Original Article

Diagnostic Methods for Endometrial Lesions and Pre-operative Imaging Study for Endometrial Cancer: Survey of Practice among Thai Gynecologic Oncologists

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Objective: To study the practice of Thai gynecologic oncologists regarding methods for diagnosis of endometrial lesions and preoperative investigation of endometrial cancer.

Materials and Methods: The present study was a part of the national practice survey of the Thai Gynecologic Cancer Society (TGCS) on the management of gynecologic cancer in Thailand. Thai gynecologic oncologists who had worked for more than 1 year were invited to respond to web-based questionnaires which were opened from August to October, 2019. The present study reviewed data of operative means to obtain endometrial tissue for diagnosis and preoperative investigations of EMC patients.

Results: Of 170 respondents, the mean age was 41.1±8.25 years old. Endometrial biopsy (70%) was more common than uterine curettage (30%). The biopsy was performed more frequently among the respondents working in government, tertiary, training hospitals and with less than 5 years duration of practice. The differences were significant between the respondents working in the tertiary or training hospitals than their comparative groups. Over 90% of the respondents also obtained endocervical tissue for histopathologic examination, however, at different frequencies. Only the respondents who worked in private hospitals 'always' performed endocervical curettage more frequently than those in government hospitals. Only 23.5% routinely requested imaging study; this was found especially among the respondents working in secondary hospitals. The other 1.8% never requested any imaging study at all whereas 74.7% selectively had imaging study; the most common indications were advanced disease or incomplete surgical staging.

Conclusion: There were variations of diagnostic methods to evaluate the endometrial lesion and the use of pre-operative imaging for EMC patients among Thai gynecologic oncologists. The differences resided in the work setting and experience of the respondents.

Keywords: Survey, Practice, Gynecologic Cancer, Endometrial Cancer, Diagnosis, Imaging

J Med Assoc Thai 2020;103(Suppl. 7): 37-42
Website: http://www.jmatonline.com

The majority of endometrial cancer (EMC) presented with abnormal uterine bleeding[(1)]. The investigations in women with this symptom include a thorough history taking and physical examination including a pelvic examination, along with bedside ultrasonography to assess endometrium and other pelvic structures[(1)]. Pathologic examination of endometrial tissue is carried out if clinical findings suggest endometrial lesions.

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The procedure which had frequently been used in the past to obtain endometrial tissue was endometrial curettage. However, the curettage procedure can induce pain requiring an anesthetic agent. Hence, other newer methods e.g. endometrial aspiration biopsy, manual vacuum aspiration biopsy (MVA), or hysteroscopic examination and biopsy have become more common in later years[(2-6)].

Together with endometrial tissue evaluation, endocervical curettage is sometimes obtained in the same setting when EMC is suspected. This endocervical pathologic evaluation may vary upon the degree of suspicion from findings from the pelvic examination and upon discretion or preference of the gynecologist or gynecologic oncologist. A pre-operative finding of endocervical involvement by EMC, aside from the designation of stage II cancer according to the

How to cite this article: Chanpanitkitchot S, Suwannarurk K, Hamontri S, Manusirivithaya S, Tangjitgamol S, Thai Gynecologic Cancer Society (TGCS). Diagnostic Methods for Endometrial Lesions and Pre-operative Imaging Study for Endometrial Cancer: Survey of Practice among Thai Gynecologic Oncologists. J Med Assoc Thai 2020;103(Suppl.7): 37-42.

International Federation of Gynecology and Obstetrics (FIGO)[7], may influence the type of primary treatment e.g. primary radiation therapy, neoadjuvant chemotherapy, or modification of surgical technique as radical instead of simple hysterectomy[8].

Another issue of pre-operative management of EMC is the use of imaging study. With an advance and more availability of radiology machines and technologies, its role in gynecologic cancer including EMC has been increasing[9,10]. In early-stage disease when cancer deems to locate only in the uterus, tumor size and degree of myometrial invasion are the indicators for retroperitoneal node surgico-pathological evaluation. Although the therapeutic benefit of lymph node (LN) resection in early-stage EMC is still being a subject of debate, it certainly has a diagnostic role for FIGO stage assignment. Endometrial cancer with nodal metastasis, which could be encountered in 10% of apparently early-stage disease[11], will instead be designated as advanced-stage cancer (stage IIIC)[7]. So, knowing the status of the lymph node by radiologic features would help to refine the surgical procedure of nodal resection. In advanced-stage cancer, pre-operative imaging study would provide information regarding the extent of EMC involvement or metastasis. This will certainly help the gynecologic oncologist plan for the appropriate surgical procedure and team preparation to achieve the optimal surgical outcomes and to minimize surgical morbidity.

Aside from the scientific or evidence-based data, these pre-operative practices for diagnosis and investigation for EMC may vary upon other factors e.g. experience or preference of the physician, financial and reimbursement condition of the patients, availability, and access to the instruments, etc. This survey study evaluated the practice of Thai gynecologic oncologists in various hospitals regarding the procedure to obtain endometrial and endocervical tissue in a patient suspected to have EMC, and the use of radiologic test before surgery for EMC patients.

Materials and Methods

This study was a part of the national practice survey on the management of gynecologic cancer conducted by the Thai Gynecologic Cancer Society (TGCS). After obtaining approval from the Ethical Review Committee of each participating institution (COAs: Faculty of Medicine Vajira Hospital, 097/2562; Rajavithi Hospital, 104/2562), a web-based questionnaire was opened for a response from August to October, 2019. The electronic questionnaire was available on the following website: https://forms.gle/e1WsBLcX5jVsXVgG8. Details of materials and methods were described in our main work[12]. In brief, all Thai Gynecologic Oncologists who had worked for at least 1 year and were currently working in the country were invited to participate in the study.

The self-administered questionnaire queried about personal and demographic data related to work and various aspects of the management of gynecologic cancer. A total of 170 gynecologic oncologists responded to the questions and were included in the study. The present study abstracted the survey data regarding the use of diagnostic methods of endometrial lesions and pre-operative imaging study for EMC patients as well as working features of the respondents.

The diagnostic methods to evaluate endometrial pathology included uterine curettage or sampling biopsy which included aspiration biopsy, hysteroscopic-directed biopsy or manual vacuum aspiration (MVA). The practice of endocervical curettage for pathologic assessment was also queried regarding the frequency of the procedure along with endometrial tissue evaluation. The practice of special pre-operative imaging (excluding ultrasonography) was categorized as never, routinely or selectively requested. The selective indications for imaging study were also assessed. The respondents were grouped according to the type of their working hospitals and duration of practice. The hospitals were classified by setting or ownership (governmental versus private), by level (secondary- versus tertiary-levels which were divided by number of $<$ or $\geq$300 in-patients bed respectively), and by type of service (gynecologic oncology fellowship training versus service only). The duration of gynecologic oncology practice with a cut-off value at 5 years was applied as a factor indicating the experience of respondents.

Statistical analyses were performed using SPSS computer software version 22 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were used to report patterns of practice in each aspect. Differences between the groups were determined by using the χ^2 and Fisher's exact test, whenever appropriate. All statistical tests were two-sided and a *p*-value of less than 0.05 was considered statistically significant.

Results

This survey found that endometrial sampling was used more commonly than other methods in endometrial pathology evaluation. Aspiration biopsy was most commonly used (63.5%) followed by hysteroscopic biopsy and manual vacuum aspiration. For endocervical tissue

Table 1. Pre-operative endometrial and endocervical tissue pathologic evaluation (n = 170)

Pre-operative endometrial and endocervical tissue evaluation	n (%)
Means of primary endometrial tissue pathologic evaluation	
Curettage	51 (30.0)
Biopsy	119 (70.0)
Aspiration biopsy	108 (63.5)
Hysteroscopic-directed biopsy	6 (3.5)
Manual vacuum aspiration (MVA)	5 (3.0)
Endocervical tissue pathologic avaluation	
Always	64 (37.6)
Occasionally	80 (47.1)
Rarely	20 (11.8)
Never	6 (3.5)

Table 2. The pre-operative procedure of endometrial tissue pathology evaluation by work setting and duration of practice of the respondents (n = 170)

Features of respondents	Means to obtain of EM tissue		*p*-value
	Biopsy*, n (%)	Curettage, n (%)	
Hospital setting			0.050
Government, n = 152	110 (72.4)	42 (27.6)	
Private, n = 18	9 (50.0)	9 (50.0)	
Level of hospital			0.038
Secondary, n = 28	15 (53.6)	13 (46.4)	
Tertiary, n = 142	104 (73.2)	38 (26.8)	
Type of service			0.001
Service/training, n = 86	70 (81.4)	16 (18.6)	
Service only, n = 84	49 (58.3)	35 (41.7)	
Duration of practice			0.084
<5 years, n = 71	54 (76.1)	17 (23.9)	
≥5 years, n = 99	65 (65.7)	34 (34.3)	
Total	119 (70.0)	51 (30.0)	

* Biopsy included aspiration biopsy, manual vacuum aspiration biopsy, and biopsy under hysteroscopy

assessment, nearly half (80 or 47.1%) 'occasionally' had cervical histopathology assessment whereas slightly more than one third 'always' had the procedure performed. Table 1 shows the pre-operative procedure to obtain endometrial tissue and practice of endocervical tissue sampling for pathologic evaluation.

The procedures of endometrial tissue assessment were assessed by the work setting and experience of the respondents (Table 2). The authors found the gynecologic oncologists who worked in tertiary-level or training hospitals performed endometrial sampling biopsy significantly more frequent than the other comparative groups. Although this was also found among those working in the government hospital or had been practicing <5 years, the differences were only marginally significant or only tended to be significant.

Of note, all 6 respondents who reported using hysteroscopy as an auxiliary tool for endometrial biopsy worked in a government hospital or had worked for ≥5 years. On the other hand, 4 of them worked in tertiary-level or training hospitals.

Pathologic evaluation of endocervical tissue before the operation was also studied by the work setting and duration of practice of the gynecologic oncologists (Table 3). Only the respondents who worked in a private hospital 'always' performed endocervical curettage significantly more frequent than those in the government hospital. No differences among the respondents who worked in other work settings or their experience were found regarding their practice of endocervical tissue assessment pre-operation.

Regarding the practice and frequency of pre-operative imaging study, three (1.8%) reported that they 'never request for any imaging study at all' whereas the others had pre-operative imaging performed ranging from 2% to 100% (median 50%). Nearly one fourth reported the use of pre-operative imaging in all patients. Among the selective criteria, the 2 most common features were clinically advanced disease (71.8%) and incomplete surgical staging (48.8%). The criteria considered by the respondents for pre-operative imaging are shown in Table 4.

The use of imaging study (all vs selected patients) was studied according to the work setting and experience of the 167 respondents (Table 5). Only the respondents who worked in secondary-level hospitals reported imaging study in all patients significantly more frequent than those in tertiary-level hospitals. There were no significant differences in practice regarding pre-operative imaging study among the respondents who worked in other work settings or experience.

Discussion

From the survey of practice of Thai gynecologic oncologists to evaluate an existing pathology in women with symptoms suggesting endometrial lesions, sampling biopsy (by one or another method) was more common than curettage. This finding was consistent with a general trend of practice that uterine curettage, which had been used as a common method to obtain endometrial tissue in the past, was less commonly practiced at present. The curettage generally requires a local anesthetic agent or even general anesthesia (which may require hospital admission) to prevent or alleviate pain or discomfort. In contrast, endometrial sampling using a small plastic cannula (e.g. Pipelle®) can be done in an out-patient setting without a requirement of any anesthetic agent. The total cost is also cheaper compared to the conventional uterine curettage method.

However, the present study found 30% of the respondents still used curettage as the primary technique to evaluate endometrial lesions. This was found significantly more frequent in the secondary-level or service only hospital and marginal or tended to be so in the private hospital or

Table 3. The practice of pre-operative endocervical tissue pathology evaluation by work setting and experience of the respondents (n=170)

Features of respondents	Endocervical tissue pathology assessment			*p*-value
	Always, n (%)	Occasional, n (%)	Rarely or never, n (%)	
Hospital setting				0.025
Government, n = 152	52 (34.2)	75 (49.4)	25 (16.4)	
Private, n = 18	12 (66.7)	5 (27.8)	1 (5.5)	
Level of hospital				0.162
Secondary, n = 28	15 (53.6)	10 (35.7)	3 (10.7)	
Tertiary, n = 142	49 (34.5)	70 (49.3)	23 (16.2)	
Type of service				0.228
Service/training, n = 86	27 (31.4)	44 (51.2)	15 (17.4)	
Service only, n = 84	37 (44.0)	36 (42.9)	11 (13.1)	
Experience				0.283
<5 years, n = 71	22 (31.0)	38 (53.5)	11 (15.5)	
>5 years, n = 99	42 (42.4)	42 (42.4)	15 (15.2)	
Total	64 (37.6)	80 (47.1)	26 (15.3)	

Table 4. Practice and indication of pre-operative imaging study for endometrial cancer patients

Practice and indication of pre-operative imaging study	n (%)
Never	3 (1.8)
Routinely done in all patients	40 (23.5)
Select in some patients*	127 (74.7)
Clinically advanced stage	122 (71.8)
Incomplete staging	83 (47.8)
Pre-laparoscopic surgery	28 (16.5)
Miscellaneous**	2 (1.2)

* One respondent may have one or more selective criteria for pre-operative imaging study
** Miscellaneous included medically inoperable (1) or high-grade non-endometrioid cancer (1)

those who had practiced ≥5 years. Being a general survey study, the underlying reason that some respondents reported curettage as the primary method were not explored in detail. The possible reasons were, instead, queried to a few of them and discussed among the authors based on the situation in our country. One possible reason was that the cannula used in sampling cannot be reimbursed by most health benefits coverages and must be paid by the woman herself. This might be a problem for patients seeking medical treatment in secondary-level or service only hospital who were not willing or could not afford an extra cost. Another possible reason was the number of visits. Although the pathology obtained by endometrial biopsy correlates well with that obtained by uterine curettage with 85% to 98% accuracy[2,3], inadequate diagnostic tissue might be found as high as 15 to 54% from biopsy specimen especially when the endometrial pathology was focal, involving an area less than 50% of the uterus, or in a presence of co-existing endo- or myometrial pathology i.e. submucous myoma obstructing the passage of soft sampling cannula[3-5]. Another situation was when endometrial hyperplasia was suspected from clinical findings or biopsy specimen or when EMC cannot be excluded. These situations mandate a more comprehensive evaluation by endometrial curettage. This would, in turn, required the patient's understanding and compliance for a few more follow-up visits. Hence, some gynecologic oncologists might select curettage as the technique to assess and to have a definite diagnosis of endometrial pathology in one setting.

Regarding the hysteroscopy, it has advantages that it allows direct visualization of endometrium enabling a primary impression of the pathology, location, and extension of the lesion. One study compared tissue obtained from hysteroscopic examination to that from curettage[6]. Although consistent findings were found in 81%, more information was yielded from hysteroscopy than curettage in 16%. However, the procedure should always be accompanied by biopsy because only 52% of EMH and 20% of EMC could be correctly diagnosed from hysteroscopy[13,14]. In this survey, only 3.5% of the respondents reported that they mainly used hysteroscopy as the primary technique to assess endometrium and to obtain endometrial tissue for pathologic examination. The reason for the uncommon use of hysteroscopy among the Thai gynecologic oncologists may be from the limited availability of the instrument and experience of the performer a well as the extra cost of the procedure. These possibilities were evidenced from subgroup analyses that all of the few respondents who performed hysteroscopy worked in the government hospitals (where the cost should be lower than private) or had worked for ≥5 years (more experience) whereas the majority (67%) were in tertiary-level or training hospitals (available instrument).

Endometrial cancer which extends to the cervix is

Table 5. The use of pre-operative imaging study by work setting and duration of practice of the respondents (n = 167)

Features of responder	Pre-operative imaging study		*p*-value
	All patients, n = 40	Selected patients, n = 127	
Hospital setting			0.143
Government, n = 149	33 (22.1)	116 (77.9)	
Private, n = 18	7 (38.9)	11 (61.1)	
Level of hospital			0.006
Secondary, n = 27	12 (44.4)	15 (55.6)	
Tertiary, n = 140	28 (20.0)	112 (80.0)	
Type of service			0.124
Service/training, n = 135	29 (21.5)	106 (78.5)	
Service only, n = 32	11 (34.4)	21 (65.6)	
Duration of practice			0.352
<5 years, n = 69	14 (20.3)	55 (79.7)	
≥5 years, n = 98	26 (26.5)	72 (73.5)	

designated as stage II by FIGO staging classification[7]. Aside from staging and associated prognosis, cervical involvement has an influence on clinical management. Radical hysterectomy may be considered instead of simple hysterectomy. From this survey, slightly more than one third always performed endocervical curettage to assess endocervical pathology whereas nearly half occasionally carried out this procedure and approximately 15% rarely or never did it. Only the respondents in private hospitals 'always' performed endocervical curettage more frequently than government hospitals. This might reflect a more cautious practice e.g. thorough counseling regarding the prognosis, surgical planning, and an estimated cost of management.

When a diagnosis of EMC is made, careful clinical evaluation is crucial before surgical staging. A thorough history and physical examination should be carried out to assess the performance status of the patients who were usually old and frequently accompanied by medical illnesses. An evaluation by imaging study will give additional information on cancer e.g. sites of the lesion, presence of extrauterine diseases or metastasis can be assessed[10,11]. From this survey, the pre-operative imaging study was performed in all patients in only 30%. The respondents working in private, secondary-level, and service only hospitals significantly requested the imaging study in all patients more frequently than their comparative groups. The possible reasons for these findings were discussed according to the situation in our country. The imaging study in the former groups of hospitals (private, secondary-level, service only) might be more readily available (in a private hospital), short waiting time due to fewer number of patients (in secondary-level, service only), so the gynecologic oncologist had no difficulties in requesting imaging study in all of their patients. Furthermore, imaging study may help categorize the patients who could undergo surgical treatment in their hospitals (secondary-level) or should be referred to a larger hospital with more advanced facilities.

Among the respondents who reported that they selectively requested for the imaging study, clinically advanced stage disease from the physical examination was the most common indication followed by incomplete staging. Findings from the imaging may help refine the surgical procedures or management i.e. considering a referral to a larger hospital or neoadjuvant therapy before surgery in advanced diseases that optimal surgery is not possible, or when repeat surgery vs. adjuvant therapy without surgery in incomplete staging[8].

Conclusion

Some different clinical practices of Thai gynecologic oncologists working in various work settings and their experiences were demonstrated regarding the diagnostic methods and pre-operative imaging study for EMC patients. Although there have been many international practice guidelines for the management of EMC, the practice may vary upon the context of each country and even the area/hospital where the gynecologic oncologists had their practice. These contexts may be influenced by national economics, the hospital budget, availability of the instruments, etc. Any option is acceptable assuming that all EMC patients received a correct diagnosis without delay and appropriate management, or else should be improved accordingly.

What is already known on this topic?

The contemporary means to evaluate endometrial lesion is by biopsy. Uterine curettage which has long been used is now rather employed as secondary measures when the result from biopsy specimen is ambiguous. Endocervical sampling may also be performed if indicated clinically. A pre-operative imaging study to assess the extent of endometrial cancer may help in surgical planning.

What this study adds?

There were variations in diagnostic methods to evaluate endometrial lesion and pre-operative imaging assessment for endometrial cancer patients among gynecologic oncologists in Thailand. Although majority (70%) performed endometrial biopsy as a primary technique to evaluate

endometrial lesion, others still used uterine curettage. Although most performed endocervical curettage, the frequency of the procedure varied among working features. A pre-operative imaging study was performed in almost all endometrial cancer patients, more likely when clinically indicated and less likely as a universal test in all endometrial cancer patients.

Acknowledgements

The present study was granted by Navamindradhiraj University Research Fund for the study conduct and by Faculty of Medicine Vajira Hospital Facilitating Research Fund for manuscript preparation and publication.

Potential conflicts of interest

The authors declare no conflicts of interest.

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วิธีการวินิจฉัยรอยโรคของเยื่อบุโพรงมดลูกและการตรวจภาพทางรังสีก่อนการผ่าตัดสำหรับมะเร็งเยื่อบุโพรงมดลูก: การสำรวจแนวปฏิบัติของแพทย์มะเร็งนรีเวชไทย

ศรัญญา ชาญพานิชกิจโชติ, คมสันติ์ สุวรรณฤกษ์, สุทธา หามนตรี, สุมนมาลย์ มนัสศิริวทยา, ศิริวรรณ ตั้งจิตกมล, สมาคมมะเร็งนรีเวชไทย

วัตถุประสงค์: เพื่อศึกษาวิธีการตรวจวินิจฉัยรอยโรคของเยื่อบุโพรงมดลูกและการตรวจภาพทางรังสีก่อนการผ่าตัดในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกของแพทย์มะเร็งนรีเวชไทย

วัสดุและวิธีการ: รายงานนี้เป็นส่วนหนึ่งของการศึกษาสำรวจของสมาคมมะเร็งนรีเวชไทยเกี่ยวกับการปฏิบัติงานแพทย์มะเร็งนรีเวชไทยที่ปฏิบัติงานมาแล้วอย่างน้อย 1 ปี แบบสอบถามผ่านเว็บซึ่งเปิดให้แพทย์ตอบคำถามตั้งแต่เดือนสิงหาคมถึงเดือนตุลาคม พ.ศ. 2562 รายงานนี้วิเคราะห์ข้อมูลของวิธีที่ใช้การตรวจวินิจฉัยรอยโรคของเยื่อบุโพรงมดลูกและการตรวจภาพทางรังสีก่อนการผ่าตัดในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก

ผลการศึกษา: อายุเฉลี่ยของผู้ตอบแบบสอบถาม 170 ราย คือ 41.1±8.25 ปี พบว่า ร้อยละ 70.0 ของผู้ตอบแบบสอบถามใช้วิธีสุ่มตัดเนื้อเยื่อจากเยื่อบุโพรงมดลูก ในขณะที่ร้อยละ 30 ใช้วิธีการขูดมดลูก โดยผู้ตอบแบบสอบถามที่ทำงานในโรงพยาบาลรัฐ โรงพยาบาลระดับตติยภูมิ โรงพยาบาลที่มีการฝึกอบรมแพทย์ประจำบ้านอนุสาขามะเร็งวิทยาและผู้ที่ทำงานมานาน ≥5 ปีจะใช้วิธีการสุ่มตัดมากกว่ากลุ่มอื่นๆ โดยความแตกต่างนี้มีนัยสำคัญเฉพาะแพทย์ในโรงพยาบาลระดับตติยภูมิและโรงพยาบาล ที่มีการฝึกอบรม พบว่า มากกว่าร้อยละ 90 ของผู้ตอบแบบสอบถามจะทำการขูดปากมดลูกร่วมด้วย แต่ด้วยความถี่ที่แตกต่างกัน โดยผู้ที่ทำงานในโรงพยาบาลเอกชนทำการขูดปากมดลูกร่วมด้วยเสมอในสัดส่วนที่สูงกว่าผู้ที่ทำงานในโรงพยาบาลรัฐอย่างมีนัยสำคัญทางสถิติ ในแง่ของการส่งตรวจภาพทางรังสีก่อนการผ่าตัดมะเร็งเยื่อบุโพรงมดลูก พบว่า ร้อยละ 23.5 ของผู้ตอบแบบสอบถามจะส่งผู้ป่วยทุกรายไปรับการตรวจทางรังสี โดยเฉพาะอย่างยิ่งผู้ที่ทำงานในโรงพยาบาลทุติยภูมิ ร้อยละ 1.8 ไม่ส่งตรวจภาพทางรังสีใดๆ เลย และอีกร้อยละ 74.7 เลือกส่งในผู้ป่วยบางราย โดยข้อบ่งชี้ที่พิจารณาบ่อยที่สุด คือ โรคน่าจะอยู่ในระยะลุกลามหรือการผ่าตัดก่อนหน้าไม่ครบถ้วน

สรุป: มีความหลากหลายของวิธีการที่แพทย์มะเร็งนรีเวชไทยใช้ในการตรวจวินิจฉัยรอยโรคในเยื่อบุโพรงมดลูกและการตรวจภาพทางรังสีก่อนการผ่าตัดในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก ความแตกต่างนี้ขึ้นอยู่กับลักษณะของโรงพยาบาลและประสบการณ์ของแพทย์