Utilization of Breast Cancer Screening in a Clinically Based Sample of Women after BRCA1/2 Testing

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Abstract
We conducted a prospective, observational study to determine breast cancer screening practices among self-referred high-risk women who pursued genetic testing for BRCA1 and BRCA2 mutations. Of the 107 unaffected women included in this study, 41 were BRCA1/2 carriers and 66 women tested negative for a mutation previously identified in their family. All of the women underwent comprehensive pre- and posttest genetic counseling, and completed baseline and 12-month follow-up telephone interviews. The baseline (pretest) interview assessed potential predictors of mammography use, including demographics and psychosocial variables. During the year after the receipt of BRCA1/2 test results, 47% of the noncarriers and 59% of the carriers reported that they had had a mammogram \(\chi^2(1, n=107)=3.13; P=0.01\). Only 39% of carriers ages 25–39 reported having a mammogram, versus 74% of carriers age \(\geq 40\) \(\chi^2(1, n=41)=5.10; P=0.02\). Among noncarriers ages 50 and older, 83% had an annual mammogram. Factors independently associated with mammography use included age \((< 40, \geq 40); \text{odds ratio}, 7.5; \text{confidence interval}, 2.6–21.5\) and test result \((\text{odds ratio}, 4.6; \text{confidence interval}, 1.1–18.7\). The effects of perceived likelihood of having a BRCA1/2 gene alteration and the interaction between test result and perceived likelihood were not significant. As expected, most carriers (95%) and noncarriers (77%) obtained a clinical breast exam within the year after the receipt of test results. These data suggest that in carriers, overall, the use of breast cancer screening including mammography is good, although there was a relatively low uptake rate of mammography in younger carriers. Noncarriers had very good adherence to general population screening guidelines.

Introduction
Since the cloning of BRCA1 and BRCA2 in the mid-1990s, genetic testing for breast cancer susceptibility has become increasingly available in both research and clinical settings. One of the most important motivations for pursuing BRCA1/2 testing is to gain risk information to guide medical management decisions (1). Therefore, it has been widely assumed that positive BRCA1/2 test results will encourage mutation carriers to engage in protective behaviors in light of the very high risks they face for breast and ovarian cancer. Breast cancer risk management options include close surveillance with or without the use of chemoprevention or prophylactic surgery (2). However, data regarding the efficacy of tamoxifen in carriers is limited because the number of identified BRCA1/2 carriers enrolled in the largest chemoprevention trial to date [National Surgical Adjuvant Breast and Bowel Project (NSABP-P1)] was extremely low (3) and is likely to be similarly low for the STAR (Study of Tamoxifen and Raloxifene) trial, because the latter is open only to postmenopausal women (4). In addition, although many women contemplate having prophylactic mastectomies, the actual uptake of this procedure after obtaining BRCA1/2-positive results appears to be relatively low, at least in the year immediately after receipt of positive results (5, 6). Thus, in the alternative, it is important to determine carriers’ utilization of breast cancer screening, particularly mammography.

A study of families in a hereditary cancer registry reported that BRCA1/2 carriers had significantly higher rates of mammography compared with noncarriers 1 year after obtaining test results (68 versus 44%), although overall rates of mammography adherence did not change from baseline among carriers (5). Data from 216 high-risk women from our cohort of self-referred women indicate that, even for women over age 50, rates of mammography utilization before BRCA1/2 testing were suboptimal, ranging from 53 to 69% (7). Although these rates are roughly comparable with those observed in the registry study, Scheuer et al. (6) found higher rates of mammography in carriers at baseline, with an overall increase noted after testing. However, that study did not examine the impact of test results on screening behavior. Thus, the present report provides the first available data on utilization of breast cancer screening and predictors of mammography use after the receipt of positive and true negative BRCA1/2 results among women who self-referred for testing.

We hypothesized that positive test results would most significantly increase utilization among carriers under age 50, and especially those under age 40. These younger women may...
have been waiting for confirmation of their risk status before initiating routine screening via mammography.

Materials and Methods

Participants

Details of study procedures and participation rates have been described elsewhere (8, 9). Briefly, participants were women who self-referred for genetic counseling to the Lombardi Cancer Center’s Cancer Assessment and Risk Evaluation Program from 1995 through 2000. To be eligible for the present analysis, participants had to be women ≥25 years old with no history of cancer or prophylactic mastectomy. Only women who received definitive BRCA1 or BRCA2 results were included (i.e., “carriers,” who tested positive for a deleterious mutation, and “noncarriers,” who tested negative for a mutation identified in their family). Three women were excluded because they developed breast cancer (n = 1) or obtained a prophylactic mastectomy within the study period (n = 2). Of 135 otherwise eligible women, 28 (21%) did not complete the 12-month interview. Thus, 107 women were included in this analysis: 41 BRCA1/2 carriers and 66 noncarriers (i.e., with “true negative” results).

Procedures

After obtaining written informed consent, free BRCA1/2 testing through Clinical Laboratory Improvement Amendments approved labs was performed in conjunction with comprehensive pre- and posttest genetic counseling. Carriers were counseled that their lifetime risk of breast cancer was between 55–85%, with a significant proportion of risk occurring before age 50 (10, 11), and age-appropriate screening recommendations were provided (adapted from Burke et al.; Ref. 2). We recommended monthly breast self-exams, CBEs 2–4 times per year, and a baseline mammogram at age 25, with the interval of regular screening to be determined by the patient and her doctor. Annual mammograms commencing by age 35 were recommended. The potential benefits and risks of tamoxifen and raloxifene were reviewed, and women were informed about available clinical trials using these medications. The option of prophylactic mastectomy was also discussed, although data regarding its risk-reducing potential specifically in carriers (>90%) was not published until 2001 (12). With respect to noncarriers, whose breast cancer risk was reduced to the level observed in the general population, they were instructed to have mammograms every 1–2 years between ages 40 and 50, and annually thereafter (13). All of the participants received a letter summarizing their test results, guidelines for cancer screening, and options for risk reduction.

Measures

Predictor Variables. Potential predictors of mammography use were assessed before genetic counseling and testing via telephone interview. These measures included: (a) sociodemographics, for which age, race, marital status, education, and income were assessed; (b) perceived risk, for which the woman’s perceived likelihood of having a BRCA1/2 mutation was assessed (likelihood was rated as “not at all likely, somewhat likely, very likely, definitively”; Ref. 14); and (c) cancer-specific distress. For the latter, we used the total score from the Impact of Event Scale to assess the degree of “intrusion” and “avoidance” that individuals experienced on learning their BRCA1/2 status (15).

Utilization of Screening. One, 6, and 12 months after receiving test results, women were asked via telephone interviews whether they had undergone any prophylactic surgical procedures, and if not, whether and when they had obtained a CBE1 and mammogram. We also measured BSE practices. However, because of limited data regarding its efficacy and difficulty in interpreting reports of excessive BSE, we chose not to include BSE in these analyses. Twelve-month interviews were completed in early 2001.

Results

Sample Characteristics. There were a total of 135 eligible women, of whom 28 did not complete the 12-month follow-up interview. Of the 107 participants, 97% were Caucasian, 92% had at least some college education, and the average age was 43 ± 12 years. The 28 women lost to follow-up were more likely to be age 40 and older [χ2 (1, n = 22) = 5.4; P = 0.02] and to have received negative test results [χ2 (1, n = 23) = 4.1; P = 0.04]. There were no significant differences between carriers and noncarriers in demographic factors, psychosocial variables, or baseline screening practices.

Uptake of CBEs. The test result was a significant predictor of whether women obtained a CBE within the year after the receipt of their BRCA1/2 test results. Of the 41 carriers, 39 (95%) had obtained at least one CBE and, among the 66 true negatives, 51 (77%) had obtained a CBE [χ2 (1, n = 107) = 6.0; P = 0.01]. Because of the small number of women who did not obtain a CBE, multivariate modeling was not performed.

Mammography Utilization. Sixty-five percent of women reported having obtained a mammogram during the year before genetic testing. Overall, the proportion of participants reporting mammograms during the year after the receipt of BRCA1/2 test results was 47% for noncarriers and 59% for carriers [χ2 (1, n = 107) = 1.35; P = 0.24]. Because annual mammography is not explicitly recommended for carriers under age 35, we looked at whether testing led to the receipt of a baseline mammogram among women under age 35. Among women 25–35 years of age (n = 30), only 10 (33%) had never had a mammogram before testing, and none of these women obtained a mammogram in the year after receiving test results, although only 3 tested positive. Of the 20 women under age 35 who had previously undergone mammography, 20% of the true negatives (2 of 10) and 40% of the positives had another mammogram within the year after test results were obtained.

Predictors of Mammography Utilization. Mammography rates by age and carrier status are shown in Fig. 1. Only 39% of carriers ages 25–39 (7 of 18) reported having a mammogram, as compared with 17 (74%) of 23 of carriers ages 40 and older [χ2 (1, n = 41) = 5.10; P = 0.02]. With respect to noncarriers, surprisingly, 23% of women under age 40 (7/31) had a mammogram within 1 year after disclosure, which suggests that these women may not have felt reassured about their breast cancer risk. Among noncarriers ages 40–49, the uptake of mammography 1 year after genetic testing was 53% (9/17). However, the other 8 women had obtained a mammogram within the year before study entry, so they were also adherent to recommendations. In noncarriers ≥50 years old, 83% (15/18) had an annual mammogram, consistent with recommendations.

Among the other predictors examined, only precounseling perception of the likelihood of having a mutation was margin-

1 The abbreviations used are: CBE, clinical breast exam; BSE, breast self-examination; OR, odds ratio; CI, confidence interval.
examined in a logistic regression model. Only age (status, and perceived likelihood of having a mutation were independent predictors of subsequent mammography use. The effects of perceived likelihood of having a mutation (OR, 0.17; CI, 0.02–1.154; CI, 0.4–18.7) were not significant.

Fig. 1. Mammography rates within the year before BRCA1/2 testing (baseline) and during the year after the receipt of test results, by age and carrier status.

Discussion

A potential benefit of obtaining BRCA1/2 test results is that such knowledge could promote screening behaviors or lead women to choose risk-reduction options, which may decrease mortality from breast cancer. However, previous research has shown that only a relatively small proportion of unaffected carriers undergo prophylactic mastectomy (5, 6). Thus, it is important to determine whether and what screening practices most carriers are choosing to adopt. Although our sample size is small, the present report is the first to describe the impact of receiving BRCA1/2 test results on breast cancer screening in the year after the receipt of test results. These data suggest that in a self-referred sample, women ages ≥40 report high rates of mammography utilization. However, the 39% rate of mammography in younger carriers was lower than we expected and suggests that such women may need additional reinforcement about screening guidelines. Importantly, our data suggest that these women are obtaining CBE. However, it is conceivable that the physicians following these women are not recommending mammography because of their young age. On the other hand, the high rate of mammography and CBE in noncarriers, especially in women over age 50, suggests that they were not falsely reassured about their risk of breast cancer.

There are some limitations to this study. Utilization of mammography was based on participants’ self-reports and not on medical record verification. However, data suggest that self-reports of mammography use are generally reliable (16). Although our retention rate was good (79%), noncarriers and women ages 40 and older were more likely to be lost to follow-up, and as such were probably less likely to be compliant with recommendations. Thus, mammography rates for these women may have been inflated. However, as mentioned, there were no differences in demographic factors or baseline psychosocial variables among women lost to follow-up versus those included in this analysis. In addition, participants in our study received counseling and testing at no cost; therefore, they may not be truly representative of clinic-based populations in which individuals must pay for testing out-of-pocket or via insurance.

This brief report raises several important issues, including the need to perform long-term follow-up of individuals who have participated in genetic counseling and testing programs. This will enable us to ascertain what medical decisions women make over time, as well as how they adapt psychologically to test results. For example, future research should examine whether younger carriers adopt annual mammograms once they reach age 35. If not, exploration of potential barriers to screening will be important. We have demonstrated that 6 months after testing, participants who receive positive test results do report higher levels of distress than those who test negative, although the levels of distress are only modestly elevated (9). This distress may, nevertheless, hamper the decision-making process as women strive to choose their best or most comfortable course of action. Thus, adjuncts to genetic counseling may be useful in helping women to cope with their test results and to make medical decisions. In addition, forthcoming data about the efficacy of screening and chemoprophylaxis in carriers will also help women make more informed decisions about the available options, especially in carriers age 35 and younger, for whom the screening guidelines in particular are very vague. Obtaining such data are becoming increasingly important as carriers also consider the potential breast cancer risk reduction potential associated with oophorectomy, a procedure undertaken by a significant number of carriers mainly to diminish the potential associated with oophorectomy, a procedure undertaken by a significant number of carriers mainly to diminish the risk of ovarian cancer (17). In the meantime, clinical trials specifically targeted to mutation carriers will offer a promising opportunity to explore methods of recruitment into such studies and a mechanism to offer regular screening, perhaps with novel detection methods, to these high-risk women.

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