Role of sonography in the diagnosis of axillary lymph node metastases in breast cancer: a systematic review

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CRD summary
This review found that axillary sonography has moderate sensitivity and good specificity for the diagnosis of axillary metastatic involvement in women with breast cancer, and that sonographically guided biopsy has excellent specificity but poor sensitivity. These conclusions should be interpreted with caution given the limited literature search, possible bias in the review process and differences between the studies.

Authors' objectives
To determine the accuracy of sonography and sonographically guided biopsy for the pre-operative diagnosis of axillary lymph node metastases in patients with breast cancer.

Searching
MEDLINE was searched from 1980 to 2004 for articles written in English, Spanish, French or Italian; the search terms were reported. The reference lists of retrieved articles were screened for additional studies.

Study selection
Study designs of evaluations included in the review
No inclusion criteria relating to the study design were specified. The included studies used both prospective and retrospective designs; some included consecutive patients.

Specific interventions included in the review
Studies that assessed axillary sonography performed using transducers of 7 MHz or higher and carried out before axillary lymph node dissection or sentinel node biopsy were eligible for inclusion. Studies had to use sonographic criteria as to size and morphology, or sonographically guided biopsy, to classify lymph nodes as positive or negative for metastases. The transducer strength ranged from 5 to 15 MHz. Criteria for positivity included a size greater than 5 mm, visible node of any size, and various descriptions of node morphology.

Reference standard test against which the new test was compared
Studies that included histopathologic results of total lymph node dissection or the results of dissection of first (nodes outside the smaller pectoral muscle) and second (behind the smaller pectoral muscle) levels, or sentinel node biopsy, as the reference standard were eligible for inclusion. The reference standard used in the included studies was lymphadenectomy, which in some cases followed or included sentinel node biopsy.

Participants included in the review
Studies of patients with breast cancer were eligible for inclusion.

Outcomes assessed in the review
Studies had to report sufficient data to construct a 2x2 table of test performance to be eligible for inclusion. The primary outcomes reported in the review were sensitivity and specificity.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The studies were assessed for the following methodological features: prospective or retrospective design; selection and number of patients; blind interpretation of the tests; and 'any other data that may prove useful'. The authors did not state
how many reviewers performed the validity assessment.

Data extraction
The sensitivity, specificity and 95% confidence intervals (CIs) were calculated for each study. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The pooled sensitivity and specificity, weighted by sample size, were calculated together with their 95% CIs.

How were differences between studies investigated?
The chi-squared test was used to assess heterogeneity. The studies were grouped according to the presence of palpable/non-palpable nodes and criteria for positivity before pooling.

Results of the review
Sixteen studies were included (total number of participants unclear).

Fourteen studies were prospective and eight of these recruited consecutive patients. Three studies reported blind assessment of the reference standard or sonography.

Studies that included axillae with both palpable and non-palpable nodes.

There were 5 studies in which the criterion for positivity was based on size. The sensitivity ranged from 66 to 73% and the pooled sensitivity was 69% (95% CI: 63, 75); there was no evidence of heterogeneity (p=0.95). The specificity ranged from 44 to 98% and the pooled specificity was 75% (95% CI: 70, 80); there was strong evidence of heterogeneity (p<0.001).

There were 6 studies in which the criterion for positivity was based on morphology. The sensitivity ranged from 55 to 92% and the specificity from 80 to 97%. The pooled sensitivity and pooled specificity were 71% (95% CI: 65, 76) and 86% (95% CI: 83, 89), respectively; there was strong evidence of heterogeneity in both measures (p<0.003).

Studies that included axillae with non-palpable nodes only.

There were 4 studies in which the criterion for positivity was based on size. The sensitivity ranged from 49 to 87% and the specificity from 78 to 97%. The pooled sensitivity and pooled specificity were 61% (95% CI: 55, 67) and 77% (95% CI: 72, 82), respectively; there was strong evidence of heterogeneity in both measures (p<0.001).

There were 4 studies in which the criterion for positivity was based on morphology. The sensitivity ranged from 26 to 76% and the specificity from 89 to 98%. The pooled sensitivity and pooled specificity were 44% (95% CI: 65, 76) and 92% (95% CI: 89, 95%), respectively; there was strong evidence of heterogeneity in both measures (p<0.02).

Sonographically guided biopsy.

There were 8 studies of only needle biopsy. The sensitivity ranged from 25 to 95% and the pooled sensitivity was 75% (95% CI: 70, 79); there was strong evidence of heterogeneity (p<0.001). Specificity was 97% in 1 study and 100% in all other studies.

There were 5 studies of all axillae. The sensitivity ranged from 6 to 63% and the pooled sensitivity was 45% (95% CI: 40, 51); there was strong evidence of heterogeneity (p<0.001). Specificity was 100% in all studies.

Authors' conclusions
Axillary sonography has moderate sensitivity and good specificity for the diagnosis of axillary metastatic involvement.
Sonographically guided biopsy shows excellent specificity but poor sensitivity.

**CRD commentary**
This review addressed a focused objective supported by clearly defined inclusion criteria. The literature search was limited to one electronic database and to studies in a small number of languages. No attempts to locate unpublished studies were made. It is therefore likely that relevant studies have been missed and the review may be subject to language and publication bias. Details of the review process were not reported, so it is not possible to determine whether appropriate steps were taken to minimise bias. Some methodological features were assessed, but the authors also stated that they also extracted "any other data that may prove useful", which suggests that the quality assessment was not objective. The methods used to pool the results were adequate and the 'Results' section did not overemphasise the pooled estimates, which was appropriate given the heterogeneity between the studies. The influence of the reference standard and sonography criteria on heterogeneity was examined. The authors’ conclusions are supported by the results presented but should be interpreted with caution given the limitations in the literature search, the possibility for bias in the review process and differences between the studies.

**Implications of the review for practice and research**
Practice: The authors stated that axillary sonography cannot be used in isolation to make decisions regarding whether to perform axillary lymph node dissection. If axillary sonography is used before sentinel node biopsy, then morphologic sonographic criteria should be used to determine malignancy. Sonographically guided biopsy can be used to increase specificity.

Research: The authors did not state any implications for research.

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