Complete Summary

GUIDELINE TITLE

Management of ductal carcinoma in situ of the breast.

BIBLIOGRAPHIC SOURCE(S)

Breast Cancer Disease Site Group. Management of ductal carcinoma in situ of the breast [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2003 Jan [online update]. 18 p. (Practice guideline; no. 1-10). [46 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.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Ductal carcinoma in situ (DCIS) of the breast

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Oncology
Radiation Oncology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To make recommendations about the management of ductal carcinoma in situ (DCIS) of the breast

TARGET POPULATION

Adult patients with ductal carcinoma in situ (DCIS) of the breast

INTERVENTIONS AND PRACTICES CONSIDERED

Original: January 1998

1. Breast conserving surgery (lumpectomy)
2. Total mastectomy
3. Total mastectomy with reconstruction
4. Radiation therapy

Update: November 2002

1. Tamoxifen therapy

MAJOR OUTCOMES CONSIDERED

- Overall survival
- Disease-free survival
- Local recurrence
- Distant recurrence
- Quality of life

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

Original: January 1998
A CANCERLIT search was completed for January 1983 to May 1997. The search was updated in January 1998 using MEDLINE. Search terms included carcinoma in situ, noninvasive, intraductal, classification, diagnosis, epidemiology, pathology, radiation, surgery, and therapy. Bibliographies from recently published reviews were examined and relevant articles were retrieved. The proceedings of the 1997 meeting of the American Society of Clinical Oncology were also reviewed.

All randomized controlled trials and all prospective studies that involved patients with carcinoma in situ of the breast were reviewed.

Update: November 2002
The literature search strategy was revised to combine disease-specific text words and subject headings (breast, mammary, cancer, carcinoma, neoplasm[s], ductal carcinoma in situ [DCIS], carcinoma in situ), and design-specific terms (meta-analysis, randomized controlled trial[s]).

The literature search has been updated using MEDLINE (through January Week 2, 2003), CANCERLIT (to November 2002), the Cochrane Library (Issue 4, 2002) and abstracts published in the proceedings of the annual meetings of the American Society of Clinical Oncology (2000-2002), the American Society for Therapeutic Radiology and Oncology (2000-2002), and the European Society for Medical Oncology (2000). Literature searches were not restricted by language of publication.

Inclusion Criteria

Original: January 1998
Articles were selected for inclusion in this systematic review of the evidence if they met the following criteria:

1. Studies reported after 1983, due to the significant evolution of our understanding of the biology of ductal carcinoma in situ with the maturation of screening mammography.
2. All randomized controlled trials and all prospective studies that involved patients with carcinoma in situ of the breast.

Update: November 2002
Articles were selected if they were randomized controlled trials comparing treatment options for ductal carcinoma in situ. Outcomes of interest included overall survival, disease-free survival, local recurrence, distant recurrence, and quality of life. Evidence-based practice guidelines addressing the guideline questions and meta-analyses of data from randomized controlled trials were also included. Both abstracts and full reports were eligible.

NUMBER OF SOURCE DOCUMENTS

Original: January 1998
Only evidence from non-randomized studies comparing mastectomy versus breast conserving surgery in patients with ductal carcinoma in situ (DCIS) exists. However, there is indirect evidence from subgroup analysis of a randomized trial

in invasive disease. There is evidence from one randomized controlled trial (RCT) of adjuvant radiation versus observation post lumpectomy in women with DCIS. There are no randomized trials confined to patients at low risk of local recurrence. Evidence on prognostic factors is available from a retrospective analysis of data from one randomized trial. Data on survival and local recurrence are also available from a case series of 625 patients with DCIS.

Update: November 2002
Since the publication of the original guideline, literature search results have uncovered five practice guidelines, one updated consensus document, two new randomized trials, one updated randomized trial with updated pathologic considerations, and one retrospective study.

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

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Original: January 1998
High quality evidence regarding the clinical management of ductal carcinoma in situ (DCIS) is lacking. The natural history of DCIS remains poorly understood and available treatment options have been poorly evaluated.

Mastectomy with the option for reconstruction is indicated for women with large tumours (>5 cm). It remains an acceptable choice for women preferring to maximize local control and may be more relevant for women at higher risk of local recurrence, e.g., high-grade lesions or comedo necrosis.

Given the importance of breast conservation for the patient and the potential for salvage, lumpectomy is an equally acceptable option for women with DCIS. The evidence supporting equivalent overall survival is weak. There is currently one prospective randomized trial that supports the routine use of postoperative

radiation following radical lumpectomy for patients with DCIS of the breast. Radiation resulted in reduced rates of breast recurrence (both invasive and non-invasive) and mastectomy. For patients treated with breast irradiation following lumpectomy, similar doses and fractionation schedules recommended for invasive disease are suggested.

The ability to identify a group of patients treated with breast conserving surgery that does not require radiation is lacking. Current data suggest that tumour size, margin status, grade and comedo type necrosis are important predictors for local recurrence. Recent studies are provocative in suggesting that there may be different risk groups for local failure (e.g., low, intermediate, high) where different treatments may be more desirable, e.g., low risk -- lumpectomy alone; moderate risk -- lumpectomy plus radiation; and high risk -- total mastectomy plus or minus reconstructive surgery. Further evidence is necessary before making firm recommendations. Until then, it is recommended that pathologic descriptions including assessment of size, margin status, nuclear grade and evidence of comedo necrosis be more consistently reported. Patients interested in breast conserving surgery alone should participate in ongoing prospective clinical trials.

Update: November 2002
In the surgical management of DCIS, the choice between mastectomy and lumpectomy should be dependent upon patient preference and the results of clinical, mammographic and pathologic evaluation. Mastectomy is indicated for patients at high risk of recurrence. High-risk factors include large size tumours (>5 cm), multi-area tumours, or extensive DCIS with close margins. Mastectomy with the option of reconstruction is also an acceptable option for women preferring to maximize local control or who are at higher risk (e.g., high grade lesions or comedo necrosis). Given the importance of breast conservation for the patient, the potential for salvage, and that breast conserving surgery is often performed in patients with more aggressive tumour types; lumpectomy is an equally acceptable option for eligible women with DCIS.

While the risk of tumours developing in the contralateral breast is greater in patients who receive radiotherapy, it must be weighed against the greater benefit of a lower risk of recurrence in the ipsilateral breast for those patients who receive radiotherapy.

There is some evidence to suggest that patients with small, low-grade lesions with clear margins greater than 10 mm have a sufficiently low risk of recurrence to forgo breast irradiation. Eligible patients should be encouraged to participate in ongoing clinical trials.

It would be premature to recommend the routine use of tamoxifen in patients with DCIS based on the evidence available. Although a randomized trial reported a lower rate of recurrence with tamoxifen, these patients already have a low risk of recurrence, and the benefits of tamoxifen as demonstrated by this trial were small in absolute terms.

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 performed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This describes the external review activities undertaken for the original guideline report.

External review of the original guideline (January 1998) was obtained through a mailed survey of 147 practitioners in Ontario. The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The results of the survey were reviewed by the Breast Cancer Disease Site Group.

The practice guideline was approved 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

- Women with ductal carcinoma in situ (DCIS) of the breast who are candidates for breast conserving surgery should be offered the choice of lumpectomy or total mastectomy.
- Mastectomy with the option for reconstruction remains an acceptable choice for women preferring to maximize local control.
- When lumpectomy is performed, all evidence of disease should be resected.
- Standard reporting of pathologic features, including assessment of tumour size, margin status, nuclear grade and the presence/absence of comedo necrosis, is recommended.
- Women who have undergone breast conserving surgery should be offered postoperative breast irradiation. Women with small (less than 2.5 cm) well-differentiated tumours that are fully resected with clear margins (greater than 10 mm) should consider participating in clinical trials exploring radiation versus wide excision alone.
- Women with ductal carcinoma in situ should be informed of the option of five years of tamoxifen therapy and of the harms and benefits associated with tamoxifen use. While there is some evidence to suggest that tamoxifen is effective in the reduction of ipsilateral recurrence and contralateral incidence, the absolute benefit is small, particularly in patients with negative resection

margins, and should be weighed against the known toxicities of this medication.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Original: January 1998
Only evidence from non-randomized studies comparing mastectomy versus breast conserving surgery in patients with ductal carcinoma in situ (DCIS) exists. However, there is indirect evidence from subgroup analysis of a randomized trial in invasive disease.

There is evidence from one randomized controlled trial (RCT) of adjuvant radiation versus observation post lumpectomy in women with DCIS.

There are no randomized trials confined to patients at low risk of local recurrence. Evidence on prognostic factors is available from a retrospective analysis of data from one randomized trial.

Data on survival and local recurrence are also available from a case series of 625 patients with DCIS.

Update: November 2002
Since the publication of the original guideline, literature search results have uncovered five practice guidelines, one updated consensus document, two new randomized trials, one updated randomized trial with updated pathologic considerations and one retrospective study.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- In two large randomized trials, ipsilateral breast irradiation following breast conserving surgery significantly reduced the risk of invasive and non-invasive breast recurrence in the ipsilateral breast. In both trials, an association was observed between radiotherapy and an increased risk of developing contralateral breast cancer.
- There are no published reports of studies that randomized patients at low risk for local recurrence of ductal carcinoma in situ following breast conserving surgery to observation versus adjuvant radiotherapy. There is some evidence from non-randomized studies to suggest that patients with small, low-grade lesions with clear margins greater than 10 mm have a sufficiently low risk of recurrence to forgo breast irradiation.
- A randomized trial reported a lower rate of disease recurrence with tamoxifen plus radiotherapy compared to placebo plus radiotherapy as adjuvant therapy

for ductal carcinoma in situ. However, the benefit of tamoxifen in this trial was small in absolute terms. The benefit of tamoxifen was even smaller in patients with negative resection margins compared to those with positive or unknown margins.

POTENTIAL HARMS

There are limited data addressing the toxicity of radiation specifically for non-invasive disease, but given similar technical issues one could predict acute and chronic toxicity comparable to radiation treatment for invasive disease.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Pathological Classification of DCIS

Original: January 1998
There was no evidence on this topic when the original guideline report was developed.

Update: November 2002

- Several new pathologic classification systems have been proposed recently, to address the need to identify those lesions more likely to recur or progress to invasive cancer in women treated by breast conserving therapy. These classification systems are based primarily on nuclear grade and/or necrosis. Recent studies have supported the clinical relevance of this approach, showing that high nuclear grade and/or necrosis, particularly extensive comedo necrosis, are associated with a higher risk of early local recurrence following breast conservation therapy. No classification system to date, however, has been useful in predicting whether local disease is likely to recur as in-situ or invasive carcinoma.
- A consensus conference on the classification of ductal carcinoma in situ was convened in 1997. Although a single classification system for ductal carcinoma in situ was not endorsed at this meeting, it was recommended that the pathologist should clearly report the nuclear grade of the lesion and the presence or absence of necrosis and cell polarization. If a specific grading system for ductal carcinoma in situ is used, this should be stated in the pathology report. The report should also include the architectural patterns present, since this may be clinically important. It has been shown, for instance, that the micropapillary pattern, when present in pure form, tends to be more extensive.
- The issue of consistency among pathologists in categorizing ductal carcinoma in situ has been addressed in a few recent studies using the newer classification systems. In general, greatest consistency is achieved using classification systems based primarily on nuclear grade, particularly the Van Nuys scheme. Use of a synoptic report is recommended.
- 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 judgement 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.

IMPLEMENTATION TOOLS

Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Breast Cancer Disease Site Group. Management of ductal carcinoma in situ of the breast [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2003 Jan [online update]. 18 p. (Practice guideline; no. 1-10). [46 references]

ADAPTATION

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

DATE RELEASED

1998 Jan 20 (updated online 2003 Jan)

GUIDELINE DEVELOPER(S)

Practice Guidelines Initiative - 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

Provincial Breast Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

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

GUIDELINE STATUS

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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:

- Management of ductal carcinoma in situ of the breast. Summary. Toronto (ON): Cancer Care Ontario. Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, 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 August 19, 1999. The information was verified by the guideline developer as of September 17, 1999. This summary was updated by ECRI on July 3, 2001, July 5, 2002, and most recently on July 21, 2003. The most recent information was verified by the guideline developer as of August 6, 2003.

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