BENEFITS AND SAFETY OF MULTIGENE PANEL TESTING IN PATIENTS AT RISK FOR HEREDITARY BREAST CANCER

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BACKGROUND

- Genetic testing for hereditary breast cancer risk has been in rapid evolution.
- Conventional testing required initial testing for BRCA1/2 mutations followed by sequential testing for other breast cancer-related gene mutations when applicable.
- New multi-gene panel testing evaluates up to 43 genetic mutations at once, including BRCA1/2.
- Some concern has been raised regarding the ability of multigene panel tests to evaluate BRCA1/2 genetic mutations.

OBJECTIVES

- Compare multigene panel testing with limited BRCA1/2 testing in the detection of pathogenic BRCA1/2 mutations and variants of uncertain significance (VUS).
- Evaluate total yield of pathogenic mutations detected by multigene panels.

METHODS

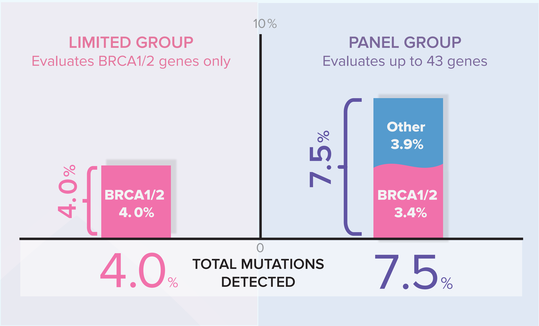
Data was collected retrospectively from 966 patients who underwent genetic testing at one of three Breastlink sites from January 2008 to September 2014 while under the supervision of a breast surgeon. Test results for 629 patients who received limited BRCA1/2 testing were compared with test results for 337 patients who received multigene panel testing through Ambry Genetics for 5 to 43 breast cancer-related genes. Multivariate analysis was used to control for variables.

	Limited Group *n*=629		Panel Group *n*=337		*p*-Value
Personal History of Breast Cancer	443	70.3	205	60.8%	0.003
Median Age at Breast Cancer Onset	49		52.5		0.002
Personal History of Ovarian Cancer	10	1.6	6	1.8%	NS
Ethnicity					0.006
African American	11	1.7%	3	0.9%	
Asian	23	3.8%	22	6.5%	
Caucasian	377	59.9%	180	53.5%	
Hispanic	13	2.1%	25	7.4%	
Ashkenazi Jewish	52	8.4%	48	7.4%	
Middle Eastern	15	2.4%	7	2.1%	
Multiple Ethnicities	49	7.8%	37	11.0%	
Native American	2	0.3%	1	0.3%	
Unknown/Other	87	13.5%	14	4.2%	
Family History of Breast Cancer	484/620	78.1%	248	73.6%	NS
≥1 Family Member with Breast Cancer at Age <50	264/620	42.6%	127	37.7%	
Family History of Ovarian Cancer	132/620	21.3%	67	19.9%	NS
Pathogenic BRCA 1/2 mutation	25	4.0%	12	3.6%	NS
Variant of Uncertain Significance in BRCA1/2	28	4.5%	11	3.3%	NS

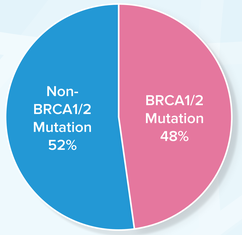
RESULTS

Pathogenic BRCA1/2 mutations were identified in 37 patients, with equivalent rates between limited and multigene panel groups. Of patients undergoing multigene testing, an additional 13 had non-BRCA pathogenic mutations. Mutations in PALB2, CHEK2 and ATM were the most common non-BRCA1/2 mutations observed. A total of 39 patients had BRCA1/2 VUS, with similar rates between limited and multigene groups. An additional 45 patients in the multigene group had non-BRCA1/2 VUS.

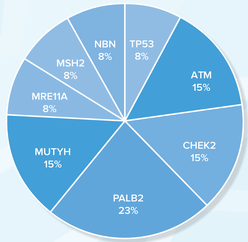
PATHOGENIC MUTATIONS DETECTED



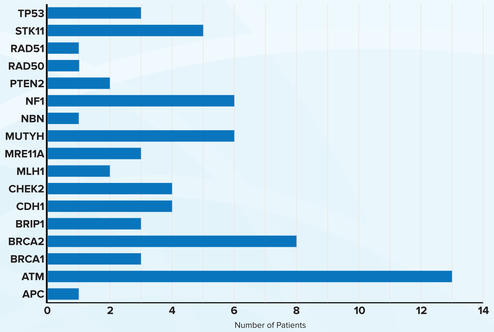
PATHOGENIC MUTATIONS IN MULTIGENE PANEL GROUP



NON-BRCA1/2 PAHTOGENIC MUTATIONS



FREQUENCY OF VUS IN MULTIGENE GROUP



CONCLUSIONS

- Multigene panel testing safely and effectively evaluates BRCA1/2 pathogenic mutations and VUS.
- Pathogenic mutations in non-BRCA1/2 genes have important implications for risk management and treatment algorithms.
- Multigene panel testing nearly doubles the total rate of detection of pathogenic mutations.
- Breast surgeons and oncologists have an important opportunity to discuss the benefits of multigene panel testing with their patients.

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