Role of fluorodeoxyglucose-PET versus fluorodeoxyglucose-PET/computed tomography in detection of unknown primary tumor: a meta-analysis of the literature

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CRD summary
This review pooled heterogeneous accuracy data for the imaging methods fluorodeoxyglucose-PET (positron emission tomography) and fluorodeoxyglucose-PET/CT (computed tomography), for the detection of unknown primary tumours, concluding that both methods had value over conventional work-up. The review had some methodological flaws and the included studies reported generally moderate/poor values for sensitivity, specificity and likelihood ratios, so this conclusion may be optimistic.

Authors' objectives
To assess the accuracy and comparative accuracy of fluorodeoxyglucose-PET (positron emission tomography) and fluorodeoxyglucose-PET/CT (computed tomography) for the detection of primary tumours in patients presenting with carcinoma of unknown primary unidentified by conventional work-up.

Searching
MEDLINE, Cancerlit and EMBASE were searched from January 1990 to September 2007. Search terms were reported.

Study selection
Studies of the detection of carcinoma of unknown primary using fluorodeoxyglucose-PET or fluorodeoxyglucose-PET/CT, where the carcinoma of unknown primary was diagnosed after physical examination and conventional work-up had failed to detect a primary tumour, were eligible for inclusion. Included studies were required to have a minimum of four participants with unknown primary tumours, and report sufficient data to calculate sensitivity and specificity for primary tumour detection. Included studies also had to use histology and/or follow-up as the reference standard. Abstracts, editorials, letters and comments were excluded.

The mean age of study participants ranged from 51 to 64 years, where reported. The characteristics of unknown primary carcinomas varied widely across the included studies (details presented in the paper). Conventional work-up most frequently included physical examination, CT/MRI (magnetic resonance imaging) and chest radiograph.

Two reviewers independently assessed studies for inclusion and disagreements were resolved by discussion.

Assessment of study quality
Study quality was assessed on seven criteria: description of study design and selection criteria; participant characteristics; indications for the use of fluorodeoxyglucose-PET; details of the imaging methods used and interpretation issues; reference standard method; sensitivity and specificity data; change-in-management information. Methodological quality was classified as high (more than 70%), acceptable (50 to 70%) or low (less than 50%) for overall adherence to these criteria.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Data were extracted on the number and location (where reported) of tumours detected by each imaging method, and the numbers of true positives, false positives, false negatives and true negatives. Sensitivity, specificity, positive and negative likelihood ratios, log diagnostic odds ratio, and their 95% confidence intervals (CIs) were calculated for each study and imaging method.

The authors stated that reviewers independently constructed 2x2 contingency tables, but did not specify how many reviewers performed the data extraction.
**Methods of synthesis**
The Q test was used to assess statistical heterogeneity. Pooled estimates of sensitivity, specificity, positive and negative likelihood ratios and log diagnostic odds ratios and their 95% confidence intervals were generated, using a fixed-effect model when p>0.10 and a random-effects model was used where p<0.05.

Summary receiver operating characteristic curves were also presented, but the method used to generate these was not reported.

**Results of the review**
A total of 28 studies (n=910) were included in the review. The mean overall % adherence to quality criteria for included studies was 68.44% (range 58.06% to 87.10%).

**Fluorodeoxyglucose-PET (positron emission tomography):** The pooled sensitivity of fluorodeoxyglucose-PET for the detection of unknown primary tumours was 0.78 (95% CI 0.72 to 0.84) and the specificity was 0.79 (95% CI 0.74 to 0.83), based on 21 studies with 480 participants. Significant between study heterogeneity was identified for specificity. The maximal joint sensitivity and specificity (Q*), derived from the summary receiver operating characteristic curve, was 0.78. Fluorodeoxyglucose-PET had a lower sensitivity for tumours at the base of the tongue (0.68) and tonsils (0.77).

**Fluorodeoxyglucose-PET/CT (computed tomography):** The pooled sensitivity of fluorodeoxyglucose-PET/CT for the detection of unknown primary tumours was 0.81 (95% CI 0.74 to 0.87) and specificity was 0.83 (95% CI 0.78 to 0.87), based on eight studies with 430 participants. Significant between study heterogeneity was identified for both sensitivity and specificity. The maximal joint sensitivity and specificity (Q*), derived from the summary receiver operating characteristic curve, was 0.83.

Pooled estimates of likelihood ratios and log diagnostic odds ratios were also reported.

No data were reported comparing the accuracy of fluorodeoxyglucose-PET with fluorodeoxyglucose-PET/CT.

**Authors' conclusions**
Fluorodeoxyglucose-PET and fluorodeoxyglucose-PET/CT had value in patients presenting with carcinoma of unknown primary, beyond that provided by conventional work-up.

**CRD commentary**
The research question was clearly stated and defined using appropriate inclusion criteria. A number of bibliographic databases were searched to identify relevant studies. Searches appeared to be based on target condition and tests only (likely to increase search sensitivity). No attempts to identify unpublished studies were reported. Reporting of the review process was incomplete, although measures to reduce error and bias were reported for the inclusion screening process and elements of data extraction. The methodological quality of included studies was assessed, but the results of this assessment were not used in the analysis and reporting was limited. Relevant characteristics and results of included studies were fully reported. The generation of pooled estimates of accuracy measures, in the presence of significant between study heterogeneity and without assessment of the impact of any variation in diagnostic threshold, was of questionable value; the forest plots could have been usefully presented without pooled estimates. The summary receiver operating characteristic curve was the more appropriate of the methods used for pooling studies. Given the values for sensitivity, specificity and likelihood ratios presented, the authors' conclusions seem optimistic.

**Implications of the review for practice and research**
**Practice:** The authors stated that fluorodeoxyglucose-PET and fluorodeoxyglucose-PET/CT can detect primary tumours undetected by physical examination and conventional work up.

**Research:** The authors made no recommendations for future research.
Funding
Not stated.

Bibliographic details

PubMedID
18677207

DOI
10.1097/MNM.0b013e328302cd26

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Databases, Bibliographic; False Positive Reactions; Fluorodeoxyglucose F18 /pharmacology; Humans; Medical Oncology /methods; Neoplasms /diagnosis; Positron-Emission Tomography /instrumentation /methods; ROC Curve; Radiopharmaceuticals /pharmacology; Sensitivity and Specificity; Tomography, X-Ray Computed /methods

AccessionNumber
12008106601

Date bibliographic record published
03/02/2009

Date abstract record published
23/12/2009

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.