Re: Magnetic Resonance Imaging and Mammography in Women With a Hereditary Risk of Breast Cancer

In a recent report, Stoutjesdijk et al. (1) determined that the operating characteristics of magnetic resonance imaging (MRI) were superior to mammography in a cohort of women, predominantly less than 50 years of age, who were at high risk for breast cancer. Similarly, other studies have found that mammography is a suboptimal screening method in BRCA1/2 mutation carriers (2,3) and that MRI may be superior (4,5).

We examined the sensitivity of mammography in a retrospective cohort of Ashkenazi Jewish women who were diagnosed with primary invasive breast cancer at age less than 65 years at one institution in Montreal, Canada, between 1980 and 1995 and who were tested for the three Ashkenazi Jewish founder mutations in BRCA1/2. Details of the mammogram performed before surgery were obtained by chart review by two physicians who were blinded to the BRCA1/2 status of the patients. We used Fisher’s exact test and the Mann–Whitney rank-sum test to assess the statistical significance of our results.

Mammography reports were available for 161 patients. Nineteen and four patients had mutations in BRCA1 or BRCA2, respectively. BRCA1/2 mutation carriers (hereafter “BRCA1/2 carriers”) were younger (median age, 45.8 years versus 54.3 years; P = .02) and had larger tumors at diagnosis (median tumor size, 1.9 cm versus 1.4 cm; P = .05) than noncarriers, but there was no difference in the median interval between mammography and the surgical diagnosis of breast cancer between the two groups (13 versus 11 days for BRCA1/2 carriers and noncarriers, respectively; P = .99). Suspicious lesions were found in 15 (65.2%) of 23 of the BRCA1/2 carriers and in 119 (86.2%) of 138 of the noncarriers (P = .03). We stratified the data by tumor size (≤2 cm versus >2 cm) or age at diagnosis (<50 years versus >50 years). When BRCA1/2 carriers were compared with noncarriers, there was no statistically significant difference in the number of detectable cancers if the cancers were greater than 2 cm (P = .65) or the patients were greater than 50 years of age (P = .53). However, breast cancers less than or equal to 2 cm in size occurring in BRCA1/2 carriers (median cancer size, 1.3 cm) were statistically significantly less likely to be detectable than similar-sized cancers in noncarriers (median cancer size, 1.2 cm) (six [46%] of 13 versus 96 [89%] of 108; P < .001). In women diagnosed at age 50 years or less with breast cancers less than or equal to 2 cm in size, only two (25%) of eight breast cancers were detected in BRCA1 mutation carriers compared with 27 (77%) of 35 in noncarriers (P = .009). Although it is uncertain why breast cancers occurring in BRCA1/2 carriers were less detectable by mammography than those occurring in noncarriers, one likely explanation is that the smooth, noninfiltrative edge of many BRCA1/2-related breast cancers (6) reduces their mammographic detectability. Of interest, in one study of symptomatic women who underwent mammography, medullary breast cancers were overrepresented in the false-negative group (5.5%) when compared with the true-positive group (0.8%) (7). Other possible explanations include a deficit of ductal carcinoma in situ (6) (which could be associated with less microcalcification surrounding BRCA1-related cancers) or increased mammographic density (2).

Recommendations regarding the use of mammography in BRCA1/2 carriers have not been based on clinical studies. Our data support the emerging evidence (1–5) that mammography is insensitive in detecting invasive breast cancer in BRCA1/2 carriers. Furthermore, such data suggest that, for BRCA1/2 carriers, alternative forms of early detection and an increased focus on prevention are likely to be more beneficial than a reliance on mammography as an early diagnostic tool.

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We thank Dr. Goffin et al. for their contribution. Their work and several recent studies (1–4) strongly suggest that mammography is not the best modality to screen BRCA1/2 carriers and other women with an increased hereditary risk of breast cancer. Although this may be so, screening by means of magnetic resonance imaging (MRI) still has to prove its merit in prospective multicenter studies. Furthermore, no direct link between MRI screening and decreased risk of dying of breast cancer has been made.

Regarding Goffin et al.’s suggested reasons for the decreased mammographic sensitivity in BRCA1/2 carriers, we would like to make two comments. First, parenchymal density is usually higher for BRCA1/2 carriers than for noncarriers in a regular screening program, who are mostly age 50 years and older. We agree with Goffin et al. that this may be part of the reason why mammography performs rather badly on BRCA1/2 carriers. Second, we would also like to point out that in our study (2) malignancies were missed, even on mammograms of women with low or normal parenchymal density. Low mammographic density does not equal adequate sensitivity.

The sensitivity of MRI of the breast may be reduced for invasive lobular carcinoma and well-differentiated ductal carcinoma in situ. However, invasive lobular carcinoma is probably even more difficult to detect by mammography, and, therefore, MRI may still be the best option (5). Ductal carcinoma in situ without an invasive component is probably found less frequently in BRCA1/2 carriers than in noncarriers, perhaps because of fast progression to invasive ductal carcinoma. In light of the suspected susceptibility to radiation-induced breast cancer in BRCA1/2 carriers, and if a considerable underrepresentation of well-differentiated ductal carcinoma in situ in screening examinations can be confirmed, screening by mammography should probably be replaced with screening by MRI for these women.

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