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Screening mammography starting at age 40: Still relevant

SCREENING MAMMOGRAPHY is not a perfect test, but it still plays an important role for women even in their 40s, when the incidence of breast cancer is low but the risk of a tumor being aggressive is especially high.

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■ SCREENING DETECTS CANCER EARLY

The goal of screening mammography is to reduce breast cancer deaths by detecting cancers early, when treatment is more effective and less harmful.

Mammography detects tumors when they are smaller: the median size of breast cancers found with high-quality, two-view screening mammography is 1.0 to 1.5 cm, whereas cancers found by palpation are 2.0 to 2.5 cm.¹ In general, tumors found when they are smaller require less treatment, and patients are more likely to survive.

Moreover, about 10% of invasive cancers smaller than 1 cm have spread to lymph nodes at the time of detection, compared with 35% of those 2 cm in size and 60% of those 4 cm or larger. Women who have a positive lymph node at the time of diagnosis usually undergo more intensive treatment with chemotherapy and more radical surgery than those who do not. The 5-year disease-free survival rate is more than 98% for breast cancer with a tumor smaller than 2 cm that has not spread to lymph nodes (stage I), compared with 86% for stage II disease (tumors 2.1–5 cm or one to three positive axillary lymph nodes).²

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Treating breast cancer early is also less expensive. In a study of women enrolled in a health maintenance organization in Pennsylvania, 14% of those not screened presented with advanced breast cancer (stage III or IV) compared with 2% who had been screened. The cumulative cost of treating advanced breast cancer was two to three times that of treating early breast cancer (stage 0 or I), not accounting for time lost away from work and family, in addition to pain and suffering.³

■ SCREENING SAVES LIVES

Multiple prospective, randomized controlled trials have been conducted to assess whether inviting women between ages 40 and 74 to undergo screening mammography reduces the rate of death from breast cancer.^{4,5} Such trials tend to underestimate the effect of screening because not all women invited to be screened actually *are* screened, and some in the control group may undergo screening on their own.⁶

The Canadian National Breast Screening Study (NBSS) had additional problems that underestimated the benefits of screening. The quality of mammography came under question, and an issue with randomization became evident after the first round of screening, as the group invited to be screened had an excess of women presenting with palpable lumps and advanced breast cancer.⁶⁻⁸ Despite these issues, a meta-analysis of randomized controlled trials of screening mammography, including the NBSS data, found a 15% reduction in deaths.⁹ When the NBSS data were excluded,

The median size of breast cancers found by mammography is 1.0–1.5 cm; by palpation, 2.0–2.5 cm

the reduction was 24%.¹⁰

In 2009, the United States Preventive Services Task Force (USPSTF)¹¹ recommended against mammographic screening for women ages 40 to 49. Using results from trials including the NBSS, they estimated that the number of women needed to be invited to screening to prevent one breast cancer death was:

- 1,904 for ages 39 to 49
- 1,339 for ages 50 to 59
- 377 for ages 60 to 69.

But if the NBSS study were excluded, these results would be 950, 670, and 377, respectively.⁶

In a review on screening mammography, Feig¹² points out that the USPSTF selected the number of women invited to be screened rather than the number that were actually screened to measure the absolute benefit of screening.

Hendrick and Helvie¹³ reported that the number of women who needed to be screened to prevent one cancer death was:

- 746 for ages 40 to 49
- 351 for ages 50 to 59
- 253 for ages 60 to 69.

The benefit of screening, if analyzed by number of life years gained rather than number of deaths prevented, is even more favorable to younger women with longer life expectancy. The number needed to be screened per life year gained is:

- 28 at ages 40 to 49
- 17 at ages 50 to 59
- 16 at ages 60 to 69.¹²

These data provide additional support for screening women starting at age 40.

Observational studies, which provide a better measure of effectiveness because only women who actually undergo routine mammography are compared with those who do not, also support this conclusion. An observational study in Sweden with 20 years of follow-up found that women of all ages who participated in screening had a 44% lower risk of death from breast cancer than with those who were not screened; for women in their 40s, the risk reduction was 48%.¹⁴ Similarly, an observational study conducted in British Columbia¹⁵ found a 40% decrease in deaths in women screened annually between ages 40 and 79, and a 39% decrease in deaths in women first screened between ages 40 and 49.

■ LOW RATE OF FALSE-POSITIVE RESULTS

Like many screening programs, screening mammography does not benefit all women equally.

False-positive results occur, for which women need additional imaging or a biopsy for findings that turn out not to be cancer. But the false-positive rate is not high: for every 1,000 women screened in the United States, 80 to 100 (10% or less) are recalled for additional evaluation, 15 (1.5%) undergo biopsy, and 2 to 5 have a cancer, so only about 1% of the women screened underwent an unnecessary biopsy.¹⁶

False-positive test results can provoke unnecessary anxiety, but evidence indicates that this tends to be a temporary effect, and even women who had a false-positive result tend to support mammography. In a report by Lerman et al,¹⁷ when mood was assessed 3 months after mammography, worry was reported by 26% of women who had had a false-positive report, compared with 9% of women who had had a normal mammogram. Another report addressing the consequences of false-positive mammograms found that although short-term anxiety increased, long-term anxiety did not.¹⁸ In a random telephone survey, 98% of adults who reported having had a false-positive cancer screening result stated that they were nevertheless glad that they had undergone screening.¹⁹

■ OVERDIAGNOSIS OCCURS BUT IS LIKELY UNCOMMON

Overdiagnosis of breast cancer is a possible drawback of screening mammography. Cancers may be detected that would not have become clinically apparent in a person's lifetime²⁰ or have affected ultimate prognosis,¹⁸ and so would not have needed to be treated.

Overdiagnosis from screening mammography usually refers to finding ductal carcinoma in situ (DCIS) on breast biopsy. Because no randomized controlled study has been done in which breast cancer was diagnosed and not treated, evidence of the danger from DCIS comes from retrospective reviews of 130 cases in which excised tissue initially interpreted as benign was actually cancerous. Over 10 to 30 years, 11% to 60% of these patients developed invasive breast cancer in the same quad-

Only about 1% of the women screened underwent an unnecessary biopsy

rant from which tissue had been excised.²¹ This rate of cancer development could lead to underestimation of the invasive potential of DCIS because the patients studied all had low-grade DCIS; further, some of the baseline biopsies involved complete removal of the tumor, thereby preventing the development or progression of cancer.

All DCIS is not the same. An ongoing trial²² found a 5-year recurrence rate of 6.1% after surgery for low-grade or intermediate-grade DCIS, and 15% after surgery for high-grade DCIS. Swedish trials²³ have shown that most women who die of “early” breast cancer have high-grade DCIS. These findings suggest that although screening mammography may result in overdiagnosis and overtreatment of low-grade DCIS, high-grade DCIS can be lethal and should be treated. Thus, overdiagnosis likely represents a small fraction of all breast cancers.

Most important, it is not yet possible to accurately predict the biologic behavior of an individual tumor. Current clinical practice is to treat patients with DCIS similar to the way we treat patients with early-stage breast cancer, as we cannot determine which types of DCIS may remain indolent and which ones may become invasive.

Tumors in younger women tend to grow and spread more quickly

■ **HOW FREQUENTLY SHOULD YOUNGER WOMEN BE SCREENED?**

The frequency of screening mammography has been another area of controversy, but we believe that annual screening offers the greatest benefit, especially for younger women.

The optimum screening frequency depends on how fast breast cancer grows and spreads. Data suggest that tumors in younger women tend to be biologically aggressive and grow and spread more quickly, making the benefit of yearly mammography more dramatic for younger women. A model based on

data from Swedish studies^{24–26} predicted that the mortality reduction from breast cancer in women ages 40 to 49 would be 36% with annual screening, 18% with screening every 2 years, and 4% with screening every 3 years. For women in their 50s, the model estimated a reduction of 46% for yearly mammography, and 39% and 34% for screening every 2 or 3 years, respectively.⁶

In a prospective cohort study of the Breast Cancer Surveillance Consortium,²⁷ in women ages 40 to 49 with extremely dense breasts, screening every 2 years was associated with a higher risk of advanced-stage disease (IIB or higher) and large tumors (> 2 cm) than with annual screening. For women ages 50 to 74, screening every 2 years vs every year did not increase the odds of advanced-stage or larger tumors.

■ **AN INFORMED DECISION**

In agreement with the current recommendations from the American Cancer Society, the American College of Radiology, and the American Congress of Obstetricians and Gynecologists, we support starting breast cancer screening with mammography at age 40.

Not all cancers are visible on mammography (false negatives), as they may be masked by mammographically dense breast tissue. Women should be informed of the importance of seeking medical attention for breast symptoms, even if mammography is normal. We need to inform women of the benefits and risks of screening mammography, including the risk of false-positive results that could lead to additional imaging and anxiety, and the uncertainties related to the potential for overdiagnosis and overtreatment. This information, offered in an easily understandable format, can help the patient make an informed decision regarding screening mammography, based on her values and preferences. ■

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