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Oppong and King present a clear and concise review of the current data regarding lobular carcinoma in situ (LCIS) and discuss the rationale behind the current management recommendations for this disease. It is interesting to note that in 2011 we are still debating the clinical management of LCIS despite these lesions having first been recognized in the early 1900s.[1] Recent advances in genomic profiling have demonstrated that in some cases LCIS is no longer simply a risk factor for all types of breast cancer but also a precursor for invasive lobular cancer. It is the molecular characterization of these lesions that may potentially define those women with LCIS who are more likely to develop invasive cancer, and that can help identify targets for therapeutic interventions. However, it is still extremely difficult to determine the true incidence of LCIS in any population due to the fact that LCIS continues to be an incidental finding on biopsy or at surgery. The pleomorphic variant is an exception, since it can present with microcalcifications on mammography.[2] As stated by the authors, the proportion of LCIS in sample sets of benign breast disease is low, ranging between 0.5% and 4%, but the majority of these lesions are multicentric, suggesting a more widespread process. Further, although the risk per year of invasive cancer is 1%, the risk accumulates over time for at least 20 years.[3-7] Bilateral disease can also occur in up to 35% of cases, leading some women to opt for bilateral prophylactic mastectomy.

The management of LCIS continues to be a challenge due to the uncertainty among providers about the clinical significance of most LCIS lesions. Treatment recommendations range from core biopsy plus or minus tamoxifen, to bilateral prophylactic mastectomy. The lack of consensus reflects both individual responses to varying levels of risk and our inability to predict which women will develop breast cancer. The current National Comprehensive Cancer Network (NCCN) guidelines, as described in the article by Oppong and King, recommend surgical excision to ensure that there is no adjacent carcinoma, and then counseling regarding risk-reduction options, such as chemoprevention and prophylactic mastectomy.[8] Clear surgical margins are not considered essential, based on the fact that subsequent invasive cancer can occur in either breast. This recommendation regarding the nonessential nature of clear margins may, however, prove to be different in specific precursor lesions.

Broadly stated, there are two main areas of research that could help refine the current management of LCIS. The first is development of the ability to define at diagnosis those LCIS lesions that are precursor lesions and that are likely to progress to invasive lobular cancers. The ability to do this could then narrow down the list of possible treatment approaches. For example, the pleomorphic subtype appears to be more aggressive,[9] but it is unclear whether it is associated with a high risk of invasive cancer. E-cadherin and the α, β, and γ catenin genes that encode for cellular adhesion molecules are examples of markers that could be used to identify precursor lesions. Loss of expression of these genes has been observed in invasive lobular cancer and adjacent LCIS lesions.[10-12] Longitudinal studies are now needed to confirm the temporality of these findings and to ascertain the risk of invasive cancer associated with these specific lesions.

The second research area involves the generation of risk estimates for invasive breast cancer among younger women diagnosed with LCIS. The recent recommendation by the American Cancer Society to consider annual MRI screening at a younger age for women with a cumulative lifetime breast cancer risk of 20% to 25%,[13] along with the introduction of image-guided biopsies, is likely to result in LCIS being diagnosed more frequently and at an earlier age. By understanding the short- and long-term risk of invasive cancer in these women, we will be able to determine the appropriate time to intervene.

Lastly, it appears that the potential benefit of chemoprevention agents such as tamoxifen in women with LCIS has been underappreciated. In the National Surgical Adjuvant Breast and Bowel Project...
(NSABBP) P-1 Breast Cancer Prevention Study, the subset of women with LN who received tamoxifen once a day for 5 years had a 56% reduction in breast cancer risk compared with those who received placebo. This benefit continues to be seen after cessation of tamoxifen therapy during follow-up of at least 10 years.[14] Further, the increased risk of certain serious side effects, including blood clots and vascular events, which occurred in a small number of participants, was only observed during the treatment period. Therefore, in women with LCIS, physicians should consider recommending tamoxifen in those who are premenopausal but post-childbearing and in those who are postmenopausal; they should also consider recommending exemestane (after it is FDA-approved) in postmenopausal women, provided they have no contraindications to therapy. Based on data from nine population-based registries that were part of the Surveillance, Epidemiology, and End Results (SEER) Program, LCIS incidence rates increased fourfold between 1987 and 1999, with a particularly notable increase in postmenopausal women.[15] It is also important to remember that breast cancer risk is a dynamic process that increases with age and that is influenced by other factors, such as family and biopsy history, that can change over time. Therefore, a woman’s risk should be reassessed periodically so that decisions regarding screening and risk-reduction approaches can be optimized.

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