

Prophylactic salpingectomy and ovarian cancer: An evidence-based analysis

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Abstract

Introduction: One of the ovarian carcinogenesis theories was the presence of premalignant cells in the epithelium of the fallopian tube. Therefore, the prophylactic salpingectomy during benign gynecological surgery is now expected as the attempt to reduce the ovarian cancer incidence. We studied the effect of prophylactic bilateral salpingectomy (PBS) in reducing the ovarian cancer incidence. **Methods:** This evidence-based report resulted from critical appraisal of 5 articles. It is aimed to answer our clinical question, can bilateral prophylactic salpingectomy reduce the incidence of ovarian cancer among women underwent hysterectomy for benign condition or permanent contraception surgery? The search was conducted on the Cochrane Library®, PubMed®, and Embase® using keywords of “prophylactic salpingectomy,” and “ovarian cancer incidence.” Reference lists of relevant articles were searched for other possibly relevant articles. **Results:** Five studies were included in our appraisal. The incidence of ovarian cancer among women underwent prophylactic salpingectomy is lower compared to women who were not underwent any intervention (2.2% to 13% and 4.75% to 24.4%). The salpingectomy may reduce 29.2% to 64% of ovarian cancer incidence. No significant effect of PBS to ovarian function, quality of life, sexuality, surgery duration, and its cost-effective profile were also found throughout our literature study. **Conclusion:** PBS is suggested to be performed for women during benign gynecological surgery as a primary preventive strategy of ovarian cancer. PBS is a cost-effective procedure, risk-reducing for ovarian cancer and has no significant effect to the ovarian function.

Key words: Ovarian cancer, prophylactic salpingectomy

Introduction

The global prevalence of ovarian cancer is 22.6/100.000 women. The 5-year survival rate ranges from approximately 30%–50%.^[1] Ovarian cancer is one of lethal malignancies, approximately 14,000 deaths from the disease expected in the United States in 2013. Most cases are diagnosed at an advanced stage and no reliable methods to prevent the disease.^[2] One of the ovarian carcinogenesis theories was the presence of premalignant cells in the epithelium of the fallopian tube. The precursor of most ovarian high-grade serous carcinomas and also low-grade serous tumors may originate in the fallopian tube.^[3] This increase the gynecologists’ awareness regarding the role of fallopian tube in the development of epithelial ovarian cancer (EOC).^[4]

Prophylactic bilateral salpingectomy (PBS) is expected to be associated with reductions in the risks of ovarian, fallopian tube, and breast carcinoma. However, a number of debatable issues, i.e., regarding the timing of the procedure, nononcologic morbidity, and the safety of menopausal hormonal therapy remain unresolved.^[5] Therefore, the prophylactic salpingectomy is being studied by many authors to determine its effectivity in reducing the ovarian cancer.^[6] In addition, The American Congress of Obstetricians and Gynecologists recommends the surgeon and patient should discuss the benefits of the removal of salpingectomy during a hysterectomy in women at population risk of ovarian cancer.^[7] Other gynecological boards already declared the beneficial impact of PBS, however, no clear statement that PBS should be performed.^[8] This critical review aims to study the risk-reducing potencies of PBS for ovarian cancer.

Case Illustration

Mrs. 41-year-old, P2A1, underwent a laparotomy total hysterectomy due to adenomyosis. She suffered from abnormal uterine bleeding and dysmenorrhea VAS 3 for 4 months before admission. She felt palpable mass on the lower abdomen and had history of hospitalization for blood transfusion due

to anemia of blood loss (Hemoglobin level 6.8 g/dl). On ultrasound examination, we revealed enlarged and globular uterus, diffuse adenomyosis with the diameter of 52 mm. During hysterectomy, the Obstetrics and Gynecologist (OB-GYN) performed bilateral salpingectomy to reduce the risk of having ovarian cancer.

Clinical question

- P (patients): Women underwent hysterectomy for benign condition or permanent contraception surgery
- I (intervention): Bilateral prophylactic salpingectomy
- C (comparison): No prophylactic salpingectomy
- O (objective): Ovarian cancer incidence.

Among women underwent hysterectomy for benign condition or permanent contraception surgery, can bilateral prophylactic salpingectomy reduce the incidence of ovarian cancer?

Methods

Search strategy

We conducted the literature searching on July 27th, 2017 on the Cochrane Library®, Embase® PubMed® with the combination of keywords of “prophylactic salpingectomy,” and “ovarian cancer.” Search focused on articles in clinical trial or case–control design. Reference lists of relevant articles were searched for other possibly relevant trials [Figure 1]. Studies without ovarian cancer incidence stated in the studies’ outcome were not included in this study.

Selection

First selection was done by screening the study title and abstract [appendix Figure 1 for an overview of the selection of articles]. Five articles were available as full text and included in our analysis.

Critical appraisal

Appraisal of five studies including two cost-effectiveness studies and 3 population-based case–control studies, involving

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Table 1: Critical appraisal summary based on five published studies

Study	Type of study	Sample	Validity				Result		Applicability	Total score
			1	2	3	4	5	6		
Falconer <i>et al.</i> (2015)	Cohort	5,449,119	+	+	-	+	+	+	+	6/7
Dilley <i>et al.</i> (2017)	Cost-effectiveness study	-	-	+	-	-	+	+	+	3/7
Lesard-Anderson <i>et al.</i> (2014)	Nested case-control	582	+	+	-	+	+	+	+	6/7
Madsen <i>et al.</i> (2014)	Case-control	16,846	+	+	-	+	+	+	+	6/7
Kwon <i>et al.</i> (2015)	Cost-effectiveness study	-	-	+	-	-	+	+	+	3/7

Every item was scored based on Critical Appraisal of Prognostic studies (CEBM, University of Oxford, 2010). 1=Sample recruitment, 2=Sufficient follow-up, 3=Blinding, 4=Adjustment if needed, 5=Result how likely over time, 6=How precise prognostic estimate, 7=Applicability, +=Adequate, -=Inadequate, ?=Unknown

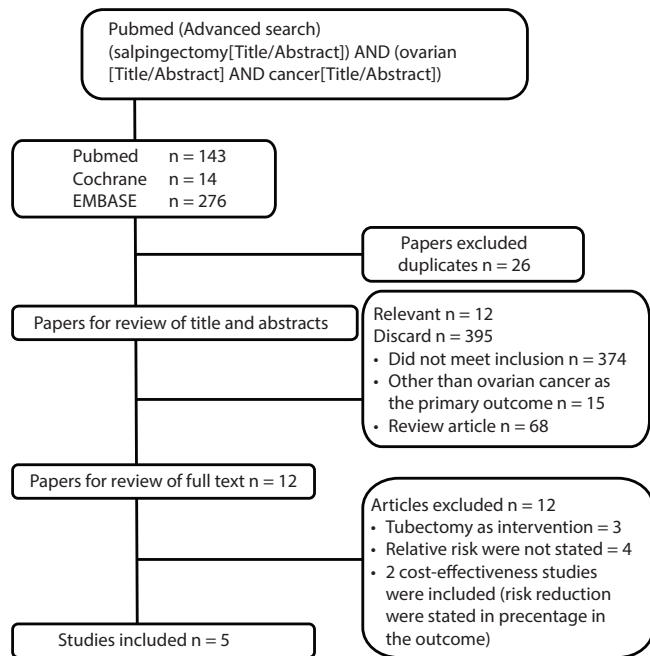


Figure 1: Searching flow

women underwent hysterectomy for benign condition or tubal sterilization were conducted finding at ovarian cancer incidence among they who underwent prophylactic salpingectomy and they who were not performed any intervention. The quality of study was evaluated using appraisal form developed by Center of Evidence-Based Medicine, University of Oxford, available from <http://www.cebm.org>.

Results

We included five studies in our appraisal. Two cost-effectiveness studies were included due to the statement of risk reduction percentage of ovarian cancer stated in the outcome of their studies [Table 1]. From two studies, the incidence of ovarian cancer among women underwent prophylactic or opportunistic salpingectomy was lower compared to they who were not underwent any intervention (2.2% to 13% and 4.75% to 24.4%). The salpingectomy might reduce 29.2% to 64% of ovarian cancer incidence.

Dilley *et al.* calculated the cost saving and ovarian cancer incidence among two population models: (1) 50,000 women aged 45 undergoing laparoscopic hysterectomy and (2) 300,000 women aged undergoing laparoscopic permanent contraception. The incidence of ovarian cancer at the age of 65 of these populations was, respectively, 2.20% (1104/50,000) among they who underwent prophylactic salpingectomy and 4.75% (2376/50,000) among they who not underwent PBS. Ovarian cancer rates were estimated based on lifetime population risk of ovarian cancer of 1.3%, and risk reduction

data from a large population-based cohort conducted by Falconer *et al.*^[9] They stated that opportunistic salpingectomy may save \$23.9 million in health-care budget.^[10]

Kwon *et al.* predicted that salpingectomy would reduce ovarian cancer risk by 38.1% (95% confidence interval [CI] 36.5-41.3%) and 29.2% (95% CI 28.0-31.4%) compared with hysterectomy alone or tubal ligation, respectively.^[11] In addition, they also stated that salpingectomy with hysterectomy was less costly than hysterectomy alone or with bilateral salpingo-oophorectomy.^[11]

In their population-based cohort study, Falconer *et al.* was clearly stated that salpingectomy might reduce ovarian cancer risk in the general population. The risk for ovarian cancer among women underwent salpingectomy was significantly lower compared with the unexposed population (hazard ratio [HR] = 0.65, 95% CI = 0.52-0.81). In addition, bilateral salpingectomy was better than the unilateral procedure to prevent the incidence of ovarian cancer (HR = 0.35, 95% CI = 0.17-0.73, and 0.71, 95% CI = 0.56-0.91, respectively).^[9]

Lessard-Anderson *et al.* studied the effects of excisional tubal sterilization on the risk of serous EOC or primary peritoneal cancer (PPC). Excisional tubal sterilization, i.e., complete salpingectomy, partial salpingectomy, and distal fimbriectomy was statistically lower the risk of serous EOC and PPC by 64% after (odds ratio [OR], 0.36 [95% CI, 0.13-1.02]; *P* = 0.054) compared with those without sterilization or with nonexcisional tubal sterilization. Tubal sterilization reduces the risk of EOC and PPC by 41%.^[12]

Madsen *et al.* conducted the Danish nationwide register-based case-control study during 1982-2011. They found that bilateral salpingectomy reduced EOC risk by 42% (OR 0.58). Tubal ligation reduced overall EOC risk (OR 0.87), the strongest risk reductions associated with endometrioid cancer (OR 0.66) and EOC of “other” histology (OR 0.60). Interval 0.43-0.83).^[13] All studies was summarized in Table 2.

Discussion

Ovarian cancer incidence after prophylactic salpingectomy

The incidence of ovarian cancer among was, respectively, 2.2% to 13% and 4.75% to 24.4% among they who underwent prophylactic salpingectomy and they who were not underwent any intervention. The risk-reducing capability of prophylactic salpingectomy in our study was similar with latest meta-analysis performed by Yoon *et al.* They revealed the risk of incidence of ovarian cancer was lower 49% among the patients who underwent bilateral salpingectomy compared to the controls (OR: 0.51, 95% CI 0.35-0.75).^[14] In our study, PBS may reduce 29.2% to 64% of ovarian cancer incidence.

Table 2: Study characteristics

Study	Population	Design	Intervention	Outcome
Falconer <i>et al.</i> (2015)	Previous surgery on benign indication (sterilization, salpingectomy, hysterectomy, and bilateral salpingo-oophorectomy hysterectomy; <i>n</i> =251,465) compared with the unexposed population (<i>n</i> =5,449,119)	Cohort	Previous salpingectomy	Salpingectomy: 13.0% (10.5-16.2) Unexposed: 24.4% (24.2-24.7) Hazard ratio: 0.65 (95% CI 0.52-0.81)
Dilley <i>et al.</i> (2017)	2 models: Women aged 45 undergoing laparoscopic hysterectomy with ovarian preservation for benign indications (50,000) Women aged 35 undergoing laparoscopic permanent contraception (300,000)	Cost-effectiveness study	Laparoscopic hysterectomy with and without salpingectomy	Salpingectomy: 2.20% (1104/50,000) Without salpingectomy: 4.75% (2376/50,000) Risk reduction: 53.68%
Lesard-Anderson <i>et al.</i> (2014)	All patients with a diagnosis of serous EOC or PPC from 1966 through 2009 194 cases of serous EOC and PPC, 388 controls	Case-control	Salpingectomy	Adjusted risk of serous EOC and PPC was decreased by 64% after excisional tubal sterilization (OR, 0.36 [95% CI 0.13-1.02]; <i>P</i> =0.054)
Madsen, <i>et al.</i> (2014)	Danish women diagnosed with epithelial ovarian cancer (<i>n</i> =13,241) or border-line ovarian tumor (<i>n</i> =3605) in the study period	Case-control	Salpingectomy	Percentage of risk reduction: 42% (ORs, 0.58 [95% CI 0.36-0.95])
Kwon, <i>et al.</i> (2015)	Hypothetical cohort of women undergoing hysterectomy for benign gynecologic conditions or surgical sterilization	Cost-effectiveness study	Hysterectomy with and without salpingectomy	Percentage of risk reduction Salpingectomy: 38.1% (95% CI 36.5%-41.3%) Hysterectomy alone or tubal ligation: 29.2% (95% CI 28.0%-31.4%)

EOC=Epithelial ovarian cancer, ORs=Odds ratios, CI=Confidence interval, PPC=Primary peritoneal cancer

Three cohort studies appraised in our study had better appraisal score due to its clearly-stated sample recruitment, duration of follow-up, and risk-reducing parameters.

Opportunistic salpingectomy at the time of pelvic surgery for a benign condition develops as an option for primary prevention of high-grade serous cancer. It was based on the theory suggests that precursor lesions of high-grade serous cancer originate in the fallopian tube. The presumed precursor tubal lesion, localized at the fimbrial end of the fallopian tubes, is termed the serous tubal intraepithelial carcinoma.^[8]

Other impact of prophylactic salpingectomy

Prophylactic salpingectomy probably has low effect to the ovarian function after surgery. It was proven by insignificant change anti-Mullerian Hormone levels three months after hysterectomy of and there were reported morbidities related to the procedure.^[2] Findley *et al.*, in their pilot randomized controlled trial revealed similar finding that PBS did not have any short-term negative effects on ovarian reserve.^[15] The latest study conducted by Venturella *et al.* revealed that follicle-stimulating hormone, anti-Mullerian hormone, 3-dimensional antral follicle count, vascular index, flow index, and vascular flow index did not show different profile up to 35 years after surgery after prophylactic salpingectomy compared to the control group.^[16]

Antosh *et al.* stated that PBS increases operating time by 11 min and blood loss by 6 ml.^[17] However, it did not increase the complication rate of surgeries.^[18] In Italia, PBS is already well-known among the Italian OBGYNs as the attempt to reduce ovarian cancer incidence.^[19] In Austria, PBS is now

widely performed during benign gynecologic surgery and cesarean section.^[20] We need further research to know the knowledge and practice among OBGYNs regarding this issue. Among low-risk women undergoing pelvic surgery, PBS is a cost-effective strategy for decreasing ovarian cancer risk.^[10] PBS also did not affect either on the general quality of life or sexuality.^[21]

We suggest that removal of the fallopian tubes is an effective attempt to reduce the ovarian cancer risk in the general population. This was similar with the latest meta-analysis. Therefore, PBS should be considered for women who require hysterectomy with benign indications or sterilization procedures.^[14] Due to its beneficiary effect, the patients should be counseled about the risks and benefits of both procedures based on the current available evidence.^[22]

Conclusion

PBS is suggested to be performed for women during benign gynecological surgery as a primary preventive strategy of ovarian cancer. PBS is a cost-effective procedure that has risk-reducing profile has no significant effect to the ovarian function.

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Conflicts of interest

There are no conflicts of interest.

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