September 15, 2011

GOC STATEMENT REGARDING
SALPINGECTOMY AND OVARIAN CANCER PREVENTION

GOC Recommendations:

1. **Due to its cancer prevention potential, it is recommended that physicians discuss the risks and benefits of bilateral salpingectomy with patients undergoing hysterectomy or requesting permanent, irreversible contraception.**

2. **Given that the total benefits and risks of this practice change have not been defined, a national ovarian cancer prevention study focused on fallopian tube removal is a GOC priority.**

Introduction

Most (>90%) ovarian cancers are epithelial cell in origin and primarily affect women over 40 years of age. Of the different epithelial cell types, high-grade serous histology is the most common subtype of ovarian cancer, accounting for 2/3 of epithelial ovarian malignancies. In contrast to other types of epithelial malignancies (clear cell, endometrioid, and mucinous), this subtype is rarely confined at the time of diagnosis. The vast majority of high-grade serous cancers are diagnosed after it has spread beyond the ovary and would be classified as stage 3 or 4. For these patients, the goal of cure remains elusive. Ovarian cancer is the most lethal gynecologic malignancy, making it the 5th leading cause of cancer death for women in Canada. [1] The recently reported Prostate, Lung, Colon, Ovarian (PLCO) Cancer Screening Trial evaluated annual screening in the general population of women aged 55-74 and found no improvement in mortality from ovarian cancer compared to usual care.[2] The absence of effective screening tools for early detection of ovarian cancer in both high-risk and general populations has led to increased interest in prevention and the identification of precursor lesions. It is hoped that identified precursor lesions could be the target for screening and early detection efforts and also possible prevention strategies.

The evidence for the tubal origin of serous cancers of the ovary

Until recently, the ovarian surface epithelium and epithelial inclusions within the ovarian cortex have been the purported origin for these serous tumours of the ovary.[3] High-grade serous carcinoma is the subtype most commonly found in *BRCA1/2* mutation carriers and up to 20% of these cancers occur in women with germ line *BRCA1/2* mutations. Many of these women with BRCA mutations have chosen to have risk-reducing surgery, which includes removal of both of the ovaries and the fallopian tubes. It was believed that meticulous inspection of the ovaries from *BRCA1/2* mutation carriers would reveal "ovarian" cancer precursors. When pathologically

780 promenade Echo Drive, Ottawa, Ontario, K1S 5R7
Tel./Tél. : 613-730-4192 ext. 250 or/ou 1-800-561-2416 ext. 250
Fax/Téléc. : 613-730-4314 WEB : WWW.G-O-C.ORG

examined after surgery, about 10% of women undergoing risk-reducing surgery were found to have an early cancer. The majority of early cancers were found in the distal fallopian tubes, not the ovaries. Once believed to originate in the ovary, evidence has accumulated since 2004 that these cancers are actually fallopian tube cancers.[4,5,6,7]

What about the origin of high-grade serous carcinomas in the low risk general population? Since 2007, research has demonstrated that the majority of these malignancies also likely arise from the distal fallopian tube epithelium. [8,9,10] In addition, the transition of cells from normal to precancerous to cancer has been identified within the distal fallopian tube but not on the ovary. Likewise, the transformation of fallopian tube epithelial cells into pathologically and immunophenotypically credible high-grade serous carcinomas has been demonstrated.[11] Therefore, the evidence is now convincing that high grade serous cancers do arise within the distal fallopian tubes.

The potential for a preventive strategy

The identification that the distal fallopian tube is the origin of these cancers provides an opportunity to explore prevention strategies on a larger scale. Evidence for the usefulness of salpingectomy as a cancer risk reduction strategy is underscored by the successful impact of bilateral oophorectomy and salpingectomy procedure in the high risk *BRCA1/2* mutation carrier population.[12,13,14,15]

The identification of a precursor lesion within the fallopian tube opens up new avenues for possible prevention in the general population. Each year, women undergo gynecologic surgery for benign and malignant conditions. Among the most common surgeries a Canadian woman will undergo in her lifetime are hysterectomy and tubal ligation. In 2008–2009, the most frequent indications for hysterectomy included uterine fibroids (35%); menstrual disorders (19%); genital prolapse (15%); gynecological cancers (15%); and endometriosis (8%).[16] Premenopausal women undergoing gynecologic surgery often prefer to keep their ovaries intact to prevent the possible adverse health effects of early menopause such as osteoporosis or vasomotor symptoms. If most “ovarian cancers” begin in the fallopian tube, it then becomes possible to remove the fallopian tubes at the time of surgery and at the same time keep the hormone producing ovaries in place.

Traditionally, when hysterectomy was performed and the ovaries were being conserved, the fallopian tubes were not removed. Knowing that most of these cancers could likely begin in the fallopian tube means that our surgical convention should be reconsidered. One approach would be to consider the fallopian tube as part of the uterus and remove both fallopian tubes at the time of each hysterectomy, regardless of whether the ovaries are being removed or not.[17] It must however be underscored that this strategy is intended exclusively for women in whom the benefits of ovarian conservation at the time of surgery exceed the benefits of salpingo-oophorectomy. An additional opportunity is to consider bilateral salpingectomy instead of tubal ligation in a woman requesting permanent, irreversible contraception. In this circumstance, removing the fallopian tubes from the fimbria to the insertion at the uterus but not the intramural segment would be recommended.

However, consideration of such a preventative strategy would depend on a documented favorable risk-benefit ratio including a clear description of the potential harms and benefits. While the evidence of the distal fallopian tube origin of high grade serous tumours is compelling, and the addition of salpingectomy to the procedures listed above may involve a limited or minimal increase in surgical morbidity when done by trained surgeons, there remains at present no data at the population level to inform this risk-benefit profile.

In view of this, the Society of Gynecologic Oncology of Canada (GOC) is highly supportive of efforts to study, in a prospective fashion, the impact that this promising and potentially significant strategy could have on risk reduction at the population level. In addition, GOC endorses efforts to address the safe implementation of this strategy. In the interim however, GOC recommends that women and/or their doctors interested in prophylactic bilateral salpingectomy as a risk reduction strategy for serous ovarian cancer should engage in a clear discussion of the risks and benefits of this strategy, as it is known to date. The potential risks of the additional surgery and the potential risks of leaving the fallopian tubes in situ should be balanced with the potential benefits of prophylactic bilateral salpingectomy in women already undergoing surgery for other indications.

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