It's Not All About Breast Density: Risk Matters

Breast density is a prickly topic. Data suggest that dense breast tissue, typically defined radiographically as heterogeneously or extremely dense breasts, confers an increased risk for breast cancer and decreases the sensitivity of mammography (1). While the medical community continues to assess optimal methods of managing breast cancer screening in women with dense breasts, legislative changes have brought this issue to the forefront. Since 2009, in response to grassroots advocacy, at least 21 states have enacted legislation mandating that women with mammographically dense breasts receive information about this finding with their mammography results. The language of the laws varies, with some requiring only patient notification and others recommending that women discuss additional imaging with their physicians. At the national level, the Breast Density and Mammography Reporting Act has been proposed and is under review. Currently, however, there is no consensus on the optimal approach to supplemental imaging in women with dense breasts (2). Perhaps because of this uncertainty, many providers, including primary care physicians, are uncomfortable answering patients' questions about breast density (3).

In this issue, a prospective cohort study by Kerlikowske and colleagues advances our knowledge about the association between dense breast tissue and risk for interval breast cancer (4). This study provides us with additional information on which women with dense breasts might benefit from supplemental screening to detect cancer that may have been missed on mammography. The study also examines potential outcomes of 6 strategies (based on breast density alone or in combination with age or 5-year breast cancer risk) to identify women for discussion of supplemental imaging. The investigators used data from the Breast Cancer Surveillance Consortium (BCSC) mammography registries from 2002 to 2011. They defined interval breast cancer as invasive cancer detected within 12 months of a negative screening mammography result and defined a high interval breast cancer rate as more than 1 case per 1000 examinations. This correlates roughly with a sensitivity less than 75%, which is considered the minimal acceptable sensitivity for screening mammography. Breast density was categorized using Breast Imaging Reporting and Data System (BI-RADS) density categories (5), and 5-year breast cancer risk was calculated using the well-validated BCSC calculator.

The study found that approximately half of all women with heterogeneously or extremely dense breasts did not meet the threshold for high rates of interval breast cancer, including all women with a BCSC 5-year risk less than 1.67%. Additional analyses found unacceptably high rates of false-positive results on digital mammography (>120 per 1000 examinations) among women with heterogeneously dense breasts and a 5-year BCSC risk less than 1.67%. Although no specific supplemental screening strategy dominated in its ability to detect additional cancer cases, the approach of screening all women with heterogeneously or extremely dense breasts required 1124 supplemental tests per additional cancer case detected. Taking the results in totality, the authors concluded that not all women with dense breasts were at sufficiently high risk to warrant consideration of supplemental screening.

The medical community continues to debate about which women with dense breasts should have supplemental screening. Data from studies by the American College of Radiology Imaging Network show that supplemental imaging with handheld ultrasonography can increase breast cancer detection by as much as 4.2 cases per 1000 women with dense breasts (6). In these studies, nearly all of the cancer cases detected with supplemental ultrasonography were node-negative invasive cancer, suggesting a potential mortality benefit from early detection.

Although this literature lends support to the use of supplemental imaging, other factors must be considered. First, any strategy recommending supplemental imaging for all women with mammographically dense breasts would affect a large population. More than 40% of women aged 40 to 74 years (an estimated 27.6 million in the United States) have heterogeneous or extremely dense breasts (7). Second, supplemental imaging for this population would substantially increase costs while producing only small benefits. Specifically, annual supplemental screening with ultrasonography in women aged 40 to 74 years with heterogeneously or extremely dense breasts would avert 0.43 cancer death, result in 1219 additional biopsies, and cost an additional $2 210 000 per 1000 women screened (8). Third, the evidence base is limited by the lack of randomized, controlled trials or studies that included a control group. As a result, there are no data on long-term outcomes, such as breast cancer–related mortality. Fourth, measurement of breast density varies substantially because radiologists currently estimate it on the basis of the amount of fibroglandular tissue seen (2). In addition, a recent change to BI-RADS (9) could substantially increase the proportion of women with dense breasts. Fifth, we do not know which supplemental screening strategy would identify the highest proportion of clinically significant breast cancer cases, maintain acceptable rates of false-positive results, and be affordable. Will emerging imaging methods, such as tomosynthesis, FAST magnetic resonance imaging, and dual-energy contrast-enhanced digital mammography, be the preferred methods of imaging for certain women? Sixth, the appropriate frequency for supplemental screening is unclear. One study examining annual supplemental ultrasonography showed persistent increases in rates of detection over 3 years, but at a high cost (10). Finally, except in a few states, supplemental screening is not routinely covered by insurance. In the context of these limitations and unanswered questions, recommending additional imaging for all

women with dense breasts may not be the appropriate approach.

Kerlikowske and colleagues' study provides compelling evidence that breast density should not be the sole criterion to guide decisions about supplemental breast cancer screening. This finding suggests that federal legislation on management of screening in women with dense breasts is premature. If enacted, such legislation would require significant additional breast cancer screening resources for a large portion of the screening population, with high costs and unclear long-term benefit. Incorporating a risk assessment, such as the BCSC 5-year risk, into the mammography report in addition to breast density information might help clarify risk and improve physicians' ability to effectively counsel patients on appropriateness of supplemental screening. In particular, this may assist primary care providers, who are currently ill-prepared to discuss breast density with their patients, even in states that have enacted legislation (3). Given the lack of scientific consensus, resources targeted for breast density legislation would be better devoted toward more accurate identification of women at high risk for interval breast cancer, research on optimal use of imaging methods, reduction of disparities in screening and early detection, and training of front-line primary care providers on breast cancer risk assessment.

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