

Current Trends in Prophylactic Mastectomies for Unaffected BRCA Mutation Carriers

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Short Communication

Breast cancer remains the most common cancer diagnosis in women, as it represents 14.6% of new cancer diagnoses in the United States and accounts for 6.8% of cancer deaths [1]. Growing research into breast cancer etiology has shed new light on genetic risk factors. It is now estimated that 5% to 10% of all breast cancers have a hereditary link [2]. This is especially true in younger patients, in whom 25% to 40% of cases have a coexisting genetic risk [2].

Perhaps the most well-known hereditary cancer syndrome is the BRCA1/BRCA2 mutation. Mutations in the tumor suppressor genes BRCA1 and BRCA2 have been identified as known risk factors for the development of breast cancer since 1994 and 1995, respectively. The increased lifetime risk of developing cancer in these individuals ranges from 56% to 87% with the onset of cancer occurring earlier in life compared with sporadic cases (age 40-50 versus 60-70) [2,3].

BRCA screening is recommended for any individual with a suggestive family history where the information would be used to affect medical treatment [4]. Concerning factors include breast cancer before age 50, bilateral breast cancers, presence of ovarian cancer, male breast cancer, multiple cases of breast cancer within a family, breast and ovarian cancer, and Ashkenazi Jewish descent. The United States Preventive Services Task Force recommends genetic counseling for any patient with these risk factors and BRCA screening when appropriate [5].

There are several risk-reducing strategies available for women with known BRCA mutation. Increased surveillance with clinical examination and radiographic screening beginning at a younger age is one option [2]. Chemoprophylaxis targeting estrogen receptor signaling pathways and oophorectomy to reduce estrogen stimulation have been shown to reduce risk [2]. Prophylactic mastectomy has also been proven to be a safe and effective method to decrease lifetime incidence of breast cancer [2].

While the most appropriate choice for breast cancer risk reduction in a woman with BRCA mutation remains a complex and personal decision, a joint American Society of Clinical Oncology and Society of Surgical Oncology Task Force stated that “the primary intervention for mutation carriers of high penetrance breast cancer is surgical” [3]. Risk reducing mastectomy was associated with a decreased risk of breast cancer in BRCA1/2 mutation carriers with a clinical study demonstrating no cancer events at three-year follow-up in this high-risk cohort [6]. Based on mathematical models, bilateral mastectomy has the greatest life expectancy gain amongst the prevention strategies [2,7]. It should be noted, however, that no randomized controlled trials have examined the potential impact of prophylactic bilateral mastectomy on survival. Additional benefits include higher level of patient satisfaction and a significant reduction in anxiety and cancer related distress when compared with patients who opted for surveillance [8].

Several unique mastectomy methods are commonly utilized. A total mastectomy removes the entire breast including the glandular tissue, nipple areola complex, and a significant portion of the overlying skin,

and it is considered to be the gold standard. Newer techniques which aim to preserve the skin envelope and/or nipple areola complex are gaining favor in appropriately selected patients. Skin sparing mastectomy has proven to be safe with Peled et al. demonstrating no new cancer cases at four-year follow-up and similarly low rates of carcinoma at the nipple margin in BRCA and sporadic cases [9]. Nipple-sparing mastectomy allows for superior cosmetic outcome and higher levels of patient satisfaction in comparison to skin-sparing mastectomy [10].

Controversy exists regarding residual breast tissue in the nipple areola complex both for long term risk and multifocal disease. Although commonly regarded as oncologically safe, long term oncologic outcomes have not been well studied. Wang et al. examined a cohort of 633 patients who underwent nipple sparing mastectomy with immediate reconstruction, and there were no cases of recurrence at the nipple areola complex [11]. Loco-regional recurrence was observed in 3% of patients, with an additional 4.2% having distant disease [11]. In patients undergoing nipple sparing mastectomy for risk reduction, 2.7% of individuals were found to have an incidentally discovered cancer, and the only documented recurrence was outside the nipple areola complex [12]. In BRCA patients, Manning et al. found no new breast cancer diagnoses in 151 patients undergoing nipple sparing mastectomy at twenty-six month follow-up [10].

Breast cancer remains a common cause of cancer and cancer related death in women. Advances in genetic diagnosis have allowed for the identification of patients who possess a high risk for breast cancer development. Trends in preventive health measures have created challenges in managing patients with a known hereditary breast cancer syndrome. Surgical treatment in these individuals promises excellent risk reduction and has been shown to be a satisfactory option for many women. In these patients, skin and nipple sparing operations are being developed which can maximize aesthetic result and simultaneously reduce overall oncologic risk.

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