Screening Mammography Under Age 50

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Mammography is a screening procedure that has decreased the risk of death from breast cancer by 25% to 30%, as shown in 7 randomized studies (TABLE 1). It can detect breast cancer or carcinoma in situ at 5 to 10 mm in diameter. Most physicians cannot reliably detect lesions smaller than 10 mm on physical examination, and patients generally seek medical attention for lesions that are 25 mm or larger.

Of women with known breast cancer who undergo mammography, 80% to 90% have a positive test result. A negative mammogram result does not preclude clinical breast cancer and should not dissuade physicians from biopsy of a palpable abnormality.

The remainder of this article discusses screening mammography only. No controversy exists over diagnostic mammography in any woman or man with a suspicious breast examination finding whether older or younger than 50 years. The most common malpractice suit against primary care physicians is failure to diagnose cancer, and, of these, failure to diagnose breast cancer is most common. A substantially higher proportion of these lawsuits involve women younger than 50 years than what is expected based on their relative incidence of breast cancer.

History of Recommendations

In 1989, after completion of the first 6 randomized mammography trials, the National Cancer Institute (NCI), the American Cancer Society, and other organizations issued joint recommendations for mammography for the ages (40-75 years) included in the trials.

However, later subset analysis suggested the benefit of mammographic early detection of breast cancer mainly accrued to screened patients 50 years and older, for whom breast cancer mortality decreased 25% to 30%. Early meta-analyses and overviews found little decrement in mortality in the 40- to 49-year age group.

In 1992, 2 Canadian trials, designed and powered specifically to evaluate mammography in women aged 40 to 49 years (Canadian 1) and in women aged 50 to 59 years (Canadian 2), reported a statistically nonsignificant excess of breast cancer mortality in the mammography group in women aged 40 to 49 years, and no significant benefit for mammography in women aged 50 to 59 years (relative risk, 0.97). In the 2 Canadian trials, volunteers, in contrast with European trials that screened populations, underwent a breast examination followed by assignment to the next position on a paper randomization log. In women aged 40 to 49 years, 19 cancers developed in the mammography group vs 5 in the clinical group during the first year of the study, an imbalance that raised concern by some that patients with subtle abnormalities on physical examination might have been assigned to the mammography arm.

Furthermore, the breast cancers were smaller in both arms of the first Canadian study (1.6 vs 1.9 cm for mammography and observation, respectively), compared with those in the combined Swedish studies (2.2 vs 2.8 cm). Perhaps self-selected volunteers were more vigilant than women in the population-based Swedish trials. Based only on the expected mortality for the lesion-size distribution observed, we would expect the Canadian study to be negative and the Swedish to be positive.

In 1993, an NCI conference considered the results of all 7 randomized clinical trials reported to date. Results of screening mammography were a 30% reduction in breast cancer mortality in the women 50 years and older who were randomized, a 15% to 17% reduction in breast cancer mortality in women aged 40 to 49 years, and a combined estimate of the benefit for women aged 40 to 49 years that was not statistically significant unless the Canadian volunteer study was excluded.

Reliable meta-analysis requires the assumption that all included studies are sufficiently valid in design and conduct to provide informative data. This assumption has been part of the controversy regarding the Canadian trial since differences in the design and conduct of the study, as well as sampling variability, may have contributed to the variability across studies in the results in the 40- to 49-year-age group.

The scientific aspects of the NCI controversy arose in relation to 2 issues. The first was whether to accept the benefit estimate of 15% to 17% reduction in breast cancer mortality in women aged 40 to 49 years since it did not meet the usual statistical criterion (P<.05) for rejecting the null hypothesis. The second was that the number screened to save 1 life is substantially lower for women 50 years and older (TABLE 2). Based on subset analysis from the 6 initial trials plus the results of the Canadian study, the committee concluded that mammography did not significantly benefit women aged 40 to 49 years. Both the data and the recommendation engendered controversy.

In 1997, new data from the Gothenburg trial demonstrated a significantly de-
creased mortality for women aged 40 to 49 years. Of note, the number of cancer cases in both groups was similar during that study. Investigators had feared that mammography detected a significant number of cancers that never would have become clinically apparent. These data suggest that small tumors detected in the screening mammography group would have become clinically detectable within a few years and were clinically significant.

Recent overviews of the 4 Swedish trials identified a 24% decrease in mortality. A meta-analysis of all published studies showed a nonsignificant 16% decrease in mortality in women aged 40 to 49 years. The difference was 24% and significant if only the population-based studies were included (ie, excluding the Canadian study done with volunteers). Investigators were concerned that this difference could result from mammograms done after the patients reached age 50 years, but the Swedish analysis demonstrated that “almost all of the effect in the 40-44 year age group at randomization was due to screening before the age of 50.”

An NCI consensus conference was convened again, but degenerated this time into what an editorial in Science described as the “NCI brawl,” basically pitting “treating physicians versus epidemiologists.” The competing values were “lives saved versus numbers screened to save one life.”

**Why the Controversy?**

How and why did this issue become so contentious? There are 7 randomized trials (Table 1) and 4 meta-analyses, but more than 30 editorials on mammography screening. Of the 7 randomized trials, 2 used single-view mammography, now generally considered suboptimal, particularly in younger women with relatively dense breasts (the ratio of glandular tissue to fat). Editorial recommendations for screening mammography range from “don’t screen any women” to “screen all beginning at age 40 years” with various positions staked out along this continuum. One of the most conservative positions is that of Wright and Mueller who conclude, “Since the benefit achieved is marginal, the harm caused is substantial, and the costs incurred are enormous, we suggest that public funding for breast cancer screening in any age group is not justifiable.”

A somewhat less conservative view was written by Eddy, who was partially supported by Blue Cross/Blue Shield. He recommended that “women at average risk have breast physical examinations annually after age 40 and mammography every 1 to 2 years starting at age 50. For high risk women mammography can be recommended annually after age 40.” He notes that mammography is very expensive, false-positive rates are high, and that “it is not known how women might respond if actually presented information on the magnitude of the expected benefits, harms and costs.”

Margolese concludes that “women closer to age 50 should be screened,” but recommends starting earlier with women with a family history and with breasts that are hard to examine but easier to view on mammography because of the increased contrast.

Sickles and Kopans, both mammographers, recommend that all women between ages 40 and 49 years should be screened. They conclude that older studies may not be reliable since equipment is now better, dense breasts are less of an issue, and cost is in the acceptable range.

Some editorialists point out that “only” 2% of 40- to 49-year-old US women develop breast cancer during their fifth decade and even fewer (0.3%) died. Others have observed that despite this low-percentage risk, cancer is the major cause of mortality (and breast cancer is the most common cancer) in this age group. Both are correct. Because of the lower prevalence of breast cancer in younger women, an abnormality on a mammogram in a younger woman is more likely to be...
nign. In addition, younger women’s breasts are more dense, decreasing the sensitivity of mammography. In an analysis of cost, more 40- to 49-year-old women need to be screened to save 1 life than 60- to 70-year-old women (Table 2). Discounting for years of life lost (eg, the number of years lost for a patient dying of breast cancer at 45 vs 65 or 70 years) decreases the cost calculated per year of life saved for younger women.

Elmore et al,25 in 1988, described a cohort of 40- to 69-year-old women who had undergone 9762 mammograms.25 The mammograms that were “interpreted as indeterminate, aroused a suspicion of cancer, or prompted recommendations for additional workup in women in whom breast cancer was not diagnosed within the next year” were defined as false-positive results. Many would not consider an indeterminate or suspicious test result as false-positive. When this broad definition was used, 24% had false-positive mammogram results. Consequences of false-positive mammogram results were 539 repeat views, 186 ultrasounds, and 188 biopsy procedures. Repeat views or ultrasounds are noninvasive and can be expensive, but physicians would like to avoid performing inappropriate biopsies. However, in this cohort, 58 cancers were detected mammographically. The number of cancers detected for the number of biopsies performed (the rate of true-positives: 58 / (188 + 58) = 23.6%) for this cohort was thus about 1 in 4, well within the US standard rate of about 1 positive biopsy result for every 5 suspicious lesions. Americans may be unwilling to tolerate the higher incidence of cancer cases to biopsies (1 of 2) found in many European screening programs. Failure to biopsy a lesion with a 30% or 40% likelihood of being cancer is unacceptable in the United States.

A Reasonable Recommendation

Many authors in this controversy have staked out positions based on screening beginning specifically at age 40 vs 50 years, without considering that the risk of breast cancer, cost-effectiveness of mammography, and age are all continuous. Patients in the 40- to 50-year-old range particularly need to be counseled regarding the available results of mammography screening, as young women overestimate their risk of dying of breast cancer in the next decade.26 Those who have substantial risk factors, particularly a family history, and those who are eager for screening could begin regular screening mammography at age 40 or 45 years. Those who have no particular risk factors might begin screening between ages 45 and 50 years.

No controlled clinical trials exist for screening young women who have multiple first-degree relatives developing breast cancer before age 45 years, or those known to carry BRCA1 or BRCA2 mutations in whom the risk of developing breast cancer is estimated to be 30% to 87%.27 Mammography screening beginning about 10 years before the first breast cancer case developed in their family is often recommended despite the lack of data. Ultrasound and magnetic resonance imaging, which both avoid radiation exposure, may prove to be cost-effective in these groups.

Breast cancer mortality is currently falling for the first time in the 6 decades for which statistics are available, probably reflecting the growing acceptance by the US public of mammography screening and use of adjuvant therapy. Mammography screening can be offered to women at higher risk beginning at age 40 years, and to those with no risk factors beginning between 45 and 50 years. Studies to determine the role of earlier screening in women with multiple affected first-degree relatives are needed. Although we favor inclusion of mammography as a covered health benefit so that women and their physicians can make their own decisions, we recommend against using mammography in women aged 40 to 49 years as a quality-of-care indicator for health plans or provider organizations.

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REFERENCES