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Multigene Panel Testing Increases Yield of Surgically-Actionable Results Among Breast Cancer Patients.

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BACKGROUND

- Germline *BRCA1/2* testing may be recommended for some patients diagnosed with breast cancer to guide surgical management.
- Studies have identified additional hereditary breast cancer genes[1].
- Multigene panel testing (MGPT) allows for simultaneous testing of *BRCA1/2 and* other breast cancer genes.
- National Comprehensive Cancer Network (NCCN®) guidelines have evolved to include surgical management considerations for multiple cancer susceptibility genes.
- This study aims to determine the likelihood of a surgically actionable result based on NCCN® guidelines beyond *BRCA1/2* when using a breast cancer-specific MGPT.

METHODS

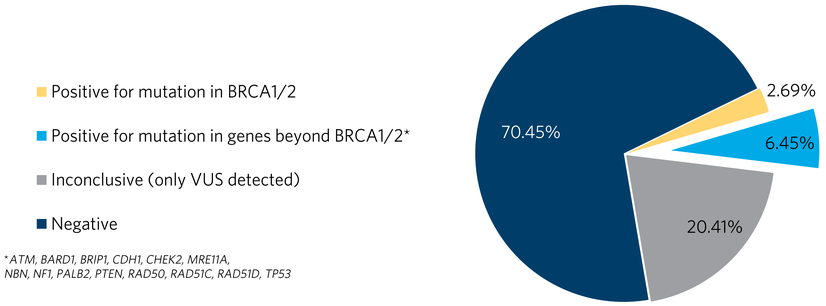
- We performed a retrospective analysis in our cohort of female patients with a breast cancer diagnosis who had testing with a 17-gene breast cancer-specific MGPT (*ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, MRE11A, MUTYH, NBN, NF1, PALB2, PTEN, RAD50, RAD51C, RAD51D, TP53*) between June 2012 and December 2016.
- The frequency of likely pathogenic and pathogenic variants (mutations) was calculated for each gene.
- NCCN® guidelines (Version 1.2018) were used to determine surgically-actionable findings for breast and other cancers.

REFERENCES

1. Castéra L, et al. Next-generation sequencing for the diagnosis of hereditary breast and ovarian cancer using genomic capture targeting multiple candidate genes. *Eur J Hum Genet.* 2014 Feb 19.

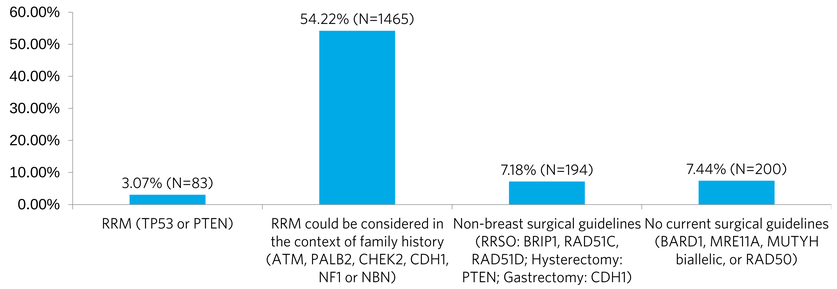
2. NCCN Clinical Practice Guidelines in Oncology®. Genetic/Familial High-Risk Assessment: Breast and Ovarian. V1.2018. Available at nccn.org

Overall Multigene Panel Testing Results



ATM, BARD1, BRIP1, CDH1, CHEK2, MRE11A, NBN, NF1, PALB2, PTEN, RAD50, RAD51C, RAD51D, TP53

Surgically Actionable Findings Among Mutation Carriers (beyond *BRCA1/2*)



Mutation Spectrum of Pathogenic or Likely Pathogenic Result

Gene	Mutation		Current NCCN guidelines
	N	%	
ATM	343	1.16	Consider RRM in context of family history
BARD1	80	0.27	None at this time
BRCA1	366	1.29	RRM and RRSO
BRCA2	429	1.52	RRM and RRSO
BRIP1	86	0.29	RRSO
CDH1	18	0.06	Consider RRM in context of family history and gastrectomy
CHEK2	762	2.58	Consider RRM in context of family history
MRE11A	39	0.13	None at this time
MUTYH (bialleic)	1	0.00	None at this time
NBN	59	0.20	Consider RRM in context of family history
NF1	49	0.18	Consider RRM in context of family history
PALB2	289	0.98	Consider RRM in context of family history
PTEN	17	0.06	RRM, hysterectomy
RAD50	80	0.27	None at this time
RAD51C	49	0.17	RRSO
RAD51D	26	0.10	RRSO
TP53	66	0.22	RRM

RESULTS

- Of 29,568 breast cancer patients tested, 9.14% (n=2702) were identified to carry a likely pathogenic or pathogenic variant in at least one breast cancer susceptibility gene (excluding *MUTYH* carriers).
- 2.69% (n=794) of patients were positive for a mutation in either *BRCA1* or *BRCA2*. One patient was positive for a mutation in both *BRCA1* and *BRCA2*.
- 6.45% (n=1908) of patients tested positive for a mutation(s) in genes beyond *BRCA1/2*.
- According to NCCN® guidelines, risk reducing mastectomy (RRM) could be considered for an additional 3.07% of positive patients (N=83).
- As indicated by NCCN® guidelines, RRM could be considered for an additional 54.22% of positive patients (N=1465) in the context of a significant family history of breast cancer.
- An additional 7.18% of positive patients (N=194) had a surgically actionable finding for sites beyond breast, including consideration of risk-reducing salpingo-oophorectomy (RRSO) (N=159), gastrectomy (N=18), and hysterectomy (N=17).

TAKE-HOME POINTS

- Expanding testing beyond *BRCA1/2* for breast cancer patients eligible for genetic testing identifies additional patients who may benefit from discussion of surgical options.
- Breast cancer-specific MGPT also identifies patients who would be at an increased risk for endometrial, ovarian, or gastric cancer and can consider surgical management options for these cancers.
- MGPT is an efficient and effective approach to identify more patients for whom discussion of surgical cancer risk management options is warranted.