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Breast Cancer—Epidemiology, Risk Factors, Classification, Pathophysiology, Histopathology, Screening, and Management —An Updated Review

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ABSTRACT

Breast cancer is by far the most common malignancy in women, accounting for over 10% of all cancer diagnoses annually. There is a mortality-to-incidence ratio of 15% for breast cancer, which affects around 30% of female cancers worldwide. Classification of breast cancer includes histological classification, luminal breast cancer, her2-enriched breast cancer, basal-like/triple-negative breast cancer, surrogate markers classification, and American Joint Committee on Cancer Classification. Lobular carcinoma in situ (LCIS) and ductal carcinoma in situ (DCIS) are the two most common types of noninvasive breast neoplasms. A higher risk of breast cancer may develop if LCIS is present. Eight separate randomized clinical trials found that screening mammography reduced breast cancer deaths by 20% or more. Multiple clinical factors impact breast cancer care. These include tumor stage, hormone receptor status, histological features, patient age, contralateral involvement, lesion size, and histological type. The surgical options for intervention include lumpectomy and bilateral mastectomy; however, most patients with unilateral illness are favored to have a breast-conserving lumpectomy. Trastuzumab and pertuzumab are HER-2 blockers that can be helpful for HER-2-positive breast cancer.

KEYWORDS: Breast cancer, Selective estrogen receptor modulator, Lobular carcinoma in situ, Ductal carcinoma in situ, Magnetic resonance imaging,

INTRODUCTION

Breast cancer is by far the most common malignancy in women, accounting for over 10% of all cancer diagnoses annually. On a global scale, it is the second most common reason why women die from cancer. The breast glands that produce milk are anatomically situated anterior to the chest wall. The pectoralis major muscle provides support, while ligaments that run down the chest wall keep the breast in place.[1] In a circular arrangement, the breast has fifteen to twenty lobes. The amount of fat that covers a woman's lobes determines the size and shape of her breasts. The glands that release milk in response to hormonal stimulation are located within the lobules that comprise each lobe.[2] As it advances, breast cancer is infamously silent. During routine screenings, most people find out about their disease. Others may show signs including a change in the breast's size or shape, the appearance of a lump, or the discharge of the nipples.[3] However, mastalgia is common. Imaging studies, including mammography, a tissue sample, and a comprehensive physical examination are necessary for a breast cancer diagnosis. The survival rate is improved with an early diagnosis. Tumors that spread through the lymphatic system or the bloodstream often have a poor prognosis and spread to other parts of the body. Given this, the importance of breast cancer screening programs becomes quite apparent.[2]

Epidemiology and risk factors

The association between economic development and breast cancer rates, as well as related social and lifestyle variables, is reflected in the incidence rates of the disease, which vary from 27 per 100,000 in North America to 97 per 100,000 in Africa and East Asia. Death rates, however, are still declining, albeit in some places more than others. There is a mortality-to-incidence ratio of 15% for breast cancer, which affects around 30% of female cancers worldwide. Although there are significant inequalities in the availability of these services, we can hasten the decrease in breast cancer deaths by guaranteeing that all women may participate in effective programs for prevention, early diagnosis, and treatment. The percentage of breast cancer cases attributable to genetic factors varies by ethnicity and nation but typically hovers around 10% overall. Germline mutations in the BRCA1 and BRCA2 genes cause breast cancer.[3,4] Next-generation sequencing in breast cancer uses gene panels that include PALB2, ATM, CHEK2, RAD51C, BARD1, and TP53, among other genes. The average total lifetime risk is roughly 70%. Mutations in mono-allelic PALB2 in the germline increase the risk of breast cancer by 53%, pancreatic cancer by 2-3%, and ovarian cancer by 5%. PALB2 is a protein that boosts the position and stability of BRCA2.[5] National guidelines for genetic testing serve as a roadmap for the therapeutic approach, which includes gathering personal and family histories, evaluating risk, and providing genetic counseling. Although Lynch syndrome and other rare inherited disorders are associated with an increased risk of

breast cancer, their penetrance is low to moderate.[6] Hormone therapy, pregnancy, and poor lifestyle choices—including obesity, insufficient physical activity, excessive alcohol use, poor dietary fiber, and smoking—are shown in Panel 1 as major risk factors for breast cancer. In high-income countries, data reveals that a third of breast cancer cases may have been avoided if people had simply changed their harmful practices. There has been much back-and-forth regarding whether or not oral hormonal contraceptives increase the risk of breast cancer; nevertheless, the actual risk is modest and not associated with a higher risk of mortality. On the other hand, there is more concrete evidence linking menopausal hormone therapy to an increased risk of breast cancer in women.[4,6]

ETIOLOGY

Finding potential breast cancer risk factors should be a standard component of women's preventative health examinations. We can classify these elements into seven main categories:

a. Age: The age-adjusted incidence of breast cancer continues to rise alongside the aging female population.

b. Females are more likely to develop breast cancer.

c. Having a first-degree relative with breast cancer increases the likelihood of getting a second primary cancer in the opposite breast.

d. Histologic risk factors: A notable portion of the breast cancer risk factors include histologic abnormalities that have been validated by a breast biopsy. Lobular carcinoma in situ (LCIS) and proliferative changes with atypia are among these abnormalities.

e. Having a first-degree relative with breast cancer increases the risk of developing the disease by a factor of two to three due to genetic predispositions and a family history of the disease. A quarter of breast cancer cases among women less than 30 years old, and another 5 to 10 percent of all instances, may be explained by genetic factors. The BRCA1 and BRCA2 genes are the most critical ones that increase the likelihood of breast cancer.

f. Factors related to reproduction: as a woman approaches reproductive milestones that expose her to higher estrogen levels throughout her life, the likelihood of her developing breast cancer is thought to rise. Such situations include menarche occurring before the age of 12, the first live birth occurring after the age of 30, nulliparity occurring after the age of 55, and menopause occurring beyond the age of 60.

g. Exogenous hormone use: estrogen and progesterone are commonly used for contraceptives by women before menopause and as hormone replacement therapy by women after menopause.[4,5,6]

CLASSIFICATION OF BREAST CANCER

Histological Classification

The clinical appearance, behavior, and tumor morphology of tumors classified as "invasive breast cancers" (IBCs) can differ substantially. The WHO has classified at least 18 different subtypes of breast cancer. Invasive ductal carcinoma, the most prevalent subtype, now known as invasive no special type (NST) breast cancer, accounts for 40-80% of all occurrences. By default, a tumor is classified when it does not cleanly match any of the established histological buckets. Subtypes of invasive breast cancer, which constitute around 25% of all cases, include neuroendocrine, mucinous A, mucinous B, tubular, and invasive lobular carcinoma. Examining gene expression levels in messenger RNA provides a biological method for classifying invasive breast cancer that is distinct from histological subtypes. Luminal, Basal-like, HER2-enriched, and Normal Breast-like were the four molecular categories used to categorize 38 breast tumors based on microarray gene expression data.[7,8] Subsequent studies separated the Luminal group into two subgroups, Luminal A and Luminal B. The normal breast-like subtype was eventually eliminated due to the belief that it represents sample contamination by normal mammary glands. More than 300 primary tumors were analyzed by the Cancer Genome Atlas Project (TCGA), which used DNA, RNA, and protein profiles to divide them into physiologically related categories.[9] Luminal A, Luminal B, HER2-enriched, and basal-like were the four main intrinsic subtypes of breast cancer determined by consensus clustering, based only on levels of mRNA gene expression. In 2007, researchers identified claudin-low breast cancer as the fifth intrinsic subtype in a study that combined data from human and animal mammary tumors. In 2009, Parker et al. developed PAM50, a 50-gene signature for subtype assignment. Using it, 93% of the time, it correctly classified individual breast tumors into the main intrinsic subtypes. Global clinical application of PAM50 is presently being carried out using the NanoString nCounter, which is the basis of the Prosigna test. By combining clinical data with the PAM50 assay, the Prosigna can assess the probability of distant recurrence in postmenopausal women with hormone receptor-positive, node-negative, or node-positive early-stage breast cancer. This everyday tool is used to evaluate the indication of adjuvant chemotherapy.[10]

Luminal Breast Cancer

Out of all breast cancers diagnosed in Western countries, more than 70% are luminal tumors (ER-positive). Most Luminal-like tumors present as IBC without a distinct subtype, while rare subtypes such as invasive lobular, tubular, invasive cribriform, mucinous, and invasive micropapillary carcinomas do occasionally emerge. Differentiating between subtypes A and B of luminal-like malignancies, which have different clinical outcomes, are two main biological processes: pathways related to proliferation and pathways regulated by luminal factors. Luminal A tumors include estrogen receptors (ER) and progesterone receptors (PR), unlike HER2-negative malignancies.[11] This subtype of luminal epithelium is defined by the activation of genes by

ER transcription factors; it lines the mammary ducts. Low levels of expression are also seen for genes that are important in cell proliferation. Because they are low-grade, slowly growing, and clinically benign, these malignancies usually have the best prognosis. Luminal B tumors have a worse grade and prognosis compared to subtype A malignancies. They may also be HER2-positive and PR-negative, in addition to ER-positive. In addition, there is an abundance of expression of genes linked to proliferation, including MKI67 and AURKA. The luminal epithelium contains genes and proteins such as PR and FOXA1, although this subtype does not express the ER at lower levels. Examining ER expression, which is constant across A and B subtypes, is one approach to distinguishing luminal from non-luminal illnesses. [7,12,13]

HER2-Enriched Breast Cancer

Approximately 10-15% of breast tumors are HER2-enriched. Specific to this malignancy is an overexpression of HER2 in the absence of ER or PR. Clusters of genes and proteins linked to proliferation (such as ERBB2/HER2 and GRB7) are mostly expressed by this subtype, in contrast to others. Additionally, the HER2-enriched subtype shows signs of APOBEC3B-mediated mutagenesis.[14] The APOBEC3B and other APOBEC cytidine deaminases are responsible for mutation clusters and cytosine mutation biases. Due to their faster growth rate compared to luminal tumors, HER2-enriched malignancies had the worst prognosis among the subtypes before the development of HER2-targeted medicines. It is important to differentiate between the HER2-enriched subtype and clinically HER2-positive breast cancer since a large number of ER-positive/HER2-positive tumors belong to the luminal B category.[15,16] Around 30% of tumors that are HER2-enriched are HER2-negative, according to immunohistochemistry (IHC) and/or fluorescence in situ hybridization (FISH) methods.[16]

Basal-Like/Triple-Negative Breast Cancer

A broad collection of breast tumors known as triple-negative breast cancer (TNBC) lack ER, PR, and HER2 markers. This type of breast cancer accounts for 20% of cases. The occurrence of TNBC was greater among women of African American heritage and in those under the age of 40. Hepatocellular non-small cell carcinomas (TNBCs) account for around 80% of breast cancers resulting from BRCA1 germline mutations, and BRCA1 or BRCA2 mutations are present in 11% to 16% of all TNBCs. It is typical for TNBC to be biologically aggressive and have a bad prognosis.[17,18] Metaplastic tumors with squamous or spindle cell differentiation, medullary-like tumors with a noticeable lymphocytic infiltrate, and extremely rare special-type tumors such as adenoid cystic carcinoma (AdCC) are other possible presentations of TNBC, though infiltrating ductal carcinoma is the most common histology. Despite the common usage of the terms, not all TNBCs are basal-type. Based on gene expression profiling, six subtypes of TNBCs can be identified: basal-like (BL1 and BL2), mesenchymal (M), immunomodulatory (IM), luminal androgen receptor (LAR), and an unknown group (UNS).[19] The therapeutic importance of subtyping in influencing therapy decisions for TNBC is not yet evident, and further research is needed to clarify.[20] The poor prognosis of Claudin-low (CL) breast cancers is because they are generally ER-negative, PR-negative, and HER2-negative. CL tumors account for 7–14% of invasive breast cancers. There was no difference in survival rates among claudin-low tumors, HER2-enriched tumors, and basal-like tumor subtypes, all of which had poor prognoses. One characteristic of the CL subtype is the reduced expression of genes related to cell-cell adhesion, including E-cadherin, occludin, and claudins 3, 4, and 7.[21,22] Furthermore, these malignancies have elevated amounts of genes contributing to the epithelial-mesenchymal transition (EMT) and gene expression patterns resembling stem cells. To add insult to injury, stromal and immunological cells flood CL tumors. On occasion, the lack of differentiation and the EMT-related transcription factor cause ZEB1 CL tumors to stay genetically stable.[23,24]

Surrogate Markers Classification

Clinical practice revolves around the core concern of how to ascertain whether patients will or will not benefit from particular therapies. Although molecular testing is costly, it enables more patients to forgo adjuvant treatment.[25] This is why commonly used immunohistochemistry (IHC) markers and surrogate subgroups based on pathological morphology are utilized to stratify risks and target adjuvant treatment. Combining the three prevalent pathological markers—ER, PR, and HER2—allows for the classification of tumors into intrinsic subtypes. Semiquantitative analysis of Ki-67 and PR can help further classify the Luminal subtype. Furthermore, by analyzing cytokeratin 5/6 and epidermal growth factor receptors, TNBC with basal-like breast cancer can be diagnosed.[26] The 2013 St. Gallen guidelines recommended surrogate subtype classification based on immunohistochemistry for use in clinical decision-making. These markers are only surrogates and cannot identify the intrinsic subtype of any specific cancer, despite the high degree of concordance (up to 30%) between IHC-based markers and gene-based tests.[27]

American Joint Committee on Cancer Classification

An essential tool for predicting the likely prognosis of breast cancer patients, the American Joint Committee on Cancer (AJCC) staging system incorporates grading, immunohistochemistry biomarkers, and the physical course of the illness. Based on three anatomical findings—tumor size (T), nodal status (N), and metastases (M)—the American Joint Committee on Cancer (AJCC) has been producing a widely used staging classification for cancer patients since 1977. However, gene expression profiling has led to the discovery of many molecular subtypes of breast cancer.[28] In their eighth edition of the staging manual, the American Joint Committee on Cancer (AJCC) laid out new criteria for the prognostic staging of breast cancer (2018). This system considers both morphological markers and biochemical factors.[29] The following criteria are used to define prognosis in practice: ER, PR, HER2, grade, and multigene screens. Breast cancer histologic grading is most commonly performed using the Elston-Ellis system, a modification of the Scarff-Bloom-Richardson system. To determine the tumor grade, tests are performed on (a) the growth of tubules, (b) the count of mitotic cells, (c) the variability of the tumor, and (d) the size and shape of human cell nuclei. We assign a value between one (the greatest) and three (the poorest) to each attribute. Grade 1 is attained with a combined score of 3-5, grade 2 with 6-7, and grade 3 with 8-9. In addition to grades and biomarkers, the AJCC 8th edition could benefit from the additional prognostic data provided by commercially accessible multigene assays. Only the Oncotype DX® 21-gene assay, which assessed gene expression by RT-PCR, was part of the staging strategy. This assay can enhance the staging of patients with hormone

receptor-positive, HER2-negative, and node-negative tumors that are smaller than 5 cm in size. The disease-free survival rate was an impressive 98.6% after 6.9 years for patients with test findings (Recurrence Score) less than 11 who received only endocrine therapy. Patients who have a low-risk multigene test can therefore safely forego systemic adjuvant treatment.[30] According to the American Joint Commission staging handbook, there are two types of stages: clinical and pathological. Before beginning systemic treatment, all patients should undergo evaluation utilizing the clinical prognostic stage group. The expression of these three biomarkers, the TNM grading system, and anatomical information are the foundation of clinical staging. After the primary tumor has been surgically removed, the results of pretreatment biomarkers are combined with the anatomical information to determine the Pathologic Prognostic Stage Group.[30,31]

PATHOPHYSIOLOGY

Because estrogen causes DNA damage and genetic mutations, it can impact the development of breast cancer. Some genes cause cancer or DNA abnormalities that run in families, such as BRCA1 and BRCA2. Having a personal or maternal history of breast cancer increases your risk of getting the disease.[22] A person's immune system attacks cells it finds to have abnormal DNA or to be growing in an unhealthy way. Unfortunately, this won't help those whose breast cancer has already spread to other parts of their bodies.[25,31]

HISTOPATHOLOGY

Breast cancer's aggressiveness or lack thereof is defined by its association with the basement membrane. Lobular carcinoma in situ (LCIS) and ductal carcinoma in situ (DCIS) are the two most common types of noninvasive breast neoplasms. A higher risk of breast cancer may develop if LCIS is present. Enlarged and filled acini resembling a typical lobule shape are characteristic of LCIS.[25] Pathologists typically divide DCIS into four types: papillary, cribriform, solid, and comedo, due to the higher degree of morphological variation in DCIS compared to LCIS. Cancer cells densely packed into tiny regions, frequently encircled by a basal cell layer of apparently normal myoepithelial cells, characterize differential stromal inflammatory bowel syndrome (DCIS). Compared to other types of DCIS, papillary and cribriform appear to be less aggressive due to their lower grade and possible delayed progression to invasive malignancy. The solid and comedo variants of DCIS are usually considered higher-grade lesions.[32] It is common for DCIS to grow into aggressive cancer if not treated. Invasive breast cancer is characterized by a lack of a coherent plan, the random invasion of cells into different thicknesses of stroma, or the formation of flattened, uniform cell sheets that fail to take into account the glandular organ's form and function. Pathologists use histological criteria to categorize invasive breast cancer as lobular or ductal. Invasive ductal carcinoma may not develop into a solid mass, but it shows up as discrete abnormalities on mammograms and feels like a tiny bump in the breast. Invasive lobular cancer is clinically occult and often goes undiscovered until the disease has advanced considerably, even after mammography and physical exams, because it usually travels in a single file across the breast. Surgical ductal cancers, also known as infiltrating ductal carcinomas, account for 50% to 70% of all invasive breast cancers.[33] Invasive lobular carcinoma accounts for 10% of breast cancer cases, and there has been an uptick in the frequency of pathology reports describing tumors that are a mix of ductal and lobular. It is possible to tell invasive ductal carcinomas apart by looking for telltale signs that they've developed. When cancer cells invade and grow into small glands encircled by a single layer of bland epithelium, the result is infiltrating tubular carcinoma. The invading cells may release a great deal of mucin, giving the impression that they are suspended in midair. This is the medical term for tumors that are filled with mucus or colloid. About 2% to 3% of invasive breast carcinomas are tubular or mucinous tumors, and they typically have a low grade (grade I).[34] The hallmarks of medullary cancer include abnormal invasive cells that do not have an in situ component, an abundance of mitoses, and high-grade nuclear features. As the cancer cells cluster in almost syncytial sheets, a small number of mononuclear lymphocytes infiltrate the area. Instead of penetrating the stroma, the tumor presses on the adjacent breast. The pure form of medullary malignancies accounts for only approximately 5% of breast tumors.[35]

SCREENING

Eight separate randomized clinical trials found that screening mammography reduced breast cancer deaths by 20% or more. Digital breast tomosynthesis improves upon traditional screening mammography by 1.6 per 1000 images, increasing the frequency of malignancies detected from 2 to 8 per 1000 images. Although the positive predictive value of ultrasonography screening is just 3-8%, it does identify an extra 4.4 malignancies per 1000 screening exams, especially in women with thick breasts. Among asymptomatic high-risk women, MRI screening had a far higher sensitivity for cancer detection (90-93% vs. 48-63% for mammography and ultrasound combined). Nevertheless, there are areas where MRI screening has not caught on.[36] A shorter magnetic resonance imaging (MRI) scan or contrast-enhanced spectral mammography can replace a standard MRI for breast cancer screening. To lower their risk, women who have a BRCA1 or BRCA2 mutation can choose to have either a bilateral mastectomy or a salpingo-oophorectomy. Medications that prevent breast cancer, such as raloxifene, tamoxifen, or aromatase inhibitors, decrease the likelihood of the disease developing, but they do not lessen the likelihood of death from the disease. In patients with intraepithelial neoplasia, a 5-milligram dose of tamoxifen seems to reduce the likelihood of ipsilateral and contralateral recurrences.[35,36]

MANAGEMENT

Multiple clinical factors impact breast cancer care. These include tumor stage, hormone receptor status, histological features, patient age, contralateral involvement, lesion size, and histological type. The surgical options for intervention include lumpectomy and bilateral mastectomy; however, most

patients with unilateral illness are favored to have a breast-conserving lumpectomy. When there is no evidence of involvement in the axillary lymph nodes, either clinically or radiographically, sentinel lymph node biopsy is the way to go instead of extensive lymph node dissection.[37] However, whether or not axillary node dissection is effective in patients with lymph node involvement is still up for dispute. The occurrence of metastatic disease, hormone receptor, HER-2 status, and Oncotype DX recurrence score are among the many criteria that inform the development of personalized chemotherapy regimens. Before surgery, patients with triple-negative breast cancer or illness that has progressed locally get neoadjuvant chemotherapy, which usually includes paclitaxel, doxorubicin, and cyclophosphamide. Doxorubicin has several side effects, including nausea, vomiting, diarrhea, exhaustion, and cardiotoxicity (which can cause heart failure), which calls for a complete evaluation of the heart and blood vessels.[38] Other side effects include staining of the nails and a crimson tint to bodily fluids. In contrast to paclitaxel's potential to induce mucositis, peripheral neuropathy, and musculoskeletal pain, cyclophosphamide's side effects include neutropenia, hair loss, and gastrointestinal issues. A histological subtype, hormone receptor status, tumor features, and surgical methods determine the course of treatment for adjuvant chemotherapy. Breast cancers that have not spread and have estrogen and progesterone receptors positive can be treated with endocrine treatments such as aromatase inhibitors and selective estrogen receptor modulators (SERMs).[38,39] Trastuzumab and pertuzumab are HER-2 blockers that can be helpful for HER-2-positive breast cancer. However, it is crucial to monitor the left ventricular ejection fraction because these drugs can cause cardiotoxicity. SERMs can be given to premenopausal patients who have developed resistance to trastuzumab or are experiencing secondary resistance. The current standard of care for hormone-positive breast cancer is a 5-year regimen of SERMs combined with aromatase inhibitors. Exemestane in conjunction with ovarian suppression by different modalities may be beneficial for high-risk patients, especially those younger than 35 with HER-2 negative tumors, high-grade disease, or big tumors. The most prevalent selective estrogen receptor modulator (SERM) used in this setting is tamoxifen.[40]

Tamoxifen increases the risk of endometrial hyperplasia and cancer, thus women using the drug should tell their gynecologist right once they notice a change in the way their uterine bleeding occurs. The effectiveness of tamoxifen may be diminished when used with the strong CYP2D6 inhibitors paroxetine, fluoxetine, bupropion, or duloxetine. Moderate CYP2D6 inhibitors include escitalopram, desvenlafaxine, citalopram, and medrol. Venlafaxine seems to have a negligible effect on aromatase, an enzyme that many women use to alleviate the symptoms of menopause (whether surgically or otherwise).[41] As per the National Comprehensive Cancer Network, menopause can be identified in breast cancer patients. To be classified as postmenopausal, a woman must fulfill the following conditions: Her age is sixty-five or more. She had her ovaries removed. Her age is less than 60, she has not had a period in at least a year, and she has not taken any medications that might influence ovarian function. Her serum estradiol and follicle-stimulating hormone levels are in line with menopause, even though she is using a selective estrogen receptor modulator (SERM) and is under the age of 60. Women using aromatase inhibitors should get their bone density evaluated frequently since the medicine accelerates bone loss. Women with hormone receptor-positive breast cancer who have gone through menopause may be prescribed bisphosphonates by their doctors to help prevent further bone loss caused by aromatase inhibitor treatment. Aromatase inhibitors can cause severe joint discomfort.[42] Education and assistance for patients can help improve adherence. Arthritis caused by aromatase can be treated with paracetamol and nonsteroidal anti-inflammatory medications. Some people may find relief through CAM techniques like exercise, acupuncture, and physical therapy. The triple-negative basal subtype of breast cancer is commonly treated with doxorubicin, cyclophosphamide, and paclitaxel. Clinical trials for targeted medicines, including immunotherapies, are currently underway. The lack of endocrine reactivity in triple-negative breast cancer makes endocrine therapy an inappropriate choice for this subtype of the disease.[43] Radiation therapy is typically given either before or after surgery. In terms of treatment, the gold standard methods are whole-breast and targeted nodal radiation. Typically, a lady will get radiation treatment five times weekly for four to seven weeks. A "boost" of less radiation may be administered to women who are very prone to recurrence. Potential candidates for accelerated partial breast irradiation include node-negative, hormone receptor-positive, and BRCA-negative women who are 50 years old and older. After breast-conserving surgery, patients get radiation therapy to the breasts and axilla. For tumors staged at T2 or higher, pre-surgical radiation therapy is frequently used, with particular criteria dictating radiation decisions.[44] When a woman has tumors bigger than 5 cm or positive lymph nodes, she may be given radiation to the axilla, supraclavicular areas, and sternum. Deodorants, antiperspirants, and underwire bras should not be worn by radiation patients. Women over the age of 65 with hormone receptor-positive cancer, node-negative disease, and a primary tumor smaller than 3 cm may be able to avoid radiation treatment, according to new research. Furthermore, patients should not use heavy amounts of topical lotions, ointments, or creams on their breasts before radiation treatments, since this could raise the radiation dosage.[45] Radiation burns can happen during radiation treatments, thus it's important to use only topical solutions designed for skin burns, such as hydrocortisone or aloe Vera. Other common adverse effects of radiation treatment include breast discoloration, pain, and fatigue. Candida dermatitis can also develop under a woman's breasts if her breasts are too large. Quick administration of a sufficient antifungal medication is of the utmost importance.[46]

CONCLUSION

Breast cancer is the most common malignancy in women and the second leading cause of cancer-related deaths in women globally. Screening programs and early diagnosis are crucial for improving survival rates. The incidence and mortality rates of breast cancer vary across regions, with economic development and lifestyle factors playing a role. Genetic factors, reproductive factors, and exogenous hormone use are also associated with breast cancer risk. Breast cancer can be classified based on histology and molecular characteristics, with luminal, HER2-enriched, basal-like/triple-negative, and claudin-low being the main subtypes. Subtyping can help guide treatment decisions. The importance of surrogate markers and classification systems in determining treatment strategies for breast cancer patients. It emphasizes the significance of molecular testing, immunohistochemistry markers, and gene expression profiling in guiding clinical decision-making and prognosis assessment. Additionally, the text underscores the role of histopathology and pathophysiology in understanding the development and progression of breast cancer, emphasizing the importance of early detection and treatment.

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