

## It is Very Important to Start Treating Breast Cancer at an Early Stage

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### Abstract

Breast cancer is the most common type of cancer in women. Most women diagnosed with breast cancer are over 50, but younger women can also get this type of cancer. There is a high possibility of cure if it is detected at an early stage. A tumor up to 1 cm in size is curable in 98% of cases. For these reasons, it is vital that women check their breasts regularly for any changes. Although rare, men can also get breast cancer.

**Keywords:** Breast; Cancer; Risk; Prevention

### Introduction

Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer death among women in the United States. Approximately one out of every eight American women will be diagnosed with breast cancer in their lifetime [1]. Since the turn of the century, an abundance of guidelines for breast cancer screening has been put forth by numerous medical organizations, each with its own variations. These include the government organization known as USPSTF (US Preventive Services Task Force), as well as nongovernmental professional medical societies such as (in alphabetical order) American Cancer Society (ACS), American College of Radiology (ACR), the American Congress of Obstetricians and Gynecologists (ACOG), and the National Comprehensive Cancer Network (NCCN).

Breast cancer is a heterogeneous disease that encompasses a number of distinct biological characteristics and clinical behaviour [2]. Breast cancer is often curable, particularly if diagnosed at an early stage. This requires early detection and a knowledge and awareness of all types of the disease, including the rarer forms of breast cancer.

Breast cancer is not a single disease, but rather there are different types of breast cancers with different prognostic features. Breast cancers arise in the terminal duct lobular unit. They are classified according to the type of tissue from which they arise and their appearance under the microscope. When making treatment decisions, the type of breast cancer may affect the choice.

Carcinoma cells confined within the terminal duct lobular unit and adjacent ducts, but which have not invaded the basement membrane, are known as carcinoma in situ. Two types have been identified: ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). DCIS arises from the ducts and is more common than LCIS, which arises from the lobules.

#### Breasts

The breasts, also known as the mammary glands, exist in both males and females but are only usually enlarged in the woman [3]. The breasts begin to develop in the foetus at around the seventh week of gestation and progress to the budding stage at the twelfth week. They are formed from the ectodermal mammary ridge that runs from the axilla to the groin, often referred to as the nipple line. Between weeks 13 and 20, the epithelial bud branches and canalises to form the 16–20 major ducts found in the adult breast.



Occasionally at birth, a baby may produce a small amount of milk. This is due to high levels of luteal and placental hormones crossing the placenta and entering the foetal circulation during the late stage of pregnancy thus stimulating the foetal breast. At birth, the foetal and maternal circulatory systems are separated, resulting in the rapid fall of sex steroids in the baby's blood, whereas the baby's pituitary gland continues to secrete prolactin. The baby's prolactin level then declines and the secretions dry up. This is classed as a normal physiological event. Accessory nipples may also be found along the ectodermal ridge, most commonly below the normal breast. These are harmless and only need to be removed if they cause distress to the individual.

The evaluation of a breast mass during pregnancy should not differ from that of a non - pregnant patient and therefore should not be delayed [4]. Mammography maybe of use but is associated with a higher rate of a false - positive test when compared with non - pregnant women because of the increased density of breast tissue in pregnancy. Because of this an ultrasound may be a useful first step in the diagnostic process. Magnetic resonance imaging (MRI) of the breast may also be useful in prenatal diagnosis of breast cancer; data are currently limited on its use in pregnancy, but it appears to be a safe modality.

If a mass appears suspicious for malignancy on radiographic evaluation, a biopsy is indicated. Ideally, this is acquired through a core biopsy. A fine needle aspiration may also yield the diagnosis but requires a pathologist with experience in pregnancy - associated breast cancer.

If a malignancy is discovered further evaluation is mandatory. In non - pregnant patients, this has been achieved through careful history and physical exam, serologic tests and chest X - ray; bone scans and CT are also performed in patients at high risk or who have suspected metastases. Traditionally, CT has been avoided in pregnancy because of concerns about exposure of the fetus especially during the first trimester. MRI may be selectively used in patients where metastasis is suspected.

When matched for stage and other prognostic factors, pregnancy does not appear to worsen the prognosis. In those women who have no evidence of metastasis, surgical management may be definitive. For smaller tumors, breast - conserving surgery can be performed; if the tumor is larger, the patient may require more substantial surgical management with modified radical or total mastectomy with axillary node staging. While radiation therapy is employed in non - pregnant women with breast - conserving surgery, this is avoided in pregnancy, because of the potential radiation exposure to the fetus. In node - positive or advanced cases, chemotherapy is recommended; current recommendations include cyclophosphamide, doxorubicin, and 5 - fluorouracil. Methotrexate can also be used beyond the first trimester.

## Prevention

Women positive for the heritable BRCA mutation may benefit from prophylactic tamoxifen and prophylactic total mastectomy [5]. AAFP (American Academy of Family Physician) recommends that women whose family history is associated with an increased risk for BRCA mutation be referred for genetic counseling and evaluation for BRCA testing. Neither routine testing nor prophylactic medication is recommended for the general population. Smoking is a risk factor for cancer development, and cessation should be recommended in all current smokers.

Breast cancer most commonly presents as a painless, irregularly bordered mass. Other presentations may include local swelling, dimpling, breast pain, and skin and nipple changes as well as nipple discharge. Advanced clinical presentations may include pain and/or fracture from bony metastasis.

## Self-Examination

Breast self-examination (BSE) was traditionally advocated as a method of self-screening [1]. Over the years, evidence has demonstrated that self-examination does not reduce breast cancer-related mortality and is associated with an increased rate of benign biopsies.

The new mantra being advocated, in place of the traditional practice of BSE, is the concept of "breast self-awareness," which is being promoted by essentially all organizations, including the ACOG, ACS, and NCCN. Rather than a methodically and routinely performed self-exam, this recommendation emphasizes the importance of patients being aware of the way their breasts normally appear and feel. The patient is encouraged to be aware of any change that may occur in their own body and to discuss these changes with their physician. A breast finding brought to a clinician's attention by the patient may be appropriately followed up with either reassurance, clinical breast exam, and/or imaging. ACOG, ACS, and NCCN. Rather than a methodically and routinely performed self-exam, this recommendation emphasizes the importance of patients being aware of the way their breasts normally appear and feel. The patient is encouraged to be aware of any change that may occur in their own body and to discuss these changes with their physician. A breast finding brought to a clinician's attention by the patient may be appropriately followed up with either reassurance, clinical breast exam, and/or imaging.

## Risk

The two most important risk factors for breast cancer are female gender and advancing age [6]. The lifetime risk of breast cancer for American women through age 85 is one in eight. Only 1% of breast cancers occur in men. Breast cancer is rare before age 30



and increases with age until declining at 80. Other factors associated with an increased risk include early menarche, late menopause, nulliparity, first birth after age 35, positive family history, and radiation exposure especially in younger women. Five to ten percent of women with breast cancer have an associated autosomal dominant suppressor gene mutation BRCA. The risk of BRCA mutation is highest in younger women with cancer especially less than age 30, bilateral disease, or family history of breast or ovarian cancer. The lifetime risk for women with a known BRCA mutation is between 40% and 85%. Women with a personal history of breast cancer have a 1% per year risk of a new primary cancer and a lifetime risk of approximately 20%. Oral contraceptive use has not conclusively been shown to increase breast cancer risk.

Proliferative breast lesions without atypia confirm a small increased risk of breast cancer and include tissue-proven fibroadenoma, ductal hyperplasia, papilloma, sclerosing adenosis, and radial scar. Proliferative breast lesions with atypia have a greater risk and include atypical ductal hyperplasia, atypical lobular hyperplasia, and lobular carcinoma in situ.

Even when genetic testing fails to reveal a predisposing genetic mutation, women with a strong family history of breast cancer are at higher risk for development of breast cancer [7]. Compared with a woman with no affected family members, a woman who has one first-degree relative (mother, daughter, or sister) with breast cancer has double the risk of developing breast cancer and a woman with two first-degree relatives with breast cancer has triple the risk of developing breast cancer. The risk is further increased for a woman whose affected family member was premenopausal at the time of diagnosis or had bilateral breast cancer. Lifestyle and reproductive factors also contribute to risk of breast cancer. Nulliparous women and women whose first full-term pregnancy occurred after the age of 30 have an elevated risk. Late menarche and artificial menopause are associated with a lower incidence, whereas early menarche (under the age of 12) and late natural menopause (after the age of 55) are associated with an increase in risk. Combined oral contraceptive pills may increase the risk of breast cancer. Several studies show that concomitant administration of progesterone and estrogen to postmenopausal women may markedly increase the incidence of breast cancer, compared with the use of estrogen alone or with no hormone replacement treatment. The Women's Health Initiative prospective randomized study of hormone replacement therapy stopped treatment with estrogen and progesterone early because of an increased risk of breast cancer compared with untreated women or women treated with estrogen alone. Alcohol consumption, high dietary intake of fat, and lack of exercise may also increase the risk of breast cancer. Fibrocystic breast condition, when accompanied by proliferative changes, papillomatosis, or atypical epithelial hyperplasia, and increased breast density on mammogram are also associated with an increased incidence. A woman who had cancer in one breast is at

increased risk for cancer developing in the other breast. In these women, a contralateral cancer develops at the rate of 1% or 2% per year. Women with cancer of the uterine corpus have a risk of breast cancer significantly higher than that of the general population, and women with breast cancer have a comparably increased risk of endometrial cancer. Socioeconomic and racial factors have also been associated with breast cancer risk. Breast cancer tends to be diagnosed more frequently in women of higher socioeconomic status and is more frequent in white women than in black women.

### Brca

BRCA1 (also known as breast cancer 1, early onset) and BRCA2 (also known as breast cancer 2, early onset) are tumor-suppressor genes that function to prevent abnormal growth and development of cellular tissue [8]. Both BRCA1 and BRCA2 interact with other proteins to repair breaks in damaged DNA resulting from environmental influences, natural causes, iatrogenic causes (e.g., radiation), and the process of cell division. BRCA2 is also thought to have significant involvement in cytokinetic pathways. BRCA1 regulates the activity of other genes and has a significant influence on embryonic development. BRCA1 mutations have implications for breast cancer, fallopian tube cancer, and pancreatic cancer. BRCA1 mutations change one or more of the amino acids needed for the BRCA1 protein. The resultant protein is unable to repair damaged or mutated DNA. As a result, defects accumulate and divide uncontrollably, forming a tumor. Over 1,000 mutations of BRCA1 have been identified.

### Pelvic Exam

The pelvic examination can be a very challenging examination to execute because of associated patient discomfort, anxiety, and embarrassment [9]. The American College of Physicians reported that 35 percent of surveyed women experience fear, anxiety, discomfort, and/or pain during their pelvic examination. Women who experienced pain with their pelvic examination were found to be less likely to return for their visit than those who did not have a negative experience. Another study sought to address suggestions to improve the examination process from patients that had negative experience. Explaining each step of the examination in advance, providing information about the reproductive organs, warming the instruments, increased gentleness, and maintaining eye contact have been suggested by the patients as ways to improve the overall experience of the basic GYN examination. All of these areas can be addressed with simulation training.

The pelvic examination is conducted to screen for pathology, with the examination made of three elements: inspection of the external genitalia; speculum examination of the vagina and cervix; and bimanual examination of the adnexa, uterus, ovaries,



and bladder and sometimes a rectovaginal examination.

Teaching the pelvic examination portion of the basic GYN exam can start with an overview of the necessary materials. Reviewing the various swabs, Pap smear collection devices, bacterial wound culture, viral culture container, review of various specula (pediatric, nulliparous, multiparous speculum), and urine culture collection are some of the many various useful materials that a learner may not have seen before. Becoming familiar with these materials, recognizing what they look like, and indications and uses of collecting samples may be very helpful for the learner and lead to a more efficient and streamlined exam.

Having the opportunity to be instructed by a standardized patient on proper techniques for performing pelvic examinations is ideal as the anatomy is real and the feedback is immediate. Standardized patients are often utilized as both instructors and patients for these sessions. The standardized patient is able to talk the learner through proper bedside manner and work through a pelvic examination and bimanual examination usually with an instructor present to further provide brief lecture to the students prior to the examination. Often, the standardized patient provides the learner with feedback and helpful critiques to allow for improvement in clinical skills as both the content expert and patient.

## Screening

Breast cancer screening has been consistently demonstrated to decrease morbidity and mortality [1]. The goal of a screening exam, whether radiographic or clinical, is to detect and diagnose breast cancer before it produces symptoms or spreads throughout the body.

Traditionally, the pillars of screening were imaging, clinical breast exam, and breast self-examination. Over time, evidence has steered screening recommendations to heavily emphasize the role of imaging and de-emphasize or even discourage the practice of physical examination by some.

The breast cancer screening recommendations regarding the frequency and modality of such screening vary based on the patient population. The method of screening should be tailored to an individual patient's risk factors, taking into account items such as age, family history, and many other factors that will be described below. There are accelerated screening regimens for women who have certain high-risk factors.

Screening with mammography has improved the chances of survival through early diagnosis when tumors are more likely to be smaller, low grade, and treatable with a less aggressive approach [6]. The mammographic window is the time sequence when a breast cancer may be discovered only by mammogram imaging. Tumors are generally pre-mammographic until they

reach at least 1 mm and are usually not clinically palpable until at least 1 cm. Screening mammography should begin at age 40 and continue annually. Diagnostic mammography for a specific problem may be obtained at any time and at any age. Dense breasts are found in many women before age 40 and may make mammography less sensitive. Abnormal areas requiring biopsy are best sampled by image-guided core-needle technique. It is mandatory that the pathology result is in concordance with the mammogram appearance. Because the core-needle biopsy takes a representative sample, some pathology findings require an open excisional biopsy to more completely sample the area. Breast ultrasound is an adjunct to mammography and is used to detect cystic from solid or complex cystic masses. Simple cysts confirmed by sonar do not need to be removed or aspirated.

## Management

Breast cancers are classified according to the site of origin, the presence or absence of invasion, the degree of differentiation, and more recently the molecular characteristics (nature of genes expressed) of the tumor cells [10]. More than 90 percent of carcinomas arise from the epithelium of the ducts and are called ductal carcinomas. The rest arise from the lobules and are designated lobular carcinomas. As previously noted, a precursor in situ lesion for ductal carcinoma (DCIS) has been defined. Lobular carcinoma in situ (LCIS) occurs but is usually not considered an in situ carcinoma requiring surgical excision. However, certain specific types of LCIS may be an in situ precursor for forms of lobular carcinoma and require excisional therapy.

The therapy and prognosis for invasive breast carcinoma depend on many variables, but current practice focuses on the molecular characteristics of the carcinoma cells, which differ from case to case. The characteristics examined include the presence of several cell surface receptors including estrogen receptors (ER) and progesterone receptors (PR), which are almost always present or absent together, and the human epidermal growth factor receptor 2 (HER-2). ER positivity is a favorable prognostic indicator and suggests that the cancer cells may still respond to hormonal stimulation. Patients with these cancers are excellent candidates for drugs that block the effects of estrogens (such as tamoxifen) and slow the growth of the cancer cells. Some breast carcinomas overexpress (make excessive amounts of) the HER-2 protein and other genes associated with HER-2. These carcinomas are aggressive and have a poor prognosis. However, they are candidates for therapy using antibodies that target the HER-2 receptor (the monoclonal antibody trastuzumab and others) or for a drug that blocks the pathway stimulated by HER-2 (lapatinib, a tyrosine kinase inhibitor). Tests that determine the gene expression profile of breast carcinomas have been devised recently. These tests determine which sets of proteins are produced by the carcinomas and divide the disease



into subtypes that have particular prognostic characteristics. Luminal A carcinomas make up about 50 percent of cases and are most like the normal (non-neoplastic) breast epithelial cells. Luminal A cancers are low grade; that is, they are most similar to the normal cells they originate from and are generally ER positive. Individuals with these carcinomas have an excellent prognosis and are treated with hormonal therapy. Luminal B tumors (15 to 20 percent of cases) have a higher grade than Luminal A tumors but usually still express some level of ER. Individuals with these carcinomas have a poorer prognosis and are treated with both hormonal and other forms of chemotherapy. Individuals with basal-like tumors (15 to 20 percent of cases) have a poor prognosis. Their pattern of gene expression is most similar to the myoepithelial cells that line breast TDLUs (terminal duct lobular unit). These tumors are commonly of the triple-negative type, lacking in ER, PR, and HER-2. Most tumors in BRCA1-positive individuals are of this type. Although the tumors are sensitive to chemotherapy, patients have a high relapse rate, and the tumors tend to metastasize to the viscera and brain. HER-2-positive tumors (10 percent of cases) are extremely aggressive. These tumors contain multiple copies of the gene responsible for the HER-2 protein and have large amounts of the HER-2 receptor on their surface. Like basal-cell-type tumors, they have very high rates of cell division but can be treated using anti-HER-2 therapy. Another important factor in deciding on the likely prognosis of breast carcinoma (and choosing a therapy) is the stage of the tumor at detection.

## Conclusion

The exact cause of breast cancer is not known, so it is difficult to say why one woman gets sick and another does not. However, it is known that it all starts due to damage and mutation of DNA in the breast tissue cell, and this causes uncontrolled growth and proliferation of breast cells. Such damaged cells divide much faster than healthy ones, accumulating to form a nodule or tumor mass. The consequence is the development of a malignant tumor.

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