A systematic review of positron emission tomography (PET) and positron emission tomography/computed tomography (PET/CT) for the diagnosis of breast cancer recurrence

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CRD summary

This generally well-conducted review concluded that positron emission tomography (PET) plus conventional imaging techniques may generally offer improved diagnostic accuracy for breast cancer recurrence compared with standard practice. PET/computed tomography (CT) appeared to show clear advantage over CT or PET alone. Despite limitations of the available evidence, the conclusions reflect the data presented.

Authors' objectives

To assess the accuracy of positron emission tomography (PET) and PET/computed tomography (PET/CT), compared with conventional diagnostic strategies or each other for the diagnosis of breast cancer recurrence.

Searching

MEDLINE and EMBASE were searched for full papers from inception to May 2009. The search strategy was reported. There were no language restrictions.

Study selection

Diagnostic accuracy studies that evaluated PET or PET/CT using a fludeoxyglucose tracer were eligible for inclusion if they used a reference standard of histological diagnosis (surgery/biopsy) and/or long-term clinical follow-up in patients with a previous diagnosis of breast cancer who had completed a course of primary treatment (whether cleared of the original disease or not). Recurrence could be local, regional or distant. Studies had to provide sufficient data to construct 2x2 tables of test performance and report the impact of tests on patient management, or report the reasons for false negative and false positive results. Studies conducted during initial breast cancer diagnosis, staging or monitoring of response to primary breast cancer treatment were excluded.

The PET camera, method of image reconstruction, contrast dose and uptake time and acquisition times varied across studies; most used visual interpretation of PET scan results. All studies used clinical follow-up as the reference standard; about 60% also used histology but seemingly not in all patients. Most studies also evaluated an alternative conventional technology, such as magnetic resonance imaging (MRI), bone scintigraphy, CT or conventional work-up. Most data were reported on a per patient basis. The reason for investigation was suspected metastases, primarily due to elevated tumour markers, symptoms or suspicious imaging results. Mean patient age, where stated, ranged from 46 to 62 years.

Studies were selected for inclusion by one reviewer; a second reviewer assessed full papers where there was doubt about inclusion.

Assessment of study quality

Study quality was conducted independently by two reviewers using an 11-point version of the QUADAS tool; disagreements were resolved by consensus.

Data extraction

Two reviewers independently extracted data to populate 2x2 contingency tables to enable calculation of sensitivity and specificity, along with 95% confidence intervals (CI). Disagreements were resolved by consensus.

Methods of synthesis

Summary receiver operating characteristic (SROC) curves were produced using a bivariate random-effects

model, from which summary estimates of sensitivity and specificity with 95% CI were calculated. Patient- and lesion-based data were analysed separately; patient-based data were used as the basis for the main analysis and for the investigation of heterogeneity. A sensitivity analysis was conducted on studies that reported direct comparisons where the analysis was restricted to studies with a delay between tests of one month or less. Subgroup analysis was used to investigate the impact of prior imaging results, location of suspected metastases, previously cleared or uncleared breast cancer and standard practice being included in the evaluation.

Results of the review

Twenty-eight studies (1,527 participants, range 10 to 291) met the inclusion criteria; 26 studies evaluated PET, six evaluated PET/CT and 16 evaluated an alternative conventional imaging technology. Twelve studies recruited a representative patient spectrum. Twenty-two studies used an acceptable reference standard. Eleven studies avoided progression bias (delay less than one month) and 19 avoided partial verification bias. Nine studies reported blinding of interpreters of the index tests. Ten studies avoided clinical review bias. Only one study reported avoiding differential verification bias and none reported avoiding incorporation bias.

Compared with conventional imaging technologies (10 studies), PET had significantly higher sensitivity (89%, 95% CI 83% to 93% versus 79%, 95% CI 72% to 85%) and specificity (93%, 95% CI 83% to 97% versus 83%, 95% CI 67% to 92%). Indirect comparisons of conventional imaging technology (11 studies) and PET (25 studies) gave the same findings.

Compared with CT (four studies), PET/CT had significantly higher sensitivity (95%, 95% CI 88% to 98% versus 80%, 95% CI 65% to 90%), but not specificity. Indirect comparisons of conventional imaging technology (11 studies) and PET/CT (five studies) showed similar results. Direct comparisons between PET/CT and conventional imaging technologies where there was clearly less than one month between tests (three studies) showed no significance.

Compared with PET (four studies), PET/CT had significantly higher sensitivity (96%, 95% CI 90% to 98% versus 85%, 95% CI 77% to 91%), but not specificity. Results were similar for indirect comparison of PET/CT (five studies) and PET (25 studies).

There were no significant differences in the sensitivity or specificity of PET when compared with MRI. Results of subgroup and sensitivity analyses were reported. Results in the abstract were on a per patient basis; results on a per lesion basis were reported (nine studies).

Authors' conclusions

Available evidence suggested that for the detection of breast cancer recurrence, PET in addition to conventional imaging techniques may generally offer improved diagnostic accuracy compared with standard practice. However, uncertainty remained around its use as a replacement for rather than an add-on to existing imaging technologies. PET/CT appeared to show clear advantage over CT and PET alone for the diagnosis of breast cancer recurrence.

CRD commentary

The review addressed a clearly stated research question defined by appropriate inclusion criteria. The search covered two main databases. No diagnostic filters or language restrictions were used and this reduced the possibility of missing studies and language bias. There was no specific search for unpublished studies, so publication bias was possible. Measures were taken to minimise error and bias during data extraction and study quality assessment. During study selection, a second reviewer was consulted only where there was doubt regarding inclusion by one reviewer.

The methodological quality of included studies was assessed and included in the interpretation of results. Studies were generally small and retrospective and this may have limited the reliability of findings. Appropriate analytical methods were used and potential heterogeneity was explored.

The review was generally well-conducted and, despite the limitations of the available evidence, the authors

cautious conclusions reflect the data presented.

Implications of the review for practice and research

Practice: The authors stated that the review supported the move to PET/CT from PET generally seen in clinical practice and it may be premature to make recommendations about the precise diagnostic role of PET/CT, but recommendations for its use in diagnosing metastatic breast cancer following equivocal findings on conventional imaging techniques were justified.

Research: The authors recommended prospective studies in clearly defined patient populations, diagnostic accuracy studies comparing PET/CT with conventional imaging technologies and whole-body MRI, investigations into using PET/CT as a replacement for conventional imaging technologies and decision modelling to assess the impact of PET/CT on patient outcomes to inform the possibility of conducting large-scale trials.

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