Case 3: Risk-reducing salpingo-oophorectomy

Susan is now 40 years of age, with a feisty four year old and has decided to undergo a risk-reducing salpingo-oophorectomy (RRSO). Susan's gynecologist performs a laparoscopic RRSO. After surgery, Susan meets with her doctor to review the pathology report, which shows some atypical cells in the fallopian tubes, called serous tubal intraepithelial carcinoma (STIC).

Questions

Are any special procedures part of a (RRSO) surgery?

RRSO is usually performed as a minimally invasive (laparoscopic) surgery that takes approximately 60 to 90 minutes. This outpatient surgery is usually performed with several small incisions. All ovarian tissue and as much fallopian tube as possible is carefully removed from its junction with the uterus. The abdomen is thoroughly inspected and a pelvic wash called cytology is performed. The ovaries and tubes are then cut into very small sections (2 to 3 mm) so that each section is carefully examined by the pathologist for early cancer or pre-cancer. It is very important that this special pathology is done in order to detect very tiny cancers that could already be present. The entire fallopian tube must be examined in careful detail as many of the pre-cancer and early cancer changes are found in the fallopian tube.

What is the benefit of risk reducing (RRSO) surgery?

RRSO prevents approximately 80 percent of ovarian/fallopian tube and peritoneal cancer in women who carry BRCA1 and BRCA2 mutations. Current guidelines recommend RRSO for women between the ages of 35 and 40, although delaying until mid-forties in women with BRCA2 mutations may be considered because the incidence of ovarian cancer is approximately 1 percent for women under age 50. Breast cancer risk may also be reduced by premenopausal RRSO. One study has shown that RRSO surgery also reduces death from all causes in women with BRCA1 and BRCA2 mutations as well as deaths specifically from breast and ovarian cancer. One caution is that women can still get primary peritoneal carcinoma, an ovarian-like cancer, after RRSO, however the risk is very low, particularly when the ovaries and fallopian tubes were carefully examined for early cancers.

Should hysterectomy be performed along with RRSO?

Generally, it has been suggested that patients with BRCA1 and BRCA2 mutations are not at increased risk of developing uterine carcinoma, although data have suggested a small increased risk of serous endometrial cancer. Another potential advantage of hysterectomy performed at the time of risk-reducing surgery is to facilitate postoperative hormonal therapy; if hysterectomy were performed, only estrogen would be needed, which confers lower risk of hormone therapy complications compared to combined therapy with estrogen and progestin. Some women choose hysterectomy because they are on tamoxifen for breast cancer risk reduction, and tamoxifen is associated with an increased uterine cancer risk. Still others may have other gynecologic reasons for desiring hysterectomy, such as fibroids or abnormal Pap smears. An argument against hysterectomy is a small increase in recovery time and surgical complications associated with the addition of hysterectomy to salpingo-oophorectomy. Generally, the decision to include hysterectomy with RRSO in BRCA1 and BRCA2 mutation carriers should be based on a full discussion of risks and potential benefits in shared decision-making between the patient and her surgeon.
What is the significance of serous tubal intraepithelial carcinoma (STIC)?

STIC was first identified in the fallopian tube specimens removed from women with a *BRCA1* or *BRCA2* mutation. It comprises cancer cells that are confined to the innermost layer of the fallopian tube, called the endothelium, and have not yet invaded to deeper tissues as a true invasive carcinoma would. They are almost always found on the fimbriae, the end of the fallopian tube furthest from the uterus.

STIC or invasive cancers are identified in 4-10% of women with *BRCA1* and *BRCA2* mutations when complete serial sectioning of the fallopian tubes is performed at RRSO. These pre-invasive and invasive lesions are more commonly found in women with BRCA1 mutations over age 45 at the time of surgery.

The management of women in whom only STIC but no invasive cancer is identified is not well established. The risk that a STIC will develop into an invasive carcinoma in the tube or spread to the ovary is not known. Pelvic washings are sometimes positive for abnormal cells in women in whom STIC has been identified, raising the possibility that a small cancer may have already spread to the peritoneal surfaces.

Based on an uncertain risk of developing carcinoma in the future, management protocols for women with STIC have ranged from surveillance to surgical staging and consideration of chemotherapy. CA-125 levels are usually normal but may be helpful to raise suspicion of more extensive disease. Each patient with STIC should discuss her options with her gynecologic oncologist.

What is the association of fallopian tube cancer with *BRCA1* and *BRCA2* mutations?

When STIC and invasive fallopian tube cancer were seen in RRSO specimens from women with *BRCA1* and *BRCA2* mutations, we realized that the fallopian tube, rather than the ovary, might be the originating site of many pelvic serous cancer cases. This has changed the thinking about the prevention of “ovarian” cancer to include an emphasis on the fallopian tube. The increased risk of ovarian cancer associated with *BRCA1* and *BRCA2* mutations is more accurately stated as an increased risk of pelvic serous cancers, including fallopian tube, ovarian and peritoneal cancers.

Are there surgical alternatives to RRSO?

Tubal ligation has been associated with some risk reduction of ovarian cancer. More recently, risk-reducing salpingectomy has been suggested as a bridge to delayed oophorectomy in young women with *BRCA1* and *BRCA2* mutations who desire risk reduction that avoids menopause. Delaying oophorectomy, however, negates the risk reduction for breast cancer in these women. In addition, cases of pelvic cancer arising in the ovaries would not be prevented. Salpingectomy instead of BSO has not yet been fully evaluated as to safety or effectiveness in women at high risk of ovarian cancer. Observational trials are ongoing in the United States and Europe to collect more information about this alternative
References


