Positron emission tomography in the diagnosis and staging of lung cancer: a systematic, quantitative review

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Authors' objectives
To assess the diagnostic value of dedicated positron emission tomography (PET) and gamma-camera PET for discriminating between malignant and benign solitary pulmonary nodules and pulmonary masses, and for staging in non-small-cell lung cancer (NSCLC).

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched for studies published between 1993 and June 2000; the search terms were listed. In addition, the bibliographies of retrieved studies were reviewed for additional papers. Studies published in English, German or French were eligible for inclusion. The authors made no attempt to locate unpublished studies.

Study selection
Study designs of evaluations included in the review
Any study design assessing the diagnostic accuracy of fluorodeoxyglucose PET in lung cancer, which described the methods and results adequately and included more than 10 participants, was eligible for inclusion in the review.

Specific interventions included in the review
Studies of either dedicated PET or gamma-camera PET assessing fluorine-18-labelled fluorodeoxyglucose in NSCLC were eligible.

Reference standard test against which the new test was compared
The authors did not specify any inclusion criteria in relation to the reference standard used. The reference standards varied between the included studies and were not always described clearly. The most common reference standard for diagnostic studies of dedicated PET was computed tomography. Bone scintigraphy and other standard methods were used in staging studies. Some studies compared gamma-camera PET and dedicated PET, using dedicated PET as the reference standard.

Participants included in the review
The authors did not specify any inclusion criteria relating to the study population. The participants were general and high-risk populations undergoing diagnostic testing for NSCLC. Seventy-one per cent of the participants were men (range: 41 to 99%). The mean reported age of the participants was 60 years (range: 56 to 66). The mean pre-test probability of NSCLC (prevalence) was 70% (range: 43 to 88%).

Outcomes assessed in the review
The authors did not specify any inclusion criteria relating to the outcomes. The main outcomes reported in the primary studies were test sensitivity and specificity. The authors calculated likelihood ratios from extracted data using 2x2 tables of true-positive, true-negative, false-positive and false-negative results. Studies that did not report sufficient data to construct 2x2 tables were excluded from the quantitative analysis. Positive and negative predictive values were also reported.

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 authors used a checklist to assess methodological quality. The factors assessed included generalisability of the findings, sample size, clinical relevance, description of clinical symptoms, appropriateness of reference standard,
technical quality and study design. Methodological quality was assessed after blinding the reviewers to the study authors’ names, year of publication, and results. The authors did not state how the papers were assessed for quality, or how many reviewers performed the quality assessment.

**Data extraction**
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data were extracted on publication details, participant characteristics, eligibility criteria for the participants, study design, imaging procedure, interpretation of scans, application of reference test, and results.

**Methods of synthesis**
How were the studies combined?
The studies were combined by pooling estimates of sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios to generate means. Diagnostic studies were pooled separately to studies of staging.

How were differences between studies investigated?
The authors described sources of variation such as participant and study characteristics. Subgroup analyses were conducted on methodological quality, interpretation of PET scans, and gamma-camera PET versus dedicated PET. A chi-squared test was used to assess whether there were significant differences between the groups.

**Results of the review**
Fifty-five relevant articles were identified, of which 19 contained insufficient data for inclusion in the quantitative analysis. Forty-six studies assessed dedicated PET and 9 focused on gamma-camera PET. The sample sizes were not provided for all studies. More than 800 participants were included in the diagnostic studies, 1,000 in studies of staging, and 400 in studies of gamma-camera PET.

The mean sensitivity of dedicated PET for diagnosing NSCLC was 96% (standard error, SE=1%) compared with 92% (SE=4%) for gamma-camera PET. The specificity was 78% (SE=3%) for dedicated PET and 86% (SE=4%) for gamma-camera PET.

The mean sensitivity of dedicated PET for mediastinal staging of NSCLC was 83% (SE=2%) compared with 81% (SE=4%) for gamma-camera PET. The specificity was 96% (SE=1%) for dedicated PET and 95% (SE=2%) for gamma-camera PET.

There was no significant correlation between methodological quality and the diagnostic performance of PET, except for negative predictive value when used for staging NSCLC.

**Cost information**
The authors reported that studies from the USA and Europe suggest that PET may be cost-effective in people at low to medium risk of NSCLC. PET may cost US$2,831 more per life-year saved when compared with a wait-and-watch strategy, but save US$6,082 per life-year saved when compared with an exploratory strategy.

**Authors’ conclusions**
The introduction of PET as a routine diagnostic tool for NSCLC would make it possible to decide whether a pulmonary nodule is malignant or benign, and to identify the stage of a potential cancer with one examination. This could be done with greater accuracy than with current noninvasive methods.

**CRD commentary**
The authors addressed a defined research question, were blinded when making quality assessments, and investigated the
The impact of study quality on the findings. However, the lack of inclusion criteria relating to a reference standard test may limit the reliability of the findings. The reference standard varied between the included studies and was not always fully defined. Although the authors reported only limited details about the studies included in the review, it seems likely that studies using different reference standards may have been pooled in the quantitative analysis. The authors did not discuss the possible effects of this.

The search strategies described were reasonably comprehensive. However, the included studies were restricted to those published in English, French or German, so the possibility of language bias remains. The authors acknowledged the possibility of publication bias and multiple publication bias, but they made no attempt to locate unpublished studies.

The authors used pooled estimates of diagnostic accuracy to generate overall means. There were methodological difficulties with many of the studies included, but the authors stated that this pooling was justified given the homogeneity of the studies. Heterogeneity test statistics were not presented, and factors other than methodological quality which may influence sensitivity and specificity estimates may not have been considered.

The review addressed the research question, but the findings should be treated with care given the quality of the included studies, the lack of details reported, and the statistical techniques used. The authors acknowledged many of the limitations of the review.

Implications of the review for practice and research
Practice: The authors suggested that dedicated PET may be a valuable tool in the diagnosis and staging of NSCLC.
Research: The authors suggested that further research is needed in populations with a lower prevalence of NSCLC.

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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.