Caring for the Patient at High Risk for Breast Cancer

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Abstract

Breast cancer remains the most common cancer among women (other than skin cancer) and the second leading cause of death from cancer. This year the American Cancer Society estimates over 212,000 new breast cancer cases.[1] As clinicians, regardless of where we work, we will most certainly be faced with the challenge of caring for a patient who is at high risk for the development of breast cancer. Caring for high risk women requires a multi-disciplinary approach and has many facets. Choosing when to start screening and what method(s) to use, counseling on the use of chemo-preventative agents, suggestions of surgical prophylaxis, genetic testing and emotional and psychological support are some of the vital issues. These issues will be discussed in this review.

Identifying Women at High Risk

Before discussing the care of high risk women it is important to decide who is high risk and how we define this. We will break this discussion down into the two main categories of breast cancer; spontaneous (or sporadic) verses genetic breast cancers. Most breast specialists talk about women at high risk for a spontaneous breast cancer by the Gail Model.[2] The Gail Model gained recognition as the model used in the National Surgical Adjuvant Breast and Bowel Project P1 Trial.[3] The Gail Model is a scoring system based on answers to seven questions that then gives an estimate of the risk for the development of breast cancer over the next five years, as well as over a women's lifetime (Table 1).[2] The P1 study used the criteria of all patients with a Gail risk estimate of at least 1.66% over the next five years as being high risk.[3]

If a Gail Model is not available, the traditional risk factors for the development of a spontaneous breast cancer are: history of atypical (ductal or lobular) hyperplasia on biopsy, lobular carcinoma in situ, early menarche, late menopause, nulliparity, late age of first birth, extended use of exogenous hormones, and history of radiation exposure (Table 2).[4,5]

Women at high risk for the development of a genetically induced breast cancer either have a documented mutation of BRCA 1/2 or a family history extremely suggestive of a mutation. In the absence of a documented gene, several characteristics can help identify a patient at high risk for a mutation including family history of a gene mutation, early age of diagnosis of breast or ovarian cancer, history of breast and ovarian cancer in a family, bilateral breast cancer, and Ashkenazi Jewish heritage.[6]

Table 1 - Gail Model Breast Cancer Risk Assessment Tool

1. Race
2. Age
3. Age of first menses
4. Age of first live birth
5. Number of mother/sister(s)/ daughter(s) with breast cancer
6. Number of previous breast biopsies
7. Biopsy with atypical hyperplasia

Approximately 5-10% of all breast cancer cases are associated with a genetic mutation.[7] Clinically significant BRCA mutations occur in 1 in 300 to 500 persons in the general population. A mutation of BRCA 1/2 increases a woman's lifetime risk for the development of breast cancer up to 85% and ovarian cancer up to 26%.[6] More than 50% of women with BRCA 1 and 2 mutations are diagnosed with breast cancer before the age of 50.[4]

Evaluation of the Women at High Risk for Developing Breast Cancer

Clearly, special intensified screening methods need to be used in this high risk population (Table 3). Annual screening mammography and annual clinical breast exam should begin in these high risk women at the age of 25.[4]

The dilemma is that we know that the sensitivity of mammography is reduced in many young women. Premenopausal women have a denser breast tissue that limits the sensitivity of mammography. Therefore, high risk premenopausal women should also undergo annual MRI. Annual screening with breast MRI is more accurate than mammograms in the population of high risk young women with dense breasts.[4,7,8,9] MRI is not limited by dense breast tissue and also does not use ionizing radiation, thus being an ideal tool for imaging young women. There has been debate regarding the sensitivity and specificity of MRI. It is known to have high sensitivity but questionably lower specificity, which may lead to additional imaging and more biopsies.[8] This concern supports the rationale that this tool be reserved for the high risk population of young women.

The question of whether MRI can be used alone in these young high risk women is still being studied. MRI works using the contrast agent gadolinium to show enhancement

Table 2 - Factors that Increase Breast Cancer Risk
History of breast biopsy with Atypical Hyperplasia (ductal or lobular) or Lobular Carcinoma in Situ
Early menarche
Late menopause
Late Age of first birth (>30)
Null parity
History of Radiation Exposure
Extended Use of Exogenous Hormones
Postmenopausal Obesity
Heavy alcohol use
Strong Family History of Breast or Ovarian Cancer

patterns of the breast. Cancerous tumors have increased vascularity (due to angiogenesis) and thus show a specific pattern on uptake and washout. DCIS (ductal carcinoma in situ) growth is less dependent on angiogenesis because the nutritional supply comes from diffusion. Thus, DCIS is less likely to enhance on MRI as compared to invasive carcinoma.[10] The reported sensitivity of MRI for DCIS ranges in the literature anywhere from 40-100%.[8,10,11] Therefore, even though mammograms are less sensitive in this group they may still be useful since MRI may be less sensitive for DCIS. How useful mammograms are for this indication is still uncertain.

Digital mammography is also a tool being studied in the high risk population. Recent data suggest that digital mammography is more accurate than traditional film screen mammograms in women under the age of 50 with radiographically dense breasts. Digital imaging associated with digital mammography allows the degree of contrast in the image to be manipulated, helping to overcome the limitations of a dense breast.[12]

Risks for Ovarian Cancer

Although we are focusing mostly on breast cancer risk and screening, it is important to recall that many of these women are at high risk for both breast and ovarian cancer. While risk of ovarian is much lower, it is an important issue to address. Women with BRCA gene mutations should have surveillance with pelvic exam, transvaginal ultrasound and CA-125 every 6-12 months.[13] Screening for ovarian cancer should also begin between the ages of 25 and 35 for these high risk women.[14]

Prophylaxis to Prevent Breast Cancer

For some women the idea of imaging alone is not enough and they consider the use of prophylactic surgery to help reduce their risk. Prophylactic surgery for breast cancer risk reduction may be either prophylactic mastectomy or prophylactic oopherectomy, or both. Neither surgery totally eliminates risk of developing breast or ovarian cancer. Risk reduction estimates from each surgery vary significantly in the literature. Prophylactic oopherectomy, however, serves two purposes; as the most important measure to reduce ovarian cancer risk and as a secondary benefit to reduce breast cancer.[7] These surgeries are not without risk. Aside from traditional surgical risks, there is potential for risk of depression, impact on sexuality, and potential changes in feelings of femininity that also need to be considered.[15,16] Referral to a psychologist or social worker is often appropriate prior to prophylactic surgery. Many options for reconstructive surgery exist; both immediate and delayed reconstruction.

Aside from screening and surgery, chemoprevention is another option for risk reduction. The largest trial analyzing chemoprevention in breast cancer is the National Surgical Adjuvant Breast and Bowel Project P1 trial. P1 studied 13,388 women randomized to Tamoxifen vs. placebo. The results from this trial have been what support use of tamoxifen in the high risk population. P1 found a 49% reduction in the risk of breast cancer, 56% reduction in women with a history of lobular carcinoma in situ, and 86% risk reduction in women with a history of atypical ductal hyperplasia. Adverse effects of clinical significance with 5-year use of Tamoxifen included endometrial cancer, stroke, deep vein thrombosis, and pulmonary embolism.[3] It should also be mentioned that while Tamoxifen is an extremely effective medicine for risk reduction in many high risk women, we do not know if there is a role with BRCA 1/2 mutation carriers.[14]

Table 3 - Management of the High Risk Breast Patient	
Mammograms	Annually starting at 25
MRI	Annually starting at 25
Clinical Breast Exam	Every 6 months
Self Breast Exam	Annually starting at 20
CA 125	Every 6- 12 months starting at 25-35
Pelvic Exam	Every 6- 12 months starting at 25-35
Transvaginal Ultrasound	Every 6- 12 months starting at 25-35
Consider Referral to Behavioral Medicine	As needed
Consider Referral to Surgeon to discuss prophylactic mastectomy and/or oopherectomy	As needed
Consider Chemoprevention	As needed
Consider Clinical Trials	As needed

Recent research has looked at other SERM's (selective estrogen receptor modulators) to assess potential for breast cancer risk reduction. Preliminary data on the drug Raloxifene (Evista) has been published showing similar efficacy for the risk reduction of invasive breast cancer. In contrast, there were fewer noninvasive breast cancers in the Tamoxifen group (although this was not of statistical significance). There was decreased incidence in uterine cancer and thromboembolic events in the Raloxifene group.[17]

Psycho-social Issues in High Risk Women

Another issue to consider is the emotional and psychological implications of being termed "high risk." Specifically, the process of genetic testing can have many psychological implications. Identifying and testing high risk patients for gene mutations has been debated and is still viewed by some as controversial. Concern has been that testing for genetic mutations provides predictive but not diagnostic information. Knowledge of high risk status can cause increased anxiety.[14] Other barriers to genetic testing include expense of testing, fear of insurance discrimination, fear of results.[14,18]

Conclusion

It is important to remember that many women today are educated and take an active part in their healthcare. Working with these patients should be "shared-decision making," a process that incorporates provider preference and patient involvement.[19] It is important to include the patient in all avenues of their personalized risk reduction and screening including risks, benefits, and alternatives, combining medical knowledge with the patient's own values.

Care of the woman at high risk for breast cancer is a multidisciplinary, multi-faceted, lifelong process. These women have specific screening needs such as modified imaging that do not fall into the traditional guidelines. They may need referrals to surgery to discuss the options of prophylactic mastectomy or oopherectomy. They may also have many psychological and emotional issues that require a referral to behavioral medicine.

Referral of high risk patients to high risk breast clinics may be useful. These are complex patients and often many of them are young. An integrated care team with knowledge of the variety of different issues these women face is a vital part of their care.

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References

1. American Cancer Society. Breast Cancer Facts and Figures, 2005-2006. www.cancer.org

2. Gail, M, Brinton, L, Byar, D, et al. Projecting individualized probabilities if developing breast cancer fir white females who are being examined annually. Journal of the National Cancer Institute 1989; 81: 1879-86.

3. Fisher, B, Constantino, J, Wickerham, L, et al. Tamoxifen for prevention of beast cancer: Report of National Surgical Adjuvant Breast and Bowel Project P-1 study. Journal of the National Cancer Institute 1998; 90: 1371-1388.

4. Hollingsworth, A, Singletary, E, Morrow, M, et al. Current comprehensive assessment and management of women at increased risk of breast cancer. The American Journal of Surgery 2004; 187: 349-362.

5. Cuzick, J. Epidemiology of breast cancer-selected highlights. The Breast 2003; 12: 405-411.

6. Nelson, H, Huffman, LH, Rongwei, F, Harris, E. Genetic risk assessment and brca mutation testing for susceptibility: Systemic evidence review for the U.S. Preventative Task Force. Annals of Internal Medicine 2005; 143: 362-379.

7. Kuhl, C, Schmutzler, R, Leutner, C, et al. Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: Preliminary results. Radiology; 2000; 215: 267-279.

8. Kriege, M, Brekelmans, C, Boetes, C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med 2004; 351: 427-237.

9. Stoutjesdijk MJ, Boetes C, Gerrit JJ, et al. Magnetic Resonance Imaging and mammography in women with hereditary risk of breast cancer. JNCI 2001; 93: 1095-1102.

10. Shah SK, Shah, SK, Greatex, KV. Current role of magnetic resonance imaging in breast imaging: A primer for the primary care physician. The Journal of the American Board of Family Practice 2005; 18: 478-490.

11. Sardinelli, F, Guiseppetti, G, Panizza, P, et al. Sensitivity of MRI versus mammography for detecting foci of multi-focal, multi-centric breast cancer in fatty and dense breasts using the whole-breast pathologic examination as a gold standard. AJR; 2004; 183: 1149-1157.

12. Pisano, ED, Gatsonis, C, Hendrick, E, et al. Diagnostic performance of digital versus film mammography for breast-cancer screening. N Engl J Med 2005; 353:1773-83.

13. Sifri, R, Gangadharappa, S, Acheson, L. Identifying and testing for hereditary susceptibility to common cancer. CA Cancer J Clin; 2004; 54: 309-326.

14. Matloff, E, Shappell, H, Brierly,K, Bernhardt, B, McKinnon, W, Peshkin, B. What would you do? Specialist's perspectives on cancer genetic testing, prophylactic surgery, and insurance discrimination. Journal of Clinical Oncology 2000; 18: 2482-2492.

15. Eisen, A, Rebbeck, T, Wood, W, Weber, B. Prophylactic surgery in women with a hereditary predisposition to breast and ovarian cancer. Journal of Clinical Oncology 2000; 18: 1980-1995.

16. Bresser, P, Seynaeve, C, Gool, A, et al. Satisfaction with prophylactic mastectomy and breast reconstruction in genetically predisposed women. Plastic and Reconstructive Surgery 2006; 117: 1675-1682.

17. Vogel, V, Constantino, J, Wickerham, L, et al. Effects of tamoxifen vs. raloxifene on the risk of developing invasive breast cancer and other disease outcomes. JAMA 2006; 295.

18. Armstrong, K, Micco, E, Carney, A, Stopfer, J, Putt, M. Racial differences in the use of BRCA 1/ 2 testing among women with a family history of breast or ovarian cancer. JAMA 2005; 293: 1729-1736.

19. Nekhlyudov, L, Bower, M., Herrinton, L, et al. Women's decision-making roles regarding contralateral prophylactic mastectomy. Journal of the National Cancer Institute; 2005; 35: 55-60.