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Hereditary breast cancer and genetic testing

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Individuals with germline BRCA1 and BRCA2 mutations have an up to 80% life time risk of breast and up to 45% life-time risk of ovarian cancer. Candidates for genetic evaluation include individuals with personal and/or family history of early onset breast cancer, personal or family history of ovarian cancer, bilateral breast cancer, and male breast cancer. Recent research has shown that there is a high prevalence of BRCA1 mutations in patients with triple negative breast cancer diagnosed at age 50 years or younger, regardless of family history. Therefore, these individuals are also recognized as candidates for genetic evaluation. Having a germline BRCA mutation has several implications on the patient as well as her/his family. For the patient, it can affect surgical treatment decisions, potential use of new agents in the neoadjuvant setting and being eligible for PARP inhibitor trials. For family members, it is an indication to undergo predictive testing (especially first degree relatives) and if found positive these high risk individuals would consider breast MRI screening in addition to yearly mammograms, and both at an earlier age. Bilateral preventive mastectomy is also an option that would reduce breast cancer risk by more than 95%. These individuals would also start ovarian screening until their late 30's and early 40's and ideally undergo bilateral salphingoohprectomy at that time. There are no completed prospective chemoprevention trials in BRCA mutation carriers; therefore, there is no standard of care in that regard. Genetic counseling and testing has recently become more complicated after several companies have started offering genetic testing fir multiple genes in their panels. Some panels include low penetrance genes, for which, if found positive, there are no standard cancer risk reduction recommendations. All of the above issues will be reviewed in a critical fashion based on available data and expert opinion.

Management of axilla in breast cancer: The saga continues

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Sentinel-lymph-node biopsy(SLNB) has not been subjected to the STARD(Standards for Reporting of Diagnostic Accuracy) for defining its role in management of axilla in breast cancer patients. Prospective trials investigating the accuracy of SLNB for cN0 (primary surgical therapy) and cN1 patients (neoadjuvant chemotherapy) have not utilized likelihood ratios(LR) to assess the impact of false negative SLNB. This review utilizes the: (i) Reported rates for pre-test probabilities of node positive disease from Surveillance, Epidemiology, and End Results(SEER) database for the cN0 patients (primary surgical therapy) for each T stage; calculatesthe negative LR from NSABP B-32 trial data; and uses the Bayesian nomogram to compute the post-test probability of missing the metastatic axillary node based on negative SLNB. (ii) Reported rates of complete axillary response in ACOSOG-Z1071 trial for cN1 patients to calculate the pre-test probabilities of residual nodal disease for each biological tumor sub-type; calculates the negative LR from ACOSOG-Z1071, and SENTINA trial data; and uses the Bayesian nomogram to compute the post-test probability of missing the residual metastatic axillary node based on negative SLNB. For cN0 disease, the odds of missing axillary disease based on negative SLNB for each T stage are: T1a=0.7%; T1b=1.1%; T1c=4%; T2=6%; T3=17%. For cN1 disease, the odds of missing residual axillary disease based on negative SLNB for each biological subtype are: HER2neu+=7%; Triple negative=13%; ER+/PR+/HER2neu-=40%. Negative LR is more accurate and superior to false negative rate for determining the clinical utility of SLNB by taking into account the changing pre-test probability of disease.