Transvaginal Ultrasonographic Measurement of Endometrial Thickness in the Detection of Endometrial Abnormalities

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Abstract : A prospective clinical study was performed to determine an appropriate cut-off point value of endometrial thickness for the detection of endometrial abnormalities among women with abnormal uterine bleeding. Two hundred and forty nine women with abnormal uterine bleeding who had indication for fractional uterine curettage were enrolled. Endometrial thickness was measured by transvaginal ultrasonographic examination in each patient before performing fractional uterine curettage on the same day. The results were compared with the final histological diagnosis from fractional uterine curettages. Endometrial abnormalities were identified in 69 out of 249 cases (27.7%) as hyperplasia in 57 cases (22.9%) and endometrial cancer in 12 cases (4.8%). The appropriate cut off point value of endometrial thickness was 4 mm below which no endometrial abnormality was found. This cut-off point yielded a sensitivity of 100%, a specificity of 18.3%, a positive predictive value of 31.9%, a negative predictive value of 100%, a false positive rate of 68.2%, a false negative rate of 0% and an accuracy of 40.5%. In conclusion, endometrial thickness measurement by transvaginal ultrasonography is a simple diagnostic method for identifying endometrial abnormalities in women with abnormal uterine bleeding. The cut-off point value of 4 mm is appropriate for identifying endometrial abnormalities, below which unnecessary fractional uterine curettage can be avoided.

เรื่องย่อ : การใช้ค่าความหนาของเยื่อบุโพรงมดลูกที่วัดโดยคลื่นเสียงความถี่สูงทางช่องคลอดในการค้นหาความผิดปกติของเยื่อบุโพรงมดลูก

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ทำการศึกษาเพื่อหาค่าจุดตัดความหนาของเยื่อบุโพรงมดลูกที่ได้จากการวัดด้วยคลื่นเสียงความถี่สูงทางช่องคลอด ที่เหมาะสมในการค้นหาความผิดปกติของเยื่อบุโพรงมดลูกในสตรีที่มีเลือดออกผิดปกติจากโพรงมดลูก โดยศึกษาในสตรี 249 รายที่มีปัญหาเลือดออกผิดปกติจากโพรงมดลูกและมีข้อบ่งชี้ของการขูดมดลูกแบบแยกส่วน ทำการวัดความหนาของเยื่อบุโพรงมดลูกด้วยคลื่นเสียงความถี่สูงผ่านทางช่องคลอดแล้วนำไปเปรียบเทียบกับผลทางพยาธิวิทยาของเนื้อเยื่อบุโพรงมดลูกที่ได้จากการขูดมดลูกแบบแยกส่วนภายในวันเดียวกัน พบความผิดปกติของเยื่อบุโพรงมดลูกทั้งหมด 69 ราย (ร้อยละ 27.7) ผลเป็นเยื่อบุโพรงมดลูกหนาตัว 57 ราย (ร้อยละ 22.9) และมะเร็งเยื่อบุโพรงมดลูก 12 ราย (ร้อยละ 4.8) ถ้าความหนาของเยื่อบุโพรงมดลูกน้อยกว่า 4 มิลลิเมตร จะไม่พบพยาธิสภาพผิดปกติของเยื่อบุโพรงมดลูกเลย การใช้ค่านี้ในการทำนายความผิดปกติของเยื่อบุโพรงมดลูกพบมีค่าความไว ร้อยละ 100, ค่าความจำเพาะ ร้อยละ 17.8, คุณค่าในการทำนายผลบวก ร้อยละ 31.8, คุณค่าในการทำนายผลลบ ร้อยละ 100, ผลบวกลวง ร้อยละ 68.2, ผลลบลวง ร้อยละ 0 และค่าความแม่นยำ ร้อยละ 40.5 ดังนั้น การวัดความหนาของเยื่อบุโพรงมดลูกด้วยคลื่นเสียงความถี่สูงผ่านทางช่องคลอดซึ่งเป็นวิธีที่ง่ายและสะดวก จึงมีประโยชน์ในการค้นหาความผิดปกติของเยื่อบุโพรงมดลูกในสตรีที่มีเลือดออกผิดปกติจากโพรงมดลูก โดยสามารถหลีกเลี่ยงการขูดมดลูกแบบแยกส่วนในกลุ่มผู้ป่วยที่มีความหนาของเยื่อบุโพรงมดลูกน้อยกว่า 4 มิลลิเมตรได้

INTRODUCTION

Cancer of the uterine corpus is the most common cancer of the female lower reproductive tract. Most of these tumors are endometrial in origin, accounting for more than 95% of cases[1] and represent 10% of all cancers diagnosed in woman. The most common symptom of endometrial cancer, abnormal uterine bleeding, occurs in more than 80% of patients.[2] The rate of endometrial cancer and hyperplasia is over 10 – 15% in cases of postmenopausal bleeding. In contrast to cervical cancer, there is no screening technique that can detect an endometrial abnormality as precisely as cytology detecting cervical cancer. Dilatation and curettage has been the gold standard for the diagnosis of endometrial pathology. However it is invasive, inconvenient and relatively insensitive with a 10% false negative rate. Many safe and noninvasive techniques are now available for detecting and diagnosing endometrial abnormality.

Advances in technology have permitted the introduction of transvaginal ultrasound scanning using higher frequency ultrasound with greater approximity to the uterus. Hence, the endometrial–myometrial interface can be more clearly delineated than with the full bladder transabdominal technique. In recent years, in women with abnormal uterine bleeding, transvaginal ultrasound has been widely used to identify women at risk who should undergo uterine curettage procedure because it is safe, easy and non-invasive. Attempts have been made to correlate endometrial thickness to pathology results in order to avoid unnecessary samplings. Cut-off values of 4 - 5 mm were recommended, below which dilatation and curettage was deemed unnecessary[3-7].

The aim of this prospective study is to correlate the endometrial thickness measured by transvaginal ultrasound to endometrial pathology diagnosed by uterine curettage and to evaluate the values of different cut-off points in detecting endometrial abnormality.

MATERIALS AND METHODS

Two hundred and forty nine patients with abnormal uterine bleeding who attended the gynecology out-patient clinic of Siriraj Hospital between June 1998 and May 1999 were studied. All patients underwent dilatation and curettage after sonographic assessment with a 6.5 MHz vaginal probe attached to a Toshiba SSA-220A scanner on the same day. The transducer was introduced into the posterior vaginal fornix and the uterus was

scanned longitudinally and transversely. Endometrial thickness was measured on a longitudinal scan of the uterus at the level of maximal thickness that included both endometrial basal layers of the anterior and posterior uterine walls. If an intrauterine fluid collection was found, its thickness was subtracted from the total thickness. Fractional uterine curettages were performed and tissue samples were examined histologically in all patients. The endometrial thickness data were compared with the final histological diagnosis from fractional uterine curettage by statistical analysis.

RESULTS

The mean age of the patients was 44.5 years old with a range of 30 – 75 (Table 1).

Table 2 shows patients' menopausal status and parity. Most of the patients were premenopause and multiparous, i.e., 82.7% and 88.0% respectively.

Table 1. Patient's age.

Age (years)*	Number	Percentage
30 – 34	24	9.6
35 – 39	40	16.1
40 – 44	60	24.1
45 – 49	70	28.1
50 – 54	32	12.9
55 – 59	17	6.8
60 – 64	4	1.6
≥ 65	2	0.8
Total	249	100

*$\bar{X} \pm SD = 44.5 \pm 7.4$ years

Table 2. Patients' menopausal status and parity.

Patients	Number	Percentage
Menopausal status		
- Premenopause	206	82.7
- Menopause	43	17.3
Parity		
- Multiparous	219	88.0
- Nulliparous	30	12.0

The number, percentage, mean and range of endometrial thickness in relation to the histological diagnosis are summarized in Table 3. Under pathological examination, 99 patients had proliferative endometrium with a mean sonographic endometrial thickness of 7.1 mm (range 2.7 – 11.7 mm), 50 patients had secretory endometrium (mean sonographic endometrial thickness 9.6 mm, range 2.9-16.2 mm), 31 patients had atrophic endometrium (mean sonographic endometrial thickness 3.9 mm, range 2.2-5.8 mm). All of these were classified as negative pathological group. The positive pathological group were simple hyperplasia, complex hyperplasia and endometrial cancer which had mean endometrial thicknesses of 8.0, 10.7 and 14.6 mm with ranges of 4.2-14.4, 7.4-14.6 and 10.3-19.2 mm respectively. The mean endometrial thickness of the negative pathological group was less than that of positive pathological group which was statistically significant (7.3 mm. vs. 9.7 mm, $p < 0.05$). The least endometrial thickness was found in atrophic endometrium whereas the greatest thickness was in endometrial cancer (3.9 vs. 14.6 mm). The positive pathological group had endometrial thickness ranging from 4.2-19.2 mm, therefore, no positive pathology was found by histology in patients with sonographic endometrial thicknesses below 4.2 mm.

Table 3. Histological diagnosis related to transvaginal ultrasonography.

Pathology	Number	Percentage	Endometrial thickness	
			Mean ± SD (mm)	Range (mm)
Negative	180		7.3 ± 3.2*	
- Proliferative endometrium	99	39.8	7.1 ± 2.4	2.7 - 11.7
- Secretory endometrium	50	20.0	9.6 ± 3.8	2.9 - 16.2
- Atrophic endometrium	31	12.5	3.9 ± 0.9	2.2 - 5.8
Positive	69		9.7 ± 3.5*	
- Simple hyperplasia	42	16.9	8.0 ± 2.3	4.2 - 14.4
- Complex hyperplasia	15	6.0	10.7 ± 2.2	7.4 - 14.6
- Endometrial cancer	12	4.8	14.6 ± 3.0	10.3 - 19.2

*P < 0.05

The sensitivity and specificity of transvaginal ultrasonography in determining endometrial pathology in patients with abnormal uterine bleeding are shown in Table 4. A cut-off point of 4 mm gave a 100% sensitivity with a low specificity (17.8%) while none of the remaining values had an acceptable sensitivity and / or specificity.

Table 4. The sensitivity and specificity of transvaginal ultrasonography in abnormal uterine bleeding.

Endometrial thickness (mm)	Sensitivity (%)	Specificity (%)
≥ 3	100	3.3
≥ 4	100	17.8
≥ 5	91.3	31.3
≥ 6	87.0	40.0
≥ 7	76.8	49.4
≥ 8	68.1	63.3
≥ 9	52.5	73.9
≥ 10	45.5	78.7

The discordance between ultrasonographic endometrial thickness and histological diagnosis is shown in Table 5. An endometrial thickness of 4 mm or more had a sensitivity and negative predictive value of 100% in predicting malignancy, meaning that a negative result (endometrial thickness < 4 mm) clearly indicated that there was no carcinoma. However, the low specificity (17.8%) and positive predictive value (31.8%) indicated that the likelihood of a patient with a positive result (endometrial thickness ≥ 4 mm) having carcinoma was low. When an endometrial thickness limit of < 4 mm was used, the false negative rate and accuracy of sonography in diagnosing endometrial pathology were 0% and 40.5% respectively.

Table 5. Diagnostic value of ultrasound scan in prediction of endometrial abnormalities.

Endometrial thickness (mm)	Pathology		
	Positive	Negative	Total
< 4	0	32	32
≥ 4	69	148	217
Total	69	180	249

Sensitivity = 100%, 95% CI 93.4-100
Specificity = 17.8%, 95% CI 12.6-24.3
Positive predictive value = 31.8%, 95% CI 25.7-38.5
Negative predictive value = 100%, 95% CI 86.7-100
False positive rate = 68.2%, 95% CI 75.7-87.4
False negative rate = 0%, 95% CI 0-6.6
Accuracy = 40.5%, 95% CI 34.5-46.9

DISCUSSION

Abnormal uterine bleeding in women is an important sign necessitating dilatation and curettage to determine any underlying endometrial abnormality after a normal pregnancy has been ruled out. Although uterine curettage is considered to be one of the best methods to evaluate endometrial pathology, it is still not considered to be 100% accurate. In about 60% of the curettages, more than half of the uterine cavity is not sampled. Early diagnosis of endometrial cancer is of utmost clinical importance since it is one of the most common gynecological malignancies. Attempts are now being made to reduce the number of curettages in order to avoid unnecessary samplings. Transvaginal sonography is a noninvasive method and yields detail images of the uterus. This has facilitated the measurement of endometrial thickness and patient acceptance remains good. Measuring endometrial thickness has been used as a diagnostic procedure to avoid unnecessary uterine curettage. Different cut-off values have been used by some authors claiming that samplings below these figures would be unnecessary. Gull B, et al. found that no endometrial cancer or hyperplasia was diagnosed among women with an endometrial thickness of ≤ 4 mm.[3] Gerber B, et al. have shown that an endometrial thickness of > 5 mm had a sensitivity of 92.5%, specificity of 71.0% and concluded that in cases with a single postmenopausal bleeding with an endometrial thickness less than 5 mm, expectative procedures with repeated ultrasound examinations of the endometrium were recommended.[4] Smith-Bindman R, et al. also used a cut-off point of 5 mm and found that 96% of women with cancer had an abnormal endovaginal ultrasound result whereas 92% of women with endometrial disease had abnormal ultrasound.[5] Briley M, et al. used a 5 mm threshold to define abnormal endometrial thickening and found no carcinoma below this (100% negative predictive value), and this cut-off point had a 29% positive predictive value.[6] The combination of sonographic evaluation of endometrial thickness, endometrial morphology and endometrial border could improve the accuracy of transvaginal sonography in detecting endometrial pathology.[7] Other advance methods, including high frequency real time intrauterine sonography and sonohysterography could also improve the accuracy[8-10], but Doppler sonography could not improve the detection rate of premalignant and malignant endometrial lesions compared with conventional ultrasound.[11] Although transvaginal ultrasound is sensitive and should be used to select women with abnormal uterine bleeding for further investigations, it is not suitable for general screening in asymptoma-tic women.[12] Other advantages of transvaginal ultrasound are evident in the evaluation of myometrial invasion and in predicting lymph node metastasis in endometrial cancer patients. Transvaginal sonography was only slightly less accurate than MRI but more sensitive than CA 125 in predicting myometrial invasion in endometrial cancer.[13,14] Grabrielli S, et al. showed that transvaginal sonography was more accurate than hysteroscopy in detecting cervical involvement of endometrial cancer (82% and 72% respectively).[15] Cheng WF, et al. indicated that preoperative ultrasound features could offer important information for predicting lymph node metastasis in endometrial cancer patients.[16] However, current staging of uterine cancer relies on the findings and histopathology obtained from an exploratory laparotomy and the decision to use adjuvant radiotherapy is based on this surgical staging.

In our study, 249 patients with abnormal uterine bleeding were evaluated. For atrophic endometrium, the endometrial thickness remained in a fairly narrow range (2.2-5.8 mm) suggesting that it could be predicted by ultrasound alone while for other negative and positive pathology, the data showed quite a wide range making it impossible to predict pathology by ultrasound. The endometrial thickness of the positive pathology (hyperplasia and cancer) ranged from 4.2 to 19.2 mm. No positive pathology was found on histology in patients with a sonographic endometrial thickness below 4.2 mm, therefore, using a cut-off point of 4 mm could exclude endometrial hyperplasia and endometrial cancer so that uterine curettage for endometrial histology was unnecessary. Transvaginal sonography had a high sensitivity (100%) and high negative predictive value (100%) but a low specificity (17.8%) and positive predictive value (31.8%) with an accuracy of only 40.5%.

In conclusion, endometrial thickness measurement by transvaginal sonography is a simple diagnostic method for excluding endometrial abnomalities in women with abnormal uterine bleeding. The cut-off point value below which endometrial abnormalities can be excluded should be 4 mm, under which circumstances an unnecessary uterine curettage can be avoided.

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