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Do we Need Prophylactic Salphingectomy for Ovary Preserving in Hysterectomy

Eddy Hartono

Department of Obstetrics and Gynecology, Hasanuddin University, Makassar, South Sulawesi, Indonesia

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Abstract: Ovarian carcinoma was believed to had arised from fallopian tubes and then spread to ovarian surface and peritoneum. In addition, Lack of ovarian lesion precursor identified and the fact that bilateral salphingo-Oopherectomy performed to protect women with BRCA mutations from ovarian carcinoma lead many authors postulated that fallopian tube is probably the origin of serous ovarian carcinoma. Lately, initial form of serous carcinoma in fallopian tubes of women with BRCA mutation has been identified and this precursor lesion is known as STIC (serous tubal intraepitelial carcinoma). Prophylactic BSO in high risk women (with BRCA mutation) after completed parity may reduce risk of ovarian carcinoma dramatically (80%). Meanwhile, prophylactic salpingectomy as an alternative may suffice to prevent ovarian carcinoma if we could ensure that serous ovarian carcinoma arise from tubal fimbriae.

Keywords: ovarian carcinoma, BRCA, STIC, salpingo-Oopherectomy, salpingectomy

Introduction

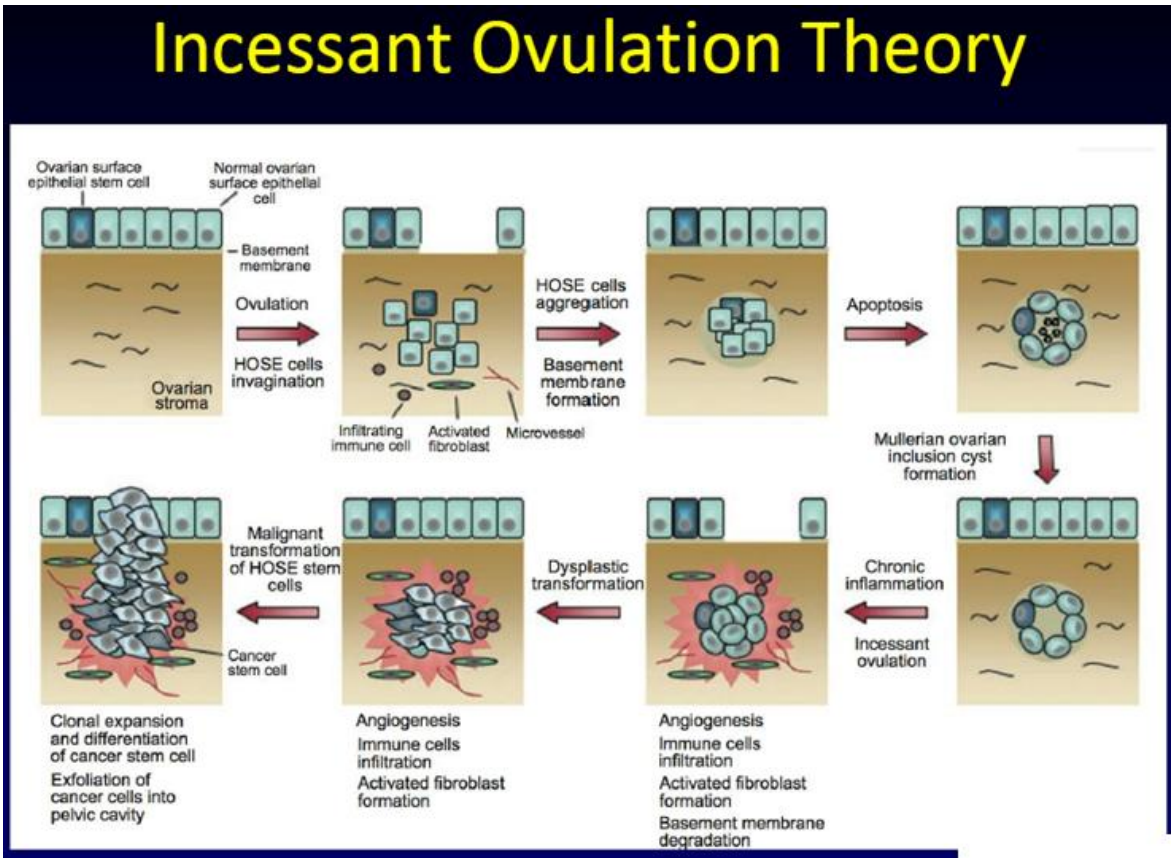
Fallopian tubes was first described by Gabrielis Fallopius (Italia, 1533-1562)and its function was first reported by Reinier DeGraaf (Belanda, 1672). Three hundred years ahead, more authors believed that ovarian carcinoma had arised from fallopian tubes and then spread to ovarian surface and peritoneum (Backes, 2014).

Etiology of Ovarian Carcinoma

Ovarian carinoma is a life-threatening gynecologic malignancy. Serous ovarian carcinoma (SOC)is the most frequent epithelial ovarian malignancy. Its incidence rate is about 70-80% (Roelofsen, 2013).

Many efforts have been attempted to screen and detect this pathology early. Transvaginal ultrasonography, Ca-125 level, and many others biomarkers have not shown any satisfying results. Early detection of ovaian carcinoma is more complicated by its histological origin which have long been an debatable issue. Till now, there is a paradigm that ovarian carcinoma is first arise from *ovarian surface* (OSE). OSE consists of squamous cells that is similar to mesothelium of peritoneal cavity. Histologically these cells are different from ovarian carcinoma histologies (serous, endometrioid, dan clear cell) which have Mullerian phenotype (Roelofsen, 2013).

Classic theory of ovarian carcinogenesis is incessant ovulation theory. This theory assumes that ovarian carcinoma arising from OSE mesothelium that undergo metaplasia and morpholigal changes. Metaplastic OSE is then undergo stromal invagination which results in epithelial inclusion cyst. This epithelial inclusion cyst is then undergo malignant transformation. This malignant transformation is triggered by incessant ovulation and chronic inflammation as its consequence. Clinicopathologic studies failed to prove this hipothesis and epithelial inclusion cyst was randomly found in both high risk and control group. (Roelofsen, 2013, Coleman, 2012).



Picture 1. Classic theory of ovarian carcinogenesis (Coleman, 2012)

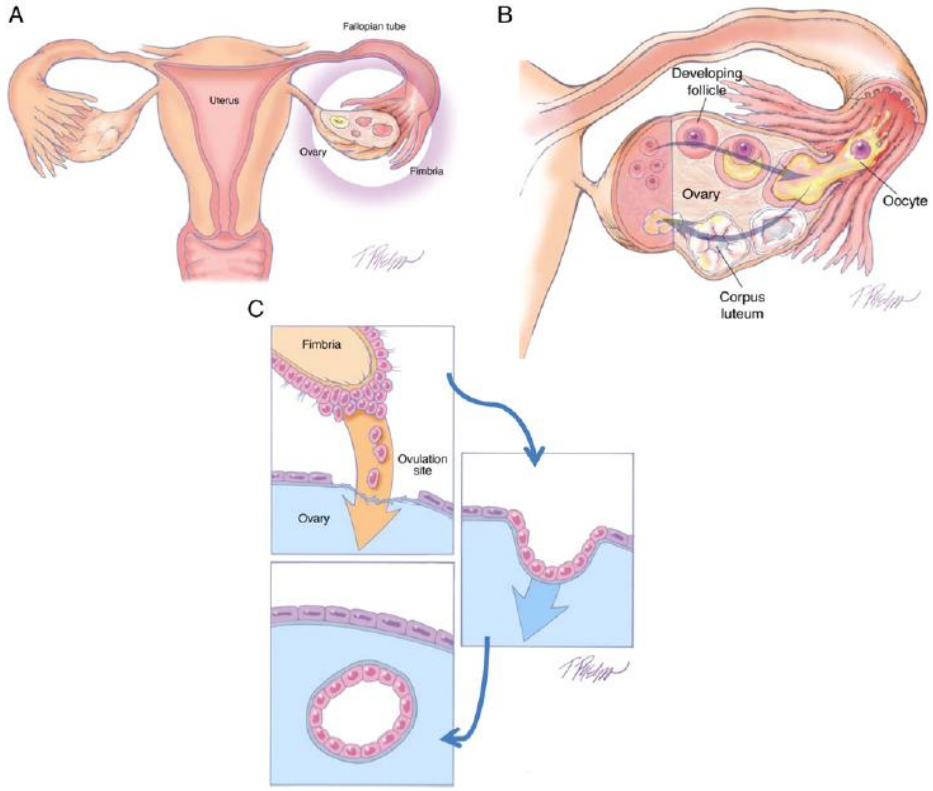
Recently, ovarian carcinogenesis theory has focused on fallopian tubes as its primary origin of serous ovarian carcinoma. Mullerian ducts (Paramesonephric) develops to upper vagina, uterus, and fallopian tube in early embriogenesis. Lack of ovarian lesion precursor identified and the fact that bilateral salphingo-Oopherectomy performed to protect women with BRCA mutations from ovarian carcinoma lead many authors postulated that fallopian tube is probably the origin of serous ovarian carcinoma. Fallopian tube consists of Mullerian type epithel and malignant transformation of this cell logically cause serous type cancer. Lately, initial form of serous carcinoma in fallopian tubes of women with BRCA mutation has been identified and this precursor lesion is known as STIC (serous tubal intraepitelial carcinoma). Cells from this precursor lesion is able to detach and impant on ovarian surface. Diagnosis and lesion findings could be difficult to established because its low reproducibility and many studies have insufficient appropriate control to differentiate premalignant lesion with other normal histologic variants of fallopian tube epithelium (Roelofsen, 2013, Li et al., 2012).

In normal individual, BRCA1 and BRCA2 could be assumed as genetic materials that contribute to genomic stability and cellular integrity. Damaged of these DNA could occur secondarily from extrinsic agents such as radiation or metabolic process. These damaged DNA can be repaired with protein encoded by BRCA1 and BRCA2. This repairing process prevent mutation accumulation and suppress cancer formation. This events may prove that BRCA gen is a tumor suppressor gen. Incidence of BRCA mutations in breast cancer and ovarian cancer is about 5-10%. BRCA1 dan BRCA2 may be linked with breast cancer in 52% and 32% of cases. Risk of ovarian cancer in BRCA1 mutation is about 28-44%, meanwhile risk of ovarian cancer in BRCA2 mutations is about 20% and tends to occur in older age. Most BRCA mutations related to serous type of ovarian cancer. BRCA mutation may also be found in ovarian adenocarcinoma enometrioid type but no correlation found between BRCA mutation and ovarian carcinoma mucinous type. Subjects with BRCA mutation are also in increased risk to have colon cancer, pancreatic cancer, prostate cancer, and melanoma (Colgan, 2003, Narod, 2013).

Mingels et al (2012) reported that 226 women with BRCA1 and BRCA2 carrier that underwent prophylactic bilateral salphingooopherectomy, invasif tubal carcinoma in BRCA 1/2 mutations subject is about 7,1%, and STIC in BRCA 1/2 subjects is about 6,2% compared with controls where no incedence of STIC found (0%). 64,3% STIC found in fimbria and 35,7% remainders found in other parts. Incidence of STIC is increased in people older than 40 years. This study reported that STIC incidence in subjects <35 y.o. was 0%, 35-40 y.o was 2,7%, 41-50 y.o. was 5,8%, and >50 years was 10,8% (Mingels et al., 2012).

Other studies found that STIC incidence was about 50% in serous ovarian carcinoma, besides prophylactic bilateral salpingo-oopherectomy may reduce ovarian cancer risk about 80% (Mingels et al., 2012, Tanner et al., 2013).

Kurman dan Shih (2010) in their study about origin and pathogenesis of epithelial ovarian carcinoma described how premalignant and malignant fallopian tube cells transferred to ovarium as shown in picture bleow. Shortly before ovulation, tubal fimbria cover the ovary (A); At ovulation, ovarian surface will rupture and followed by oocyte expulsion and transfer to fimbriae, fimbriae directly in contact with rupture ovarian surface (B); Tubal epithelium detach from fimbriae and implant on ovarian surface to form inclusion cyst (C)(Kurman and Shih, 2010).



Picture 2. Transfer of tubal epithelium to ovarian surface (Kurman and Shih, 2010)

Ovarian carcinoma prevention

Incidence of ovarian carcinoma after hysterectomy has been frequently found about 4-14% (Hickey et al., 2010).Paradigms changes in origin of ovarian carcinoma generate controversies in role of bilateral salpingectomy in ovarian carcinoma prevention. (Backes, 2014).

Traditional approach to decrease the risk of ovarian carcinoma in women with family history of ovarian cancer or BRCA1 and BRCA2 mutation is to perform hysterectomy and bilateral salpingo-oopherectomy. Many authors suggest to perform bilateral oopherectomy in women who underwent hysterectomy for benign reasons to reduce risk of ovarian carcinoma . (Kurman and Shih, 2010).

Prophylactic BSO as ovarian carcinoma prevention

Prophylactic BSO in high risk women (with BRCA mutation) after completed parity may reduce risk of ovarian carcinoma dramatically (80%).In addition, prophylactic BSO may reduce risk of breast cancer especially in premenopausal population. BSO perform before menopause may initiate severe menopausal symptoms and increase risk of cardiovascular disease, this suggest that premenopausal women should not undergo BSO concurrently with hysterectomy, except for any obvious indications(Tanner et al., 2013, Narod, 2013).

Bilateral salpingectomy as ovarian carcinoma prevention

Salpingectomy may suffice to prevent ovarian carcinoma if we could ensure that serous ovarian carcinoma arise from tubal fimbriae. This approach should be elaborated further and comparing it to traditional BSO method (Kurman and Shih, 2010).

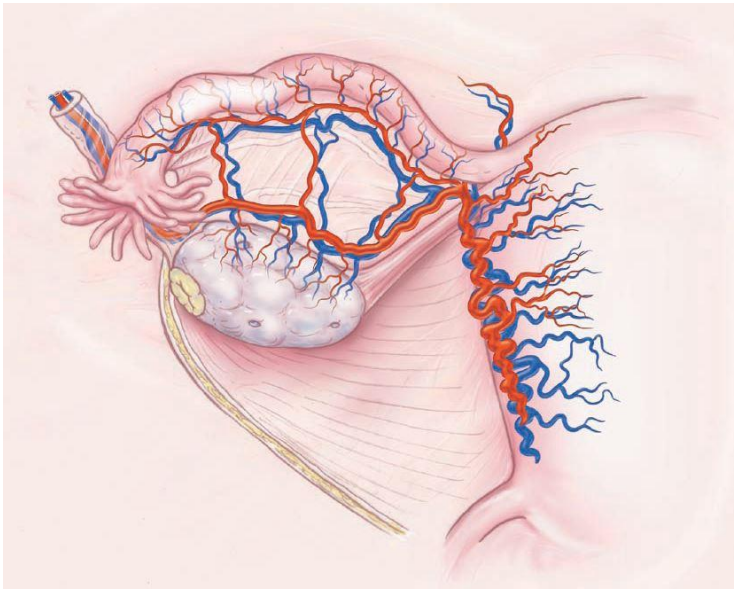
Salpingectomy may be a logical intervention if we assume that fallopian tube is the origin of serous ovarian carcinoma. Preserving fallopian tube at hysterectomy procedure with benign indications may not have any physiologic benefits because remained tube will not have any function after hysterectomy. In addition, hormonal profile is not affected after salpingectomy. (Roelofsen, 2013).

Do we Need Prophylactic Salphingectomy for Ovary Preserving in Hysterectomy

A prospective study from 30 000 women found that concommitant bilateral oopherectomy at hysterectomy procedure compared with ovarian consevation may be related to increased mortality, increased risk of coronary heart disease and lung cancer. Therefore, women whom undergo hyseterectomy with benign indications should have their fallopian tube removed and ovarian preserved to improve life quality and survival. (Kurman and Shih, 2010).

Theroritically, fallopian tube removal and ovarian preservation have hormonal benefits and could reduce risk of ovarian carcinoma. However, how far this intervention could reduce ovarian cancer risk still need to be explored. Besides, salpingectomy may compromise ovarian blood flow and results in premature menopause and produce long term consequences. Some authors considered that in general population, reduced risk of ovarian function and/or premature menopause after surgery may be more prominent and harmful than the benefits of decreased risk of ovarian carcinoma. (Backes, 2014, Kurman and Shih, 2010).

A publication reported that salpingectomy as intervention to reduce risk of ovarian carcinoma if performed meticulously and conserved ovarian hilum may not produce negative effects on ovarian function and no perioperative complications related to salpingectomy discovered.(Erickson et al., 2013). McAlpine in his study reported that concomittant salpingectomy at hysterectomy procedure as ovarian carcinoma prevention measures did not increase perioperative and operative complications (prolonged hospital care or blood transfusion rate). Besides this intervention is quite simple and safe to perform (McAlpine et al., 2014).



Picture 3. Anatomy of ovarian vessels

Recommendation

To support concomittant prophylactic salpingectomy at hysterectomy procedure with benign indications in women categorized as low risk to have ovarian carcinoma, we need to consider any evidences and rationales to accept or decline this new operative paradigm. Till now there is no prospective data from large randomised controll trial with sufficient time and life quality analysis to infer the long term implications of salpingectomy in women with low risk category to have ovarian carcinoma (Tanner et al., 2013).

In Netherland, prophylactic BSO is recommended in women with BRCA mutations at 40 years of age. This recommendation based on study that STIC and tubal invasive carcinoma incidence solely found in women with with BRCA mutations and STIC incidence is increased after 40 years of age. (Mingels et al., 2012).

Other alternative measure is to perform bilateral salpingectomy in women with completed parity and BRCA mutations then followed by ovarian removal at older ages. This alternative seems better and more safety to perform at below 40 years old because it may avoid premature menopause. In addition, prophylactic BSO itself still need further investigations about its effectivity and safety in preventing ovarian carcinoma (Mingels et al., 2012).

An ovarian carcinoma study center in Canada has made recommendations as follow:(McAlpine et al., 2014)

1. Women in general population with low risk category (1,5-2%) to have ovarian carcinoma:
   a. Consider to perform concomittant bilateral salpingectomy at hysterectomy procedure even if ovaries are preserved.
   b. Consider to perform excisional bilateral salpingectomy in tubal sterilization instead of tubal ligation.

2. Women with high risk category (>50%) to have ovarian carcinoma after incidental identification of BRCA 1/2 mutations or patients with high grade serous carcinoma is counseled about hereditary carcinoma and genetic evaluation of BRCA 1/2. Counselling and genetic evaluation also are also performed in patients as to perform preventive operative measures.

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