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Sorting through the recent controversies in breast cancer screening

EDITOR'S NOTE: This commentary, written by members of the Cleveland Clinic Breast Cancer Screening Task Force, was not independently peer-reviewed.

IN NOVEMBER 2009, the US Preventive Services Task Force (USPSTF) announced its new guidelines for breast cancer screening—and created an instant controversy by suggesting that fewer screening tests be done.¹

The November 2009 update recommended that most women wait until age 50 to get their first screening mammogram instead of getting it at age 40, that they get a mammogram every other year instead of every year, and that physicians not teach their patients breast self-examination anymore. However, on December 4, 2009, the USPSTF members voted to modify the recommendation for women under age 50, stating that the decision to start screening mammography every 2 years should be individualized, taking into account the patient's preferences after being apprised of the possible benefits and harms.²

Various professional and advocacy groups have reacted differently to the new guidelines, and as a result, women are unsure about the optimal screening for breast cancer.

NEW GUIDELINES ARE BASED ON TWO STUDIES

The USPSTF commissioned two studies, which it used to formulate the new recommendations.^{3,4} Its goal was to evaluate

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the current evidence for the efficacy of several screening tests and schedules in reducing breast cancer mortality rates.

An updated systematic review

Nelson et al³ performed a systematic review of studies of the benefit and harm of screening with mammography, clinical breast examination, and breast self-examination.

Screening mammography continued to demonstrate a reduction in deaths due to breast cancer. The risk reduction ranged from 14% to 32% in women age 50 to 69. Similarly, it was calculated to reduce the incidence of deaths due to breast cancer by 15% in women age 39 to 49. However, this younger age group has a relatively low incidence of breast cancer, and therefore, according to this analysis, 556 women need to undergo one round of screening to detect one case of invasive breast cancer, and 1,904 women need to be offered screening (over several rounds, which varied by trial) to prevent one breast cancer death.³

Most of the harm of screening in the 39-to-49-year age category was due to false-positive results, which were more common in this group than in older women. The authors calculated that after every round of screening mammography, about 84 of every 1,000 women in the younger age category need additional imaging and about 9 need a biopsy. The issue of overdiagnosis (detection of cancers that would have never been a problem in one's lifetime) was not specifically addressed for this age category, and in different studies, estimates of overdiagnosis rates for all

We still recommend yearly mammograms for most women, starting at age 40

age groups varied widely, from less than 1% to 30%.

Beyond age 70, the authors reported the data insufficient for evaluating the benefit and harm of screening mammography.

Breast self-examination was found to offer no benefit, based largely on two randomized studies, one in St. Petersburg, Russia,⁵ and the other in Shanghai, China,⁶ both places where screening mammography was not routinely offered. These studies and one observational study in the United States⁷ failed to show a reduction in breast cancer mortality rates with breast self-examination.

Clinical breast examination (ie, by a health care provider) lacked sufficient data to draw conclusions.

A study based on statistical models of mammography

Mandelblatt et al⁴ used statistical modeling to estimate the effect of mammographic screening at various ages and at different intervals.

The authors used six statistical models previously shown to give similar qualitative estimates of the contribution of screening in reducing breast cancer mortality rates. They estimated the number of mammograms required relative to the number of cancers detected, the number of breast cancer deaths prevented, and the harms (false-positive mammograms, unnecessary biopsies, and overdiagnosis) incurred with 20 different screening strategies, ie, screening with different starting and stopping ages and at intervals of either 1 or 2 years.

They estimated that screening every other year would achieve most of the benefit of screening every year, with less harm. Looking at the different strategies and models, on average, biennial screening would, by their calculations, achieve about 81% of the mortality reduction achieved with annual screening. Compared with screening women ages 50 to 69 only, extending screening to women age 40 to 49 would reduce the cancer mortality rate by 3% more, while extending it up to age 79 would reduce it by another 7% to 8%.

In terms of harm, the models predicted more false-positive studies if screening were started before age 50 and if it were done annually rather than biennially. They also predicted

that more unnecessary biopsies would be done with annual screening than with screening every 2 years. The models suggested that the risk for overdiagnosis was higher in older age groups because of higher rates of death from causes other than breast cancer, and that the overdiagnosis rate was also somewhat higher with annual than with 2-year screening.

WHAT WOULD LESS SCREENING MEAN?

Our practice has been to initiate annual screening with mammography at age 40 and to continue as long as the patient's life expectancy is at least 10 years.

According to the models used by Mandelblatt et al,⁴ screening 1,000 women every year, starting at age 40 and continuing until age 84, would result in 177 to 227 life-years gained compared with no screening. In contrast, screening only women age 50 to 74 and only every other year (as advocated in the new guidelines) would entail about one-third the number of mammograms but would result in fewer life-years gained per 1,000 women screened: between 96 and 128. If we take the mean of the estimates from the six models, adherence to the new screening guidelines would be estimated to result in about 79 fewer life-years gained for every 1,000 women screened. On the other hand, each woman screened would need to undergo about 25 fewer screening mammograms in her lifetime.⁴

KEY POINTS ABOUT BREAST CANCER SCREENING

Together, these studies demonstrate several points about breast cancer screening.

Importantly, randomized controlled trials and model analyses continue to show that screening mammography reduces the breast cancer mortality rate.

The studies and models also reinforce the concept that those at greatest risk get the most benefit from screening. Because the incidence of breast cancer rises with age, the probability of a true-positive result is higher in women over age 50 than it is in younger women, and, therefore, the screening test performs better.

On the other hand, women at high risk of dying of other causes, such as those over

Randomized trials continue to show that screening mammography reduces the breast cancer mortality rate

age 75, achieve less benefit from screening, as some of the cancers detected in this manner may not contribute to their death even if they are not detected early.

Screening is therefore best targeted at people who are healthy but who are at sufficient risk for the disease in question to justify the screening.

■ CLEVELAND CLINIC'S POSITION

In December 2009, the Cleveland Clinic Breast Cancer Screening Task Force, a multidisciplinary panel of breast cancer experts, breast radiologists, and primary care providers, convened to review the literature and set forth institutional recommendations for breast cancer screening for healthy women. The authors of this paper are members of this task force. Our consensus recommendations:

- We continue to recommend annual mammography for most healthy women over age 40.
- Screening every other year is an option for older postmenopausal women, as they are likely to achieve most of the benefit of annual screening with this schedule.
- We agree with the USPSTF finding that there are insufficient data to provide evidenced-based recommendations regarding the benefits and harms of clinical breast examination. However, breast examination was done as part of the screening in many of the randomized trials of mammography and cannot easily be separated from mammography. Therefore, we believe that careful examination of the breasts remains an important consideration in the general physical examination.
- The USPSTF recommendation not to teach breast self-examination was based on studies that probably do not apply to the US population. Therefore, we continue to recommend that women be familiar with their breasts and report any changes to their physicians.

How we reached these conclusions

The task force discussions focused heavily on at what age mammography should be started and how often it should be done. In addition to an in-depth review of the studies on which

the USPSTF recommendations were based, we considered a review posted on the Society of Breast Imaging (SBI) Web site.⁸

A key point from the SBI's review is that although breast cancer occurs less often in women under age 50, approximately 1 in 69 women are diagnosed with invasive cancer when in their 40s. Some—probably a minority—have a family history of breast cancer and thus warrant earlier screening on that basis.

Breast cancer is, therefore, an important public health concern for women ages 40 to 49. While mammography is an imperfect test, it has a demonstrated ability to find cancers at an earlier stage in this age group. The SBI statement also summarized data suggesting that the 40-to-49-year age group would experience significantly fewer lives saved by screening if the mammography interval were increased from once a year to every other year (ie, by approximately one-half—from 36% of deaths prevented with annual screening to 18% deaths prevented with screening every other year).

Screening every other year is also expected to result in fewer lives saved in women ages 50 to 69 (39% of deaths prevented by biennial screening instead of 44% to 46% with annual screening). However, this proportion of deaths prevented with more frequent (ie, annual) screening is smaller than in the younger age group. Breast cancers that arise before menopause are considered biologically more aggressive, so the longer the interval between screening tests, the lower the likelihood of detecting some of these potentially more lethal cancers.

We believe, for several reasons, that the randomized trials may have underestimated the benefit of mammography. The trials included in the USPSTF studies did not use modern mammographic techniques such as digital mammography. Some of the trials used single-view mammography, which may be less sensitive. Also, the rate of compliance with screening in these randomized trials was only about 70%, which would lead to an underestimation of the number of lives saved with mammography screening. Yet in spite of these limitations, the data continue to show a reduction in breast cancer deaths in all age categories studied.

Patients at highest risk get the most benefit from screening

Other issues the task force considered

Harms of screening are acceptable. We agree that the need for additional imaging or possibly breast biopsy is an acceptable consequence of screening for most women, especially when weighed against the potential benefit of improving survival. Nelson et al³ briefly discussed the risk of inducing other cancers through radiation exposure, and any such risk appears to be low enough that it is overshadowed by the reduction in the breast cancer mortality rate achieved from screening.

The USPSTF studies did not address the issue of cost, which is another potential harm of screening. However, screening mammography is relatively inexpensive compared with other potentially life-saving screening tests.

Our position differs from that of the American College of Physicians (ACP), which has endorsed the USPSTF recommendation for reduced breast cancer screening. The USPSTF has been a leading group in providing practice recommendations based on high-level evidence predominantly from randomized controlled clinical trials, and its recommendations have been consistently followed by the ACP and many of its members,

including Cleveland Clinic physicians. It is, therefore, not without considerable discussion that we have come to our consensus.

Evidence for less screening was not compelling. One of our concerns about the new USPSTF recommendations is that the changes are based largely on a model analysis of the efficiency of different screening strategies rather than on randomized controlled trials comparing different strategies. We did not find this level of present evidence to be sufficiently compelling to make a change in our practice that may result in loss of lives from breast cancer.

Screening guidelines will continue to change over time as technology improves and new data are introduced. In the future, risk-assessment strategies such as incorporating genetic profiles may allow us to use factors more predictive than age to target our screening population.

While we continue to strive for better means of early detection and cancer prevention, the Cleveland Clinic task force is currently recommending yearly screening with mammography and breast examination for most women, starting at age 40. ■

We believe that careful examination of the breasts remains an important consideration in the general physical examination

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