Integrating Tools for Breast Cancer Risk Assessment, Risk Reduction, and Early Detection

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In 2010, it is projected that there will be 207,090 diagnoses and 39,840 deaths from breast cancer among women in the United States. Approximately 10,300 will be diagnosed before the age of 40 (1), the age when the American Cancer Society (2) recommends mammography screening for average risk women, and approximately 45,900 will be diagnosed before age 50, the age of screening initiation for average risk women recommended by the U.S. Preventive Services Task Force (3). Although breast cancer risk assessment is particularly critical for younger women who would not otherwise be offered screening mammography, it is also important for older women at increased risk for whom additional interventions may be appropriate.

Interventions offered to women at increased risk of breast cancer include chemoprevention with tamoxifen or raloxifene, magnetic resonance imaging (MRI) screening as an adjunct to mammography, genetic counseling, and among women with BRCA1 and BRCA2 mutations, screening beginning at age 30 (4), as well as surgical options including prophylactic mastectomy and oophorectomy (4-6). Women with a 5-year projected breast cancer risk of ≥1.66 according to the National Cancer Institute Breast Cancer Risk Assessment Tool developed from the Gail model or women with lobular carcinoma in situ may be offered tamoxifen or raloxifene for 5 to 10 years to reduce their risk of estrogen receptor-positive invasive breast cancer (6). Clinical trials demonstrating the efficacy of tamoxifen and raloxifene for breast cancer risk reduction used a variety of eligibility criteria (4); some included women at average risk whereas others included only women at high risk based on family history, with consistent evidence of benefit. Based on the balance between clinical benefits and side effects, tamoxifen is generally recommended for younger women and raloxifene for older women. Both medications are contraindicated for women with specific clinical conditions (prior history of deep vein thrombosis, pulmonary embolus, stroke, or transient ischemic attack; ref. 6).

In 2006, the American Cancer Society (ACS) recommended that annual MRI screening be used as an adjunct to mammography screening among women with a known BRCA mutation, first-degree relatives of BRCA carriers who have not been tested, and women with a lifetime risk of breast cancer of ~20% to 25% or greater as defined by models that are largely dependent on complete, multigenerational family histories on the maternal and paternal side, such as the BRACAPRO, Claus, and Tyrer-Cuzick models (4). Unlike the trials of tamoxifen and raloxifene chemoprevention, clinical trials documenting the increased sensitivity of MRI screening compared with mammography for women at high risk included only women with a documented BRCA1 or BRCA2 mutation or a very strong family history of breast cancer; a few also included women with a personal history of breast cancer. ACS guidelines also recommend annual MRI screening for women who have had radiation therapy to the chest as well as a limited number of other rare genetic conditions (4). The Gail model was not recommended for risk assessment for MRI screening in the ACS guideline because it does not incorporate family history of breast or ovarian cancer in second-degree relatives (including maternal or paternal aunts, uncles, nieces, nephews, grandparents, and grandchildren).

Using the Gail model and data from the National Health Interview survey, Graubard et al., in this issue, estimate that ~1% of women ages 35 to 84 in the U.S. population have a 20% or greater lifetime risk of breast cancer and infer that they are eligible for MRI screening based on the ACS based on the ACS guidelines. They note that the Gail model has been well-validated at the population level and the proportion of women identified as having >20% lifetime risk is generally as high or higher than the proportion predicted by the BRACAPRO and Claus models. However, they do not acknowledge the important limitation that the Gail model does not detect women who are at increased risk due to family history in second-degree relatives, likely the majority of women whose family history is suggestive of being a mutation carrier. In the general population, ~6% of women have a first-degree relative with breast cancer, whereas 13% have one or more second-degree relatives with breast cancer (7). Among women diagnosed with breast cancer under age 40, 314 (50%) had family members with breast and/or ovarian cancer; 99 among first-degree relatives and 209 among second-degree relatives only (8). In addition to not identifying many women likely to benefit from MRI screening, the Gail model will identify some...
women who are unlikely to benefit based on current evidence (those with a >20% lifetime probability of breast cancer based on factors other than family history). The ACS concluded that there was insufficient evidence to recommend for or against MRI as an adjunct to mammography in women with a >20% lifetime risk based on factors other than familial risk or therapeutic radiation exposure for childhood cancer.

Breast cancer risk assessment and available interventions for prevention and early detection among women at increased risk seem to be underutilized in the U.S. population. A survey of a nationally representative sample of 351 internists, family practitioners, and obstetrician-gynecologists conducted in 2002 to 2004 found that although 88% reported discussing breast cancer risk at least once during the previous 12 months, only 48% had ordered or referred a patient for BRCA1/2 testing, and only 18% had used a software program to calculate breast cancer risk (9). Other studies have shown low use of routine mammography (10), low uptake of tamoxifen for primary prevention (11), low rates of BRCA testing among eligible women (12, 13), and delays in breast cancer diagnosis due to underuse of genetic testing and breast imaging among women under 40 years of age (8). Breast cancer risk assessment, genetic testing, and other interventions are utilized even less by racial and ethnic minority women, low-income, and uninsured women (12, 13), likely contributing to higher rates of late stage diagnosis (12, 13).

The lack of a single, simple, and accessible data collection tool that can produce risk estimates used in various guidelines might hinder the widespread adoption of breast cancer risk assessment in primary care settings. As scientific knowledge of how to identify women at increased risk of breast cancer and technology to identify premalignant and malignant disease earlier in the disease process, tools for risk assessment need to be updated, adapted, and used to benefit the largest number of women. A recent study showed 3- to 4-fold increased risk of breast cancer among women with high BIRADS breast density scores (14), suggesting that breast density may be incorporated in breast cancer risk assessment and guidelines in the future. Self-administered questionnaires that gather family history and personal risk information using a scannable form or a tablet computer system could be used to generate risk estimates and recommendations for genetic testing, chemoprevention, and MRI screening based on multiple models and guidelines (15, 16). In addition to creating tools that will allow clinicians to generate risk estimates for multiple purposes, increased efforts are needed to encourage healthcare providers to use them and ensure that all women have access to these potentially life-saving interventions.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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References
