RESEARCH ARTICLE

Subsequent Oophorectomy and Ovarian Cancer after Hysterectomy for Benign Gynecologic Conditions at Chiang Mai University Hospital

Aurapin Jitkunnatumkul, Charuwan Tantipalakorn*, Kittipat Charoenkwan, Jatupol Srisomboon

Abstract

This study was undertaken to determine the incidence of subsequent oophorectomy due to ovarian pathology or ovarian cancer in women with prior hysterectomy for benign gynecologic conditions at Chiang Mai University Hospital. Medical records of women who underwent hysterectomy for benign gynecologic diseases and pre-cancerous lesions between January 1, 2004 and December 31, 2013 at Chiang Mai University Hospital were retrospectively reviewed. The incidence and indications of oophorectomy following hysterectomy were analyzed. During the study period, 1,035 women had hysterectomy for benign gynecologic conditions. Of these, 590 women underwent hysterectomy with bilateral salpingo-oophorectomy and 445 hysterectomy with bilateral ovarian preservation or unilateral salpingo-oophorectomy. The median age was 47 years (range, 11-75 years). Ten women (2.45 %) had subsequent oophorectomy for benign ovarian cysts. No case of ovarian cancer was found. The mean time interval between hysterectomy and subsequent oophorectomy was 43.1 months (range, 2-97 months) and the mean follow-up time for this patient cohort was 51 months (range, 1.3-124.9 months). According to our hospital-based data, the incidence of subsequent oophorectomy in women with prior hysterectomy for benign gynecologic conditions is low and all represent benign conditions.

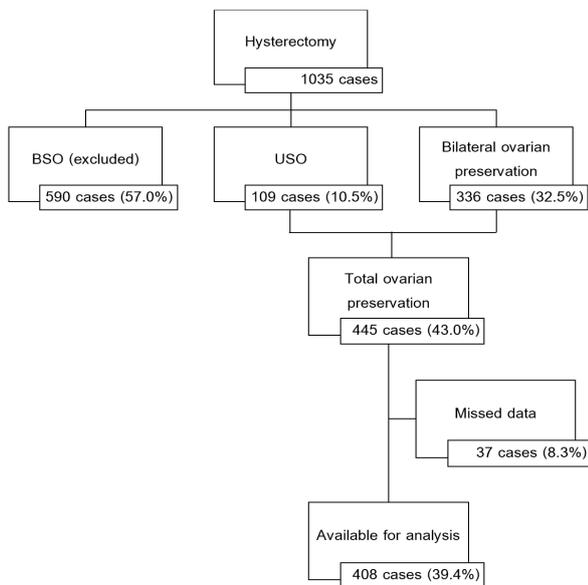Keywords: Subsequent oophorectomy- hysterectomy - ovarian preservation - ovarian cancer

Introduction

Ovarian cancer is the seventh most common cancers in female population and the eighth most common cause of death from cancer in women. Worldwide, in 2012, approximately 238,700 women were diagnosed with ovarian cancer and 151,900 died from this disease. The incidence rates are highest in developed countries (Ferlay et al., 2012). In Thailand, ovarian cancer is the second most common gynecologic cancers and the sixth most common cause of death from cancers in women. The incidence is approximately 5.4-6.8 per 100,000 women (Moore et al., 2008). Ovarian cancer has a poor prognosis because over 75% presented in an advanced stage and about 80% developed tumor recurrence (Jansaka et al., 2014). This is probably due to the fact that early-stage ovarian cancers are asymptomatic and there is no effective screening test. Therefore early detection of ovarian cancer is usually not possible. Many methods for ovarian cancer screening such as serum CA -125 or transvaginal ultrasound were ineffective (Muto et al., 1993; Woodward et al., 2007; Tantipalakorn et al., 2014). Hysterectomy is one of the

most common gynecologic operations. Women underwent hysterectomy for benign indications are commonly offered elective bilateral salpingo-oophorectomy (BSO) because this approach greatly decreases the risk of ovarian cancer and the need for future ovarian surgery (Asante et al., 2010). However, oophorectomy has potential adverse effects such as cardiovascular disease, osteoporosis, impaired cognitive function, and neurologic disease particularly if performed in women under the age of 45-50 years (Rocca et al., 2006; Parker et al., 2007; Shuster et al., 2008; Parker et al., 2009). In the previous studies, the incidence of subsequent oophorectomy in women with ovarian preservation during hysterectomy varied from 2.8–9.2 % (Plockinger et al., 1994; Dekel et al., 1996; Zalel et al., 1997; ACOG Practice Bulletin, 2008; Casiano et al., 2013) and incidence of ovarian cancer in women with ovarian preservation during hysterectomy varied from 0.07–9.9% (Naylor, 1984; Kontoravdis et al., 1996; Loft et al., 1997; Chan et al., 2014).

The objective of this study was to determine the incidence of subsequent oophorectomy due to ovarian pathology in women with prior hysterectomy for benign

Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand *For correspondence: nokctantipa@gmail.com*

Figure 1. Diagram of the Study
conditions over a period of 10 years at Chiang Mai University Hospital.

Materials and Methods

This study was a retrospective descriptive study in women who underwent hysterectomy for benign gynecologic diseases and pre-cancerous conditions at Chiang Mai University Hospital between January 1, 2004

and December 31, 2013. It was ethically approved by the Research Ethics Committee of Chiang Mai University. The data resources for review were medical records of operating section of Obstetrics and Gynecology Department and computerized database of Chiang Mai University Hospital. The patient characteristics and treatment details were thoroughly reviewed; including age at hysterectomy, indications for hysterectomy, types of hysterectomy, unilateral or bilateral ovarian preservation, date at hysterectomy and subsequent oophorectomy, and pathology of subsequent oophorectomy. The inclusion criteria were hysterectomy for benign conditions based on postoperative pathological diagnosis. The women who had history of gynecologic cancer or hysterectomy for malignant gynecologic disease were excluded. Pregnant women were also excluded. The main outcome was the incidence of subsequent oophorectomy due to ovarian pathology in women with prior hysterectomy for benign conditions.

The statistical analysis was performed using SPSS version 21.0 (IBM Corp. Released 2012; IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: USA). The descriptive data were presented as percentage / range or means ± SD, as appropriate.

Results

A total of 1,756 women undergoing hysterectomy were identified during the study period. Of these, 721

Table 1. Baseline Characteristics of Women Undergoing Hysterectomy

Characteristics	Total ovarian preservation (n = 445) Number of patients		BSO (n = 590) Number of patients	
	cases	%	cases	%
Indications for hysterectomy				
· Myoma uteri	381	85.6%	447	75.8%
· Pre-cancerous of cervix	51	11.5%	118	20.0%
· Uterine prolapse	3	0.7%	1	0.2%
· Benign ovarian cyst	7	1.5%	20	3.3%
· Others	3	0.7%	4	0.7%
Routes of hysterectomy				
· Abdominal	406	91.2%	567	96.1%
· Vaginal	5	1.2%	7	1.2%
· Laparoscopic	34	7.6%	16	2.7%

BSO= Bilateral Salpingo-Oophorectomy

Table 2. Summary of Subsequent Oophorectomy Cases

1st diagnosis	Age	1st operation	Interval	2nd operation	2nd pathologic diagnosis
Myoma uteri	44	TAH with left SO	8 yr 1 mo	Lap right SO	Corpus luteum
Myoma uteri	40	TAH with left SO	5 yr 11 mo	Right SO	Endometrioma
Myoma uteri	44	TAH with appendectomy	2 yr 9 mo	BSO	Mature teratoma
Myoma uteri	44	TAH	2 mo	Right SO	Corpus luteum
Adenomyosis	36	TAH with right SO	6 yr 8 mo	Left SO	Benign ovarian cyst
Adenomyosis	51	TAH	7 yr 4 mo	BSO	Mucinous cystadenoma
Pre-cancerous lesion of cervix	34	TAH with appendectomy	1 yr 2 mo	Right SO	Serous cystadenoma
Hypermenorrhea	45	TAH	1 yr 3 mo	BSO	Corpus luteum
Myoma uteri	43	TAH	2 yr 1 mo	Lap Left SO	Benign ovarian cyst
Pre-cancerous lesion of cervix	43	TAH	5 mo	Lap BSO	Benign ovarian cyst

TAH=Transabdominal hysterectomy, SO = Salpingo-Oophorectomy, BSO= Bilateral Salpingo-Oophorectomy, Lap =laparoscopy

(41.1%) women were excluded due to hysterectomy for ovarian, tubal and uterine cancers. The remaining 1,035 women with prior hysterectomy for benign conditions were available for analysis. Although, the data of 590 (57.0%) women who underwent hysterectomy with bilateral salpingo-oophorectomy (BSO) did not provide information for the main outcome, they were available for comparison of hysterectomy indications and routes with the ovarian preservation group. (Table 1) Three hundred thirty-six (32.5%) women underwent hysterectomy only with bilateral ovarian preservation and 109 (10.5%) women underwent hysterectomy with unilateral salpingo-oophorectomy (USO). Therefore, 445 women undergoing hysterectomy with bilateral ovarian preservation or unilateral salpingo-oophorectomy (USO) were analyzed. Thirty-seven women were lost to follow-up. Finally, 408 women were available for main analysis in Figure 1.

Median age at the date of hysterectomy was 47 years (range 11-75 years). Indications for hysterectomy included myoma uteri, pre-cancerous lesion of cervix, uterine prolapse, endometrioma, benign ovarian cyst, and unspecific benign conditions such as tubo-ovarian abscess (TOA), endometrial polyp, chronic pelvic pain, and mental retardation. Routes of hysterectomy were abdominal, vaginal and laparoscopic approaches. (Table 1).

This study found that 10 (2.45%) women had subsequent oophorectomy. The pathologic diagnosis included; corpus luteum (3 cases), endometrioma (1 case), mature cystic teratoma (1 case), serous cystadenoma (1 case), mucinous cystadenoma (1 case), and benign ovarian cysts (3 cases). None of them had ovarian cancer in the oophorectomy specimens. Among the 10 women with subsequent oophorectomy, seven women had hysterectomy only with bilateral ovarian preservation and three women had hysterectomy with unilateral salpingo-oophorectomy (USO). (Table 2).

At the time of hysterectomy, the mean age of women who needed subsequent oophorectomy was 43.5 years (range 34–51 years). The mean time interval between hysterectomy and subsequent oophorectomy was 43.1 months (range 2–97 months). The mean follow up time of this study is 51 months (range 1.3–124.9 months).

Discussion

For developed countries, the lifetime risk of ovarian cancer is 1.4 - 1.8 % (Piver, 1996; Rozario et al., 1997; Jacoby et al., 2011). The incidence of ovarian cancer in Thailand is lower than that for developed countries. In Thailand, the incidence is approximately 5.4-6.8 per 100,000 women (0.005-0.007 %) (Moore et al., 2008). This study found that women who had prior hysterectomy with bilateral ovarian preservation or unilateral salpingo-oophorectomy had low incidence of subsequent oophorectomy (2.45 %) and the pathologic diagnoses were benign in all cases. This could be explained by the low incidence of ovarian cancer in Thailand, the small number of this patient cohort, and the short follow-up time of this study. In previous studies, the incidence of ovarian cancer among women after ovarian preservation during benign hysterectomy has been reported to vary between 0.07 and 9.9 % (Naylor, 1984; Kontoravdis et al., 1996; Loft et al., 1997; Chan et al., 2014). Therefore, it is necessary to examine the risk of subsequent oophorectomy in different population. From the present study, prophylactic or concurrent oophorectomy at the time of hysterectomy in general Thai population as a preventive measure for subsequent ovarian cancer should not be recommended without complete knowledge of patients' socioeconomic background and propensity to comply with hormone replacement therapy regimens. Bilateral salpingo - oophorectomy (BSO) may reduce the risk of ovarian cancer, but resulting in long-term negative health outcomes. Other surgical procedures appear to reduce the risk of ovarian cancer (Greene et al., 2013; Morelli et al., 2013). Hysterectomy alone was associated with approximately 30% reduction in the risk of ovarian cancer in a meta-analysis (Whittemore et al., 1992). Tubal ligation was found to be associated with 34% reduction in ovarian cancer risk in meta-analysis of case-control studies (Cibula et al., 2011). The potential mechanisms of these procedures include eliminating lesions that may have originated from the fallopian tubes or limiting the upward migration of carcinogens from the lower genital tracts into the peritoneal cavity.

The incidence of subsequent oophorectomy due to benign ovarian pathology in the present study was relatively low (2.45%) when compared to some other previous studies. The mean time interval between hysterectomy to subsequent oophorectomy in present study was 43.1 months and the mean follow up time of this study is 51 months. In the literature, the incidence of subsequent oophorectomy varies (2.8-9.2%) (Plockinger et al., 1994; Dekel et al., 1996; Zalel et al., 1997; ACOG Practice Bulletin, 2008; Casiano et al., 2013). In one study, 9.2% of 4,931 women, who were followed for 30 years needed subsequent oophorectomy (Casiano et al., 2013). However all pathologic findings were reported to be benign, which is consistent with our findings. The overall risk of subsequent oophorectomy among women undergoing ovary-sparing hysterectomy was significantly higher than among women who did not undergo hysterectomy. Furthermore, among women with ovary-sparing hysterectomy, the risk of subsequent oophorectomy was significantly higher in women who had both ovaries preserved compared with those who initially had one ovary preserved (Casiano et al., 2013).

According to the present study, ovarian preservation at the time of hysterectomy for benign conditions, especially for premenopausal women appears acceptable due to the low incidence of subsequent oophorectomy. This information may be useful for counseling the patients before operation for gynecologic benign conditions. In addition, women who underwent bilateral salpingo–oophorectomy (BSO) may possibly suffer from estrogen deficiency conditions such as menopausal symptoms within 2 years after surgery, coronary heart disease, osteoporosis, cognitive dysfunction or neurologic diseases (Rocca et al., 2006; Parker et al., 2007; Shuster et al., 2008; Parker et al., 2009) and may take risk of hormone replacement therapy.

The strength of this study is the rather long follow up

Aurapin Jitkunnatumkul et al

time (51 months), which would be considered sufficient for determining the incidence of subsequent oophorectomy. The weaknesses of this study were small sample size and the short follow-up time to determine the incidence of subsequent ovarian cancer in these women.

In conclusion, In Chiang Mai University Hospital - based population, the incidence of subsequent oophorectomy in women with prior hysterectomy for benign gynecologic conditions is low and all represent benign conditions. Ovarian preservation at the time of hysterectomy for benign conditions appears reasonable.

Acknowledgements

References

ACOG Practice Bulletin No. 89 (2008). Elective and risk-reducing salpingo-oophorectomy. *Obstet Gynecol*, **111**, 231-41.

Asante A, Whiteman MK, Kulkarni A, et al (2010). Elective oophorectomy in the United States: trends and in-hospital complications, 1998-2006. *Obstet Gynecol*, **116**, 1088-95.

Casiano ER, Trabuco EC, Bharucha AE, et al (2013). Risk of oophorectomy after hysterectomy. *Obstet Gynecol*, **121**, 1069-74.

Chan JK, Urban R, Capra AM, et al (2014). Ovarian cancer rates after hysterectomy with and without salpingo-oophorectomy. *Obstet Gynecol*, **123**, 65-72.

Cibula D, Widschwendter M, Majek O (2011). Tubal ligation and the risk of ovarian cancer: review and meta-analysis. *Hum Reprod Update*, **17**, 55-67.

Dekel A, Efrat Z, Orvieto R, et al (1996). The residual ovary syndrome: a 20-year experience. *Eur J Obstet Gynecol Reprod Biol*, **68**, 159-64.

Ferlay J, Soerjomataram I, Dikshit R, et al (2012). Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*, **136**, 359-86.

Greene MH, Mai PL, Schwartz PE (2013). Does bilateral salpingectomy with ovarian retention warrant consideration as a temporary bridge to risk-reducing bilateral oophorectomy in BRCA1/2 mutation carriers? *Am J Obstet Gynecol*, **204**, 1-6.

Jacoby VL, Grady D, Wactawski-Wende J, et al (2011). Oophorectomy vs ovarian conservation with hysterectomy: cardiovascular disease, hip fracture, and cancer in the Women's Health Initiative Observational Study. *Arch Intern Med*, **171**, 760-8.

Jansaka N, Suprasert P (2014). Survival outcomes of recurrent epithelial ovarian cancer: experience from a Thailand northern tertiary care center. *Asian Pac J Cancer Prev*, **15**, 10837-40.

Kontoravdis A, Kalogirou D, Antoniou G, et al (1996). Prophylactic oophorectomy in ovarian cancer prevention. *Int J Gynaecol Obstet*, **54**, 257-62.

Loft A, Lidegaard O, Tabor A (1997). Incidence of ovarian cancer after hysterectomy: a nationwide controlled follow up. *Br J Obstet Gynaecol*, **104**, 1296-301.

Moore MA, Attasara P, Khuhaprema T, et al (2008). Cancer epidemiology in mainland South-East Asia - past, present and future. *Asian Pac J Cancer Prev*, **11**, 67-80.

Morelli M, Venturella R, Mocciaro R, et al (2013). Prophylactic salpingectomy in premenopausal low-risk women for ovarian cancer: primum non nocere. *Gynecol Oncol*, **129**, 448-51.

Muto MG, Cramer DW, Brown DL, et al (1993). Screening for ovarian cancer: the preliminary experience of a familial ovarian cancer center. *Gynecol Oncol*, **51**, 12-20.

Naylor AC (1984). Hysterectomy--analysis of 2901 personally performed procedures. *S Afr Med J*, **65**, 242-5.

Parker WH, Broder MS, Liu Z, et al (2007). Ovarian conservation at the time of hysterectomy for benign disease. *Clin Obstet Gynecol*, **50**, 354-61.

Parker WH, Feskanich D, Broder MS, et al (2009). Long-term mortality associated with oophorectomy compared with ovarian conservation in the nurses' health study. *Obstet Gynecol*, **121**, 709-16.

Piver MS (1996). Prophylactic oophorectomy: reducing the U.S. death rate from epithelial ovarian cancer. A Continuing Debate. *Oncologist*, **1**, 326-30.

Plockinger B, Kolbl H (1994). Development of ovarian pathology after hysterectomy without oophorectomy. *J Am Coll Surg*, **178**, 581-5.

Rocca WA, Grossardt BR, de Andrade M, et al (2006). Survival patterns after oophorectomy in premenopausal women: a population-based cohort study. *Lancet Oncol*, **7**, 821-8.

Rozario D, Brown I, Fung MF, et al (1997). Is incidental prophylactic oophorectomy an acceptable means to reduce the incidence of ovarian cancer? *Am J Surg*, **173**, 495-8.

Shuster LT, Gostout BS, Grossardt BR, et al (2008). Prophylactic oophorectomy in premenopausal women and long-term health. *Menopause Int*, **14**, 111-6.

Tantipalakorn C, Wanapirak C, Khunamornpong S, et al (2014). IOTA simple rules in differentiating between benign and malignant ovarian tumors. *Asian Pac J Cancer Prev*, **15**, 5123-6.

Whittemore AS, Harris R, Itnyre J (1992). Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies. IV. The pathogenesis of epithelial ovarian cancer. collaborative ovarian cancer group. *Am J Epidemiol*, **136**, 1212-20.

Woodward ER, Sleightholme HV, Considine AM, et al (2007). Annual surveillance by CA125 and transvaginal ultrasound for ovarian cancer in both high-risk and population risk women is ineffective. *BJOG*, **114,** 1500-9.

Zalel Y, Lurie S, Beyth Y, et al (1997). Is it necessary to perform a prophylactic oophorectomy during hysterectomy? *Eur J Obstet Gynecol Reprod Biol*, **73**, 67-70.