Prophylactic Surgery in Hereditary Breast/Ovarian Cancer Syndrome

Drs. Levine and Gemignani have composed an excellent comprehensive review of the issues surrounding prophylactic surgery in patients at high risk for breast and ovarian cancer. Their article focuses on the role of BRCA1/2 mutations in the risk of developing hereditary breast and ovarian cancer and the data supporting risk reduction in mutation carriers undergoing prophylactic surgery.

Approximately 10% of ovarian cancer and 5% of breast cancer cases are due to an inherited predisposition, with the majority due to mutations in the BRCA1 and BRCA2 genes. For mutation carriers, the authors have estimated the lifetime risk of developing breast cancer to range from 35% to 75%, and the risk of ovarian cancer, from 20% to 40%. When considering prophylactic surgery, the elevated risk of cancer in these patients must be balanced against several factors, such as the availability of effective cancer screening techniques, the cost and morbidity of surgical prophylaxis, the effectiveness of such prophylaxis, and the available alternatives to surgery.

Prophylactic Oophorectomy

The case for prophylactic oophorectomy seems more clear. Laparoscopic oophorectomy may be performed on an outpatient basis in the majority of women, with low surgical morbidity and acceptable financial cost. Data from Rebbeck et al[1] clearly demonstrate a significant reduction in the risk of developing ovarian or primary peritoneal cancer following prophylactic oophorectomy. Among 259 women with germ-line BRCA1 and BRCA2 mutations who underwent prophylactic surgery, 6 (2.3%) were diagnosed with occult ovarian cancer at the time of surgery and 2 (0.8%) developed primary peritoneal cancer, compared to 58 cases (19.9%) of ovarian cancer among 292 matched controls. Although the use of oral contraceptives is under investigation as a means to mitigate ovarian cancer risk, current data do not support as great a reduction in risk as that achieved with prophylactic oophorectomy. Promising, intensive screening techniques have yet to be proven effective in reducing mortality from ovarian cancer in high-risk women, and many women may not adhere to surveillance recommendations. Botkin et al[2] recently showed that among mutation carriers, only 26% obtained an ultrasound in the first year and 11% in the second year after mutation testing. CA-125 testing was only used by 32% and 37% in the first and second year after testing, respectively. Similarly, Lerman et al[3] reported that among mutation carriers, only 21% underwent CA-125 testing, and 15% underwent transvaginal ultrasound in the year following testing. In contrast, women in the Botkin et al study[2] appeared to demonstrate a preference for prophylactic oophorectomy over screening, and 46% of all mutation carriers and 78% of those age 40 or older underwent the procedure. Meijers-Heijboer[4] found similar results, with 49% of women requesting the surgery. Others have demonstrated a high level of satisfaction with the procedure, with a concomitant reduction in anxiety.[5] Although the incidence of mutation-associated ovarian cancer is lower than that of breast cancer, the absence of reliable screening methods to detect early tumors combined with the high mortality of late-stage disease make prophylactic surgery a reasonable option for high-risk women.

Prophylactic Mastectomy

Recommendations for prophylactic mastectomy are more problematic. Although studies have clearly demonstrated a marked reduction in the risk of breast cancer,[6,7] there is an inherent irony in recommending bilateral mastectomy for healthy women who are merely at risk for cancer, when those who actually develop the disease may be treated with breastconserving therapy. The use of prophylactic mastectomy varies in the reported literature from 0%[2] to 35%[4] of mutation carriers. Multiple factors make prophylactic mastectomy an unattractive option for many women. Aside from significant issues regarding body image and sexuality, women may prefer other options to ameliorate cancer risk. Intensive screening typically involves annual mammography beginning at
age 25 combined with clinical and self-breast examination; the use of magnetic resonance imaging as a screening tool is currently under investigation. These options appear to be acceptable to patients and are used by a high percentage of mutation carriers. Botkin et al.[2] demonstrated that 71% of women obtained a mammogram within 2 years post-mutation testing. Over 80% adhered to recommendations for self-examination and clinical examination. However, this enthusiasm for surveillance must be tempered by the realization that screening is imperfect and may be less sensitive in both BRCA1 and BRCA2 mutation carriers, and in women under age 40.[8] Safe, effective chemoprevention for breast cancer is another active area of investigation. The Breast Cancer Prevention Trial[9] demonstrated that tamoxifen reduced the risk of invasive cancer by 49% among women at elevated risk. However, among the 288 women who developed invasive cancer, only 19 BRCA1 and BRCA2 mutation carriers were identified, making it difficult to base firm recommendations for mutation carriers on the available data, especially given the concern that the majority of BRCA1 mutation-associated cancers do not express estrogen receptors. The Study of Tamoxifen and Raloxifene (STAR) trial, in which patients at elevated risk of breast cancer by Gail criteria are randomized to either daily tamoxifen or raloxifene (Evista), is currently accruing patients to examine study end points of invasive and noninvasive breast cancer, cardiovascular disease, endometrial cancer, bone fracture, and thromboembolic events.

Conclusions

Recommendations regarding surgical prophylaxis for patients with BRCA1/2 mutations need to be individualized. The clear reduction in ovarian cancer risk, weighed with the lack of proven effective screening techniques, and the generally tolerable side effects of early estrogen deprivation provide a strong argument for prophylactic oophorectomy. The decision to undergo prophylactic mastectomy may be more difficult for patients. Given the distinct reduction in cancer risk, mastectomy may be preferable to many patients. However, for others, intensive screening, chemoprophylaxis, and prophylactic oophorectomy, which has also has been shown to decrease breast cancer risk,[1,10,11] may be realistic alternatives.

Disclosures: The author(s) have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.


Source URL: http://www.cancernetwork.com/review-article/prophylactic-surgery-hereditary-breastovarian-cancer-syndrome-0

Links: