Cancer Incidence in First and Second Degree Relatives of BRCA1 and BRCA2 Mutation Carriers

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Mutations in the BRCA1 or BRCA2 genes are associated with increased risks for breast, ovarian, and several other cancers. The purpose of this study was to evaluate the incidence of cancers other than breast and ovarian in first and second degree relatives of BRCA mutation carriers compared to the general population. A total of 1086 pedigrees of BRCA mutation carriers was obtained from a prospectively maintained, internal review board approved study of persons referred for clinical genetic counseling at The University of Texas MD Anderson Cancer Center. We identified 9032 first and second degree relatives from 784 pedigrees which demonstrated a clear indication of parental origin of mutation. Standardized incidence ratios (SIRs) were used to compare the observed incidence of 20 primary cancer sites to the expected incidence of each cancer based on calculated risk estimates according to a subject’s age.

BRCA1 families had increased SIRs for breast and ovarian cancer (p<0.001) and decreased SIRs for kidney, lung, Non-Hodgkin's lymphoma, prostate, and thyroid cancer (p<0.001). BRCA2 families had increased SIRs for breast, ovarian, and pancreatic cancer (p<0.001) and decreased SIRs for kidney, lung, Non-Hodgkin's lymphoma, thyroid, and uterine cancer (p<0.0025). Analysis of only first degree relatives (4099 individuals) identified no decreased SIRs and agreed with the increased SIRs observed in the overall study population. We confirmed previous reports of an association between breast, ovarian, and pancreatic cancers with BRCA mutations. Additional research to quantify the relative risks of these cancers for BRCA mutation carriers can help tailor recommendations for risk reduction.

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