Positron emission tomography (PET) and magnetic resonance imaging (MRI) for the assessment of axillary lymph node metastases in early breast cancer: systematic review and economic evaluation

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CRD summary

This review concluded that there was higher sensitivity for magnetic resonance imaging (MRI) than positron emission tomography (PET) for detecting axillary lymph node metastases in patients with newly diagnosed early stage breast cancer. Because no studies directly compared PET with MRI, caution should be taken when comparing these estimates. These conclusions reflect limitations in the evidence base and are appropriate.

Authors' objectives

To assess the diagnostic accuracy and effect on patient outcomes of positron emission tomography (PET), with or without computed tomography (CT) and magnetic resonance imaging (MRI) in the evaluation of axillary lymph node metastases in patients with newly diagnosed early stage breast cancer. This abstract only addresses part of the report that related to diagnostic accuracy results.

Searching

The following databases were searched up to April 2009: MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, DARE, NHS EED, HTA databases, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Science Citation Index and BIOSIS Previews. Search terms were reported. Research registers and relevant conference proceedings were also searched for addition studies. Studies not published in English were excluded.

Study selection

Studies that evaluated the diagnostic accuracy of PET or MRI for the assessment of axillary metastases in patients newly diagnosed with early stage invasive primary breast cancer were eligible for inclusion. Eligible studies had to report data that allowed calculation of diagnostic accuracy measures for PET or MRI scanning compared with a reference standard test. PET studies were required to have at least 20 analysable patients. Studies that involved more than 20% of patients with non-early stage, non-newly diagnosed breast cancer or ductal carcinoma *in situ* were excluded. The outcomes of interest were sensitivity, specificity and adverse effects.

Most PET studies evaluated PET alone while the remaining studies evaluated PET combined with computed tomography (CT). The MRI studies assessed the following types of MRI: ultrasmall superparamagnetic iron oxide (USPIO)-enhanced MRI, dynamic gadolinium-enhanced MRI, (non-dynamic) gadolinium-enhanced MRI and *in vivo* proton MR spectroscopy. Reference standards used in most of studies were axillary lymph node dissection or a mixture of axillary lymph node dissection and sentinel lymph node biopsy. A small proportion of studies did not specify the reference standard or used a method other than axillary lymph node dissection/sentinel lymph node biopsy for some patients. The mean age of participants in PET studies ranged from 49 to 67 years and most were female.

Two reviewers assessed studies for inclusion, with any disagreements resolved by consensus.

Assessment of study quality

The quality of studies was assessed using the quality assessment of diagnostic accuracy studies (QUADAS) checklist, with three items being omitted (see details on the report).

The quality assessment was performed by one reviewer and checked by a second.

Data extraction

Data were extracted on the number of true positive, false positive, false negative and true negative to enable the calculation of sensitivity and specificity with 95% confidence intervals (CIs).

Data extraction was performed by one reviewer and checked by a second reviewer, with any disagreements resolved by discussion.

Methods of synthesis

Pooled estimates of sensitivity and specificity, with 95% confidence intervals, were calculated using a bivariate random-effects model. Study results were plotted in receiver operating characteristic (ROC) space. Subgroup analyses were performed on the basis of a range of variables, such as: clinical nodal status; size of breast tumour; number of axillary metastases; size of axillary metastases; patient sample; and type of reference standard.

Results of the review

Thirty-five studies were included in the review; 26 studies of PET (2,591 patients) and nine studies of MRI (307 patients). For all studies, quality items that scored poorly were: representative patient spectrum; availability of relevant clinical information; handling/reporting of uninterpretable results; interpretation of reference standard with blinding to index test results; and description of the reference standard.

For all studies that evaluated PET and PET/CT, the pooled sensitivity was 63% (95% CI 52% to 74%; 26 studies) and specificity 94% (95% CI 91% to 96%; 26 studies) for the detection of axillary lymph node metastases. For studies that evaluated PET/CT, the pooled sensitivity was 56% (95% CI 44% to 67%; seven studies) and specificity 96% (95% CI 90% to 99%; seven studies). For studies that evaluated PET only, the pooled sensitivity was 66% (95% CI 50% to 79%; 19 studies) and specificity 93% (95% CI 89% to 96%; 19 studies).

For all studies that evaluated MRI, the pooled sensitivity was 90% (95% CI 78% to 96%; nine studies) and specificity 90% (95% CI 75% to 96%; nine studies) for the detection of axillary lymph node metastases. For studies that evaluated USPIO-enhanced MRI, the pooled sensitivity was 98% (95% CI 61% to 100%; five studies) and specificity 96% (95% CI 72% to 100%; five studies). For studies that evaluated gadolinium-enhanced MRI, the pooled sensitivity was 88% (95% CI 78% to 94%; three studies) and mean specificity 73% (95% CI 63% to 81%; three studies).

No adverse effects were reported for PET. Studies of MRI reported mild to moderate adverse effects such as mild rash following USPIO administration, claustrophobia and back pain.

Results for subgroup analyses were also reported.

Authors' conclusions

The results demonstrated a higher sensitivity for MRI than PET for the detection of axillary lymph node metastases in patients with newly diagnosed early stage breast cancer. USPIO-enhanced MRI provided the highest sensitivity. No studies directly compared PET with MRI, so caution should be taken when comparing these estimates.

CRD commentary

This review's inclusion criteria were clear. Several relevant databases were searched. Efforts were made to find both published and unpublished studies, which minimised the risk of publication bias. Studies not published in English were excluded, which may have increased the risk of language bias, but sufficient attempts were made to minimise biases and errors in the review process.

Appropriate criteria were used to assess study quality, and results on study quality were reported in detail. Appropriate methods were used to pool the results and sources of heterogeneity were explored through a range of subgroup analyses. The authors acknowledged limitations such as lack of studies that directly compared PET with MRI and the high variation of sensitivity and specificity PET and MRI between studies. The authors' cautious conclusions reflected the limitations in evidence base and appeared to be reliable.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that further large and well-conducted studies of MRI (particularly using USPIO) were required to obtain more robust data on sensitivity and specificity, adverse effects and the optimum criteria for defining a node as metastatic. Studies of the comparative effectiveness between PET and MRI were also required for the detection of axillary lymph node metastases in patients with newly diagnosed early stage breast cancer.

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Other publications of related interest
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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.