9. Follow-up after treatment for breast cancer

The Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer

Abstract

Objective: To assist patients and their physicians in arriving at the most effective follow-up strategy after treatment for breast cancer.

Outcomes: Survival, metastasis-free survival, local recurrence, quality of life.

Evidence: Evidence was based on a literature review using MEDLINE for the years 1991 to 1996, references cited in reviews and consensus conference proceedings.

Recommendations:

• All patients who have completed their primary treatment for breast cancer should have regular follow-up surveillance.

• The frequency of follow-up visits should be adjusted according to individual patient’s needs. The following issues and schedule should be considered:
  (a) The need to discuss and manage early side effects of therapy, plan a follow-up program and provide general support. (This visit is usually scheduled 4 to 6 weeks after therapy.)
  (b) The need to establish a post-treatment baseline, detect early recurrences and teach breast self-examination. (This visit is usually 4 to 6 months after therapy.)
  (c) The need for regular physical and mammographic examination to detect potentially curable disease. (These examinations should be at approximately 1-year intervals indefinitely thereafter.)
  (d) The need to provide support and counselling may require additional visits for some women, particularly for the first few years.
  (e) If metastases develop, the frequency of visits must be determined by the symptoms, course of disease and need for further treatment.

• All visits should include a medical history. For women who are taking tamoxifen, it is important to ask about vaginal bleeding. Physical examination should include both breasts, regional lymph nodes, chest wall and abdomen. The arms should be examined for lymphedema. Annual visits should include mammographic examination.

• Routine laboratory and radiographic investigations should not be carried out for the purpose of detecting distant metastases.

• Patients should be encouraged to report new, persistent symptoms promptly, without waiting for the next scheduled appointment.

• Breast self-examination should be taught to those women who wish to carry it out.

• Psychosocial support should be encouraged and facilitated.

• Participation in clinical trials should be facilitated and encouraged.

• The responsibility for follow-up care should be formally allocated to a single physician, with the patient participating as much as possible. The patients should always be fully informed of these arrangements.

• Communication between all members of the therapeutic team must be ensured to avoid duplication of visits and tests.

Validation: Successive reviews and revisions of this document were carried out by a writing committee, expert primary reviewers, secondary reviewers from across Canada, and by the Steering Committee. This final version reflects a substantial consensus of all individuals involved. This guideline has been reviewed and approved by the Canadian Association of Radiation Oncologists.

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Once the primary treatment for breast cancer is complete, patients should be kept under surveillance for some years. However, there is a lack of agreement regarding how frequently follow-up visits should be scheduled, what tests and procedures should be carried out and who should be responsible for their scheduling and processing. Because of differences in cancers, and in patients and their needs, no
single follow-up schedule is appropriate for all. The evidence concerning these issues is considered in this guideline, with the objective of assisting patients and their medical advisers in developing the optimal follow-up strategy for each individual.

Method

A MEDLINE search of the English language literature was initiated using the key words breast cancer and follow-up for the years 1991 to 1996 (inclusive). Other references were obtained from review articles. The proceedings of recent Italian and Australian consensus conferences were also reviewed.1,2

This guideline is based as much as possible on experimental evidence. When no direct evidence was available, recommendations were based on expert opinion and currently accepted practice. Current practices were established by a literature review and a questionnaire sent to Canadian cancer centres. (The results are summarized in Table 1.) The nature of the evidence used is classified into 5 levels (see page S2).

The initial draft guideline document was prepared by the authors, after which it underwent a process of iterative review and revision by a writing committee consisting of 9 members of The Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer, 2 expert primary reviewers, and by all members of the Steering Committee. It was then submitted to 17 secondary reviewers selected from across Canada, including surgical, medical and radiation oncologists, nurses, family physicians and breast cancer patients, before final approval by the entire Steering Committee. All changes were reviewed by Dr. Murphy. These guidelines were also reviewed and endorsed by the Canadian Association of Radiation Oncologists. The final document reflects a consensus of all those involved.

Recommendations (including evidence and rationale)

- All patients who have completed their primary treatment for breast cancer should have regular follow-up surveillance.

Objectives

Regular follow-up surveillance should aim to achieve 4 principal objectives:

The first objective is to provide patients with support and counselling.

This is especially necessary in the early months after the end of primary treatment (surgery, radiotherapy and chemotherapy). Certain types of early symptoms, such as soft-tissue swelling, hematomas, seromas of the breast area and numbness or stiffness of the upper arm, are attributable to surgery. Later symptoms may be due to the effects of surgery (e.g., postmastectomy syndrome), irradiation (e.g., erythema, swelling, tenderness and skin edema) or to menopause induced by tamoxifen, ovarian ablation or chemotherapy. Lymphedema requires counselling on the avoidance of trauma and the prompt treatment of infection. Early intervention with external compression and massage is more effective than treatment of established lymphedema.1,4 Stiffness and limitation of shoulder movement may require physiotherapy (level IV evidence).1 Management of chronic pain after mastectomy is discussed in guideline 10 (page S71).

A major concern for many patients is fear of recurrence. Will the cancer recur and how can recurrence be recognized? These matters demand ample time for discussion. Patients may also ask for advice on issues such as genetic testing, what to do about contraception or pregnancy, or about issues that influence their quality of life, such as coping with menopausal symptoms or maintaining a healthy diet and exercise program. Follow-up visits to discuss these issues, to give treatment when necessary and to give reassurance are needed more often in the early post-treatment period than later (level IV evidence).

The second objective is to detect potentially curable conditions such as local recurrence of cancer in the breast following breast-conserving surgery and new cancers in the opposite breast.1

Early detection is facilitated when clinical and mammographic examinations have been carried out to establish a “baseline” after the inflammatory changes resulting from surgery and radiotherapy have subsided.

Detecting local recurrence early

In patients treated with breast-conserving surgery (BCS)

Table 1: Summary of survey of Canadian follow-up practices for women treated for breast cancer

Fourteen Canadian Breast Centres responded to a questionnaire concerning the details of their follow-up practices. Their replies are summarized as follows:

- All centres follow their patients at short intervals for 2 to 5 yr, after which routine visits are carried out annually. 4 centres begin their follow-up visits at 6-mo intervals for 5 yr, after which the interval is increased to yearly for at least 10 yr or indefinitely. The range of planned, fixed visits varies from 9 to 30. The average is approximately 20, which would be every 6 mo for 5 yr, then annually for 10 yr.

- 3 of the 14 Canadian centres do regular laboratory tests, radiographic examinations and scanning.

- None of the 14 Canadian centres utilize the tumour marker CA-15-3 for continued surveillance.

- All centres perform regular mammographic examinations after irradiation of the breast, usually at 12-mo intervals.

- All centres but 1 carry out mammographic examinations of the contralateral breast annually. One centre performs follow-up mammographic examinations at 24-mo intervals.

- 11 of 14 Canadian centres utilize more than 1 type of medical personnel for follow-up. This may be a function of necessity imposed by geography rather than intent. 1 centre has nurses involved in follow-up.

- About half of the Canadian centres tend to schedule follow-up visits more frequently for high-risk patients than for low-risk patients.
Follow-up

and radiotherapy local recurrence may develop in the same breast. In one study this occurred at a rate of approximately 7% at 5 years and 20% at 20 years. These cancers can be detected earlier by mammographic examination than by physical examination and are potentially curable by mastectomy. Thus, after BCS, regular examination is recommended with the aim of detecting local recurrences early (level IV evidence). Nevertheless, early treatment of metastases will lead to curative treatment and some evidence that it will improve survival. However, any such benefit is likely to be small because of the small numbers of second cancers involved and the competing mortality related to the first cancer.

Detecting a new cancer in the contralateral breast

Women who have had breast cancer are, on average, at about 3 times greater risk for cancer in the opposite breast than age-matched women in the general population (level III evidence). Since the absolute risk is about 0.75% per year, the number of cases detected through yearly follow-up will be relatively small. However, those cancers that are detected by annual mammographic examination will be found at an earlier stage. There is, again, no direct proof in this context that early detection will improve survival. However, it is accepted, based on level I evidence, that regular mammographic screening of healthy populations results in earlier detection of breast cancer and reduced mortality due to breast cancer in women over 50 years of age. Therefore, since regular clinical and mammographic examination of such patients after treatment is, in effect, screening of a high-risk population, these measures should result in improved survival. However, any such benefit is likely to be small because of the small numbers of second cancers involved and the competing mortality related to the first cancer.

The third objective of follow-up is to provide care for patients in whom metastatic disease develops.

There is no evidence that early diagnosis of distant metastases will lead to curative treatment and some evidence that it will not. In a 1991 review of 5 studies on the effect of routine follow-up on the course of recurrent cancer, it was found that symptoms developed between visits in 75% to 95% of patients and that physicians detected abnormalities in only 15% of asymptomatic patients. The authors concluded that “once patients with breast cancer develop metastases they are essentially incurable regardless of the tumour load at the time of recurrence,” and that “postoperative surveillance therefore, does not lead to earlier detection of metastases or affect cure rates” (level III evidence). Nevertheless, early treatment of metastases can clearly influence morbidity; thus, with this objective in mind, patients should be encouraged to report new symptoms promptly.

The fourth objective of follow-up is to determine outcome.

It is important for physicians who treat women with breast cancer to learn which treatments produce the best outcomes in terms of survival, morbidity and quality of life. Accordingly, the monitoring of outcomes is considered to be important (level IV evidence). Thus, in addition to clinical trials, the outcomes of all interventions, including side effects of treatment, should be systematically recorded and collected. In this way health care providers and institutions can be aware of their own results and how they compare with national or international standards.

- The frequency of follow-up visits should be adjusted according to individual patient’s needs. The following issues and schedule should be considered:
  - (a) The need to discuss and manage early side effects of therapy, plan a follow-up program and provide general support. (This visit is usually scheduled 4 to 6 weeks after therapy.)
  - (b) The need to establish a post-treatment baseline, detect early recurrences and teach breast self-examination. (This visit is usually 4 to 6 months after therapy.)
  - (c) The need for regular physical and mammographic examination to detect potentially curable disease. (These examinations should be at approximately 1-year intervals indefinitely thereafter.)
  - (d) The need to provide support and counselling may require additional visits for some women, particularly for the first few years.
  - (e) If metastases develop, the frequency of visits must be determined by the symptoms, course of disease and need for further treatment.

Scheduling of visits

Because of individual differences, there is no single optimal schedule of follow-up visits. The Bari consensus conference suggested 4 visits per year for 2 years, 2 visits per year for the next 3 years and annual visits thereafter, but no evidence was cited to support this frequency. In a recent British study, women were randomized to a follow-up schedule of visits every 3 months in year 1, every 4 months in year 2, and every 6 months in years 3 to 5 versus 1 visit every 1 or 2 years. No benefit was detected from the more frequent visits, and patients in both groups expressed a preference for reducing rather than increasing the number of follow-up visits. Most Canadian centres recommend visits every 6 months for 2 to 5 years with annual visits thereafter (Table 1).

There is no compelling evidence to support any particular frequency of visits. The decision requires a balancing of the probable health benefits against the inconvenience, stress, and the costs of frequent visits and number of false-positive tests they may generate. Although follow-up visits can reassure patients, they can also cause anxiety and remind women of their disease without ever being able to provide complete reassurance that they are cured.

The annual rate of potentially curable cancers suggests that intervals of more than 1 year between visits may be suboptimal. In an average 11-year follow-up of 1593 patients...
with stages I and II breast cancer who were treated with local excision and radiotherapy, 159 local recurrences were found that were considered operable. In addition, 98 cancers were diagnosed in the opposite breast. Thus, in this series, the number of potentially curable cancers in 11 years was 159 + 98 = 257, giving an overall rate of approximately 1.5% per year. Although more frequent visits than 1 per year could not detect more cancers, each visit generates false-positive findings at a rate, according to one estimate, of 2.5% per visit. Since these visits will cause unnecessary anxiety and frequently lead to additional biopsies, it is necessary to put some limit on the frequency of visits (level V evidence). Thus, after the first few years, during which time visits are generally more frequent, a reasonable compromise seems to be the interval of 12 months between visits. This is the interval adopted by most Canadian centres (Table 1) (level IV evidence). The fact that the local recurrence rate appears to be higher in the first 3 years than in subsequent years lends support to a more frequent schedule in earlier years.

Some women are at increased risk of relapse.

Women under 35 years of age are at greater risk of both local and distant recurrences than older women, and may also be at higher risk for the development of a contralateral breast cancer (level III evidence). There is also greater risk of local recurrence when tumours are not removed with wide tumour-free margins or when they exhibit an extensive intraductal component (level III evidence). Although there is no proof of benefit, the presence of such factors is added reason for a more frequent schedule of visits for the first few years (level V evidence).

Regular follow-up surveillance should be continued for life.

The value of regular screening using physical and mammographic examination is accepted for women over 50 years of age who have never had breast cancer. For those who have had breast cancer, it should be of at least equal value. However, the benefit of regular follow-up for the very elderly or for those with reduced life expectancy due to other causes becomes more questionable due to other factors that increase the risk of death (level III evidence).

- All visits should include a medical history. For women who are taking tamoxifen, it is important to ask about vaginal bleeding. Physical examination should include both breasts, regional lymph nodes, chest wall and abdomen. The arms should be examined for lymphedema. Annual visits should include mammographic examination.

Treatment with tamoxifen causes a small increase in the risk of endometrial cancer (level I evidence). Thus, inquiry concerning vaginal bleeding should be specifically included in the history. When such bleeding is present in the absence of obvious cause, endometrial biopsy should be carried out (level V evidence).

Physical and mammographic examinations are complementary: a mammographic examination may be normal even when a palpable cancer is present, and nonpalpable cancers may be detected by mammographic examination (level III evidence). Therefore, both physical and mammographic examinations should be part of the annual follow-up visit.

- Routine laboratory and radiographic investigations should not be carried out for the purpose of detecting distant metastases.

In the absence of evidence that early treatment of metastatic disease will prolong life, one should avoid the inconvenience and expense of carrying out routine tests to detect it. In a recent study, 655 patients randomized to receive intensive surveillance consisting of physician visits, bone scanning, liver echographic examination, chest radiography and laboratory tests had an almost identical 6-year survival and quality of life compared to a control group of 665 women who received only tests that were clinically indicated. Both groups had annual mammographic examination of the contralateral breast (level I evidence). In another study of similar size and duration, chest radiographs and bone scans obtained every 6 months had no influence on mortality at 5 years. Except for mammographic examination, scientific evidence does not call for the routine use of any other instrumental or laboratory test, including biologic markers (level IV evidence).

- Patients should be encouraged to report new, persistent symptoms promptly, without waiting for the next scheduled appointment.

Patients should understand clearly that the presence of persistent symptoms such as bone pain, cough, breast lumps, mastectomy scar changes, fatigue or anorexia should be reported, without waiting for a scheduled visit (level V evidence). Even slight swelling of the arm should be reported immediately, since this may indicate early lymphedema, which is more responsive to treatment than when it has been present for some months.

- Breast self-examination should be taught to those women who wish to carry it out.

Evidence is lacking that breast self-examination (BSE) can improve survival. However, for those who practise it, new cancers in the opposite breast may be detected at an earlier stage (level III evidence). In a follow-up study of 1004 women, the cancers found by women who practised BSE were smaller and associated with fewer involved axillary lymph nodes. Thus, it is possible that earlier diagnosis may improve survival, and women should be informed of the possible benefit of achieving earlier diagnosis through BSE (level IV evidence).
Psychosocial support has been defined as information, advice or tangible aid provided through contact with a social network that has beneficial effects for the recipient. It has been widely accepted that effective support can be given to patients with breast cancer by other survivors of breast cancer (level IV evidence). In a randomized study, support provided by a breast care nurse was shown to reduce psychological morbidity, hospital-related anxiety and depression (level I evidence). There is now some level I evidence that psychosocial support may even influence the survival of patients with cancer. In 1989, Speigel and colleagues reported significantly longer survival of patients with breast cancer who were randomized to receive a supportive intervention compared with those who did not. Others have confirmed a positive effect on survival related to psychosocial support of various types. In a Quebec study reported in 1993, 224 patients with breast cancer were interviewed 3 months after surgery. The 7-year survival of women who had a confidant in the 3 months after surgery was 72% compared to 56% for those who did not (p = 0.063) (level III evidence).

Not all studies have documented a survival benefit. However, irrespective of any influence on mortality, there is increasing evidence that psychosocial interventions can produce measurable improvement in outcomes such as emotional and functional adjustment, nausea and pain. In a review of the evidence, Fallowfield concluded recently that it begins “to place psychological interventions firmly on the list of requirements for good cancer care.” Thus, psychosocial support, whether provided by health care workers, family, friends or organized support groups, should be facilitated and encouraged.

Participation in clinical trials should be facilitated and encouraged.

As has been frequently noted, the knowledge base for many of the interventions involved in the treatment of breast cancer often does not exist or is extremely weak. These areas of uncertainty, where recommendations must, at present, be based on level II to V evidence, can only be eliminated by well-designed, randomized, controlled trials. Improvement in the care of future patients with breast cancer thus depends on the participation of sufficient numbers of patients in such trials. Physicians treating patients with breast cancer should therefore be aware of currently available trials, and the option of participation should be offered to patients.

The responsibility for follow-up care should be formally allocated to a single physician, with the patient participating as much as possible. The patients should always be fully informed of these arrangements.

Although early follow-up visits are normally carried out by the surgeon or the medical or radiation oncologist who has been responsible for treatment, the responsibility for long-term follow-up care is frequently not defined. In an Italian study, one-third of 284 women complained of difficulties in follow-up due to lack of cooperation and integration of follow-up procedures among specialists (level III evidence). The individuals or organizations that are the most appropriate for carrying out follow-up may differ according to the circumstances. In a British study, a general practice-centred follow-up was found to be acceptable to both patients and general practitioners (level III evidence). In this study involving 296 women randomized to receive follow-up care in the hospital or in general practice, there was no significant difference in the time to confirmation of recurrence or in scores for social functioning, mental health or general health perception (level I evidence). In Canada, continuing care is usually carried out by specialists. In a recent study in southwestern Ontario, the family physician was involved in the care of only 17.5% of 183 women with stage I cancer.

The Bari Consensus Conference concluded that after long periods of care by their various oncologists, women may feel abandoned when discharged from their cancer clinic. They concluded that patients want a “team” of health care professionals to be accessible, when necessary, for their care and treatment. Researchers in the UK have reached the same conclusions (level III evidence). Thus, when family physicians assume responsibility for follow-up, contact should be maintained with the treating specialists. When responsibility is transferred, irrespective of who is responsible for the follow-up surveillance, the patient must take part in the decision and be kept fully informed of the follow-up plans from the beginning to avoid any feelings of abandonment (level V evidence).

Communication between all members of the therapeutic team must be ensured to avoid duplication of visits and tests.

Not all of the health professionals who have taken part in the diagnosis and management of a woman’s breast cancer will necessarily wish to be kept informed of the patient’s progress during follow-up. However, for those who do, clear arrangements for the transfer of follow-up information will make for improved care and avoid unnecessary repetition of tests (level IV evidence).

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