A metaanalysis of 18F-2-deoxy-2-fluoro-D-glucose positron emission tomography in the staging and restaging of patients with lymphoma

Isasi C R, Lu P, Blaufox M D

CRD summary
This review assessed the accuracy of 18F-2-deoxy-2-fluoro-D-glucose positron emission tomography (FDG-PET) for cancer staging in patients with lymphoma. The authors concluded that FDG-PET has a high sensitivity and specificity for this purpose. These conclusions are supported by the data presented but should be interpreted with caution given the limitations in the review methods, especially in relation to the selection criteria and literature search.

Authors' objectives
To evaluate the accuracy of 18F-2-deoxy-2-fluoro-D-glucose positron emission tomography (FDG-PET) in the staging of patients with lymphoma.

Searching
MEDLINE was searched from 1995 to June 2004 for published studies. No language restrictions were applied. The reference lists of original and review articles were screened for additional studies. The search terms were reported.

Study selection
Study designs of evaluations included in the review
Diagnostic accuracy studies were eligible. No restrictions relating to sample size were applied.

Specific interventions included in the review
Studies of FDG-PET were eligible for inclusion; studies using a coincident gamma camera were apparently excluded. Some included studies used an attenuation correction. PET interpretation was either visual or SUV (not defined in paper). Some studies reported using a fasting period of 4 to 6 hours or less. The uptake period of FDG, where reported, ranged from 15 to 90 minutes. Image reconstruction was by iterative reconstruction, filtered-back projection, or both.

Reference standard test against which the new test was compared
No inclusion criteria relating to the reference standard were specified. The reference standards used were pathology and/or clinical follow-up. Among studies that used clinical follow-up, this ranged from 3 to 72 months.

Participants included in the review
No inclusion criteria relating to the participants were specified. The patients had Hodgkin's disease and non-Hodgkin lymphoma, and were aged from 7 to 90 years (mean age: 29 to 66). The proportion of male patients ranged from 45 to 68%.

Outcomes assessed in the review
To be included, studies had to report sufficient data to enable the calculation of the sensitivity and specificity.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The quality of the studies was assessed using adapted published criteria: technical quality of PET, description of the reference standard, independence of test interpretation, description of the study sample, and cohort assembly. The authors did not state how the validity assessment was performed.
Data extraction
Data were extracted on the unit of analysis (patients or lesions) and the numbers of true-positive, false-positive, true-negative and false-negative results. The sensitivity and specificity were calculated for each study. Two reviewers extracted the data and any discrepancies were resolved by consensus.

Methods of synthesis
How were the studies combined?
Pooled sensitivity and false-positive rates with respective confidence intervals (CIs) were calculated (method not reported). Summary receiver operating characteristic curves were constructed using random-effects methods. Q* (the point of equal sensitivity and specificity) was calculated as a global measure of diagnostic accuracy. The presence of publication bias was evaluated with funnel plots and the Begg test.

How were differences between studies investigated?
Heterogeneity was investigated using the chi-squared test. The following subgroup analyses were performed to investigate heterogeneity: use of attenuation correction, visual interpretation of scans, whole-body scans and blinding. The effect of study characteristics on estimates of diagnostic accuracy was evaluated using regression methods. Separate analyses were conducted for those using patient-based data and those using lesion-based data.

Results of the review
Twenty studies were included: 14 reported patient-based data (854 patients) and 7 reported lesion-based data (3,658 lesions); 1 study reported both patient- and lesion-based data.

Seven of the 20 studies were conducted prospectively. PET images were interpreted blind to the results of the reference standard in 12 of the 20 studies; 4 studies did not report on blinding.

Studies with patient-based data (n=14).
The sensitivity ranged from 71 to 100% and the specificity from 50 to 100%. The pooled sensitivity was 91% (95% CI: 88, 93) and the pooled specificity was 90% (95% CI: 86, 93). Q* was 88%. There was no statistical evidence of heterogeneity. One study reported a very low specificity of 50% (the next lowest estimate was 81%). This study was restricted to patients with Hodgkin's disease. Another study reported a low sensitivity of 70%. This study evaluated the accuracy of PET in the detection of bone marrow involvement. Pooled sensitivity and false-positive rates were higher in patients with Hodgkin's disease when stratified according to whether the patients had Hodgkin's disease or non-Hodgkin lymphoma.

Studies with lesion-based data (n=7).
The sensitivity ranged from 92 to 99% and the specificity from 33 to 100% (but it was greater than 95% in all but 1 study). The pooled sensitivity was 96% (95% CI: 94, 97) and the pooled specificity was 99% (95% CI: 98.7, 99.4). There was statistical evidence of heterogeneity. This heterogeneity was removed when the study with very low specificity was excluded.

Authors' conclusions
PET has high sensitivity and specificity for the staging of patients with lymphoma.

CRD commentary
The study addressed a focused question but the inclusion criteria were poorly defined. The literature search was limited to one electronic database and the search terms restricted to those related to diagnosis. It is therefore likely that relevant studies have been missed. The review was restricted to published studies, thus there is the possibility of publication bias. Some details of the review process were reported and these included appropriate steps to minimise bias. However, details of how the study selection and quality assessment processes were undertaken were lacking.
Although pooling was appropriate given the data, the authors did not report the methods used to pool data; it is therefore not possible to comment on their validity. Regression analyses were undertaken to investigate possible reasons for heterogeneity but, given that the results were found to be relatively homogeneous and the very small number of studies and resulting generalisability issues, the clinical value of these analyses is questionable. The authors’ conclusions are supported by the data presented but should be interpreted with caution due to the limitations highlighted, especially in relation to the selection criteria and literature search.

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

Practice: The authors stated that clinicians may consider adding FDG-PET to the staging workup of patients with lymphoma.

Research: The authors did not state any implications for further research.

**Funding**

Integral PET Associates.

**Bibliographic details**


**PubMedID**

16047335

**DOI**

10.1002/cncr.21253

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Fluorodeoxyglucose F18; Humans; Lymphoma /pathology /radionuclide imaging; Neoplasm Staging; Positron-Emission Tomography

**AccessionNumber**

12005001234

**Date bibliographic record published**

30/04/2007

**Date abstract record published**

30/04/2007

**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.