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Role of Familial and Genetic Risks in Breast Health

DR. TRAN TU HUYNH

MEDICAL DIRECTOR

COMPREHENSIVE BREAST PROGRAM

CAYUGA MEDICAL ASSOCIATES

*NOT INTENDED TO DIAGNOSE OR TREAT ANY DISEASE

**PLEASE CONSULT YOUR DOCTOR WITH ANY HEALTH CONCERNS

Disclosure

- Cayuga Health System
- OpticSurg Inc.

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Overview

- What is Familial and Genetic risks in relation to Breast Cancer?
- Who should have testing?
- What tests are available?
  - Should an updated/repeated test be done?
- Limitations of Genetic Testing
- Brief overview of hereditary Breast Cancer Syndromes
- Impact of Genetic testing results
- Variance of Unknown Significance (VUS)
- Screenings and Risks reductions

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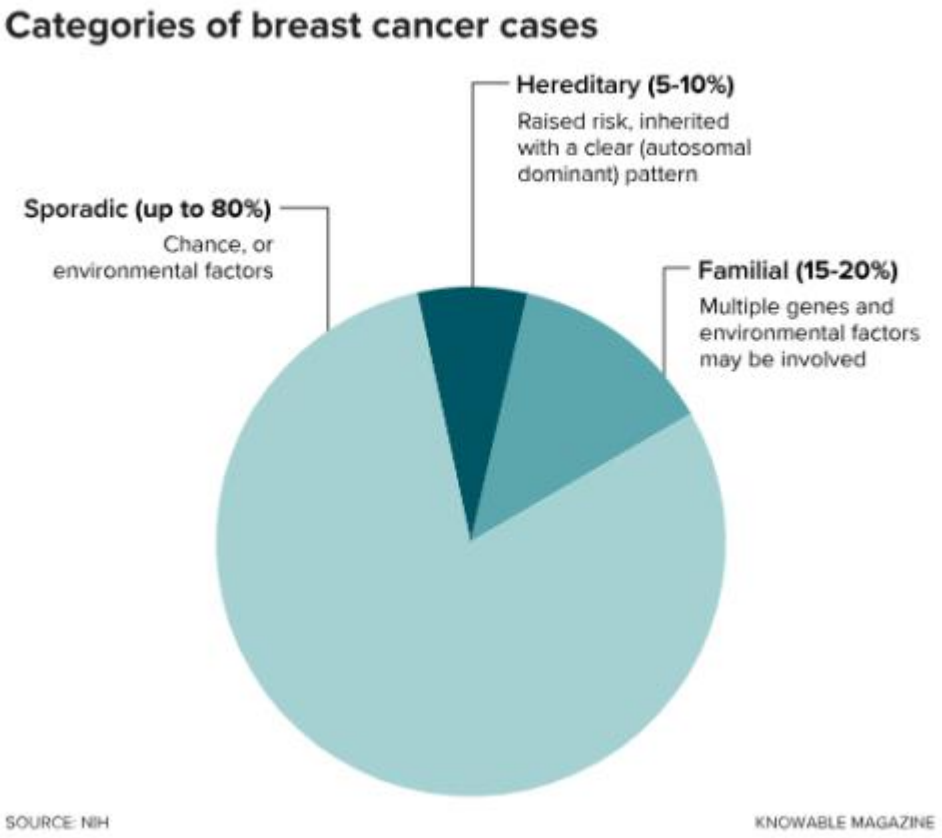
What is Familial and Genetic risks in relation to Breast Cancer?



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Who should have testing?

- Known blood relative with genetic abnormalities
- Personal history of cancer
  - Before 50 for receptor positive tumors
  - Before 60 for triple negative tumors
  - Ashkenazi Jewish ancestry with cancer at any age
    - Or close relative
  - Other cancers (Ovarian, Pancreatic, Prostate)
  - Aid in decision making of therapy, prophylaxis treatments
  - Strong family history of Breast, Ovarian, Pancreatic Cancers

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What tests are available?

- Multigenes panel

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Should an updated/repeated test be done?

- If testing was done before 2013

35 Genes Across 8 Important Cancer Types

GENES	BREAST	OVARIAN	COLORECTAL	UTERINE	MELANOMA	PANCREATIC	GASTRIC	PROSTATE	OTHER
BRCA1	●	●				●		●	
BRCA2	●	●			●	●		●	
MLH1		●	●	●		●	●	●	●
MSH2		●	●	●		●	●	●	●
MSH6		●	●	●		●	●	●	●
PMS2		●	●	●		●	●	●	●
EPCAM		●	●	●		●	●	●	●
APC			●			●	●		●
MUTYH Biallelic			●						●
MUTYH Monoallelic			●						
CDKN2A (p16INK4a)					●	●			
CDKN2A (p14ARF)					●	●			
CDK4					●	●			
TP53	●	●	●	●	●	●	●	●	●
PTEN	●		●	●	●				●
STK11	●	●	●	●		●	●		●
CDH1	●		●				●		
BMPR1A			●			●	●		●
SMAD4			●			●	●		●
PALB2	●					●			
CHEK2	●		●						
ATM	●					●			
NBN	●							●	
BARD1	●								

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Limitations of Genetic Testing

- Genetic testing is one of the tools
- Not every genetic test will yield straightforward answers
- Negative results do not mean tester is not at increased risk
- Insurance coverage for test
- How results may affect tester Life insurance coverage

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What are the hereditary Breast Cancer Syndromes?

- BRCA1, BRCA 2, PTEN, and TP53
- ATM, CDH1, CHEK2, NBN, NF1, PALB2, an
- BARD1, MSH2, MLH1, MSH6, PMS2, EPCAM, BRIP1, RAD51C, RAD51Dd STK11

NCCN National Comprehensive Cancer Network®

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Brief overview of hereditary Breast Cancer Syndromes?

- Hereditary mutations to be considered include **BRCA 1&2, PALB2**, and other hereditary breast cancer syndromes, which include but are not limited to:
- **Li-Fraumeni syndrome (TP53 pathogenic variant**),
- **Cowden syndrome (PTEN pathogenic variant),**
- **Hereditary diffuse gastric cancer syndrome (CDH1 pathogenic variant)**,
- **Peutz-Jegher syndrome (STK11 pathogenic variant)**
- The **ATM** gene is typically associated with an autosomal recessive condition called **ataxia-telangiectasia (AT).**

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Impact of Genetic testing results – Positive Results

- Positive Results → Increased Screening Exams and Surveillance
  - BRCA 1 and BRCA 2
  - The presence of mutations in ATM, CDH1, CHEK2, NBN, NF1, PALB2, and STK11 are likely to be associated with lifetime breast cancer risks of greater than 20% and therefore, in the United States, at least support a decision for enhanced surveillance with annual mammography with tomosynthesis and breast MRI with contrast.
  - Just because a patient tests positive for a hereditary breast cancer syndrome does not mean that patient will develop breast cancer

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Impact of Genetic testing results – Negative or VUS results

- Negative & VUS results → Risk stratify via patient's other risk factors for breast cancer (age, medical history, family history, etc.) to formulate the appropriate risk management plan

- For BARD1, MSH2, MLH1, MSH6, PMS2, EPCAM, BRIP1, RAD51C, RAD51D, there are some data suggesting an elevated lifetime risk of breast cancer; however, there is insufficient evidence to support change in breast cancer risk management based on the presence of a mutation alone.

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Variance of Unknown Significance (VUS)

- These are DNA sequences about which the lab is still accruing data for definitive classification as to benign or pathogenic.
- Variants of uncertain significance are DNA sequences that are NOT clinically actionable.
- For example, a patient who receives a genetic testing result of "BRCA1 variant of uncertain significance" should NOT be recommended for a change in management based on that test result alone.
- No clinical treatment plan or risk management plan should be influenced by a VUS.
- The vast majority are re-classified as benign when enough data are collected. Usually it takes several years for the reclassification to take place.

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HIGH Risk Screening/Follow up:

- 1. MRI annually, starting now.
- 2. Mammogram Annually - If above MRI is stable, I will obtain repeat mammography in approximately 6 months, so as to stagger her breast imaging.
- 3. Every 6 month clinical breast exams
- 4. Monthly self breast exams
- 5. Institute risk reduction strategies such as: Maintain a healthy lifestyle (low fat diet, exercise and decreasing alcohol consumption and maintaining an ideal body weight),
- 6. Consider chemoprevention medications such as Tamoxifen/Aromatase Inhibitor
  - Hormones/Ovarian suppression in known genetic penetrance
- 7. Consider prophylactic surgical risk reduction.

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Breast cancer screening and prevention be performed

- 1. Initiate annual screening mammography for asymptomatic patients at age 40. High risk women may benefit from earlier screening.
- 2. Perform monthly self breast examinations both in the standing and supine positions. Examination of the axillary lymph nodes should also be performed, with attention to increasing adenopathy.
- 3. Breast cancer risk can be reduced by:
  - - Exercising 2.5 hours weekly
  - - Maintaining the ideal body weight
  - - Eating a low-fat diet
  - - Limit alcohol consumption to less than 2.5 drinks weekly
  - - Not smoking

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Thank you & Resources

breast360.org
engage • educate • empower

ASK2ME™ | All Syndromes Known to Man Evaluator

- ask2me.org can be useful in understanding the penetrance and the management for most cancer-causing genes
- BRCA Decision Tool, http://brcatool.stanford.edu/brca.html, can be useful in known BRCA pathogenic variant carriers to predict likelihood of developing breast or ovarian cancer and likelihood of dying from either disease based on patient age and a variety of interventions chosen for screening and prophylaxis.
- Breast360.org
- NCCN

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