Mammography Screening: After the Storm, Calls for More Personalized Approaches

By Judy Peres

It was déjà vu all over again.

A body of independent scientists conducted a comprehensive review of the evidence and concluded that the net benefit of screening mammography for women younger than 50 years was too small to justify universal screening. The balance of benefits and harms was close, the U.S. Preventive Services Task Force (USPSTF) said in issuing its revised guidelines, so each woman in her 40s should be helped to decide for herself when to start getting mammograms.

It could have been a replay of the 1997 National Institutes of Health Consensus Development Conference, which came to a similar conclusion. As in 1997, the denunciations of the latest recommendation were swift and loud, and their defense was muted. Back then, National Cancer Institute director Richard Klausner, M.D., asked his National Cancer Advisory Board to re-review the evidence and make its own recommendation. That body produced guidelines—the only official screening guidelines NCI has ever issued—which called for mammograms every 1 or 2 years between ages 40 and 49. Similar recommendations from the American Cancer Society, and later the USPSTF, formed the basis for screening younger women until November 2009, when the task force published its revised recommendations. Now it appears that these recommendations may meet the same fate as those of the consensus conference 12 years ago.

Experts on medical prevention and cancer screening are still trying to understand why the task force recommendations on breast cancer screening have drawn such intense fire. Government officials, advocacy groups, and medical organizations immediately announced that they would ignore the revised guidelines, with the harshest critics accusing the panel of jeopardizing women’s lives.

The USPSTF is an independent panel of experts in prevention and primary care established in 1984. The Agency for Healthcare Research and Quality, part of the U.S. Department of Health and Human Services, appoints task force members. Their mandate is to periodically review the evidence and make recommendations for a wide range of clinical preventive services. In their latest update of the breast cancer screening guidelines (published in the Nov. 17 Annals of Internal Medicine), the task force said women at average risk for breast cancer should usually start getting mammograms at age 50 years and should have them every 2 years through age 74. It gave the recommendation grade B, saying there is “moderate certainty that the net benefit is moderate.” That contrasted with the grade C the panel gave to the recommendation on screening for women in their 40s, which it said reflected “moderate certainty that the net benefit is small.” (A grade C recommendation in USPSTF parlance means that the agency recommends against providing the service routinely, but “there may be considerations that support providing the service in an individual patient.”)

The task force also recommended against physicians’ teaching their patients to perform monthly breast self-exams. That received a D grade, indicating adequate evidence that teaching women to do breast self-exams does not reduce breast cancer mortality, although panel members later explained that this was not intended to stop women from examining their own breasts and reporting anything unusual to their doctors.

The task force made no recommendation on whether women aged 75 years or older should continue to be screened, saying there was insufficient evidence “to assess the additional benefits and harms.” Likewise, it said insufficient evidence existed to recommend clinical breast exams for women who are already getting mammograms, or to recommend digital mammography or magnetic resonance imaging instead of film mammography for routine screening. Each of those three statements received an I grade, meaning that the balance of benefits and harms cannot be determined.

Some of the flak that greeted the new guidelines appeared to have been provoked by the timing of the report. Politicians opposed to health care reform bills now under consideration used the guidelines as evidence that the Obama administration intended to ration care. Supporters of the guidelines pointed out that the task force does not consider costs, so rationing could have nothing to do with it.

On a somewhat more scientific level, critics argued that the evidence showed that screening would avert breast cancer deaths among women younger than 50 years but “just not enough” from a public health point of view. (Among women in their 40s, one breast cancer death would be averted for every 1,904 women screened; and for
those in their 60s, one for every 377 screened.)

Task force supporters shot back that the attackers (such as radiologists) were motivated by financial considerations or were influenced by anecdotal experience rather than scientific evidence.

Despite the many expressions of shock, the recommendations should not have come as a surprise, said Russell Harris, M.D., professor of medicine at the University of North Carolina. The task force started work on them 2 years ago and circulated them widely for peer review, including to advocacy and professional organizations. “It wasn’t a closed group,” said Harris, who was a member of the task force when the discussions were taking place but rotated off before the vote.

Moreover, the recommendations did not differ much from the task force’s last iteration, issued in 2002. At that time the group recommended screening mammograms every year or two for women older than 40 years, but it made clear that the benefit–risk ratio was small for younger women and improved with age. Nevertheless, those recommendations were widely interpreted as endorsing screening women in their 40s.

The task force’s revision rested in part on two new studies: a British trial looking at mammography screening in women aged 40–49 years, which detected only a small mortality benefit, and an analysis of screening schedules conducted by researchers from CISNET (the NCI-funded Cancer Intervention and Surveillance Modeling Network), which found that biennial screening of women aged 50–74 years achieves most of the benefits of annual screening with about half the harms.

Consistent With Biology

Jeanne Mandelblatt, M.D., of Georgetown University Medical Center, lead author of the CISNET report, said that finding—the unanimous result from six independent modeling teams—was consistent with what is now known about the biology of breast cancer. Most women have slow-growing tumors, so there is little loss in benefit if they have mammograms every other year. And for those with fast-growing, aggressive tumors, even annual screening can’t make much of a difference because by the time they’re detected they have already spread. Screening is helpful only for breast cancers that could potentially become lethal but grow slowly enough so that early detection and treatment can change the outcome. On the basis of the evidence from several meta-analyses of the randomized clinical trials of mammography screening, only about 15% of the breast cancers that have the potential to kill are in that middle group.

Most of the criticism was aimed at the recommendation to skip every other year but at the notion that the start of routine screening should be delayed from age 40 to 50. Many experts pointed out that breast cancer mortality has been declining for two decades, and at least some of that improvement is attributable to early detection through mammography screening. A CISNET study published in The New England Journal of Medicine in 2005 found that screening by itself reduced deaths by somewhere between 7% and 23%, or an average of 15%, whereas the average benefit of improved adjuvant therapies was 19%.

As emotions began to calm down, at least some critics and supporters of the new guidelines seemed to be seeking common ground. Members of the task force were at pains to stress that they weren’t suggesting that women in their 40s should never be screened, only that they should be allowed to weigh the benefits and harms and factor in their preferences. Eleven public health groups sent a letter to Congress, which had scheduled hearings, expressing support for the task force. The letter stressed the same point—that the task force “simply recommends...a full discussion about the potential pros and cons of screening.”

At the same time, some opponents conceded that mammography does have important downsides. The Mayo Clinic, for example, rejected the USPSTF guidelines and said it would continue to recommend annual mammograms for all women starting at age 40 years. But Sandhya Pruthi, M.D., director of the breast clinic, also acknowledged, “We do need more time to analyze the [new data]. . . . In the meantime, women are encouraged to meet with their health care providers to ask questions about screening because, indeed, there are some risks as well as benefits, and some limitations.”

All sides agree that, although mammography remains the best breast cancer screening test, it is an imperfect one. The technique flags an enormous number of lesions that turn out not to be cancer, it misses one in five real cancers, and even the most experienced radiologists can disagree on what the images mean. Perhaps the most serious, but least understood, problem with mammography screening is that it finds slow-growing cancers (both invasive and noninvasive) that might never have become clinically significant.

Harris estimated that, of the 1,904 women who the task force said would have to be screened regularly in their 40s to avert one breast cancer death, about half would have at least one false positive, “and about five, I’m guessing, will be diagnosed with the kind of cancer that would never hurt them. They’ll be treated—with surgery, radiation, and chemotherapy—for something that doesn’t need to be treated.”

Many agree that the greatest harm of screening is overdiagnosis—detecting a cancer that would not have been diagnosed in a person’s lifetime without screening—or its frequent consequence, overtreatment. But no one really knows the extent of the problem. A meta-analysis that accompanied the new guidelines estimated the rate of overdiagnosis at between 1% and 10%. Others have put it as high as 52%, while several recent studies estimate that one in three screen-detected cancers represents overdiagnosis.

According to Leslie Laufman, M.D., a member of the NCI’s PDQ Screening and Prevention Editorial Board, “There are many studies showing that mammograms find low-risk, well-behaved cancers preferentially and miss the bad actors preferentially. There’s paper after paper saying mammograms pick up cancers that don’t need to be found.”
In October, an article by Laura Esserman, M.D., of the University of California, San Francisco, lent support to the idea that the biology of breast cancer may limit the utility of screening. Writing in the *Journal of the American Medical Association*, Esserman said overall breast cancer incidence had increased 40% since mammography was introduced, and the incidence of early-stage cancers had nearly doubled. But there was only a 10% drop in aggressive cancers—an indication, she argued, that screening is finding mostly indolent cancers, rather than detecting potentially lethal ones earlier.

Molecular tools such as DNA microarrays and genomewide association studies are making slow progress toward the goal of identifying different subsets of breast cancer so that treatments can be better targeted. Experts now are also calling for better assessment of individual risk to identify groups of women who should be screened or offered chemoprevention. “If you’re in a high-risk group,” said Laufman, “it might make more sense to take a tamoxifen or raloxifene pill once a day [both of which reduce the risk for invasive breast cancer] than to mess with mammograms and recalls and biopsies, and then radiation if they find something precancerous. The downstream risks of radiation therapy are just starting to show up, and they could become epidemic in the next 20 years.”

Ann Partridge, M.D., and Eric Winer, M.D., of the Dana–Farber Cancer Institute said the USPSTF recommendations should be viewed as a step toward more personalized cancer screening. Writing in the Nov. 25 issue of *The New England Journal of Medicine*, they opined that advances in molecular biology are likely to lead to a better understanding of breast cancer risk.

“Our understanding of the molecular basis of breast cancer continues to evolve,” they said, “and we now view it as a family of distinct disease subtypes—which may well require their own screening tools.”