

Clinical Area: FDG PET for esophageal cancer staging.
Keywords: FDG PET, Esophageal cancer, Staging.
Reference: Flamen P, Lerut A, VanCutsem E, De Wever W, Peeters M, et al. Utility of Positron Emission Tomography for the Staging of Patients with Potentially Operable Esophageal Carcinoma. *J Clin Oncol* 2000; 18:3202-3210

Study Type: Comparison of diagnostic tests.
Study Aim: To assess the performance of FDG PET in the staging of esophageal carcinoma.

Outcomes

- *Primary:* Staging, sensitivity and specificity.

Design

- *Number of subjects:* N=74. n=43 with carcinomas of the esophagus, and n=31 with carcinomas of the gastroesophageal junction.
- *Description of study population:* These were patients sent to the University hospital of Leuven for evaluation of resectability. There was no reference to the age, or sex of the patients.
- *Inclusion criteria:* Patients with newly diagnosed, biopsy proven esophageal carcinoma.
- *Exclusion criteria:* Prior Esophageal carcinoma treatment, diabetes mellitus, inflammatory lung disease, and inoperability for medical reasons.
- *Procedure:* All patients underwent standard staging procedures, including history and physical examination, lab tests, ultrasound examination of the neck, barium esophagogram, bronchoscopy, spiral CT of the chest and abdomen, and a transesophageal EUS. Within the same week, a FDG PET scan was performed.

Validity

- *Independent blind comparison with a gold standard or follow-up of those not receiving the gold standard test?* Interpretation of PET was blinded. The gold standard for T stage was defined by histology and that for LN by histologic examination in the patients who had lymphadenectomy in conjunction with the esophagogastrectomy. The gold standard for Stage IV disease (M1 stage with organ and/or distant metastases) was, histology, dedicated radiographic techniques, or clinical and radiographic follow-up.
- *Was “normal” defined?* Yes
- *Appropriate spectrum of disease?* Yes, only patients with esophageal carcinoma well included.
- *Consecutive patients?* Yes.
- *Methods described in enough detail to enable you to replicate the test?* Yes.
- *Reproducible results?* Yes.

Conclusions regarding validity of methods: This is a reasonably well done study to evaluate a diagnostic test. However, the exclusion of patients with inflammatory lung diseases was a selection bias that could affect the specificity of the results. The gold standard for stage IV disease was not well defined (histology, radiography, or clinical) which can limit the accuracy of staging.

Results:

PET was 95% sensitive in detecting primary esophageal carcinomas. False negative images were found in four patients with tumors < 8mm diameter. This sensitivity was not compared to that of CT or endoscopic esophageal ultrasound (EUS).

There was no correlation between the intensity of the primary tumor FDG uptake (SUV) and the pT stage of the tumor. In resectable, non-obstructing carcinomas (n=42) the EUS was accurate for assessing the depth of tumor infiltration in 64% of cases, over-staged the T stage in 19%, and under-staged it in 17% of patients.

Detection of Stage IV in Patients With Esophageal Cancer (n=74)

	<i>Sensitivity</i>	<i>Specificity</i>
PET	74%	90%
CT	41%	83%
EUS*	42%	94%
CT+EUS	47%	78%

* Complete passage of endoscope, at primary tumor, was possible in only 55 patients.

PET had a significantly higher sensitivity compared to the combined CT+EUS (p=0 .004) in detecting stage IV cancer.

Detection of Malignant LN Involvement in Patients Who Underwent Extensive Lymph Adenectomies with the Esophagectomy (n=39)

	<i>Sensitivity</i>	<i>Specificity</i>
PET:		
All LN	39%	97%
Local LN	33%	89%
Regional & Distant LN	43%	98%
EUS:		
All LN	63%	88%
Local LN	81%	67%
Regional & Distant LN	50%	91%
CT:		
All LN	22%	96%
Local LN	0%	100%
Regional & Distant LN	33%	95%
CT + EUS		
All LN	54%	90%
Local LN	62%	67%
Regional & DistantLN	48%	90%

For local lymph nodes, the sensitivity of PET (33%) was significantly lower than that of EUS (81%). P=0.027.

Specificity was higher but not statistically significant. CT did not detect any local LN (sensitivity: 0%)

For regional and distant lymph nodes, PET had a significantly higher specificity (98%) compared to the combined use of CT&EUS (90%) P= 0.025. The sensitivity was similar for both.

Authors' Conclusions:

The study confirms the high sensitivity of FDG-PET for primary tumor visualization. It has the limitation of missing small volume tumors (5% false negatives). The uptake of PET is not related to the clinicopathologic tumor grading. The study also shows that PET has a superior accuracy for diagnosing stage IV disease compared with the combined use of CT / EUS. EUS is the preferred method for assessment of local LN, and the combined CT / EUS for the regional and distant LN. FDG- PET had a high diagnostic specificity, but still incorrectly over staged some patients. Finally histologic and radiographic confirmation should be done on any patient diagnosed, with an unresectable disease, based on PET.

Reviewer's Conclusions:

This was a reasonably well-done study comparing FDG PET with other diagnostic and staging procedures for esophageal carcinoma. However, the exclusion of patients with inflammatory lung diseases led to a selection bias, which could have falsely raised the specificity of FDG PET. In addition, more than one gold standard was used which limits the accuracy of staging.