Psychological and behavioral implications of screening for breast or ovarian cancer predisposition genes *BRCA1* and *BRCA2*

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Recently discovered mutations in 2 genes, *BRCA1* and *BRCA2*, account for most hereditary cases of breast cancer. Individuals with mutations in either *BRCA1* or *BRCA2* carry an elevated lifetime risk of breast or ovarian cancer. Genetic testing for these mutations now allows individuals to learn if they are at heightened cancer risk. This genetic testing may have entered the health care system without the development of adequate notification protocols. This paper reviews the psychological and behavioral sequelae of being at increased risk for breast or ovarian cancer due to personal or family history. Similar issues relating to the *BRCA1* and *BRCA2* genetic screening and the notification process also are discussed.

Breast cancer is a common illness affecting approximately 1 in 8 women (1). Although most breast cancers are sporadic, occurring in individuals without a family cancer history, 5% to 10% of breast cancer patients harbor an inherited mutation that predisposes them to the development of breast and other cancers (1, 2).

Recently discovered mutations in 2 genes, *BRCA1* and *BRCA2*, are estimated to account for most hereditary breast cancer cases. Inheritance is autosomal dominant; either men or women may carry these genetic mutations. Incidence rates of mutations found in *BRCA1* and *BRCA2* have varied from the initial linkage studies. These incidence rates are lower in population-based studies. Women who inherit a mutated form of either *BRCA1* or *BRCA2* have a 50% to 85% lifetime risk of developing breast cancer (3, 4). Their lifetime chances of developing ovarian cancer range from 15% to 45% for *BRCA1* mutation carriers and from 10% to 20% for *BRCA2* mutation carriers (4, 5). *BRCA1* mutation carriers also have an elevated risk of colon and prostate cancer, whereas *BRCA2* mutations are associated with rare male breast cancer as well as other cancers (5, 6). Other genes may contribute to inherited breast cancer, including *p53* and *PTEN* (7, 8). It is possible that additional cancer susceptibility genes will be discovered in the future. Although inherited mutations in other genes may play important roles, *BRCA1* and *BRCA2* contribute to most breast cancers with a hereditary cause.

*BRCA1* and *BRCA2* were identified and cloned in 1994 and 1995, respectively (6, 9). Genetic testing for these breast cancer susceptibility genes is now commercially available. This new
technology has made it possible for women in high-risk families and in the general population to request genetic analysis. Lerman et al found that 91% of first-degree relatives (FDRs) of breast cancer patients intended to seek genetic evaluation when it became available (10). Lerman believes that with increasing medical and public interest and commercial pressures, genetic testing will become an integral component of routine medical care for this high-risk population (11).

Technological advances in molecular genetics presently are outpacing research on the social and psychological effects of this technology. Kodish and colleagues point out that the recent identification of BRCA1 and BRCA2 breast cancer susceptibility genes has not allowed enough time or experience to produce appropriate protocols for distribution of this genetic status information (12). Population-based clinical analysis of the effects of these data on genetic mutation carriers is inadequate. Multiple psychosocial concerns relate to the cancer susceptibility risk notification process and potential psychological sequelae that may affect those involved. Examination of these issues has become more pressing, as this technology makes its way from tightly controlled research protocols to uncontrolled commercial availability. An overview and understanding of the issues associated with the risk notification process will enable health care professionals to better serve the unique needs of this high-risk population.

ASPECTS OF GENETIC SCREENING

Pursuing the discovery of disease-predisposing genes affords some advantages (13). Individuals and society may benefit by reducing the impact of disease, improving the health of the population, and lowering the burden on the health care system with the use of genetic information in epidemiology, diagnosis, prognosis, and treatment. Genetic screening provides new possibilities (13–15). Testing offers the ability to learn whether one has a significantly heightened chance of developing cancer or the potential to genetically transmit a mutation to offspring. Individuals found to carry a genetic mutation can be advised and encouraged to follow breast cancer screening recommendations. Intensive surveillance efforts may allow for earlier diagnosis in these individuals and thereby culminate in decreased morbidity and mortality. However, at present there is no intervention proven effective for individuals who harbor a mutation in either the BRCA1 or BRCA2 genes. The awareness of one’s positive carrier status can facilitate preventive medical decision-making processes and enable health care providers to remain vigilant for early indications of the disease. Carriers can also practice preventive health behaviors that may help avert the onset of the disease. Furthermore, noncarriers have the opportunity to avoid taking irrevocable actions such as prophylactic surgery (i.e., mastectomy or oophorectomy). Monitoring these patients and continuing with this line of research may aid in the discovery of improved cancer treatments or cures.

Concomitant with the benefits of this recently accessible technology come a variety of potential problems due to the multiple unique aspects and limits involved in testing for breast cancer genetic mutations (14, 16). It must be emphasized that the information provided is qualitatively different from the typical medical data provided to other patient populations in several ways:

1. Unlike most medical tests, positive genetic mutation results provide information to individuals who are typically healthy regarding potential future risk. Therefore, these findings forecast events that may transpire far into the future.
2. Test results can predict where the cancer is likely to occur and even provide some approximate time frame.

3. There is a large element of uncertainty in the meaning of one’s mutation carrier status, as genetic susceptibility testing is probabilistic. Unlike a definitive disease diagnosis, these mutated susceptibility genes only confer an elevated chance of developing these forms of cancers. Thus, not everyone who harbors a mutation in a breast cancer susceptibility gene will develop the disease. The reality is more complex. Additional genetic factors or environmental events are necessary for the disease to be expressed.

4. Inaccurate or inconclusive genetic screening results are plausible; therefore, breast cancer susceptibility testing may not be reliable.

5. Genetic test findings are pedigree sensitive. The information can disclose the genetic status of other family members. Issues related to previously undisclosed nonpaternity may arise. Test results are also likely to impact familial dynamics. Lerman and Croyle believe it is critical to discuss with these patients the potential influence this information may have on family relationships both before and after test result notification (14).

6. There are no guaranteed methods of primary breast cancer prevention, and until the technology exists to alter one’s genome, harboring a mutation in a breast cancer susceptibility gene is permanent.

For those identified to be *BRCA1* or *BRCA2* mutation carriers, treatment decisions must be reached that may affect the rest of their lives. For example, mutation carriers may consider whether to undergo prophylactic mastectomy or oophorectomy (17). However, this type of surgery does not completely eliminate the risk of developing breast or ovarian cancer (1). Moreover, prophylactic mastectomy patients must confront issues regarding body image and sexuality. Some of these patients may elect to undergo reconstructive surgery following the mastectomy. Carriers may also choose to enroll in clinical chemoprevention trials. Further, those found to be mutation carriers must make reproductive decisions. Issues related to prenatal genetic testing have arisen and, concurrently, the question of whether to continue the pregnancy if the fetus is identified as a carrier (18). As can be surmised, genetic screening information can be powerful; alterations in the course of behaviors, plans, and even lives could result.

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There remain many unresolved questions regarding a range of psychosocial issues (19). Confidentiality becomes a matter of utmost importance, as uncertainty exists over how to shield this genetic testing information and from whom. Multiple concerns are being voiced regarding predictive testing in healthy individuals, such as how to prevent the possibility of “quality of life” deterioration, social stigmatization, prejudice, discrimination by employers and insurers (i.e., health, life, disability), family stress, and psychological stress (1, 17).

This new ability to anticipate health threats can create auxiliary factors that the individual and her family must address. Ascertaining a woman’s motivation to seek genetic screening will enable health care professionals to respond more fully to her needs. In a population-based screening program with high-risk women, Kash conducted interviews with those being screened to determine their interest in genetic evaluation (20). The most important reason indicated was to obtain a degree of certainty, preferring to hear bad news to none at all. Some believed a positive status notification would help them increase their breast cancer surveillance behaviors. Women also sought genetic screening to assist them in their decisions regarding marriage, future childbearing plans, or the
possibility of undergoing preventive procedures such as prophylactic surgery. Others wished to learn the genetic risk to their children or to inform family members. Finally, some women believed learning their genetic risk status would not assist them, but they participated to further the research, thereby benefitting others in the future.

The reasons for not desiring to undergo genetic evaluation are equally important to consider. A preference for living with the uncertainty of not knowing the test results is the overwhelming reason why high-risk women decline genetic screening (20). Therefore, the decision not to undergo genetic evaluation, in fact, may be the most appropriate decision for some women. Breast cancer surveillance behaviors have not yet proven to increase survival from breast cancer in BRCA1 and BRCA2 mutation carriers. Neither is there a proven role for surveillance and detection in ovarian cancer. Therefore, some women prefer not to discover if they are at an increased cancer risk. Others expressed concern regarding the possible negative impact of a mutation carrier status upon family members. Furthermore, many feel unable to cope with positive results and do not want to deal with the potential corresponding emotional consequences. Desiring to avoid additional distress is not surprising in light of evidence revealing that heightened levels of psychological distress may be primary distinctions of women having familial breast or ovarian cancer histories.

CHARACTERISTIC FEATURES OF HIGH-RISK WOMEN

Characteristics of BRCA1 and BRCA2 cancer expression can manifest as increased disease incidence within these high-risk families, and frequently with cancer onset at a much younger age as compared with families not at high risk. Disease expression may also include rare phenotypes. The behavioral and psychological ramifications associated with having a familial cancer history can be far-reaching. Kash and associates contend that these family cancer histories impact high-risk women’s lives because they live with fear, anxiety, and uncertainty regarding their own and their loved ones’ cancer risk every day (21). Compared with normal controls, high-risk women experience significantly more life events involving loss and illness such as watching loved ones struggle with and sometimes succumb to cancer. These adversities can have a psychological impact, as Lerman and colleagues discovered (22). In their population-based study of FDRs of breast cancer patients, 53% reported intrusive thoughts about breast cancer, 33% experienced daily functioning impairments due to breast cancer worries, and 20% noted sleep disturbances. Kash evidenced comparable findings in which >50% of the high-risk women responding to a self-report survey described psychological responses such as anger, depression, guilt, sleep disturbance, and emotional lability (20). Kash et al likewise found increased levels of psychological distress in a population of high-risk women (23). Twenty-seven percent of these women manifested a level of psychological distress consistent with a need for counseling. In a follow-up study, Kash and colleagues documented similar results, with their at-risk sample demonstrating elevations in psychological distress one-half to 1 standard deviation above the mean, compared with women in the general population (21). Such elevated levels are directly attributable to the psychological impact these disease characteristics have upon this population. Furthermore, Lerman and Croyle reported that women with a family history of ovarian cancer might be especially vulnerable to psychological distress (14). The protracted morbidity and high mortality rates associated with this disease are believed to be the cause.

The heightened psychological distress high-risk women experience influences their willingness to
engage in breast cancer surveillance behaviors, such as mammography, clinical breast examination (CBE), and breast self-examination (BSE). These procedures are the most recommended methods for breast cancer detection to date for high-risk individuals (17). To be effective, these techniques must be performed consistently. Adherence to screening recommendations by high-risk women is essential for detecting early signs of the disease, for taking action, and for having a more positive prognosis for survival. However, Kash and colleagues documented that the higher the psychological distress indexes, the lower the levels of adherence to guidelines for CBE and BSE as well as general preventive health behaviors practiced in their sample (23). Likewise, Kash et al observed a negative relation between psychological distress levels and the practice of CBE, BSE, and mammography (21). Similarly, Lerman and Schwartz noted that high-risk women attempted to alleviate their anxiety, which was caused by intrusive thoughts about breast cancer, by avoiding mammography adherence (24). Therefore, it appears that some high-risk women may attempt to allay distress by evading experiences related to cancer, such as early detection screening measures.

Overestimation of cancer risk is a major barrier to practicing early detection methods and a primary contributor to heightened levels of psychological distress (21). Kash et al assert that a woman at risk for genetic breast cancer will likely feel susceptible to the disease. This sense of vulnerability leads to an overestimation of her cancer risk which, in turn, serves to increase her subjective certainty of developing the disease. In this study, 80% of their high-risk sample overestimated their chances of developing breast cancer by as much as 4 times the actual rate. Consistent with these findings, an examination of women at risk for developing ovarian cancer also demonstrated that the higher their level of distress, the greater their overestimation of their objective risk for ovarian cancer (25).

A relation between distorted cancer risk perceptions, heightened distress indexes, and low levels of perceived control over developing cancer are noted in high-risk subjects. For example, Audrain and associates examined the characterization of at-risk women self-referring for genetic counseling and BRCA1 testing (26). Results revealed that higher levels of general distress are attributable to heightened breast cancer risk perceptions, accompanied by low perceptions of control over being afflicted with breast cancer. The psychological distress that one may associate with the development of cancer is referred to as cancer-specific distress. These low perceptions of control significantly contributed to higher levels of cancer-specific distress as well. Moreover, cancer-specific distress can impact the effectiveness of genetic counseling. The ability to process information may be impaired by the individual’s emotional state at the time the information is provided. For instance, Lerman et al discovered that women experiencing heightened levels of cancer-specific distress were more likely to continue to overestimate their lifetime chances of developing breast cancer following risk counseling versus women with lower cancer-specific distress indexes (10).

Because psychological distress can interfere with the comprehension of risk information, Lerman and Croyle raised important concerns regarding the medical management of this population (14). Overestimation of breast cancer risk may lead these patients to choose preventive medical treatment options, such as prophylactic surgeries, based upon erroneous beliefs concerning personal risk.

Alterations in psychological and behavioral functioning occur in some high-risk women, who may
be different from women in the general population across a number of behaviors. Several investigators have documented altered levels of functioning in interpersonal relations and procreation practices in their at-risk subjects. In comparison with age-matched controls, Wellisch et al discovered significant decrements in sexual satisfaction and in the frequency of sexual activity in the daughters of breast cancer patients they examined (27). Kash and associates found that some at-risk women may have postponed marriage or decided not to have children because they were certain they would develop and ultimately die from breast cancer (23). Recently, Croyle examined the variables of fertility and the time at which at-risk women became cognizant of their status (Croyle R: Genetic testing for cancer susceptibility. Ann Behav Med: 18th Annual Meeting 1997;19[suppl]:S036[SYM25]). Although the women reported no awareness of their high-risk situation having an impact upon their reproductive decisions, a significant reduction in childbearing occurred relative to the time of recognition of their at-risk profile. If the FDR affected with breast cancer was the patient’s mother, the effect did not manifest; however, the consequence did occur when the patient’s sister was afflicted.

POTENTIAL PSYCHOLOGICAL REACTIONS TO GENETIC RESULTS

As members of families with a cancer history, at-risk women typically experience alterations in several areas of life. Therefore, Lerman and Croyle voice an important concern regarding the clinical application of this new genetic technology—the potential adverse emotional reaction of this population to genetic status results (14). Not all sequelae to risk notification may be negative, as disclosure of a noncarrier status can be a time of great relief (28). However, researchers in this field agree the amount of evidence to date does not provide a clear understanding of the psychological impact of one’s mutation carrier status (14, 19, 29). At present, possible emotional sequelae to the susceptibility risk notification process remain largely speculative. Nevertheless, certain psychological sequelae to genetic test results may be anticipated (14).

Anxiety may manifest in women found to be mutation carriers and may take many forms, including hypervigilance, intrusive thoughts, sleep disturbances, confusion, somatic symptoms, and worry about the future. Recently, Croyle et al investigated the short-term psychological responses of high-risk patients tested for the BRCA1 gene mutation (29). Results indicated that elevated baseline levels of generalized anxiety predicted heightened indexes of notification-related psychological distress. In comparison with noncarriers, higher levels of general as well as genetic test-specific distress occurred in women identified as mutation carriers. The greatest levels of distress pre- and postnotification manifested in carriers and noncarriers who never personally experienced cancer or cancer-related surgery. As demonstrated, anxiety may be present in noncarriers as well. Another study reported on a subset of noncarriers who continued to manifest anxiety 6 weeks postnotification (30). The distress experienced by these noncarriers was understandable, especially for those who had made irreversible life decisions (i.e., prior prophylactic cancer surgery) based on an inaccurate assumption of risk. The receipt of genetic status findings, however, may have resulted in lowered distress levels for both carriers and noncarriers (29). Croyle et al documented an approximately 20% decrease in anxiety 2 weeks posttest across both groups, suggesting alleviation of anxiety due to the provision of carrier status information.

Lerman and Croyle also identify guilt as a potential side effect of genetic testing (14). For carriers, this may reflect remorse regarding the possible transmission of a mutated gene to one’s offspring.
In noncarriers, “survivor guilt” may manifest. These individuals may experience distress by virtue of being spared while other family members are afflicted.

Depression, another possible emotional response to notification of genetic findings, may be exhibited. Lynch and associates observed depressive symptoms in both carriers and noncarriers 6 weeks postnotification (30). Lerman et al reported the preliminary impact of BRCA1 test notification on depression, functional health status, and medical decision making for high-risk patients (31). Contrary to the findings of Lynch et al, carriers in Lerman’s study demonstrated no evidence of increases in depressive symptoms and functional impairment following disclosure of their test results at the 1-month follow-up, whereas noncarriers evidenced significant improvements in psychosocial functioning. Lerman and colleagues further explored the relation between psychological distress to BRCA1 genetic test utilization and posttest depression in a group of high-risk women (15). These findings suggested that cancer-specific distress was significantly related to BRCA1 test use. Among individuals identified as gene mutation carriers, those scoring highest on cancer-specific distress prenotification exhibited significant increases in depressive symptoms at 1 month following testing.

Adverse psychological reactions also may be experienced by high-risk family members who decline to undergo genetic testing. Lerman et al recently investigated a sample of high-risk women and men who elected not to participate in genetic counseling and screening after they discovered the positive carrier status of other family members (28). Results revealed increases in psychological distress and depressive symptoms among the decliners at the 1-month follow-up in comparison with baseline levels. In addition, heightened cancer-specific stress indexes upon initial assessment predicted depression among the decliners on follow-up. These findings suggested that high-risk family members who decline genetic education and evaluation might benefit from follow-up services aimed at reducing psychological sequelae through genetic counseling.

Because heightened levels of psychological distress may manifest in some at-risk individuals, and further alterations in psychological functioning may occur after notification of a positive carrier status, Kash emphatically states that psychological assessment must be amalgamated into the genetic evaluation and notification process (20). If a woman has a familial cancer history, it is important to determine its impact on her coping ability, role functioning, and psychological distress. For a woman already experiencing heightened distress levels, it might be in her best interest to postpone testing until she is able to handle the results. Additional stressors at the time of testing may also preclude her ability to manage news of positive test results successfully at that date. Kash believes health care professionals must remain sensitive to the psychological status of those being screened throughout all stages of the risk notification process, and they must ensure that adequate psychological resources are available for referral as needed (20).

**PSYCHOLOGICALLY BASED NOTIFICATION PROTOCOLS NEEDED**

Given that psychological processes permeate the risk notification process for breast and ovarian cancer susceptibility testing, the behavioral sciences could provide the necessary expertise to address the psychological and emotional impact of this process on the individuals involved. Historically, patient education has been the method of anticipated behavior change used in other health risk assessment settings. Many times, knowledge has not translated into automatic behavior
change, regardless of risk level. Patient education alone, although important, is likely to be ineffective in this setting against the central concerns of reducing psychological distress and increasing adherence to surveillance behaviors for breast and ovarian cancer.

Because the recent commercial availability of breast cancer genetic screening is expected to generate a great demand for these services, it is imperative that adequate protocols be created to facilitate this technology’s transition to standard of care in medical practice. A need for psychologically based notification protocols is acknowledged, including psychological preparation for genetic testing (14, 20). As previously detailed, testing for cancer predisposition genes involves complex psychosocial aspects. Therefore, education and counseling related to this process are essential to fully inform those undergoing presymptomatic testing of the potential risks, limitations, and benefits (16). In addition, high-risk women often fail to adhere to recommended breast cancer surveillance practices. Because compliance with breast cancer screening behaviors is important for this at-risk population, the genetic evaluation process should include an educational component aimed at promoting surveillance behaviors (14). Kash and associates advocate a psychoeducational group intervention approach to the risk notification process (21). Further, Mark and McGowan endorse uniting health care professionals from fields such as genetics, oncology, and psychology to provide services as part of a standard cancer risk assessment program (32).

The components recommended by these previous investigators will be integrated into a pilot study for women participating in the Baylor-Charles A. Sammons Cancer Center–Texas Oncology, PA, Breast Cancer Risk Evaluation Program. Participants will include patients possessing a familial or personal history of breast or ovarian cancer. These patients will receive genetic counseling, with genetic testing being offered to patients meeting Registry guidelines for these services. Participants will be followed longitudinally for approximately 1 year. Psychosocial questionnaires will be administered at critical points in the risk notification process and will include the Hopkins Symptom Checklist; the Coping Responses Inventory; the Impact of Event Scale; the Quality of Life, Enjoyment, and Satisfaction Questionnaire; the Social Support Questionnaire; the Multidimensional Health Locus of Control; and the Family Environment Scale. Comparisons of these measures will be made between women who are found to be mutation carriers, women who are noncarriers, and a control group. Those identified as $BRCA1$ or $BRCA2$ genetic mutation carriers will be invited to participate in a 6-week psychoeducational group intervention. The women who participate may benefit from this group intervention, as it will provide them with education, skills training, and group support after risk notification. Overall, the investigation will expand our understanding of the characteristics of this high-risk population. Health care protocols may then be developed and implemented to provide the best possible quality of care to women throughout the genetic screening process.

CONCLUSIONS

Genetic screening for breast-ovarian cancer predisposition genes has recently emerged on our medical landscape. Positive aspects of this new technology include the identification of those having a significantly increased risk of developing breast or ovarian cancer, the capability to more actively practice preventive health behaviors that may help avert cancer onset, and the ability to intensify screening efforts that may allow for earlier diagnosis in these individuals, resulting in a decrease in related morbidity and mortality. Continuing to monitor these patients may lead to
advances in cancer treatments or cures.

Because genetic testing for breast cancer susceptibility genes is relatively new, there has been limited opportunity to address important ramifications connected with the risk notification process. Among the most prominent concerns are the potential psychological and social sequelae that participants may experience postnotification. Harboring a genetic mutation and anticipating the possibility of developing a life-threatening disease may create psychological consequences, such as fear, anxiety, guilt, and depression, for those being screened and their family members. Mutation carriers may be vulnerable to discrimination, such as the loss of insurance or employment, as a result of their altered risk status.

Despite the current paucity of evidence regarding the ramifications of the breast cancer genetic screening process, genetic susceptibility testing has entered the commercial marketplace. Market pressures felt elsewhere in health care—to provide services in a more streamlined, profit-sensitive manner—appear, at first glance, to be contrary to the need for greater services to adequately assist the population of individuals who will participate in this screening. The provision of intervention programs and skills training (e.g., coping and problem solving) could be done in a relatively cost-efficient manner and could more effectively counter negative psychological and emotional sequelae of this process. Benefits would be seen more immediately in the improved quality of life for the patients involved, whereas reduced impact of these diseases on our health care system would be seen in the long run. Without the understanding of and attention to psychological issues in this process, the potential for genetic susceptibility testing to decrease morbidity and mortality may go unrealized.

References


