BREAST CANCER, PREGNANCY, AND BREASTFEEDING

This document was developed by the Breast Disease Committee and approved by Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Abstract
Objective: The primary objective of this guideline is to provide Canadian physicians up-to-date, accurate information and recommendations regarding:

1) impact of pregnancy and lactation on risk of breast cancer;
2) prognosis of breast cancer diagnosed during pregnancy and lactation;
3) risk of recurrence of breast cancer with the occurrence of subsequent pregnancies;
4) feasibility of breastfeeding and its impact on the prognosis of women with breast cancer.

Options: This guideline reviews evidence on whether pregnancy and breastfeeding change the lifetime risk for breast cancer in women, and whether breast cancer diagnosed during pregnancy or during lactation has a different prognosis. It offers the clinician advice on the diagnostic options to help identify breast cancer in pregnancy and/or during lactation, and offers evidence-based recommendations in managing an ongoing pregnancy and/or lactation when treatment for breast cancer is being planned. It also offers recommendations to clinicians in counselling their patients regarding future pregnancy and future breastfeeding for women who have been treated for breast cancer.

Outcomes: These guidelines should help physicians counsel patients using evidence-based recommendations. These recommendations may also improve the prognosis of patients diagnosed with breast cancer during pregnancy and lactation, or of those patients who had breast cancer and are contemplating future pregnancies.

Evidence: A Medline search was carried out for all publications from 1990 through 2000, in the English language, related to breast cancer and pregnancy in terms of diagnosis, prognosis, and treatment, as well as for breast cancer and breastfeeding, with particular focus on impact of treatment of breast cancer on lactation and prognosis of breast cancer after lactation. The authors submitted the manuscript for review to members of the Breast Disease Committee, who also validated the levels of evidence. The final manuscript was submitted to the SOGC Council for approval and dissemination. The levels of evidence for recommendations have been determined using the criteria described by the Canadian Task Force on the Periodic Health Examination.

Benefits, Harms, and Costs: Canadian physicians will be able to counsel their patients on the impact of pregnancy and lactation on a woman's lifetime risk for breast cancer. Physicians and patients will be empowered to decide how to manage pregnancy and lactation when breast cancer is diagnosed in pregnancy, and to appreciate the ramifications of reproduction and breastfeeding after breast cancer. This guideline identifies areas where good evidence is lacking and advocates research in those areas.

Recommendations: Women should be counselled regarding their risk for breast cancer and be informed that:

1. There is good evidence that there is a transient increase in risk of breast cancer in the first three to four years after delivery of a singleton baby (II-2B). Subsequently, their lifetime risk seems lower than that of women who remain nulliparous (II-2B).

2. There is good evidence that the risk for premenopausal breast cancer is reduced with lactation (II-2A). This protective effect seems to be best for women who had extended periods of breastfeeding during their lifetime (II-2B). Women with familial risks could potentially benefit most from breastfeeding (II-2C).

These guidelines reflect emerging clinical and scientific advances as of the date issued and are subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of the contents may be reproduced in any form without prior written permission of SOGC.
Since breast milk is the ideal nutrient for the newborn, and since breastfeeding is a modifiable risk factor, all women should be encouraged to breastfeed their children (II-2A).

3. All women should be encouraged to practice breast self-examination in pregnancy and during lactation (II-2B). Clinicians should screen all pregnant patients for breast cancer with thorough breast examination early in pregnancy (III-B). The clinician is advised to examine the breast in the postpartum period if the woman is not breastfeeding. The obstetrician is advised to examine the breast at any time in the postpartum period if the woman presents with breast symptoms (III-B).

4. Physicians should be encouraged to use ultrasonography, mammography, needle aspiration, or breast biopsies to assess suspicious breast masses in pregnancy and during lactation, in the same timely fashion as for non-pregnant or non-lactating women (II-2A). Interruption of lactation during investigation is not necessary, nor is it recommended unless nuclear studies are entertained (III-B).

5. Once breast cancer is diagnosed, a multidisciplinary approach should be taken. This includes the obstetrician, surgeons, medical and radiation oncologists, and breast cancer counsellors (II-2A).

6. In early pregnancy, the patient should be counselled regarding the effect of proposed therapy on the fetus and on overall maternal prognosis. Termination of pregnancy should be discussed, but the patient should be counselled that prognosis is not altered by termination of pregnancy. Women should be advised that premature menopause may result from breast cancer treatments, especially if chemotherapy is given to patients who are past the age of 30. (II-2C)

7. Up until now, modified radical mastectomy was the cornerstone of surgical treatment of breast cancer during pregnancy. Adjuvant chemotherapy should be entertained and, if required, administered without delay. The patient should be counselled regarding the effect of chemotherapy on the fetus and/or the future reproductive potential of the patient (II-2B). In the third trimester, the risks and benefits of early delivery versus continuation of pregnancy, and the effect of chemotherapy on the fetus, should be addressed (II-2B). Women undergoing chemotherapy or tamoxifen treatment should not breastfeed (III-B).

8. Women treated for breast cancer and who wish to become pregnant should be counselled that pregnancy is possible and does not seem to be associated with a worse prognosis for their breast cancer (II-3C). However, they should be made aware that the evidence to support such advice is relatively poor.

9. Since most breast cancer recurrences appear within two to three years after initial diagnosis, patients should be advised to postpone pregnancy for three years (III-C). If a patient has axillary node involvement, the recommendation to defer pregnancy should be extended to five years, but this recommendation is based on opinion only (III-C). Prior to attempting pregnancy, a breast cancer survivor should be referred for a full oncologic evaluation.

10. There is no evidence that breastfeeding increases the risk of breast cancer recurring or of a second breast cancer developing, nor that it carries any health risk to the child. Women previously treated for breast cancer, who do not show any evidence of residual tumour, should be encouraged to breastfeed their children (III-B).

Validation: Level of evidence, quality of research in the recruited publications, and ensuing recommendations were reviewed and discussed by members of the SOGC Breast Disease Committee as well as by a member of the Gynaecological Oncology Committee. External reviewers with expertise in the area were also solicited for comments and criticism.

INTRODUCTION

The risk of breast cancer after pregnancy, the prognosis of breast cancer diagnosed in pregnancy or during lactation, and the prospect of future pregnancies and of nursing after the occurrence of breast cancer are areas of great concern to clinicians. Breast cancer is the most common cancer in Canadian women, and one quarter of cases are diagnosed in the premenopausal period.\(^1,2\) While breast cancer occurs in 1/20,000 women at age 25, this rate increases steadily to become 1/1000 in the third decade, 1/500 in the fourth decade, and 1/300 in the fifth decade.

Most publications on breast cancer in pregnancy report a prevalence of 3 per 10,000 pregnancies, accounting for 3% of all breast carcinomas diagnosed.\(^3\) In addition, 7% of the fertile women treated for breast cancer will subsequently become pregnant, and this more often during the first five years of their diagnosis and treatment.\(^4,6\)

This Guideline addresses the issue of breast cancer, pregnancy, and breastfeeding in four areas:

1. Impact of pregnancy and lactation on subsequent risk of breast cancer
2. Breast cancer diagnosed during pregnancy and lactation
3. Pregnancy after breast cancer

The level of evidence has been determined using the criteria described by the Canadian Task Force on the Periodic Health Examination (Table 1).\(^7\)

IMPACT OF PREGNANCY AND LACTATION ON SUBSEQUENT RISK OF BREAST CANCER

Observational data indicate that the risk of breast cancer increases with nulliparity and late age at first conception.\(^8,12\) However, there is also evidence to suggest there may be a transient increase in breast cancer in the first three or four years following pregnancy.\(^13-16\) In a population-based prospective study of 802,457 Norwegian women aged 20 to 56 years, a short-term increase in breast cancer after full-term pregnancy was observed, with a peak three to four years after the delivery (RR 1.99, 95% CI 1.7–2.3).\(^13\) Similar findings were documented in a case-control study of Swedish women matched for age.\(^14\) After adjusting for parity and age at first birth, the relative risk of breast cancer within three years of the last birth was 1.2 times that of those women whose last birth was 10 or more years earlier (95% CI 1.02–1.44).\(^14\) The risk seems reduced in women who deliver twins compared to those who have singleton births (OR 0.88, 95% CI 0.78–0.99).\(^15,16\) Others, how-
ever, have disputed the theory that term pregnancy is transiently associated with a higher risk of breast cancer, and that multiple births are associated with a lower risk for breast cancer.

Some evidence suggests that there is an increased risk of breast cancer in women who have spontaneous or induced abortions. After adjusting for parity, age at first birth, and other risk factors, pregnancy termination was associated with a RR of 1.12 (95% CI 1.0–1.5).

Breastfeeding offers undeniable benefits to both the mother and the child. Indeed, national and international child care organizations have taken a strong position favouring breastfeeding. It is therefore expected that an increasing number of women will choose to breastfeed their children.

There is consistent evidence that lactation has either a protective effect against breast cancer or a neutral one. Observations from case-control studies, adjusted for age at delivery, conducted in Mexico, USA, and Greece, show that the relative risk for breast cancer occurring in the premenopausal years in women who breastfed is reduced to 0.5 (95% CI 0.24–0.62). A longer duration of lactation, especially if extended to 24 months during a patient’s lifetime, and younger age at first lactation seem to confer a more beneficial effect. Such a protective effect was not consistently observed for postmenopausal breast cancer, but three recent North American retrospective studies showed a 30–80% reduction in risk in women aged 50–79 years who nursed their children. Other case-control studies have disputed the beneficial effect of breastfeeding on the risk of breast cancer in premenopausal and postmenopausal years when the risk is adjusted for age at first pregnancy, age at menarche, age at menopause, and body mass index.

On a strict biological basis, it is plausible that breastfeeding may contribute to a reduction in the development and growth risk of breast cancer. Breastfeeding reduces the number of ovulations proportionally to its duration and intensity, and maintains a lower estrogen level than the level observed during the menstrual cycle. Lactation induces several significant histological and functional modifications in the breast. Breastfeeding can mobilize endogenous and exogenous carcinogens present in the ductal and lobular epithelial cell environment. Its influence on this local cellular milieu was studied in South-East Asian women who, for cultural reasons, breastfed only from the right breast. They reported that their breast cancer risk is four times greater on the left side than on the right.

**RECOMMENDATIONS**

Women should be informed that:

1. There is good evidence that there is a transient increase in risk of breast cancer in the first three to four years after

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**TABLE I**

<table>
<thead>
<tr>
<th>QUALITY OF EVIDENCE ASSESSMENT</th>
<th>CLASSIFICATION OF RECOMMENDATIONS</th>
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<tbody>
<tr>
<td>The quality of evidence reported in these guidelines has been described using the Evaluation of Evidence criteria outlined in the Report of the Canadian Task Force on the Periodic Health Exam.</td>
<td>Recommendations included in these guidelines have been adapted from the ranking method described in the Classification of Recommendations found in the Canadian Task Force on the Periodic Health Exam.</td>
</tr>
<tr>
<td>I: Evidence obtained from at least one properly randomized controlled trial.</td>
<td>A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination.</td>
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<tr>
<td>II-1: Evidence from well-designed controlled trials without randomization.</td>
<td>B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination.</td>
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<tr>
<td>II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group.</td>
<td>C. There is poor evidence regarding the inclusion or exclusion of the condition in a periodic health examination.</td>
</tr>
<tr>
<td>II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.</td>
<td>D. There is fair evidence to support the recommendation that the condition not be considered in a periodic health examination.</td>
</tr>
<tr>
<td>III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.</td>
<td>E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.</td>
</tr>
</tbody>
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delivery of a singleton baby (II-2B). Subsequently, their lifelong risk seems lower than that of women who remain nulliparous (II-2B).

2. There is good evidence that the risk for premenopausal breast cancer is reduced with lactation (II-2A). This protective effect seems to be best for women who had extended periods of breastfeeding during their lifetime (II-2B). Women with familial risks could potentially benefit most from breastfeeding (II-2C). Since breast milk is the ideal nutrient for the newborn, and since breastfeeding is a modifiable risk factor, all women should be encouraged to breastfeed their children (II-2A).

**BREAST CANCER DIAGNOSED DURING PREGNANCY AND LACTATION**

Breast cancer is the most common cancer in pregnant women, with a prevalence of 1–3 per 10,000 pregnancies. Canadian clinicians would probably be involved in the care of two to three cases of breast cancer in pregnancy during their professional lives. There is no evidence that pregnancy is responsible for either the generation or progression of breast cancer. The diagnosis of breast cancer in pregnancy is difficult because of the changes that occur in the breast, especially during lactation. Detection of abnormalities in breast tissue through breast examination is more difficult when the woman is lactating and for this reason some physicians prefer to wait until the woman has concluded breastfeeding before performing routine breast examinations. Women who develop breast cancer during pregnancy and lactation may suffer from a delay in detection, diagnosis, and management. Because of this, patients with pregnancy-associated breast cancer tend to have larger tumours, nodal metastasis, and advanced stage disease. A thorough breast examination at the first prenatal visit, before breast engorgement occurs, may diagnose these patients more rapidly.

Matched for age and stage, women with pregnancy-associated breast cancer tend to have similar five- and ten-year survival rates as non-pregnant patients. However, some retrospective case-control studies suggested pregnancy-associated breast cancer may have a worse prognosis, irrespective of disease stage. One such study documented a higher proportion of inflammatory breast cancer, larger tumours, negative receptor status, lower five-year recurrence-free survival, and lower metastasis-free survival. Another prospective cohort study suggested that lactation is also associated with worse prognosis, after adjusting for nodal status, tumour size, and age.

Placental metastasis of breast cancer not affecting the fetus has been reported.

During lactation, a woman with breast cancer will sometimes present with symptoms suggesting an obstructed galactophoric duct. The obstructed duct should respond within 72 hours to conservative management (local heat, massages, changes in the positioning of the infant). A persisting mass warrants further investigation. Breast cancer should be suspected in women with either recurrent mastitis of the same site or afebrile mastitis unresolved with antibiotics. Rejection of the diseased breast by the infant may be a subtle indication of an underlying malignant lesion.

Breast self-examination should be encouraged during pregnancy and lactation, as 90% of breast cancers are detected this way. Once a breast cancer is suspected, mammography with abdominal shielding and ultrasonography to identify solid or cystic tumours should be ordered without hesitation. Mammography is not contraindicated in pregnant or lactating women. Modern techniques and proper abdominal and pelvic shielding minimize fetal exposure (<50 mrad). Mammography, however, produces false negatives of 37% in pregnancy because of the relative increase in water density and hyperplastic changes to the gland. Mammography appears to be neither less sensitive nor less specific during lactation. A negative mammography result should never defer evaluation of a painless mass. Nuclear scans should be used only if there is expected benefit.

Needle aspiration and breast biopsy of suspicious masses can be performed safely during pregnancy/lactation. Fine needle aspiration shows good sensitivity but a slightly higher risk of false positive interpretation during lactation because of abundant cellularity, prominent nucleoli, and cellular debris, features that are shared with cancer. Any diagnostic procedure to rule out breast cancer, including the biopsy, may be undertaken without weaning the infant. Milk fistulas can be a complication following excisional biopsy in a central or deep position within the breast.

When breast cancer is diagnosed in a nursing woman, breastfeeding should be interrupted and definitive treatment should be undertaken without delay. The use of radiopharmaceutical agents for bone, liver, and pulmonary scans sometimes impose the interruption of breastfeeding for a period determined by the nature of the isotope itself and its dosage. A consultation with a nuclear medicine physician before performing the diagnostic study is suggested so that the radionuclide that has the shortest excretion time in breast milk can be used. Discussion of interruption of breastfeeding rather than weaning baby from the breast should always occur in this scenario.

Women undergoing active chemotherapy should not breastfeed. The cytotoxic agents used in adjuvant chemotherapy can be detected in small quantities in breast milk and are potentially toxic for the newborn. There is no current information about tamoxifen transfer into maternal milk, but this agent does inhibit milk production and should not be used by the lactating mother.

The issue of termination of pregnancy may be raised in early pregnancy with patient counselling. Termination of pregnancy may allow earlier adjuvant radiotherapy, but does not seem to improve prognosis or survival.
The mainstay of breast cancer treatment in pregnancy has been modified radical mastectomy. For some patients, conservative treatment that combines tumor resection and radiation has been used, but may create some uncertainty and delay. Radiotherapy is best avoided in pregnancy, although it appears that with appropriate shielding in very early pregnancy, the fetal exposure is low (3–9 Gy) for a total tumor dose of 46 Gy. The tolerable fetal dose may be higher in the latter stages of pregnancy. Usually, efforts are made to discourage patients from choosing treatment approaches that require radiotherapy. No studies have documented the long-term effects on children who were exposed in utero to radiotherapy used in their mother's breast cancer treatment.

Adjuvant chemotherapy may be given in the second and third trimesters. The drugs of choice are doxorubicin, cyclophosphamide, and fluorouracil. Chemotherapy may be associated with intrauterine growth retardation, premature labour, prematurity, neonatal neutropenia and alopecia, and may result in premature menopause in one-third of patients, especially when it is given to patients who are past the age of 30. Optimal timing of delivery should be individualized and decided upon by the obstetrician and the oncologist.

**RECOMMENDATIONS**

3. All women should be encouraged to practice breast self-examination in pregnancy and during lactation (II-2B). Clinicians should screen all pregnant patients for breast cancer with thorough breast examination early in pregnancy (III-B). The clinician is advised to examine the breast in the postpartum period, if the woman is not breastfeeding. The obstetrician is advised to examine the breast at any time in the postpartum period if the woman presents with breast symptoms. (III-B)

4. Physicians should be encouraged to use ultrasonography, mammography, needle aspiration, or breast biopsies to assess suspicious breast masses in pregnancy and during lactation, in the same timely fashion as for non-pregnant or non-lactating women (II-2A). Interruption of lactation during investigation is not necessary, nor is it recommended unless nuclear studies are entertained (III-B).

5. Once breast cancer is diagnosed, a multidisciplinary approach should be taken. This includes the obstetrician, surgeons, medical and radiation oncologists, and breast cancer councilors (II-2A).

6. In early pregnancy, the patient should be counselled regarding the effect of proposed therapy on the fetus and on overall maternal prognosis. Termination of pregnancy should be discussed, but the patient should be counselled that prognosis is not altered by termination of pregnancy. Women should be advised that premature menopause may result from breast cancer treatments, especially if chemotherapy is given to patients who are past the age of 30. (II-2C)

7. Up until now, modified radical mastectomy was the cornerstone of surgical treatment of breast cancer during pregnancy. Adjuvant chemotherapy should be entertained and, if required, administered without delay. The patient should be counselled regarding the effect of chemotherapy on the fetus and/or the future reproductive potential of the patient (II-2B). In the third trimester, the risks and benefits of early delivery versus continuation of pregnancy, and the effect of chemotherapy on the fetus, should be addressed (II-2B). Women undergoing chemotherapy or tamoxifen treatment should not breastfeed (III-B).

**PREGNANCY AFTER BREAST CANCER**

Tremendous emphasis has been placed on the physical and psychological rehabilitation of breast cancer patients. It is therefore natural for premenopausal patients to hope for pregnancy after breast cancer treatment. All women diagnosed with premenopausal breast cancer should be counselled about their reproductive potential.

Pregnancy after breast cancer is possible. However, most of the available evidence regarding its safety, impact on recurrence, or future prognosis are retrospective, involving small numbers of patients, carrying numerous biases, and often gathered over several decades. The evidence is further compromised, in that many subsequent pregnancies are not reported. The survival of pregnant women subsequent to breast cancer treatment does not appear to be decreased. However, there are serious limitations in the literature that allow only evidence at Level II-3 or III.

The reported good prognosis for women who conceive after treatment of breast cancer may be the result of a self-selection bias for the "healthy mother." In a study from Finland, controls who did not conceive after breast cancer had a 4.8 RR of death (95% CI 2.2–10.3) compared to those who delivered after diagnosis of breast cancer. Subsequent pregnancy may also serve as a stimulus for young women to “get well” again. In small, matched, cohort studies conducted between 1954 and 1986, women who had breast cancer and who subsequently conceived were compared to a control group of patients who did not conceive, with no detrimental effect of subsequent pregnancy noted. In a Danish population-based retrospective cohort study, women who conceived had a non-significant reduced risk of death (RR 0.55, 95% CI 0.28–1.06). A large series from the Princess Margaret Hospital in Toronto, following 136 patients diagnosed over five decades, demonstrated an overall five-year survival rate of 78%. As recurrence tends to be most likely within the first three years after diagnosis and treatment of breast cancer, women are advised to postpone subsequent pregnancy to beyond this time period. However, there is no strong evidence that conception prior to that time worsens the patient’s prognosis.
Infant. In the advent of a unilateral total mastectomy, or in an adequate lactogenesis, allowing them to breastfeed their infants following radiation therapy for breast cancer demonstrated a significant risk of recurrence in the ipsilateral breast (II-3C). However, it is important to note that the evidence to support breastfeeding is relatively poor.

9. Since most breast cancer recurrences appear within two to three years after initial diagnosis, patients should be advised to postpone pregnancy for three years (III-C). If a patient has axillary node involvement, the recommendation to defer pregnancy should be extended to five years, but this is based on opinion only (III-C). Prior to attempting pregnancy, a breast cancer survivor should be referred for a full oncologic evaluation.

**REFERENCES**


**BREASTFEEDING AFTER BREAST CANCER**

There is no epidemiological data on the impact of breastfeeding on the risk of a second breast cancer or the risk of recurrence in the ipsilateral breast (III-C).

Breast cancer treatment may impair the capability of nursing. For instance, the circumaureolar incision often used for cosmetic purpose at the time of tumour excision may reduce the quantity of milk for the infant, if several collecting ducts or lactiferous sinuses have been damaged. Radiation therapy may negatively influence the functional potential of the treated breast, although our knowledge on this is mainly based on anecdotal cases. Lactation is less likely to be possible in cases of previous centrally located lesions. Radiation to the breast induces perilobar and periductal fibrosis, lobular atrophy, and stenosis of the galactophorous ducts. The elasticity of the nipple may be impaired, creating difficulty for the infant to latch and suckle properly. Radiation therapy may also induce a decrease in the milk production from the treated breast. Tralins reported that only 34% of women who delivered following radiation therapy for breast cancer demonstrated an adequate lactogenesis, allowing them to breastfeed their infant. In the advent of a unilateral total mastectomy, or in the case of compromised milk production from the treated breast, the woman should be advised that nursing is still possible from a single breast.

For unfavourable genetic factors, the daughters of mothers treated for breast cancer may carry an increased risk of breast cancer, but there is no evidence that milk from a mother previously treated for breast cancer increases the risk of disease for the child. The oncogenic viral transmission via their milk production has been shown in certain mouse strains, but never in humans. Potential carcinogens are retrieved in the human maternal milk, but there is no known impact or risk factor associated for the infant regarding the risk of any cancer.

Case-control studies, looking at the appearance of breast cancer over a lifetime in the daughter who was breastfed as a child, showed either an unmodified risk or a reduction of breast cancer risk of between 25 and 35%. There is no evidence that breastfeeding increases the risk of breast cancer recurring or of a second breast cancer developing, nor that it carries any health risk to the child. Women previously treated for breast cancer who do not show any evidence of residual tumour, should be encouraged to breastfeed their infants. (III-B)


