Esophageal Cancer: A Multimodality Approach to Detection and Staging

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Topic: Esophageal Cancer Imaging

A multimodality approach

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CME Objectives:
1. Overview of role of PET/CT in the initial work-up and subsequent management of esophageal cancer.
2. Discussing limitations, technical issues and pitfalls, related to hybrid imaging in oncologic application of PET/CT in esophageal malignancies.
3. An update on current literature, comparing PET/CT with CECT (contrast enhanced CT); MRT and EUS (endoscopic ultrasound).

Appreciation Note:
Society of Thoracic Radiology (STR-2014) Scientific Committee

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| Oncologic Imaging: Esophageal Cancer |
| Overview |

>US incidence: 1 in 200
>Worldwide: 10-100 x of US

ACC > SCC
SCC > ACC

| 2 main subtypes |
| Squamous cell carcinoma |
| Adenocarcinoma |

| Location |
| Upper 2/3 |
| Lower 1/3 |

Predisposing factor:
Tobacco & Alcohol
Reflux & Barrett's

| Poor 5 year survival (≈SYS) |
| Advanced at the time of Dx |
| Main survival factor: Extent at the time of Dx |
| Confined: 5YS = 37 |
| Regional: 17 |
| Distant: 3 |

| Sensitivity for detecting the primary tumor: |
| PET alone: 70-100 |
| CT alone: 65-90 |
| Wieder et al 2011 |
| Debashish & Siegel 2004 |

| Uptake values: |
| Adenoca ≈ Squamous CA |
| Cannot be distinguished by SUVs |

| Higher overall uptake: |
| Worse prognosis |
| SUV has prognostic value |
| Supporting papers: |
| Contradictory papers: |
Oncologic Imaging: Esophageal Cancer

**Overview**

- **Accuracy** for staging:
  - PET alone: 83%
  - PET/CT: 90%

- **Specificity** for staging:
  - PET alone: 59%
  - PET/CT: 81%

- Reasons:
  1. T-staging: No distant esophageal wall thickening + Hyper-metabolic foci
  2. N-staging: Normal size node (CT) + Hyper-metabolism
  3. M-staging: No liver lesion seen on CT + Hyper-metabolic foci

  - Yarem et al
  - Julevar et al

**PETCT cont.:**

- PET/CT contraindications to curative (radical) surgery:
  - Liver
  - Lung
  - Bone
  - Supraclavicular LN
  - Peri-esophageal nodes

**Distant met assessment:

- **Accuracy**
  - PET: 80%
  - PET/CT: 90%

- Reason: Some are hot but not big, some are big but not hot!

- PET/CT changes the management in 22% over CT alone and PET alone:
  - Finding CT anomalies after reviewing PET images!
  - Better localization of PET activities
  - Guiding endoscopy
  - Preventing subsequent work ups with PET and CT

- PETCT contraindications to curative (radical) surgery:
  - Liver
  - Lung
  - Bone
  - Supraclavicular LN
  - Peri-esophageal nodes

**CT alone**

- **Accuracy**
  - T-staging: 40-45%
  - N-staging: 40-75%
  - M-staging: 37% have occult metastasis

- CT provides info on:
  - Wall thickening
  - Mediastinal invasion/ involvement
  - Regional nodes
  - Liver/lung/adrenal / distant nodal / peritoneal mets

- **PET alone**
  - Detects almost 100% of esophageal cancers

**Accuracy**

- PET/CT:
  - Combined sensitivity for regional lymph node detection
  - Easier to mark activity of nearby lymph nodes
  - Potential advantage of PET/CT specificity over CT
  - Enlarged nodes with no activity (avoiding FP of CT)
  - PET/CT is more accurate than CT for distant metastases
  - Clinical point:
    - Regional nodes are resectable at surgery.
    - Positive regional node doesn’t preclude curative resection.
    - PET/CT is not good for regional node detection!
    - Staging PET/CT is accurate for distant metastases.
    - What matters!

**N-staging:

- Non-regional nodes:
  - Adenomatous:
    - Upper 1/3: 40%
    - Subcarinal LN: 10%
    - Lower (50%): Lung(20%) Bone (9%) Peritoneal (2%)
  - Gastric/Pancreatic/Pancreatic/Skin/Abd/Wall/Pericard./Spleen
  - CNS (2%)

**M-staging:

- Local:
  - For upper 1/3 cancers: Cervical nodes
  - For lower 1/3 cancers: Celiac nodes

- Non-regional nodes:
  - Adenomatous:
    - Upper 1/3: 40%
    - Subcarinal LN: 10%
    - Lower (50%): Lung(20%) Bone (9%) Peritoneal (2%)
  - Stomach/Pancreatic/Pancreatic/Skin/Abd/Wall/Pericard./Spleen
  - CNS (2%)

**Overview Overview

**N-staging:

- Usually (75%) nodal spread is one step/chain at a time
- Skip nodal spread incidence: up to 25%

- Loco-regional nodal staging with PET/CT (not that great):
  - Sensitivity: 51% (EUS+CT: 83%)
  - Specificity: 84%

**M-staging:

- T@Mid thorax: Super poor prognosis

- M1a:
  - Peritoneal mets
  - Supraclavicular LN
  - Bone
  - Liver

- M1b:
  - All other Ns are actually M1!

- Regional node:
  - No regional node
  - N0: No resection!
  - All other Ns are actually M1!
Oncologic Imaging: Esophageal Cancer: Initial Detection & Staging

### AJCC Staging of Esophageal Cancer according to the TNM Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>5YS</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>In situ</td>
<td>100</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
<td>100</td>
</tr>
<tr>
<td>T1</td>
<td>Carcinoma confined to the mucosa or submucosa</td>
<td>30</td>
</tr>
<tr>
<td>T2</td>
<td>Carcinoma invades the muscularis propria; T3 = carcinomas invade adjacent structures; N0 = no regional lymph node metastases</td>
<td>15</td>
</tr>
<tr>
<td>T3</td>
<td>Carcinoma invades the pericardium or pericardial structures; N1 = regional lymph node metastases</td>
<td>15</td>
</tr>
<tr>
<td>T4</td>
<td>Carcinoma invades other organs</td>
<td>15</td>
</tr>
</tbody>
</table>

**Endoscopic US > CT > PET**: Sensitivity: 80% Specificity: 90%

### M-staging

- **M1a**: For upper 2/3 cancers: Cervical nodes
- **M1b**: For lower 1/3 cancers: Celiac nodes

**Non-regional nodes**:
- Mediastinal nodes: 80%
- Supraclavicular LN: 10%
- Liver/Lung, Brain, Bone: 10%
- Peritoneal: 10%

**Local**:
- Endoscopic US > CT > PET

### Metastasis to Regional Lymph Nodes in Patients with Esophageal Squamous Cancer

**Conclusions**:
- Local node involvement
- Metastatic cervical lymph nodes
- PET/CT > CT
- PET/CT > PETCT
- PET/CT > FDG PET

**Checklist**:
- Lung
- Thyroid
- Colon
- Breast
- Bones
- Peritoneum
- Genitalia
- Skin
- Lymphoma

**Synchrony**
- DNA defect
- Environmental factors

**Reason**
- Multifocal Esophagus (Adeno)
- Barrett's
- Squamous (Esophagus)
- Colon
- Squamous (Esophageal)
- Lung

**Initial Detection & Staging**

**Reason**
- PETCT > CT
- PET/CT > PETCT
- PETCT > FDG PET

**Conclusion**
- Initial PET/CT baseline scanner
- PET scans done with no contrast.
TUESDAY

**Oncologic Imaging: Esophageal Cancer**

Initial Detection & Staging

- 11C-Choline PET better sensitivity than FDG and CT for mediastinal node assessment.
- 11C-Choline PET: marked hepatic activity: not useful for upper abdominal nodal assessment.

Non-Surgical Imaging:

- Best time would be before onset of therapy.
- CTx can induce inflammation: usually causing increase in FDG uptake.
- More accurate assessment of longitudinal extension of tumor.
- PET is more accurate due to structure: PET can assess the extent accurately.
- Marked impact on GTV & PTV:
  - 56% planning change by PETCT!

**Oncologic Imaging: Esophageal Cancer**

Radiation Planning

- PET improves the accuracy of RT Planning
- CT shows the radial extension of tumor
- PET:
  - More accurate nodal assessment (except those nearby primary lesion).
  - More accurate assessment of longitudinal extension of tumor.
  - PET: primary lesion is tumor due to structure: PET can assess the extent accurately.
  - Marked impact on GTV & PTV.
  - >50% planning change by PETCT!

**Oncologic Imaging: Esophageal Cancer**

Response to Therapy

**Fact:**
- 50-60% failure of response to Neoadjuvant CTx
- Great need for a tool for early response assessment!

1. PETCT is not particularly reliable modality to assess response to therapy in the primary lesion
   - Not for reassessment!

2. If done during therapy:
   - New foci may be found: Up-stage the cancer
   - 8-17% new metastatic can develop during the course of therapy.
   - Many of them are occult to conventional imaging modalities.
   - Able to re-assess for N and M
   - OK for N- & M-reassessment

3. Post neoadjuvant /RT: fat planes become blurry
   - Limited value of CT in accurate assessment
   - PETCT may be more useful than CECT alone

1. PETCT is not particularly reliable modality to assess response to therapy in the primary lesion
   - Not for reassessment!

2. Upon completion of therapy (CTx/RTx) repeat scan can provide insight for prognosis:
   - Residual activity: Non-responder. Poor prognosis
   - Best time for scanning:
     - Post RTx: 2 months
     - Post CTx: 1 month

**Oncologic Imaging: Esophageal Cancer**

Response to Therapy

**Best time to image (Controversial):**
- CTx/RTx can induce inflammation usually causing increase in FDG avidity.
- Time of onset of Post-Tx esophagitis: 14-35 day
  - So best time would be before onset of esophagitis, limiting FP results.
  - Within 2 weeks of initiation of therapy.
- Upon completion of therapy (CTx/RTx) repeat scan can provide insight for prognosis:
  - Residual activity: Non-responder. Poor prognosis
  - Best time for scanning:
    - Post RTx: 2 months
    - Post CTx: 1 month
Oncologic Imaging: Esophageal Cancer: Response to Therapy

**Data:**
- **Brucher et al.** (n=27): Those with 52% SUV drop in post-tx:
  - Differentiate Responders from Non-responders
  - Sensitivity: 100%
  - Specificity: 55%
  - 2-Shorter 5 year survival

- **Flamen et al.** (n=36): 3-4 weeks post-Tx: 80% drop Tumor/Liver ratio:
  - Differentiate Responders from Non-responders
  - Sensitivity: 71%
  - Specificity: 82%

- **Downey et al.** (n=17): Post-CTx: 60% drop in max SUV:
  - 2 year survival: 67% vs. 38%

- **Swisher et al.** (n=103): Post-CTx max SUV threshold of 4:
  - 18 month survival: maxSUV > 4: 34%
  - maxSUV ≤ 4: 77%

**Blub (4/20)**

Thank you for your attention.

**Bijan Bijan, MD**

Questions & Comments