

Fallopian Tubes: Keep or Remove?

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ABSTRACT

Ovarian cancer is a devastating disease. The pathogenesis of ovarian carcinomas always remained unclear. Enough evidence is now available clearly highlighting distal fallopian tube as the site of origin for serous ovarian carcinomas particularly in women with BRCA mutations. The ovaries and fallopian tubes may not be simultaneously involved. After the completion of childbearing, there exists no known physiological benefit of retaining the fallopian tubes. Post-salpingectomy, the ovarian endocrine function remains unaffected. Removal of premenopausal ovaries leads to attainment of early surgical menopause. Prophylactic salpingectomy at hysterectomy for benign reasons or sterilization rules out any subsequent tubal pathology and offers considerable protection against later tumor development. Risk reducing salpingectomy even if the ovaries are retained are beneficial especially in young women with BRCA mutations.

INTRODUCTION

Epithelial ovarian cancers (EOCs) are the leading cause of death in women dying from gynecological cancer in the developed world. Serous EOC's (68%) are the commonest pathological subtype followed by clear cell (13%), endometrioid (9%) and mucinous (3%). Crum et al classified serous ovarian carcinomas (SOC's) into low-grade (type I, LGSC) and high-grade (type II, HGSC) serous ovarian carcinomas.¹ Ovarian HGSC's are more aggressive and often women present with advanced stage disease. There is now enough evidence to support that these type II tumors derive from epithelium of fallopian tube.² Most deaths from ovarian cancer are attributable to the ovarian HGSC's.³ Hereditary genetic abnormalities can be identified in approximately 10-25% of ovarian cancers.⁴ Ovarian

HGSC's develop in women with hereditary BRCA1 or BRCA2 mutation.⁵

The pathogenesis of ovarian cancer was not clearly understood till date. This had been the key factor in non-identification of screening strategies for this deadly disease. This article reviews knowledge and understanding of ovarian carcinogenesis as well as assess the impact of clinical preventive strategies in ovarian cancer primarily salpingectomy.

"If you're brave enough to say goodbye, life will reward you with a new hello" – Paul Coelho.

Origin of Ovarian Cancer – The New Concept

Ovarian carcinogenesis has a dualistic model that proposes all ovarian cancers into two groups: Type I and Type II (see Table 1).⁶ This model is supported by clinical, pathologic and molecular evidence. The last decade has witnessed weakening of the theory of ovarian serous epithelium (OSE) as origin of EOC and emergence of the fallopian tube as site of origin for ovarian HGSC.

Contrary to the popular belief, HGSCs result from the clonal expansion of the secretory cells in the distal

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Table 1: Characteristics of Type I and II ovarian cancers – Dualistic model⁶

| | Type I ovarian tumors | Type II ovarian tumors |
|-------------------------------------------|--------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Frequency | 20% | 80% |
| Precursors | Adenoma/borderline tumors/endometriosis | De novo |
| Histologic sub-types | Low grade serous carcinoma (LG-SC), low grade endometrioid, mucinous, clear cell, Brenner tumors | High-grade serous carcinomas (HG-SC), high grade endometrioid carcinomas, malignant mixed mesodermal tumors (carcinosarcomas) and undifferentiated carcinomas |
| TP53 mutation | Absent | Present |
| Specific cell signaling pathway mutations | KRAS, BRAF, ERBB2, PTEN, CTNNB1, PIK3CA, ARID1A, and PPP2R1A | Genetically unstable |
| Aggressiveness | Less aggressive | More aggressive |

fallopian tube, rather than the ovary.^{7,8} Ovarian LGSC's are believed to evolve in a stepwise fashion from ovarian epithelial inclusions (OEIs)/serous cystadenomas to serous borderline tumors to invasive carcinoma.^{9,10}

Li et al showed that the majority of ovarian epithelial inclusions (OEIs) are derived from the fallopian tube rather than OSE. LGSCs arise from the tubal secretory cell.¹¹ The fallopian tube is considered the site of origin for most adnexal serous carcinomas. Therefore, preventive strategies, such as salpingectomies, have found their place. The fallopian tubes provide no known benefit, after hysterectomy for benign uterine disease. The woman's hormonal profile remains unaffected after salpingectomy as the ovarian function is preserved.

Time of Fallopian Tube Removal – Opportunistic or Prophylactic

Three strategies for ovarian cancer risk reduction have been proposed in women with BRCA mutations. The options are risk reducing bilateral salpingo-oophorectomy (RRBSO), risk reducing bilateral salpingectomy (RRBS) and risk reducing bilateral salpingectomy (RRBS) with delayed risk reducing bilateral oophorectomy (RRBO).¹²

RRBSO seems to be the most effective risk-reducing strategy. Women unwilling to have their ovaries removed can be offered RRBS with delayed RRBO.¹³

In young women with BRCA mutation declining RRBSO after completion of family, some form of risk reducing surgical intervention would always be welcome rather than none at all. All women should be fully informed regarding the range of available surgical prevention options along with their risks and benefits. The mortality risk and breast cancer risk reduction benefits of RRBSO must be clearly understood by the woman. The strategies to combat the effects of premature menopause should be discussed. A staged procedure with initially RRBS and then RRBO at a later date closer to the age of natural menopause can be offered. The advantage of this dual staged strategy is the avoidance of morbidity of premature menopause. The disadvantage is the uncertain impact on overall mortality, ovarian cancer-

specific mortality and complete loss of breast cancer risk reduction. The woman's informed decision should be honored. The medical professionals should support her in the choice to maximize benefit and minimize risk.

Where Do We Stand in 2015?

The American College of Obstetricians and Gynecologists (ACOG) have released their committee opinion in January 2015¹⁴ based on the recent understanding of ovarian carcinogenesis. The benefits of fallopian tube removal at the time of hysterectomy for benign disease should be discussed with women at risk of having ovarian cancer not undergoing oophorectomy. The women opting for laparoscopic sterilization, can be counseled regarding the availability of bilateral salpingectomy as an effective method of contraception. Removal of fallopian tubes prophylactically provides an opportunity to prevent ovarian cancer. All women undergoing hysterectomy for benign reasons should be informed of the risks and benefits of bilateral salpingectomy and bilateral salpingo-oophorectomy. Only after obtaining an informed consent, the woman should undergo the surgery.

Surgical Minutiae

Some questions do crop up in our minds when we think of removing fallopian tubes. How much of the fallopian tube should be removed? What happens to the ovarian blood supply after salpingectomy? The answers are simple. The fallopian tube should be removed from the fimbriated end up to the uterotubal junction. The interstitial portion of the fallopian tube can be spared.¹⁴ Any fimbrial attachments to the ovary should be cauterized or removed. Preservation of the ovarian blood supply is crucial. The removed fallopian tube must be sectioned in entirety by the pathologist.

Women with BRCA1 or BRCA2 mutation are at high risk of developing serous ovarian carcinoma. They are strongly recommended to have prophylactic RRBSO after completion of childbearing.¹⁵⁻¹⁷ This approach offers the best risk reduction for ovarian cancer and significant risk reduction for breast cancer. Women who are not at high risk for BRCA mutation and have completed their families should be carefully considered for RRBS with

conservation of ovaries at the time of gynecological or other intraperitoneal surgery.

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