The feasibility and accuracy of sentinel lymph node biopsy in clinically node-negative patients after neoadjuvant chemotherapy for breast cancer: a systematic review and meta-analysis
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CRD summary
This review concluded that sentinel lymph node biopsy was a feasible and accurate method of diagnosing metastases in patients who were clinically node-negative after neoadjuvant chemotherapy. These conclusions reflect the data presented, but should be interpreted cautiously due to the small number and size of included studies and some limitations in review methods and reporting.

Authors' objectives
To assess the feasibility and the accuracy of sentinel lymph node biopsy in patients who were clinically node-negative after neoadjuvant chemotherapy for breast cancer.

Searching
MEDLINE, EMBASE and The Cochrane library were searched to December 2008 for studies in English. Search terms were reported. The bibliographies of included studies were screened for additional articles.

Study selection
Eligible studies included patients with histologically proven breast cancer who had a clinically node negative axilla after neoadjuvant chemotherapy. Patients had to have undergone both the reference standard of axillary lymph node dissection and sentinel lymph node biopsy, regardless of the results of the biopsy. The diagnosis of metastases had to be made from permanent paraffin sections.

Studies where patients received only neoadjuvant hormonal therapy and those where patients had prior axillary surgery or non-conventional sentinel lymph node identification methods were excluded.

Studies were published from 2000 to 2008; most were conducted in the USA or Japan. Where reported, the age of participants ranged from 27 to 79 years. Initial cancer stage varied (T1 to T4; N0 to N2). Neoadjuvant chemotherapy regimens differed within and between studies (details reported in the paper). All studies used either blue dye, radionuclide or a combination of both for sentinel lymph node mapping. Half of the studies used additional immunohistochemical staining on sentinel lymph nodes found to be negative for metastases on routine staining.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
The methodological quality of studies was assessed with a modified version of the QUADAS tool which omitted the items on incorporation bias and reporting of indeterminate test results. An overall QUADAS score (maximum 12) was calculated for each study.

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

Data extraction
Data were extracted on successful identification rate (number of women with successfully identified sentinel lymph nodes/number in whom sentinel lymph node biopsy was attempted) and the numbers of true positive, false negative and true negative test results. No false positives were possible as a positive sentinel lymph node biopsy means that the axillary lymph node dissection was always positive for metastases.

Extracted data were used to calculate sensitivity, false negative rate (false negatives/true positives plus false negatives), negative predictive value and overall accuracy, with 95% confidence intervals (CIs).
The authors did not state how many reviewers performed the data extraction.

**Methods of synthesis**

Pooled estimates of sentinel lymph node identification rate and measures of test performance were calculated with a bivariate mixed effects model, weighted by study size and inverse variance. Between study heterogeneity was assessed using $I^2$. The effect of lymph node mapping technique on identification rate and the effect of the use of immunohistochemical staining on accuracy was assessed using $X^2$. Publication bias was assessed with funnel plots.

**Results of the review**

Ten studies (449 patients) were included in the review. Eight studies had a QUADAS score of 12 and the remaining two scored 11 and 9.

The pooled estimate of successful identification rate was 94% (95% CI 92 to 97%), $I^2=4.3%$. No significant difference in successful identification rate was found between the different mapping methods used (blue dye, radionuclide or both).

The summary estimates for sensitivity were 93% (95% CI 88 to 97%), false negative rate 7% (95% CI 3 to 12%), negative predictive value 94% (95% CI 90 to 98%) and overall accuracy 95% (95% CI 93 to 98%). Heterogeneity was low ($I^2$ less than 25%) for all measures. The use of immunohistochemical did not significantly affect the accuracy of sentinel lymph node biopsy.

There was no evidence of publication bias.

**Authors’ conclusions**

For patients who were clinically node-negative after neoadjuvant chemotherapy, sentinel lymph node biopsy was technically feasible. Results predict those obtained on axillary lymph node dissection with accuracy comparable to that of sentinel lymph node biopsy for patients with early breast cancer.

**CRD commentary**

The review stated a clear objective and defined appropriate inclusion criteria. Several sources were searched for relevant studies, but (as acknowledged by the authors) the restriction to studies in English raised the possibility of language bias. Although a test for publication bias was reported, these tests were known to be unreliable for reviews of test accuracy studies. Therefore, the possibility of publication bias cannot be excluded. Reporting of the review methods was limited and it was not clear whether any measures were taken to minimise error and/or bias in the review process.

Methodological quality of included studies was assessed with an appropriate tool. However, results were only reported as summary quality scores, which minimised the informative value of the assessment. The results of individual included studies were reported and the meta-analytic methods used were appropriate.

The authors’ conclusions reflect the data presented, but should be interpreted cautiously due to the limitations described and the small number and size of the included studies.

**Implications of the review for practice and research**

**Practice:** The authors stated that it may be possible to maximize the benefits of neoadjuvant chemotherapy by using the less morbid sentinel lymph node biopsy to stage the axilla in patients who were node negative after neoadjuvant chemotherapy, but cautioned that results may be dependent upon the experience of surgeons.

**Research:** The authors did not specify any recommendations for future research.

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