Newly Diagnosed Breast Cancer Patients Choose Bilateral Mastectomy Over Breast-Conserving Surgery When Testing Positive for a BRCA1/2 Mutation

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In women diagnosed with breast cancer and testing positive for a BRCA1/2 mutation, decisions as to whether to undergo prophylactic risk-reduction surgery may differ from those women who test positive in a presymptomatic phase. Eighty-four women were identified who had undergone genetic testing at the time of breast cancer diagnosis. The study group consisted of 46 of these women who had initially undergone breast-conserving surgery. Eight patients (17.4%) tested positive for a mutation. Seven of the eight underwent bilateral prophylactic mastectomy prior to receiving radiation therapy. The only patient not undergoing bilateral mastectomy was awaiting liver transplant. Women who are candidates for breast-conserving surgery and who test positive for a breast cancer gene mutation choose mastectomy over surveillance.

In patients who test positive for deleterious mutation in the BRCA1/2 genes, the decision as to the appropriate course of action is a complicated one. Currently, affected patients must choose between surveillance, tamoxifen, bilateral prophylactic mastectomy (BPM), and salpingo-oophorectomy. The decision-making process is difficult, and it is likely that decisions differ based on cultural attitudes and possibly the bias of those presenting the options. In those women who have tested positive for a gene mutation but have not been diagnosed with cancer, the process generally involves multiple counseling sessions and may include psychological assessment.[1] For those who chose to undergo BPM, the entire process may last as long as 6–12 months.[1]

However, the perspective of women who undergo genetic testing only when they are first diagnosed with breast cancer seems inherently different than those who have not been diagnosed with cancer. Theoretic risks are put aside as the disease now becomes a reality. Concerns prior to diagnosis were focused on the potential risk of developing breast and ovarian cancer as well as the risk to siblings and children. With the diagnosis of cancer, additional concerns enter the picture such as the fear of dying and the potential need for chemotherapy and radiation.

The intent of this study was to determine what surgical decisions were made by women who tested positive for a BRCA1/2 gene mutation at the time of breast cancer diagnosis and who were candidates for breast conservation surgery (BCS).

Patients and Methods

A record review was undertaken of women who underwent BCS for cancer and also underwent genetic testing for BRCA1/2 mutations. All women were treated for breast cancer between March 2000 and March 2005. Surgical therapy was carried out at the Memorial Medical Center or the Ochsner Clinic Foundation in New Orleans, Louisiana. All patients underwent genetic counseling prior to testing. In most instances, counseling on newly diagnosed breast cancer patients was performed by the breast surgeon. In some instances, the patients were seen in a high-risk clinic and were counseled by a trained nurse practitioner, overseen by a medical geneticist. An attempt was made to counsel all newly diagnosed high-risk women at the time of their diagnosis or soon thereafter. All genetic tests were performed by Myriad Genetics, Inc. (Salt Lake City, UT). Age at diagnosis, results of the genetic test, subsequent prophylactic surgery, and the use of reconstructive surgery were noted.

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Results

Eighty-four women were identified who had undergone genetic testing after being diagnosed with breast cancer. Twenty-three (27.4%) underwent unilateral mastectomy as their initial surgical procedure and 15 (17.9%) underwent bilateral mastectomy. The initial surgical procedure was BCS in 46 (54.7%) women. The study group is composed of the 46 women who had BCS as their initial procedure and underwent BRCA1/2 genetic testing.

Patient characteristics, information on genetic tests, results, and outcomes are noted in Table 1. Age range was 24–76 years with a mean age of 46. The mean age was 40 for those testing positive for a mutation.

Of the 46 women who underwent genetic testing, 41 underwent complete sequencing (BRACAanalysis), and 5 had testing for the 3 known Ashkenazi mutations (MultiSite3). Thirty-seven of the 46 (80.4%) tested negative for a deleterious mutation, whereas 4 tested positive for a mutation in BRCA1 and 4 for a mutation in BRCA2. One variant of uncertain malignant potential was reported.

Forty-two of the 46 women in the study group had no prior history of breast cancer; whereas 3 had a history of cancer in the contralateral breast and 1 a history of a prior ipsilateral cancer.

Of the 8 women testing positive for a mutation, 7 subsequently underwent bilateral prophylactic mastectomy with immediate reconstruction. All 8 patients were diagnosed with ductal carcinoma, 7 invasive, 1 *in situ*. Seven of the 8 women testing positive had a family history of breast cancer. Five of the 8 women were less than 45 years old at the time of diagnosis. The one patient without a family history of breast or ovarian cancer was diagnosed at age 24 and was adopted. The only patient not having prophylactic surgery was 55 years old at diagnosis with a strong family history and was a liver transplant candidate as a result of chronic hepatitis.

Two women elected to undergo BPM despite a negative genetic test. One underwent BPM when she developed what was presumed to be a second cancer in the ipsilateral breast. The other, with a very strong family history, underwent BPM prior to learning the results of her genetic test.

TABLE 1. *Patient Characteristics, Genetic Tests, and Outcomes*

Patient Characteristic	Number (%)
Age	
Range	24–76
Median	46
Genetic test: total	46
Complete sequencing	41 (89.1)
Ashkenazi panel (Multisite 3)	5 (10.9)
Prior history of breast cancer	
None	42 (91.3)
Ipsilateral	1 (2.2)
Contralateral	3 (6.5)
Genetic test results	
Negative	37 (80.4)
Variant	1 (2.2)
Positive BRCA1	4 (8.7)
Positive BRCA2	4 (8.7)
Bilateral prophylactic mastectomy in those testing positive	
Yes	7
No	1

Discussion

Currently, risk-reduction strategies for women who test positive for a deleterious mutation in the BRCA1/2 genes include surveillance, chemoprevention, and prophylactic surgery. Reports indicate that 0 to 54 per cent of female BRCA carriers, unaffected by cancer, choose to undergo BPM.[2–6] It is also more likely that unaffected women are more likely to undergo risk-reduction surgery for ovarian cancer risk than for breast cancer risk. Botkin et al. reporting a series of presymptomatic women who were studied up to 2 years after genetic testing. They noted that none of the 37 women carriers elected to undergo BPM compared to 30 per cent who underwent salpingo-oophorectomy (BSO).[2] Lerman et al. also examined decisions made by presymptomatic mutation positive women and found that 1 of 29 affected women elected BPM compared to 5 of 39 electing BSO.[3] In a study from Memorial Sloan-Kettering Cancer Center, 14.9 per cent of unaffected gene positive women elected to undergo BPM in contrast to 50.3 per cent of women who elected to undergo bilateral salpingo-oophorectomy.[6]

Intuitively, the perspective of women who are found to be BRCA1/2 carriers after the diagnosis of breast cancer might differ considerably from those who are unaffected carriers. They are no longer dealing with the statistical probability of developing an initial breast cancer but a life-threatening illness and the risk of a second cancer. Furthermore, the decision-making process is complicated by the potential cancer treatments that loom in the near future.

Schwartz et al. reported on 194 patients who underwent genetic testing at the time of breast cancer diagnosis.[7] Of these, 31 tested positive and 16 (52%) elected to undergo bilateral mastectomy, which is similar to the decisions made in some series by unaffected carriers.[4, 5] Similar to our series, Weitzel et al. reported a series of 37 newly diagnosed patients from City of Hope National Medical Center who underwent genetic testing.[8] Seven women were found to harbor a deleterious mutation and all 7 chose bilateral mastectomy as their initial surgical procedure.

Does the presence of a family history of either breast or ovarian cancer influence the decision-making process for this group of affected women? Though a logical inference, our study is too small to draw such conclusions. Does the presence or absence of a family history affect the risk of developing breast cancer in unaffected BRCA1/2 positive women? King et al. reported on 104 Ashkenazi women who tested positive for a BRCA1 or BRCA2 mutation.[9] They found that the risk of developing breast cancer was similar in families with many cases compared to families with just one affected relative. They also noted that in almost all of these low-incidence families, the mutations were proved to come from the father.

Our own surgical approach to the newly diagnosed breast cancer patient who is at high risk for a BRCA1/2 mutation has been previously reported[10] (Fig. 1). Briefly, in high-risk women who are breast conservation candidates, BCS is carried out but radiation is withheld until test results are known. Results may take 3–5 weeks to become available. Women who test negative undergo radiation therapy in the appropriate sequence. Those testing positive are counseled regarding available options. This would currently include surveillance, tamoxifen and/or oophorectomy and BPM with immediate reconstruction. In our study, 46 high-risk women underwent BCS and genetic testing. Eight (17%) tested positive and 7 elected to have BPM with reconstruction. The only patient not electing BPM was awaiting liver transplant. Although these series are small, they suggest that in most instances, women who are found to carry a BRCA1/2 mutation at the time of breast cancer diagnosis will choose bilateral prophylactic mastectomy.

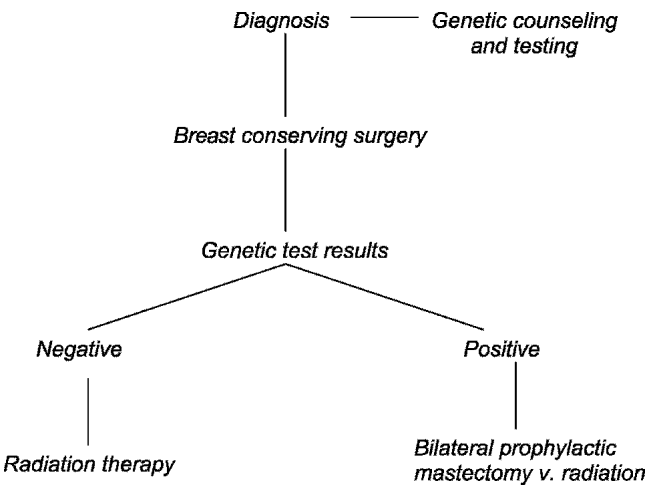

FIG. 1. Algorithm for women who are candidates for breast-conserving surgery and are at high risk for BRCA1/2 mutation.

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