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Gynecologic Cancer and Surgical Decision-Making in BRCA1 and BRCA2 Carriers

It has been well established that women who carry mutations in BRCA1 or BRCA2 have a high lifetime risk of developing ovarian cancer. The lifetime risk for a mutation carrier to develop ovarian cancer ranges from 15-60%, depending on the population studied; however, even the lowest end of this range is much greater than the population risk of 1-2%. Ovarian cancer is very difficult to detect at an early, treatable stage (even when using CA-125 and transvaginal ultrasounds)¹. Therefore, it is recommended that women who carry BRCA mutations consider having their ovaries and fallopian tubes removed by the time they are forty, when they are done having children or 10 years before the first ovarian cancer diagnosis in their family, which ever occurs first².

BRCA carriers are at risk for ovarian cancers, and cancers of the fallopian tube and peritoneum (a thin membrane that lines the abdominal cavity). Therefore all BRCA carriers who opt for prophylactic surgery should have their ovaries AND fallopian tubes removed (bilateral salpingo-oophorectomy = BSO)³ and examined using rigorous operative and pathologic guidelines⁴. In women whose pathology comes back normal, this surgery reduces the risk of ovarian and fallopian tube cancers by >90%. It also significantly reduces the *future risk* of breast cancer, particularly in young women who have the surgery before they go through menopause⁵⁻⁶.

The use of hormone replacement therapy (HRT) in healthy pre-menopausal BRCA carriers who have their ovaries removed is somewhat controversial because of the risk that these hormones may increase the risk of breast cancer. A recent study of 462 BRCA carriers compared the rate of breast cancer in women who had their ovaries removed and took HRT to women in the group who never had their ovaries removed and had never taken HRT. Women who had their ovaries removed and took HRT had approximately a third of the risk to develop breast cancer as compared to women who did not have their ovaries removed⁷. Therefore, short-term HRT does not appear to diminish the protective effects of ovary removal in BRCA carriers and should be considered in young women with no previous history of cancer who carry BRCA mutations and are considering having their ovaries removed.

There has also been debate about whether BRCA carriers are also at risk for endometrial cancer, and should therefore be offered total abdominal hysterectomies (TAH) as the minimum prophylactic procedure. The risk of Uterine Serous Papillary Carcinoma (USPC) is of special concern because it is pathologically similar to both peritoneal and ovarian serous malignancies and is very aggressive. A few case reports have shown that BRCA1 carriers have had USPC⁸. However, a study of Jewish women with endometrial cancer (including 17 cases of USPC) did not show an excess of BRCA mutations⁹. In a separate study of 56 non-Jewish women diagnosed with USPC, none (0/56) were found to carry a BRCA mutation¹⁰. If a causal

relationship does exist between BRCA mutations and endometrial cancer, the penetrance for endometrial cancer appears to be low and is not significantly elevated over that of the general population¹¹. Some have argued that BSO alone may leave at-risk stumps of fallopian tube that are still attached to the wall of the uterus. However, the histology of this segment of the fallopian tube is distinct from the remainder of the tube¹², and BSO alone as been shown to reduce the risk of ovarian and fallopian tube cancers by >90%. It is therefore premature to offer total abdominal hysterectomy as the **only** prophylactic surgical choice for BRCA carriers.

Ultimately, the patient must decide whether she wants BSO or TAH-BSO. Some important points to consider and discuss with your physician:

- Do you have any other indication for TAH (e.g. fibroids, endometriosis)?
- You may be a candidate for hormone replacement therapy, particularly if you have not had breast cancer. If you have your uterus removed you may be a candidate for estrogen alone (instead of combined with progestin). Estrogen alone may be associated with a lower risk of subsequent breast cancer than combined hormone replacement therapy.
- Tamoxifen is associated with a small, but increased risk of uterine cancer (<1%). If you have your uterus removed, this risk will be eliminated if you ever need to take tamoxifen.
- BSO is a smaller surgery than TAH-BSO. It is usually done laparoscopically and is an outpatient procedure. TAH-BSO generally requires hospitalization and is associated with a longer recovery time than BSO. TAH-BSO is also associated with more complications. Please speak to your physician about the risks/benefits of each procedure (including possible sexual and urinary side effects).
- Studies have shown that BSO, alone, significantly reduces the risk of ovarian and breast cancer in BRCA carriers.
- There is little evidence to suggest that removal of the uterus to prevent uterine or fallopian tube cancer is indicated at the time of prophylactic BSO.

References

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