

BRCA1 and BRCA2 Mutation Prevalence in Individuals Undergoing Clinical Testing at Myriad Genetic Laboratories

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Abstract

Accurate risk assessment for hereditary breast and ovarian cancer (HBOC) is dependent on clinical expertise and the models available to evaluate an individual's risk. These models depend heavily, if not exclusively, on estimates of mutation prevalence in individuals presenting with various personal and family histories of cancer. In order to assess the BRCA1 and BRCA2 mutation prevalence in individuals tested in a clinical setting through our diagnostic laboratory, the results of 32,346 consecutive full-gene-sequence analyses and Ashkenazi Jewish founder mutation analyses were correlated with clinical information provided on a routine test requisition form. The prevalence of deleterious mutations was correlated with personal and family histories of breast and ovarian cancer, as well as ethnicity and gender. Patients tested through specific research protocols and patients for whom relevant information was not provided were not included.

The results of this correlation were published initially in 2002 by Frank et al. and have been updated periodically; they are available on the Myriad Web site as mutation prevalence tables.^{1,2} Two tables exist: one for patients of Ashkenazi Jewish ancestry and another for all other patients. Overall, deleterious mutations were identified in 1,688 (18.7%) of the 9,029 individuals tested who indicated Ashkenazi ancestry, and in 3,508 (15.0%) of the 23,317 individuals tested who did not indicate Ashkenazi ancestry. Of the individuals who indicated Ashkenazi ancestry, mutations were identified in 554 (23.8%) of 2,324 women with breast cancer diagnosed before age 50 and in 170 (35.9%) of 473 with ovarian cancer at any age. Of all other individuals, mutations were identified in 1,937 (19.5%) of 9,950 women diagnosed with breast cancer before age 50 and in 388 (27.0%) of 1,438 with ovarian cancer at any age.

One limitation of this analysis is the variability that likely exists in the clinical histories recorded on the test requisition forms, both from patient recall and from accurate documentation of cancer history on the form. However, the histories reported are expected to be similar to what is seen in comparable clinical settings. We therefore conclude that this large series of individuals tested for BRCA1 and BRCA2 mutations in a clinical setting provides useful estimates of the prevalence of mutations in patients with personal and/or family histories of breast and ovarian cancer. Further studies in a controlled setting are needed to resolve outstanding differences in the levels of risk predicted by these mutation prevalence tables and other current HBOC risk prediction models.

References

1. Frank TS, Deffenbaugh AM, Reid JE, Hulick M, Ward BE, Lingenfelter B, et al. Clinical characteristics of individuals with germline mutations in BRCA1 and BRCA2: Analysis of 10,000 individuals. *J Clin Oncol* 2002;20:1480-90.
2. www.myriadtests.com/provider/mutprev