Systematic review of the staging performance of 18F-fluorodeoxyglucose positron emission tomography in esophageal cancer


CRD summary
This review evaluated the diagnostic performance of 18-fluorodeoxyglucose positron emission tomography (FDG-PET) in the pre-operative staging of oesophageal cancer. The authors concluded that FDG-PET was more likely to be of clinical value in M-staging of oesophageal cancer than N-staging. The authors stated that, given the methodological limitations of the included studies, their results should be viewed with caution.

Authors’ objectives
To evaluate the diagnostic performance of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) in the pre-operative staging of oesophageal cancer.

Searching
MEDLINE, EMBASE and the Cochrane Library were searched in June 2003; the search terms were reported. The bibliographies of identified studies and relevant reviews were also checked. Unpublished data and conference proceedings were excluded. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
No inclusion criteria for the study design were specified. The review included both prospective and retrospective studies.

Specific interventions included in the review
Studies evaluating the diagnostic accuracy of FDG-PET for the staging of oesophageal cancer were eligible for inclusion. Other investigations in the pre-operative work-up of patients in the included studies were (in various combinations) computed tomography (CT), chest X-ray, barium swallow, endoscopy, endoscopic ultrasonography, bone scintigraphy, bronchoscopy, and ultrasound of the neck; CT was used in the majority of studies. No further details of the imaging protocols used in the included studies were reported.

Reference standard test against which the new test was compared
The included studies were required to use pathology or surgery as the reference standard. All of the included studies used histopathology of resected specimens or surgical biopsies (alone or in radiological follow-up) as the reference standard.

Participants included in the review
Studies conducted in patients with histologically proven cancer of the oesophagus or gastro-oesophageal junction were eligible for inclusion. Where reported, the age of the participants ranged from 22 to 90 years for staging studies, and the proportion of male participants ranged from 72 to 100%. Most studies included a mix of patients with either squamous cell carcinoma or adenocarcinoma.

Outcomes assessed in the review
The included studies were required to report sufficient data for the construction of 2x2 contingency tables. Calculated values for sensitivity, specificity, positive and negative predictive values, and prevalence were reported for each included study.

How were decisions on the relevance of primary studies made?
Two reviewers independently screened articles for inclusion. Any disagreements were resolved by consensus.
Assessment of study quality
Two reviewers independently assessed the methodological quality of the included studies. Any disagreements were resolved by consensus. Quality was assessed using the criteria recommended by the Cochrane Methods Working Group on Systematic Review of Screening and Diagnostic Tests, with some review-specific modifications. The criteria assessed aspects of internal and external validity: the former included validity of the reference standard, blinded interpretation of the index test and reference standard, avoidance of verification bias, interpretation of index test blind to clinical data, prospective or retrospective study design; the latter included disease and demographic spectrum, inclusion and exclusion criteria, avoidance of selection bias, standard execution of index test. Overall quality scores were calculated for internal and external validity.

Data extraction
Two reviewers independently extracted data with which to calculate the sensitivity, specificity, and positive and negative predictive values for locoregional and distant metastases. For articles that did not present data based on the TNM classification system, reviewers re-staged patients according to this system wherever possible.

Methods of synthesis
How were the studies combined?
Meta-analysis was performed using a bivariate random-effects model to generate pooled estimates of sensitivity and specificity for locoregional and distant metastases.

How were differences between studies investigated?
No investigation of sources of between-study heterogeneity was reported.

Results of the review
Twelve studies with a total of 490 participants were included.

All studies had a valid reference standard, but most did not describe whether or not interpretation was blinded. Nine studies avoided verification bias. Eight studies were prospective and six recruited patients consecutively. The majority of the studies included all stages of disease.

Detection of locoregional lymph node metastases (N stage) (421 patients, 12 studies).

The pooled estimates for sensitivity and specificity were 0.51 (95% confidence interval, CI: 0.34, 0.69) and 0.84 (95% CI: 0.76, 0.91), respectively. The positive and negative predictive values derived from the included studies ranged from 0.70 to 1.00 and from 0.64 to 1.00, respectively. Detection of distant lymph node and organ metastases (M stage) (452 patients, 11 studies).

The pooled estimates for sensitivity and specificity were 0.67 (95% CI: 0.58, 0.76) and 0.97 (95% CI: 0.90, 1.00), respectively. The positive and negative predictive values derived from the included studies ranged from 0.60 to 1.00 and from 0.24 to 0.88, respectively.

An update study, published in 2006 (see Other Publications of Related Interest), identified 4 additional studies. These studies did not substantively alter the findings of the current review.

Authors' conclusions
‘FDG-PET showed moderate sensitivity and specificity for the detection of locoregional metastases, and reasonable sensitivity and specificity in the detection of distant lymphatic and hematogenous metastases.’

CRD commentary
This was a generally well-conducted and clearly defined review. The search strategy was reasonable and no language
restrictions were applied. The exclusion of unpublished and conference data leaves open the possibility of publication bias, the significance of which is uncertain with respect to diagnostic accuracy studies. The review methodology was reported clearly and included methods to minimise error and bias. Details of the included studies, including an assessment of methodological quality and individual results, were also reported clearly. The methodological quality assessment used criteria appropriate to diagnostic accuracy studies.

The meta-analytic method used was appropriate and was clearly stated and referenced. It is worth noting that the bivariate model used can be expanded to assess the impact of factors thought to contribute to between-study heterogeneity; this was not done or proposed in the current review, although the authors acknowledged the presence of significant heterogeneity which was probably due to the small size of the data set. The authors stated that, given the methodological limitations of the included studies, their results should be viewed with caution. In addition, their conclusions could be said to be somewhat optimistic given the low values for pooled sensitivity.

**Implications of the review for practice and research**

Practice: The authors stated that the moderate sensitivity of FDG-PET for the detection of locoregional metastases (N stage) means that it is not thought suitable for sole use in determining the allocation of neoadjuvant therapy in these patients. The presence of distant haematogenous metastases (M stage) excludes an intended curative surgical option; relatively high specificity of FDG-PET for M stage metastases therefore means that its potential impact upon the management of these patients is greater.

Research: The authors stated that larger prospective studies are needed to quantify the extent to which FDG-PET leads to changes in management and better outcomes for these patients. They suggested that future studies compare FDG-PET with multislice CT after an endoscopic ultrasonography fine-needle aspiration examination, and they recommended that studies use the International Union Against Cancer (UICC) classification system for staging of oesophageal cancer.

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**Other publications of related interest**


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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.