

Position Statement



Position statements on genetic test for peritoneal, ovarian, and fallopian tubal cancers: Korean Society of Gynecologic Oncology (KSGO)

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This statement sets out the position of the Korean Society of Gynecologic Oncology regarding the assessment of genetic tests on women with peritoneal, ovarian, and fallopian tubal (POFT) cancers and their families.

Two high susceptibility genes (*BRCA1* and *BRCA2*) have been identified for hereditary breast and ovarian cancer (HBOC) and these genes normally function as tumor suppressor genes [1,2]. Women with *BRCA1* or *BRCA2* mutations have a 39% or 11% (1.3% in normal population) cumulative risk for ovarian cancer by the age of 70 years, respectively [3]. The prevalence of *BRCA* mutations in Korean women with POFT cancers regardless of family history has been reported to be as high as 23.8% to 25.7% [4,5]. The substantial frequency of *BRCA* mutations in the Korean population is expected to be higher than that reported in previous studies, because of the limitations involved in confirming the exact family history in Korea [6]. Approximately 15% cases of ovarian cancer are due to germline genetic mutations and the prevalence of peritoneal and fallopian tubal cancers is higher than that of ovarian cancer [7]. Studies concerning other genes (*PTEN*, *TP53*, *BRIP1*, and *RAD51D*) known to cause HBOC are also in progress [8-11], but it is difficult to apply those genes clinically in Korea at the present.

Genetic counseling and clinical genetic testing allow physicians to precisely identify women who are at substantial risk for POFT and breast cancer. For these individuals, surveillance and risk reducing strategies can be instituted to reduce the risk to them and their family. If one of the parents harbors the *BRCA* mutation, the prevalence of *BRCA* mutation in each child is found

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to be 50%. The candidates for *BRCA* genetic tests focusing on the proband are patients with POFT cancers and their families, especially first degree relatives (parents, siblings, and offspring).

The recommendations of the Korean Society of Gynecologic Oncology for *BRCA* genetic testing are follows:

- POFT cancers or breast cancer diagnosed with the first or second degree relative with POFT or breast cancer
- Epithelial ovarian cancer, fallopian tubal cancer, or peritoneal cancer
- A personal history of both POFT and breast cancer
- Early onset breast cancer (diagnosed ≤ 40 years)
- Bilateral breast cancer
- Multiple organ cancers including breast cancer
- Male breast cancer
- First degree relatives of an individual with a known *BRCA1* or *BRCA2* mutation

A germline mutation in *BRCA* was associated with improved 5-year overall survival among patients with epithelial ovarian cancer [12]. Poly (ADP-ribose) polymerase inhibitors (niraparib, olaparib, rucaparib, or veliparib) can be used in patients with POFT cancer harboring *BRCA* mutations and better treatment options are promising [13,14].

The opportunity to provide tailored screening and risk reducing strategies such as surveillance, chemoprevention and risk-reducing surgery may reduce the morbidity and mortality in *BRCA* carriers.

PRACTICAL INFORMATION

There are several programs to calculate the prevalence of *BRCA* mutations considering the clinical environment and family history of individuals.

- <http://www.myriadpro.com/brca-risk-calculator/calc.html>
- <http://www.ibreast.kr/BRCA/BRCA.html> (Korean model)
- <http://www4.utsouthwestern.edu/breasthealth/cagene>

The probability of harboring the *BRCA* genetic mutation according to the clinical environment is as follows:

- The prevalence of *BRCA* mutation in high grade serous epithelial ovarian cancer is approximately 23% to 40% [15,16].
- The prevalence of *BRCA* mutation in Korean ovarian cancer patients with a family history of ovarian cancer in a first degree relative is approximately 63% [17].
- The prevalence of *BRCA* mutation in Korean ovarian cancer patients with a family history of breast cancer in a first degree relative is approximately 21% [17].
- The prevalence of *BRCA* mutation in Korean ovarian cancer patients with a family history of ovarian or breast cancer in a first degree relative is approximately 33% to 61% [16,17].
- The prevalence of *BRCA* mutation in Korean ovarian cancer patients without a family history of ovarian cancer in a first degree relative is approximately 9% to 13% [16,17].

For *BRCA* carriers, the need for strict adherence to screening schedules for peritoneal, ovarian, and fallopian tubal (POFT) cancers such as transvaginal sonograms or serum CA-125

tests every 4 months and frequent screening for POFT cancers might offer a better chance for early stage detection [18].

Transvaginal ultrasound and serum CA125 tests can be performed when the prevalence of POFT cancer is predicted to be more than 10% as follows [18].

1. Known carriers of one of the predisposing genes (BRCA1, BRCA2, MLH1, MSH2, MSH6, PMS1, or PMS2).
2. Families with two or more individuals suffering from POFT cancer who were first-degree relatives.
3. Families with one individual suffering from POFT cancer and one individual with breast cancer diagnosed at age <50 years who were first-degree relatives.
4. Families with one individual suffering from POFT cancer and two individuals with breast cancer diagnosed at age <60 years who were first-degree relatives.
5. Families with three individuals suffering from colorectal cancer, at least one of whom was diagnosed at age <50 years as well as one individual suffering from POFT cancer, and all of these individuals were connected by first-degree relationships.

If the patients are clinically suspected of POFT cancer, they should be assessed for a family history of POFT cancer and breast cancer. Genetic counseling and genetic testing are provided after pathological diagnosis. BRCA carriers should be counseled about risk-reducing bilateral salpingo-oophorectomy, ideally between 35 to 40 years and upon completion of child-bearing or in an individualized manner based on the earliest age of onset of ovarian cancer in the family.

Even in families with the BRCA mutation, the risk of developing POFT cancer or breast cancer in a woman under the age of 21 years is extremely low. Therefore, and considering the potential negative impact of genetic testing, the Korean Society of Gynecologic Oncology panel does not recommend genetic testing for women under the age of 21 years for hereditary breast and ovarian cancer in the absence of a family history of early-onset cancer.

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