

Editorial

Is it possible to preserve the ovaries during surgical intervention in younger women diagnosed with endometrial cancer?



Lau et al. authored a valuable article entitled “Impact of ovarian preservation in women with endometrial cancer”.¹ This retrospective cohort study enrolled 529 patients with endometrial cancer between 2000 and 2010. Among these, 17 were in the ovarian preservation group and 517 in the bilateral salpingo-oophorectomy (BSO) group. The authors investigated the impact of ovarian preservation on the outcome of patients with endometrial cancer.¹ We recognize the probity of this publication.

The relationship between hormones and endometrial cancer is well-known because disease states, such as chronic anovulation and endogenous estrogen production from hormone-secreting organ or tumors, are related to excess estrogen, and unopposed estrogen use might lead to endometrial overgrowth, hyperplasia, and subsequent development of endometrial cancer.^{2–5} Since the concern regarding ovarian preservation is that continued ovarian estrogen production might increase the risk of endometrial cancer recurrence,⁴ preservation of the ovaries—a main organ producing estrogen, and of course progesterone—in patients with endometrial cancer is the biggest challenge and unresolved issue that is worthy of further discussion.

The standard treatment for endometrial cancers is a complete and thorough staging surgery, including washing cytology, total hysterectomy (TH), BSO, retroperitoneal lymph node sampling or dissection and randomized biopsy for any suspicious lesion. BSO is typically performed in conjunction with TH to exclude occult ovarian metastases and to decrease estrogen production, which might be beneficial in type I endometrioid cancer therapy.⁴ Despite the theoretical benefits of BSO during endometrial cancer treatment, this procedure results in surgical menopause with the subsequently increasing risk of long-term sequelae of estrogen deprivation, such as cardiovascular disease or osteoporosis.⁶ By contrast, ovarian preservation may lead to the potentially fatal risk of overlooking occult ovarian metastases and coexisting synchronous ovarian primary tumors and the potential risk of endocrine stimulation of residual microscopic endometrial cancers.⁴ Therefore, how to balance the benefit and risk ratio might be a big challenge. The following will be focused on rationale and evidence of the use of ovarian preservation in the management women with endometrial cancer.

First, endometrial cancer can be classified as 2 categories: type I (incidence >80%, endometrioid cell type, low grade of differentiation, strong estrogen-related disease, obesity, indolent clinical behavior, less frequency of extrauterine spreading, frequently nulliparous, PTEN [phosphatase and tensin homolog] gene mutation, and younger age) and type II (incidence < 20%, postmenopausal status, serous or clear cell type, high grade of differentiation, aggressive clinical behavior, frequent extrauterine spreading, non-hormone-related disease, p53 mutation, and older age).⁴ Lau et al.'s study¹ suggested that ovarian preservation might be considered in premenopausal women with early-stage endometrial cancer, pointing that the candidates of ovarian preservation might be those women with Type I endometrial cancer. However, it is conflicted, since these Type I endometrial cancer is hormone-dependent. The rationale of ovary preservation supposed by Lau et al. might be based on the benefits of maintenance of hormone for women's health.^{4,6,7}

Second, endometrial cancers commonly present in an early stage and are staged surgically according to the 2009 French Federation Internationale de Gynecologie et d'Obstetrique (FIGO) staging system, a revision of the 1988 FIGO staging system.⁸ In the Lau et al.'s study,¹ Stage I endometrial cancer was 77.9% of all-stage endometrial cancers. In addition, the recurrence rate was as low as 6.6% from all-stage endometrial cancers, suggesting that the survival of these supposed Stage I endometrial cancer patients after treatment, regardless of performing BSO or not is excellent. In fact, the 5-year survival rate is more than 95% for early-stage endometrial cancer in the United State, with 95.8% and 98% of 1988 FIGO Stage I and 1988 FIGO IA endometrial cancers, respectively.⁹ The similarly excellent 5-year survival rate is 99.0%, 98.6%, and 98.7% for 1988 FIGO IA, 1988 FIGO IB, and 2009 FIGO IA, respectively in Taiwan.¹⁰ The rationale of ovarian preservation might be based on the high percentage of early-stage endometrial cancer and an excellent survival rate.

Third, the rationale of ovarian preservation might be based on an extremely low incidence of extrauterine spreading, including occult ovarian metastases in those patients with early-stage endometrial cancer. Much evidence had supported the possibility,^{9,11–13} including Dr. Lau et al.'s publication.¹ The data of the Surveillance, Epidemiology, and End Results (SEER) study enrolled a total of 3269 women 45 years of age

or younger with Stage I endometrial cancers, including 402 patients (12%) with ovarian preservation, showed that 5-year survival was similar between the patients who received TH with and without BSO.⁹ Among patients with 1988 FIGO IA (2009 FIGO IA) endometrial cancer, 5-year survival rate was excellent up to 98%, regardless of whether the ovaries were preserved or moved. Among patients with 1988 FIGO IC (2009 FIGO IB) endometrial cancer, 5-year survival rate was 89% and 86% in women who underwent BSO and those who did not, respectively. The difference of 5-year survival rate failed to reach a statistical significance. In addition, Cox proportional hazards models of survival based on performance of BSO also confirm no difference of 5-year survival rate between patients with and without BSO. Taken together, the SEER study suggested that ovarian preservation in premenopausal women with early-stage endometrial cancer might be safe and not increase cancer-related mortality. Furthermore, many studies, including Korean¹³ and Yale University¹⁴ reports also supported the concept that ovarian preservation does not adversely affect the recurrence, disease-free and overall survival of patients with Stage I endometrial cancer.

However, although most studies^{13,14} showed that clinical Stage I endometrial cancer with metastasis to the ovary is rare, the incidence of any stage of endometrial cancer with a synchronous ovarian malignancy may be as high as 10–29%, which is at least fivefold greater than the incidence in women older than 45 years with endometrial cancer.¹⁴ However, it is fortunate that premenopausal women with concomitant ovarian and endometrial cancers often had Stage I ovarian cancer and Stage I endometrial cancers, and that women with grade I tumors of each type of cancer had an excellent prognosis after surgical treatment.¹⁴ In addition, the incidence of coexisting ovarian cancer in clinical Stage I endometrial cancer might not be as high as 10–29%, because one study showed that synchronous ovarian primary cancer was only 0.31%.¹⁵ The same study found that 17 of 976 women (1.74%) with clinical Stage I endometrial cancer had ovarian metastases, contributing to a total of 2.05% for the incidence of coexisting ovarian cancer in clinical Stage I endometrial cancer.¹⁵

Taken together, we conclude that ovarian preservation for younger women with early-stage endometrial cancer is still not a standard therapy, although it is a reasonable choice. Before attempting this approach, concerns should be adequately explored between the patients and physicians. Of course, careful counseling, including anxiety about relapse and metastases, should be included in the final decision.

Conflicts of interest

The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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