Impact of Timing of Diagnosis of Genetic Mutation on Surgical Decision Making and Outcome of BRCA1/BRCA2 Mutation Carriers with Breast Cancer

Akiko Chiba, MD, Tanya Hoskin, MS, Emily Hallberg, MPH, Jodie Cogswell, Courtney Heins, BS, Fergus J. Couch, PhD, Judy C. Boughey, MD
Mayo Clinic, Rochester, MN

Background

- The BRCA1 and BRCA2 genes were sequenced in 1994 and 1995 respectively. Approximately 3-5% of all newly diagnosed breast cancer have a deleterious BRCA1/2 mutation.
- It is well established that BRCA mutation carriers have increased lifetime risk of developing breast cancer, and that mutation carriers with breast cancer are at increased risk of future breast cancer events.
- Knowledge of BRCA mutation carrier status can strongly influence surgical treatment decisions for patients diagnosed with breast cancer.
- We evaluated how the surgical decisions of BRCA mutation carriers with breast cancer varied based on timing of identification of mutation relative to surgery for their index breast cancer.

Study Design

- Aims: 1. Evaluate the surgical choices of BRCA mutation carriers diagnosed with breast cancer before and after identification of their BRCA mutation. 2. Evaluate the impact of timing of BRCA testing on surgical decisions and on outcome.
- Background: All BRCA mutation carriers diagnosed with breast cancer at our institution between 1996 and 2015 were identified. Patient surveys, medical record, and institutional databases were used to collect data.
- Data collected included: timing of BRCA test result, operation performed for initial breast cancer treatment and any subsequent breast operations. Patients were categorized into 3 groups based on timing of identification of BRCA mutation relative to breast cancer diagnosis and surgery:
  - Group 1: BRCA+ status not known until after cancer diagnosis.
  - Group 2: BRCA+ identified during workup.
  - Group 3: BRCA+ identified after surgery.
- Differences in surgical choice were analyzed using chi square test, rates of subsequent breast cancer events were estimated using Kaplan-Meier method.

Results

- A cohort of 179 BRCA carriers with breast cancer were identified. 100 BRCA1 and 76 BRCA2.
- In 13 patients with bilateral cancer, 9 (69%) underwent subsequent bilateral mastectomy (BM).
- Among 13 patients with bilateral cancer, 9 (69%) elected bilateral mastectomy and 4 (31%) elected for bilateral BCT. None of the 4 woman selecting bilateral BCT knew of their BRCA+ mutation status at the time of surgical decision making.

Analysis

- In the 159 women with unilateral breast cancer (stage 0-3), surgical choice differed significantly between the 2 groups. (p=0.0001)
- Patients with BRCA mutation identified after surgery who underwent breast-conserving therapy (BCT) or unilateral mastectomy (UM) at index surgery, 33/66 (50%) underwent subsequent bilateral mastectomy (BM).
- Differences in surgical choice were analyzed using chi square test, rates of subsequent breast cancer events were estimated using Kaplan-Meier method.

Discussion

- The BRCA1 and BRCA2 genes were sequenced in 1994 and 1995 respectively. Approximately 3-5% of all newly diagnosed breast cancer have a deleterious BRCA1/2 mutation.
- It is well established that BRCA mutation carriers have increased lifetime risk of developing breast cancer, and that mutation carriers with breast cancer are at increased risk of future breast cancer events.
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Aims

1. Evaluate the surgical choices of BRCA mutation carriers diagnosed with breast cancer.
2. Evaluate the impact of timing of BRCA testing on surgical decisions and on outcome.

Clinical Stage Distribution

- In patients with BRCA mutation identified after surgery who underwent breast-conserving therapy (BCT) or unilateral mastectomy (UM) at index surgery, 33/66 (50%) underwent subsequent bilateral mastectomy (BM).

Outcomes: Unilateral Breast Cancer

- Rates of BM were significantly higher among patients aware of their BRCA mutation compared to patients whose BRCA mutation status was identified after surgical treatment.
- Identification of BRCA mutation after definitive surgery led to subsequent breast surgery in 59% of patients who had not undergone BM.
- Contralateral prophylactic mastectomy significantly decreases risk of contralateral breast cancer in patients with BRCA mutations.
- These data highlight the importance of genetic testing prior to definitive surgical treatment of breast cancer in patients with elevated risk of genetic mutation.

Summary

- BRCA mutation positive status strongly influences surgical decision making.
- Rates of BM are significantly higher among patients aware of their BRCA mutation compared to patients whose BRCA mutation status was identified after surgical treatment.
- Identification of BRCA mutation after definitive surgery led to subsequent breast surgery in 59% of patients who had not undergone BM.
- Contralateral prophylactic mastectomy significantly decreases risk of contralateral breast cancer in patients with BRCA mutations.
- These data highlight the importance of genetic testing prior to definitive surgical treatment of breast cancer in patients with elevated risk of genetic mutation.