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Breast Cancer Screening in Women at Higher-Than-Average Risk: Recommendations From the ACR

SA-CME

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Abstract

Early detection decreases breast cancer mortality. The ACR recommends annual mammographic screening beginning at age 40 for women of average risk. Higher-risk women should start mammographic screening earlier and may benefit from supplemental screening modalities. For women with genetics-based increased risk (and their untested first-degree relatives), with a calculated lifetime risk of 20% or more or a history of chest or mantle radiation therapy at a young age, supplemental screening with contrast-enhanced breast MRI is recommended. Breast MRI is also recommended for women with personal histories of breast cancer and dense tissue, or those diagnosed by age 50. Others with histories of breast cancer and those with atypia at biopsy should consider additional surveillance with MRI, especially if other risk factors are present. Ultrasound can be considered for those who qualify for but cannot undergo MRI. All women, especially black women and those of Ashkenazi Jewish descent, should be evaluated for breast cancer risk no later than age 30, so that those at higher risk can be identified and can benefit from supplemental screening.

Key Words: Breast cancer screening, breast cancer, higher risk populations, breast MRI, digital breast tomosynthesis, breast cancer risk assessment

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INTRODUCTION

Early detection decreases mortality for women with breast cancer [1-3]. The ACR currently recommends annual mammographic screening beginning at age 40 for women at average risk for breast cancer, on the basis of extensive literature review [4]. Women with additional risk factors placing them at higher-than-average risk for developing breast cancer need further consideration for earlier and/or more intensive screening [5]. These women typically have, at age < 40 years, risk equivalent to or higher than that of an average-risk woman at age 40.

Breast imaging experts from the ACR Commission on Breast Imaging have reviewed a wide body of literature regarding the screening of higher-risk women. Our analysis again includes consideration of the ACR Appropriateness

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Criteria, which use robust strength-of-evidence methodology accepted by the National Guidelines Clearinghouse [6,7]. Our recommendations for women in the higher-risk population are based on the latest data available regarding the use of MRI, ultrasound, molecular breast imaging (MBI), and digital breast tomosynthesis (DBT) in addition to digital mammography (DM).

POPULATION SUBGROUPS AT HIGHER RISK

There are several factors that increase a woman's risk for breast cancer. Known genetic predisposition is found in about 5% to 10% of breast cancers [8], with the *BRCA1* or *BRCA2* mutation the most widely recognized [9]. The lifetime risk for breast cancer is 50% to 85% among *BRCA1* carriers and approximately 45% among *BRCA2* carriers [10,11]. Women of Ashkenazi Jewish descent are known to be at high risk for the *BRCA* mutation, although they may also have higher rates for other actionable mutations [12]. Other less common gene mutations include *TP53* and *CHEK2* (Li-Fraumeni syndrome), *PTEN* (Cowden and Bannayan-Riley-Ruvalcaba syndromes), *CDH1* (hereditary diffuse gastric cancer), *STK11* (Peutz-Jeghers syndrome), *PALB2* (interacts with *BRCA2*), and *ATM* (ataxia-telangiectasia) genes.

Women with strong family histories are at higher risk, even in the absence of known genetic mutations. The number of family members with breast cancer, especially first-degree relatives, and their age at diagnosis are important considerations that add complexity to the assessment (see "Models for Risk Assessment" later in this article).

Women treated with chest or mantle radiation therapy at a young age, such as those with Hodgkin lymphoma, are at increased risk for developing breast cancer, starting approximately 8 years after the completion of radiation treatment [13,14]. The cumulative risk for a Hodgkin lymphoma survivor treated at age 25 will be 20% to 25% by age 45 [15,16]. This is similar to *BRCA1/2* carriers, whose cumulative risk by age 40 is 15% to 18% [17]. Recipients of $\geq$20 Gy and those treated at younger ages (first and second decades of life) are at greatest risk. Any woman who has received a cumulative dose of 10 Gy or more before age 30 is considered high risk [18].

Women with personal histories of breast cancer are at risk for recurrence or a second breast cancer. A meta-analysis of 10,801 women treated with breast-conserving therapy found a 10-year recurrence rate of 19.3% and a 15-year cancer death rate of 21.4% [19]. The risk for contralateral cancer is 0.5% to 1% per year during the 10 years after diagnosis [20]. Although hormone therapy and/or chemotherapy lowers this risk, women diagnosed with early estrogen receptor–positive cancers remain at increased risk for future cancer (approximately 10% and 20% at 5- and 10-year follow-up, respectively) [21-24]. Age at diagnosis matters. Risk analysis shows that all women diagnosed at or before age 50 and treated with breast-conserving therapy have a 20% or higher lifetime risk for a new breast cancer [25].

Women with lobular neoplasia—atypical lobular hyperplasia or lobular carcinoma in situ (LCIS)—have a lifetime risk of 10% to 20% [26]. For women with LCIS at biopsy, breast cancer risk is bilateral, and most cancers occur more than 15 years after the diagnosis. Atypical ductal hyperplasia (ADH) confers increased risk but to a lesser degree than LCIS. At a median follow-up of 17 years, the relative risk for invasive cancer is 4- to 5-fold for women with ADH and 6- to 10-fold for women with LCIS [27]. Recent work shows the cumulative risk for invasive cancer 10 years after a diagnosis of ADH was 2.6 times higher than without ADH [28].

White and black women have the highest incidence rates of breast cancer of any group, and their occurrence rates are now similar [29]; however, a meta-analysis found that black women were 19% more likely to die of their disease [30]. Recent data from the American Cancer Society show that non-Hispanic black women have death rates 39% higher than non-Hispanic whites [31]. Reasons may include access to mammography, health care delivery patterns, and tumor biology [32]. Black women experience delays in diagnosis and treatment initiation, which negatively affect survival [33-36]. Although stage at diagnosis, tumor characteristics, and body mass index contribute to racial differences in survival, disparities persist after accounting for those factors [37]. Black women are less likely to be diagnosed with stage I cancer but are twice as likely to die of early breast cancers [38]. This difference may be attributed to the higher incidence of triple-negative (estrogen receptor, progesterone receptor, and Her2 receptor negative) breast cancer among black women. In fact, intrinsic differences in tumor aggressiveness may exist [38]. Recent data show a 2-fold higher population-based incidence rate of triple-negative breast cancer in African American women compared with white American women in all age categories [39-41]. Among 46,276 women, *BRCA1* and *BRCA2* mutation prevalence, respectively, was 10.2% and 5.7% with African ancestry, compared with 6.9%