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A REVIEW ON BREAST CANCER

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ABSTRACT

Breast cancer is the most frequently diagnosed malignant tumor in women worldwide and the leading cause of malignant tumor-related death. Everywhere in the world, there is an ongoing increase in the incidence of breast cancer. The most frequent type, infiltrative ductal carcinoma, was discovered to be 77% common, and lobular carcinoma, 5% common. Over the previous ten years, death rates have significantly decreased in 36 states and the District of Columbia, but have remained level in 14 other states. The single most crucial action that doctors can take to lessen suffering and mortality from breast cancer is to encourage patients aged 40 and older to undergo annual mammography and a clinical breast examination.

KEYWORDS: *Introduction, pathalogy of breast cancer, Risk factor for development of breast cancer, relationship of benign breast disease with breast cancer, detection of breast cancer, DCIS:intra intestinal (dUCtal) carcinoma in situ, In situ lobular carsinoma, conclusion.*

INTRODUCTION

Carcinogenesis, which has six key characteristics, can happen in every cell, tissue, and organ, resulting in the degenerative changes that cause a large proportion of malignancies. Resistance to apoptosis, an infinite capacity for division, increased angiogenesis, and evasion of apoptosis are the main processes that permit its growth. the ability to metastasis, induction of own growth signals, and anti-growth signals.[1]

With an estimated 2.3 million new cases worldwide, breast cancer is currently one of the most often diagnosed cancers and the fifth leading cause of cancer-related deaths, according to GLOBOCAN 2020 estimates.[2]

When compared to transitioned nations (Australia/New Zealand, Western Europe, Northern America, and Northern Europe), deaths from breast cancer are more frequently reported (incidence rate is about 88% higher) in Melanesia, Western Africa, Micronesia/Polynesia, and the Caribbean. Regarding a potential reduction in the incidence rate of breast cancer and the adoption of early treatment, a number of procedures including preventative practices generally as well as screening programs are essential. Currently, the Breast Health Global Initiative (BHGI) is in charge of creating appropriate guidelines and strategies to offer the most effective breast cancer control globally.[3]

Since female breast cancer is currently the most common cancer among females, as was said above, we have specifically concentrated on it in this review article.[4]

Epidermology

The WHO estimates that malignant neoplasms cause 107.8 million Disability-Adjusted Life Years (DALYs) for women worldwide, of which 19.6 million DALYs are attributable to breast cancer.[5]

In extremely high HDI countries, the ASIR was the highest (75.6 per 100,000), while in medium and low HDI countries, it was more than 200% lower (27.8 per 100,000 and 36.1 per 100,000, respectively). 2.26 million [95% UI, 2.24-2.79 million] new cases of breast cancer will be detected in women worldwide in 2020.[6]

In the US, breast cancer will likely represent 29% of all new cases of cancer in females.[7]

Age-standardized incidence rates (ASIR) of breast cancer are highly and favorably correlated with the Human Development Index (HDI), according to GLOBOCAN data from 2018.[8]

Worldwide, incidence varies, with high-income regions (92 per 100,000 in North America) having a higher frequency than low-income regions (27 per 100,000 in middle Africa and eastern Europe, Asia).[9,10]

The likelihood of a recurrence can last up to 20 years, even if 60% to 80% of them happen in the first three years.[11,12]

Pathalogy of breast cancer

Ninety-five percent of breast malignancies are carcinomas, meaning that breast epithe- lial components constitute their source. There are two main forms of breast cancer: invasive (or infiltrating) carcinomas and in situ carcinomas. In situ cancers can develop in the ductal or lobular epithelium.

Table 1: A Woman's Age-Specific Risk of Breast Cancer.

By Age	Normal Risk	Genetic Risk
45	1 in 93 (1%)	42%
55	1 in 33 (3%)	72%
65	1 in 17 (6%)	80%
75	1 in 11 (9%)	84%

- The breast cancer-related antigens BRCA-1 and BRCA-2. Data from Cancer Facts from the American Cancer Society

. The type of bronchial extension that would go beyond epithelial borders.

It is referred to as an invading (or infiltrating) ductal or lobular carcinoma when the tumor extends below the basement membrane that makes up the epithelial border.

- **RISK FACTORS FOR DEVELOPMENT OF BREAST CANCER**

The incidence of breast cancer is lowest in Asia and Africa and greatest in North America and Northern Europe. Given that the incidence rates of second-, third-, and fourth-generation Asian immigrants are steadily rising in the United States, studies of migration patterns there imply that genetic reasons do not fully explain the incidence variation among nations. Environmental and/or lifestyle variables so seem to be significant risk factors for breast cancer.[13]

Breast cancer incidence rates in women increase significantly with age (see Table 1) until ages 45 to 50, after which the increase becomes less pronounced.[14]

A small but significant part of breast cancer risk comes from genetics. Only 5 to 6 percent of breast cancers are thought to be hereditary.[15]

Women who are BRCA-1 and/or BRCA-2 positive have a lifetime risk of 50% to 85% for breast cancer (see Table 1) and a lifetime risk of 15% to 65% for ovarian cancer starting at age 25.[16]

It was determined that combined es- trogen plus progestin use increased the risk of invasive breast cancer in the Women's Health Initiative (WHI), a randomized controlled trial of 16,608 post-menopausal women comparing effects of es- trogen plus progestin with placebo on chron- ic disease risk.[17]

The relative risk of breast cancer appears to be correlated with the breast's cumulative exposure to estrogen and progesterone, suggesting that a woman's hormonal history may be a risk factor.

Early menarche (the start of menstruation at age 13), not having children or having them after the age of 30, menopause after the age of 50, particularly after the age of 55, all result in more menstrual cycles and higher hormone exposure.[18]

In postmenopausal women, the Nurses' Health Study discovered that weight increase of more than 45 pounds beyond the age of 18 was associated as a separate risk factor for breast cancer (fat tissue releases hormones that are converted to estrogen).[19]

The rationale for the decreased risk in physically active women may be connected to the delayed menarche in young girls who participate in vigorous exercise. Additionally, premenopausal women who engage in moderate physical activity have anovulatory cycles, which are likewise linked to a lower risk.[20]

A new second cancer developing in either the treated breast or the other breast is around 1% more likely to occur in women who have had breast cancer treatment each year. Therefore, having had breast cancer in the past is a recognized risk factor for developing breast cancer.[21]

High doses of radiation administered to the chest before the age of 45, typically for Hodgkin's disease, considerably increase a woman's risk of developing breast cancer later in life. Radiation exposure after the age of 45 does not increase risk. The prepubertal years of 10 to 14 seem to be the most vulnerable. These women should start getting annual mammograms and clinical breast exams 10 years after their radiation treatments or by the time they are 35.[22]

Sex

Nearly all (99%) incidences of breast cancer are found in females. Men are only affected by this malignant tumor in 1% of instances, with a standardized incidence rate of 0.4/105 in Poland. Each year, no more than 100 instances are documented.[23]

However, much like in women, there is a gradual increase in the incidence of breast cancer in men, which is most likely related to obesity and longer survival times.[24]

Age

Age is the most significant known risk factor for breast cancer, after gender.[25] The incidence of breast cancer rises sharply with advancing age, peaks after menopause, and then either steadily declines or stays unchanged.[26]

Younger women, on the other hand, tend to have breast tumors that are larger, in advanced stages, positive lymph nodes, and have a worse prognosis.[28]

In a case-control study, the incidence rate of breast cancer was correlated with age greater than 50.[27]

Blood group

According to the findings of a review study, women who belong to blood group AB and are Rhesus negative are less likely to get breast cancer than women who belong to blood group A and are Rhesus positive.[29]

Numerous researchers were unable to find any connection between breast cancer and blood group.[30,31]

RELATIONSHIP OF BENIGN BREAST DISEASE WITH BREAST CANCER

Given that certain illnesses clearly raise the risk of cancer while others do not, this is a matter of great worry for patients, doctors, and insurance companies alike.

Breast biopsies that do not result in a markedly elevated risk of cancer include any lesion that exhibits non-proliferative change.[32,33]

Apart from the possibility of overlooking a malignant mass, there is no elevated risk of cancer associated with fibrocystic change (cysts and/or fibrous tissue without symptoms) or

fibrocystic disease (fibrocystic changes occurring in conjunction with pain, nipple discharge, or a degree of lumpiness sufficient to cause suspicion of cancer).[34]

Ductal hyperplasia without atypia is one condition associated with an increased risk of cancer. This is the most frequently seen breast biopsy result, which carries a two-fold greater risk and is unquestionably linked to an elevated risk of developing breast cancer in the future. Although there is an increase in the quantity, size, and form of epithelial cells lining duct basement membranes, the histology does not meet the requirements for malignancy. A higher risk of Invasive breast cancer is linked to the reduction of transforming growth factor-b receptor II expression in the impacted epithelial cells.[35]

There is also a nearly two-fold greater chance of developing breast cancer from a variety of other benign tumors. These include fibroadenomas with proliferative disease, which are tumors that contain cysts larger than 3 mm in diameter, with sclerosing adenosis, epithelial calcification, or papillary apocrine change; diffuse papillomatosis, which is the formation of multiple papillomas; and sclerosing adenosis, where lobular tissue undergoes hyperplastic change with increased fibr- brous tissue and interspaced glandular cells. Benign breast lesions with an unclear etiology known as radial scars are typically found by coincidence after a breast tumor is removed for medical purposes. The fibroelastic core of radial scars is surrounded by radiating ducts and lobules.[36]

Although non-bloody and bilateral breast discharge are typically the result of benign causes, women and their doctors frequently worry about breast discharge as an indication of cancer. Papilloma-affecte women frequently have bloody discharge. Invasive breast cancer rarely causes breast discharge; when it does, it is always unilateral and typically accompanied by a palpable lump.[37]

In a similar vein, breast pain is a rare sign of breast cancer. Just 4 women (0.4%) out of 987 women who were referred for breast imaging due to breast pain alone were found to have invasive breast cancer; this percentage was the same as that of the control group of women who did not exhibit any symptoms.[38]

DETECTION OF BREAST CANCER

Since breast cancer rarely hurts, a lump without any pain is far more suspicious of malignancy than one that is exhibiting symptoms. For women without any risk factors, the current recommended is a yearly mammogram starting at age 40.[39]

The most significant regularly available predictor of recurrence and survival is involvement of the axillary lymph nodes.[40]

Refer to the discussion that follows on DNA microarrays and cyclin E assays, which could refute this claim in the future. A poor prognosis is always indicated by an axillary recurrence or tumor involvement in the supraclavicular or internal mammary lymph nodes.[41]

A biopsy of the level I axillary lymph nodes is known as a sentinel lymph node biopsy. Its sensitivity is 89%, its specificity is 100%, and its positive predictive value is about 100%.[42]

A recent edition of this publication has a more thorough explanation of sentinel lymph node biopsy.[43]

Compared to receptor-negative tumors, estrogen and/or progesterone receptor-positive tumors have a better prognosis and respond better to hormone therapy. The flow cytometer Quantifies the DNA content, or DNA index, with Cancer cells with diploid DNA (normal DNA content, With a DNA index of 1, the prognosis is better. As opposed to aneuploidy.[44]

The percentage of cells actively synthesizing DNA is known as the S-phase fraction. Low S-phase cell counts in tumors result in worse differentiation and a worse prognosis.[45]

Numerous women with metastatic breast cancer have elevated levels of the tumor marker CA 15-3. c-erbB-2, also known as the HER-2/neu oncoprotein, is linked to a worse prognosis, a shorter time to relapse, and a shorter survival rate.1. Particular significance has been placed on this tumor marker since trastuzumab became a treatment option. First approved by the FDA in June 1996, CA 27.29 is a blood test for breast cancer recurrence.[46]

These studies should correctly identify patients who are most likely to benefit from adjuvant treatment, if they are validated.[47]

DCIS: Intra-intestinal (dUCtal) carcinoma in situ

The proliferation of malignant epithelial cells restricted to ducts without any indication of invasion through the basement membrane is known as intraductal (or ductal) carcinoma in situ, or DCIS. DCIS existed before mammography. Constituted a rare diagnosis. When routine mammography was implemented, the age-adjusted incidence of DCIS increased from 2.3 to 15.8 per 100,000 women, a rise of 587%. Invasive breast cancer cases increased in new cases. 34% during the identical time frame.[48]

Approximately 85% of intraductal cancers are detected by clustered microcalcifications on mammography; these tumors are frequently smaller than 1 cm. Mammography microcalcifications can also be seen in other conditions such as atypical ductal hyperplasia and sclerosing adenosis. The primary determinant of benign versus malignant calcification is the morphology of the microcalcifications. Findings such as fine linear branching calcifications, segmental distribution calcifications, or heterogeneous clustered calcifications are indicative of malignancy. When benign findings are magnified, they frequently display several clusters of finely granular microcalcification, but when DCIS-related findings are magnified, they typically appear as coarser microcalcifications.[49]

The microscopic and radiographic extents of the illness are highly correlated in women with poorly differentiated DCIS. On the other hand, well-differentiated DCIS's mammographic appearance may significantly underestimate its microscopic extent. A residual tumor with a positive-predictive value of 65% to 70% is indicated by residual microcalcifications on the post-surgery mammography.[50]

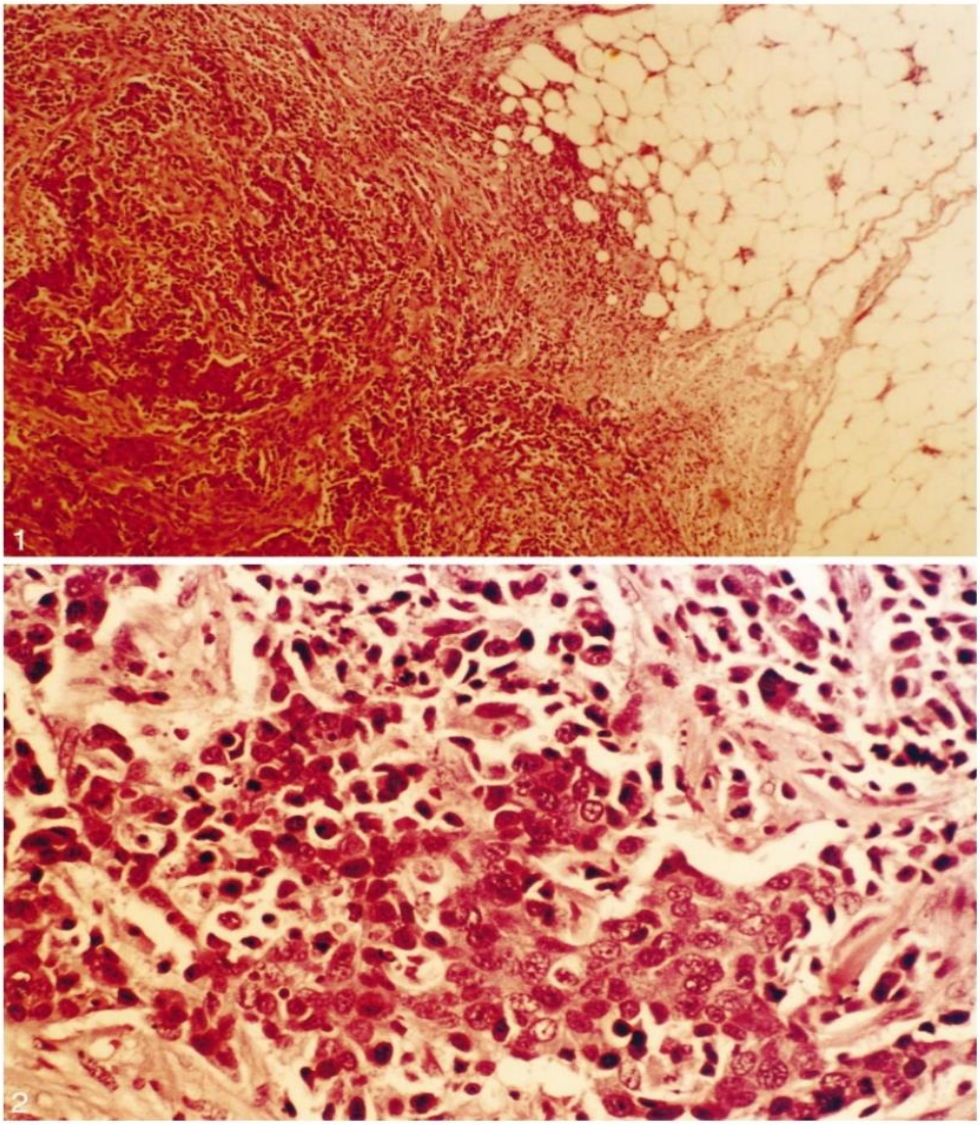
If post-operative mammography reveals more than five microcalcifications, the probability of remaining malignancy rises to 90%.[51]

When a lesion is clinically palpable, occult invasion is more likely than when it is solely detected by mammography. Six out of the 54 women (11%) who had palpable DCIS had invasive cancer, compared to none of the 16 women who had non-palpable DCIS.[52]

When DCIS is diagnosed with needle biopsy, 20% of cases had regions of invasive cancer discovered during the subsequent surgical excision (note that pathologists may find it challenging to differentiate DCIS from very atypical hyperplasia).[53]

In DCIS, axillary node involvement is extremely rare. Just 3.6% of 10,946 DCIS patients who received axillary node dissection between 1985 and 1991, according to a National Center Data Base analysis, had axillary Metastasizes.[54]

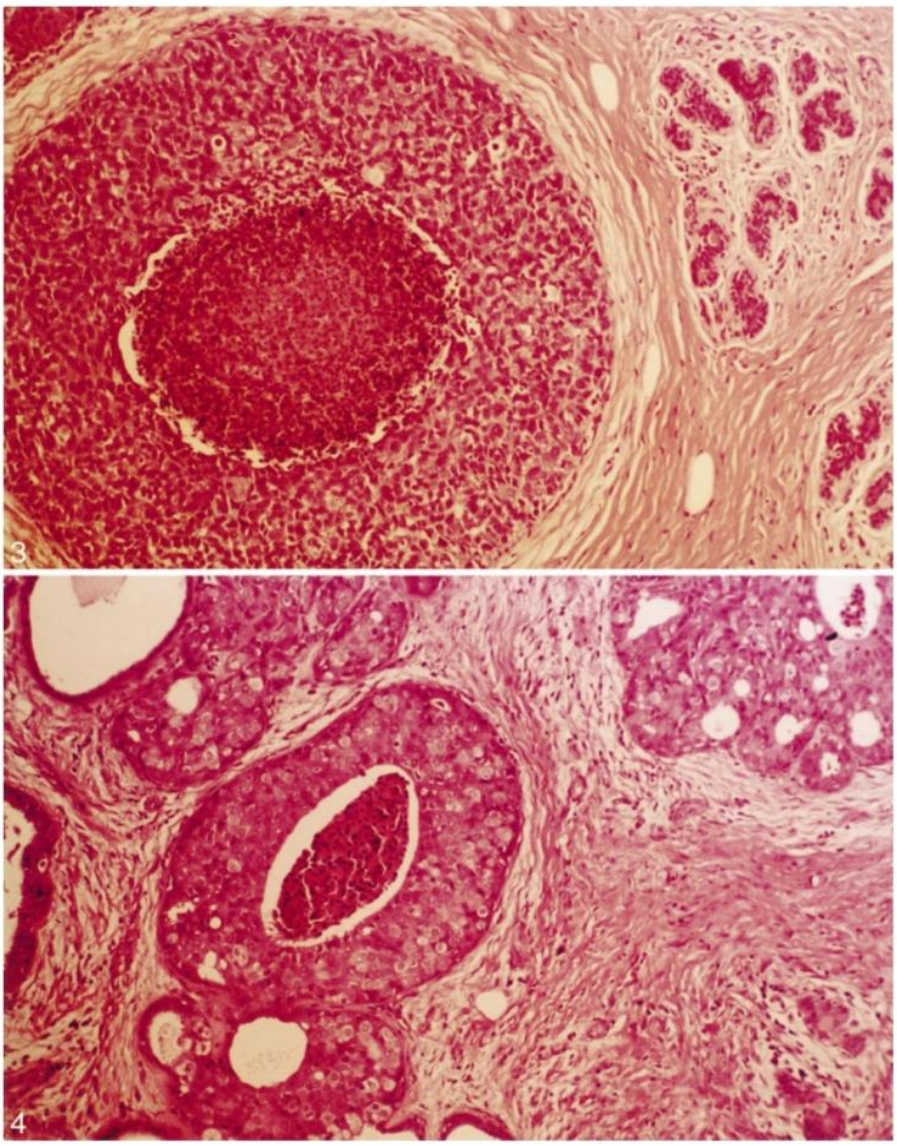
None of the 189 women with DCIS in a different series who had their axillary nodes removed had positive nodes.[55]



Figures 1 and 2. Low-power (Fig. 1) and high-power (Fig. 2) views demonstrating poorly differentiated infiltrating adenocarcinoma. The disorganized pattern is characteristic of a poorly differentiated cancer. Photomicrographs courtesy of E.Morrison, MD, Waco, TX.

Comedo-type DCIS (Figures 3 and 4) is likely intermediate between invasive cancer and DCIS, with a higher malignancy than other types of DCIS. In the end, 12 of the 19 cases

(63%) of DCIS with comedo necrosis had invasive breast cancer, compared to 4 of the 36 cases (11%) without comedo necrosis.[56]



Figures 3 and 4. Low-power (Fig. 3) and high-power (Fig. 4) views show ductal carcinoma in situ, comedo-type (comedocarcinoma). The tumor is contained within the basement membrane. Central necrosis is characteristic of comedocarcinoma. Photomicrographs courtesy of E. Morrison, MD, Waco, TX.

Regarding the so-called micro-invasive DCIS lesion, pathologists and breast surgeons continue to disagree. Microinvasion is defined by the American Joint Committee on Cancer (AJCC) as the spread of cancer cells into neighboring tissues past the basement membrane, with no concentration greater than 0.1 cm in Maximum dimension. Lesions that satisfy these T1mic, a subset of T1 breast cancer, meets the staging criteria.[57]

The term "microinvasion" in the context of the breast should ideally be used to refer to invasive lesions of such a small extent that the risk of them spreading is negligible, much like it does in the cervix. Regretfully, the data that are available are insufficient. In order to enable the repeatable identification of Such a division. When it comes to DCIS treatment, mastectomy is almost always curative (98%).[58,59,60]

If the following conditions are satisfied, breastconserving therapy (also known as a "lumpectomy") is nearly as curative: the lesion is three centimeters in size, the histologic margins are negative, and the nuclear grade is low, intermediate, or at least most definitely not high grade.[61]

Most frequently, radiation therapy is administered after breast-conserving surgery. At 15 years, 16% of treated breasts experience local failure; the median time to local failure is 5.0 years (mean 5.7 years, range 1.0–15.2 years).[62]

In treating DCIS, age and margin status are crucial, as demonstrated by a study involving 418 women who had breast radiation and breast-conserving surgery, or "lumpectomy." In 48 cases (11%) there was a recurrence within ten years. In women with retrospectively positive margins, recurrence occurred in 24% of cases, in women with uncertain margin status in 12% of cases, and in 9% of cases with negative margins. Age of the woman at initial diagnosis and surgery is statistically associated with the likelihood of local recurrence; recurrences are 31% for those under 39, 13% for those 40–49, 8% for those 50–59, and 6% for those over 60 ($p < 0.0001$).[62]

About half of the women who experience a local recurrence after radiation and lumpectomy for DCIS also have invasive ductal carcinoma, while the other half have DCIS once more. When a recurrence occurs, salvage therapy usually entails a mastectomy (88%) without adjuvant chemotherapy or tamoxifen (69%). In one series, 8 years after salvage treatment, 92% of patients were still alive and 88% showed no signs of recurrent disease. Following salvage treatment, DCIS as the local recurrence's histology and mammography alone as the means of local recurrence detection were favorable prognostic factors.[63]

It's interesting to note that a diagnosis of DCIS rather than the more serious invasive ductal breast cancer does not always indicate a less complex surgical outcome. In one series, women

with DCIS had a higher percentage of contraindications to breast preservation surgery (33%), compared to women with stage I invasive ductal carcinoma (10%).[64]

Two randomized trials have compared Lumpectomy alone for DCIS with lumpectomy with radiation.[65,66]

In terms of cancer recurrence (whether it was DCIS or invasive ductal disease), both trials supported lumpectomy with radiation therapy; however, the overall survival rates of the two groups were comparable (95% vs. 94%), indicating the effectiveness of salvage mastectomy. It seems that as mallsubset of DCIS patients with small tumor sizes, no comedo-type necrosis, and low histologic grade can be treated with lumpectomy alone.[67]

When local failure does occur, it usually takes longer to manifest, and in half of the instances, invasive cancer is still present compared to lumpectomy plus radiation therapy.[68,69,70]

For women with DCIS who have had a lumpectomy or a lumpectomy combined with radiation therapy, tamoxifen is recommended. 1804 women with DCIS receiving breast conservation therapy were randomly randomized to receive either tamoxifen (20 mg daily for five years) or placebo in a trial designed to particularly address this issue. Tamoxifen decreased the rate of invasive recurrence from 9 to 5 per 1000 patients (relative risk reduction 0.56, p 5 0.03) and the rate of recurrent DCIS from 11% to 9% per 100 patients (relative risk reduction 0.82, p 5 0.043) after an average follow-up of 62 months. Overall, in the tamoxifen group, the ipsilateral recurrence of either local or invasive cancer decreased from 13% to 8% after 5 years.[66]

In Situ Lobular Carcinoma (LCIS)

The actual incidence of LCIS is unclear because it is clinically undefinable (there is never a palpable lump and lacks distinctive mammographic characteristics). The incidence of 69 LCIS in breast tumors excised has ranged from From 0.05% to 10% and beyond.[71,72,73]

In the United States, white women have a ten-fold higher incidence of LCIS than African-American women.[74]

This diagnosis is always made as a byproduct of a needle biopsy or mass removal performed for fibroadenoma, fibrocystic change, or a mass that may be cancerous.[75]

Premenopausal women are more likely than postmenopausal women to have LCIS, which may indicate that hormones play a role in the genesis or maintenance of these lesions.[76,77]

Careful follow-up, a semiannual physical examination of the breasts, and an annual mammography are the recommended treatments for LCIS. 826 women with LCIS participated in the NSABP tamoxifen prevention trial (NSABP protocol P1). Invasive breast cancer was less common in the tamoxifen arm at 4 years of follow-up (2% vs 4% with placebo, 5.7 vs 13 per 1000 women, a 56% reduction in risk).[78]

But many experts advise against tamoxifen in this group, citing the drug's side effects (hot flashes, an estrogen antagonist effect, and an increased risk of endometrial cancer and venous thromboembolism in postmenopausal women) as well as its expense (20 mg tablets per day for five years).

CONCLUSION

While breast cancer is a leading cause of morbidity and death in women, which is understandable for life underwriters to be concerned about, a basic understanding of the disease often permits aggressive underwriting in certain situations. While underwriting women with cumulative risk factors discussed in this treatise, as well as unfavorable pathology and particularly the presence of axillary metastases, calls for ever-increasing caution, women with DCIS and LCIS who have been properly managed should still be eligible for optimistic ratings.

The more recent reports on the discriminating power of cyclin E measurements and simultaneous analysis of thousands of gene expression levels with DNA microarray technology in identifying women with stage I and II breast cancers with both much better and those with much worse prognoses than is currently available with knowledge of estrogen-receptor status and the presence or absence of lymph node metastases are particularly noteworthy for underwriting department.

We have examined the data as of the time of writing on the contentious use of hormone replacement therapy (HRT) in postmenopausal women in the section Risk Factors for Development of Breast Cancer.

There seems to be growing evidence that hormone replacement therapy (HRT) involving both estrogen and progestin carries risks that should be taken into account when making underwriting decisions, despite the persistence of some contentious issues.

Our review's most important conclusion may have been that between 70% and 75% of women who die from invasive breast cancer do so from causes other than the cancer itself. Despite the fact that these women's underwriting should raise serious concerns due to certain red flags, many "breast cancer survivors" are just that—apparently survivors of their disease. However, the selection of these insurable cases will only be possible with a thorough comprehension of all the issues covered in this review.

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