DANA-FARBER/BRIGHAM AND WOMEN'S CANCER CENTER

Pathogenic variants among female breast cancer patients with a subsequent cancer demonstrate potential preventable cancer burden

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INTRODUCTION

- With both improved breast cancer (BC) survivorship and increasing genetic testing of patients (pts) with Stage 2-3 BC who are eligible for adjuvant Olaparib, it is important to identify and manage pts with pathogenic variants for additional cancer risks.
- Identification of PVs in cancer susceptibility genes impacts screening and options for risk-reduction in addition to cancer treatment.
- Herein, we report the burden of potentially preventable cancers.

OBJECTIVES

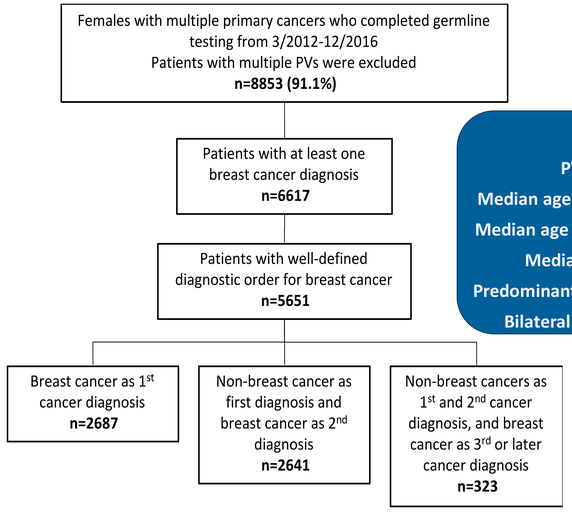
- Primary aim: To delineate the frequency and distribution of germline PVs among females with BC and cancer of another site.
- To determine germline PV prevalence by diagnostic order of BC.
- Characterize the preventable cancer burden among females with MPCs and a germline PVs who were first diagnosed with BC.

METHODS

- *Study population*: Patients age≥18 with MPCs who underwent germline testing from March 2012-December 2016 with Ambry Genetics for the following 21 genes: *ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, NBN, NF1, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11,* and *TP53.*
- Multiple cancers at one site were counted once only.
- Clinical characteristics were obtained from clinician-completed requisition forms and from clinical pedigrees and chart notes when provided.
- *Statistical analysis*: Descriptive statistics were used. T-tests were used to examine differences in ages at panel testing, first and second primary cancer diagnosis. For diagnostic order of BC, we performed χ^2 test. All statistical tests were two-sided, and a *P* value of <0.05 was considered statistically significant.

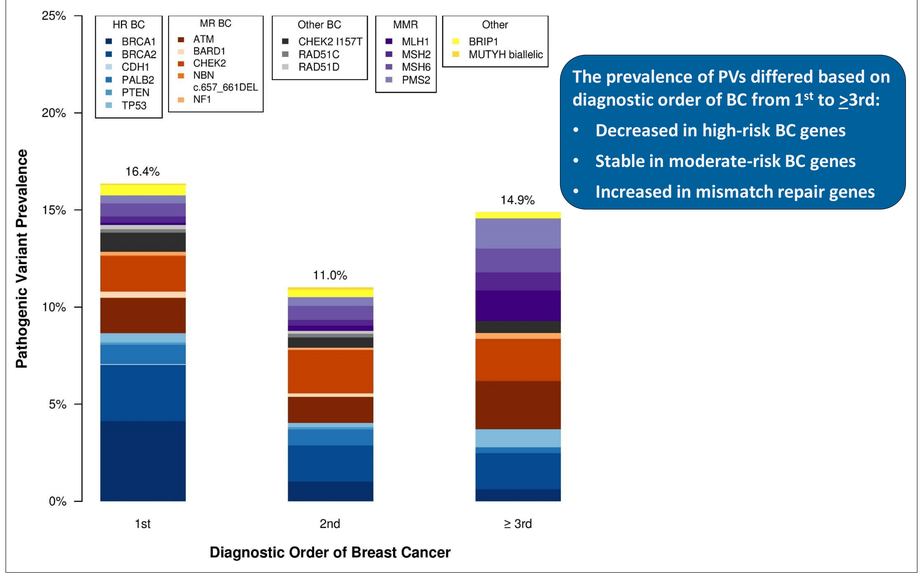
RESULTS

Prevalence of PVs among females with BC and a non-breast cancer diagnosis



At a glance

- PV in tested genes = 12.7%
- Median age at 1st cancer diagnosis = 49 (IQR:18)
- Median age at 2nd cancer diagnosis = 59 (IQR:16)
- Median age at testing = 63 (IQR: 16)
- Predominantly non-Hispanic white (4687, 70.8%)
- Bilateral BC rates were low (1007, 15.2%)

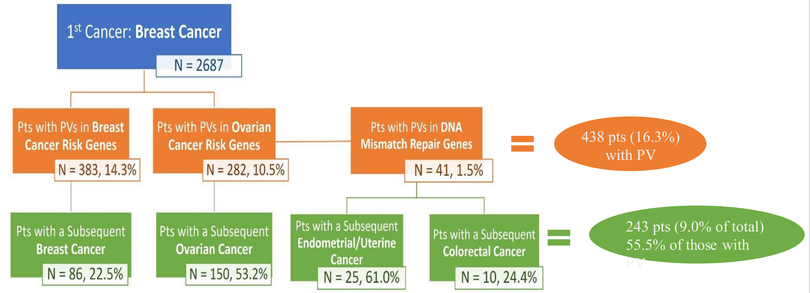


The prevalence of PVs differed based on diagnostic order of BC from 1st to ≥3rd:

- Decreased in high-risk BC genes
- Stable in moderate-risk BC genes
- Increased in mismatch repair genes

RESULTS

Cancer diagnoses subject to intervention based on PV among females diagnosed 1st with breast cancer



Breast cancer genes = *ATM, BARD1, BRCA1/2, CDH1, CHEK1, NBN 657del, NF1, PALB2, PTEN, RAD51C/D & TP53*
Ovarian cancer genes = *BRCA1/2, BRIP1, PALB2, RAD51C/D* & MMR genes (*MLH1, MSH2, MSH6, PMS2*)
Mismatch repair genes = *MLH1, MSH2, MSH6, & PMS2*

Amongst females with a PV identified, 55.5% (243) were subsequently diagnosed with cancers for which guidelines-based interventions may have resulted in a different outcome.

CONCLUSIONS

- Of 6617 females included in this study, 843 (12.7%) were identified to have a single PV in one of 21-cancer genes tested.
- By diagnostic order of breast cancer, PV prevalence was 16.4% (95% CI:15-17.8%) with BC as 1st cancer, 11.0% (95% CI:9.9-12.3%) for 2nd and 14.8% (95% CI:11.4-19.2%) as >3rd diagnostic order (p<0.001).
- Prevalence of PVs was high >10% regardless of diagnostic order of breast cancer in this cohort.
- Among females first were diagnosed with breast cancer who later developed a subsequent cancer, 16.3% (438/2687) had a hereditary cancer gene that may have impacted breast, ovarian, endometrial and/or colon cancer care, and among these pts, 55.5% (243/438) would have had different care prior to their subsequent cancer diagnosis had this gene been identified.

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