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Gender Disparity: Overlooking Hereditary Prostate Cancer and Implications for Urology Practice

Abstract#17-8316

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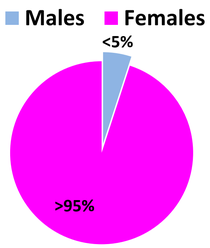
BACKGROUND

- Prostate cancer (PC) has been associated with germline mutations in several genes, most often *BRCA2*[1]
- Recently, 11.8% of men with metastatic prostate cancer were found to have germline mutations in *BRCA* and other DNA-repair genes[2]
- Men and women are equally likely to carry mutations in hereditary cancer genes and both have elevated cancer risks.
- NCCN guidelines recommend genetic testing for men with a personal and/or family history of high Gleason score prostate cancer with family history of breast, ovarian, and/or pancreatic cancers[3]. Despite this, over 95% of patients undergoing hereditary cancer multi-gene panel testing (MGPT) are women.
- We sought to describe results of MGPT in men with prostate cancer compared to women with breast cancer (BC)

BRCA-Related Multi-Gene Panel Testing (N>100,000)

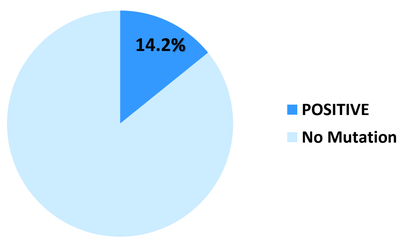


METHODS

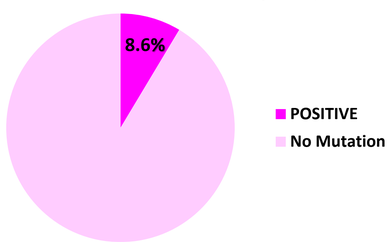
- Test results were reviewed for PC patients and female BC patients undergoing MGPT (June 2013 – June 2016) for up to 49 genes. Clinical history was obtained from ordering providers

MUTATION-POSITIVE RATES: MALES vs. FEMALES

Males w/Personal History of Prostate Cancer (N=654)

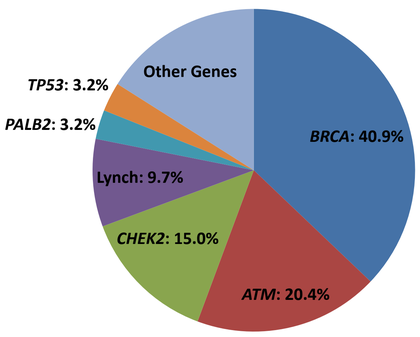


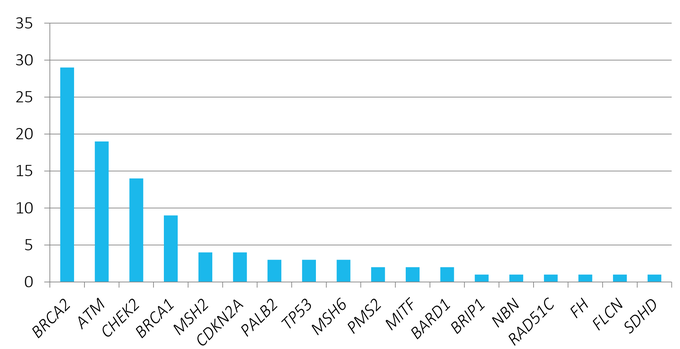
Females w/Personal History of Breast Cancer (N>71,000)



- 14.2% (93/654) of PC probands tested positive for one or more mutations, compared to 8.6% of women with BC
- Average age at PC diagnosis was 60.1yr for mutation-positive men and 59.9yr for mutation-negative men

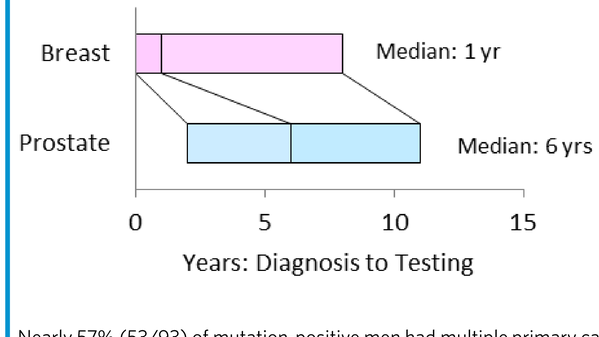
MULTI-GENE PANEL RESULTS FOR PROSTATE CANCER CASES





- 100 germline mutations were found in 93 men with PC, across 18 different genes
- *BRCA* mutations made up 40.9% of PC positives (38/93); *BRCA2* mutations accounted for over 31%, followed by *ATM* (20.4%), *CHEK2* (15.0%), and Lynch syndrome-associated genes (9.7%)
- Of the 100 total mutations, 94% were in genes that would impact management recommendations for PC probands and/or their relatives[3,4]

TIMING OF GENETIC TESTING



The median time from cancer diagnosis to MGPT was 6 years for PC probands, compared to 1 year for women with BC

Nearly 57% (53/93) of mutation-positive men had multiple primary cancers

- ~80% developed PC followed by additional cancer(s) which ultimately prompted genetic testing
- Of *BRCA* positives with multiple primaries (n=21), over 90% developed PC followed by subsequent cancers, yet testing was not initiated until another cancer developed

TAKE-HOME POINTS

- MGPT identified mutations in men with prostate cancer at rates almost 2-fold higher than females with breast cancer
- 59.1% of mutation positive PC probands had a *BRCA* or *ATM* mutation, making them possibly eligible for a PARP-inhibitor clinical trial
- Unfortunately, time from PC diagnosis to MGPT was several years longer than women, allowing many to develop subsequent cancers that may have been prevented or detected earlier with knowledge of the germline mutation
- Revisions to NCCN guidelines recognize the contribution of PC to Hereditary Breast and Ovarian Cancer; however increased awareness is needed to identify more male mutation carriers to enable appropriate cancer risk management for patients and their relatives
- Further studies are needed to explore possible explanations for the difference in mutation detection rates

REFERENCES

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2. Pritchard et al. N Engl J Med. 2016;375(5):443-53
3. Daly M, Pilarski R, et al: Genetic/Familial High-Risk Assessment: Breast and Ovarian Version 2.2017, NCCN Clinical Practice Guidelines in Oncology
4. Provenzale D, Gupta S, Ahnen DJ, et al: Genetic/Familial High-Risk Assessment: Colorectal Version 2.2016, NCCN Clinical Practice Guidelines in Oncology

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