Value of 18F-FDG-PET/PET-CT in differentiated thyroid carcinoma with radioiodine-negative whole-body scan: a meta-analysis

CRD summary
The review concluded that 18F-fluorodeoxyglucose-positron emission tomography/computed tomography was the more sensitive method in the follow-up of thyroid cancer recurrence or metastases, particularly in patients with negative whole-body scintigraphy. Limitations relating to both the review and the included studies indicate that the authors' conclusions should be interpreted with caution.

Authors' objectives
To evaluate the diagnostic accuracy of 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) and FDG-PET/computed tomography (FDG-PET/CT) in the detection of recurrent or metastatic differentiated thyroid cancer that was not identified by radioiodine whole-body scintigraphy.

Searching
PubMed, CANCERLIT and EMBASE were searched from January 1990 to September 2008 for published studies; search terms were reported.

Study selection
Studies of whole-body FDG-PET or FDG-PET/computed tomography that used histology and/or follow-up as a gold standard and reported data that allowed calculation of both sensitivity and specificity for primary tumour detection were eligible. All patients had to have undergone a total thyroidectomy for differentiated thyroid carcinoma followed by 131I ablation of residual thyroid tissue or radioiodine therapy. All patients had to be suspected of having recurrences or metastases, but had negative prior radioiodine whole-body scintigraphy results. Studies had to include at least four patients.

Participant age ranged from eight to 87 years (range from 37 to 66 years). Participants had a range of disorders; papillary carcinoma was the most common.

Two reviewers independently selected studies for inclusion. Disagreements were resolved through discussion.

Assessment of study quality
Study quality was evaluated with the criteria: description of study design and patient selection; characteristics of patients; patient indications; details of technologies used; final diagnostic confirmation; and sensitivity and specificity data. Each criterion was rated as either adequately or partially adhered to, not addressed or not applicable; based on this, studies were classed as high, acceptable or low quality.

The authors did not state how many reviewers assessed study quality.

Data extraction
Data were extracted independently by two reviewers in order to calculate sensitivity, specificity, diagnostic odds ratios (DOR) and positive and negative likelihood ratios with 95% confidence intervals (CI).

Methods of synthesis
Pooled estimates for sensitivity, specificity, likelihood ratios and diagnostic odds ratios were calculated using a random-effects model. A summary receiver operating characteristic (ROC) curve was presented. Subgroup analyses were performed and investigated histology, localisation, lesions in the cervical region, serum thyroglobulin levels and negative 131I whole body scintigraphy. The X² test and I² statistic were used to assess heterogeneity.
Results of the review
Twenty-five studies (n=789, range seven to 166) were included (16 were retrospective studies). Twenty-one studies were classed as high quality and four were of acceptable quality.

In the 17 studies (n=571) that used FDG-PET, pooled sensitivity was 0.84 (95% CI 0.79 to 0.87, I^2=65%) and pooled specificity was 0.84 (95% CI 0.79 to 0.89, I^2=69%). Positive likelihood ratio was 3.35 (95% CI 1.67 to 6.73), Negative likelihood ratio was 0.24 (95% CI 0.15 to 0.38). The area under the summary ROC curve was 0.89. Six studies included lesion-based data (n=237 lesions). Pooled (lesion-based) sensitivity was 0.92 (95% CI 0.86 to 0.95) and pooled specificity was 0.78 (95% CI 0.66 to 0.87) for specificity. In patients who presented with elevated serum thyroglobulin and negative ^131^I scan (eight studies, n=217) pooled sensitivity was 0.89 (95% CI 0.83 to 0.93) and pooled specificity was 0.85 (95% CI 0.72 to 0.93). The area under the SROC curve was 0.93.

In the six studies (n=165) that used FDG-PET/CT, pooled sensitivity was 0.94 (95% CI 0.87 to 0.97, I^2=15%) and pooled specificity was 0.84 (95% CI 0.72 to 0.92, I^2=59%), specificity. Positive likelihood ratio was 4.33 (95% CI 1.83 to 10.21) and negative likelihood ratio 0.1 (95% CI 0.04 to 0.23). The area under the SROC curve was 0.97.

Authors' conclusions
FDG-PET was especially effective for detection of patients with elevated thyroglobulin levels and normal radiiodine whole-body scintigraphy; FDG-PET/CT was a more sensitive method in the follow-up of thyroid cancer recurrence or metastases, particularly in patients with negative whole-body scintigraphy.

CRD commentary
The review addressed a clear question and was supported by appropriate inclusion criteria. Three electronic databases were searched. There appeared to be no search for unpublished studies and it was unclear whether any language restrictions were used, so some relevant studies may have been missed. Suitable methods were employed to reduce risks of reviewer error and bias during study selection and data extraction; the authors did not report whether such methods were during study quality assessment. The quality assessment used appeared adequate, but sample sizes varied greatly and the quality results were not presented for individual studies, which made it difficult to interpret the reliability of the pooled results. Many analyses were accompanied by statistically significant heterogeneity (the causes of which were not investigated), which made the appropriateness of pooling the results uncertain. The pooled likelihood ratios had wide confidence intervals, which raised further uncertainty about their reliability. No studies directly compared the two tests in the same population. These limitations indicate that the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that large studies were needed to define the exact role of FDG-PET/CT in the detection of recurrent or metastatic disease.

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