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SGO Committee Statement

Society of Gynecologic Oncologists Clinical Practice Committee Statement on Prophylactic Salpingo-oophorectomy ☆

Since the recent publication of several studies demonstrating that prophylactic (or risk-reducing) salpingo-oophorectomy significantly reduces the risk of subsequent breast, ovarian, and fallopian tubes cancers in women at inherited risk for these malignancies, these procedures have been increasingly offered to women with personal and family histories suggestive of hereditary breast–ovarian cancer syndrome. These studies have provided compelling evidence to support the use of risk-reducing surgery in high-risk women, but several important questions remain regarding this procedure, including: (1) who should be offered the procedure; (2) how should the procedure technically be performed; (3) what are the minimal requirements for pathologic evaluation; (4) what is the optimal timing for the procedure; and (5) how should patients undergoing the procedure be followed long term? This position statement will attempt to provide some guidance on each of the issues as well as identify areas for future study.

Women with documented *BRCA1* or *BRCA2* mutations have a 10–60% lifetime risk of ovarian cancer and a 60–85% lifetime risk of breast cancer [1,2]. Three studies have now demonstrated that carriers of *BRCA* mutations who undergo risk-reducing salpingo-oophorectomy have a 71–96% reduction in the risk of subsequent ovarian, fallopian tube, and primary peritoneal cancer [3–5]. Additionally, if the procedure is done premenopausally, risk-reducing salpingo-oophorectomy is associated with a 50–68% reduction in the risk of subsequent breast cancer. On the basis of these studies, there is clear evidence to support offering risk-reducing salpingo-oophorectomy to women with known mutations in either *BRCA1* or *BRCA2*.

In individuals with a personal or family history suggestive of an inherited predisposition to breast and ovarian cancer who have not had genetic testing or who have undergone genetic testing and have not had a deleterious *BRCA1* or *BRCA2* mutation identified, less information is available regarding the relative risks and benefits of salpingo-oophorectomy. These individuals are best managed by a multidisciplinary team of gynecologists, gynecologic oncologists, and geneticists experienced in the care of women at inherited risk for cancer.

For women with *BRCA1* mutations, the risk of ovarian cancer begins to rise in the late 30s and early 40s. For women with *BRCA2* mutations, the ovarian cancer risk does not begin to rise until approximately 10 years later [6,7]. For women with *BRCA1* mutations, risk-reducing salpingo-oophorectomy should be offered after the completion of childbearing and only deferred beyond the early 40s following a careful discussion of the risk and benefits. For women with *BRCA2* mutations, the ovarian cancer risk is only 2–3% by age 50 [6,7]. It is important to remember, however, that the risk of breast cancer in *BRCA2* mutation carriers by age 50 may be as high as 26–34% [1,2,7], and that deferral of risk-reducing salpingo-oophorectomy until the time of natural menopause may cause the loss of the substantial protection against breast cancer that salpingo-oophorectomy affords [8].

Occult ovarian and fallopian tube cancers have been detected in 2–10% of surgical specimens from *BRCA* mutation carriers undergoing risk-reducing salpingo-oophorectomy [3,4,9–11]. As many of these cancers are microscopic, it is imperative that the entire ovaries and fallopian tubes be serially sectioned and examined by an experienced gynecologic pathologist. It is not clear at this time if routine cytologic evaluation of peritoneal washings should be recommended. Case reports have suggested that peritoneal washings at the time of risk-reducing salpingo-oophorectomy may identify cancers that would be missed even on detailed pathologic evaluation of the entire surgical specimen [12]. Until more information becomes

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available, cytologic evaluation is reasonable but not required part of the risk-reducing surgical procedure.

To maximize the efficacy of the procedure, as much of the ovaries and fallopian tubes as possible should be removed. Surgeons performing risk-reducing salpingo-oophorectomy must be comfortable operating in the retroperitoneal space to facilitate isolation of the ovarian blood supply adequately proximal to its insertion into the ovarian hilum. Surgeons also should take appropriate steps to minimize the possibility that adhesions, endometriosis, or other inflammatory process lead to the creation of an ovarian remnant. As the fallopian tube is also at risk for malignant transformation in hereditary breast–ovarian cancer syndrome [13], if the surgical procedure does not include hysterectomy, the fallopian tube should be amputated as close as possible to the uterine cornua. It is not clear whether or not hysterectomy should be included as part of the risk-reducing surgical procedure [14]. Studies have demonstrated that hysterectomy in addition to bilateral salpingo-oophorectomy is associated with increased hospital stay, morbidity, and costs. Some reports suggest that patients who do not undergo hysterectomy are at increased risk of papillary serous carcinoma of the uterus [15]; however, existing data are conflicting. Additionally, it has been suggested that the residual interstitial fallopian tube may be at risk for malignant transformation, but there are no reports in the literature to date that this has occurred following risk-reducing salpingo-oophorectomy. Lastly, hysterectomy may simplify hormone replacement or tamoxifen administration. There are currently no conclusive answers regarding the relative risks and benefits of including hysterectomy as part of the risk-reducing surgical procedure. Pending further studies, patients considering risk-reducing surgery should be apprised of the available data and its limitations, and make an individualized decision following a careful discussion with the health care team.

Limited information is available regarding management of women following risk-reducing salpingo-oophorectomy. While hormone replacement may be a reasonable option in selected women, there is some evidence to suggest that hormone replacement in this setting may be associated with a decrease in the breast cancer risk-reduction associated with the procedure [8]. Until further data are available, decisions regarding hormone replacement are best individualized in the context of a patient's specific symptoms. Premature surgical menopause is also associated with an increased risk of osteoporosis and may be associated with an increased risk of cardiovascular disease. Patients who are considering risk-reducing salpingo-oophorectomy should undergo careful assessment of risk factors for each of these processes and may benefit from long-term treatment to reduce the risks of each of these diseases.

Patients who have undergone risk-reducing salpingo-oophorectomy and who have not undergone bilateral mastectomy are still at increased risk of breast cancer and should participate in breast screening appropriate for women who are at inherited risk. It is less clear whether or not women who have had salpingo-oophorectomy benefit from continued screening for gynecologic cancers. It is estimated that women with *BRCA* mutations have a residual lifetime risk of peritoneal cancer of 1–6% after salpingo-oophorectomy. Some have suggested, on the bases of case reports, that serial CA125 determinations may have a role in screening for peritoneal cancer following salpingo-oophorectomy [16]. At this time, there is no information available regarding the efficacy of this approach. However, an ongoing study currently being conducted by the Gynecologic Oncology Group (GOG 199) should provide data pertinent to this question.

Risk-reducing salpingo-oophorectomy clearly has the potential to decrease the risk of breast and gynecologic cancers in women at inherited risk for these malignancies. However, multiple unanswered questions remain regarding this procedure. These questions will be best answered in the context of well-designed clinical trials. One such trial is GOG 190. This study evaluates the role of oral fenretinide as a chemoprotective agent in women undergoing risk-reducing salpingo-oophorectomy. Patients contemplating risk-reducing salpingo-oophorectomy should be encouraged to participate in such trials whenever possible.

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