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Breast Cancer: A Review

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A B S T R A C T

Breast cancer is cancer that develops from breast tissue. In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or yellow skin. Breast cancer most commonly develops in cells from the lining of milk ducts and the lobules that supply the ducts with milk. Worldwide, breast cancer is the leading type of cancer in women, accounting for 25% of all cases. The diagnosis of breast cancer is confirmed by taking a biopsy of the concerning lump. A malignant tumor can spread to other parts of the body. A breast cancer that starts off in the lobules is known as *lobular carcinoma*, while one that develops from the ducts is called *ductal carcinoma*.
Keywords: Breast Cancer , Breast Cancer Awareness , Women's Cancer

A R T I C L E   I N F O

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1. Introduction

Breast cancer is a malignant tumor that starts in the cells of the breast. A malignant tumor is a group of cancer cells that can grow into (invade) surrounding tissues or spread (metastasize) to distant areas of the body. The disease occurs almost entirely in women, but men can get it, too. Breast cancer is cancer that develops from breast tissue. [1] Signs of breast cancer may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, or a red scaly patch of skin.[2] In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or yellow skin.[3]

Risk factors for developing breast cancer include: female sex, obesity, lack of physical exercise, drinking alcohol, hormone replacement therapy during menopause, ionizing radiation, early age at first menstruation, having children late or not at all, and older age.[2][4]

About 5–10% of cases are due to genes inherited from a person's parents, including BRCA1 and BRCA2 among others. Breast cancer most commonly develops in cells from the lining of milk ducts and the lobules that supply the ducts with milk. Cancers developing from the ducts are known as ductal carcinomas, while those developing from lobules are known as lobular carcinomas. [2]

In addition, there are more than 18 other sub-types of breast cancer. Some cancers develop from pre-invasive lesions such asductal carcinoma in situ.[4] The diagnosis of breast cancer is confirmed by taking a biopsy of the concerning lump. Once the diagnosis is made, further tests are done to determine if the cancer has spread beyond the breast and which treatments it may respond to.[2]

The balance of benefits versus harms of breast cancer screening is controversial. A 2013 Cochrane review stated that it is unclear if mammographic screening does more good or harm.[5] A 2009 review for the US Preventive Services Task Force found evidence of benefit in those 40 to 70 years of age [6] and the organization recommends screening every two years in women 50 to 74 years old.[7] The medications tamoxifen or raloxifene may be used in an effort to prevent breast cancer in those who are at high risk of developing it.[4] Surgical removal of both breasts is another useful preventative measure in some high risk women.[4] In those who have been diagnosed with cancer, a number of treatments may be used, including surgery, radiation therapy, chemotherapy, hormonal therapy and targeted therapy.[2] Types of surgery vary from breast-conserving surgery to mastectomy [8] [9].

Breast reconstruction may take place at the time of surgery or at a later date. In those in whom the cancer has spread to other parts of the body, treatments are mostly aimed at improving quality of life and comfort.[9] Outcomes for breast cancer vary depending on the cancer type, extent of disease, and person's age.[9] Survival rates in the developed world are high,[10] with between 80% and 90% of those in England and the United States alive for at least 5 years.[11][12] In developing countries survival rates are poorer.[4] Worldwide, breast cancer is the leading type of cancer in women common in developed countries [4] and is more than 100 times more common in women than in men.[10][14], accounting for 25% of all cases.[13] In 2012 it resulted in 1.68 million cases and 522,000 deaths.[13] It is more

2. Classification

Breast cancers are classified by several grading systems

Histopathology

Breast cancer is usually classified primarily by its histological appearance. Most breast cancers are derived from the epithelium lining the ducts or lobules, and these cancers are classified as lobular carcinoma. *Carcinoma in situ* is growth of low grade cancerous or precancerous cells within a particular tissue compartment such as the mammary duct without invasion of the surrounding tissue. In contrast, *invasive carcinoma* does not confine itself to the initial tissue compartment. [17]

Grade:

Grading compares the appearance of the breast cancer cells to the appearance of normal breast tissue. Normal cells in an organ like the breast become differentiated, meaning that they take on specific shapes and forms that reflect their function as part of that organ. Cancerous cells lose that differentiation. In cancer, the cells that would normally line up in an orderly way to make up the milk ducts become disorganized.

Cell division becomes uncontrolled. Cell nuclei become less uniform. Pathologists describe cells as well differentiated (low grade), moderately differentiated (intermediate grade), and poorly differentiated (high grade) as the cells progressively lose the features seen in normal breast cells. Poorly differentiated cancers (the ones whose tissue is least like normal breast tissue) have a worse prognosis.
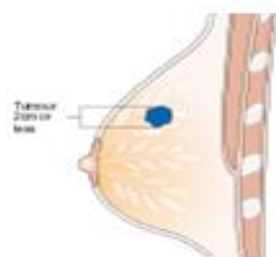
Stage:

Breast cancer staging using the TNM system is based on the size of the tumor (**T**), whether or not the tumor has spread to the lymph nodes (**N**) in the armpits, and whether the tumor has metastasized (**M**) (i.e. spread to a more distant part of the body). Larger size, nodal spread, and metastasis have a larger stage number and a worse prognosis.
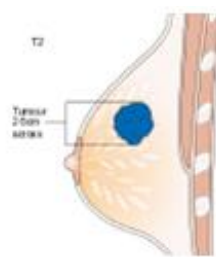
The main stages are:

Stage 0 is a pre-cancerous or marker condition, either ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS).
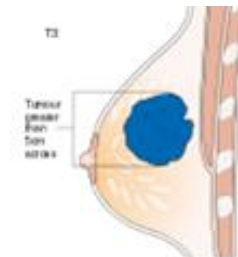
 a. Stages 1–3 are within the breast or regional lymph nodes.
 b. Stage 4 is 'metastatic' cancer that has a less favorable prognosis.

Stage T1 breast cancer

Stage T2 breast cancer   Stage T3 breast cancer

The lymph (lymphatic) system of the breast

The lymph system is important to understand because it is one way breast cancers can spread. This system has several parts. Lymph nodes are small, bean-shaped collections of immune system cells (cells that are important in fighting infections) that are connected by lymphatic vessels. Lymphatic vessels are like small veins, except that they carry a clear fluid called *lymph* (instead of blood) away from the breast. Lymph contains tissue fluid and waste products, as well as immune system cells. Breast cancer cells can enter lymphatic vessels and begin to grow in lymph nodes. Most lymphatic vessels in the breast connect to lymph nodes under the arm (*auxiliary nodes*). Some lymphatic vessels connect to lymph nodes inside the chest (*internal mammary nodes*) and either above or below the collarbone (*infraclavicular nodes*).
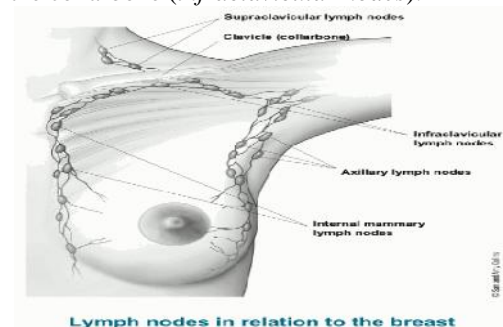
Lymph nodes in relation to the breast

3. Signs and Symptoms

The first noticeable symptom of breast cancer is typically a lump that feels different from the rest of the breast tissue. More than 80% of breast cancer cases are discovered when the woman feels a lump.[15] The earliest breast cancers are detected by a mammogram.[16] Lumps found in lymph nodes located in the armpits[15] can also indicate breast cancer. Indications of breast cancer other than a lump may include thickening different from the other breast tissue, one breast becoming larger or lower, a nipple changing position or shape or becoming inverted, skin puckering or dimpling, a rash on or around a nipple, discharge from nipples, constant pain in part of the breast or armpit, and swelling beneath the armpit or around the collarbone. [17] Pain (mastodynia) is an unreliable tool in determining the presence or absence of breast cancer, but may be indicative of other breast health issues. [15][16][18] Inflammatory breast cancer is a particular type of breast cancer which can pose a substantial diagnostic challenge. Symptoms may resemble a breast inflammation and may include itching, pain, swelling, nipple inversion, warmth and redness throughout the breast, as well as an orange-peel texture to the skin referred to as peau d'orange [15] as inflammatory breast cancer doesn't show as a lump there's sometimes a delay in diagnosis. Most symptoms of breast disorders, including most lumps, do not turn out to represent underlying breast cancer. Fewer than 20% of lumps, for example, are cancerous [23] and benign breast diseases such as mastitis and fibro adenoma of the breast are more common causes of breast disorder symptoms. Nevertheless, the appearance of a new symptom should be taken seriously by both patients and their doctors, because of the possibility of an underlying breast cancer at almost any age.[24]

Risk factors:

The primary risk factors for breast cancer are female sex and older age.[25] Other potential risk factors include: genetics,[26] lack of childbearing or lack of breastfeeding, [27] higher levels of certain hormones, [28][29] certain dietary patterns, and obesity. Recent studies have indicated that exposure to light pollution is a risk factor for the development of breast cancer.[30]

4. Lifestyle

Smoking tobacco appears to increase the risk of breast cancer, with the greater the amount smoked and the earlier in life that smoking began, the higher the risk.[11] In those who are long-term smokers, the risk is increased 35% to 50%.[13] A lack of physical activity has been linked to ~10% of cases.[12] Sitting regularly for prolonged periods is associated with higher mortality from breast cancer. The risk is not negated by regular exercise, though it is lowered. [13] There may be an association between use of oral contraceptives and the development of premenopausal breast cancer, [34] but whether oral contraceptives use may actually cause premenopausal breast cancer is a matter of debate. If there is indeed a link, the absolute effect is small.[15][16] In those with mutations in the breast cancer susceptibility genes *BRCA1* or *BRCA2*, or who have a family history of breast cancer, use of modern oral contraceptives does not appear to affect the risk of breast cancer.[17][18]

The association between breast feeding and breast cancer has not been clearly determined; some studies have found support for an association while others have not.[39] In the 1980s, the abortion–breast cancer hypothesis posited

that induced abortion increased the risk of developing breast cancer.[20] This hypothesis was the subject of extensive scientific inquiry, which concluded that neither miscarriages nor abortions are associated with a heightened risk for breast cancer.[11] There is a relationship between diet and breast cancer, including an increased risk with a high fat diet,[12] alcohol intake, [13] and obesity, [14] related to higher cholesterol levels.[15] Dietary iodine deficiency may also play a role.[16] Other risk factors include radiation,[17] and shift-work.[18] A number of chemicals have also been linked including: polychlorinated biphenyls, organic solvents, polycyclic aromatic hydrocarbons, [19] and a number of pesticides. [15] Although the radiation from mammography is a low dose, it is estimated that yearly screening from 40 to 80 years of age will cause approximately 225 cases of fatal breast cancer per million women screened.[51]

Genetics

Some genetic susceptibility may play a minor role in most cases.[22] Overall, however, genetics is believed to be the primary cause of 5–10% of all cases.[23] In those with zero, one or two affected relatives, the risk of breast cancer before the age of 80 is 7.8%, 13.3%, and 21.1% with a subsequent mortality from the disease of 2.3%, 4.2%, and 7.6% respectively.[54] In those with a first degree relative with the disease the risk of breast cancer between the age of 40 and 50 is double that of the general population.[15] In less than 5% of cases, genetics plays a more significant role by causing a hereditary breast–ovarian cancer syndrome. This includes those who carry the BRCA1 and BRCA2 gene mutation. These mutations account for up to 90% of the total genetic influence with a risk of breast cancer of 60–80% in those affected. In 2012, researchers said that there are four genetically distinct types of the breast cancer and that in each type, hallmark genetic changes lead to many cancers.

5. Medical conditions

Breast changes like atypical ductal hyperplasia [7] and lobular carcinoma *in situ*,[18] found in benign breast conditions such as fibrocystic breast changes, are correlated with an increased breast cancer risk. Diabetes mellitus might also increase the risk of breast cancer.[11]

Precautions:

a. Avoid becoming overweight. Obesity raises the risk of breast cancer after menopause, the time of life when breast cancer most often occurs. Avoid gaining weight over time, and try to maintain a body-mass index under 25 (calculators can be found online).

b. Eat healthy to avoid tipping the scale. Embrace a diet high in vegetables and fruit and low in sugared drinks, refined carbohydrates and fatty

foods. Eat lean protein such as fish or chicken breast and eat red meat in moderation, if at all. Eat whole grains. Choose vegetable oils over animal fats.

c. Keep physically active. Research suggests that increased physical activity, even when begun later in life, reduces overall breast-cancer risk by about 10 percent to 30 percent. All it takes is moderate exercise like a 30-minute walk five days a week to get this protective effect.

d. Drink little or no alcohol. Alcohol use is associated with an increased risk of breast cancer. Women should limit intake to no more than one drink per day, regardless of the type of alcohol.

6. Conclusion

Screening may identify early noninvasive cancers and allow treatment before they become invasive or identify invasive cancers at an early treatable stage. But screening does not, per se, prevent cancer. Breast cancer prevention really must be understood as risk reduction. In extremely high-risk patients, such as those who have BRCA mutations, risk reduction may involve prophylactic surgical removal of the breasts and ovaries. For the average patient, lifestyle modifications (diet, exercise, weight loss, etc.) may be easily recommended and have many other benefits. For patients who have an increased risk based on other factors, the use of hormone-blocking agents, in addition to the usual lifestyle recommendations, may also be considered.

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