

Is prophylactic breast surgery essential in BRCA mutation carriers following diagnosis of ovarian cancer?

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Background

- Breast cancer risk in the general population is - **12.4%**
- In women with a BRCA+ - **69-72%**.
- Risk reducing (RR) salpingo-oophorectomy significantly reduces ovarian and Breast cancer risk in BRCA mutation carriers
- The role of RR breast surgery after a diagnosis of OC is less studied.
- These patients may be
 - followed with screening procedures including MRI/mammogram
 - offered RR breast surgery to mitigate potential cancer risk.
- Our objective is to define **actuarial risks of breast cancer and overall mortality** in a multi-ethnic cohort of BRCA1 and BRCA2 mutation carriers after a diagnosis of ovarian cancer.

Inherited BRCA1/2 mutation

- The risk of developing **breast cancer** (BC) to age 70 is
 - approximately **70%** for carriers of either a BRCA1 or BRCA2 mutation
- The risk of developing **epithelial ovarian cancer** (EOC) to age 70 is
 - approximately **40%** for BRCA1 mutation carriers
 - Approximately **20%** for BRCA2 mutation carriers .
- The **annual** risk of BRCA-associated **breast cancer**
 - Ages 30-60 - is approximately 2%
 - Ages 60–80 - is approximately 1%

Treatment Options: BRCA1/2 Carriers

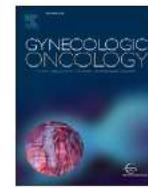
- Chemoprevention
 - Tamoxifen reduces risk in BRCA2 carriers, (still questionable in BRCA1 carriers)
- Prophylactic bilateral mastectomy
 - ~90% reduction in breast CA risk
- Prophylactic bilateral oophorectomy
 - ~90% reduction in ovarian CA risk
 - ~50% reduction in breast CA risk

Cancer Prevention

- Breast cancer screening with MRI
- Prophylactic bilateral mastectomy (PBM)
 - The value of PMB is greater for women with **long life expectancy**
 - PMB is rarely offered to women after age 70.

Ovarian cancer in BRCA carriers

- Women with **ovarian cancer** -
 - a reduced life expectancy
 - most are not offered preventive mastectomy
- The probability of ultimately surviving ovarian cancer increases with time already survived after diagnosis
- Long survivors
 - wish to avoid second primary (breast) cancers.
 - Some might benefit from preventive mastectomy or MRI screening.
- Currently - no guidelines for BRCA+ with a diagnosis of OC



Risk of breast cancer after a diagnosis of ovarian cancer in *BRCA* mutation carriers: Is preventive mastectomy warranted?



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Results

- **N= 509** - OC with BRCA +
 - Twenty (**3.9%**) developed breast cancer **within 10 years** following OC diagnosis.
- At **10 years** post OC diagnosis- actuarial risk of **7.8%**
- BRCA mutation-carrying patients diagnosed with stage III/IV ovarian cancer at age 50, the chance of dying before age 80 was **reduced**
 - by less than 1% with MRI
 - by less than 2% with mastectomy
- Greater improvements in survival with MRI or mastectomy were observed
 - for women who had already survived 10 years after ovarian cancer,
 - for women with stage I or II ovarian cancer.

Conclusions

- Preventive mastectomy or MRI screening is warranted only for those
 - 10 years without recurrence
 - early stage ovarian cancer.

Research

Original Investigation | PACIFIC COAST SURGICAL ASSOCIATION

Breast Cancer Following Ovarian Cancer in *BRCA* Mutation Carriers

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Results

- **N= 135-** OC with *BRCA+*
- 12 (**8.9%**) developed breast cancer.
- **50.5m** - The **median time** from diagnosis of EOC to BC
- Annual mammography in **59.3%**, annual MRI in **44.4%**
- 13 (**9.6%**) underwent a bilateral prophylactic mastectomy at a median of 23 months following EOC diagnosis.
- All patients had **early-stage breast cancer** (stages 0-II).
 - Four patients (33.3%) received adjuvant chemotherapy.
 - 4 of the 12 patients (33.3%) died of recurrent EOC after a diagnosis of BC , median follow-up of 6.3 years
- **10-year** survival rate for the entire cohort (N-135) was **17.0%**.

Conclusions

- The risk of metachronous breast cancer is low in patients with known *BRCA* mutations and EOC.
- A majority of these cases of breast cancer at an early stage are detected by use of mammography.
- These results suggest that
 - optimal breast cancer surveillance for patients with *BRCA*-associated EOC **needs to be reevaluated**
 - given the **low incidence of breast cancer** among these high-risk patients.
- Confirmation of our findings from larger studies seems to be indicated.

Original Article

The Risk of Primary and Contralateral Breast Cancer After Ovarian Cancer in *BRCA1/BRCA2* Mutation Carriers

Implications for Counseling

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Cancer March 1, 2013

N=79 - OC patients with BRCA+, no history of breast cancer (BC)

N=37 - OC patients with BRCA+, with history of breast cancer (BC)

The control groups

N = 351 - unaffected *BRCA* mutation carriers

N = 294 - mutation carriers who had a previous unilateral BC

RESULTS

- Women with *BRCA*-associated OC had **lower** 2-year, 5-year, and 10-year risks of PBC (3%, 6%, and 11%, respectively)
 - compared with unaffected mutation carriers (6%, 16%, and 28%, respectively; $P = .03$),
- A considerably higher mortality rate at similar time points (13%, 33%, and 61%, respectively, vs 1%, 2%, and 2%, respectively; $P < .001$).
- In *BRCA* mutation carriers with a previous unilateral BC,
 - the 2-year, 5-year, and 10-year risks of CBC were nonsignificantly lower in patients with OC than in those without OC (0%, 7%, and 7%, respectively, vs 6%, 16%, and 34%, respectively; $P = .06$)
 - the **mortality** rate was **higher** in patients with OC (19%, 34%, and 55%, respectively, vs 4%, 11%, and 21%, respectively; $P < .001$).

CONCLUSIONS:

- Patients with *BRCA*-associated OC had
 - a lower risk of developing a subsequent PBC or CBC than mutation carriers without OC
 - whereas the risk of dying from OC was greater than the risk of developing BC.
 - These data may facilitate more tailored counseling for this patient subgroup
 - confirmative studies are warranted.

Our Study

- BRCA+ diagnosed with OC 2000 to 2017 at
 - New York University (n=102)
 - Tel Aviv Sourasky Medical Center (n=124).
- Clinical data regarding PBS, diagnosis of subsequent breast cancers, and type of BRCA 1 or 2 deleterious mutations were analyzed.

Results

- During this time period, 6 women underwent PBS.
- The cumulative risk of breast cancer following OC in BRCA carriers was lower than projected.
- Within the 124 Israeli BRCA carriers OC patients, with annual MRI, none went through PBS and only 3(2.4%) developed sequential Breast cancer.
- Issues to be studied further include risk according to specific BRCA mutations, instances of synchronous presentations, pre-existing breast pathology, and the emerging role of PARP inhibitors.

Conclusions

- Lower than expected rates of breast cancer
 - Might be attributed to
 - ovarian cancer mortality
 - Chemotherapy treatment
 - Other
- Our data are consistent with prior series of BRCA mutation carriers diagnosed with ovarian cancer
- PBS and/or MRI breast surveillance are unlikely to affect outcomes until ovarian cancer survivors have been disease-free for 10 years.

Conclusions

- No guidelines
- The **cumulative risk of breast cancer** after a diagnosis of ovarian cancer is lower than projected for BRCA carriers.
-
- Might be due to **mortality from ovarian cancer**, which occurs before the affected patients develop breast cancer.
- **PBM or MRI/mammo breast surveillance** are unlikely to affect outcomes until ovarian cancer survivors have been **disease-free for 10 years**.
- Further studies
 - ascertaining risk according to specific BRCA mutations
 - instances of synchronous presentations
 - pre-existing breast pathology
 - incidence after PARP inhibitors use for ovary cancer will be important.
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Thank you!