Is FDG-PET suitable for evaluating neoadjuvant therapy in non-small cell lung cancer?
Evidence with systematic review of the literature
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CRD summary
This review concluded that positron emission tomography should not be used as the only reassessment tool following induction therapy for non-small cell lung cancer. Substantial heterogeneity between studies, the small number and size of included studies, a possibility of publication bias, limitations in quality assessment and lack of details regarding synthesis, make these conclusions unlikely to be reliable.

Authors' objectives
To determine the accuracy of 18-F fluorodeoxyglucose (FDG) positron emission tomography (PET) in evaluating induction therapy response in patients with non-small cell lung cancer (NSCLC).

Searching
MEDLINE, EMBASE, The Cochrane Library, ClinicalTrials.gov, NRR, INAHTA, DARE and NHS EED were searched from 1999 to August 2006 without language restrictions. Search terms were reported. Relevant articles, reference lists of retrieved articles and relevant websites were screened. The review was restricted to studies published as full-text articles.

Study selection
Prospective studies that evaluated PET or PET/computed tomography (CT) in at least 10 patients with non-small cell lung cancer suitable for neoadjuvant therapy were eligible for inclusion. Studies needed to use pathology confirmation, other imaging techniques or clinical follow-up over a year as the reference standard. Studies had to report data on the accuracy of the test or the clinical value of information about patient management and PET or PET/CT had to be performed before and/or after neoadjuvant therapy.

Studies were conducted in USA, Japan and Europe. All included studies assessed PET in preoperative restaging after induction therapy for locally advanced non-small cell lung cancer. Studies aimed to assess pathological response after neoadjuvant therapy or early during neoadjuvant treatment, or assessed restaging after neoadjuvant therapy. The cytotoxic drugs involved in neoadjuvant therapy varied between studies; most included platinum-based agents. Radiotherapy regimes varied. Surgery after neoadjuvant therapy was carried out in 76% of participants. Most studies used PET scanners; two used hybrid PET/CT scanners. Technical protocol of the PET procedure and interpretation of scans varied between studies.

Assessment of study quality
Two reviewers independently assessed study quality using QUADAS criteria. Summary scores out of a maximum of 14 points were calculated based on the number of items fulfilled.

Data extraction
One reviewer extracted or calculated accuracy data from the included studies. Estimates of accuracy presented included sensitivity, specificity, positive and negative predictive values and accuracy.

Methods of synthesis
Pooled estimates of sensitivity and specificity were reported and a summary receiver operating characteristic (SROC) analysis conducted; no details on methods used to estimate these were reported. Heterogeneity was assessed using the X² statistic.

Results of the review
Nine studies (n=367) were included in the review. Study quality scored between 5 and 11 points on the QUADAS score. Main weaknesses in study quality were selection criteria, independence of interpretation of test results and...
inclusion of intermediate results.

Sensitivity ranged from 80% to 100% and specificity ranged from 0% to 100%. Seven studies reported data on results of N2 restaging; data from these studies were pooled. Summary sensitivity was 64% (95% CI 53% to 74%) and summary specificity was 85% (95% CI 80% to 89%). There was some evidence of heterogeneity in sensitivity (p=0.06); data for specificity were lacking.

Authors' conclusions
The results did not support use of FDG-PET as the only reassessment tool for mediastinal lymph node evaluation for routine clinical use. FDG-PET seemed to predict primary tumour response to induction therapy, but it could not be shown by this analysis.

CRD commentary
The review addressed a clear question supported by defined inclusion criteria. The literature search was adequate, but restriction of the review to published studies raised the possibility of publication bias. Appropriate steps were taken to minimise bias and errors in the quality assessment; no such steps were taken for data extraction and it was unclear whether inclusion assessment was performed in duplicate. Appropriate criteria were used to assess study quality, but the results were presented as summary quality scores and were inappropriate for QUADAS. Details on the individual QUADAS items fulfilled were lacking. No details on how data were pooled were reported and so it was not possible to determine whether appropriate methods were used. There was considerable heterogeneity between studies; this was particularly apparent from the SROC plot and was not investigated further. Therefore, the pooled estimates should be interpreted with extreme caution.

Given differences between studies, the small number and size of the included studies, the possibility of publication bias and errors during data extraction, limitations in the quality assessment and a lack of details regarding methods of synthesis, the authors' conclusions are unlikely to be reliable.

Implications of the review for practice and research
Practi ce: The authors stated that the evidence did not support use of FDG-PET as the only reassessment tool for mediastinal lymph node evaluation following induction therapy for non-small cell lung cancer.

Research: The authors stated that larger prospective studies were required to confirm the diagnostic accuracy of FDG-PET in the evaluation of neoadjuvant therapy response in patients with non-small cell lung cancer.

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