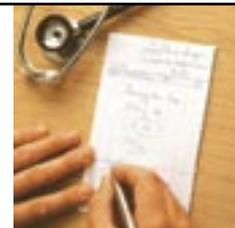




Breast cancer in young women



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This eighth article in our series on breast disease focusses on breast cancer in young women. There are several challenges in the diagnosis of breast cancer in young women, and special consideration must be given to the woman's fertility and body image issues. The difficulty in distinguishing benign from malignant lesions on clinical and imaging assessment in this group stresses the importance of the triple test of clinical examination, mammography or ultrasound, and biopsy.

Breast cancer is uncommon in young women, with only 6% of breast cancers in Australia diagnosed in women under the age of 40 years.¹ Breast cancer in young women deserves special consideration as there are complex issues raised by a cancer diagnosis at a young age. Breast cancer in these women may present differently to breast cancer in older women and may be more difficult to diagnose. For women under the age of 40 years there are also the special considerations of pregnancy, fertility and contraception, sexuality and body image, as well as familial and genetic issues.

Breast cancers in women under the age of 40 years tend to be larger (median tumour size 2 cm in young women vs. 1.5 cm in older women), more advanced at diagnosis (more likely to be lymph node positive) and more aggressive (less well differentiated) than breast cancer in older women.^{2,3} Cancer in young women also has a higher mortality and shorter

disease free survival than in older women, and is more likely to recur after treatment both locally and at distant sites.^{4,5}

Diagnosis

There are several ways in which the presentation of breast cancer may differ in women under the age of 40 years compared to its presentation in older women. The majority of young women with breast cancer present with symptoms (93% in one Australian study³). Older women, on the other hand, are more likely to present with screen detected breast cancer than symptomatic cancer because of established population screening.

There are several challenges in the diagnosis of breast cancer in young women: clinical examination and breast imaging may be limited and this may contribute to a delay in diagnosis, which is more common in young women;⁶ clinical breast examination is less sensitive in young women (but improves with

increasing age⁷); and breast cancer is rare in this group, whereas benign and physiological conditions of the breast are very common. As a result there is an inherently lower level of suspicion for cancer when assessing a young woman with breast symptoms.

Mammography has much lower accuracy in women under 40 years of age compared with older women.^{8,9} This is partly due to the greater tissue (glandular) density in younger women which may obscure lesions, and partly due to the fact that some breast cancers in this group don't have typical malignant features on mammography. A recent Australian series showed that only 54% of mammograms with cancer were reported as suspicious or malignant in women younger than 40 years compared to 70% in women over 40 years.³

Ultrasound has been shown to be more accurate than mammography in younger women^{8,9} and is considered the imaging test of choice.¹⁰ However, a proportion of

cancers in young women will have benign sonographic features.^{3,9} It has been reported that 10% of malignant lesions in young women have features typical of, or consistent with, fibroadenomas – even in retrospect.³ A combination of the two imaging tests, mammography and ultrasound, is therefore often used to maximise imaging accuracy, especially in young women where there are significant clinical findings.¹⁰

The difficulty in distinguishing benign from malignant lesions on clinical and imaging assessment in young women stresses the importance of the triple test. The addition of percutaneous biopsy (fine needle aspiration biopsy [FNAB] or core biopsy) to the clinical and imaging findings increases the chances of correctly diagnosing a malignant lesion, with over 90% showing an atypical, suspicious, or malignant result on biopsy alone.³ While one report states that the accuracy of the triple test may be lower in young women than the 99–100% accuracy quoted for the general population,¹¹ an Australian report shows that the triple test in young women is in line with reported estimates and approaches 100%.¹² It is likely that most errors in diagnosis of breast cancer in young women result from falsely reassuring clinical and/or imaging findings. New palpable masses in women of any age should undergo imaging and biopsy to establish a diagnosis.

Treatment

Treatment options for breast cancer treatment are the same in young women as they are for older women. Options for local treatment are mastectomy and breast conserving surgery followed by radiotherapy. As in older women, treatment recommendations should be guided by factors such as tumour size and location, the likely cosmetic outcome, and patient preference. Local recurrence rates following breast conserving surgery may be higher in young women following breast conserving treatment,⁴ and it is recommended that radiotherapy include a boost of radiation to the tumour bed in an attempt to reduce the risk of local recurrence.¹³ It is critical that surgical resection margins are clear after

breast conservation. Re-excision should be considered if risk factors such as an extensive intraductal component or extensive lymphatic vessel invasion are seen in the pathology report, particularly if there is doubt that the margins are clear. When mastectomy is recommended or chosen, the option of breast reconstruction should be offered, either as an immediate or as a delayed procedure.

Adjuvant chemotherapy is usually recommended for women under the age of 40 years, as the absolute benefit they gain from chemotherapy is greater than for older women. The incidence of oestrogen receptor positive tumours is lower in younger women than it is in older women.¹⁴ Women with hormone receptor positive breast cancer should be offered endocrine therapy, which may be given in the form of Tamoxifen, ovarian suppression (oophorectomy or luteinising hormone releasing hormone [LHRH] agonists, eg. goserelin), or a combination of these options.¹³ Aromatase inhibitors are newer hormonal agents which may be used instead of Tamoxifen in postmenopausal women. Their role in young women who are rendered postmenopausal by treatment is uncertain.

Premature menopause and loss of fertility

Premature menopause and loss of fertility are significant considerations in young women undergoing treatment for breast cancer. The adjuvant treatments for breast cancer that may induce menopause are chemotherapy and hormone therapies such as Tamoxifen and oophorectomy. Studies have shown that patients with hormone receptor positive tumours who are amenorrhoeic after breast cancer treatment may have a better outcome than those in whom menses return following treatment,¹⁵ although results are inconsistent.

The risk of menopause with chemotherapy is dependent on age and the intensity of chemotherapy. The likelihood of menopause following chemotherapy increases with increasing age. The use of Tamoxifen is also associated with an increase in the risk of menopause. *Figure 1* shows the likelihood of menopause based on age and treatment.

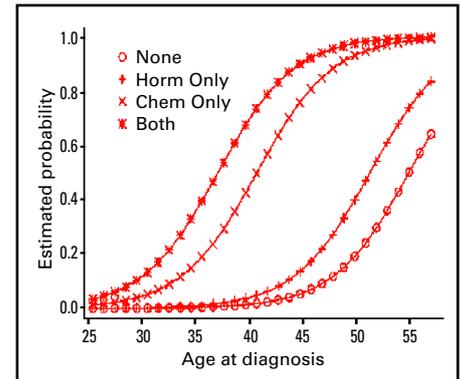


Figure 1. Probability of menopause during the first year after diagnosis, showing the effect of patient age and type of adjuvant treatment
Reprinted with permission: Goodwin et al¹⁶

A woman who has chemotherapy at age 30 years is unlikely to become menopausal with treatment; at age 35 the risk is around 18%, and at age 40 years the risk is around 40%.¹⁶

If future childbearing is planned, the option of using assisted reproduction techniques before chemotherapy and hormone therapy should be considered. Generally, this is more successful if the woman has a partner so that embryos (rather than oocytes) can be frozen for future use following one or more cycles of in-vitro fertilisation.

Young women, if treated successfully, may live for many years following breast cancer treatment. Even if future childbearing is not a consideration, other side effects of menopause such as heart disease, osteoporosis, hot flushes, urinary symptoms, weight gain and psychological and sexual symptoms may be troublesome for a long period of time. The use of hormone therapy is generally avoided in women who have had breast cancer, but may be an option, particularly for women with oestrogen receptor negative tumours who are suffering severe symptoms. The woman's symptoms should be assessed individually, and treatment, preferably nonhormonal, should be targeted to the most troublesome complaints.

Breast cancer during pregnancy

Breast cancer may present during pregnancy, and may be more difficult to diagnose than breast cancer in the young nonpregnant woman due to the hormonal effects of

pregnancy on breast tissue. Young women who present with breast cancer during pregnancy tend to have larger, more advanced cancer at diagnosis and a poorer outcome than other women the same age with breast cancer.^{17,18}

Treatment options for breast cancer that presents during pregnancy depend on the gestational stage at diagnosis. While many women will assume that the pregnancy must be terminated, this is not necessarily the case as breast cancer can be treated successfully during pregnancy. Surgery may be performed at any gestation. It is a commonly held misconception that general anaesthesia increases the risk of spontaneous abortion. While there may be a very small increase in risk to the fetus, this is not of clinical significance. The surgical options of breast conserving surgery and mastectomy are the same as for any breast cancer, with the same considerations of tumour size and location, breast size, likely cosmetic outcome, and patient preference.

Breast conserving surgery may be performed during pregnancy, but is generally not recommended in the first and second trimesters as adjuvant radiotherapy must be delayed until after confinement. The use of lymphoscintigraphy and sentinel node biopsy during pregnancy has not been studied extensively. Some small studies suggest it may be safe.^{19,20}

Chemotherapy may be given during the second and third trimesters of pregnancy with some commonly used agents. The incidence of spontaneous abortion or birth defects associated with chemotherapy in the second and third trimesters is very low and most babies are born with hair. Chemotherapy is contraindicated in the first trimester.²¹⁻²³

Pregnancy after breast cancer

While there is a theoretical concern that the hormonal effects of a pregnancy after breast cancer may cause relapse, the evidence does not support this. While fertility may be reduced, pregnancy following treatment for breast cancer does not increase the risk of relapse and is therefore not contraindicated.²⁴

Table 1. Features in the family history that suggest an inherited gene mutation

The presence of:

- A number of women affected by either breast or ovarian cancer in different generations on one side of the family (maternal or paternal)
- Women who have developed breast cancer under 40 years of age
- Women who have developed bilateral breast cancer
- Women who have developed ovarian cancer
- Men who have developed breast cancer
- Ashkenazi Jewish ancestry

Some oncologists recommend delaying pregnancy for a period of 2 years as particularly aggressive disease may relapse in that time, but there is no evidence that a delay is required.

Breastfeeding from a breast previously treated for cancer is not usually possible as radiotherapy diminishes the ability of the breast to produce milk. Successful breastfeeding from one breast may be possible. The untreated breast will usually enlarge with pregnancy and lactation but the treated breast may not.

The difficult areas for discussion are timing of a pregnancy and whether pre-pregnancy metastatic screening tests such as a computerised tomography and bone scan should be performed. Before a pregnancy, other sensitive issues about the amount of family support available if the mother subsequently relapses or dies from the cancer need to be discussed.

Genetic issues

Young women who develop breast cancer are more likely than older women to have an affected first degree relative.²⁵ While only about 5% of all breast cancer occurs in women who carry a heritable mutation in genes such as BRCA1 or BRCA2 (ie. are 'gene mutation positive'), women who develop breast cancer at a young age are more likely to carry a mutation than women who develop breast cancer later in life. If a young woman with breast cancer has other relatives who have breast or ovarian cancer, or has other risk factors for a genetic mutation in the family (*Table 1*) it may be appropriate to refer her to

a family cancer clinic for assessment. Genetic testing may be recommended.

Options for treating breast cancer in women who are carry a BRCA1 or BRCA2 gene mutation are the same as for women who do not carry a mutation. However, knowledge that a woman carries a gene mutation implies a high risk of cancer developing in the contralateral breast or in the ovary/fallopian tube, and this may affect treatment choices.^{26,27} For example, she may elect to have her cancer treated with mastectomy rather than conservation, as she may be considering risk reducing mastectomy to decrease the risk of contralateral breast cancer. She may also consider the option of salpingo-oophorectomy to further reduce her risk of breast cancer as well as decrease her risk of developing ovarian cancer. Such an approach may also play a role in the adjuvant therapy or a hormone receptor positive breast cancer.

Psychological factors

Evidence has shown that the psychological impact of breast cancer diagnosis and treatment is greater in young women than in older women. Younger women often suffer from a worse body image and have more 'negative feelings' such as guilt, sadness, anger and frustration than older women following treatment for breast cancer.²⁸ Problems in sexual functioning such as lack of interest, inability to enjoy sex and difficulty with arousal and orgasm are more common in breast cancer survivors than in women without a history of breast cancer.²⁹ Some of these symptoms may occur as a direct result of treatment such as the menopausal effects of

chemotherapy and endocrine therapy, and some may be related to changes in body image and sexual relationships following breast cancer. Some women may feel a 'loss of womanhood' and feel more vulnerable after having breast cancer and this may translate into difficulty in sexual functioning. The reality for young women is that they must adjust to an 'altered sexual self' following treatment. This transition seems to be more successful in women who are married or partnered and have strong existing intimate relationships.^{30,31}

Young women may therefore require more support during their treatment than older women. Young women are often faced with additional difficulties such as dealing with young children, dealing with issues related to future fertility, and continuing to work during cancer treatment.

Conclusion

Although a diagnosis of breast cancer is rare in women under the age of 40 years, it can have a greater impact than in older women. It tends to present at a later stage, be more aggressive and have a poorer prognosis. In addition, other complex issues such as future fertility and genetic issues need to be considered. This presents – in addition to the usual elements of breast cancer management – a new set of challenging dilemmas to the treating team.

Conflict of interest: none.

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