Predictors of Future Breast Cancer Risk

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Breast cancer is the second leading cause of death from cancer among women in the United States. Its incidence rose from 94.6 to 124.3 cases per 100,000 women between 1980 and 1987, although the mortality remained stable at 31.1 deaths per 100,000 (1). Mammography screening offers the most promising potential avenue for reduction of breast cancer mortality. The pooled results of several large randomized clinical trials suggest that mammographic screening reduces breast cancer mortality among women 50–69 years of age by approximately 39% (1). To achieve this goal, screening programs must adhere strictly to quality assurance guidelines, and women with abnormal screening results must be referred promptly for diagnosis and treatment. However, there continues to be controversy over the frequency of screening and the age groups that benefit most from participating in screening programs.

In this issue of Cancer Epidemiology, Biomarkers & Prevention, Holowaty et al. (2) suggest that risk factor information obtained at the time of initial breast screening may have more discriminatory power than etiological risk factors in predicting the short-term risk for breast cancer. They used a nested case-control design drawn from the study population of the Canadian National Breast Screening Study. The analysis is based on women 40–59 years old who presented with breast cancer up to 4 years following the initial breast screen, which consisted of a two-view mammographic examination and physical examination plus a risk factor survey. Of the etiological risk factors considered, only age at entry (or years menstruating) was significant for later breast cancer. Women with a mammographic film parenchymal pattern classified as either P-2 or DY had a 2-fold risk of breast cancer. An abnormality reported by either the radiologist or a nurse examiner was also associated with an independent significant risk. The authors conclude that although some discrimination was achieved, this was not sufficient to determine the frequency of rescreening.

The fact that breast parenchymal pattern could predict for future breast cancer risk among women participating in a screening program is intriguing but controversial. Wolfe (3) published a classification schema that groups the mammographic appearance of the breast into four categories: N-1, when the breasts appear to contain almost all fat with little radiographic density; P-1, when the breast is mostly fat with visible ducts occupying up to 25% of the breast volume; P-2, if more than 25% of the breast is occupied by visible ducts; and DY, if the breasts contain structures producing diffuse areas of radiographic density. The latter was an unfortunate choice of term, since it suggested this density was synonymous with mammary dysplasia. There have been no satisfactory clinical pathologic studies of this classification system. Moreover, Wolfe used xerography, a technique which when compared to film-screen mammography, produces more variable images, lacks contrast capability, and can miss subtle abnormalities.

In 1976, Wolfe (3) reported that women with dense mammary parenchyma were at 37 times greater risk for developing breast cancer than women with the N-1 pattern. Two prospective studies that used data from the Breast Cancer Detection Demonstration Project and one from hospital-based mammography units in Boston and Livingston, New Jersey, have shown an association between Wolfe patterns P-2 and DY and breast cancer occurrence with relative risks of approximately 2–3 (4–6). Boyd et al. (7) criticize the methodology of some of these studies; nevertheless, the magnitude and significance of parenchymal patterns as risk factors remain in question. It is unlikely that the differences attributed to the P-2 and DY category are due to “masking,” i.e., denser breast parenchyma obscuring an extant breast cancer, resulting in an initially negative mammogram and a delay in diagnosis. The report by Holowaty et al. is another prospectively designed study to test this association; however, while the data are statistically significant, they do not have a clinical application at this time.

Unfortunately, the Canadian Study did not establish a formal system to train radiologists to consistently apply the parenchymal pattern classification. Misclassification errors have been blamed for inconsistencies in study results and for the inability of many investigators to replicate Wolfe’s findings. Grove et al. (8) have shown that as the proportion of women misclassified increases, “true” relative risks are increasingly underestimated. Tonilolo et al. (9) have demonstrated that consensus conferences between radiologists to resolve classification conflicts provide a simple, reliable, and easily applicable method which could impact on future studies in this area. The American College of Radiology has developed a standardized nomenclature for breast image reporting (10). The use of this 5-category reporting system with well-defined and agreed-upon descriptors would help to reduce errors in interpretation that undoubtedly occurred in the Canadian Study.

We have reported that women with suspicious mammograms had substantial mammography-related anxiety and worries about breast cancer (11). Such worries affected the moods and daily functioning of these women, despite diagnostic evaluation excluding malignancy. Our study suggests that risk notification and subsequent cancer-related concerns are key motivators of continued adherence to recommended health behaviors such as participation in annual screening mammography. Holowaty et al. do not comment on the adherence rate or the psychological effect in women determined to have un-
favorable parenchymal patterns or abnormalities detected by the radiologist or the nurse examiner.

The Canadian investigators are to be commended for initiating a population-based breast cancer screening program which has been used to study mammographic parenchymal patterns as a risk factor for breast cancer. I look forward to their future analyses, especially if they include a more quantitative assessment of the mammographic pattern and better clinical-pathological correlations between imaging patterns and breast dysplasia.

References
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