Original Article

Conservative Treatment for Endometrial Cancer: Survey of Practice among Thai Gynecologic Oncologists

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Objective: To evaluate the practice of Thai gynecologic oncologists on conservative treatment for endometrial cancer patients and influencing factors.

Materials and Methods: This study was a part of the national survey by the Thai Gynecologic Cancer Society (TGCS) on the management of gynecologic cancer. All Thai Gynecologic Oncologists who had been in practice for at least 1 year were invited to respond to the web-based questionnaire which was active from August to October, 2019. Data involving the practice of conservative treatment for endometrial cancer patients were abstracted and analyzed.

Results: of 170 respondents, 85.3% considered conservative treatment options if the patient needed childbearing. Among the respondents who considered conservative treatment, 84.1% considered one or more clinic-pathological features for conservative treatment. The two most frequent features of which included an absence of myometrial invasion (82.8%) and low-grade tumor (78.6%). The respondents working in training hospitals considered tumors without myometrial invasion more frequently than those in service-only hospitals (89.6% vs. 75.0%; p = 0.020. No significant differences of other clinic-pathological features were noted across the different hospital settings or duration of practice.

Conclusion: Most of Thai gynecologic oncologists considered conservative treatment option if the patient needed childbearing. The most frequently considered features were an absence of myometrial invasion and low-grade tumor.

Keywords: Survey, Practice, Endometrial cancer, Conservative treatment

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Endometrial cancer (EMC) is the most common pelvic gynecologic malignancy in developed countries wherein the age-standardized incidence rate (ASR) is 14.7 per 100,000 women-years[1,2]. Lower incidence of EMC was found in developing countries where cervical cancer is more common. In Thailand, EMC is the third most common gynecologic cancer after cancer of cervix and ovary, with an incidence of 4.5 per 100,000 women-year from the report of the Ministry of Public Health and the National Cancer Institute[3].

Although the peak incidence of EMC was between 55 and 64 years of age, 6.4% occur between 35 and 44 years, and 1.5% can occur between 20 and 34 years[4]. In Thailand, the incidence of EMC in women aged less than 40 years and 45 years were 3% and 6%, respectively[3]. Few studies reported more favorable prognostic features of EMC in young patients than older patients resulting in a better survival outcome[5]. Hence, conservative management can be considered in a young or reproductive-age patient who has not completed family life[6-8].

The most important issue when considering a conservative treatment is a thorough assessment of the clinical and pathological characteristics of the patient and her cancer. The patient should be healthy, are in reproductive age, and has no history or evidence of any pelvic pathology or co-medical diseases which may hinder her reproductive function. The tumor should be of low-grade endometrioid histology without lymphovascular invasion (LVSI), lower uterine involvement, myometrial invasion or extrauterine disease[9,10]. In the conservative treatment setting, dilatation and curettage are preferred over endometrial biopsy in terms of better accuracy of tumor grading[11]. An enhanced pelvic magnetic resonance imaging (MRI) should be done to ensure the exclusion of myometrial invasion and extra-uterine cancer involvement[12].

The American Society of Clinical Oncology[13] and American Society for Reproductive Medicine[14] recommend that information regarding the options of fertility-sparing

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treatment and their possible adverse effects on the fertility outcomes should be given to the couple before considering conservative treatment[13,14]. Good compliance during and after the treatment is needed. Hysterectomy as a definite treatment should be accepted in an event when the conservative treatment is not feasible and/or after pregnancies have been achieved.

Most information regarding conservative treatment for EMC is based on retrospective studies with few numbers of patients[6,15,16]. Therefore, the clinician may be reluctant to consider and propose a conservative treatment to the patient because of many caveats in management and follow-up.

This study was conducted to evaluate the insights of Thai gynecologic oncologists regarding conservative treatment for EMC patients. The pathologic factors taken into consideration for the conservative management as well as the impact of working features of the respondents on the practice were also assessed.

Materials and Methods

The Thai Gynecologic Cancer Society (TGCS) had launched a survey on the practice of Thai gynecologic oncologists on gynecologic cancer management. After obtaining approval from the Ethical Review Committee of each participating institution (COAs: Faculty of Medicine Vajira Hospital, 097/2562; Rajavithi Hospital, 104/2562; HRH Princess Chulabhorn College of Medical Science, 052/2562), the web-based survey questionnaire was open for response (website: https://forms.gle/e1WsBLcX5jVsXVgG8) from August to October, 2019. Thai gynecologic oncologists who had worked for at least 1 year were invited to participate in the study. The description of materials and methods, as well as questions for each cancer management, were presented elsewhere in detail[17].

This study abstracted the survey data that related to the practice in the conservative management of EMC. The results were stratified by the type of hospitals and duration of practice of the respondents. The type of hospitals, as detailed in the main report, were categorized as governmental or private, secondary or tertiary, and gynecologic fellowship training or service only[17]. The experience of respondents was determined as 'experienced' if the duration of gynecologic oncology practice was 5 years or longer[17].

Statistical analyses were performed using SPSS computer software version 22 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were presented and compared with χ^2 and Fisher's exact test as appropriate. The *p*-value of less than 0.05 was considered statistically significant.

Results

Of 258 gynecologic oncologists who met inclusion criteria, 170 participated in the survey (65.9%). The majority were female (63.5%), worked in government (89.4%) or tertiary-level hospitals (83.5%), with slightly over half involved in gynecologic fellowship training (50.6%).

One hundred and forty-five (85.3%) respondents reported that they would consider conservative treatment if the patient still required childbearing. Although the respondents who worked in the government hospitals or had a duration of practice less than 5 years tended to consider conservative treatment more frequently, the differences were not significantly from those in the comparative groups (Table 1).

Among 145 respondents who reported an option of conservative treatment for the patients, 23 (15.9%) did not specify any factors to be considered during treatment decision making whereas the remaining 122 respondents

Table 1. Characteristic features of the respondents and consideration for conservative treatment for endometrial cancer (n = 170)

Features	Conservative treatment		
	No, n (%)	Yes, n (%)	*p*-value
Gender			0.615
Male, n = 62	8 (12.9)	54 (87.1)	
Female, n = 108	17 (15.7)	91 (84.3)	
Hospital setting			0.098
Government, n = 152	20 (13.2)	132 (86.8)	
Private, n = 18	5 (27.8)	13 (72.2)	
Level of hospital			0.257
Secondary, n = 28	6 (21.4)	22 (78.6)	
Tertiary, n = 142	19 (13.4)	123 (86.6)	
Type of service			0.114
Training, n = 86	9 (10.5)	77 (89.5)	
Service only, n = 84	16 (19.0)	68 (81.0)	
Practice duration			0.051
<5 years, n = 71	6 (8.5)	65 (91.5)	
≥5 years, n = 99	19 (19.2)	80 (80.8)	
Total	25 (14.7)	145 (85.3)	

reported one or more factors were taken into consideration: 5 respondents (3.4%) selected only one factor, 28 (19.3%) with two factors, 38 (26.2%) with three factors, and 51 (35.2%) with four factors. Overall, the two most frequently factors taken into the planning for conservative treatment were an absence of myometrial invasion (82.8%) and low-grade tumor (78.6%) (Table 2).

Regarding the cancer features which were considered for conservative treatment, the respondents working in training hospitals considered tumors without myometrial invasion more frequently than those in service-only hospitals. There were no significant differences in other factors across the hospital settings and practice durations of the respondents (Table 3).

Discussion

Data on conservative treatment for EMC patients from previous studies were mostly from individual hospital-based information[5]. This was the first survey study evaluating the insights of practice and influencing factors for conservative treatment for EMC of Thai gynecologic oncologists. The survey revealed that most of the respondents would consider conservative treatment options for EMC patients if they still needed childbearing.

Finding from this survey demonstrated a high rate of respondents (85%) would consider an option of conservative treatment if the patients expressed their concern about childbearing. This was in line with findings from one recent survey study of the European Network of Young Gynecological Oncologists which found 94% of the respondents believed that fertility-sparing treatment was possible in selected EMC patients[18]. Although the surveys could not indicate the actual rate of this practice, the high rates of positive responses reflected the optimistic attitude towards this treatment option[18].

This study classified practices of gynecologic oncologists by the working features and found that the respondents who reported positive response for conservative treatment were those who worked in the government hospitals or had practice duration fewer than 5 years tended to consider conservative treatment more frequently. The underlying reasons for these findings were probably because the respondents in the government hospital which harbored a high number of patients in service may encounter more patients who had not completed their family lives than those in private hospitals. On the other hand, the respondents who had practiced fewer than 5 years may be more familiar with a concept of conservative management which has been emerging only in recent years[6-8,19-21].

The successful outcome of childbearing must be weighed with the oncological safety when considering conservative treatment for EMC. The characteristic features of the patient and her diseases must be carefully scrutinized. The first pre-requisite is the patient herself. The patient

Table 2. Factors considered for conservative treatment of endometrial cancer (n = 145)

Features	n (%)
Not otherwise specified	23 (15.9)
No myometrial invasion	120 (82.8)
Low-grade tumor	114 (78.6)
Negative lymphovascular invasion	81 (55.9)
Tumor size	59 (40.7)
Others*	6 (4.1)

* Others included young age without contraindication for progesterone (n = 1), no medical morbidity or good performance status (n = 2), no evidence of extra-uterine metastasis (n = 2), and patient's acceptance for the risk of failure (n = 1)

Table 3. Association between working features of the respondents and conservative treatment in endometrial cancer (n=145)

Features	Factors considered before conservative treatment							
	Small tumor size		Low tumor grade		No myometrial invasion		No LVSI	
	n (%)	*p*-value	n (%)	*p*-value	n (%)	*p*-value	n (%)	*p*-value
Hospital setting		0.674		0.300*		0.468		0.309
Government, n = 132	53 (40.2)		102 (77.3)		108 (81.8)		72 (54.5)	
Private, n = 13	6 (46.2)		12 (92.3)		12 (92.3)		9 (69.2)	
Level of hospital		0.621		0.572*		0.218*		0.548
Secondary, n = 22	10 (45.5)		16 (72.7)		16 (72.7)		11 (50.0)	
Tertiary, n = 123	49 (39.8)		98 (79.7)		104 (84.6)		70 (56.9)	
Type of service		0.821		0.160		0.020		0.317
Training, n = 86	32 (41.6)		64 (83.1)		69 (89.6)		46 (59.7)	
Service only, n = 84	27 (39.7)		50 (73.5)		51 (75.0)		35 (51.5)	
Practice duration		0.405		0.392		0.428		0.147
<5 years, n = 65	24 (36.9)		49 (75.4)		52 (80.0)		32 (49.2)	
≥5 years, n = 80	35 (43.8)		65 (81.3)		68 (85.0)		49 (61.3)	

should accept the risk of failure by the conservative treatment. Her health should be optimal without any co-morbidities which can be notorious causes of subfertility[13-15,19,22-24]. These concerns were also reported in a few respondents in this survey that they would assess the general health of the patients as pre-requisite before considering conservative treatment.

Of note, the familial cancer risk particularly Lynch syndrome was not specifically mentioned in any respondents of this study. This was probably due to the unknown prevalence of this syndrome in Thai patients, leading to low recognition and awareness. In contrast, the survey from Europe, wherein the familial cancer syndrome was well recognized, found nearly half of their respondents (49%) considered Lynch syndrome as a factor influencing conservative treatment options[18]. The authors from that survey emphasized that the patients with Lynch syndrome should have cautious counseling about the pros and cons of conservative treatment and definitive treatment of hysterectomy after completion of the family[18,24].

The second important pre-requisite was that EMC should have good prognostic features (i.e. low-grade tumor, endometrioid histology, no LVSI, no myometrial invasion, and no extra-uterine metastasis) to ensure the oncological safety[5]. The two most frequent tumor features the respondents in this survey took into consideration were an absence of myometrial invasion (83%), followed by a low-grade tumor (79%). These findings reflected that the respondents were well aware of existing data which noted that tumor without myometrial invasion and being low-grade were unlikely to have extra-uterine metastasis[25,26]. Furthermore, a tumor of low-grade nature generally has higher estrogen and progesterone receptors thus it is likely to respond to hormonal therapy[27]. The findings in this study were consistent with the results from the European survey which noted that 92% of respondents included no myometrial invasion and low-grade tumor as an important criterion for offering conservative management[18].

Of interest, this study also found that among the respondents who required selective factors for conservative treatment, more of the respondents selected more number of cancer features (35% for four features, 26% for three, 19% for two, and only three for one feature). Although there had not been any clear evidence that all these favorable features should be met before conservative treatment, each factor has its prognostic impact. Thus, to be on the safe side, all or more favorable features should theoretically be preferred.

When the factors considered for conservative treatment were explored by working features of the respondents, the myometrial invasion was the only factor that was more frequently considered among the respondents working in training- than the service-only hospitals. The authors could not find any specific reason for this finding but proposed that the ones in training hospital may be more cautious of myometrial invasion as an important feature which was directly associated with pelvic node metastases and extra-uterine diseases[24]. Furthermore, the contrast-enhanced MRI or PET scan which has better diagnostic performance than a CT scan to evaluate myometrial invasion are not widely available in service-hospitals which are mostly equipped with only a CT scan.

Few limitations of this survey were recognized. First, data simply represented the knowledge and opinion of the respondents rather than the actual practice. Second, this reported data was a part of the general practice survey, so the reported data was likely to lack details or depth on the issue assessed. Nevertheless, these findings should generate an enthusiasm for cooperation in data collection among the hospitals for cancer care to have more rigid data of the conservative treatment for EMC.

In summary, a high percentage of the Thai gynecologic oncologist considered a conservative treatment option for young EMC patients. The factors the respondents considered were more of the characteristic features of cancer and less with the general health, underlying disease, or co-medical illnesses. Among the pathologic factor, an absence of myometrial invasion and low-grade tumor were the most frequently concern before conservative treatment.

What is already known on this topic?

Few organizations e.g. the American Society of Clinical Oncology and American Society for Reproductive Medicine recommend that the physician should counsel the reproductive-age patients about the effect of cancer treatment on fertility outcomes. Conservative treatment should be considered. However, the attitudes, as well as the insights toward this practice of the involved physician, including gynecologic oncologists, reproductive endocrinologists, and the patients themselves, are not known.

What this study adds?

The present study found that the majority of the Thai gynecologic oncologists considered a conservative treatment for endometrial cancer patients who needed childbearing. Most of them had selective criteria for conservative treatment that cancer should be of low risk especially an absence of myometrial invasion.

Acknowledgements

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Potential conflicts of interest

The authors declare no conflicts of interest.

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การรักษาเชิงอนุรักษ์สำหรับมะเร็งเยื่อบุโพรงมดลูก: การสำรวจแนวปฏิบัติของแพทย์มะเร็งนรีเวชไทย

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

วัตถุประสงค์: เพื่อศึกษาความคิดเห็น แนวปฏิบัติและปัจจัยที่อาจมีผลต่อการพิจารณาของแพทย์มะเร็งนรีเวชไทยในการรักษาผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกแบบอนุรักษ์

วัสดุและวิธีการ: การศึกษานี้เป็นส่วนหนึ่งของโครงการสำรวจระดับชาติโดยสมาคมมะเร็งนรีเวชไทยเกี่ยวกับแนวปฏิบัติในการดูแลรักษามะเร็งนรีเวช โดยเชิญแพทย์มะเร็งนรีเวชไทยที่ปฏิบัติงานมาแล้วอย่างน้อย 1 ปีให้เข้าร่วมตอบคำถามทางเว็บตั้งแต่เดือนสิงหาคมถึงเดือนตุลาคม พ.ศ. 2562 รายงานนี้นำข้อมูลความคิดเห็น แนวปฏิบัติและปัจจัยที่แพทย์ใช้ในการประเมินผู้ป่วยก่อนการพิจารณารักษามะเร็งเยื่อบุโพรงมดลูกแบบอนุรักษ์มาศึกษาวิเคราะห์

ผลการศึกษา: จากผู้ตอบแบบสอบถามทั้งหมด 170 ราย พบว่าร้อยละ 85.3 จะพิจารณาการรักษาแบบอนุรักษ์สำหรับผู้ป่วยที่ยังต้องการมีบุตรโดยร้อยละ 84.1 จะนำลักษณะทางคลินิกและพยาธิวิทยา 1 ประการหรือมากกว่ามาพิจารณาก่อนให้การรักษาแบบอนุรักษ์ โดยลักษณะ 2 ประการที่ผู้ตอบแบบสอบถามนำมาพิจารณาบ่อยที่สุด คือ มะเร็งไม่ลุกลามเข้ากล้ามเนื้อมดลูก คิดเป็นร้อยละ 82.8 และเป็นมะเร็งเกรดต่ำ คิดเป็นร้อยละ 78.6 โดยผู้ที่ปฏิบัติงานในโรงพยาบาลที่มีการฝึกอบรมพิจารณาปัจจัยที่มะเร็งไม่ลุกลามของเข้ากล้ามเนื้อมดลูกบ่อยมากกว่าผู้ที่ปฏิบัติงานในโรงพยาบาลที่ให้บริการเพียงอย่างเดียวอย่างมีนัยสำคัญทางสถิติ คือ ร้อยละ 89.6 เทียบกับ ร้อยละ 75.0 (p = 0.020) ไม่พบความแตกต่างของปัจจัยอื่นที่นำมาพิจารณาระหว่างผู้ตอบแบบสอบถามที่ทำงานในโรงพยาบาลต่างๆ หรือระยะเวลาการปฏิบัติงาน

สรุป: แพทย์มะเร็งนรีเวชส่วนใหญ่พิจารณารักษาผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกแบบอนุรักษ์สำหรับผู้ป่วยที่ยังต้องการมีบุตร ลักษณะที่มีผลในการเลือกวิธีการรักษานี้มากที่สุด คือ การไม่มีการลุกลามของมะเร็งเข้ากล้ามเนื้อมดลูกและมะเร็งเกรดต่ำ