EDITORIAL
Salpingectomy as a Potential Ovarian Cancer Risk-Reducing Procedure

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Accumulated evidence over the past 10 years has strongly indicated that the fallopian tube is the site of origin for many high-grade serous carcinomas (1), which represent 50% to 60% of all epithelial ovarian cancers. This multi-origin model of ovarian cancer development has important implications for prevention of ovarian cancer: if some or all high-grade serous tumors develop in the fallopian tube, then bilateral salpingectomy could prevent this most aggressive form of ovarian cancer. However, to date, no large-scale data regarding the impact of salpingectomy on ovarian cancer incidence have been available. The article by Falconer et al. (2) is the first to address this question. This study combined data from several population registries in Sweden to compare incidence of ovarian cancer in women with a previous gynecologic procedure for benign indications (salpingectomy, tubal ligation, total abdominal hysterectomy with bilateral salpingo-oophorectomy [BSO], and hysterectomy without concomitant bilateral salpingo-oophorectomy [TAH]) to women with no history of these surgeries. They reported a statistically significant 35% lower risk of ovarian cancer among women with a previous salpingectomy compared with women with no previous surgeries. Consistent with previous studies, all other gynecologic surgeries evaluated in this study were associated with lower ovarian cancer risk, ranging from a 21% lower risk associated with TAH to a 94% lower risk with BSO.

It is well established that BSO almost entirely eliminates the risk of ovarian cancer; BSO is commonly used as an ovarian cancer risk-reducing measure in women with inherited BRCA mutations. However, BSO is not without side effects. First, in young women, this surgery results in early menopause, which is associated with increased risk of cardiovascular diseases, neurological diseases, psychiatric diseases, osteoporosis, and overall mortality (3). Further, studies have demonstrated that postmenopausal women with BSO compared with TAH alone have increased overall mortality and increased risks of cardiovascular and neurologic diseases (4). Therefore, given the risks associated with BSO compared with the low lifetime risk of ovarian cancer in women without BRCA mutations (1 in 72), BSO is not recommended on a population level for prevention of ovarian cancer. The finding that many high-grade serous ovarian cancers arise in the fallopian tube has thus prompted the question: Could salpingectomy be a safer, but still effective, alternative to BSO for ovarian cancer prevention?

The results provided in the Swedish study suggest that salpingectomy may reduce the risk of ovarian cancer, but to a lesser degree than BSO. The relative risk for carcinoma following salpingectomy was very similar to those for tubal ligation or TAH alone, both of which are established preventive factors for ovarian cancer. This suggests that salpingectomy may have a preventive effect. However, when evaluating the results of this study, its limitations should be taken into account. First, even this very large study is limited by the small number of ovarian cancer case patients, particularly among groups with BSO and salpingectomy, comprising seven and 81 case patients, respectively. Notably, the analysis of bilateral salpingectomy, which had an intermediate relative risk estimate between unilateral salpingectomy and BSO, only included seven ovarian cancer case patients. Second, this study did not specifically address risk of high-grade serous tumors, the tumors that putatively arise in fallopian tubes. If the authors could have demonstrated that salpingectomy specifically prevents these types of tumors, they would have provided stronger evidence for the potential of this surgery to prevent this aggressive tumor subtype. Third, as the authors acknowledge, their ability to control for potentially important confounders, notably use of oral contraceptives, was limited. Fourth, the authors address the issue of potential confounding by indication, specifically discussing whether pelvic inflammatory disease or endometriosis could explain the associations observed in this study. However, in the current study, most salpingectomies were unilateral, most likely because of ectopic pregnancies, which have not been studied for their...
association with ovarian cancer risk. Therefore, more research is needed to demonstrate whether the association of salpingectomy represents, in part, confounding by indication by the conditions leading to salpingectomy or a true inverse association of the surgery with risk.

Although these results require replication in other study populations, particularly those that can address the limitations of the current study, this study is a very important first step in providing population-level evidence that salpingectomy may be preventive. Further study will be needed to complement the author’s findings by addressing additional questions. First, it is unclear whether salpingectomy is effective in BRCA+ women. Other gynecologic surgeries seem to have similar associations in BRCA+ and “normal risk” women (4–8), but resolving the effectiveness of salpingectomy in BRCA+ women is of paramount importance, given that these are the women most likely to elect risk-reducing BSO. Second, the long-term health effects of salpingectomy are not well established. Given the long-term health consequences of BSO, it should be clearly demonstrated that salpingectomy does not have long-term adverse effects before it could be adopted as a feasible preventive strategy. Lastly, women receiving TAH at many institutions are being encouraged to also have salpingectomy. The impacts of these “opportunistic salpingectomies” on ovarian cancer risk should also be evaluated.

In conclusion, the study by Falconer et al. (2) provides the first evidence that removing the fallopian tubes, but leaving the ovaries intact, may provide some benefit for reducing risk of ovarian cancer. However, replication of these results and further evaluation of the long-term health impacts of salpingectomy are needed so that women who elect salpingectomy alone instead of BSO do so with a realistic understanding of both the potential complications of this procedure and the degree to which it will protect them from a high-grade serous cancer later in life. Given the large numbers of women who are now undergoing opportunistic salpingectomy, the long-term safety and efficacy of this procedure should be resolved over the next two decades and we will see if salpingectomy yields tangible benefits in terms of preventing the most aggressive form of ovarian cancer.

References