Baseline staging tests in primary breast cancer: a practice guideline

Robert E. Myers,* Mary Johnston,† Kathy Pritchard,‡ Mark Levine,§ Tom Oliver,† and the Breast Cancer Disease Site Group of the Cancer Care Ontario Practice Guidelines Initiative¶

Abstract

Background: Breast cancer develops in over 7000 women each year in Ontario. These patients will all undergo some staging work-up at diagnosis. The Breast Cancer Disease Site Group of the Cancer Care Ontario Practice Guidelines Initiative reviewed the evidence and indications for routine bone scanning, liver ultrasonography and chest radiography in asymptomatic women who have undergone surgery for breast cancer.

Methods: A systematic review of the published literature was combined with a consensus interpretation of the evidence in the context of conventional practice.

Results: There were 11 studies of bone scanning reported between 1972 and 1980, involving a total of 1307 women; bone scans detected skeletal metastases in 6.8% of those with stage I breast cancer, 8.8% with stage II and 24.5% with stage III. A total of 5407 women participated in 9 studies of bone scanning reported between 1985 and 1995; in these studies, bone scans detected skeletal metastases in only 0.5% of women with stage I disease, 2.4% with stage II and 8.3% with stage III. Among 1625 women in 4 studies of liver ultrasonography reported between 1988 and 1993, hepatic metastases were detected in 0% of patients with stage I disease, 0.4% with stage II and 2.0% with stage III. Among 3884 patients in 2 studies of chest radiography published in 1988 and 1991, lung metastases were detected in 0.1% of those with stage I, 0.2% with stage II and 1.7% with stage III. False-positive rates ranged from 10% to 22% for bone scanning, 33% to 66% for liver ultrasonography and 0% to 23% for chest radiography. The false-negative rate for bone scanning was about 10%.

Recommendations: The following recommendations apply to women with newly diagnosed breast cancer who have undergone surgical resection and who have no symptoms, physical signs or biochemical evidence of metastases.

- Routine bone scanning, liver ultrasonography and chest radiography are not indicated before surgery.
- In women with intraductal and pathological stage I tumours, routine bone scanning, liver ultrasonography and chest radiography are not indicated as part of baseline staging.
- In women who have pathological stage II tumours, a postoperative bone scan is recommended as part of baseline staging. Routine liver ultrasonography and chest radiography are not indicated in this group but could be considered for patients with 4 or more positive lymph nodes.
- In women with pathological stage III tumours, bone scanning, liver ultrasonography and chest radiography are recommended postoperatively as part of baseline staging.
- In women for whom treatment options are restricted to tamoxifen or hormone therapy, or for whom no further treatment is indicated because of age or other factors, routine bone scanning, liver ultrasonography and chest radiography are not indicated as part of baseline staging.

This article has been peer reviewed.

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¶ Members of the Breast Cancer Disease Site Group appear at the end of the article.
Breast cancer develops in over 7000 women each year in Ontario. These patients will all undergo some staging work-up at the time of diagnosis. One purpose of staging is to rule out distant disease that would render the patient’s condition incurable with conventional therapy. Staging may occasionally occur before surgery, but more commonly it is performed after surgery at the hospital where primary therapy is given. In many cases, the tests may be repeated at secondary or tertiary referral centres.

Staging in cancer, specifically breast cancer, has been a cornerstone in management. It has gradually become apparent that the yield of these tests has been exceedingly low, and yet the practice has remained. It must be recognized that staging tools are continually evolving and will become increasingly sophisticated. The tests of today are more sensitive and specific than those of the past. Indeed, a study involving women at high risk for breast cancer recurrence showed that an aggressive staging program could uncover previously undetected metastatic disease. Another study of cytokeratin-positive cells in bone marrow revealed that the presence of these cells correlated with risk of death from breast cancer.

This practice guideline limits itself to the discussion of the commonly used tests for breast cancer staging in Ontario, namely bone scanning, liver ultrasonography and chest radiography. These staging tests are expensive and time consuming and provoke anxiety. The clinical experience of the members of the Breast Cancer Disease Site Group of the Cancer Care Ontario Practice Guidelines Initiative has been that the prevalence of detectable metastases at initial diagnosis is very low in most stages of breast cancer. Hence, the group decided to review the evidence and indications for routine testing in the context of the following questions: Does evaluation with bone scanning, liver ultrasonography and chest radiography help to determine the extent of metastatic disease in women with newly diagnosed, operable breast cancer who are otherwise asymptomatic? In what stages of breast cancer is the prevalence of detectable metastatic disease high enough to justify routine testing with bone scanning, liver ultrasonography and chest radiography? Is there a role for performing these tests before surgery or, for cases in which they are necessary, should they be performed only after surgery?

Methods

The MEDLINE and CANCERLIT databases were searched without language restrictions for articles published from 1966 to July 1998 using the search terms “breast neoplasms,” “neoplasm staging,” “neoplasm metastasis,” “bone neoplasms/sc,” “liver neoplasms/sc” and “lung neoplasms/sc” and the text words “preop,” “stag:” and “baseline.” The search was updated in March and November 1999 and again in April 2000. These terms were also used to search the Cochrane Library (1999 [Issues 1 and 4] and 2000 [Issue 1]). Articles identified by the searches, cited in the relevant papers or known to the lead author of this practice guideline (R.E.M.) were retrieved.
prevalence of detectable metastatic disease in this population is exceedingly low.

In general, studies up to 1980 (Table 1) tended to report higher rates of positive bone scan results than those published after 1980 (Table 2). This trend was most likely brought about by changes in practice and in bone scan technology. After reviewing the literature, the Breast Cancer Disease Site Group felt that it was appropriate to divide the studies into older or more recent ones and arbitrarily chose 1980 as the cutoff date. Data collection appeared to be retrospective in 10 studies7,8,12,17,23–28 and prospective in 10.10,13–16,18–22 Bone scans were performed before surgery in 8 studies7,15–18,20,21,27 and after surgery in 4;8,12,19,28 the remaining studies included both preoperative and postoperative tests or did not state clearly when the tests were done. There did not appear to be any consistent difference in detection rates between prospective and retrospective studies and preoperative and postoperative studies.

Liver ultrasonography

The liver is not involved by metastatic breast cancer as frequently as bone is.22,29 Although the evidence surrounding the best test to determine liver involvement is conflicting1,10,27,30–33 the test currently used most often for staging is ultrasonography.

Table 3 summarizes the results of 4 studies of baseline ultrasonography of the liver, tabulated by stage of disease. All of these studies were reported after 1980. Data were collected retrospectively in 2 studies7,9 and prospectively in 2.10,30 Liver scans were performed before surgery in 2 studies,7,30 after surgery in 1,9 and before or after in the fourth.10 Based on these data, the chance of an abnormal test result appears to be even lower than that observed in the studies of bone scanning. Depending on how strictly one defines abnormalities in the liver, the false-positive rate may vary from 33% (2 of 6 cases) to 52% (11 of 21 cases).9
These rates are probably higher than one can expect currently in terms of false-positive results. However, there are many benign incidental findings with routine ultrasonography; in one study, 100 benign findings were noted among 346 patients.10

Chest radiography

The lung, although not as common a site as bone for the development of metastatic disease, is still routinely assessed in the staging of breast cancer. Only 2 studies have reported chest radiography results by stage of disease (Table 4). Both studies collected data retrospectively; the test was performed before surgery in one study7 and after surgery in the other.9

Like the other staging tests, chest radiography appears to have an appreciable false-positive rate — 23% (3 of 13 cases) when equivocal results are considered.9 However, when stricter criteria were used in 8 positive cases, none was false positive.9

Summary

Many studies have assessed the value of bone scanning, liver ultrasonography and chest radiography in breast cancer staging. All studies in which results were reported according to the conventional TNM classification system4 were reviewed for this practice guideline. Those reported up to 1980 tended to demonstrate higher rates of positive bone scans than the studies reported after 1980. This difference is probably due to the use of more specific scans in recent years and a much higher preponderance of smaller tumours frequently detected by mammography alone. The yield of baseline testing increases with disease stage but overall is very low for all 3 sites of metastases in asymptomatic patients. The pooled detection rates (the proportion of tests that were positive for metastases) among patients with stage I breast cancer, from studies published after 1980, were 0.5% for bone scanning, 0% for liver ultrasonography and 0.1% for chest radiography. Among women with stage II disease, the detection rates were 2.4%, 0.4% and 0.2% respectively, and among women with stage III disease they were 8.3%, 2.0% and 1.7% respectively. The strength of the available evidence lies not in study design, which in some cases was quite weak, but principally in the number of patients studied — 5407 patients with bone scanning, 1625 with liver ultrasonography and 3884 with chest radiography — and in the corresponding narrow confidence intervals for the estimated detection rates.

Breast Cancer Disease Site Group consensus process and discussion

As is often the practice with the Cancer Care Ontario Practice Guideline Initiative, the draft guideline was sent out for practitioner feedback. We received feedback from 92 physicians from across the province, and the guideline was revised accordingly.

The final part of the guideline development process involved consensus building among the members of the Breast Cancer Disease Site Group. The first issue, related to follow-up assessment of patients with breast cancer, has been dealt with in a published national clinical practice guideline34 and will not be discussed here. The group has reviewed the research results summarized in this report in

<table>
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<th>Study</th>
<th>Year of report</th>
<th>Cancer stage; % (and no.) of patients with positive result</th>
<th>Total</th>
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<td>Stage I</td>
<td>Stage II</td>
</tr>
<tr>
<td>Ciatto et al7</td>
<td>1988</td>
<td>0 (0/132)</td>
<td>0.2 (1/462)</td>
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<tr>
<td>Clark et al10</td>
<td>1988</td>
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<td>0 (0/86)</td>
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<td>Glynne-Jones et al9</td>
<td>1991</td>
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<td>1.8 (3/167)</td>
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<tr>
<td>Cox et al10</td>
<td>1992</td>
<td>0 (0/127)</td>
<td>0 (0/182)</td>
</tr>
<tr>
<td>All studies</td>
<td>1988</td>
<td>0 (0/423)</td>
<td>0.4 (4/897)</td>
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95% CI

0.0
0.0 – 0.8
0.4 – 3.6
0.2 – 1.0

<table>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Stage I</td>
<td>Stage II</td>
</tr>
<tr>
<td>Ciatto et al7</td>
<td>1988</td>
<td>0.1 (1/873)</td>
<td>0.2 (3/1943)</td>
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<tr>
<td>Glynne-Jones et al9</td>
<td>1991</td>
<td>0 (0/64)</td>
<td>0.8 (2/240)</td>
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<tr>
<td>All studies</td>
<td>1988</td>
<td>0.1 (1/937)</td>
<td>0.2 (5/2183)</td>
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95% CI

0 – 0.3
0 – 0.4
0.8 – 2.6
0.3 – 0.7

100% CI

0
0 – 0.8
0.4 – 3.6
0.2 – 1.0

95% CI
Routine bone scanning, liver ultrasonography and chest radiography are not indicated as part of baseline staging.

In women who have pathological stage II tumours, a postoperative bone scan is recommended as part of baseline staging. Routine liver ultrasonography and chest radiography are not indicated in this group but could be considered for patients with 4 or more positive lymph nodes.

In women with pathological stage III tumours, bone scanning, liver ultrasonography and chest radiography are recommended postoperatively as part of baseline staging.

In women for whom treatment options are restricted to tamoxifen or hormone therapy, or for whom no further treatment is indicated because of age or other factors, routine bone scanning, liver ultrasonography and chest radiography are not indicated as part of baseline staging.

Practice guideline date

Feb. 8, 2000. Practice guidelines of the Cancer Care Ontario Practice Guidelines Initiative are reviewed and updated regularly. Please visit www.cancercare.on.ca/ccopgi for updates to this guideline.

Competing interests: None declared.

Contributors: Dr. Myers was the principal author. Ms. Johnston assisted with the literature search and data extraction and contributed to the writing of the article. Drs. Pritchard and Levine contributed to the writing of the article. Mr. Oliver assisted with the literature search and contributed to the writing of the article. All of the authors and members of the Breast Cancer Disease Site Group were involved in the discussion and interpretation of the findings from the studies reviewed.

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