Breast Cancer Prevention Across the Cancer Care Continuum

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Objectives: *To review the current state of breast cancer prevention from primary prevention through survivorship, highlight cross-cutting issues, and discuss strategies for clinical integration and future research.*

Data Sources: *Published articles between 1985 and 2015 and original research.*

Conclusion: *Cancer risk persists across the lifespan. Interprofessional strategies to reduce morbidity and mortality from cancer include primary, secondary, and tertiary prevention (survivorship). Prevention strategies across the cancer care continuum are cross-cutting and focus on measures to: prevent the onset of disease, identify and treat asymptomatic persons who have already developed risk factors or preclinical disease, and restore function, minimize the negative effects of disease, and prevent disease-related complications.*

Implications for Nursing Practice: *Oncology nurses and advanced practice nurses are vital in the delivery of breast cancer prevention strategies.*

Key Words: *Breast cancer prevention, breast cancer risk*

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Breast cancer remains the most common cancer in women, affecting more than 200,000 women annually and killing more than 40,000 women each year.[1] In the United States, more than $20 billion is spent annually to screen and treat this disease.[2] Personalized breast cancer prevention strategies are necessary to accurately predict the risk of developing breast cancer and to find better ways to prevent the disease altogether.

Breast cancer prevention is the "action taken to decrease the chance of developing cancer."[3] This definition is challenging to put into action because it requires an individual to play an active role in avoiding risk factors such as smoking,

obesity, lack of exercise, alcohol consumption, and radiation exposure, and increasing protective factors such as engaging in regular physical activity and maintaining a healthy weight and a healthy diet.[3]

In addition to lifestyle modification, cancer prevention can be achieved through chemoprevention and risk-reducing surgery. However, few interventions to date have demonstrated a survival advantage.

The challenge is to determine which women are at highest risk for developing a primary or secondary breast cancer. The ability to risk stratify has been enhanced by years of epidemiologic and clinical research and the understanding of how certain risk factors impact the short- and long-term risk of developing breast cancer. General recommendations should include lifestyle modification focused on increasing exercise and weight control. A more personalized approach focused on individualized risk is necessary to recommend appropriate breast cancer screening, chemoprevention, and preventive surgery. This review will cover the current state of breast cancer prevention, from primary prevention through survivorship, highlight cross-cutting issues, and will discuss strategies for clinical integration and future research.

Understanding Breast Cancer Risk

Assessing breast cancer risk has been enhanced over the past two decades, with more comprehensive risk assessment models and the ability to calculate and integrate risk factors and estimates into electronic health records. Models include many factors for assessing breast cancer risk a age, reproductive factors and sex hormone exposure, biopsy history and results, and family history of breast and ovarian cancer. Models for a high-risk population, especially those with precancerous changes, include the Breast Cancer Risk Assessment Tool (BCRAT or GAIL Model)[4,5] or the International Breast Cancer Intervention Study (IBIS) or Tyrer-Cuzick model,[6] and those more specific to the probability of carrying a BRCA1 or BRCA2 mutation include the BOAD ICEA, CLAUS, and BRCAPRO (an upcoming enhancement to the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) will include PALB2 and RAD51).[7-12]

Hereditary Cancer Risk

Having a germline mutation can increase the risk of breast cancer from 1.5RR to >5RR. BRCA1 and BRCA2 mutations are the most common genes associated with hereditary breast (and related) cancers. However, with next-generation sequencing of multiple genes there is the ability to test for many genes, regardless of penetrance. Table 1 includes a list of high- and moderate-penetrance mutations and the types and lifetime risks of cancer. Genetic testing and the review of personal and family history is recommended across the cancer control continuum: prior to, at the time of, and ongoing into breast cancer survivorship.[13]

Single-Nucleotide Polymorphisms

In addition to germline testing for high- and moderate-penetrance gene mutations, there are also panels of low-penetrance genetic risk factors or single-nucleotide polymorphisms (SNPs). Although SNPs are not used as part of standard clinical practice, current estimates suggest that there are over 65 SNPs that might, either by themselves or in combination, be helpful in refining breast cancer risk assessment. The challenge will be to incorporate SNP testing into a clinical workflow and to interpret the impact on risk beyond of those factors already established.[14,15]

Mammographic Breast Density

Having dense breast tissue (heterogeneously or extremely dense by mammogram) is linked to an increased risk of developing breast cancer compared with women with less dense breast tissue. However, there is not a standard for measuring breast density. In addition, many states have passed laws requiring breast density to be included in patient result letters, but there are limited follow-up options outside of additional imaging for certain individuals with increased breast density.[16]

Intra-Epithelial Neoplasia

Because of widespread use of breast cancer imaging, early proliferative lesions or intraepithelial neoplasia (IEN) has become more prevalent.[17] IEN includes proliferative breast disease without atypia, atypical ductal and lobular hyperplasia, and in situ breast cancer (Fig. 1). IEN is an established risk biomarker with the closest direct biologic association with invasive breast cancer.[17] Normal or non-proliferative tissue