidisciplinary approach
- Earlier diagnosis
- Better patient selection
- Improved perioperative management
- Enhanced recovery programmes
The surgical option
Stage wise management

In general

• Stage I-IIA(T1,T2,N0,M0)-Upfront surgery if the candidate is fit

• Stage II B-III –Multimodality therapy
  1. Neoadjuvant chemo → surgery (± post-op chemo)
  2. Neoadjuvant chemoradiation → surgery

• Stage IV - Palliative
Superficial cancer (HGD /T1a/T1bN0M0)

- Rate of conversion of barretts
- 0.6%/year – Low grade dysplasia
- 5%/year – High grade dysplasia

Esophagectomy- Gold standard
ER+ Ablation – reasonable alternative
RADIATION +/- CT(Investigational)
EMR

- Early T1a
- Confined to mucosa
- < / =2cm
- Non ulcerated
- Not P/D
- No LVI
<table>
<thead>
<tr>
<th>Depth of invasion</th>
<th>% of LN</th>
<th>% of LN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>m1</td>
<td>barely breaks the basement membrane</td>
<td>0%</td>
</tr>
<tr>
<td>m2</td>
<td>3.3%</td>
<td></td>
</tr>
<tr>
<td>m3</td>
<td>infiltrates the lamina muscularis mucosae</td>
<td>12.2%</td>
</tr>
<tr>
<td>Submucosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sm1</td>
<td>26.5%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Sm2</td>
<td>35.8%</td>
<td>10%</td>
</tr>
<tr>
<td>Sm3</td>
<td>45.9%</td>
<td>45%</td>
</tr>
</tbody>
</table>

Endoscopic Ablation

- **Thermal Forms**
  - Multipolar coagulation
  - Heat probe therapy
  - Argon plasma coagulation
  - Laser therapy (many types)
  - Radiofrequency ablation

- **Photodynamic Therapy**
  - Systemic photosensitizer
    - Preferentially taken up by dysplastic tissue/tumor
  - Expose tissue to light of specific wavelength
  - Debride devitalized tissue
Endoscopic Ablation

• Deficiencies
  – No tissue removed to assure adequate targeting
  – Islands of Barrett’s esophagus +/- cancer can still exist under ablated tissue
  – Surveillance afterward difficult
Endoscopic Mucosal Resection

• Technique
  – Create pseudo polyp with epinephrine
  – Snare

• Shortcomings
  – Technically difficult
  – Difficult to perform in long segment Barrett’s
  – High recurrence rate (30%)

• May have diagnostic value
Endoscopic Mucosal Resection

Inject and Cut

Inject, Lift, and Cut

Inject, Suction, and Cut

Ligate, then Snare
NCCN Guidelines Version 2.2013
Esophageal and Esophagogastric Junction Cancers

TUMOR CLASSIFICATION:

Tis l
T1a m
T1b, n N0
Adenocarcinomas
T1b, n N+, T2-T4a, N0-N+, h,o
T4b p

PRIMARY TREATMENT OPTIONS FOR MEDICALLY FIT PATIENTS:

Endoscopic mucosal resection (EMR) a,r
or
Ablation a
EMR a.r followed by ablation a (preferred)
or
Esophagectomy d,t,u

Periodic endoscopic surveillance
See ESOPH-A (3 of 4)

See Surgical Outcomes After
Esophagectomy (ESOPH-13)

Preoperative chemoradiation v,w,dd (preferred)
(RT, 41.4-50.4 Gy + concurrent chemotherapy)
or
Definitive chemoradiation (only for patients who decline surgery) v,w
(RT, 50-50.4 Gy + concurrent chemotherapy)
or
Preoperative chemotherapy v
or
Esophagectomy d,t,u (low risk lesions, < 2cm, well differentiated lesions)

See Response Assessment
(ESOPH-12)

See Surgical Outcomes After
Esophagectomy (ESOPH-13)

Definitive chemoradiation v,w
(RT, 50-50.4 Gy + concurrent chemotherapy)

See Response Assessment
(ESOPH-12)
Post treatment surveillance

• Check endoscopy 5-6 weeks
• Biopsy of all mucosal abnormalities, strictures (Combination with EUS increases sensitivity)
• Look for barretts- 4 quadrant biopsy
• Biopsy neo squamous areas (buried glands)
• Every 3 months → 1 year → Annually
Methods of Esophagectomy
optimal free CRM should be >1 mm.

Patients with unfavorable CRM involvement (1 mm) may be considered for adjuvant
Prerequisites for surgery

- Complete (R0) resection
- 4 cm distal gastric margin
- 5 cm esophageal margin
- At least 15 nodes - appropriate for the primary tumor location

Early stage carcinoma esophagus is surgically curable disease – No controversy

I:Surgery alone
- cT1N0M0 lesions
- cT2N0M0 lesions(some centres)
CHOICE OF SURGICAL APPROACH

• DEPENDS UPON:
  • Tumor location and length, submucosal extension, and adherence to surrounding structures
  • The type of lymphadenectomy desired
  • The conduit to be used for replacement
  • The preference of the surgeon
Surgical Options

Approach
- Transhiatal
- Transthoracic
- Tri incisional
- Minimally Invasive

Conduit
- Stomach
- Colon
- Jejunum
- Skin Tube

Anastomosis
- Neck
- Chest
- Abdomen

Route
- Post. Mediast.
- Retrosternal
- Subcutaneous
Approach

**TRANSHIATAL-Orringer**
- Laparotomy and cervical approach

**TRANSTHORACIC**
- Ivor Lewis
  - Right thoracotomy and laparotomy
- McKeown or “three hole”
  - Right thoracotomy, laparotomy, cervical approach
- Left thoracotomy/Left thoracoabdominal
Transhiatal Esophagectomy
Transhiatal Esophagectomy
Transhiatal Esophagectomy
Transhiatal Esophagectomy

Diagram showing gastric pull-up with the stomach replacing the esophagus and the normal location of the stomach before surgery.
Ivor-Lewis Esophagectomy

Transthoracic (Ivor-Lewis) Approach
Ivor-Lewis Esophagectomy
Ivor Lewis Esophagectomy
Type of anastamosis

- Hand sewn-single/double layer
- **Stapler**
- Circular –EEA
- Linear side to side
- Hybrid –Modified Collard technique
- Circular stapled anastomosis - significantly higher rate of anastomotic stricture
- Leak rates similar
<table>
<thead>
<tr>
<th></th>
<th>TH</th>
<th>TTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>lymph nodes retrieved</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>OS at completed 5 years</td>
<td>34%</td>
<td>36%</td>
</tr>
</tbody>
</table>

Comparison of Approach
Transhiatal vs. Transthoracic

• No difference in operative time, blood loss, morbidity or mortality

• 5 year Survival similar

• Anastomotic Leak rate
  – Cervical 11%
  – Thoracic 6%

Putnam et al., Annal Thor Surg, 1994
Gluch et al.: Transhiatal vs. Ivor Lewis Esophagectomy

Table 4. Complications: morbidity and mortality.

<table>
<thead>
<tr>
<th>Complications</th>
<th>ILO (n = 33)</th>
<th>THO (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
<td>6.1</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1</td>
<td>3.0</td>
</tr>
<tr>
<td>Wound</td>
<td>6</td>
<td>18.2</td>
</tr>
<tr>
<td>Sepsis</td>
<td>4</td>
<td>12.1</td>
</tr>
<tr>
<td>Leak</td>
<td>3</td>
<td>9.1</td>
</tr>
<tr>
<td>Stricture</td>
<td>4</td>
<td>12.1</td>
</tr>
<tr>
<td>RLN</td>
<td>2</td>
<td>6.1</td>
</tr>
<tr>
<td>Respiratory problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>5</td>
<td>15.2</td>
</tr>
<tr>
<td>Intermediate</td>
<td>7</td>
<td>21.2</td>
</tr>
<tr>
<td>Major</td>
<td>4</td>
<td>12.1</td>
</tr>
</tbody>
</table>

RLN: recurrent laryngeal nerve.

There were no significant differences between the two groups for any of the parameters according to Fisher’s exact test.
Transhiatal Esophagectomy

• Experienced centers report <5% mortality
• Overall survival: 20-25%
• Stage I: 60-70%
• Stage III: 5%
• 40% rate of local recurrence
• Major complication rate of 30-40%
Summary

• Transthoracic (Ivor Lewis)
  – Pros: Lower rate of leaks, More extensive lymphadenectomy, decreased stricture rate, no risk to recurrent laryngeal nerve
  – Cons: Increased pain (thoracotomy)

• Intrathoracic leak not associated with increased mortality
Perioperative Mortality After Intrathoracic Leak

Historical

Overall Operative Mortality: 11%
Leak Associated Mortality: 43%

Modern

Overall Operative Mortality: 2.5%
Leak Associated Mortality: 3.3%

P = 0.03

Martin et al., Ann Surg, 2006
Summary

• Debate continues as to optimal approach
  – Transhiatal
    • Pros: Avoid thoracotomy
      Technically easier operation
    • Cons: Increase rate of anastomotic leak
      Recurrent laryngeal nerve injury (aspiration)
      Limited thoracic lymphadenectomy
Summary

• There is no ideal approach to esophagectomy

• Outcomes are best when performed in high volume centers
Problem

• Both TTE and THE are equally effective in Carcinoma esophagus

• Both are an accepted form of management

• The problem is dismal 5 year survival that ranges from 25-35% in various studies. (Even lesser for locally advanced lesions)
The answer-Extended Esophagectomy

- Two concepts
  - *en bloc*
  - *Lymph node dissection*
Rationale for lymphadenectomy

- A rich network of submucosal lymphatics
- Prone to longitudinal spread of tumor.
- Intramural metastases
  - subepithelial spread
  - skip lesions
  - satellite nodules
- The incidence of intramural metastasis and multiple tumors is up to 30%
- Adequate axial margin in esophagectomy is important to prevent anastomotic recurrence

• Rationale of 3 field lymphadenectomy
  – Overall involvement of cervical nodes – 30%
  
  – Cervical lymph nodes are involved in 60%, 20%, and 12.5% of upper-, middle-, and lower-third tumors respectively
  
  – Radical esophagectomy should encompass all lymph node stations having a greater than 10% incidence of metastases. 

Radical Three Field Esophagectomy

• Thoracic, abdominal and cervical incisions
• Three field lymphadenectomy
• Increased complications:
  – RLN Injury: 56 vs 30%
  – Tracheostomy: 53 vs 10%
  – Phrenic nerve injury: 13 vs 0%
  – No difference in 5-year survival
• Significant increase in morbidity with no improvement in survival
<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>101:</td>
<td>Cervical paraesophageal lymph nodes</td>
</tr>
<tr>
<td>102:</td>
<td>Deep cervical lymph nodes</td>
</tr>
<tr>
<td>104:</td>
<td>Supraclavicular lymph nodes</td>
</tr>
<tr>
<td>105:</td>
<td>Upper thoracic paraesophageal lymph nodes</td>
</tr>
<tr>
<td>106-rec:</td>
<td>Recurrent nerve lymph nodes</td>
</tr>
<tr>
<td>106-tbL:</td>
<td>Left tracheobronchial lymph nodes</td>
</tr>
<tr>
<td>107:</td>
<td>Subcarinal lymph nodes</td>
</tr>
<tr>
<td>108:</td>
<td>Middle thoracic paraesophageal lymph nodes</td>
</tr>
<tr>
<td>109:</td>
<td>Main bronchus lymph nodes</td>
</tr>
<tr>
<td>110:</td>
<td>Lower thoracic paraesophageal lymph nodes</td>
</tr>
<tr>
<td>111:</td>
<td>Supradiaphragmatic lymph nodes</td>
</tr>
<tr>
<td>112:</td>
<td>Posterior mediastinal lymph nodes</td>
</tr>
<tr>
<td>TD:</td>
<td>Lymph nodes along the thoracic duct</td>
</tr>
<tr>
<td>1:</td>
<td>Right cardial lymph nodes</td>
</tr>
<tr>
<td>2:</td>
<td>Left cardial lymph nodes</td>
</tr>
<tr>
<td>3:</td>
<td>Lymph nodes along the lesser curvature</td>
</tr>
<tr>
<td>7:</td>
<td>Lymph nodes along the left gastric artery</td>
</tr>
<tr>
<td>8:</td>
<td>Lymph nodes along the common hepatic artery</td>
</tr>
<tr>
<td>9:</td>
<td>Lymph nodes along the celiac artery</td>
</tr>
<tr>
<td>11:</td>
<td>Lymph nodes along the splenic artery</td>
</tr>
</tbody>
</table>


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Standard esophagectomy

- Paraesophageal nodes
- Subcarinal nodes
- Right and Left bronchial nodes below the tracheal bifurcation
Two field Esophagectomy

All nodal groups between the tracheal bifurcation superiorly to the celiac axis inferiorly
Three field esophagectomy

Excision of the nodes along both recurrent nerves as they course through the mediastinum and neck, as well as a modified cervical node dissection

Includes the nodes posterior and lateral to the internal jugular vein and an infraomohyoid node dissection bilaterally
ABDOMINAL FIELD:
Lymph nodes around the celiac trifurcation should be resected
Rationale of 3 field lymphadenectomy

- Overall involvement of cervical nodes – 30%
  - Upper - 60%
  - Middle - 20%
  - Lower - 12.5%

- Radical esophagectomy should include all lymph node stations having a greater than 10% incidence of metastases.

DISADVANTAGES OF 3-FIELD DISSECTION

- The greater the extent of dissection, the better the prognosis and local control might be; but the higher would be the surgical risks.

- Double edged sword
Three field lymphadenectomy

- Early stage esophageal carcinoma
- SCC of cervical and thoracic esophagus
- Backup of extremely good ICU care
- Careful selection of cases
• Although the optimal extent of lymph node clearance has always been under debate, the superiority of extended lymphadenectomy has rendered it a standard procedure in more than 70% of institutions in Japan.


• It provides more accurate tumor staging

• Japanese Association of Esophageal Oncology Group carried out a nationwide survey on lymphadenectomy among 96 institutions in 1991

Indicates more thorough lymph node clearance

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<thead>
<tr>
<th></th>
<th>2-field</th>
<th>3 – field</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of lymph node metastasis</td>
<td>58.7%</td>
<td>72.9%</td>
</tr>
<tr>
<td>Rate of mediastinal metastasis</td>
<td>40.8%</td>
<td>55.8%</td>
</tr>
</tbody>
</table>
Predicting systemic disease in patients with esophageal cancer after esophagectomy: study on the significance of the pN+

- Multinational retrospective review

- 700 Adenoca, 353 SCC undergoing oesophagectomy alone

- Systemic disease recurrence:
  - 40% Overall
  - 16% if pN0 Lymph nodes
  - 93% with >8 involved

MERITS OF EXTENDED LYMPH NODE DISSECTION FOR ESOPHAGEAL CANCER

- The chance of cure would be increased

- Risk of early local-regional recurrence reduced

- Lack of other effective adjuvant therapies, it is not surprising to observe a high recurrence rate in mediastinal or cervical lymph nodes shortly after surgery

Lymphadenectomy-

How many?
Which all?
Does it make a difference?
Optimum Lymphadenectomy for Esophageal Cancer

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Carolyn E. Reed, MD,†† Jarmo A. Salo, MD,‡ Walter J. Scott, MD,§ Wayne L. Hofstetter, MD,¶¶
Thomas J. Watson, MD,||| Mark S. Allen, MD,*** Valerie W. Rusch, MD,* and Eugene H. Blackstone, MD†

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(Ann Surg 2010;251: 46–50)
Method

• Database: Worldwide Esophageal Cancer Collaboration data.
• The entire project was approved by the Case Cancer Institutional Review Board of Case Western Reserve University.
• Method: total of 4627 patients who had esophagectomy alone for esophageal cancer (no pre- or postoperative adjuvant therapy) for esophageal cancer and had follow-up for all-cause mortality.
• Risk-adjusted 5-year survival was averaged for each number of lymph nodes resected.
Result

pN0M0 Cancers
pTis cancers
regardless of histopathologic cell type, survival was excellent and not associated with extent of lymphadenectomy.

T1N0M0 cancers
G1: survival was unrelated to extent of lymphadenectomy
G2/G3 cancers: survival was increased with more extensive lymphadenectomy
Result

pN0M0 Cancers
T2N0M0 and T3/T4N0M0 cancers
G1: limited data, due to few case number
G2/G3 cancers: survival was increased with more extensive lymphadenectomy
Result

**N+M0 Cancers**
1 to 6 nodes positive (N1~2)  
*survival increased* with extent of lymphadenectomy for all T classifications
7 or more nodes positive  
T2 and T3/T4 cancers: *Survival increased*, albeit minimally, with extent of lymphadenectomy

**T1**: very few case number to assessing the survival value
Discussion

- Extent of lymphadenectomy was either unassociated with or minimally increased survival for patients with extremes of esophageal cancer (TisN0M0 and T2N3 lesion) and those with well-differentiated (G1) pN0 cancer.
- pN+ cancers
  - improved survival!!
  - more accurate determination of number of positive nodes (stage purification), or therapeutic effect of removing micrometastases.
Recommendations

• If there is uncertainty as to T and histopathologic grade, it is recommended that 30 or more nodes be resected to maximize 5-year survival.
  ■ It is recommended that to maximize 5-year survival, a minimum of 10 nodes be resected for T1 cancer, 20 nodes for T2 cancer, and 30 or more nodes for T3/T4 cancers.
Optimum Lymphadenectomy

- pTis
  - no optimum extent of lymphadenectomy
- pT1 N0M0 cancers
  - 10 for adenocarcinomas
  - 12 for squamous cell carcinomas
- pT2 N0M0 cancers
  - 15 for adenocarcinomas
  - 22 for squamous cell carcinomas
- T3/T4N0M0 cancers
  - 31 for Adenocarcinomas
  - 42 for squamous cell carcinomas

Optimum number of nodes resected was determined by the value at which standardized VIMP first dropped below 5%.
Lymphadenectomy-AJCC 7

- Prognosis is Dichotomized between LN positive and LN negative
- Based on pooled data of 7800 esophagectomy predominantly squamous cell type
- The data has been validated in adenocarcinoma
- Worldwide Esophageal Cancer Collaboration (WECC)

<table>
<thead>
<tr>
<th>Stage</th>
<th>LN No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>10</td>
</tr>
<tr>
<td>T2</td>
<td>20</td>
</tr>
<tr>
<td>T3-4</td>
<td>30</td>
</tr>
</tbody>
</table>
En-Bloc Esophagectomy

- Concept of en-bloc resection, as originally proposed by Logan and later reintroduced by Skinner 1968

- Resecting the tumor-bearing esophagus within a wide envelope of surrounding tissues

- *Pericardium anteriorly and both pleural surfaces laterally, as well as the azygous vein, thoracic duct and all other lympho-areolar tissue wedged posteriorly between the esophagus and the spine*

- *1-in cuff of diaphragm is excised circumferentially for GE junction tumor*

- Concept is valid for lower thoracic and GE junction tumor

- Aims to maximize local tumor control

- Can be combined with a two field or three field esophagectomy
En-Bloc Esophagectomy
### COMPLICATIONS

<table>
<thead>
<tr>
<th>Mortality rate</th>
<th>4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastomotic leaks</td>
<td>19% to 30%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>27%</td>
</tr>
<tr>
<td>Recurrent laryngeal nerve palsy</td>
<td>&gt;50%</td>
</tr>
<tr>
<td></td>
<td>long-term quality of life in terms of speech, swallowing, and respiratory functions</td>
</tr>
</tbody>
</table>

Tracheal ischemic necrosis is specific for extensive superior mediastinal dissection

GE JN CANCER
• Incidence of adenocarcinoma of the EGJ has been increasing at 5 to 10 percent annually since the mid 1970s

• Most rapidly increasing cancer in many Western countries
What is the GE Junction
Definition

- **Anatomical**: EGJ is localized at the level of the angle of His, paraesophageal pad of fat.
- **Physiological**: Distal border of the lower esophageal sphincter, as determined by manometry.
- **Endoscopically**: - Z line- squamo columnar junction - 3 to 10 mm proximal to the anatomically defined EGJ - Proximal most extent of gastric rugosal folds → transitioning to smooth lined esophageal mucosa.
- **Pathological**: In an opened esophagogastrectomy specimen as the most proximal aspect of the gastric folds.
Classification

• Siewert’s classification
Adenocarcinoma of the Esophagogastric Junction

Results of Surgical Therapy Based on Anatomical/Topographic Classification in 1,002 Consecutive Patients

J. Rüdiger Siewert, MD, FACS(Hon), FRCS, FASA,* Marcus Feith, MD,* M. Werner, MD,† and Hubert J. Stein, MD*

From the *Chirurgische Klinik und Poliklinik and †Institut für Pathologie und Pathologische Anatomie, Klinikum rechts der Isar, Technische Universität München, Munich, Germany

2000 Modified Siewert’s classification
AJCC 7th edition

Siewert Types I and II - esophageal cancer
Siewert Type III - gastric cancer
## Esophagectomy Morbidity

<table>
<thead>
<tr>
<th></th>
<th>Michigan</th>
<th>VA</th>
<th>MSKCC</th>
<th>Duke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leak</td>
<td>12%</td>
<td>NR</td>
<td>21%</td>
<td>14%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2%</td>
<td>21%</td>
<td>21%</td>
<td>16%</td>
</tr>
<tr>
<td>RLN Injury</td>
<td>4.5%</td>
<td>NR</td>
<td>4%</td>
<td>NR</td>
</tr>
<tr>
<td>Conduit Necrosis</td>
<td>2%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Chylothorax</td>
<td>1%</td>
<td>0.02%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>MI</td>
<td>NR</td>
<td>1.2%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Tracheal Injury</td>
<td>0.4%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>2%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Diaphragm Hernia</td>
<td>NR</td>
<td>NR</td>
<td>1.2%</td>
<td>NR</td>
</tr>
</tbody>
</table>
High Volume Centers for Esophagectomy: Number needed to achieve low post-operative mortality

- Reduction in post-op mortality with increasing case volumes per year
- Post-op complication rates are lower in high-volume hospitals

*Metzger, R. et al. Dis of the Esophagus, Vol17(4)310, Dec, 2004*
Surgery, future...?
MIE Techniques

• Thoracoscopic; laparotomy

• Laparoscopic; thoracotomy

• Laparoscopic; transhiatal

• Thoracoscopic; laparoscopic
## MIE vs Open

<table>
<thead>
<tr>
<th></th>
<th>MIE</th>
<th>Transthoracic</th>
<th>Transhiatal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time</td>
<td>364</td>
<td>437</td>
<td>391</td>
</tr>
<tr>
<td>Blood Loss</td>
<td>297</td>
<td>1046</td>
<td>1142</td>
</tr>
<tr>
<td>Intraop Transfusion</td>
<td>0.3</td>
<td>1.8</td>
<td>2.9</td>
</tr>
<tr>
<td>ICU Stay</td>
<td>6.1</td>
<td>9.9</td>
<td>11.1</td>
</tr>
<tr>
<td>Hospital Stay</td>
<td>11.3</td>
<td>23.0</td>
<td>22.3</td>
</tr>
<tr>
<td>No. LN’s Removed</td>
<td>10.8</td>
<td>6.3</td>
<td>6.9</td>
</tr>
</tbody>
</table>
MIE

- Minor complications 53 (24%)
- Major complications 71 (32%)

<table>
<thead>
<tr>
<th>Complication</th>
<th>N (%)</th>
<th>Complication</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>3 (1.4)</td>
<td>Chylothorax</td>
<td>7 (3.2)</td>
</tr>
<tr>
<td>Leak</td>
<td>26 (11.7)</td>
<td>Gastric necrosis</td>
<td>7 (3.2)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>17 (7.7)</td>
<td>Delayed gastric empying</td>
<td>4 (1.8)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>14 (6.3)</td>
<td>Tracheal injury</td>
<td>4 (1.8)</td>
</tr>
<tr>
<td>Recurrent nerve palsy</td>
<td>8 (3.6)</td>
<td>ARDS</td>
<td>4 (1.8)</td>
</tr>
</tbody>
</table>
Minimally invasive versus open - RCT

• Multicentre, RCT – Only RCT available

• June 1, 2009, and March 31, 2011

• Primary outcomes - Pulmonary infections

<table>
<thead>
<tr>
<th></th>
<th>Open (n=56)</th>
<th>MIS (n=59)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulm Infection</td>
<td>29%</td>
<td>9%</td>
<td>0.005</td>
</tr>
<tr>
<td>Pulm Infection (Hosp)</td>
<td>34%</td>
<td>12%</td>
<td>0.005</td>
</tr>
</tbody>
</table>

# Minimally invasive versus open -RCT
## Secondary outcomes

<table>
<thead>
<tr>
<th>Secondary outcomes</th>
<th>Open(n=56)</th>
<th>MIS(n=59)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital stay</td>
<td>14 Days</td>
<td>11 Days</td>
<td>0.04</td>
</tr>
<tr>
<td>SF-36</td>
<td>36</td>
<td>42</td>
<td>0.007</td>
</tr>
<tr>
<td>Lymphnode</td>
<td>21</td>
<td>20</td>
<td>0.8</td>
</tr>
<tr>
<td>Margins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>84%</td>
<td>92%</td>
<td></td>
</tr>
<tr>
<td>R1</td>
<td>9%</td>
<td>2%</td>
<td></td>
</tr>
</tbody>
</table>

Hospital-Volume Outcome: Esophagectomy

Metzger et al. Dis Esoph; 2004, 17:310-314

![Mortality rate distribution by volume categories](image)
High Volume Centers: What is the number needed to achieve low post-operative mortality

• Management of complications is more successful in high-volume hospitals

• Long-term prognosis is also correlated to case-volume

• With the experience of > 20 esophagectomies/yr mortality <5% can be achieved

Metzger, R. et al. Dis of the Esophagus, Vol17(4)310, Dec, 2004
## Results of surgery alone

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgical mortality</strong></td>
<td>&lt;10 %</td>
</tr>
<tr>
<td><strong>Med survival</strong></td>
<td>16m</td>
</tr>
<tr>
<td><strong>Med survival - R0</strong></td>
<td>27m</td>
</tr>
<tr>
<td><strong>3 yr survival</strong></td>
<td>26 %</td>
</tr>
</tbody>
</table>

Underscores need for adjuvant therapy
Most recurrences following esophagectomy are **systemic**

<table>
<thead>
<tr>
<th>Pattern of Recurrence post Esophageal Cancer Resection (%)</th>
<th>Locoregional</th>
<th>Hematogenous / distant</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osugi Oncol Rep 2003</td>
<td>11</td>
<td>58</td>
<td>-</td>
</tr>
<tr>
<td>Kato Anticancer Rsrch 2005</td>
<td>22</td>
<td>51</td>
<td>27</td>
</tr>
<tr>
<td>Fahn ATS 1994</td>
<td>33</td>
<td>61</td>
<td>-</td>
</tr>
<tr>
<td>Abate JACS 2010</td>
<td>30</td>
<td>60</td>
<td>10</td>
</tr>
</tbody>
</table>
Results of surgery alone: patterns of failure

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence</td>
<td>30 %</td>
</tr>
<tr>
<td>Distant mets</td>
<td>50 %</td>
</tr>
</tbody>
</table>

Underscores need for adjuvant therapy
Neoadjuvant

- NA Chemotherapy
- NA Radiotherapy
- NA chemoradiotherapy
- Chemoradiotherapy Vs Chemotherapy
Neoadjuvant Chemotherapy +/- Radiation Therapy

• Rationale
  – Down-staging of tumor
    • Increase “resectability” rate
    • Improve the ability of surgeon to perform a complete (R0) oncologic resection
  – Potentially prevent systemic spread at the earliest time-point of treatment
  – Tumor “oxygenation” may be better prior to surgery, thus enhancing effectiveness
  – Better compliance than if given post-operative
  – Better assessment of biology of tumor
    • 20% have complete pathologic response
  – Recent data has shown a survival advantage
Meta-analysis

- Ten randomised comparisons of neoadjuvant chemoradiotherapy versus surgery alone (n=1209) and
- Eight neoadjuvant chemotherapy versus surgery alone (n=1724) in patients with local operable oesophageal carcinoma

- Survival benefit was evident for preoperative chemoradiotherapy (13% at two years)
- No survival benefit of chemotherapy in squamous cell carcinoma and lesser survival benefit (7%) with adenocarcinoma of the oesophagus.

Lancet Oncol 2007
Palliative Therapy

• Epidemiology
  – >50% patients are inoperable due to:
    • Unresectable tumor
    • Metastatic disease
    • Poor medical condition

• Goal
  – Relieve dysphagia rapidly with no hospital stay

• Basic principles
  – Currently, no indication for “palliative esophagectomy”
  – Treatment should be individualized
    • Wide range of options