Have You Been Checked?

BRCA Gene Mutation

Introduction

- According to The Center for Disease Control and Prevention, breast cancer is the second most common cancer among women in the United States.
- The most common inherited gene that affects breast cancer is BRCA1 and BRCA2.
- Imaging such as MRI and mammography, play a very special role in helping identify potential cancers associated with these mutations.

BRCA Gene

- BRCA stands for BReast CAncer gene indicating its relevance in breast cancer pathogenesis.
- BRCA1 and BRCA2 were discovered in 1994 and 1995.3
- These genes are very large, due to their size, there are more than 400 mutations have been reported.4
- Each person has BRCA1 and BRCA2, but only some patient's genes are mutated, which in turn increases the risk for breast and ovarian cancers.4
- When these genes are unaffected and normal, their function is to be a tumor suppressor gene.
- When mutated, it can cause irregularities in DNA synthesis which means the cells are more likely to develop additional genetic alterations that can lead to cancer.[3]
- Inherited breast cancer is an autosomal dominant genetic condition. This means both male and female children of a parent who has the mutation have a 50-50 chance of inheriting it as well .
- According to Mayo Clinic, the BRCA gene mutations cannot skip generations, meaning if your parents have it and it skips you, you cannot pass it on to your own children.[5]

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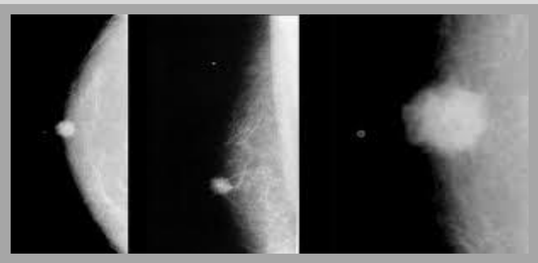
Who is at Risk?

- BRCA1 and BRCA2 gene mutation can affect both men and women since it is a hereditary gene that can be passed down.
- 0.1-0.2% of the general population are carriers of the gene mutation. [4]
- 2-3% of all breast cancers cases have detected BRCA1 and BRCA2 genes.[4]
- Ashkenazi Jews carry these mutations at higher rates than most.
- BRCA associated cancers tend to progress directly to invasive disease without development of a precancerous component.[4]
- According to Mayo Clinic, you may have a BRCA gene mutation risk if you have had:
  - breast cancer or bilateral breast cancer before the age 50
  - ovarian cancer
  - both breast and ovarian cancer
  - fallopian tube cancer or primary peritoneal cancer
  - pancreatic cancer
  - two or more close relatives with breast, ovarian, or pancreatic cancer.
- Indications that you may have a BRCA gene mutation due to family health history:
  - two or more close relatives with breast or ovarian cancer at a young age
  - close male relatives with breast cancer
  - close relatives with breast and/or bilateral breast cancer
  - two or more close relatives with pancreatic cancer
  - relative with a known BRCA1 or BRCA2 gene mutation.[5]

Men at Risk

- The general male population has a 0.1% chance for breast cancer and those with BRCA2 have a 7% chance for breast cancer.[9,10]
- Those with BRCA1 have a 2-3% risk and with BRCA2 have a 3-5% risk for pancreatic cancer.[9,10]
- Those with BRCA2 have a 20-30% increased risk for prostate cancer.[10]
- Studies have shown those who have the BRCA2 mutation have a 3-5% increased risk for melanoma compared to 1-2% in the general population.[10]

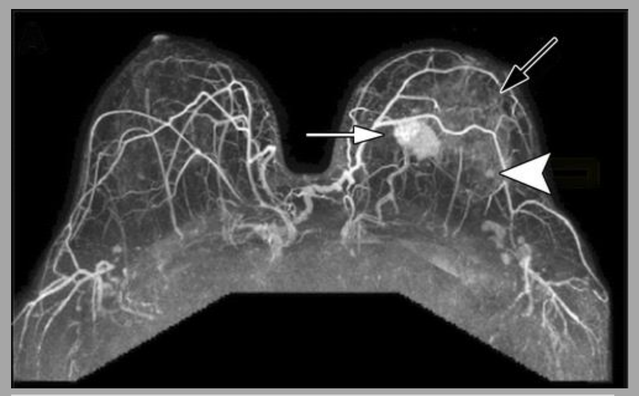


Women at risk

- Women who inherited these mutations tend to develop breast and ovarian cancers at younger ages compared to those who don't have the mutation.[6]
- Studies have shown that patients with BRCA1/2 mutant high grade serous ovarian cancer have improved survival compared to those with BRCA wild type HGSOC.[7]
- Clinically, 4-7% of women tested in large studies using multi-gene analyses presented with BRCA1 and BRCA2 mutations
- According to the National Comprehensive Cancer Network, individuals with mutations in BRCA1 Hereditary Breast and Ovarian Cancer syndrome (HBOC).[4]
- HBOC increase the risk for breast cancer over the 12% lifetime risk for women of the general population in the US.[5]
- Those with BRCA1 gene, the breast cancer risk is 60-80% compared to the 12% for the general population.[9]
- In a large study, it showed that about 72% of women who inherit BRCA1 mutation, and about 69% of women who inherit BRCA2, will develop breast cancer by the age of 80.[8]
- ovarian cancer risk is increased to 33-44% for BRCA1 and BRCA2, compared to a 1-2% risk for the general population.[4]

Detecting the Mutation

- Testing may be costly for some patients; the United States now offers patient pay prices of $250-400 for panel tests not billed to insurance.[6]
- Only 20-30% of eligible patients are referred for testing or have access to it.
- It is estimated that 97% of carriers in the population remain unidentified and end up missing opportunities for prevention.
- American Society of Clinical Oncology recommends that genetic testing should be offered to affected and unaffected patients with familial cancers affected by this mutation
- National Comprehensive Cancer Network states genetic counseling and testing for all patients diagnosed with pancreatic adenocarcinoma and those with metastatic prostate cancer.[6]
- Genetic test is usually done by a blood test.
- Today, multi gene panels including broad genomic rearrangements may be chosen for a higher affordability in risk assessment.
- For those patients who have a family member with a specific mutation, a single site targeted mutation analysis may be done.
- There is a very low chance that genetic testing would miss the BRCA1/2 mutation, but it could happen.[8]



Risk Reducing Measures

- A mastectomy increases protection from cancer development by 96%.[4]
- Salpingo-oophorectomy can be done to help reduce the risk for ovarian cancer along with breast cancer.
- Doctors can perform a pelvic exam to feel the ovaries for size, shape, and consistency. Most early ovarian tumors are difficult or impossible to feel, because early ovarian cancers often cause no symptoms.
- The American Cancer Society says women who used oral contraceptives for 5 or more years have about a 50% lower risk of developing ovarian cancer compared to those who don't. This may help lower ovarian cancer risk; it may slightly increase the breast cancer risk.[16]
- Serum CA-125 levels can be measured every 6-12 months for ovarian screening starting at age 30 or 5-10 years before the earliest age of the first diagnosis in the family.[4]
- Currently the most effective way to screen for prostate cancer is by doing a blood test that looks for the prostate-specific antigen (PSA), which can be done yearly.

Imaging for BRCA

Breast:

- BRCA1 and BRCA2 patients are recommended to undergo yearly mammograms and breast MRIs alternating every 6 months after the age of 25, or 10 years before the earliest age at which the cancer was detected in the family.[4]
- MRI has shown to detect earlier stage cancers and has a higher sensitivity in BRCA carriers than mammography, ultrasound, and clinical breast exams.[12]
- Although MRI may be better to find tumors, mammography can also identify some breast cancers that are not identified in MRI.
- MRI may be less specific than mammography.[8]
- Patients with dense breast tissue have a risk of breast cancer that is about 1 ½ to 2 times that of women with average breast tissue. Dense breast tissue also makes it harder to detect cancers on mammograms.[13]
- Breast tomosynthesis or digital breast tomosynthesis allows the doctors to see the breast tissue more clearly in three dimensions.
- Many studies have found that 3D mammography lowers the chance of being called back for follow up testing.[14]

Ovarian:

- Ovarian cancer is one of the hardest cancers to detect at an early stage.
- Only about 20% of ovarian cancers are found at an early stage.15
- Transvaginal ultrasound may detect ovarian cancer.
- Patients with a new epithelial ovarian cancer are routinely imaged with CT, but unfortunately it is unknown if the presence of BRCA can be reliably recognized on a CT.[8]