Benefits and safety of multigene panel testing in patients at risk for hereditary breast cancer.

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Abstract Disclosures

Abstract:

Background: Recently introduced multi-gene panel testing including *BRCA1* and *BRCA2* genes (*BRCA1/2*) for hereditary cancer risk has raised concerns with the ability to detect all deleterious *BRCA1/2* mutations compared to older methods of sequentially testing *BRCA1/2* separately. The purpose of this study is to evaluate rates of pathogenic *BRCA1/2*mutations and variants of uncertain significance (VUS) between previous restricted algorithms of genetic testing and newer approaches of multi-gene testing. **Methods:** Data was collected retrospectively from 966 patients who underwent genetic testing at one of three sites from a single institution. Test results were compared between patients who underwent *BRCA1/2*testing only (limited group, n = 629) to those who underwent multi-gene testing with 5-43 cancer-related genes (panel group, n = 337). **Results:** Deleterious *BRCA1/2* mutations were identified in 37 patients, with equivalent rates between limited and panel groups (4.0% vs 3.6%, respectively, p = 0.86). Thirty-nine patients had a *BRCA1/2* VUS, with similar rates between limited and panel groups (4.5% vs 3.3%, respectively, p = 0.49). On multivariate analysis, there was no difference in detection of either *BRCA1/2* mutations or VUS between both groups. Of patients undergoing panel testing, an additional 3.9% (n = 13) had non-BRCA pathogenic mutations and 13.4% (n = 45) had non-BRCA VUSs. Mutations in *PALB2*, *CHEK2*, and *ATM* were the most common non-BRCA mutations identified.**Conclusions:** Multi-gene panel testing detects pathogenic *BRCA1/2* mutations at equivalent rates as limited testing and increases the diagnostic yield. Panel testing increases the VUS rate, mainly due to non-BRCA genes. Patients at risk for hereditary breast cancer can safely benefit from upfront, more efficient, multi-gene panel testing.