Breast Cancer Screening

Expires Thursday, October 31, 2019 Nursing John Link , M.D.

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2. Discuss the importance of screening, who should be screened, and when screening should occur.
3. Describe the different techniques that might be used (now and in the future) for detecting breast cancer including mammography, digital mammography, magnetic resonance imaging, and positron emission tomography.

Article

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Introduction

Breast cancer is a major health problem for modern society. It is the leading cancer of women (excluding skin cancer) and is second behind lung cancer in female mortality. The absolute numbers of new cases of breast cancer will markedly increase in the next twenty years due to the population increase of women over 50 years of age. However, the incidence of breast cancer has leveled off at about 120 cases per 100,000 population per year (figure 1).

This topic is important for the nursing profession because nurses are in an advantageous position for educating the population (primarily women). This article will help nurses understand the significance of this disorder and will give them the knowledge regarding the need for screening, how screening is performed, and what the imaging techniques might depict.

Much has been investigated and written about risk factors for breast cancer. The two most definite major risk factors are being a woman and aging. Well over 95% of all breast cancer cases occur in women. In the United States, the risk of a woman developing breast cancer between the ages of 20 and 40 is about 0.5% compared to 5% after the age of 65 (a 10 fold increase in risk).

Endocrine factors also seem to play a role in the development of this cancer. Factors such as early age of menarche, late onset of menopause, nulliparity (no pregnancies that carry to the delivery of a child), and late age at first pregnancy all appear to be independently associated with an increased risk. A woman's age at the time of her first full-term pregnancy seems to be a more important determinant than the number of pregnancies. The relative risk of a woman developing breast cancer is four times higher for a woman whose first pregnancy is after the age of 30 compared to a woman whose first pregnancy occurs before the age of 18. Some investigations have actually found a slightly higher risk in women whose first pregnancy occurs after the age of 30 compared to nulliparous women. It is these observations that lead to the hypothesis that events between menarche and the first pregnancy are important in determining the lifetime probability of developing breast cancer. Unfortunately, none of these issues help in identifying the woman who will ultimately develop the cancer compared to those who don't.

Long-term estrogen exposure also appears to increase the incidence somewhat. This issue has been evaluated extensively and many conflicting reports exist. The majority of studies regarding oral contraceptives have failed to establish a definite link. However, large studies that involve the use of estrogen for 10 or more years have found that the risk of developing breast cancer is about double. In addition, there has been a tremendous amount of discussion regarding the "Women's Health Initiative" that was recently stopped (results published in JAMA in 2002) because of a higher incidence of cardiovascular events in the women on the estrogen / progestin arm compared to placebo. This study also showed a higher rate of breast cancer in the estrogen / progestin arm, though the majority of cases were caught early and there was no difference in overall outcome.

Approximately 10% of breast cancer is caused by inherited genetic abnormalities. Two genes have now been identified and sequenced. The first is Breast Cancer Gene 1 (BRCA1), which resides on the 17th chromosome. The second is Breast Cancer Gene 2 (BRCA2), which resides on the 11th chromosome. Both genes are associated with an increased risk of developing breast cancer (60% to 80%) usually before the age of 60. There is also an increased risk of developing ovarian cancer (15% to 30%) in women who carry either of these genes (figure 2). Both genes are autosomal dominant and thus, can be passed through the father's as well as the mother's side of the family. The BRCA1 gene is also associated with Ashkenasi Jewish families. Males that carry the BRCA-2 gene also appear to have a higher incidence of male breast cancer than the normal population.

Environmental factors have also been extensively analyzed. The incidence of breast cancer varies widely around the world with the highest rates seen in affluent and westernized countries. Asian countries, such as Japan, have the lowest incidence; however, the risk increases for Japanese women who immigrate to Hawaii and California. Unfortunately, the environmental factor that is responsible for this phenomenon is unknown. A large emphasis has been placed on diet, especially dietary fat. However, the majority of epidemiologic studies have failed in demonstrating the link between dietary fat and breast cancer. Most studies do show that obese postmenopausal women have a higher risk than postmenopausal women who are not obese. Obesity in women, however, also increases endogenous estrogen production and this relationship could be hormonal (though excess dietary fat can lead to obesity). Other environmental factors that may be associated with an increase in the development of breast cancer include high dose radiation exposure at an early age (data from atomic bomb victims) and moderate to excessive alcohol consumption.

The mortality from breast cancer has steadily fallen over the last 30 years (figure 3), and this is due largely to screening mammography and its ability to detect early breast cancer before the disease spreads. The use of systemic agents in at-risk women for systemic spread (adjuvant chemotherapy and tamoxifen) has also reduced mortality from breast cancer. African-American women have not experienced the same drop in mortality when compared to White woman and this may be explained by the lack of consistent mammography screening in this population.

Screening mammography reduces breast cancer mortality because it can discover a breast cancer before it has spread systemically. Breast cancer is a progressively systemic disease. The risk of systemic spread and death increases with tumor size and lymph node involvement. If a cancer can be found before it becomes larger than 1 cm in size, the 20-year disease free survival exceeds 95% (figure 3), compared to only 20% for tumors that are 5 cm or larger. Likewise, the ten-year survival for cancers with negative lymph nodes is greater than 80%, dropping to only 40% if nodes are positive.

A number of randomized studies have demonstrated the benefit of screening mammography. The first major study performed was the HIP Study (Health Insurance Plan of New York). This early randomized screening trial demonstrated a decreased mortality from breast cancer in the screened group versus the control group. The Swedish Two-Country Study confirmed the HIP study. This trial beginning in 1977 randomized 77,080 women to receive an invitation to mammography screening and 55,985 to receive no invitation. The end point of the trial was death from breast cancer. There was a 30% decrease in breast cancer mortality in the screened group. Several other studies on this topic performed in other countries have also shown a decrease in death in the screened group compared to the unscreened group during observations of 7 to 12 years, though not all trials were statistically significant based on odds ratios. However, when these studies are all combined, the decrease is statistically significant.

Screening Mammography

Modern screen-film mammography typically calls for two views of each breast taken while the breast is spread and compressed. The screen is repeated on an annual basis. There has been some controversy over the age at when screening should start, but there is now general consensus to begin at age 40 and repeat annually thereafter. There is some evidence that the repeat interval can be lengthened after age sixty to every two years without increasing mortality from breast cancer.

Screening mammography prior to age 40 is not cost effective because of the lower incidence of breast cancer in this age group and the number of false positive and false negative exams. Some of this is due to increased breast density in the premenopausal woman. However, certain groups of high-risk women that are genetically predisposed to breast cancer may benefit from screening at a younger age. Screening mammography is not completely reliable in finding non-palpable breast cancer. Approximately 10% of palpable breast cancers are not visible on the two-view mammogram. This "false negative" group (patients who actually have cancer that is not detected on the mammogram) tends to have increased breast density that obscures cancer and a large percentage of these cancers are the infiltrating lobular type which grow in a pattern that can prevent mammographic recognition.

The quality of mammography has improved dramatically over the last ten years due to improving technology and regulatory standards imposed upon centers performing mammography. Radiologists performing mammograms are required to read sufficient numbers of films to maintain their skills. For optimal management of small cancers, there needs to be close collaboration between the radiologist, the pathologist, and the surgeon. This has led to the development of centers that are dedicated to breast imaging and breast cancer management.

Mammographic Characteristics of Cancer

Breast cancers are recognized on a mammogram by three distinct findings that are often seen in combination.

- **Calcifications**: There are a number of conditions that can cause calcifications on a mammogram and most are benign. However, when breast cancer has a pre-invasive phase known as ductal carcinoma in situ (DCIS), it often shows up as a cluster of branching linear calcifications, which represent petrified necrotic cellular debris from the DCIS (figure 4). A second type of calcification known as "powdery" calcification is also associated with DCIS. Calcifications can also be seen with the other two mammographic patterns of malignancy, namely architectural distortion and a "stellate" or spiculated mass. Ductal carcinoma in situ accounts for about 15% to 20% of mammographically detected cancer.
- **Stellate or Spiculated Mass**: This is the classic cancer seen on a mammogram. The mammographer recognizes it because of its straight radiating lines away from a central density giving a sunburst or stellate pattern. It is most often associated with "invasive ductal cancer" and when associated with ductal calcifications, it almost always represents a malignancy (figure 5).
- **Architectural Distortions**: Both breasts have similar patterns of fat interspersed with fibrous and glandular tissue giving a characteristic scalloped appearance. When a cancer grows in this matrix, it can disrupt this pattern by "pulling" on the surrounding tissue. This leads to a distortion of the architecture of that breast (different from the opposite breast) producing "straight lines," "funnels" and increased densities (figure 6). This pattern is frequently associated with the "infiltrating lobular" type of breast cancer.

The Work Up

If a patient is sent for mammography, the images are often obtained by a technologist who then shows the films to a radiologist. If the radiologist concludes that the exam is normal, the patient receives a "well" post card and is instructed to return in one year. If it is not normal, then the patient is called to return for a definitive work-up. Approximately 5% to 10% of women are typically asked to return. Mammographic accuracy can be improved by having two independent readings of each screening study. This increases the number of discovered cancers by approximately 20%.

The definitive work up consists of special magnification x-rays known as "mags" that allow for better definition. It also may include image-guided biopsy using either ultrasound or stereotactic x-rays (figure 7). The use of stereotactic localization and biopsy is becoming the standard approach for indeterminate calcifications and small stellate lesions that are not seen with the ultrasound. This method of management has markedly reduced the number of open surgical biopsies for benign lesions (procedures that are expensive and can produce scars).

There are also a number of advantages to having a preoperative needle diagnosis of cancer. The surgeon can use this information to plan the appropriate operation and determine if lymph node sampling is indicated. In addition, with a preoperative diagnosis, the surgeon less frequently needs to do a second operation to clear involved margins or do lymph node sampling.

Digital Mammography and Newer Imaging Techniques

Digitalization of mammographic images is now a reality. This allows for manipulation of the images and may allow for

more accuracy, though this has not been demonstrated to date in a randomized study. The technology allows for image transmission and better storage, which also can be very advantageous. Presently, the cost of digital mammography precludes a rapid conversion from traditional film mammography. This is partly due to the thin profit margins in the area of radiology.

Magnetic resonance imaging (MRI) of the breast is too expensive at this point in time to be used as a screening tool but does have some utility for high-risk women with dense breasts (figure 8). Positron emission tomography (PET scanning) like MRI is also expensive. Present studies are looking at the ability of PET scanning in imaging the axilla for possible tumor extension or nodal involvement.

Film screen mammography as it exists today is a "static technique" that allows the detection of early cancers based on density changes due to cancer or the disruption of the normal surrounding tissue architecture. The term "early cancer" which usually refers to mammographically detected lesions less than 15 mm is a relative term in that these cancers may be five to seven years old from their birth. The future may allow us to develop "dynamic" scanning with labeled or "tagged" antibodies that recognize even smaller cancers. However, while we are waiting for these advancements, we need to continue to refine and promote film screen mammography, a process that prevents breast cancer death in tens of thousands of women each year.

Figures

1. Graph that demonstrates the incidence of breast cancer in the White and African-American populations and mortality related to the disease per 100,000 population from 1973 through 1996.
2. Graph that demonstrates the increase in risk for developing breast cancer and ovarian cancer related to the presence of the BRCA1 and BRCA2 genes.
3. Graph that depicts the cumulative survival rates based on breast cancer tumor size for women between 40 and 70 years of age (Swedish Two-County Trial) (Reproduced with permission – L. Tabar) (1) is ductal carcinoma in situ DCIS; (2) tumor 1 to 9 mm in size; (3) tumor 10 to 14 mm in size; (4) tumor 15 to 19 mm in size; (5) tumor 20 to 29 mm in size; (6) tumor 30 mm or greater in size; (7) tumor 50 mm or greater in size.
4. Mammogram image that shows calcifications in a patient with a malignancy.
5. Mammogram image of a breast carcinoma that demonstrates the stellate or spiculated mass appearance.
6. Mammogram image that shows tissue distortion with straight lines and increased density.
7. Figure of a patient undergoing further work up.
8. Magnetic resonance imaging (MRI) evaluation of a breast carcinoma.

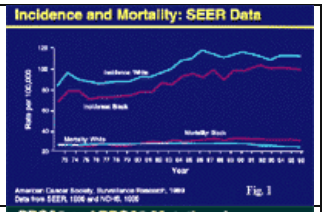
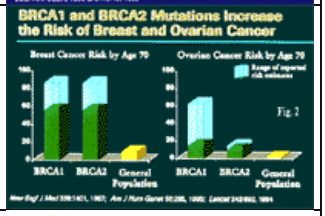
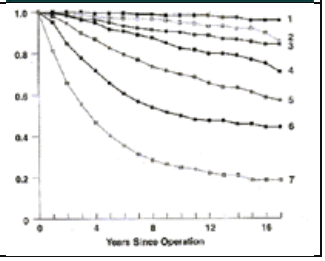
Figure 1	
Figure 2	
Figure 3	

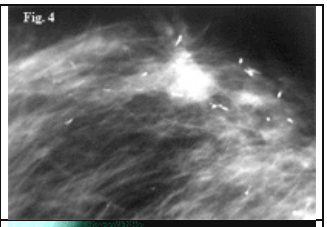
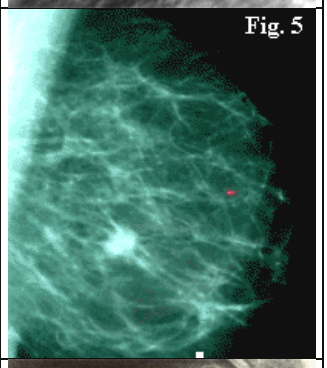
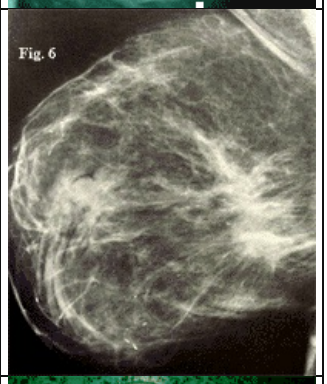
Figure 4	
Figure 5	
Figure 6	
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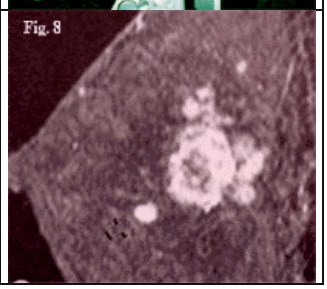
Figure 8	

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About the Author(s)

Dr. John Link is an Internist and Oncologist who is the founding medical director of two Breast Care Centers in California - the Long Beach MemorialCare Breast Center in Long Beach, California (ranked by Self Magazine as one of America's ten best breast cancer centers) and the Orange Coast MemorialCare Breast Center in Fountain Valley, California.

Dr. Link is Board Certified by the American Board of Internal Medicine and the American Board of Oncology. He is also a member of the American Society of Breast Disease and American College of Physicians. Dr. Link is an international lecturer / teacher and researcher. He has presented over 40 major courses on breast cancer management since 1988. He is the principal research investigator for the National Cancer Institute approved National Surgical Adjuvant Breast Project (NSABP) and the NSABP Breast Cancer Prevention Trial.

In addition, He has written numerous scientific papers for peer-review medical journals and has published two books: The Breast Cancer Survival Manual and A Step-by Step Guide for the Woman with Newly Diagnosed Breast Cancer.

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