Original Article

Ovarian Preservation during Surgery for Early Stage Endometrial Cancer: Survey of Practice among Thai Gynecologic Oncologists

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Objective: To evaluate the insights of the Thai gynecologic oncologists towards ovarian preservation during staging surgery for early-stage endometrial cancer.

Materials and Methods: The Thai Gynecologic Cancer Society (TGCS) conducted a national survey study on the management of gynecologic cancer among Thai gynecologic oncologists who had been in practice for longer than one year. An electronic online questionnaire was opened for a response during August 2nd and October 31st, 2019. This study retrieved and analyzed data about the concept and practice of ovarian preservation during surgery for early-stage endometrial cancer patients.

Results: Among 170 gynecologic oncologists who responded to the questionnaires, 108 respondents (63.5%) considered ovarian preservation during surgical staging for early-stage endometrial cancer. Young age patients (<40 years old) and low-grade tumors were the 2 most common features taken into consideration. No significant differences in hospital setting grade and practice duration of the respondents were associated with the consideration of ovarian preservation.

Conclusion: Nearly two-third of Thai gynecologic oncologists considered ovarian preservation during surgical staging for early-stage endometrial cancer. The most common features taken into consideration were young age and low-grade tumor.

Keywords: Ovarian preservation, Endometrial cancer, Gynecologic oncologists, Survey

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The fundamental procedure of surgical staging for endometrial cancer is removal of both ovaries along with the uterus[1]. Ovarian resection aim to take away the major hormonal producing organ and to eradicate the possible sites of metastasis or co-existing synchronous cancer[1]. The ovarian resection which has no effect of hormone deprivation in post-menopausal patients certainly affects the reproductive age patients. The physiologic derangement will lead to cardiovascular diseases, neurological diseases, osteoporosis and/or psychiatric disorders, etc[2].

Many studies reported young endometrial cancer patients who aged <40 years or 45 years had better prognostic features compared to older age groups in terms of having low-grade tumor[3], endometrioid histopathology[4], less myometrial invasion[3,5,6], less nodal metastasis[3], lower stage diseases[5,6], and longer survival[5,6]. These young patients with good prognosis and long survival would have long-term risk from hormonal deprivation from ovarian resection.

Recent publications showed that ovarian preservation in early-stage endometrial cancer surgery especially in premenopausal cohorts did not impact oncologic outcome; instead, it may have a benefit to the quality of life due to the absence of menopausal-related effects[7,8].

This ovarian preservation had been increasing in many countries especially in low risk young endometrial cancer patients. However, studies or reports of this particular practice in Thailand were limited. This study aimed to evaluate insights of the Thai gynecologic oncologists towards ovarian preservation during endometrial cancer surgery.

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Materials and Methods

A cross-sectional survey study was conducted by the Thai Gynecologic Cancer Society in 2019. The research working group discussed the possible variations of the current working situation and practice of the Thai gynecologic oncologists. The survey was to evaluate the current practice

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of gynecologic cancer management of the Thai gynecologic oncologists who had been working for at least one year and were still working in the country. Each collaborator independently obtained approval from the institutional Ethics Committees for Human Research (Ethic approval number 052/2562 by Human Research Ethic Committee of Chulabhorn Research Institute).

Approximately a total number of 258 gynecologic oncologists or gynecologists having practiced in gynecologic cancer care (collectively called gynecologic oncologists in the present study) in Thailand was planned. A list of gynecologic oncologists was retrieved from the membership registry of the Thai Gynecologic Cancer Society. Inclusion criteria were Thai gynecologic oncologists who had been practicing in this field of gynecologic oncology for at least 1 year and being literate in Thai. Exclusion criteria were individuals who were not having clinical practice in the country at the time of this survey and those who were registered members but perform only benign gynecologic lesions or tumors. In brief, the questionnaire was constructed and discussed among the research group members, revised, and finalized with consensus. The questionnaire contained 2 major parts: (1) personal and demographic data: age, gender, years of practice, a setting of the main hospital of practice (government or private, service with or without gynecologic fellowship training, and secondary or tertiary level determined by < or = 300 in-patient beds respectively); (2) current clinical practice for cancers of the cervix, endometrium, and epithelial ovarian cancer in various aspects. The detailed description and questions of cancer-specific sites were detailed and presented elsewhere.

The electronic online questionnaire was opened for responses from August 2nd to October 31st, 2019. This study extracted data about the concept and current practice of ovarian preservation in early-stage endometrial cancer as well as the gynecologic oncologists' working features which might be associated with their practice.

Data were analyzed using SPSS statistical software, version 22 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were used to analyze demographic data and were summarized as numbers with percentages, mean with standard deviation (SD) or median with range. Chi-square or Fisher exact tests were used to compare data between groups as appropriate. The *p*-value <0.05 was considered significant.

Results

A total of 170 gynecologic oncologists responded to the questionnaire. Among these, 107 (63.5%) were female. Most worked in government or tertiary-level hospitals: 152 or 89.4% vs. 142 or 83.5%, respectively. Slightly over half of the respondents involved in gynecologic fellowship training (86 or 50.6%). The median duration of practice was 5 years (range 1 to 42 years).

Regarding the response to the question whether they performed ovarian preservation, 62 (36.5%) did not have this practice at all whereas 108 (63.5%) considered ovarian preservation during surgical staging for early-stage endometrial cancer. The association of the respondents' working features and the practice of ovarian preservation is shown in Table 1. Only the respondents working in the training hospitals tended to do ovarian preservation more frequently than those in service-only hospitals. However, the difference was not statistically significant: 60 (69.8%) versus 48 (57.1%), $p = 0.087$. No other working features were associated with this ovarian preservation surgery.

Among the 108 respondents who considered this ovarian preservation in their practice, the 3 most common features they considered were age <40 years, low-grade tumor, and absence of myometrial invasion (Table 2).

Of note, 20 out of 108 respondents (18.5%) who selected ovarian preservation considered only young age <40

Table 1. Association between the respondents' working features and the practice ovarian preservation during endometrial cancer surgery (n = 170)

Working features of the respondents	The practice of ovarian preservation		*p*-value
	No, n (%)	Yes, n (%)	
Hospital setting			0.457
Government, n = 152	54 (35.5)	98 (64.5)	
Private, n = 18	8 (44.4)	10 (55.6)	
Level of hospital			0.735
Secondary, n = 28	11 (39.3)	17 (60.7)	
Tertiary, n = 142	51 (35.9)	91 (64.1)	
Type of service			0.087
Service/training, n = 86	26 (30.2)	60 (69.8)	
Service only, n = 84	36 (42.9)	48 (57.1)	
Practice duration			0.185
<5 years, n = 71	30 (42.3)	41 (57.7)	
≥5 years, n = 99	32 (32.3)	67 (67.7)	
Total	62 (36.5)	108 (63.5)	

or 45 years as the only criteria. The other respondents selected ed 2 features: 19 (17.6%) considered 2 factors, 65 (60.2%) 3 factors, and 4 (3.7%) required 4 factors as criteria for ovarian preservation.

The association between common clinic-pathologic factors considered for ovarian preservation with workplace and professional experience of the respondents was assessed (Table 3). Only the respondents working in tertiary-level hospitals concerned about young age (<40 or <45 years) more frequently than those in secondary-level hospitals. No significant differences of other factors considered between the respondents in other work settings and experience.

Discussion

This study, which was a part of the survey study of the Thai Gynecologic Cancer Society on gynecologic cancer management among the Thai gynecologic oncologists, evaluated the practice of ovarian preservation in early-stage endometrial cancer surgery.

The results revealed that nearly two-thirds of the respondents (64%) considered this ovarian preservation strategy whereas others reported that they had never have considered this treatment option for their endometrial cancer patients. Being a survey study, the reason why this type of management was not included in their practice could not be explored in detail. Our group discussed and agreed on one obvious reason that endometrial cancer has well-recognized pathogenesis of hormone-dependent (type I), so bilateral salpingo-oophorectomy (BSO) is logical management. This concept, as has been stated by FIGO, had long been trained and practiced among gynecologic oncologists for decades[9]. However, this concept had recently been challenged with data from few retrospective studies which showed no survival difference between endometrial cancer patients with early-stage diseases who had complete standard treatment or ovarian preservation[10-13]. Although more information from a few systematic reviews/meta-analysis also showed no association between ovarian preservation and lower survival rate[7,8], the respondents may be reluctant to consider the ovarian preservation for their patients from limited available data.

No association of ovarian preservation practice and working features of the respondents were demonstrated except for the more common practice in the respondents working in training-hospital. It might be possible that the respondents involved in gynecologic fellowship training would be more up-to-date regarding the emerging data and knowledge, so they tended to consider more current treatment options. This information should also be interpreted with caution. Data from this survey of practice concept could not be referred to an actual data of their real clinical practice until a clinical study would be conducted.

To minimize the negative impact of ovarian preservation and survival outcomes of endometrial cancer patients, careful selection of an appropriate candidate must

Table 2. Factors considered for ovarian preservation during endometrial cancer surgery (n = 108)

Variables	n (%)
Age <40 years	94 (87.0)
Age <45 years	8 (7.4)
Low-grade tumor	86 (79.6)
No myometrial invasion	77 (71.3)
Others*	4 (3.7)

* Others included having no risk of familial cancer (n = 2), accepted the risk after counseling or expected to have good compliance for follow-up (n = 2)

Table 3. Factors considered ovarian preservation during endometrial cancer surgery by working features of the respondents (n=108)

Working features of the respondents who considered ovarian preservation (n = 108)	Factors considered for ovarian preservation					
	Age <40 or 45 years		Low tumor grade		No myometrium invasion	
	n (%)	*p*-value	n (%)	*p*-value	n (%)	*p*-value
Hospital setting						
Government, n = 98	92 (93.9)	0.504	76 (77.6)	0.209	69 (70.4)	0.721
Private, n = 10	9 (90.0)		10 (100.0)		8 (80.0)	
Level of hospital						
Secondary, n = 17	13 (76.5)	0.011	12 (70.6)	0.332	11 (64.7)	0.563
Tertiary, n = 91	88 (96.7)		74 (81.3)		66 (72.5)	
Type of service						
Training, n = 60	58 (96.7)	0.238	48 (80.0)	1.000	43 (71.7)	0.924
Service, n = 48	43 (89.6)		38 (79.2)		34 (70.8)	
Practice duration						
<5 years, n = 41	38 (92.7)	1.000	32 (78.0)	0.750	30 (73.2)	0.736
≥5 years, n = 67	63 (94.0)		54 (80.6)		47 (70.1)	
Total	101 (93.5)		86 (79.6)		77 (71.3)	

be exercised. First, the patients should have an adequate ovarian hormonal function, represented at a young age, so the preservation procedure would not be futile. This factor was quite well aware of among our Thai gynecologic oncologists that younger age of 40 years or 45 years old or less as the most common feature the respondents considered. This was significantly more frequent among those who worked in tertiary-level hospitals. We postulated that the greater number of patients in service, so the more rigid selective criteria were applied. One important note was an additional concern in a few respondents regarding familial ovarian cancer risk which is associated with other cancers. This uncommon but has a possible impact on prognosis should be aware.

The second pre-requisite and probably more important was endometrial cancer should be of low risk for extra-uterine metastasis or having the early-stage disease. Although the risk of ovarian metastasis in early-stage endometrial cancer reported from previous studies ranged from 4.2 to 6.1%[14-17], the 0% rate of this event should be preferred to prevent any relapse of cancer at the remaining tissue. Hence, other risk features that were commonly associated with ovarian metastasis should be excluded e.g. high grade or non-endometrioid tumor, >50% myometrial invasion, and lymph and vascular space invasion (LVSI)[14]. The patients without any of these features had a very low rate (0.5%) of ovarian metastasis[14]. This study also found a low-grade tumor and without myometrial invasions as other factors the respondents considered.

Although these prognostic factors were frequently related to each other, they might be encountered independently. Hence, the more rigid criteria considering all or most features should be encouraged. This was reflected by our survey that only 12% considered only young age as a selective factor, the others reported ≥2 factors before ovarian preservation.

One caveat in ovarian preservation in endometrial cancer was a common feature of co-existing ovarian malignancy. Previous studies reported 4.5 to 25% rates of synchronous ovarian cancer in the young[18-20]. This wide range of this event may partly lie in the characteristic features of the patients studied. One multicenter retrospective study found synchronous ovarian carcinoma as high as 25% among 102 young women with endometrium cancer[4]. However, this figure included patients with cancer of all stages and grades. The rate dropped to only one patient (3.8%) among those with grade 1 and no myometrial invasion and who were treated conservatively[4]. The low or negligible risk of synchronous cancer was supported by one study from Korea which reported 4.5% synchronous ovarian cancer in all their young endometrial cancer patients, with specifically none in the low-risk patients[20]. Another study reported an 11% rate of synchronous ovarian cancer, however, data of grading and staging were not described[19]. The heterogeneous data from different studies did not allow the definite suggestion of the clinic-pathological risk features of synchronous cancer aside from age.

In summary, careful preoperative evaluation and selection of the patients who might benefit without any risk of cancer failure from ovarian preservation should be practiced. Selective criteria should be the patients with no history of familial ovarian cancer, young age with good ovarian function, low-grade tumor, no or less than 50% myometrial invasion, and no extra-uterine lesion. Extensive intraoperative exploration of the ovaries to detect the presence of metastatic or synchronous cancer is a crucial final step before ovarian preservation in endometrial cancer patients. Lastly, thorough counseling with the patients and their families about the benefit, potential consequences, and cancer-specific outcomes should be done before formal inform consent.

Conclusion

This study showed that two-thirds of Thai gynecologic oncologist considered ovarian preservation in endometrial cancer surgery for young and low-risk patients. Further education or guideline development should implement to promote this practice in Thailand.

What is already known on this topic?

The benefit of this ovarian preservation surgery, assuming that there is no risk of cancer metastasis, is to preserve hormonal function leading to a decrease of physiologic deterioration in many systems of the patients after treatment. The trend of ovarian preservation during endometrial cancer surgery is increasing all over the world. However, the attitudes, as well as the insights toward this practice of Thai gynecologic oncologists, are not known.

What this study adds?

The present study found nearly two-thirds of Thai gynecologic oncologists considered ovarian preservation during endometrial cancer surgery. The most common features taken into consideration were young age and low-grade tumor.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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การอนุรักษ์รังไข่ระหว่างการผ่าตัดมะเร็งเยื่อบุโพรงมดลูกระยะต้น: การสำรวจแนวปฏิบัติของแพทย์มะเร็งนรีเวชไทย

ณัฐวุฒิ กันตถาวร, ศรัญญา ชาญพานิชกิจโชติ, ณัฐพร จันทร์ดียิ่ง, ศิริวรรณ ตั้งจิตกมล, สมาคมมะเร็งนรีเวชไทย

วัตถุประสงค์: เพื่อสำรวจแนวปฏิบัติการเก็บรังไข่ระหว่างการผ่าตัดมะเร็งเยื่อบุโพรงมดลูกระยะต้นของแพทย์มะเร็งนรีเวชไทย

วัสดุและวิธีการ: การศึกษานี้เป็นส่วนหนึ่งของโครงการสำรวจระดับประเทศเกี่ยวกับแนวปฏิบัติในการดูแลรักษามะเร็งนรีเวชของแพทย์มะเร็งนรีเวชไทยที่ปฏิบัติงานมาแล้วอย่างน้อย 1 ปี จัดทำโดยสมาคมมะเร็งนรีเวชไทย การศึกษารวบรวมข้อมูลจากการตอบแบบสอบถามออนไลน์ระหว่างวันที่ 2 สิงหาคม ถึง 31 ตุลาคม พ.ศ. 2562 รายงานนี้ศึกษาวิเคราะห์ ข้อมูลที่เกี่ยวกับปัจจัยที่แพทย์พิจารณาเก็บรังไข่ระหว่างผ่าตัดผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกระยะต้น

ผลการศึกษา: จากผู้ที่ตอบแบบสอบถามทั้งหมด 170 ราย พบว่าผู้ตอบแบบสอบถามจะพิจารณาเก็บรังไข่ระหว่างผ่าตัดผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกระยะต้น 108 คน (ร้อยละ 63.5) และพบว่าปัจจัยที่ใช้พิจารณาในการเก็บรังไข่มากที่สุด ได้แก่ อายุที่น้อยกว่า 40 ปี และมะเร็งเกรดต่ำ โดยลักษณะของโรงพยาบาลหรือประสบการณ์การทำงานไม่มีผลต่อการพิจารณาเก็บรังไข่ระหว่างผ่าตัดผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกระยะต้นแต่อย่างใด

สรุป: ประมาณสองในสามของแพทย์มะเร็งนรีเวชไทยจะพิจารณาเก็บรังไข่ระหว่างผ่าตัดผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกระยะต้น โดยปัจจัยที่ใช้ในพิจารณามากที่สุดคือ อายุ และ มะเร็งเกรดต่ำ