Prevalence of \textit{BRCA1} and \textit{BRCA2} Mutations in Patients with Ductal Carcinoma In Situ (DCIS)

It is well documented that \textit{BRCA1} and \textit{BRCA2} mutations are responsible for the majority of cases of hereditary breast and ovarian cancer. Factors such as personal and family history of premenopausal breast cancer, ovarian cancer at any age or multiple primary cancers have all been shown to increase the likelihood of carrying a mutation in one of these genes. Nearly all of the studies on \textit{BRCA1} and \textit{BRCA2} limit breast cancer diagnoses to invasive breast cancer, not considering in situ breast cancers. The following data examines the prevalence of mutations in patients with DCIS.


Design and Methods: The 369 participants in this case-control population-based study were diagnosed with DCIS between the ages of 20 and 79. All women underwent full sequencing of \textit{BRCA1} and \textit{BRCA2} between 1994 and 1998.

Results:

- 3% (11/369) of women were identified to carry deleterious mutations
- 36% (4/11) of the carriers did not report a family history of breast and ovarian cancer
- 54% (6/11) of carriers developed a second breast lesion or ovarian cancer within 7 years of initial diagnosis
- 5.4% (7/131) of patients diagnosed with DCIS under age 50 had a mutation

Conclusion: DCIS is part of the hereditary breast and ovarian cancer syndrome. These findings suggest that women with DCIS should be considered candidates for \textit{BRCA1/2} testing in the same manner as women with invasive breast cancer so appropriate medical management strategies can be implemented.


Design and Methods: This is a cross-sectional study looking at 7,296 women with a personal history of carcinoma in situ (CIS) who had genetic testing between 2006 to 2008. This study included both ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS), but LCIS was believed to account for less than 10% of cases. All women underwent full sequencing of \textit{BRCA1} and \textit{BRCA2} and break-point analysis for 5 common large genomic rearrangements in \textit{BRCA1} (5-site large rearrangement panel). Additionally, a small subset of women had additional testing for large gene deletions and rearrangements.

Results:

- 5.9% (428/7295) of women were identified to carry deleterious mutations
- 2.3% (17/738) of the carriers did not report a family history of breast and ovarian cancer
- 10.3% (162/1572) of women with CIS and personal and family history of invasive breast cancer and/or ovarian cancer were found to carry deleterious mutations

Conclusion: DCIS is part of the cancer spectrum in \textit{BRCA1/2} carriers. There was increasing prevalence of these mutations in women with more severe personal and/or family histories of invasive breast cancer and/or ovarian cancer. There was also a significant association of these mutations being found in those with young onset breast CIS.

Professional practice guidelines, including the National Comprehensive Cancer Network (NCCN), include invasive breast cancer \textit{as well as} DCIS as a risk factor for \textit{BRCA} mutations.

Bottom Line: These data highlight the importance of evaluating women diagnosed with DCIS for hereditary breast and ovarian cancer syndrome especially when it is diagnosed prior to 50 years of age or in conjunction with a suggestive family history.