SESSION 5

Primary Prevention of Breast Cancer I: Ovarian Suppression and Ablation in Premenopausal Women at Risk

S12. The Problems of Risk Selection: Scientific and Psychosocial Aspects

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Nine to eighteen thousand new cases of breast cancer per year in the United States are associated with a genetically-defined predisposition [1,2]. Mutations in BRCA1 and 2 account for greater than 60% of inherited breast cancer. Mutations in additional undiscovered high and low penetrance genes may account for the other 40% of inherited breast cancer cases and possibly a subset of familial breast cancer cases that lacks an autosomal dominant pattern of inheritance. False negative rates resulting from gene sequencing of BRCA1 and 2 may be as high as 10-15% making the identification of high-risk individuals a complex and often futile process for both patient and physician. As a consequence of technical limitations in BRCA1 and 2 genetic testing and the lack of comprehensive breast cancer prediction models that take into account both genetic and environmental factors, we are unable to quantify future breast cancer risk for many patients. This uncertainty often leads to the exclusion of high-risk individuals in screening and prevention trials, which is perhaps most evident in breast cancer screening trials incorporating the use of MRI to identify early cancers [3–5]. These studies demonstrate that MRI increases the sensitivity of a screening protocol in mutation carriers and succeeds at detecting earlier stage cancers [6–8]. Eligibility criterion for most of these trials was documented mutations in BRCA1 and 2 or future breast cancer risk predicted by family history or models, thereby possibly excluding women at significantly elevated risk that testing failed to identify or whose risk is not adequately reflected based on current models used in risk assessment. We may be turning very high-risk women away from screening trials, recommending yearly mammography and clinical breast exam, when neither will be adequate for detecting their cancers early. In addition, the impact of risk-reducing strategies including bilateral prophylactic oophorectomy (BSO) and tamoxifen has not been analyzed in these studies. For example, a 40-year old BRCA2 carrier may only have a 10% and 50% lifetime risk of ovarian and breast cancer, respectively, and interventions including tamoxifen and breast MRI screening may significantly reduce the risk of both getting breast cancer and dying from it, thereby obviating the need for early screening or prophylactic surgeries, permitting these women to defer the quality of life struggles until they are older. A larger sample size is needed to determine the degree to which different subgroups of high-risk patients will benefit from MRI screening, with particular attention to women who have undergone BSO or who are taking tamoxifen. The challenges in risk selection are numerous and produce more questions than answers with regard to screening and management of high-risk individuals. In the future, we hope that early detection tools, risk-reduction strategies, and risk assessment preclude the need for prophylactic surgeries, inappropriate selection of patients for screening, and the associated decisions that compromise our patients' quality of life.

References

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