A systematic review and meta-analysis of the role of positron emission tomography in the follow up of head and neck squamous cell carcinoma following radiotherapy or chemoradiotherapy

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CRD summary
This review concluded that positron emission tomography (PET) was highly accurate for detecting recurrent or residual head and neck squamous cell carcinoma following chemoradiotherapy, but was less sensitive less than 10 weeks after treatment and had poor anatomical detail. These conclusions should be viewed with caution due to weaknesses in the review process and data from small heterogeneous studies.

Authors' objectives
To determine the accuracy of ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET) for detecting recurrent or residual head and neck squamous cell carcinoma after radiotherapy or chemoradiotherapy.

Searching
MEDLINE and The Cochrane database were searched for English-language studies published before the end of October 2007. Search terms were reported. Bibliographies of included studies and review articles were screened for additional studies.

Study selection
Prospective and retrospective studies of FDG-PET for detecting recurrent or residual cancer following radiotherapy or chemotherapy in patients with head and neck squamous cell carcinoma were eligible for inclusion. Included studies were required to report sensitivity and specificity or false positive and false negative rates for either primary site or neck disease.

The primary site of disease varied. Reference standards used to determine disease recurrence varied and included histology from biopsy or surgical specimen and length of disease-free survival. Reporting of follow-up was generally poor; mean follow-up duration, where reported, ranged from 5.2 to 41 months.

The authors did not report how many reviewers assessed studies for inclusion.

Assessment of study quality
Methodological quality was assessed using the 14-item QUADAS tool to assess aspects of reporting quality, adequacy and independence of the reference standard, blinding, avoidance of verification biases, avoidance of disease progression bias and handling of uninterpretable results and withdrawals. An overall score (out of a maximum of 14) was calculated for each study.

The authors did not state how many reviewers performed quality assessment.

Data extraction
Data were extracted on the sensitivity and specificity, positive and negative predictive values and accuracy of FDG-PET for detecting recurrent/residual disease at the primary site and recurrent disease in the neck (nodal metastases). Where these values were not reported directly, they were calculated from reported data.

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
Summary receiver operating characteristic (SROC) curves and corresponding pooled estimates of sensitivity and
specificity with 95% confidence intervals (CIs) were calculated using a bivariate model. Separate models were constructed for primary site recurrence and for nodal metastases. A further analysis on data for the neck was performed after exclusion of the most outlying study.

Exploration of the following possible sources of heterogeneity (included as covariates in the model) was planned: timing from treatment to FDG-PET scan; reference standard used to confirm diagnosis; treatment mode (radiotherapy or chemoradiotherapy); and QUADAS score.

Results of the review
Twenty-seven studies (917 participants, range eight to 97) were included in the review. QUADAS scores ranged from 8 to 12 out of 14. All papers were scored highly for reporting quality.

Primary site recurrence/residual disease: Twenty studies (27 data sets) assessed recurrence/residual disease at the primary site. Pooled estimate of sensitivity was 94% (95% CI 87% to 97%) and pooled estimate of specificity was 82% (95% CI 76% to 86%). Pooled estimate of positive predictive value was 75% (95% CI 68 to 82%) and the pooled estimate of negative predictive value was 95% (95% CI 92 to 97%). QUADAS score did not effect the estimate of sensitivity, but higher QUADAS scores were correlated with lower specificity (p=0.04).

Recurrence/residual disease of nodal metastasis: Thirteen studies (14 data sets) assessed recurrence/residual disease in the neck. Pooled estimate of sensitivity was 74% (95% CI 50% to 89%), and pooled estimate of specificity was 88% (95% CI 74 to 95%). Pooled estimate of positive predictive value was 49% (95% CI 29% to 70%) and pooled estimate of negative predictive value was 96% (95% CI 84 to 99%). Exclusion of the outlying study made no significant difference to sensitivity and specificity.

The bivariate model indicated that estimates of sensitivity were significantly higher where FDG-PET was performed more than 10 weeks after treatment (p=0.002); no difference in specificity was identified. There were insufficient data to investigate other possible sources of heterogeneity (radiotherapy versus chemoradiotherapy, type of reference standard).

Authors' conclusions
Positive emission tomography (PET) was highly accurate for detecting recurrent or residual head and neck squamous cell carcinoma following chemoradiotherapy. However, it was less sensitive early after treatment (<10 weeks) and had poor anatomical detail. PET may reduce the requirement for check endoscopies and planned neck dissections.

CRD commentary
The review addressed a clearly stated research question defined by appropriate inclusion criteria. Although no inclusion criteria were specified for the reference standard, the reference standards used in included studies were described. A limited number of sources were searched to identify studies for inclusion in the review; this together with the restriction to studies published in English may have resulted in a loss of some relevant data. Restriction to English-language studies left open the possibility of language bias. It was unclear whether measures were taken to avoid error and/or bias in the review process. Methodological quality of included studies was assessed using QUADAS and the results of assessment incorporated in the meta-analysis as an overall quality score. However, as acknowledged by the authors, use of an overall score is not recommended for QUADAS. Appropriate meta-analytic methods were used. The authors' conclusions broadly reflected the data presented, but should be viewed with some caution given that they were based on data from small, heterogeneous studies and there were some weaknesses in the review process.

Implications of the review for practice and research
Practice: The authors stated that the findings of their analysis strongly suggested that PET could be incorporated a surveillance policy for nodal disease following chemoradiotherapy. A negative PET scan was highly predictive of the absence of disease, with a negative predictive value of 95%. As a result PET may have the potential to reduce the requirement for planned neck dissections or surveillance endoscopies.

Research: Early studies of coregistered PET/computed tomography (CT) scanning had yet to demonstrate superior
accuracy to PET alone for post-treatment surveillance; more research was needed to clarify the role of this technique. A multicentre trial of a PET–CT guided watch and wait policy compared to planned neck dissection for management of advanced nodal disease in head and neck cancer patients was underway in the UK.

Funding
Not stated.

Bibliographic details
Isles MG, McConkey C, Mehanna HM. A systematic review and meta-analysis of the role of positron emission tomography in the follow up of head and neck squamous cell carcinoma following radiotherapy or chemoradiotherapy. Clinical Otolaryngology 2008; 33(3): 210-222

PubMedID
18559026

DOI

Original Paper URL

Additional Data URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Carcinoma, Squamous Cell /radionuclide imaging /therapy; Combined Modality Therapy; Follow-Up Studies; Head and Neck Neoplasms /radionuclide imaging /therapy; Humans; Neoplasm Recurrence, Local /radionuclide imaging; Positron-Emission Tomography; Predictive Value of Tests; Sensitivity and Specificity

AccessionNumber
12008104934

Date bibliographic record published
31/03/2009

Date abstract record published
23/06/2010

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.