The Role of 18F-FDG PET/CT in the Management of Gastric Cancers: A comprehensive review

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Disclosures

• None
Outline

• Background
• Gastric cancer characteristics
• Staging
  - Primary tumor
  - Lymph node disease
  - Distant metastases
  - Synchronous primary tumor
• Treatment Response Assessment
• Disease Recurrence
• Prognosis
Background

- 7.4 new cases of gastric cancer per 100,000 per year in the US
- 15th leading cause of cancer death
- Lifetime risk: 0.9%
- New cases in 2016: 26,370
- Number of deaths: 10,730
- 5 year survival rate: 30.4% (66.9% in localized disease; 30.9% in regional disease; 5.0% in distant disease)
NCCN guidelines

- Treatment ranges from Surgery, peri or pre operative chemotherapy/radiation, chemoradiation or palliative management
- Work-up: H&P, Upper GI endoscopy and biopsy, Chest/abdomen/pelvis CT with oral and IV contrast, PET/CT if no evidence of M1 disease and if clinically indicated
- Restaging/Post-treatment assessment: CAP CT with contrast, PET/CT as clinically indicated (Unresectable disease or non-surgical candidate following primary treatment)
- Follow-up/surveillance: CAP CT with contrast or upper GI endoscopy

Pathology

- Majority arise from gastric mucosa and are classified as adenocarcinomas.
- Lymphoid tissue, neuroendocrine cells or from the muscular layers of the stomach wall.
- Most are sporadic. True hereditary cancers are rare.
PET/CT in Gastric Cancers

- 18F-FDG PET/CT has been evaluated in the staging, treatment response evaluation, recurrence detection, follow-up and prognosis
- 18F-Fluorothymidine (FLT) – can be useful in tumors without or low FDG activity
Staging

- Primary tumor evaluation, locoregional and distant lymph node involvement, distant metastases
- Accurate staging and thereby impact on management
- Change in stage in 28.9% gastric adenocarcinoma patients
- Of those who were upstaged 64.5% developed progressive disease
- In patients with primary gastric lymphoma – change in stage in up to 35% of patients

• Chen R, et al. Relationship Between 18F-FDG PET/CT Findings and HER2 Expression in Gastric Cancer. J Nucl Med. 2016 Jul;57(7):1040-1044
Primary tumor

- No significant difference in SN and SP between CECT and 18F-FDG PET/CT
- Level of FDG activity in the primary tumor and lymph nodes may predict non-curative resection (p=0.001)
- Primary tumor peak-SUV associated with age (p=0.009), tumor depth (p<0.001), size (p<0.001), LN metastases (p<0.001)
- SUV-max higher in
  - T3/T4 tumors in comparison to T1/T2 tumors (9.0 vs. 3.8, p<0.001)
  - Distant metastases vs. no metastases (9.5 vs. 7.7, p=0.018)
  - Stage III/IV vs. stage I/II (9.0 vs. 4.7, p=0.017)

Oh HH et al. The peak-standardized uptake value (P-SUV) by preoperative positron emission tomography-computed tomography (PET-CT) is a useful indicator of lymph node metastasis in gastric cancer. J Surg Oncol. 2011 Oct;104(5):530-533.
Primary tumor

- SUV-max significantly higher in HER-2 negative patients
- Tumor FDG uptake correlates with Ki-67 expression in GIST tumors (Correlation coefficient 0.72)

Primary tumor

- **Differentiating lesions with FDG uptake?**
  - Dual-time point imaging at 1 and 2h after injection has been evaluated
  - 85% with increased SUVmax had a malignant lesion
  - 90% with decreased SUVmax had a benign lesion (p<0.001)
- **Differentiating tumors based on their histopathology**
  - Aggressive NHL exhibits higher SUVmax than gastric adenocarcinoma and MALT (p<0.05)
  - Pattern of FDG uptake may help differentiate gastric cancer from lymphoma

Pattern of FDG uptake

- **Type I**: Diffuse thickening of the gastric wall with increased FDG uptake of more than $1/3^{rd}$ of the stomach
- **Type II**: Segmental thickening of the gastric wall with increased FDG uptake involving less than $1/3^{rd}$ of the stomach
- **Type III**: Local thickening with focal FDG uptake
- Gastric lymphoma: Type I and II
- Gastric carcinoma: Type II and III
- The incidence of the involvement of more than one region of the stomach was higher in gastric lymphoma

Pattern of FDG uptake based on histopathology

- Increased FDG uptake in 89% gastric lymphoma and 71% MALT
- FDG avidity of SRCC, MAC significantly lower than well to poorly differentiated, papillary adenocarcinomas (SUVmax 6.43 vs 8.95)
- Gastric sarcomas: intense peripheral uptake with central photopenia within ill-defined heterogeneous masses

Valls-Ferrusola E, et al. Patterns of extension of gastrointestinal stromal tumors (GIST) treated with imatinib (Gleevec(R)) by 18F-FDG PET/CT. Rev Esp Enferm Dig. 2012 Jul;104(7):360-366.
Case Example
Lymph node metastases

• May have a higher SP and PPV in the detection of LN metastases than CECT
• No significant difference in the detection of regional LN metastases
• Significantly better patient-based SN, SP and accuracy for distant LN metastases
• Improvement in SN (p<0.005) and regional LN metastases detection (p<0.01) with regional PET/CT over gastric area performed 80min after injection with water gastric inflation

<table>
<thead>
<tr>
<th>Study</th>
<th>Modality</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy</th>
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<tbody>
<tr>
<td>Yang et al (2008)</td>
<td>CT</td>
<td>60.5%</td>
<td>83.3%</td>
<td>82.1%</td>
<td>62.5%</td>
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<td></td>
<td>PET/CT</td>
<td>31.0%</td>
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<td>Kim et al (2011) Regional LN metastases</td>
<td>CECT</td>
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<td>Namikawa et al (2014)</td>
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<td>64.5%</td>
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<td>PET/CT</td>
<td>64.7%</td>
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<td>Altini et al (2015)</td>
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<td>PET/CT</td>
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<td>Distant LN metastases</td>
<td>PET/CT+CECT</td>
<td><strong>67.6%</strong></td>
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<td><strong>86.0%</strong></td>
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<td>Kawanaka et al (2016)</td>
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<tr>
<td>Regional LN metastases</td>
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<td>80.0%</td>
<td>70.0%</td>
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<td>78.8%</td>
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</table>
Detection of synchronous primary cancers

- High diagnostic accuracy in detecting a synchronous colorectal cancer in 4.7% patients

Distant metastases

- Can detect occult metastases in 10% patients
- Addition of 18F-FDG PET/CT to the standard evaluation resulted in an estimated cost savings of USD 13000 per patient
- High SN, PPV and accuracy in detecting bone metastases, comparable to bone scan
- 15.0% of solitary bone metastases positive only on PET/CT

Ma DW et al. 18F-fluorodeoxyglucose positron emission tomography-computed tomography for the evaluation of bone metastasis in patients with gastric cancer. Dig Liver Dis. 2013 Sep;45(9):769-775
Treatment Response Assessment

- Small study evaluating tumor to liver ratio demonstrating a wide spectrum of response with a 22% median reduction.
- 30% reduction correlated with improvement in symptoms and anatomic imaging
- Short survival associated with increased tumor to liver ratio

Case Example
Detection of Recurrence

- Diagnostic accuracy higher in FDG-avid tumors and in non-anastomosis site recurrence
- After surgical resection the SN, SP, PLR and NLR: 86%, 88%, 17.0 and 0.16.
- PET/CT performance equal to or higher than CECT
- Higher diagnostic accuracy in peritoneal carcinomatosis

Detection of Recurrence

- FDG uptake of tumor at baseline predicts recurrence (24-mo RFS) in patients with adenocarcinoma (p=0.0001). Marginally significant in SRRC and mucinous carcinoma (p=0.05)
- Diagnostic accuracy lower in local recurrence as compared to liver (p=0.012) and bone (p=0.012)
- Cautious interpretation to be considered when FDG uptake at anastomotic sites noted and may persist over several follow-up scans.

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of study</th>
<th>SN</th>
<th>SP</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>PLR</th>
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<td>Park et al (2009)</td>
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<tr>
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<td>0.85</td>
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<td>0.78</td>
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<td>Lee et al (2011)</td>
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<td>Wu et al (2012)</td>
<td>Meta-analysis (n=526)</td>
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<td>3.9</td>
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Prognosis

- SUVmax of primary tumor >8 significant predictor of OS (p=0.048)
- SUVmax >5.74 poor prognostic predictor of PFS (p=0.034, HR 3.6)
- TLG was a significant predictor of OS (p=0.047) and time to metastasis (p=0.02)
- SUVpeak and max/liver ratio significantly unfavorable for RFS (p<0.05)
- SUVmax of nodal disease measure pre-operatively was an independent risk factor for RFS(p<0.0001) and OS (p<0.0001)
- ∆%SUVmax ≥70% predicted histopathological tumor response (p=0.047)

• 30% tumor size reduction was associated with a 50% SUVmax reduction (p<0.001).
• Better OS and PFS in patients with both tumor size and SUVmax reduction than in patients with either size or SUVmax reduction only (OS, p=0.003; PFS, p=0.038)

Thank you