Accuracy of Transvaginal Ultrasound for the Evaluation of Myometrial Invasion in Endometrial Carcinoma

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Abstract

Objective : To evaluate the accuracy of transvaginal ultrasound for the evaluation of myometrial invasion in endometrial carcinoma in comparison with standard paraffin section.

Method : A total of 111 patients with endometrial carcinoma diagnosed from fractional curettage underwent pre-operative transvaginal ultrasonography to assess myometrial invasion. Operation for surgical staging was subsequently performed and the hysterectomy specimen was evaluated for depth of myometrial invasion by standard paraffin section blinded from transvaginal ultrasound results. Final histopathologic diagnosis and depth of myometrial invasion were obtained from standard paraffin section. Ultrasonographic assessment was compared with the histopathological results.

Results : In evaluation of myometrial invasion, transvaginal ultrasound yielded the sensitivity of 69.4 per cent, specificity of 70.6 per cent, positive predictive value of 53.2 per cent, negative predictive value of 82.8 per cent, and accuracy of 70.3 per cent. The accuracy, sensitivity, specificity, negative predictive value, false positive and negative rates were comparable between grade 3 and grade 1 and 2 tumors. However, the positive predictive value was significantly higher among grade 3 than grade 1 and 2 tumors. The Kappa coefficients were 0.57 and 0.22 for grade 3 and grade 1 and 2 tumors respectively.

Conclusion : Transvaginal ultrasound for assessment of depth of myometrial invasion in endometrial carcinoma provided acceptable accuracy compared with standard paraffin section. This technique might be of value for the decision making in the intra-operative management of endometrial carcinoma.

Key word : Endometrial Carcinoma, Myometrial Invasion, Transvaginal Ultrasonography

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J Med Assoc Thai 2004; 87: 47-52

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Endometrial carcinoma is the ninth commonest cancer in Thailand and is the third most common genital cancer in Thai women[1]. Patients usually present with abnormal uterine bleeding especially post- or peri-menopausally. Risk factors include late menopause, nulliparity, obesity, hormonal producing ovarian tumors, exogenous hormones, and diabetes mellitus[2-5]. Treatment modalities include surgery, radiation, chemotherapy, hormonal therapy and various combinations of these according to patient situation. Usually surgery is carried out initially to determine cancer stage and in some cases is at the same time the definitive treatment.

Depth of myometrial invasion in endometrial carcinoma is an important feature in patient management as it is a prognostic as well as a treatment-determining factor. In cases with deep invasion, lymphatic spreading is likely and pelvic and paraaortic lymph node sampling should be performed. According to the International Federation of Gynecology and Obstetrics (FIGO), assigning a specimen as a deep or superficial invasion has a cutoff point at the half of myometrial thickness by standard pathological section. At present, the assessment is performed with naked eye or frozen section during the operation and is post-operatively confirmed for the extent of invasion on standard pathological section.

Pre-operative myometrial invasion may be beneficial as additional information for physicians in judgement for patient management. Transvaginal ultrasonography has been studied in a number of publications[6-11]. The procedure is simple, not expensive, available in many hospitals and can be performed pre-operatively. The authors therefore aimed to study if transvaginal ultrasonography could be used to assess myometrial invasion in endometrial carcinoma compared to pathological results. If its accuracy is acceptable, it would help in patient planning and management.

MATERIAL AND METHOD

A total of 111 patients diagnosed with endometrial carcinoma by fractional curettage and scheduled for an operation in the Department of Obstetrics and Gynecology, Siriraj Hospital, were recruited in the study with informed consent. The patients had no prior chemotherapy or radiotherapy, and had not previously received any high dose exogenous hormone before surgery. Demographic data were collected and the patients underwent an ultrasonographic evaluation by one of the authors (P.S) less than a week prior

to surgery. The results were categorized into 2 groups, the first being no invasion or invasion equal to or less than half of the myometrial thickness and the second group being invasion more than half of the myometrial thickness. The patient would be operated on according to the standard treatment. Extent of the operation depended on the judgement of the surgeon who assessed the myometrial invasion by naked eye. The pathological results, concluded by pathologists who were blinded to the ultrasonographic results, were collected.

Statistical analysis was carried out as a Diagnostic Test study using pathological section as the gold standard. Kappa values were calculated for agreement between ultrasonographic and the pathological section assessment of myometrial invasion.

RESULTS

From 1st March 2001 to 30th September 2002, 111 patients with endometrial cancer were enrolled into the study and their demographic data are presented in Table 1. The average age of the patients was 55 years old and the average body mass index

Table 1. Demographic data of the patients (total 111 cases).

Characteristics	Mean ± SD	
Age (years)	55.1 ± 10.7	
BMI (kg/m^2)	26.8 ± 5.1	
	Number	%
Family history of cancer		
Positive	26	23.4
Negative	85	76.6
Parity		
Nulliparous	35	31.5
Multiparous	76	68.5
Hormonal usage (either as HRT or contraception)		
Positive	36	32.4
Negative	75	67.6
Menopausal status		
Menopause	71	64.0
Premenopause	40	36.0
Presenting symptom		
Vaginal discharge	3	2.7
Abnormal vaginal bleeding	105	94.6
Abdominal pain	1	0.9
Check up	2	1.8
History of medical disease		
Positive	67	60.3
Negative	44	39.7

Table 2. Details of pathological results from surgical specimens of the studied patients.

Pathological results	Number	%
Myometrial invasion		
Deep	36	32.4
Superficial	75	67.6
Histologic subtype		
Endometrioid	86	77.5
Non-endometrioid	25	22.5
Histologic grade		
1	39	35.2
2	35	31.5
3	37	33.3
Cervical involvement		
Yes	21	18.9
No	90	81.1

(BMI) was 26.8. Most of the patients sought attention because of abnormal vaginal bleeding. The majority of the patients were menopausal. More than half of the patients had a medical disease. Interestingly, the patients were nulliparous in merely a third of the cases.

Table 2 reveals the details of pathological results, namely myometrial invasion, histologic subtype, histologic grade and cervical involvement. In two-thirds of the cases, the myometrial invasion was only superficial. The majority of cases were endometrioid tumor. The histological severity was equally distributed among the three grades. The cervix was free of disease in 80 per cent of cases. In cases with cervical involvement, the primary lesion was considered to be endometrial or cervical according to the main tumor site in relation to the squamocolumnar junction. If this was not clear, cell type would come into consideration. As most endometrial cancers are of the endometrioid type and cervical cancer squamous, the tumor would be considered as such. As about 80 per cent of cervical adenocarcinomas are of the endocervical type with mucin production, a mucin producing tumor would be considered as cervical in origin except when some features were present. Features that favor a primary endometrial carcinoma were the merging of the tumor with areas of normal endometrial tissue, presence of foamy endometrial stromal cells, presence of squamous metaplasia, or presence of areas of typical endometrioid carcinoma.

Comparison between the ultrasonographic and pathologic results is shown in Table 3. Using the pathologic results as gold standard, sensitivity and specificity of ultrasonographic assessment of myometrial invasion were about 70 per cent and 70 per cent accuracy with only poor agreement as indicated by Kappa = 0.37.

Table 4 shows the diagnostic values of ultrasonographic assessment of myometrial invasion compared to pathological results according to tumor grades. Apart from positive predictive value which was slightly higher in grade 3 tumors, no statistically significant differences were found between diagnostic values of ultrasonographic and pathological results in low and high grade tumors.

DISCUSSION

Endometrial cancer is an important cancer in Thailand. It is the third most common cancer in Thai

Table 3. Myometrial invasion assessed by ultrasonographic and pathological results.

Transvaginal ultrasound	Paraffin section		Total
	Deep	Superficial	
Deep	25	22	47
Superficial	11	53	64
Total	36	75	111

Sensitivity	= 69.4% (95% CI = 51.7-83.1)
Specificity	= 70.6% (95% CI = 58.9-80.3)
Positive predictive value	= 53.2% (95% CI = 38.2-67.6)
Negative predictive value	= 82.8% (95% CI = 70.9-90.7)
False positive rate	= 29.3% (95% CI = 19.7-42.1)
False negative rate	= 30.6% (95% CI = 16.9-48.3)
Accuracy	= 70.3% (95% CI = 60.7-78.4)

Table 4.   Diagnostic values of myometrial invasion assessment between ultrasonographic and pathological results according to tumor grade.

Diagnostic value (95% CI)	Grade 1-2 (95% CI)	Grade 3 (95% CI)	P value*
Sensitivity	58.8% (33.5-80.6)	78.9% (53.9-93.0)	0.191
Specificity	68.4% (54.6-79.7)	77.7% (51.9-92.6)	0.447
PPV	35.7% (19.3-55.9)	78.9% (53.9-93.0)	0.004
NPV	84.7% (70.5-93.2)	77.7% (51.9-92.6)	0.487**
False positive rate	31.6% (20.3-45.4)	22.2% (7.4-48.1)	0.447
False negative rate	41.1% (19.4-66.5)	21.0% (7.0-46.1)	0.191
Accuracy	66.2% (54.2976.5)	78.4% (61.3-89.6)	0.186
Kappa	0.22	0.57	

* Chi-square test, ** Fisher exact test.
PPV = Positive predictive value, NPV = Negative predictive value.

women[1]. Its staging is based on pathological results on surgically removed specimens. Exploration during the operation is essential as it indicates the extent of surgery needed, which basically consists of total hysterectomy with bilateral salpingo-oophorectomy and peritoneal cytology. Presence of several factors warrants pelvic and para-aortic lymph node sampling. These factors are highly malignant histologic subtype, high grade, deep myometrial invasion, and suspicious lymphadenopathy[3,5,12].

Myometrial invasion is also a prognostic factor. According to The International Federation of Gynecology and Obstetrics (FIGO), assigning a specimen as a deep or superficial invasion has a cutoff point at half of the myometrial thickness by standard pathological section. However, the result is available only after the operation. Intra-operatively, the surgeon has to rely on the naked eye or frozen section to assess myometrial invasion. Several pre-operative assessment strategies have been attempted. Examples include ultrasonography, hysteroscopy, Doppler ultrasound, magnetic resonance imaging (MRI), computerized tomography (CT) and tumor markers such as CA-125[2-5].

Transvaginal ultrasonography had been shown to be beneficial in the pre-operative assessment of myometrial invasion in a number of studies as the results were in agreement with the pathological results[6,7,9]. Artner et al demonstrated more accuracy in transvaginal ultrasonographic assessment compared to intra-operative naked-eye assessment or frozen section[8]. Transvaginal ultrasonography has been compared to MRI in myometrial invasion assessment with contradict results in two studies[13,14]. Its

sensitivity was shown to be better than CA-125 in another study[15]. As for tumor grading, Fishman et al reported better performance of transvaginal ultrasonography in grade 2-3 tumors compared with grade 1 tumor, in which frozen section was more accurate[11].

Since transvaginal ultrasonography is more widely available than frozen section in Thai rural hospitals, it would be of interest to study the performance of transvaginal ultrasonography in myometrial assessment in a Thai population to see if it can aid in referring the patients to the cancer center for the proper management. In the present study, only one operator performed the ultrasonography to avoid interobserver bias. The procedure was carried out less than a week ahead of the surgery to avoid error from progression of tumor. Only 70 per cent accuracy was achieved from the present study. The errors in the remaining 30 per cent might have been associated with the operator's experience especially in early stage cases. In addition, a third of the patients, even though married, were nulliparous, rendering slight difficulty in the examination. In addition, other pathologies such as adenomyosis might hamper ultrasound image clarity. Moreover, the position and the size of the cancer might be other attributing factors to the error. Indeed, tumors that grew into the cavity could flag the operator's attention to the tumor site and myometrial invasion better than the flat ones and this can affect the results in Tables 3 and 4. However, the number of cases was too small to pinpoint any of these as the definite obstacles of study.

Nevertheless, considering tumor grades, positive predictive value of transvaginal ultrasonography was higher in grade 3 tumor than that from grade 1-

2. This might be explained by a higher grade tumor being more invasive and invasion is more readily and correctly recognized.

All in all, transvaginal ultrasonography may be used pre-operatively in assessment of myometrial invasion. The accuracy may be improved with the operator's experience. For the time being, the limitations in accuracy due to various causes cited above should be borne in mind and the patient should be counseled accordingly. Also, other additional investigations such as tumor marker or other imaging studies may be considered together to give the surgeon some idea beforehand and, incorporated with intra-operative findings, all information will hopefully help in the proper decision making for the surgical procedure to obtain the best benefit for the patient.

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ความถูกต้องแม่นยำของการตรวจคลื่นเสียงความถี่สูงทางช่องคลอดในการประเมินการลุกลามของกล้ามเนื้อมดลูกของมะเร็งเยื่อบุโพรงมดลูก

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วัตถุประสงค์ : เพื่อศึกษาความถูกต้องแม่นยำของการตรวจหาความลึกของการลุกลามชั้นกล้ามเนื้อในมะเร็งเยื่อบุโพรงมดลูก โดยใช้คลื่นเสียงความถี่สูงทางช่องคลอด เปรียบเทียบกับวิธีสไลด์ถาวรซึ่งเป็นวิธีมาตรฐาน

วิธีการวิจัย : ผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นมะเร็งเยื่อบุโพรงมดลูกโดยการขูดมดลูกแบบแยกส่วน จำนวน 111 ราย ได้รับการตรวจคลื่นเสียงความถี่สูงทางช่องคลอดก่อนการผ่าตัด เพื่อประเมินการลุกลามชั้นกล้ามเนื้อมดลูก หลังจากนั้นได้ทำการผ่าตัดเพื่อกำหนดระยะของโรค มดลูกที่ผ่าตัดออกมาจะได้รับการตรวจหาความลึกของการลุกลามของชั้นกล้ามเนื้อมดลูกโดยวิธีสไลด์ถาวรซึ่งเป็นวิธีมาตรฐาน โดยไม่ทราบผลการตรวจคลื่นเสียงความถี่สูง ผลทางพยาธิวิทยาและความลึกของการลุกลามชั้นกล้ามเนื้อมดลูกถือตามการตรวจทางพยาธิวิทยามาตรฐานนี้ การตรวจคลื่นเสียงความถี่สูงจะถูกเปรียบเทียบกับผลการตรวจทางพยาธิวิทยา

ผลการวิจัย : การตรวจคลื่นเสียงความถี่สูงเพื่อประเมินการลุกลามของชั้นกล้ามเนื้อมดลูก มีความไวร้อยละ 69.4, ความจำเพาะร้อยละ 70.6, คุณค่าในการทำนายผลบวกร้อยละ 53.2, คุณค่าในการทำนายผลลบร้อยละ 82.8, และค่าความถูกต้องร้อยละ 70.3 ค่าความถูกต้อง, ค่าความไว, ค่าความจำเพาะ, คุณค่าในการทำนายผลลบ, ผลบวกลวง, และผลลบลวงของเนื้องอก grade 3 เปรียบเทียบกับ grade 1–2 ไม่แตกต่างกันในทางสถิติ ส่วนคุณค่าในการทำนายผลบวกของเนื้องอก grade 3 มากกว่าของ grade 1–2 อย่างมีนัยสำคัญทางสถิติ ค่าความสอดคล้องของ grade 3 และ grade 1–2 เท่ากับ 0.57 และ 0.22 ตามลำดับ

สรุป : การตรวจหาความลึกของการลุกลามเข้าสู่ชั้นกล้ามเนื้อมดลูกของมะเร็งเยื่อบุโพรงมดลูก โดยใช้คลื่นเสียงความถี่สูงทางช่องคลอดนั้นสามารถยอมรับได้เมื่อเปรียบเทียบกับวิธีสไลด์ถาวรมาตรฐาน เทคนิคนี้สามารถเป็นประโยชน์ช่วยในการตัดสินวิธีการผ่าตัดในขณะผ่าตัดในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก

คำสำคัญ : มะเร็งเยื่อบุโพรงมดลูก, การลุกลามชั้นกล้ามเนื้อ, การตรวจคลื่นเสียงความถี่สูงทางช่องคลอด

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