18FDG-PET/CT for detection of mediastinal nodal metastasis in non-small cell lung cancer: a meta-analysis
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CRD summary
This review concluded that 18F-fluorodeoxyglucose positron emission tomography computed tomography (18FDG-PET-CT) had high specificity but low sensitivity for mediastinal nodal metastasis in patients with non-small cell lung cancer. The review process was generally well-conducted, but limitations with analyses and uncertainty regarding biases included studies were subject to, means the conclusions should be treated with caution.

Authors' objectives
To evaluate the role of 18F-fluorodeoxyglucose positron emission tomography computed tomography (PET-CT) in detecting mediastinal nodal metastasis in patients with non-small cell lung cancer (NSCLC).

Searching
MEDLINE, EMBASE and Evidence Based Medicine Review databases were searched without language restrictions 2000 to July 2011; studies that were published in languages other than English and Chinese were subsequently excluded. Search terms were reported. Reference lists were scanned for additional studies. Conference abstracts were excluded.

Study selection
Studies that used PET-CT to detect mediastinal nodal metastasis in at least ten patients with NSCLC at staging were eligible for inclusion. Studies had to use histopathologic findings as the reference standard and report sufficient data to construct 2x2 tables of test performance on a per patient or per nodal-station basis. Half the studies were conducted in Asia, with the others conducted in USA or Western Europe. Where reported, the age of study participants ranged from 23 to 90 years, and the proportion male from 42% to 95%. The studies varied considerably in terms of patient population, imaging techniques used and the histopathologic analyses.

Two reviewers independently selected studies for the review; disagreements were resolved by consensus.

Assessment of study quality
Two reviewers independently assessed study quality using the 14-point QUADAS tool.

Data extraction
Data were extracted to construct 2x2 tables of test performance. These data were used to calculate sensitivity, specificity and positive and negative likelihood ratios.

Two reviewers independently extracted data; disagreements were resolved by consensus.

Methods of synthesis
Pooled estimates of sensitivity, specificity, positive likelihood ratios and negative likelihood ratios with 95% confidence intervals (CI) were calculated using a random-effects model. Heterogeneity was assessed using X² (p<0.05 signified significant heterogeneity) and I² statistics. Summary receiver operating characteristic (SROC) curves were produced using the Moses-Littenberg model, from which the area under the curve (AUC) and Q* were calculated.

Results of the review
Twenty studies met the inclusion criteria (3,028 participants; range 36 to 674). Of the 20 studies, six reported results on a per patient basis, six on a nodal-station basis and eight reported both. The studies score between 11 and 13 out of a possible 14 on QUADAS. Eleven studies were prospective and nine retrospective.

Using the per patient data, the pooled estimate of sensitivity was 72% (95% CI 68 to 75), specificity was 90% (95% CI 88 to 91), positive likelihood ratios was 6.119 (4.612 to 8.119), and negative likelihood ratios was 0.286 (0.213 to 0.385); the AUC was 0.9138 and Q* was 0.8464. Using the per nodal station data, the pooled estimate of sensitivity was
61% (95% CI 58 to 64), specificity was 92% (95% CI 92 to 93), positive likelihood ratios was 7.970 (5.186 to 12.247), and negative likelihood ratios was 0.383 (0.307 to 0.478); the AUC was 0.8763 and Q* was 0.8067. There was substantial heterogeneity for all four analyses (I² ranged from 78.3 to 97.9).

Authors’ conclusions
PET-CT had high specificity but low sensitivity for mediastinal nodal metastasis in patients with NSCLC.

CRD commentary
The review addressed a clear research question with reproducible inclusion criteria. Relevant sources were searched without a methodological filter, but inclusion was restricted to published studies and two languages. Each stage of the review was conducted in duplicate, which reduced the risk of error and bias. Study quality was assessed using appropriate criteria, but the results were only reported as a summary overall score. Although all the trials failed only up to three criteria, the reader was not able to determine which bias each study was subject to, so the reliability of the estimates from the primary studies was unclear.

Pooled estimates of sensitivity and specificity were derived separately from extremely heterogeneous data; this may over-estimate accuracy. Therefore, both the reliability and generalisability of the pooled estimates was uncertain. More robust methods for the synthesis of such data were available that produce summary estimates of sensitivity and specificity whilst maintaining the within-study relationship of these measures. In addition, the potential causes of the heterogeneity were not investigated. Although the review process was generally conducted well, there are the limitations with the analyses and uncertainty surrounding the biases that the included studies are subject to, therefore the conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors stated that the positive likelihood ratios were not high enough to diagnose mediastinal nodal metastasis, and the negative likelihood ratios could not be used alone as a justification to rule out mediastinal nodal metastasis in patients with NSCLC.

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

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