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

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Disclosures

- None

Outline

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- 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)

NIH. SEER Stat Fact Sheets: Stomach Cancer 2011-2013; . Accessed 1/6/2017, 2016

NCCN guidelines

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- 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

NCCN. National Comprehensive Cancer Network Guidelines: Gastric Cancer. 2017; Accessed 1/6/2017, 2017

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

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- 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

- Altini C, et al. 18F-FDG PET/CT role in staging of gastric carcinomas: comparison with conventional contrast enhancement computed tomography. Medicine (Baltimore). 2015 May;94(20):e864.
- 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, $p=0.017$)

Hur H et al. The efficacy of preoperative PET/CT for prediction of curability in surgery for locally advanced gastric carcinoma. World J Surg Oncol. 2010 Oct 11;8:86.
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.
Namikawa T et al. Assessment of (18)F-fluorodeoxyglucose positron emission tomography combined with computed tomography in the preoperative management of patients with gastric cancer. Int J Clin Oncol. 2014 Aug;19(4):649-655.

Primary tumor

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

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
Deng SM et al Correlation between the Uptake of 18F-Fluorodeoxyglucose (18F-FDG) and the Expression of Proliferation-Associated Antigen Ki-67 in Cancer Patients: A Meta-Analysis. 2015 PLoS One.10(6):e0129028

Primary tumor

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- **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

Cui J, et al. Evaluation of Dual Time Point Imaging 18F-FDG PET/CT in Differentiating Malignancy From Benign Gastric Disease. Medicine (Baltimore). 2015 Aug;94(33):e1356.
Fu L et al. SUVmax/THKmax as a biomarker for distinguishing advanced gastric carcinoma from primary gastric lymphoma. 2012 PLoS One.7(12):e50914.
Wu J et al. 18F-fluorodeoxyglucose positron emission tomography/computed tomography findings of gastric lymphoma: Comparisons with gastric cancer. Oncol Lett. 2014 Oct;8(4):1757-1764.

Pattern of FDG uptake

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- **Type I**: Diffuse thickening of the gastric wall with increased FDG uptake of more than 1/3rd of the stomach
- **Type II**: Segmental thickening of the gastric wall with increased FDG uptake involving less than 1/3rd 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

Wu J, et al. 18F-fluorodeoxyglucose positron emission tomography/computed tomography findings of gastric lymphoma: Comparisons with gastric cancer. Oncol Lett. 2014 Oct;8(4):1757-1764

Pattern of FDG uptake based on histopathology

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- 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

Radan L, et al. FDG avidity and PET/CT patterns in primary gastric lymphoma. Eur J Nucl Med Mol Imaging. Aug 2008;35(8):1424-1430.
Kawanaka Y et al. Added value of pretreatment (18)F-FDG PET/CT for staging of advanced gastric cancer: Comparison with contrast-enhanced MDCT. Eur J Radiol. 2016 May;85(5):989-995.
Yi JH, et al. 18F-FDG uptake and its clinical relevance in primary gastric lymphoma. Hematol Oncol. Jun;28(2):57-61.
Gamble B, Meka M, Ho L. F-18 FDG PET-CT imaging in gastric sarcoma. Clin Nucl Med. Sep 2009;34(9):564-565.
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

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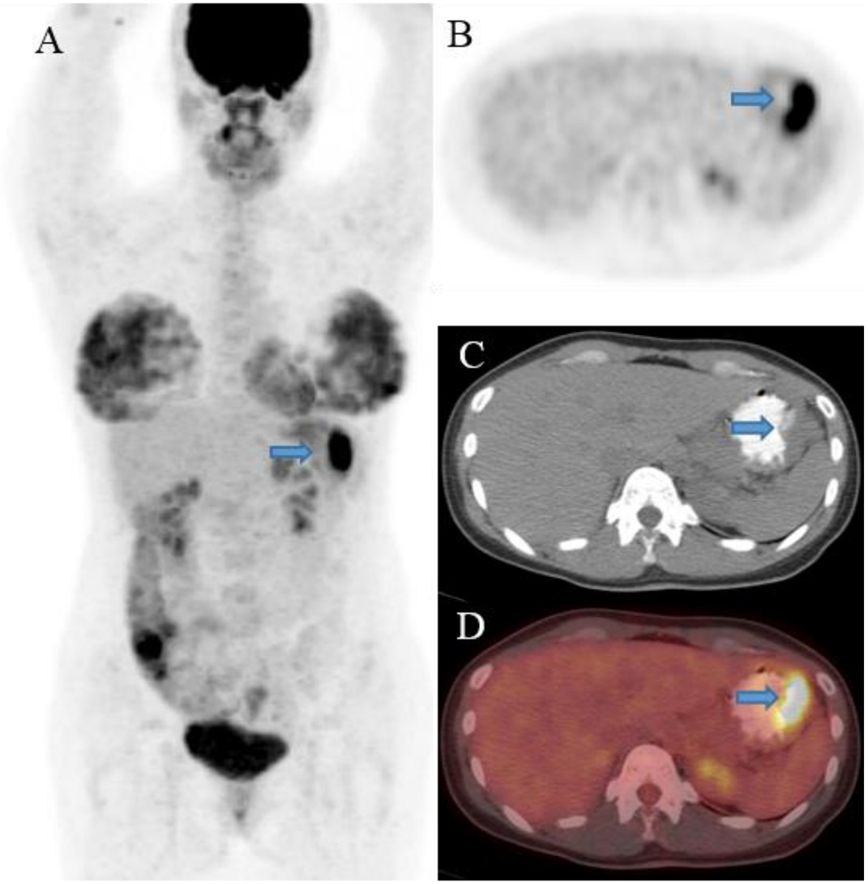
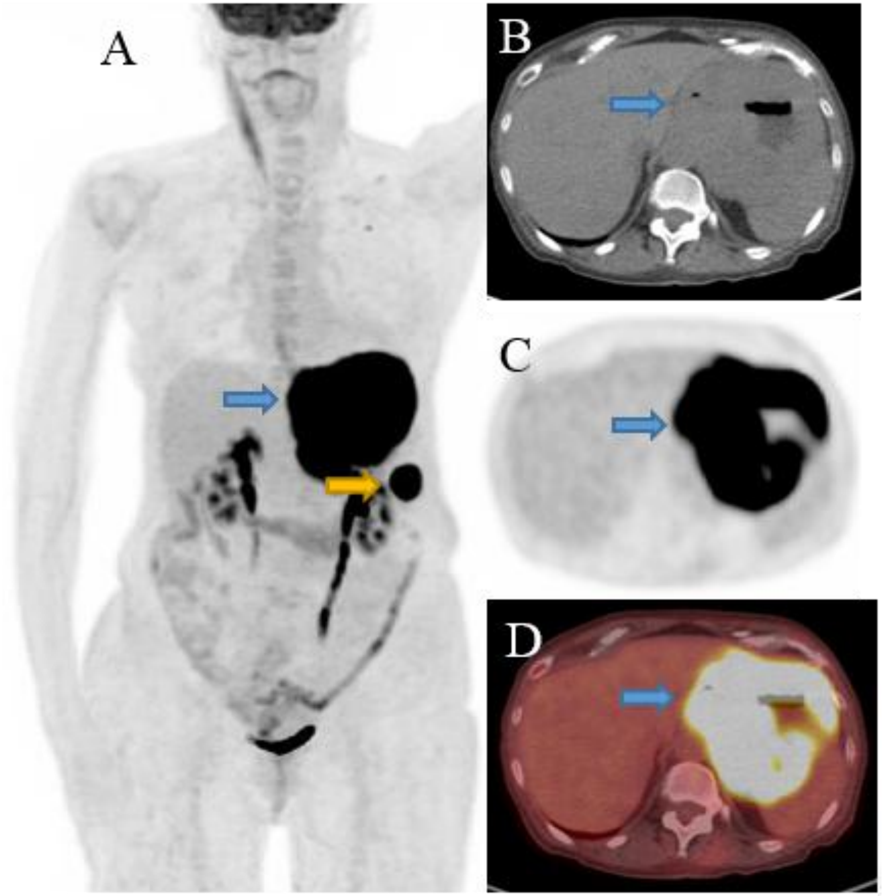
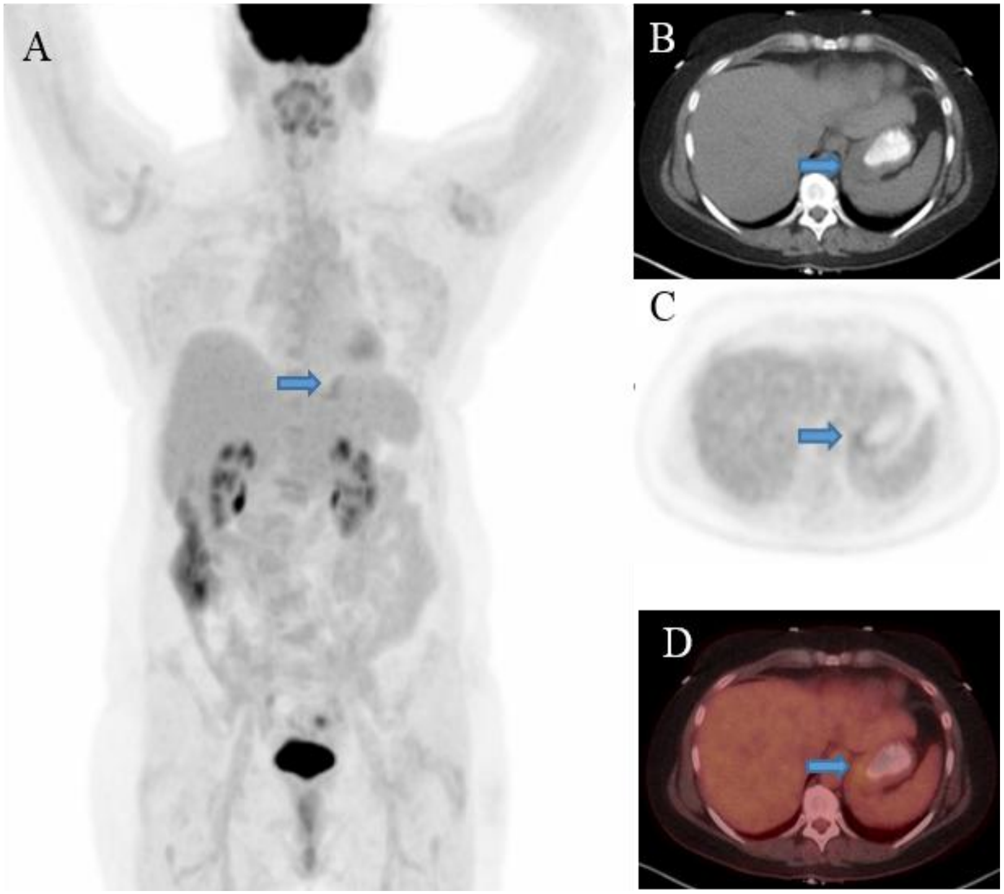


Case Example



Case Example



Lymph node metastases

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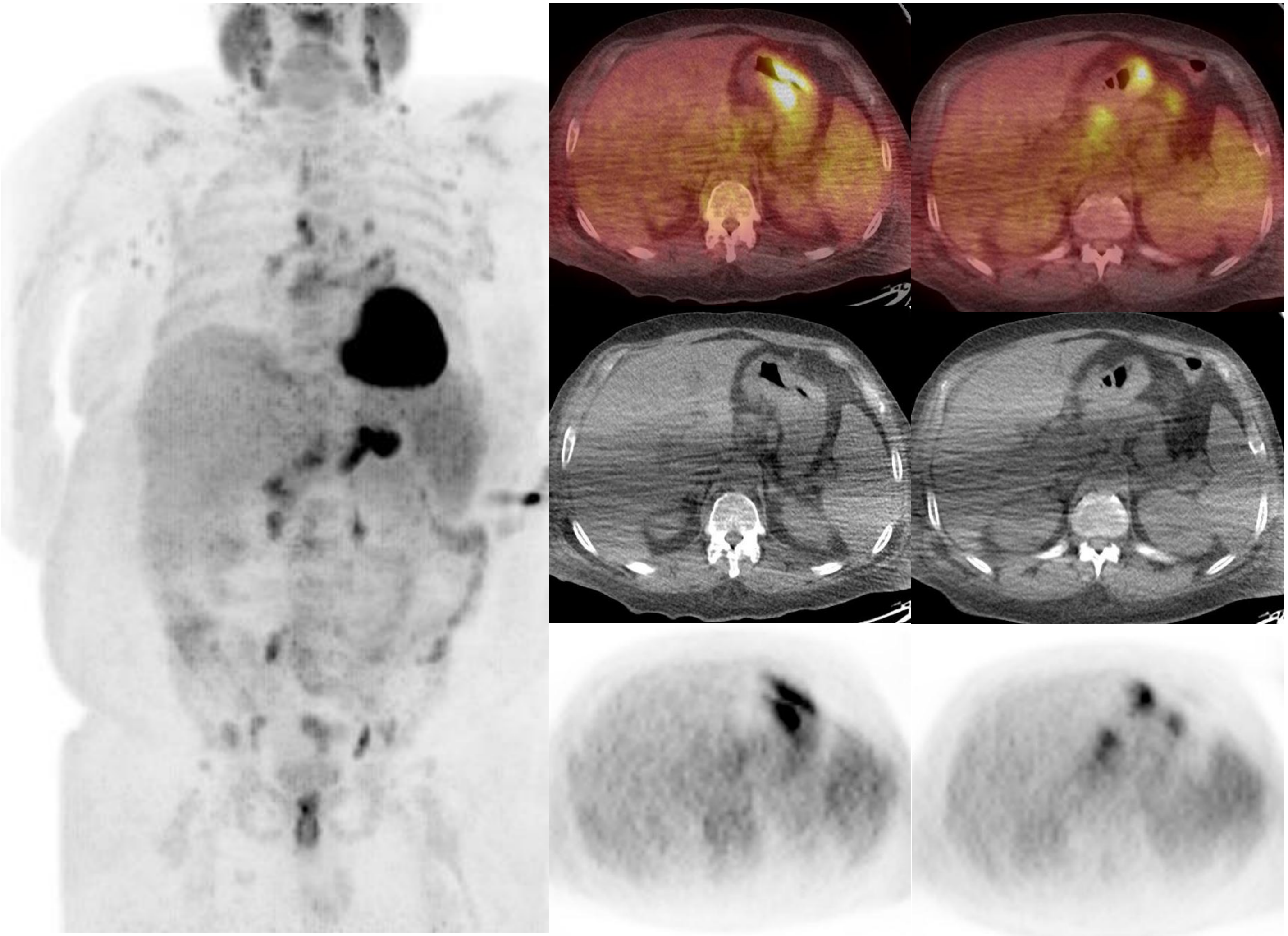
- May have a higher SP and PPV in the detection of LN metastases than CECT
- No significant difference in the detection of regional LN metastases
- Significantly better patient-based SN, SP and accuracy for distant LN metastases
- Improvement in SN ($p<0.005$) and regional LN metastases detection ($p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

Kawanaka Y et al. Added value of pretreatment (18)F-FDG PET/CT for staging of advanced gastric cancer: Comparison with contrast-enhanced MDCT. Eur J Radiol. 2016 May;85(5):989-995.
Lee SJ, et al. Regional PET/CT after water gastric inflation for evaluating loco-regional disease of gastric cancer. Eur J Radiol. 2013 Jun;82(6):935-942

Study	Modality	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
Yang et al (2008)	CT	60.5%	83.3%	82.1%	62.5%	70.6%
	PET/CT	31.0%	**97.2%**	**92.9%**	54.7%	61.5%
Kim et al (2011) Regional LN metastases	CECT	75.0%	92.0%	98.0%	42.0%	77.0%
	PET/CT	41.0%	**100.0%**	**100.0%**	26.0%	51.0%
Namikawa et al (2014)	PET/CT	64.5%	**85.7%**	**90.9%**	52.2%	71.1%
Park et al (2014) Regional LN metastases	CECT	51.0%	79.0%			64.0%
	PET/CT	34.0%	**88.0%**			58.0%
Filik et al (2015)	CECT	83.3%	75.0%	87.5%	66.6%	80.0%
	PET/CT	64.7%	**100.0%**	**100.0%**	57.1%	76.0%
Altini et al (2015)	CECT	70.83%	61.90%	68.0%	65.0%	66.66%
	PET/CT	58.33%	**95.24%**	**93.33%**	66.67%	75.55%
Kawanaka et al (2016) Distant LN metastases	CECT	45.9%	98.0%			75.6%
	PET/CT+CECT	**67.6%**	**100.0%**			**86.0%**
Kawanaka et al (2016) Regional LN metastases	CECT	84.0%	70.0%			82.4%
	PET/CT+CECT	80.0%	**70.0%**			78.8%



Detection of synchronous primary cancers

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

Choi BW, et al. Diagnostic accuracy of 18F-FDG PET/CT for detecting synchronous advanced colorectal neoplasia in patients with gastric cancer. Medicine (Baltimore). 2016 Sep;95(36):e4741.

Distant metastases

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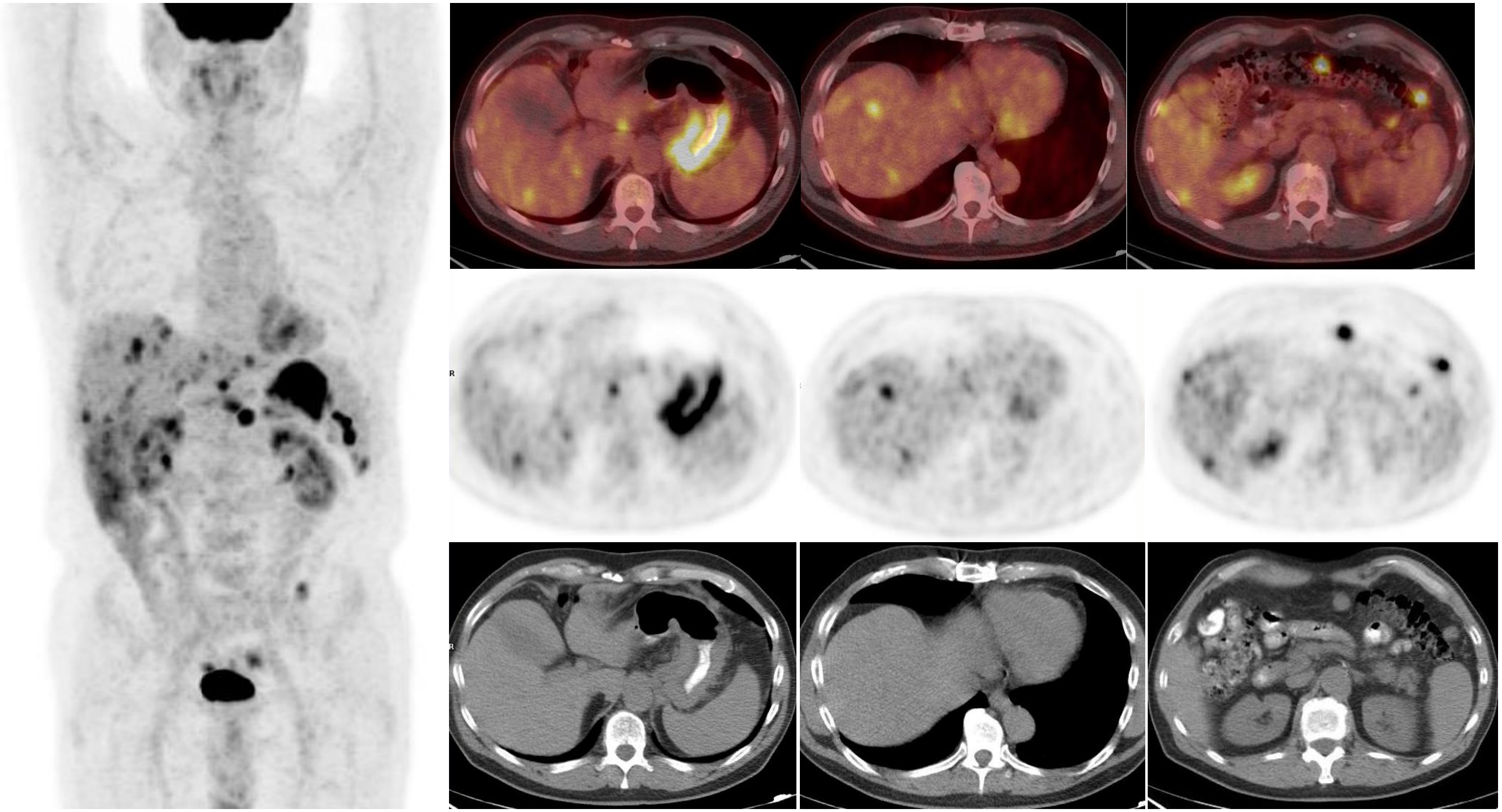
- Can detect occult metastases in 10% patients
- Addition of 18F-FDG PET/CT to the standard evaluation resulted in an estimated cost savings of USD 13000 per patient
- High SN, PPV and accuracy in detecting bone metastases, comparable to bone scan
- 15.0% of solitary bone metastases positive only on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

Smyth E al. A prospective evaluation of the utility of 2-deoxy-2-[(18) F]fluoro-D-glucose positron emission tomography and computed tomography in staging locally advanced gastric cancer. Cancer. 2012 Nov 15;118(22):5481-5488.
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

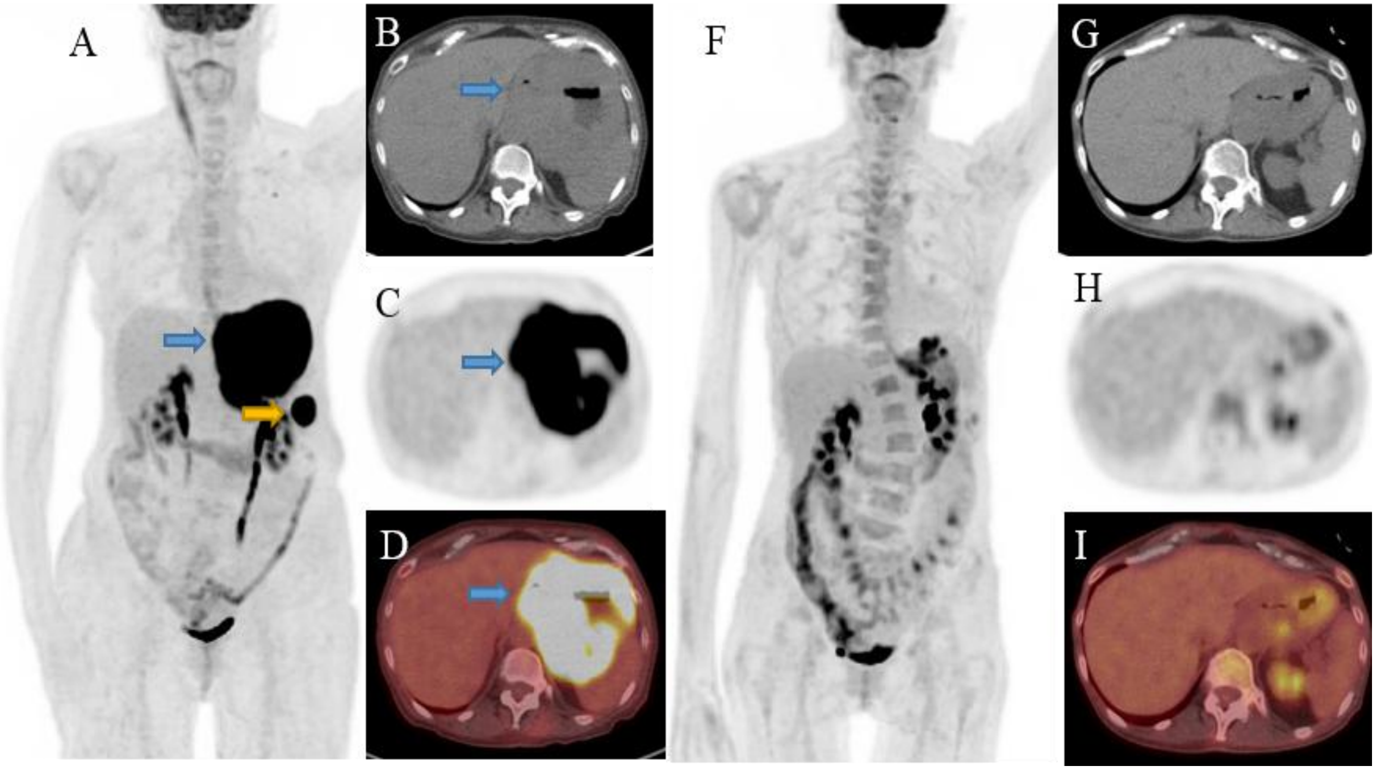


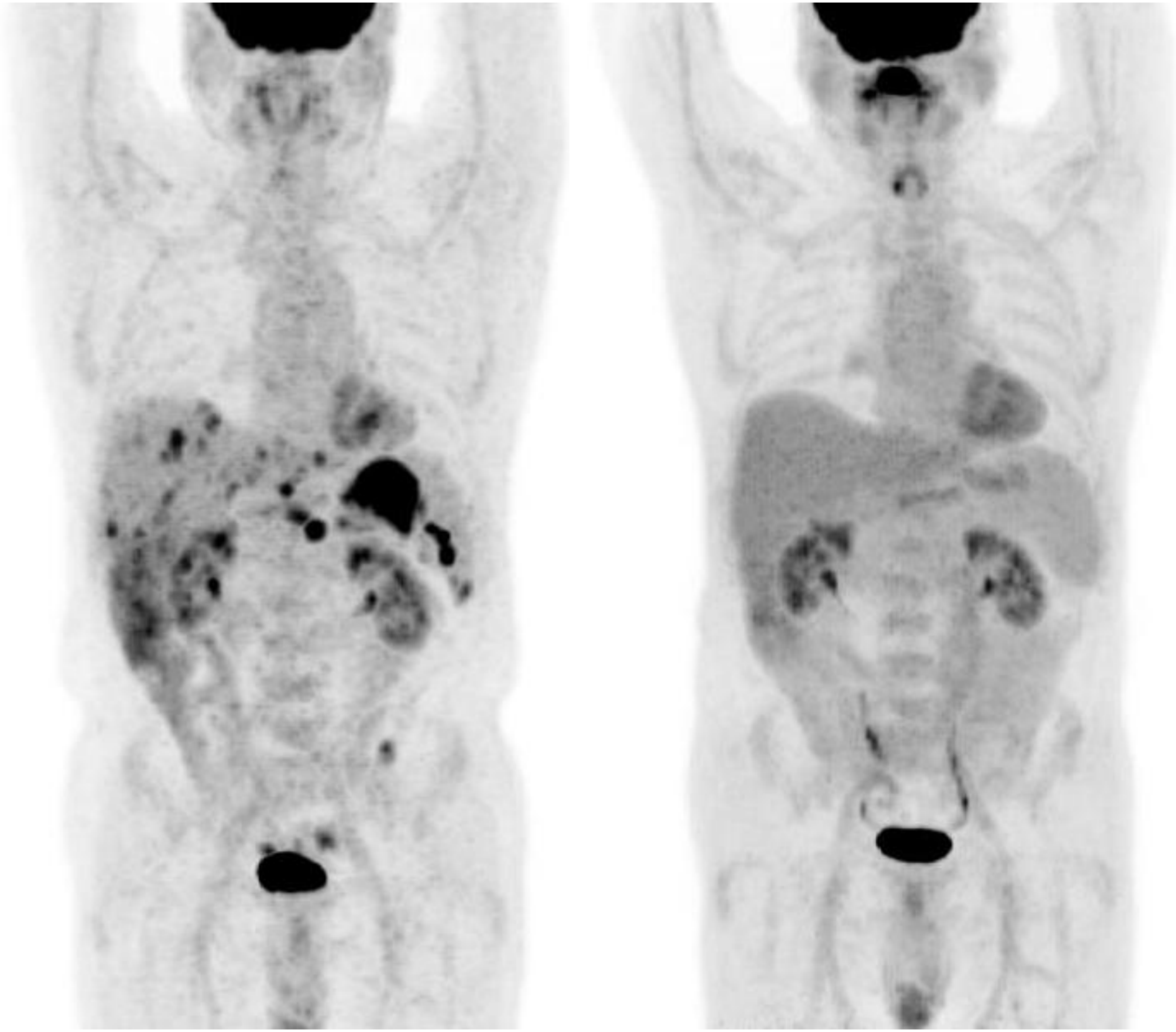
Treatment Response Assessment

- 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

Couper GW, McAteer D, Wallis F, et al. Detection of response to chemotherapy using positron emission tomography in patients with oesophageal and gastric cancer. Br J Surg. Oct 1998;85(10):1403-1406

Case Example





Detection of Recurrence

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- 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

Kim SJ, et al. Primary Tumor (1)(8)F-FDG Avidity Affects the Performance of (1)(8)F-FDG PET/CT for Detecting Gastric Cancer Recurrence. J Nucl Med. Apr;57(4):544-550.
Zou H, et al.18FDG PET-CT for detecting gastric cancer recurrence after surgical resection: a meta-analysis. Surg Oncol. Sep;22(3):162-166.
Wu LM, et al. 18 F-fluorodeoxyglucose positron emission tomography to evaluate recurrent gastric cancer: a systematic review and meta-analysis. J Gastroenterol Hepatol. Mar;27(3):472-480.
Kim DW et al. Detecting the recurrence of gastric cancer after curative resection: comparison of FDG PET/CT and contrast-enhanced abdominal CT. J Korean Med Sci. Jul;26(7):875-880.

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.

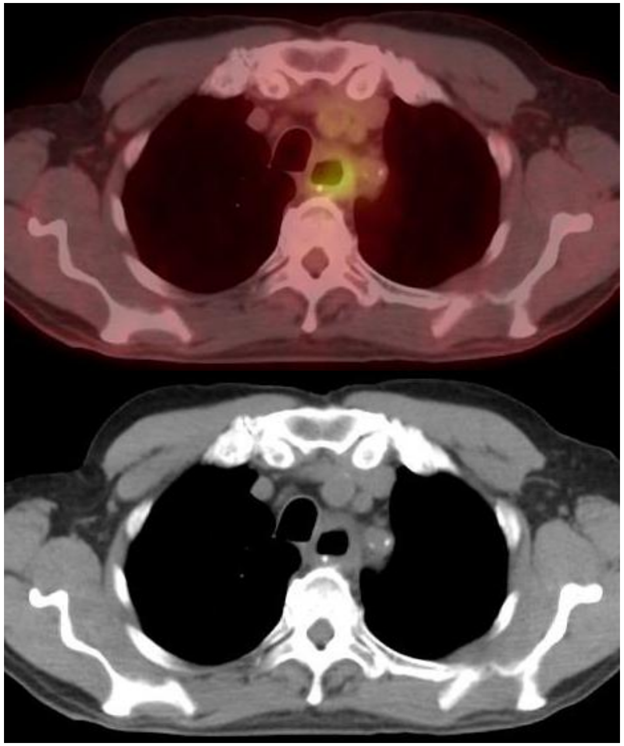
Lee JW, Lee SM, Lee MS, Shin HC. Role of (1)(8)F-FDG PET/CT in the prediction of gastric cancer recurrence after curative surgical resection. Eur J Nucl Med Mol Imaging. Sep;39(9):1425-1434.

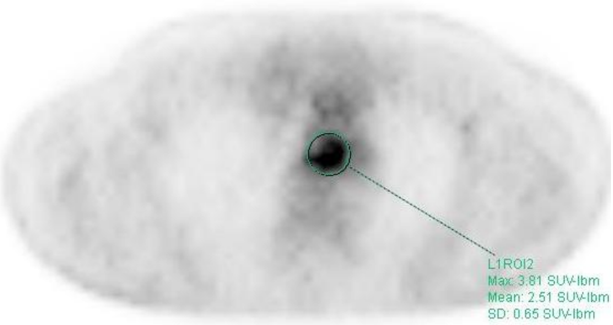
Sharma P, Singh H, Suman SK, et al. 18F-FDG PET-CT for detecting recurrent gastric adenocarcinoma: results from a Non-Oriental Asian population. Nucl Med Commun. Sep;33(9):960-966.

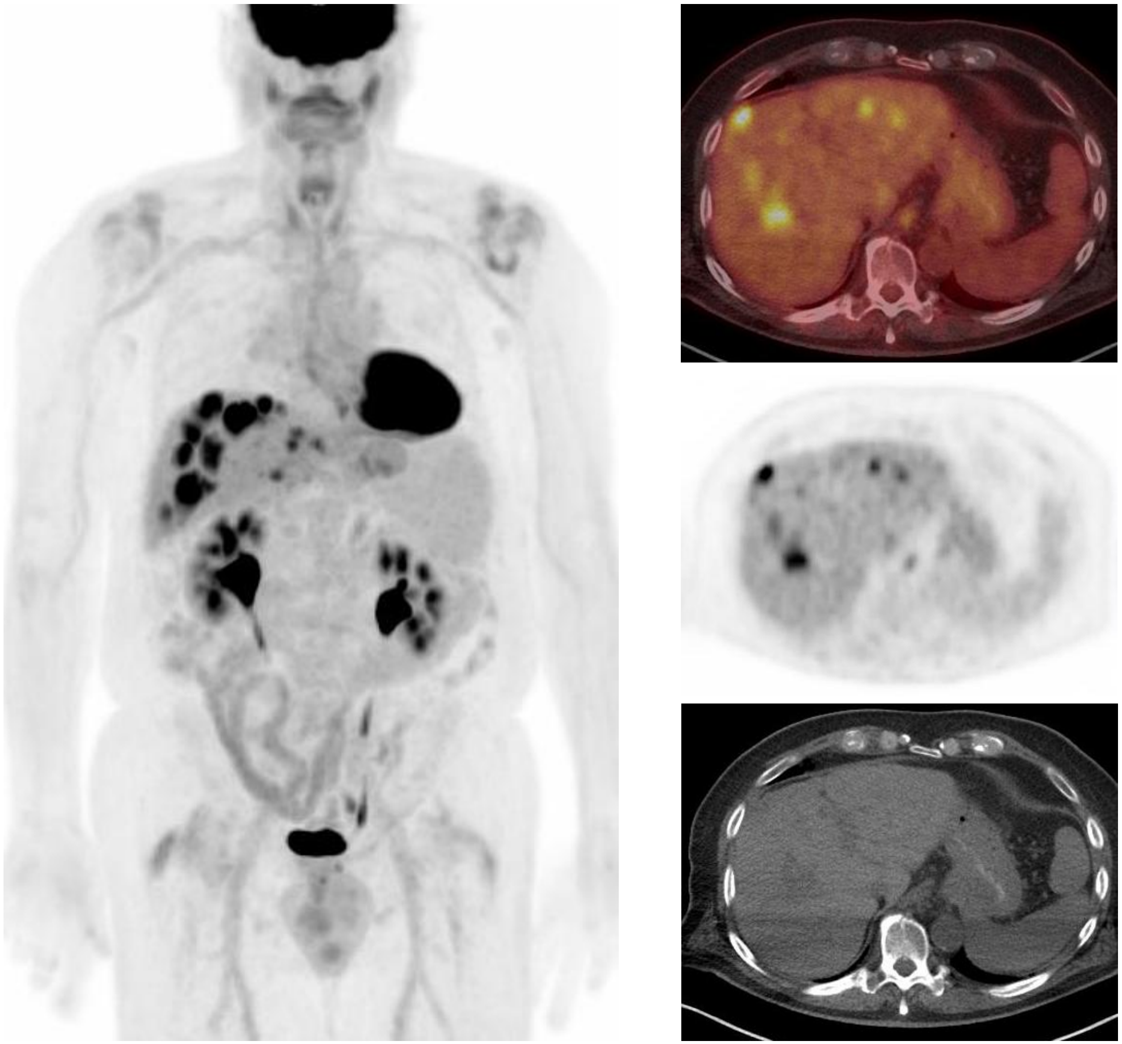
Lee DY, Lee CH, Seo MJ, Lee SH, Ryu JS, Lee JJ. Performance of (18)F-FDG PET/CT as a postoperative surveillance imaging modality for asymptomatic advanced gastric cancer patients. Ann Nucl Med. Oct;28(8):789-795.

Choi BW, Zeon SK, Kim SH, Jo I, Kim HW, Won KS. Significance of SUV on Follow-up F-18 FDG PET at the Anastomotic Site of Gastroduodenostomy after Distal Subtotal Gastrectomy in Patients with Gastric Cancer. Nucl Med Mol Imaging. Dec;45(4):285-290

Study	Type of study	SN	SP	PPV	NPV	Accuracy	PLR	NLR
Park et al (2009)	Retrospective (n=105)	0.75	0.77	0.89	0.55	0.75		
Nakamoto et al (2009)	Retrospective (n=92)	0.86	0.94	0.96	0.79	0.89		
Sim et al (2009)	Retrospective (n=52)	0.68	0.71	0.86				
Kim et al (2011)	Retrospective (n=139)	0.54	0.85			0.78		
Lee et al (2011)	Retrospective (n=89)	0.43	0.60	0.29	0.78	0.57		
Wu et al (2012)	Meta-analysis (n=526)	0.78	0.82				3.52	0.32
Zou et al (2013)	Meta-analysis (n=500)	0.86	0.88				17.0	0.16
Cayvarli et al (2014)	Retrospective (n=130)	0.91	0.62	0.85	0.75	0.82		
Lee et al (2014)	Retrospective (n=46)	1.00	0.88	0.44	1.00			
Li et al (2016)	Meta-analysis (n=828)	0.85	0.78				3.9	0.19




L1ROI2
Max: 3.81 SUV-lbm
Mean: 2.51 SUV-lbm
SD: 0.65 SUV-lbm



Prognosis

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- 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 ($p<0.0001$)
- Δ%SUVmax ≥70% predicted histopathological tumor response ($p=0.047$)

Chung HW, Lee EJ, Cho YH, et al. High FDG uptake in PET/CT predicts worse prognosis in patients with metastatic gastric adenocarcinoma. J Cancer Res Clin Oncol. Dec;136(12):1929-1935.
Kim J, Lim ST, Na CJ, et al. Pretreatment F-18 FDG PET/CT Parameters to Evaluate Progression-Free Survival in Gastric Cancer. Nucl Med Mol Imaging. Mar;48(1):33-40.
Park JC, Lee JH, Cheoi K, et al. Predictive value of pretreatment metabolic activity measured by fluorodeoxyglucose positron emission tomography in patients with metastatic advanced gastric cancer: the maximal SUV of the stomach is a prognostic factor. Eur J Nucl Med Mol Imaging. Jul;39(7):1107-1116.
Park JW, Cho CH, Jeong DS, Chae HD. Role of F-fluoro-2-deoxyglucose Positron Emission Tomography in Gastric GIST: Predicting Malignant Potential Pre-operatively. J Gastric Cancer. Sep;11(3):173-179.
Grabinska K, Pelak M, Wydmanski J, Tukiendorf A, d'Amico A. Prognostic value and clinical correlations of 18-fluorodeoxyglucose metabolism quantifiers in gastric cancer. World J Gastroenterol. May 21;21(19):5901-5909.
Na SJ, O JH, Park JM, et al. Prognostic value of metabolic parameters on preoperative 18F-Fluorodeoxyglucose positron emission tomography/ computed tomography in patients with stage III gastric cancer. Oncotarget. Sep 27;7(39):63968-63980.
Song BI, Kim HW, Won KS, Ryu SW, Sohn SS, Kang YN. Preoperative Standardized Uptake Value of Metastatic Lymph Nodes Measured by 18F-FDG PET/CT Improves the Prediction of Prognosis in Gastric Cancer. Medicine (Baltimore). Jul;94(26):e1037
Manhohran et al. Serial imaging using [18F]Fluorodeoxyglucose positron emission tomography and histopathologic assessment in predicting survival in a population of surgically resectable distal oesophageal and gastric adenocarcinoma following neoadjuvant therapy.Ann Nucl Med 2017 March 15.

Prognosis

- 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, $p=0.038$)

Park et al. Prospective evaluation of changes in tumor size and tumor metabolism in advanced gastric cancer undergoing chemotherapy: association and clinical implication. J Nucl Med. 2016 Nov 10. pii: jnumed.116.182675. doi: 10.2967/jnumed.116.182675

Thank you