The Importance of Identifying Women at Risk for BRCA1/2 Mutations for Referral to Cancer Genetics Services

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Alliance Webinar
11/21/14
Breast Cancer Genomics

- Familial: 15-20%
- Hereditary: 5-10%
- Sporadic: 70-75%
Hereditary Breast and Ovarian Cancer Syndrome (HBOC)

Inherited mutations in the *BRCA1* or *BRCA2* genes account for:
- ~3-5% of all breast cancers
- ~15 + % of all ovarian cancers (fallopian tube, primary peritoneal)
Red Flags for *BRCA1/2* Mutations

- Early onset breast cancer (< age 50)
- Ovarian* cancer
- Triple negative breast cancers (ER/PR/Her2)
- Multiple cases of breast and/or ovarian cancer in the same family
- Breast and ovarian* cancer in the same woman
- Bilateral breast cancer (at least one < age 50)
- Male breast cancer
- Ashkenazi Jewish heritage

*Fallopian tube/Primary peritoneal*
Prevalence of *BRCA1/2* Mutations

General Population

Women with Breast Cancer

**Percent**

**BRCA1**

**BRCA2**
BRCA1/2-Associated Cancers: Lifetime Risks

- Breast cancer (50%-85%)
- 2nd breast cancer (40-60%)
- Ovarian cancer (BRCA1: 20-45%, BRCA2: 10-20%)
- Male breast cancer (5-10%)

Risks for other cancers also appear to be increased 2-5 fold: pancreatic, melanoma, prostate < 65
Management Options for *BRCA1/2* Mutation Carriers

- Early clinical surveillance (begin by age 25) annual or semi annual:
  - clinical breast exam, mammogram, **breast MRI**
  - CA125, transvaginal ultrasound (uncertain efficacy)
- Chemoprevention
  - tamoxifen
  - oral contraceptives
Breast MRI vs. Mammogram in “High Risk” Women

*Warner, JCO 2011
Management Options for BRCA1/2 Mutation Carriers

- Prophylactic mastectomy – 90%+ reduction in breast cancer risk
- Prophylactic bilateral salpingoophorectomy
  - 80-96% reduction in ovarian/fallopian tube cancer risk
  - 50%+ reduction in breast cancer risk
  - Reduction in all cause and breast & ovarian cancer-specific mortality (Domcheck, JAMA, 2010)
Impact of Genetic Test Results

Bonnie:
- Risk for second breast cancer
- Risk for ovarian cancer

Sara:
No increased risk for breast or ovarian cancer beyond anyone in the general population.

*BRCA1 mutation = True Negative

**Negative for BRCA1 mutation found in sister**
Cancer Genetic Counseling

- Collect and review detailed personal and family cancer histories
- Assess likelihood for a hereditary cancer syndrome and cancer risk probabilities
- Determine appropriateness of genetic testing, who best to test, and which test to order
- Educate patient about cancer genetics, personal risks, pros/cons/limitations of genetic testing – including possible test results
Cancer Genetic Counseling - cont.

- Address patient’s risk perceptions and psychosocial concerns
- Review options of screening, management, risk reduction
- Coordinate testing and insurance coverage
- Post-test disclosure session
  - implications of test results for patient/family
  - management plan based on result
  - additional testing needed/available
  - psychosocial adjustment to results/implications
United States Preventive Services Task Force (USPSTF) 2005 Recommendation

“....women whose family history is associated with an increased risk for deleterious mutations in the BRCA1 or BRCA2 genes [should] be referred for genetic counseling and evaluation for BRCA testing.”

Healthy People 2020 Genomics Objective

“Increase the proportion of women with a family history of breast and/or ovarian cancer who receive genetic counseling”
Standard 2.3: Risk Assessment and Genetic Counseling

All programs are required to provide cancer risk assessment as well as genetic counseling and testing, on-site or by referral, by a qualified genetics professional [who has]

... extensive experience and educational background in genetics, cancer genetics, counseling, and hereditary cancer syndromes to provide risk assessment and empathetic genetic counseling to patients with cancer and their families
The USPSTF recommends that primary care providers screen women who have family members with breast, ovarian, tubal, or peritoneal cancer with 1 of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (BRCA1 or BRCA2). Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing. (B recommendation)
B-RST is a screening tool that asks questions about family history to assess if you (or your patient) may be at risk for Hereditary Breast and Ovarian Cancer.

This tool is designed to quickly identify who should be referred for cancer genetic counseling to formally evaluate their family history and discuss the benefits and limitations of genetic testing for Hereditary Breast and Ovarian Cancer.

www.breastcancergenescreen.org
## B-RST Validation

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<th>BD</th>
<th>BR</th>
<th>MII</th>
<th>FH</th>
<th>Overall*</th>
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*High-risk by at least one of the models = actual positive state
BD = BOADICEA Model; BR = BRCAPRO Model; MII = Myriad II Tables; FH = Family History Assessment Tool, AUC = Area under the curve

Public Health Implications

• Approximately 1/400 individuals carry a mutation in *BRCA1/2* (1/40 individuals of Jewish descent)
• This implies ~ 800,000 plus *BRCA1/2* mutation carriers in the US – the majority of which have not been identified
• Identification of an individual with a *BRCA1/2* mutation allows for live saving interventions which reduce morbidity and mortality associated with early onset breast cancer and ovarian cancer
• For each *BRCA1/2* mutation carrier identified, multiple family members are at risk and can benefit from the knowledge of their mutation status