

Abstract #1575: Population Genetic Screening for Hereditary Breast and Ovarian Cancer in At-Risk Patients: A Novel Testing and Prevention Model for Community Hospitals Reveals High Mutation Rates Rurally

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Background

Genetic testing for at-risk non-cancer patients continues to increase

We hypothesized rural areas could harbor higher than expected familial risks of breast and ovarian cancers due to demographic and social factors such as propinquity

We created a model to 1) assess our population for familial cancer risk, 2) provide genetic counseling and testing, and 3) offer risk reduction strategies based on outcomes

Methods

Study Design

Family history questionnaire designed to assess for the risk of HBOC using current NCCN guidelines and used at key intake points within the *unaffected* population to determine eligibility for genetic testing (and risk stratification).

First it was offered at the time of routine screening mammography for *all women* presenting to our rural hospital (which includes both unaffected and affected patients).

Second it was offered in a primary gynecology care setting to capture younger patients not yet participating in screening mammography (unaffected, and age <40).

Patients meeting HBOC criteria were sent a letter and two phone calls to schedule genetic counseling. Analysis by descriptive statistics.

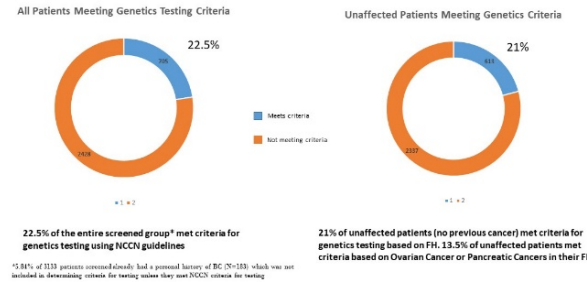
Study Endpoints

Number of screened patients (affected and unaffected by cancer), number meeting criteria for germline testing, number seen and tested, number of positives, number of negatives, and actions based on results:

- **3133** rural women screened at Critical Access Hospital in pilot study over first 8 months using our systematic approach to genetic risk assessment using a genetics extender (nurse with additional training in genetics through City of Hope). (TS)
- 22.5% of all female patients at intake met NCCN criteria for testing for HBOC, which was higher than we had anticipated. All patients offered counseling and testing. (41% of screened pts had + FH of BC, 8.1% + FH of OC, 5.4% + FH Panc Ca)
- 6% of women screened at time of mammogram had personal histories of BC or OC (affected pts), and 94% of women screened with questionnaire were *unaffected* (N=2950). Previous BC patients were still considered appropriate for testing if they met NCCN guidelines and were analyzed separately. The unaffected at-risk patients form the main group for this analysis, but the existing BC patients offer a nice comparison since it is from same provider group.

Patients Meeting Criteria for Germline Testing

Percentage Meeting Criteria for Germline Testing



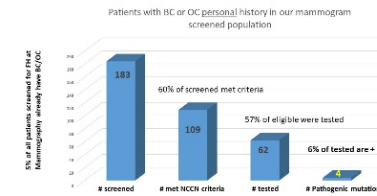
Conclusions

This rural model of screening and prevention of at risk patients is successful at detecting unknown background germline risks for cancers before they are diagnosed with cancer

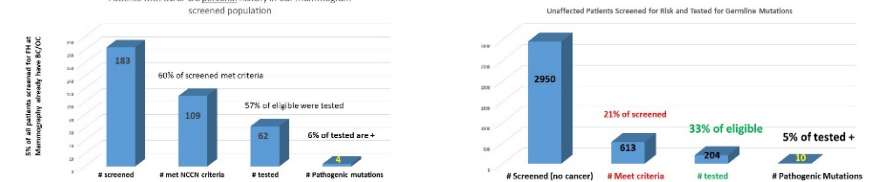
- The rate of +ve pathogenic mutations in tested (unaffected) patients without cancer (5% rate) is roughly similar to the known rates of germline mutations in existing (breast) cancer patients, which in our experience is 5-10% on any given year (last analysis was 5.3% of our aggressively tested patients).
- Discovering a pathogenic mutation before cancer of course is valuable in that it allows targeted screening for cancer and risk reduction strategies as well.
- We plan to expand this model to the male screening population in 2021, engage more primary clinics and offer testing for the larger population at risk using our FH questionnaire, which would increase testing.
- We also plan to use more expanded panel testing as newer mutations become linked to HBOC (currently all that are part of NCCN guidelines are included in our 19+ gene panels) and as testing becomes cheaper. In theory, with a high population carrier rate as we noted (1 in 295) of some pathogenic mutation, one might argue population testing might consider the most common few mutations as part of a mass screening program. We did not screen for Lynch Syndrome outside of the HBOC testing criteria, but it is worth noting the second most common cancers in our family histories were colorectal cancers (17% of screened families had +FH of CRC, none of whom we screened unless they also met HBOC criteria) with the population incidence of LS estimated to be 1 in 279.

Results

Patients counseled and tested (affected by Cancer)



Patients counseled and tested (unaffected)



Multi-gene panel test done for all patients agreeable to testing (19 to 84 genes), median was 19-gene high/moderate risk panel for breast and gynecological cancers. VUS not counted.

To date with a backlog of patients due to the higher numbers of eligible unaffected patients than anticipated (N=613), 210 patients have completed counseling, 204 completed panel testing, and 204 received post-testing counseling. Few patients deferred testing, mostly for personal reasons (e.g. disability, life insurance, etc.). 10 path mutations found in 204 patients.

10 pathogenic mutations found out of 2950 *unaffected* patients screened by FH questionnaires (3133 total patients minus 183 existing BC patients).

5 BRCA, 5 non-BRCA (PMS2, PMS2, CHEK2, CHEK2, PALB2) mutations in 204 tests. 1 patient had both BRCA and PMS2, 1 patient had both CHEK2 and PALB2. Cascade testing done (not counted in our figures) with appropriate management of all positives based on NCCN guidelines.

A pathogenic germline mutation rate occurred in ~5% of our screened and tested *unaffected* patients. The screening mammogram population was used to analyze our rates of eligibility and our testing rates as we had both controlled numerators and denominators to allow analysis.

Many patients did not follow-up to our letters or phone calls to agree to be tested and therefore could not be tested in this pilot study as desired to establish a much larger data set. They will be contacted again on subsequent intake as they will still meet criteria for testing.

In our *unaffected* population, 1 of 590 patients screened for HBOC carry a known BRCA mutation which is roughly the estimated population rate of 1 in 500 to 1 in 600.

In our *unaffected* population, some pathogenic mutation (BRCA or non-BRCA) occurs at a rate 1 out of 295 that increases the patient risk for HBOC-related Ca.

13 patients screened during this time developed BC (as a result of their imaging), and all were tested for genetic mutations (only 4 met NCCN guidelines and were negative, and the other 9 met ASocBS recommendations and were tested with 1 +ve for pathogenic mutation in PALB2 (and counted in affected group).