Are the Breast Cancer Screening Recommendations Clear or Confusing?

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The American public is convinced that cancer screening tests are valuable. Breast cancer screening recommendations have recently received a great deal of attention. Careful review of the available data reveals that combined annual mammography and clinical breast examination is the appropriate breast cancer screening program for most women over the age of 40. However, a small group of women with a genetic susceptibility for breast cancer may benefit from additional imaging. In this article, the criteria for a good screening program are identified.

Although public health officials, physicians, and disease advocacy groups have convinced the American public that cancer-screening tests are valuable, health care providers and the public are inadequately educated as to how these tests should be evaluated and interpreted. Understanding the goals and limitations of cancer-screening programs is important both for health care providers and the targeted population. The best reason for undergoing these periodic exams is to detect cancer in asymptomatic individuals, based on the premise that early cancer detection can change the course of the disease and save lives.[1]

Noninvasive screening tests, such as blood tests and diagnostic imaging, are attractive because they provide a potential benefit and have low associated risks. However, the media often provide overly optimistic expectations for the public based on the results of clinical trials, which cannot be met by the medical community.[2–4] The result has been strong public support for cancer screening and "an environment ripe for the premature diffusion of technologies"[5] and misunderstanding.

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MEDICAL IMAGING AS A CANCER SCREENING TEST

Healthy individuals undergo medical imaging tests to detect potentially serious disease before it is symptomatically evident. These tests must be held to high standards of safety, sensitivity (probability that the test will be positive in a person who has the disease, i.e., few false-negative exams), and specificity (probability that the test will be negative in a patient who does not have the disease, i.e., few false-positive exams). They must be widely available at reasonable cost, have reproducible results, and, most importantly, produce benefits for the screened population.

Obuchowski and co-workers[6] defined 10 criteria that screening tests should meet. They include:

1. The disease has serious consequences.
2. There is a high prevalence of detectable disease before it becomes clinically apparent.
3. There is a low false-positive rate.
4. The test has a high positive-predictive value.
5. The test detects disease at an early stage.
6. The test is associated with a low morbidity.
7. The test is cost effective.
8. There is effective treatment for the disease.
9. The treatment is more effective if instituted before the disease is clinically evident.
10. The treatment has low risks and toxicity.

Health care providers and the public must understand that the perfect cancer-screening test does not exist. Medical imaging tests do not have 100% sensitivity and

100% specificity; all screening tests have false-positive and false-negative results. False-positive results can cause anxiety,[5,7] lost time from work, and potential complications from the resulting tests and biopsies needed to clarify the findings of the erroneous screening exam.

A false-negative study fails to yield the very benefit that a screening test is performed to provide: detection of disease at an early stage when it may be most effectively treated.

Moreover, detecting cancer early does not guarantee that the patient will have a good outcome. Kopans and associates,[8] found that if the cancer has already spread before it is detected by the screening test, then its early detection may not alter the course of the disease. Additionally, some cancers are so slow-growing (e.g., prostate cancer) that they will have no significant effect on the quality of an individual's life, and the treatment for a non–life threatening cancer may be associated with significant morbidity.[8]

BREAST CANCER SCREENING AND MAMMOGRAPHY

Breast cancer screening has received much attention from the news media, women's groups, the American Cancer Society (Atlanta), the National Cancer Institute, and health care providers. Information and disinformation about breast cancer screening is readily available on the Internet. In 2004, the National Institute of Medicine published a report titled *Saving Women's Lives, Strategies for Improving Breast Cancer Detection and Diagnosis* that found the public has "an insatiable appetite for news about breast cancer."[9] The authors indicate that as a result of news reports and advertising, the public has an unrealistic expectation about the effectiveness of breast cancer screening programs and the risk of developing the disease. Patient advocates have effectively focused the public's attention on this disease, but they have often used scare tactics, which distort the truth about a woman's risk of being diagnosed with and dying from breast cancer.[10] It is important that the average American woman's risk of developing breast cancer be put into perspective.

Screening for the Average-Risk, Asymptomatic Woman. A recent editorial noted that cardiovascular disease kills more women than all cancers combined, yet the public seems convinced that breast cancer is the disease most threatening to women.[11] The author stated that 8.6 million American women die of cardiovascular disease annually as compared with 40,000 women who die of breast cancer.[12] A balanced approach to preventive health care is needed so that women understand their actual risk of developing breast cancer, as well as other significant diseases.[10]

According to estimates from the American Cancer Society, 211,300 new cases of breast cancer were diagnosed in 2003, making it the most common cancer (32% of all newly diagnosed malignancies) found in women.[12] However, 25% of cancer deaths in women were from lung cancer and only 15% from breast cancer. Eighty-six percent of women with breast cancer (all stages) survive at least five years, and 97% of patients with local breast cancer (in situ and stage I) survive five years. Only 15% of women who are diagnosed with lung cancer will survive for five years.[12]

To encourage women to comply with mammography screening recommendations in the 1990s, the American Cancer Society advertised that one in nine American women would develop breast cancer in her lifetime. Phillips and colleagues[13] analyzed this claim in 1999, and determined that this statistic represented the cumulative lifetime risk of developing breast cancer for a woman who lived to the age of 85 years. Their analysis found that a woman in her 30s "has a one in 250 chance of developing breast cancer within 10 years," and a woman in her 40s has a risk of one in 77. According to these authors, for any given decade, the risk that the average woman will develop breast cancer never exceeds one in 34. Aging is the average woman's greatest risk factor.

Today, most health care providers and breast cancer advocacy groups agree that asymptomatic women should begin breast cancer screening at age 40. The recommended program consists of an annual clinical breast examination and annual mammography. Additional American Cancer Society recommendations for breast cancer screening include a clinical breast examination at least once every three years between age 20 and 30, and annually after age 40.[14] Breast self-examination is no longer recommended, but the Society does advise that patients should be educated, as early as age 20, on the importance of seeking medical attention for any new breast cancer symptom(s).[15]

Screening mammography has been the subject of much debate. However, it is generally accepted as a good screening test and results in decreased breast cancer mortality.[14,16] According to the Institute of Medicine and the National Research Council (Washington, DC), mammography is the best breast cancer–screening test presently available.[9]

Breast cancer screening, does

have limitations. Unfortunately, public perception that mammography is 100% accurate has only recently begun to change.[17] Many papers in the radiology literature address mammography and its interpretation error rate.[18–20] Both false-negative and false-positive errors are the result of a combination of factors, including patient characteristics such as age, risk, breast density, and tumor growth rates; and provider factors, such as technical limitations, poor positioning, perceptual failures, incorrect interpretation, subtle signs of malignancy, slow-growing malignancies, and quality-assurance issues. Most experts believe that the false-negative rate for mammography is 10% to 30%.[14,21]

Screening for the Asymptomatic Woman Who Is at High Risk. Controversy exists as to whether different strategies should be used for women who are asymptomatic but yet are at "high-risk."[22,23]

A family history of breast cancer increases risk, but not as much as the public believes.[23] Eighty-nine percent of women who develop breast cancer have no family history.[9] Other risks include a previous biopsy with atypical ductal hyperplasia or lobular carcinoma in situ and prior chest irradiation for the treatment of Hodgkin's disease.[23,24]

The two most commonly used models[25] that assess breast cancer risk are those developed by Gail and associates[26] and Claus and co-workers.[27] The National Cancer Institute cautions that these models should probably not be used for patients with a family history suggestive of a genetic predisposition to breast cancer.[25] These models use limited information about family history and therefore underestimate the risk in patients with this genetic susceptibility.

WHO IS AT HIGHEST RISK? HOW ARE THEY IDENTIFIED? The women at greatest risk for breast cancer are the carriers of the BRCA 1 and BRCA 2 breast/ovarian cancer susceptibility genes. These women comprise approximately 5% to 10% of the breast cancer population. The lifetime risk of developing breast cancer in this small population of women may be as high as 80%.[28]

A carefully taken history can help identify these individuals. Although family history is important in identifying this subset of patients, most breast cancers are not genetically predisposed.

The important items to look for in this group are:

- At least two relatives with breast or ovarian cancer
- Breast cancer before age 50 in the affected relative
- Relatives with both breast and ovarian cancer
- At least one relative with both breast and ovarian cancer
- Breast cancer in a male relative
- A family history of breast or ovarian cancer and an Ashkenazi Jewish heritage

Genetic testing for BRCA 1 and BCRA 2 is controversial. It is not clear what women should do with this information. If testing demonstrates that an individual is a carrier of either of these mutations, it may result in greater motivation for more careful surveillance, participation in chemoprevention studies, or possibly prophylactic mastectomy. On the other hand, because of the limited preventive options for these individuals, genetic testing may result in a severe psychological burden, anxiety, and/or depression.[25] The closer the affected relative, the greater the chance of inherited breast cancer, i.e., the risk will be greater for a woman whose mother or sister had breast cancer than if her grandmother had breast cancer.[14]

Once these women are identified, should their screening program be modified? Much has been written about this dilemima, and the debate continues. However, data are accumulating to support the possibility of a different screening program for this group.[22,29,30]

Kriege and colleagues[22] recently published their results of more intense screening in women at increased risk for breast cancer. Their protocol called for clinical breast examination every six months, annual two-view mammography (supplemented by diagnostic views if needed), and contrast-enhanced magnetic resonance imaging (MRI). They found that in the very-high-risk patient population, those with a genetic susceptibility to breast cancer, MRI was able to find more cancers than mammography.[22] In this study, the sensitivity of MRI was 71% as compared with a sensitivity of 40% for mammography. The specificity of MRI was close to 90%, whereas for mammography the specificity was 95%. However, this study had only a 2.9-year follow-up, and it is unclear whether finding these lesions earlier by MRI will decrease mortality in these women. The findings are nonetheless encouraging, since most of the tumors detected were small and node-negative. A smaller study also found MRI to have a higher sensitivity than mammography in patients with a breast cancer susceptibility gene.[31]

It remains to be shown that breast MRI in this population of women meets most, if not all, of the basic criteria for a viable screening test. Obstacles that must be overcome include cost (MRI is very expensive compared with mammography),

reproducibility (MRI acquisition techniques are extremely variable),[25] and long-term research must show an improved outcome for the patient.

CONCLUSION

Not only are many women confused about the recommendations for breast cancer screening, but many health care providers are as well. Mammography is a well-tested screening exam for most women. It is not perfect, but it is the best available for the average woman.

A small group of women exist with a genetic susceptibility for breast cancer for which additional imaging may be beneficial. In these patients, the risk of developing breast cancer is so high that modifications to the standard screening recommendations may be necessary.

Physicians should obtain a complete and detailed family history from every woman to identify patients likely to be carriers of the BRCA 1 or BRCA 2 genes. They should encourage these patients to participate in clinical breast cancer screening trials designed to evaluate the role of MRI in high-risk women. As the results of better-designed studies with larger numbers of women become available, the indications for additional screening in certain targeted populations may become clearer.

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