Complete Summary

GUIDELINE TITLE

Baseline staging tests in primary breast cancer.

BIBLIOGRAPHIC SOURCE(S)

Breast Cancer Disease Site Group. Baseline staging tests in primary breast cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2003 Apr 30 [online update]. 14 p. (Practice guideline report; no. 1-14). [33 references]

GUIDELINE STATUS

This is the current release of the guideline.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

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SCOPE

DISEASE/CONDITION(S)

Breast cancer

GUIDELINE CATEGORY

Diagnosis
Evaluation

Management
Risk Assessment

CLINICAL SPECIALTY

Oncology
Radiation Oncology
Radiology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To determine whether evaluation with bone scanning, liver ultrasonography, and chest radiography helps to determine the extent of metastatic disease in women with newly diagnosed operable breast cancer who are otherwise asymptomatic
- To evaluate in what stages of breast cancer the prevalence of detectable metastatic disease is high enough to justify routine testing with bone scanning, liver ultrasonography, and chest radiography
- To determine if there is a role for performing bone scanning, liver ultrasonography, and chest radiography before surgery, or, for cases in which they are necessary, if these tests should be performed only after surgery

TARGET POPULATION

Women with newly diagnosed breast cancer who have undergone surgical resection and who have no symptoms, physical signs, or biomedical evidence of metastases

INTERVENTIONS AND PRACTICES CONSIDERED

Routine use of the following baseline staging tests, either preoperatively or postoperatively, in women with operable breast cancer:

1. Bone scan
2. Liver ultrasonography
3. Chest radiography

MAJOR OUTCOMES CONSIDERED

Primary Outcome

Detection rate (number of patients with abnormal tests that were indicative of metastases divided by the total number of patients tested)

Secondary Outcomes

- False-positive rate
- False-negative rate

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

2000 Guideline
The MEDLINE and CancerLit databases (Ovid) were searched from 1966 to July 1998 using the medical subject heading (MeSH) "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 found by the searches, cited in the relevant papers, or known to the lead author of the practice guideline were retrieved and reviewed.

The literature search described above was not restricted by language; it uncovered three reports on bone scanning published in French and one in German. Because a large body of literature published in English was available and resources for translation were limited, these foreign-language publications were excluded from the practice guideline.

2003 Update
The literature search was updated using subject headings (breast neoplasms, neoplasm staging, neoplasm metastases, bone neoplasms/sc, liver neoplasms/sc, lung neoplasms/sc, clinical trial{s}, exp evaluation studies) and text words (breast, mammary, cancer, carcinoma, neoplasm, stag:, baseline). MEDLINE (2000-April 2003), the Cochrane Library (Issue 1, 2003), and the PDQ Clinical Trials Database (www.cancer.gov/search/clinical_trials, accessed April 30, 2003) were searched for clinical trials of bone scanning, liver ultrasonography or chest radiography as staging tests in breast cancer.

Inclusion Criteria

Studies were eligible for inclusion in this overview of the evidence if they reported the number of women with newly diagnosed breast cancer who had metastases detected by bone scan, liver ultrasound, or chest radiograph. These tests could be performed either before or after surgery. Both full reports and abstracts were eligible. Studies were included only if they reported the rates of positive tests by stage of disease and the staging system was similar to that currently in use (see Appendix 1 in the original guideline document).

The primary outcome of interest was the detection rate, that is, the number of patients with abnormal tests that were indicative of metastases divided by the

total number of patients tested. Detection rates were calculated by the guideline authors from data appearing in the study reports. Also of interest were the false-positive and the false-negative rates; these were given in some of the study reports reviewed for this guideline.

NUMBER OF SOURCE DOCUMENTS

22 studies

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Summarized Patient Data
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

In order to get overall estimates of detection rates, results were pooled across studies. Study results were tabulated according to the stage of disease (I, II, and III) and summed across studies. For each stage, the detection rates were pooled by dividing the total number of patients who tested positive for metastases by the total number of patients tested in the studies; the 95% confidence intervals (CI) were calculated for the pooled rates. Results from all stages were also pooled to produce an estimate of the overall detection rate.

The information obtained from the original guideline document remains current for the 2003 update. No new information has emerged.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Breast Cancer Disease Site Group (DSG) has reviewed the research results summarized in this report in detail. Evidence from studies reported after 1980 was used as the basis for the draft recommendations because it was considered more relevant to current practice than was evidence from earlier studies. DSG members felt that tests that detected metastases in less than one percent of patients and also resulted in a significant number of false-positives were not clinically useful. Where to place the cut-off for detection rate was a subjective decision, but after discussion at a DSG meeting, the members agreed on one percent.

There were several areas where decision-making was easier than others. In stage I patients, where the yield for all tests was less than 1%, it seems appropriate to recommend the elimination of routine testing. Although studies of staging have not been performed in women with intraductal disease, there is good reason to assume that the yield from staging tests would be even less than in stage I cases. For this reason, the Breast Cancer DSG recommends the elimination of staging tests in this group. Among stage III patients, the proportion of abnormal tests was higher, exceeding 1% for all three tests. In this group, it was felt that the tests should be retained.

The longest discussion by the DSG concerned the use of staging tests in women with stage II breast cancer. The yield of positive results in this group was 2% for bone scan and less than 1% for ultrasound and chest radiograph. A good case could be made for retaining bone scanning and eliminating liver ultrasound and chest radiograph in this group. The DSG considered the possibility of dividing the stage II group according to size of tumour or number of positive lymph nodes (<4 versus $\geq$4 positive nodes). This approach was based on the assumption that risk might vary across the range of stage II patients. For example, a larger number of positive nodes could be associated with a higher likelihood of detecting metastases with staging tests. However, data were not available to answer this question.

Finally, some discussion occurred concerning patients who, because of comorbid illness, age, or personal preference, would not be candidates for chemotherapy but would either be treated with tamoxifen or receive no further treatment after surgery (with or without radiotherapy). Because one of the main purposes of staging is to rule out distant disease that would render the patient incurable with conventional therapy, the DSG did not recommend the use of baseline staging tests in this group of patients, provided they were asymptomatic. In asymptomatic patients where the decision to use tamoxifen or hormone therapy or to undergo no further treatment has already been made, there seems to be little need to perform staging tests as the results would not change treatment.

The DSG discussed what other tests should be performed at the time of diagnosis. Although a review of the literature related to this topic was beyond the scope of the practice guideline, the DSG easily reached consensus on the following recommendations: in women with newly diagnosed breast cancer that has been resected, baseline testing should consist of a careful history, physical examination, complete blood count and liver function, serum calcium, and renal function tests. Other specific tests may be ordered to assess abnormalities detected by the history, physical exam, or laboratory tests. These tests will help the clinician decide whether further tests or imaging are needed. They will also help determine which patients can tolerate chemotherapy.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 147 practitioners in Ontario (48 medical oncologists, 39 radiation oncologists, 44 surgeons, and 16 diagnostic radiologists). The survey consisted of 20 questions about the quality of the practice-guideline-in-progress report and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (postcard) and four weeks (complete package mailed again). The results of the survey have been reviewed by the Breast Cancer Disease Site Group.

Final approval of the original guideline report was obtained from the Practice Guidelines Coordinating Committee.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- 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 four 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.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by 22 reports of 21 case series evaluating one or more of the staging tests in question: 20 studies evaluated bone scan, 4

liver ultrasound, and 2 chest radiography. The strength of the available evidence lies not in study design, which in some cases is quite weak, but principally in the number of patients that have been studied (5,407 for bone scans, 1,625 with liver ultrasounds and 3,884 with chest x-rays) and the corresponding narrow confidence intervals for the estimates of detection rate.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Eleven studies of bone scanning reported between 1972 and 1980 involved a total of 1,307 women; bone scans detected skeletal metastases in 6.8% of those with stage I disease, in 8.8% with stage II, and in 24.5% with stage III. A total of 5,407 women participated in nine studies of bone scanning reported between 1985 and 1995; in these studies, bone scans detected skeletal metastases in 0.5% of women with stage I disease, in 2.4% with stage II, and in 8.3% with stage III.
- Among 1,625 women in four studies of liver ultrasound reported between 1988 and 1993, liver ultrasound detected hepatic metastases in no patients with stage I disease, in 0.4% of patients with stage II, and in 2.0% with stage III.
- Among 3,884 cases in two studies published in 1988 and 1991, chest radiographs detected lung metastases in 0.1% of stage I patients, 0.2% of stage II, and 1.7% of stage III.

POTENTIAL HARMS

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 approximately 10%.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

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Breast Cancer Disease Site Group. Baseline staging tests in primary breast cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2003 Apr 30 [online update]. 14 p. (Practice guideline report; no. 1-14). [33 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Feb 8 (updated online 2003 Apr 30)

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario, Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Breast Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Breast Cancer Disease Site Group disclosed potential conflict of interest information.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Baseline staging tests in primary breast cancer. Summary. Toronto (ON): Cancer Care Ontario (CCO), 2003 Apr. Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RS, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on June 5, 2002. The information was verified by the guideline developer as of July 8, 2002. This summary was updated by ECRI on April 19, 2004. The information was verified by the guideline developer on April 29, 2004.

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