Prophylactic Mastectomy: Obstacles and Benefits


News in medicine, such as the potential lifesaving effects of bilateral prophylactic mastectomy as reported in this issue of the Journal by Hartmann et al. (1) and its implementation in clinical practice, does not, unfortunately, always travel fast! Bilateral prophylactic mastectomy for women at increased risk for breast cancer has been highly controversial, in part because of strong concerns such as, “Will it work? Will patients accept it? Will physicians recommend it?” Physicians often are reluctant to advocate new and particularly radical medical changes, such as bilateral prophylactic mastectomy, even though their patients may be at inordinately high risk for the hereditary breast–ovarian cancer syndrome because they carry a deleterious cancer-causing BRCA1 or BRCA2 gene mutation.

In their initial study, Hartmann et al. (2) used “high-risk” criteria to identify familial or hereditary status, such as the number of breast cancer affected first- and second-degree relatives, whereas in their current report (1), they used genetic testing to identify the BRCA1/BRCA2 mutation carriers. Their initial study, therefore, showed a decreased risk of breast cancer after bilateral prophylactic mastectomy in high-risk women; now the decreased risk is confirmed in BRCA1/BRCA2 mutation carriers in their present report. A recent prospective study by Meijers-Heijboer et al. (3) also showed a statistically significant risk reduction after bilateral prophylactic mastectomy among BRCA1/BRCA2 mutation carriers.

The role of hereditary factors as a contributing cause of breast cancer was proposed more than three decades ago (4–10). At that time, hereditary cancer risk was computed primarily on the patient’s position within their pedigree, which often contained multiple primary and secondary relatives affected with breast and/or ovarian carcinomas. These publications constituted the first reports of what is now known as hereditary breast–ovarian cancer (6,8). Early reports (7,9) suggested that women at inordinately high risk of familial breast cancer required special cancer control measures. Bilateral prophylactic mastectomy was, therefore, suggested as an option for members of breast cancer-prone families wherein the risks to first-degree relatives of the proband “…approach 50%, consistent with an autosomal dominant factor . . . .” (9). The same article (9) then stated, “Prophylactic mastectomy may be considered (in such families) under certain circumstances. For example, a relative . . . who developed a crippling cancer phobia because of her awareness of this disease in her family may express a strong desire to have what she correctly considers her cancer-prone breast tissue excised . . . .” We initially recommended contralateral prophylactic mastectomy when ipsilateral breast cancer was present, as well as bilateral prophylactic mastectomy and bilateral prophylactic oophorectomy in such high-risk women (10).

Patients who were candidates for the option of bilateral prophylactic mastectomy included those who failed to comply with screening recommendations, often because of their fear of “finding” breast cancer (5). Also included as candidates for the procedure were women at high risk of hereditary breast cancer who manifested severe fibrocystic breast disease that made it difficult for them and their physicians to determine which masses were clinically significant (9). Even in those “early days,” we recommended that such women seek genetic counseling and consultation with a medical geneticist when weighing genetic risk factors relevant to considerations of prophylactic surgery (5,10).

What is the current status of bilateral prophylactic mastectomy and its benefits? Women who were at high risk of breast cancer in the initial study by Hartmann et al. (2), by and large, did not have high pretest probabilities of being BRCA mutation carriers. Their risks of developing breast cancer generally did not approach the risk of a mutation carrier; therefore, the potential benefits of bilateral prophylactic mastectomy were less (i.e., they had less of an absolute reduction in breast cancer risk).

With the ability to distinguish women who are definitely at exceptionally high risk (because of a known BRCA1 or BRCA2 mutation), we can now more strongly support bilateral prophylactic mastectomy as a medical option. The flip side, of course, is that a major detraction of bilateral prophylactic mastectomy is erased: Women within a family harboring a known mutation who are themselves BRCA1/BRCA2 mutation negative can avoid surgery.

However, even in the face of these cancer control benefits, for a variety of reasons, women may find bilateral prophylactic mastectomy unacceptable. Indeed, they may not understand what the procedure entails and/or the potential benefits of subsequent breast reconstruction. In short, they need to be educated. Health insurance carriers’ unwillingness to defray costs for the procedure in these high-risk women may continue to pose barriers to bilateral prophylactic mastectomy and/or bilateral prophylactic oophorectomy (11,12). Thus, logic, particularly the reduction of morbidity and mortality, and even likely long-term expense reduction (avoidance of more radical surgery, chemotherapy, and radiation therapy), through bilateral prophylactic mastectomy or bilateral prophylactic oophorectomy, may not immediately prevail.

Genetic counseling is mandatory when working with patients from high-risk families (5). But will counseling make a difference? With the discovery of mutations in the BRCA1 and BRCA2 genes that predispose individuals to breast cancer, we have been able to counsel these women with greater precision about their breast cancer risk and about screening and manage-

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ment options, including chemoprevention and prophylactic surgery.

For example, we have determined the germline BRCA1/BRCA2 mutation status of 1252 individuals from 95 families with hereditary breast–ovarian cancer. To date, we have counseled 687 women from 83 of these families, and pertinent insights have emerged (Lynch HT: unpublished data). For example, before knowing their mutation status, we asked 362 of these women if they would consider the option of bilateral prophylactic mastectomy if they had a mutation. One hundred thirty-eight (38%) said they would consider the procedure if they were positive for a BRCA1 or BRCA2 mutation. Conversely, five (2%) of 307 women queried said that they would still consider bilateral prophylactic mastectomy even if they were negative, reflecting, in part, their concern about the one in eight to one in nine lifetime risk of breast cancer in the general population. These women may also have believed that a negative mutation finding would not have decreased their greater lifetime risk of breast cancer, given that “... so many of my relatives are affected with breast cancer.” After learning their BRCA1 or BRCA2 mutation status, 172 (51%) of the 336 mutation-positive women and 14 (5%) of the 289 mutation-negative women who responded said that they would consider bilateral prophylactic oophorectomy. Following disclosure of BRCA1 and/or BRCA2 mutation status, our follow-up survey found that 27 (19%) of 142 mutation-positive women had undergone bilateral prophylactic oophorectomy, while 46 (35%) of 131 mutation-positive women had had a bilateral prophylactic oophorectomy.

What will be the public health impact of the findings of Hartmann et al. (1,2) given the enormous magnitude of breast cancer in the general population, particularly in women in highly industrialized Western nations? How will physicians take family histories that are sufficiently detailed to enable them to make hereditary risk determinations? Are there enough genetic counselors who are sufficiently knowledgeable about cancer genetics and the pros and cons of bilateral prophylactic mastectomy (as well as bilateral prophylactic oophorectomy), particularly the potential physical and psychologic sequelae, to adequately and responsibly advise their consultands? Indeed, should offering such options be the responsibility of the nonmedically trained genetic counselor? Are the skills of these counselors being sufficiently utilized? Will insurers defray the cost of genetic counseling, genetic testing, and prophylactic surgery? Will there be insurance discrimination? Will women accept the loss of sexual stimulation following bilateral prophylactic mastectomy, particularly with sacrifice of the nipple areola complex, and/or the change in their body image due to disfigurement? What will be the spouse’s response? Only time will tell!

REFERENCES