Access this article online

Quick Response Code:

Website: www.pogsjournal.org

DOI: 10.4103/pjog.pjog_58_23

A comparative study of subjective and objective techniques using two-dimensional ultrasound in the preoperative assessment of cervical and myometrial invasion in patients with endometrial cancer

Doreen Baco Abria-Ybañez[1], Lara Marie David-Bustamante[1], Kareen Nora Reforma[1]

Abstract:

CONTEXT: Endometrial cancer is the third most common malignancy of the female genital tract in the Philippines, following cervical and ovarian cancer. Ultrasound as the first line in imaging has a major role in preoperative treatment and planning.

AIMS: To compare the diagnostic accuracy of subjective versus objective ultrasound measurement techniques in detecting cervical stromal invasion (CSI) and deep myometrial invasion (MI).

MATERIALS AND METHODS: Fifty-seven patients were enrolled in this cross-sectional study. Deep MI and CSI were evaluated both subjectively and objectively by measuring tumor-free distance (TFD), distance from the outer cervical os to lowest edge of the tumor border (Dist-OCO), and distance from the internal cervical os to caudal tumor border (Dist-ICO). Histopathological result used as the gold standard.

RESULTS: Subjective assessment for deep (MI) had 79.3% sensitivity, 82.1% specificity, 82.1% positive predictive value (PPV), 82.1% negative predictive value (NPV), and 80.7%. Subjective assessment for CSI had a sensitivity, specificity, PPV, NPV, and overall accuracy of 80%, 90.4%, 44.4%, 97.9%, and 89.5%. Objective measurement (TFD $\leq$0.8 cm) to detect deep MI had 86.2% sensitivity, 57.1% specificity, 67.4% PPV, 80% NPV, and 71.9% overall accuracy. Adjusting TFD cutoff to 0.65 increased to 71.4% specificity, making it comparable with subjective assessment. Dist-OCO ($\leq$2.1 cm) yielded 100% sensitivity, 86.3% specificity, 30% PPV, 100% NPV, and 87% overall accuracy. Dist-ICO was first used in this study, hence no cutoff yet. By using receiver operating characteristics, cutoff was 0.45 cm, which yielded a 60% sensitivity and 92% specificity (area under the curve 0.731, $P = 0.09$).

CONCLUSIONS: Subjective assessment of CSI and deep MI performs better than objective measurement techniques. TFD and Dist-OCO as the objective measurements showed clinically comparable accuracy to subjective assessment by an expert. Dist-ICO needs to be validated to a larger population to determine its clinical value in predicting CSI.

Keywords:

Cervical invasion, endometrial cancer, myometrial invasion, ultrasound

[1]Division of Ultrasound, UP-Philippine General Hospital, Manila, Philippines

Address for correspondence:
Dr. Doreen Baco Abria-Ybañez,
22-0, Mango Avenue,
Zapatera, Cebu City
6000, Philippines.
E-mail: doreenabria@gmail.com

Submitted: 24-Aug-2023
Revised: 11-Sep-2023
Accepted: 12-Nov-2023
Published: 27-Dec-2023

How to cite this article: Abria-Ybañez DB, David-Bustamante LM, Reforma KN. A comparative study of subjective and objective techniques using two-dimensional ultrasound in the preoperative assessment of cervical and myometrial invasion in patients with endometrial cancer. Philipp J Obstet Gynecol 2023;47:249-59.

Introduction

Endometrial cancer (EC) is the third most common malignancy of the female genital tract in the Philippines, following cervical and ovarian cancer.[1,2] Treatment and prognosis are influenced by tumor histology, tumor grade (FIGO grade), size, extent of myometrial invasion (MI), cervical stromal invasion (CSI), and nodal metastasis.[2] Hence, it is important to have accurate preoperative diagnosis to come up with appropriate treatment planning.[3] It will help in determining which among those patients will undergo a more radical surgery or irradiation as first treatment while avoiding overtreatment in low risk cases.

Transvaginal/transrectal/transabdominal ultrasound offers the possibility to evaluate the extent of the disease. There are two approaches in evaluating EC patients. Subjective evaluation is an assessment done by an expert sonologist and objective measurements are techniques employed to have the accuracy as comparable to a subjective assessment. There has been no consensus yet to date as to the best objective measurement technique for EC ultrasound assessment.

Objectives

General

To compare the diagnostic accuracy of subjective evaluation with objective measurement technique using two-dimensional (2D) ultrasound in the diagnosis of cervical and MI in women with EC using histopathology result as the gold standard.

Specific

1. To determine the diagnostic accuracy in terms of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of subjective evaluation which is done by an expert which will determine if there is deep myometrial or CSI using 2D ultrasound
2. To determine the sensitivity, specificity, PPV, and NPV of objective measurement techniques in the diagnosis of cervical invasion in terms of:
   a. Distance from the outer cervical os to lowest edge of the tumor border (Dist-OCO) – distance from the outer cervical os to the lowest edge of the tumor border of ≥2.1 cm as cut-off value based on the study of Mascilini *et al*. [Figure 1][4]
   b. Distance from the internal cervical os to caudal tumor border (Dist-ICO) - Distance of the lowest edge of the tumor protruding into the endocervical canal from the internal cervical os. For tumors that do not protrude or just confined to the endometrial cavity, it will be automatically designated as zero [Figure 2].
3. To determine the sensitivity, specificity, PPV, and NPV of tumor-free distance (TFD) =/<0.8 cm as cutoff value based on the local study by Navarete and Bustamante (2016) [Figure 3a and b][5]
4. To describe the clinicopathological profiles of patients
5. To determine the association between positive cervical and deep MI (subjective versus objective

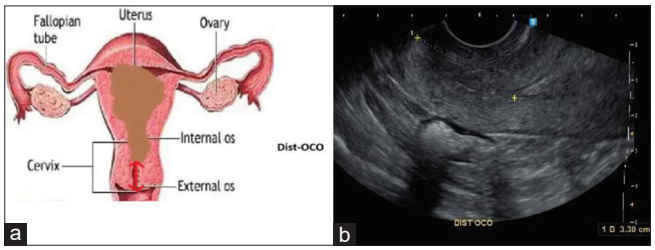

Figure 1: Objective measurement technique for cervical stromal invasion: (a) Distance from the outer cervical os to lowest edge of the tumor border (Dist-OCO) or the distance from lowest edge of the tumor to the outer cervical os. Image on the left (b) is the illustration sample and on the right is the actual Dist-OCO measurement

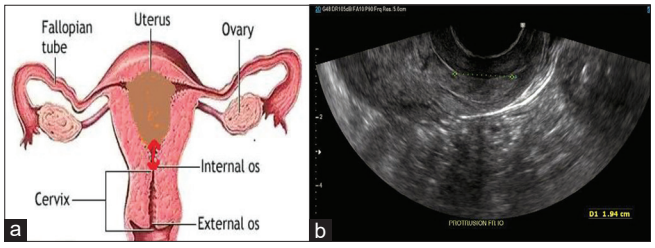

Figure 2: Objective measurement technique for cervical stromal invasion: (a) Distance from the outer cervical os to lowest edge of the tumor border (Dist-ICO) or distance measured from the lowest edge of the tumor to the internal cervical os. Image on the left (b) is the illustration sample and on the right is the actual Dist-ICO measurement

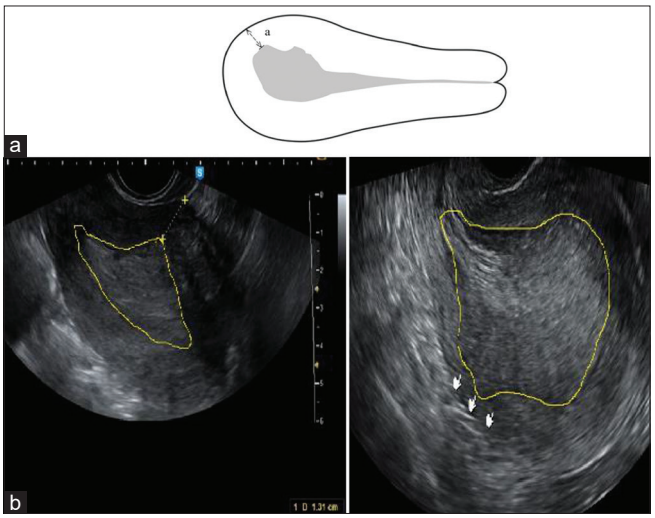

Figure 3: (a) Sagittal view of the uterus: The shortest myometrial tumor-free distance (TFD) to the serosa, which is a measure of the distance between maximal myometrial invasion and the uterine serosa, measured in cm. This will be the objective measurement in assessing myometrial invasion. A TFD ≤ 0.8 cm will signify deep myometrial invasion or ≥ 50% myometrial invasion, (b) Ultrasound image measuring TFD at the site of deepest tumor invasion

evaluation technique) in terms of lymph node metastases.

Study design

This study is a cross-sectional study. All patients who consented to the study and met the inclusion criteria were included.

Inclusion criteria

a. All patients with a new diagnosis of EC through biopsy and were admitted for elective surgery and surgical staging
b. Transvaginal/transrectal/transabdominal ultrasound was done at least 2 weeks prior to the elective surgery.

Exclusion criteria

a. Without informed consent
b. Older patients who have cognitive, psychiatric, and functional problems that may affect their capacity to give informed consent and without legally acceptable representative
c. Time interval between ultrasound and surgery was more than 2 weeks
d. Patients without histopathology results
e. Patients with histologically diagnosed with EC but not operated
f. Patients diagnosed with other primary carcinoma aside from EC
g. Patients with neo-adjuvant treatment prior to surgery
h. Patient's retraction of her informed consent.

Materials and Methods

Fifty-seven subjects were included in the study. Routine ultrasound procedure was done. Data collection from ultrasound report was obtained in terms of tumor size and color Doppler features, subjective evaluation of cervical and MI, objective evaluation of cervical and MI (TFD, Dist-OCO and Dist-ICO) and International Endometrial Tumor Analysis features of the endometrium [Figures 4-8].[6] The ultrasound findings were correlated with surgical report and final histopathologic result as gold standard.

Description of analysis

All the information was manually entered into an electronic spreadsheet after the data were extracted. Data processing and analysis were carried out using IBM SPSS version 19 (IBM Corp. Released 2010.IBM SPSS Statistics for Windows Version 19.0.Armonk, NY)and SAS program.

The patient's clinicopathological profile is categorized and presented using frequency and percentage

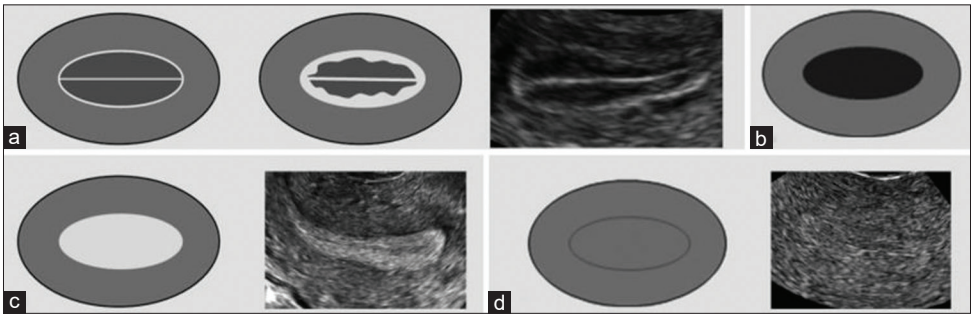

Figure 4: International endometrial tumor analysis: Uniform' endometrial echogenicity: three-layer pattern (a), hypoechogenic (b), hyperechogenic (c) and isoechogenic (d)

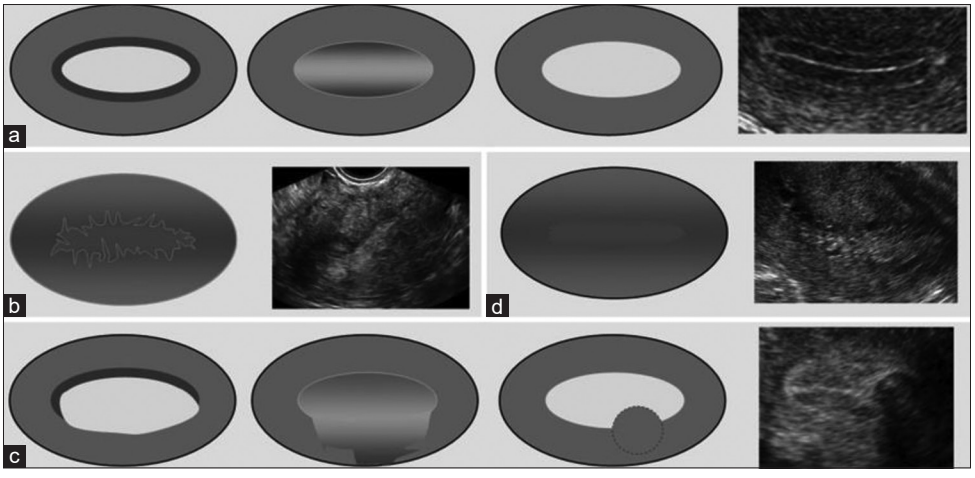

Figure 5: International endometrial tumor analysis: Endometrial–myometrial junction: "regular" (a), "irregular" (b), "interrupted" (c) (dark gray area denotes the endometrial–myometrial halo; in this case the halo is interrupted) and "not defined" (d)

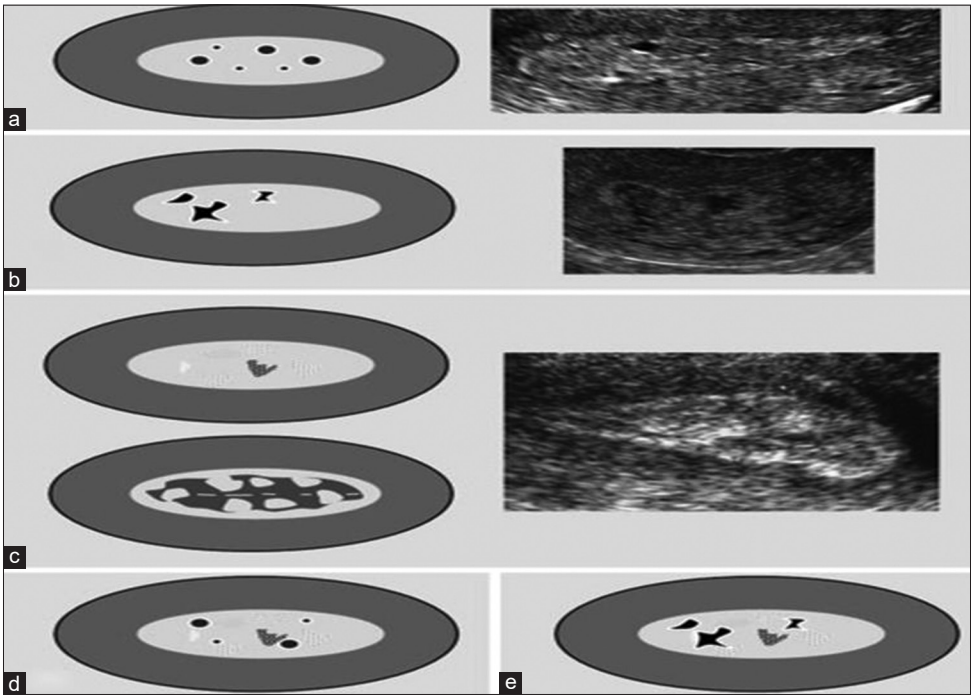

Figure 6: International endometrial tumor analysis: "Nonuniform" endometrial echogenicity: homogeneous background with regular cystic areas (a), homogeneous background with irregular cystic areas (b), heterogeneous background without cystic areas (c), heterogeneous background with regular cystic areas (d) and heterogeneous background with irregular cystic areas (e); black color denotes cystic spaces

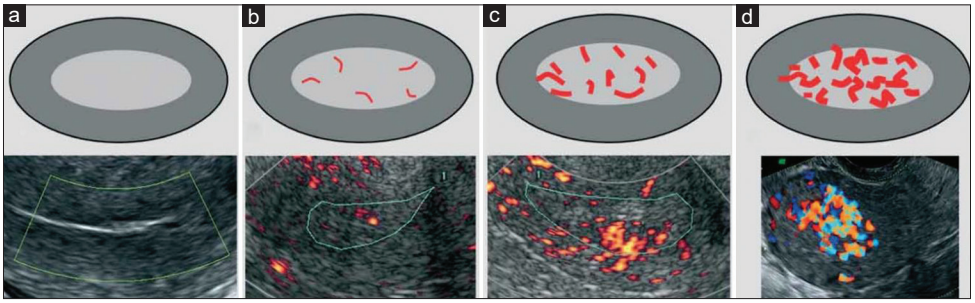

Figure 7: International endometrial tumor analysis: The color score is a subjective semiquantitative assessment of the amount of blood flow present: a color score of 1 is given when no color (a) flow signals redirecting blood floow can be found in the endometrium, a score of 2 when only minimal color can be detected (b), a color score of 3 when moderate color is present (c), and a score of 4 when abundant color if detected (d)

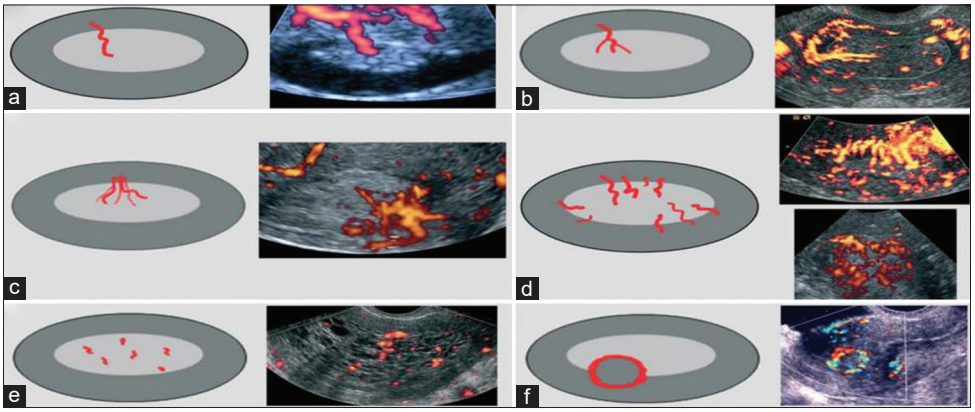

Figure 8: International endometrial tumor analysis: Vascular patterns: single "dominant" vessel without branching (a) and with branching (b), multiple vessels with "focal origin" (two or more vessels appear to share a common stem) (c) and with "multifocal origin" at the myometrial-endoemtrial junction (d), "scattered" vessels (dispersed color signals within the endometrium but without visible origin at the myometrial-endometrial junction) (e) and circular flow (f)

distribution. The ultrasound measurement techniques, TFD, Dist-OCO and Dist-ICO were expressed in frequency and percentage distributions.

The sensitivity, specificity, negative and PPVs, and overall accuracy of the cut-off values of the 3 objective measurement techniques (TFD, Dist-ICO and Dist-OCO) and the subjective evaluation of the presence of cervical and deep MI were computed.

Table 1: Age, gravidity, parity, body mass index, grade, personal history of other cancer, and family history of cancer of patients with endometrial cancer

Characteristic	Mean±SD or *n* (%)
Age	52.8±10.3
BMI (kg/m^2)	26.4±4.5
Postmenopausal	46 (80.7)
Gravidity	
Nulli	16 (29.6)
Primi	1 (1.8)
Multi (2 above)	40 (70.2)
Parity	
Nulli	16 (28.1)
Primi	1 (1.8)
Multi (2 above)	40 (70.2)
Risk factors	
Hypertension	31 (54.4)
Diabetes	19 (33.3)
Dyslipidemia	3 (5.3)
PCOS	4 (7)
Thyroid disease	3 (5.3)
Personal history of cancer	0
Family history of breast and/or gynecological cancer	9 (15.8)

BMI: Body mass index, PCOS: Polycystic ovary syndrome, SD: Standard deviation

Table 2: FIGO stage, tumor grade, and lymphovascular space invasion between patients with endometrial cancer

Characteristic	*n* (%)
Tumor grade	
Endometrioid adenocarcinoma, grade 1	19 (33.3)
Endometrioid adenocarcinoma, grade 2	22 (38.6)
Endometrioid adenocarcinoma, grade 3	9 (15.8)
Nonendometrioid (serous, malignant mixed mullerian tumor, hyperplasia with focal atypia)	7 (12.3)
FIGO stage	
IA	22 (38.6)
IB	25 (43.9)
II	1 (1.8)
IIIA	4 (7)
IIIB	2 (3.5)
IIIC1	4 (7)
IIIC2	0
IV-A	0
LVSI	
Yes	15 (26.3)
No	43 (75.4)

LVSI: Lymphovascular space invasion, FIGO: 2009 Classification

The Chi-square test was used to see if there was significant difference between those with invasion and without with regard to lymph node metastases, then if there was significant difference, odds ratio was done to determine association.

Results

A total of 57 patients were included. Tables 1 and 2 showed that the mean age is 52–53 years, postmenopausal, multigravid, preobese and with hypertension, diabetes and family history of breast and/or gynecologic cancer as risk factors. Young patients with EC have polycystic ovaries on ultrasound and are overweight or obese but with early-stage grade 1 tumors at the time of diagnosis. Postmenopausal patients are usually of higher stage and grade.

Table 3 shows that the sonographic features of patients with <50% MI mostly are hyperechogenic (10/11, 91%), with regular endometrial-myometrial junction (20/22, 90.9) and minimal flow on color and power Doppler (13/15, 86.7%). On the other hand, deep ≥50% MI usually is nonuniform in echogenicity (81%). Majority were of heterogeneous background without cystic areas (12/28, 42.9%), regular cystic areas (5/28, 17.9%) and with irregular cystic areas (8/28, 28.6%). Deep MI were often with multiple dominant vessels of multifocal origin (15/28, 53.6%) with moderate to abundant in flow (26/28, 92.9%) on color and power Doppler [Figure 9] and interrupted endometrial-myometrial junction (26/28, 92.9%).

Table 4 shows that for MI, subjective assessment on ultrasound appeared to catch the true positives and negatives (80.7%) more accurately as compared to TFD (71.9%). Comparing subjective assessment and TFD results for positive and negative MI showed, the two tests have statistically different results which become clearer when you look at the negative results, with a significant statistical difference [$P < 0.005$, Table 5].

Receiver operating characteristic (ROC) was employed to generate an area under the curve (AUC) and

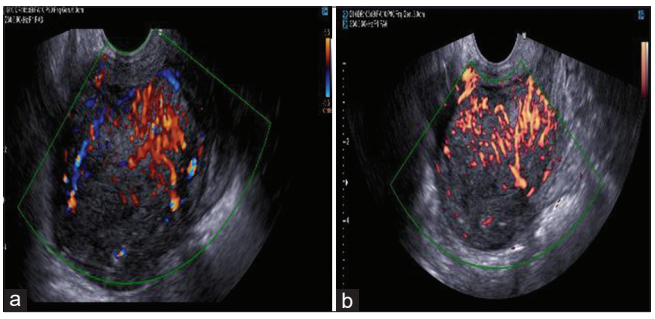

Figure 9: Color (a) and Power (b) Dopplers flow of endometrial mass showing moderate flow of multifocal origin. Final histopathology result showed deep myometrial invasion

Table 3: Endometrial mass description according to echogenicity, color Doppler, and vascular pattern between endometrioid and nonendometrioid type cancers

Echogenicity	Endometrioid		Nonendometrioid	
	Number (*n*=50)	Deep MI (*n*=22)	Number (*n*=7)	Deep MI (*n*=6)
Uniform (three layer pattern)				
Hypoechogenic	0	0	0	0
Hyperechogenic	11	1	0	0
Isoechogenic	0	0	0	0
Nonuniform				
Homogeneous background with regular cystic areas	1	0	0	0
Homogeneous background with irregular cystic areas	4	2	0	0
Heterogeneous background without cystic areas	13	9	3	3
Heterogeneous background with regular cystic areas	4	3	2	2
Heterogeneous background with irregular cystic areas	17	7	2	1
Endometrial-myometrial junction				
Regular	21	2	1	0
Irregular	1	0	0	0
Interrupted	28	20	6	6
Not defined	0	0	0	0
Color score				
Absent	0	0	0	0
Minimal	15	2	0	0
Moderate	20	11	6	5
Abundant	15	9	1	1
Color doppler vascular pattern				
Single dominant vessel with branching	1	1	0	
Single dominant vessel without branching	3	0	0	
Multiple dominant vessels of multifocal origin	18	13	2	2
Multiple dominant vessels of focal origin	13	3	2	1
Scattered	15	5	3	3
Circular flow	0	0	0	
No detectable color signs	0	0	0	

possible cutoffs that would yield a better balance between sensitivity and specificity to lessen possible overtreatment with the relatively low specificity using the TFD cut-off of the study (0.8 cm).[5] Table 6 and Figure 10 show the AUC to be almost 0.8 and with a lower cut-off of 0.65, the specificity rose from 57.1% to 71.4%.

Table 7 shows a higher sensitivity for Dist-OCO over subjective assessment (100% vs. 80%). Specificity was slightly higher for subjective assessment (90.4%) and is slightly higher in the overall accuracy rate by two points compared to the objective measurement of Dist-OCO.

By adjusting the Dist-OCO cut off to 2.05 cm in predicting deep MI, with an AUC of 0.954, the 100% sensitivity is retained and with two points improvement in specificity [Table 8].

Dist-ICO was explored as a possible predictor of cervical invasion which did not have a recommended cut-off yet. ROC was utilized [Table 9] yielding an AUC that is 0.731. The results were not statistically significant in diagnosing disease states [P = 0.091, Tables 9 and 10].

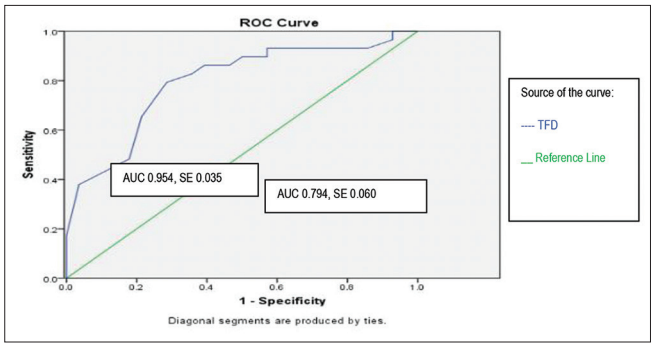

Figure 10: Receiver's operating curve generated by tumor-free distance accuracy in predicting >50% myometrial infiltration using final histopathology as the gold standard. AUC: Area under the curve, SE: Standard error, TFD: Tumor-free distance, ROC: Receiver operating characteristic

Table 10 shows that there was no significant association between lymph node metastasis and presence of CSI (P = 0.109) and deep MI (P = 0.226).

The possibility of a prolapsed mass into the vagina having CSI was likewise explored [Table 11]. Out of the 3 considered prolapsed via ultrasound, 2 eventually were found out to have cervical invasion (66.7%). However, the difference between the histopathologic

Table 4: Comparison of diagnostic accuracy of subjective assessment with that of objective ultrasound measurement tumor free distance in predicting deep myometrial involvement in women with endometrial cancer using 2×2 table

MI		Percentage (95% CI)					
	Cut-off	Sensitivity	Specificity	PPV	NPV	Likelihood ratio positive	Accuracy
Subjective assessment		79.3 (64.6–94.1)	82.1 (67.9–96.3)	82.1 (67.9–96.3)	79.3 (64.6–94.1)	4.4 (1.9–10.0)	80.7
TFD (cm)	0.8*	86.2 (73.7–98.8)	57.1 (38.8–75.5)	67.6 (52.5–82.7)	80 (62.5–97.5)	2.0 (1.3–3.2)	71.9

*Cut off used in the study. TFD: Tumor-free distance, PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval, MI: Myometrial invasion

Table 5: Comparison of subjective and objective tumor-free distance evaluation in determining deep myometrial invasion

Subjective evaluation of deep MI	Objective TFD		
	Positive	Negative	Total
Positive	28	0	28
Percentage within subjective deep MI	100.0	0.0	100.0
Percentage within TFD	75.7	0.0	49.1
Negative	9	20	29
Percentage within subjective deep MI	31.0	69.0	100.0
Percentage within TFD	24.3	100.0	50.9

P<0.004. TFD: Tumor-free distance, MI: Myometrial invasion

Table 6: Sensitivity and specificity of objective measurement tumor-free distance in predicting deep myometrial invasion in women with endometrial cancer when cut off is adjusted to 0.65

Deep MI	Cut-off	AUC	Sensitivity (%)	Specificity (%)
TFD	0.65	0.794 (0.675–0.912)	79.3	71.4

TFD: Tumor-free distance, MI: Myometrial invasion, AUC: Area under the curve

and ultrasound results was not statistically significant test ($P = 0.625$).

Discussion

Ultrasound has been widely used and is the first line in imaging patients with EC. It is cheaper, widely available and noninvasive with excellent imaging in real time.

Common profiles of patients in this study with EC were consistent with the findings in literature: mean age of 52 years old, multigravidas (70%) and nulliparas (30%), preobese (body mass index [BMI] 26.4), comorbidities such as hypertension and diabetes, and with family history of cancer, hypertension, and diabetes. The common risk factors were all leading to the pathogenesis of excess source of estrogen which will continually stimulate the endometrium leading to endometrial hyperplasia and possible progression to cancer.[7] EC patients are usually presenting at an early stage with low grade tumors and mostly of the endometrioid type which were also congruent in this study.[8]

EC in young patients common risk factor aside from increase BMI and nulliparity is the presence of polycystic ovaries on ultrasound.[9] Seventy-five percent of patients

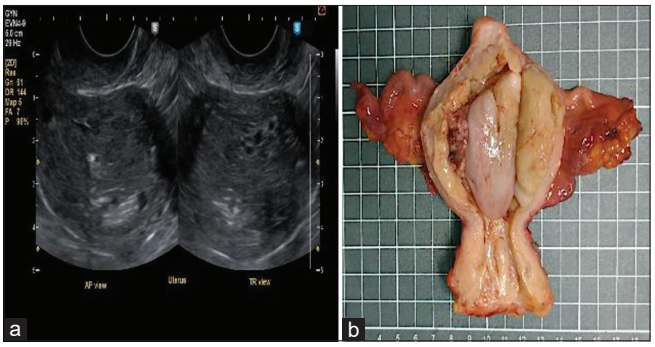

Figure 11: Ultrasound (a) appearance of a heterogeneous endometrial mass with irregular cystic areas. Gross (b) findings showed a polypoid mass bulging into the myometrium

were also presenting as grade 1 early stage tumor. On the other hand, older patients (>50 yo) tend to have higher grade tumors and higher stage.[10]

Sonographic features have shown that patients with <50% MI mostly had uniform echogenicity and hyperechogenic, regular endometrial-myometrial junction, single vessel or multiple vessels with focal origin, and minimal vascularization on color and power Doppler. On the other hand, deep mi (≥50% MI) usually are nonuniform with heterogeneous background (without cystic areas, with regular/irregular cystic areas), interrupted endometrial-myometrial junction, and moderate to abundant flow with multiple dominant vessels of multifocal origin on vascular pattern [Table 3]. These findings were concurrent with the meta-analysis by Epstein and Blomqvist (2011).[13]

Determining the extent of myometrial and cervical invasion preoperatively through imaging is vital in determining high risk patients who need more extensive surgery.[7,12] There are two methods of assessment: subjective evaluation by an expert and objective measurement techniques. To date, there is no consensus yet on which is the best way to assess MI, by subjective or objective evaluation.[4]

In this study, subjective ultrasound assessment by an expert performed better than the TFD (80.7% vs. 71.9%) with a sensitivity of 79.3% and specificity of 82.1% [Table 3]. The results have also been similar with large- and small-scale studies[3-5,7,8,10-12] with sensitivity

Table 7: Comparison of subjective assessment and objective measurement distance from outer cervical os to lower margin of tumor for prediction of cervical invasion in women with endometrial cancer

CSI	Percentage (95% CI)						
	Cut-off	Sensitivity	Specificity	PPV	NPV	Likelihood ratio positive	Accuracy
Subjective assessment		80 (44.9–115.1)	90.4 (82.4–98.4)	44.4 (11.9–76.9)	97.9 (93.9–101.9)	8.3 (3.2–21.3)	89.5
Dist-OCO	2.1 cm*	100	86.3 (76.8–95.7)	30 (1.6–58.4)	100	100	87.0

*Cut-off used in the study. Dist-OCO: Distance from outer cervical os, PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval, CSI: Cervical stromal invasion

Table 8: Sensitivity and specificity of objective measurement (distance from outer cervical os) in predicting deep myometrial invasion in women with endometrial cancer when cut off is adjusted to distance from outer cervical os 2.05

Cervical invasion	Cut-off	AUC	Sensitivity (%)	Specificity (%)
Dist-OCO	2.05	0.954 (0.886–1.00)	100	88.2

Dist-OCO: Distance from outer cervical os, AUC: Area under the curve

Table 9: Sensitivity and specificity of objective measurement (distance from outer cervical os) in predicting cervical stromal invasion in women with endometrial cancer with the different cut-offs

Positive if greater than or equal to	Sensitivity	1 - Specificity
−1.0000	1.000	1.000
0.1000	0.600	0.115
0.2500	0.600	0.096
0.4500	0.600	0.077 (92%)
1.0500	0.400	0.077
1.6000	0.000	0.077
1.7500	0.000	0.058
2.0500	0.000	0.019
3.3000	0.000	0.000

AUC=0.731; P=0.091. AUC: Area under the curve

of 68%–100% and specificity of 46.9%–90% [Table 12]. Sensitivities and specificities of ultrasound were comparable to MRI based on the large meta-analysis.[13]

We tested the 0.8 cm cutoff for the TFD and results showed that it has higher sensitivity than subjective assessment (86.2% vs. 79.3%) but lower specificity (57.1% vs. 82.1%) in accurately detecting deep MI. The study by Navarete and Bustamante (2016) showed a higher sensitivity of 100% but with a relatively lower specificity at 46.9%.[5] The cutoff of 0.8 cm is a good screening tool but is at risk for potential over diagnosis and possible overtreatment. Fischerova noted that the risk of overestimation was in large polypoid tumors, stretching the myometrium with thin TFD [Figure 11 for actual ultrasound and gross picture].[14]

This study aims to achieve the accuracy of objective technique to be as comparable with the subjective assessment and can be applicable also to the less experienced sonologists. Hence, we adjusted the cutoff to balance the relatively low specificity of 0.8 cm in

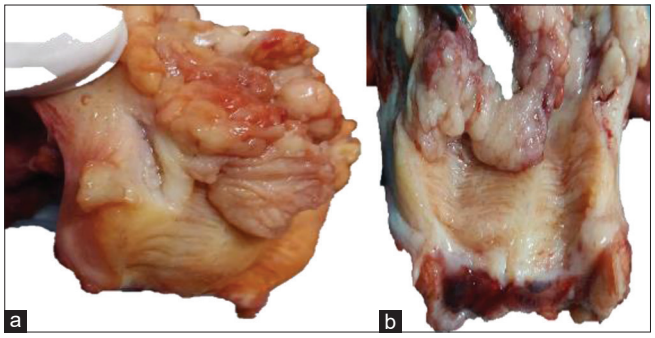

Figure 12: Gross (a) appearance of endometrial mass protruding into the endocervical canal (b) with no cervical stromal invasion

this study by using ROC. With AUC of 0.8, which is considered a good diagnostic test, TFD cut off was lowered to 0.65 cm. The specificity increased from 57.1% to 71.4%, with the sensitivity of 79.3%. The sensitivity and specificity were almost comparable already with the subjective assessment using the cutoff of 0.65 cm. Hence, it can be used by the general sonologists in assessing deep MI. Having this ≤0.65 cm cutoff of TFD would be of help in determining deep MI, especially in those far flung areas where there is a scarcity of expert sonologists who can do the subjective assessment.

Other studies have set different cutoffs in determining deep MI [Table 12]. Mascilini *et al*., used cutoff TFD value of 7.1 mm which showed higher sensitivity (85%) but with a significantly lower specificity (50%).[4] The ideal one was the study by Alcázar *et al*. using the three-dimensional (3D) ultrasound in virtual uterine navigation in assessing patients with EC.[15] The results of the study suggested cutoff value of <9 mm in detecting women with deep MI which had a sensitivity of 100% but with a low specificity of 61%,[16] which could be a risk for overtreatment. This 3D technique is supposedly better because of better image quality; however, this is operator dependent, more expensive, and takes time.

There are very few publications [Table 13] on the use of 2D transvaginal ultrasound to assess CSI, but the results are generally good. In this study, objective measurements (Dist-OCO and Dist-ICO) in determining CSI, performed better than subjective evaluation with

Table 10: Association of deep myometrial invasion and cervical stromal invasion in detecting lymph node metastases

	Lymph node metastasis (%)		Total (%)	*P*
	Yes	No		
Histopathological deep MI				
Negative				
Number	2	26	28	0.226
Percentage within histopath deep MI	7.1	92.9	100.0	
Percentage within lymph node metastasis	28.6	52.0	49.1	
Positive				
Count	5	24	29	
Percentage within histopath deep MI	17.2	82.8	100.0	
Percentage within lymph node metastasis	71.4	48.0	50.9	
Histopath CSI				
Negative				
Number	5	47	52	0.109
Percentage within histopathological cervical invasion	9.6	90.4	100.0	
Percentage within lymph node metastasis	71.4	94.0	91.2	
Positive				
Count	2	3		
Percentage within histopathological cervical invasion	40.0	60.0	5	
Percentage within lymph node metastasis	28.6%	6.0	100.0	

MI: Myometrial invasion, CSI: Cervical stromal invasion

Table 11: Prolapsed endometrial mass association with cervical stromal invasion

Prolapsed endometrial mass	Histopath cervical invasion (%)	
	Positive	Negative
Yes		
n	2	1
Percentage within prolapsed	66.7	33.3
Percentage within histopath cervical invasion	40.0	1.9
No		
n	3	51
Percentage within prolapsed	5.6	94.4
Percentage within histopath cervical invasion	60.0	98.1
Total		
n - 52	5	57
Percentage within prolapsed - 91.2%	8.8	100.0

P=0.625

Table 12: Comparison of previous studies and current study diagnostic accuracy of subjective ultrasound assessment of myometrial invasion on previous studies

Author	Year of publication	Number of women	Sensitivity (%)	Specificity (%)
Szantho *et al*.[17]	2001	52	86	90
Savelli *et al*.[12]	2008	74	84	83
Alcazar *et al*.[14]	2009	96	93	82
Akbayir *et al*.[8]	2011	298	68	82
Mascillini *et al*.[4]	2013	144	77	81
Navarete *et al*.[5]	2016	49	100	46.9
Current study	2019	57	79.3	82.1

sensitivity of 100% both for Dist-OCO and Dist-ICO and specificities of 86.3% and 89.6%, respectively. The 2.1 cm cutoff for Dist-OCO from the study of Mascilini *et al*.[4] was rounded off, instead of 20.5 mm (for uniformity purposes since the institution uses cm instead of mm). The results of this study in comparison with Mascilini *et al*., [Table 14] has higher sensitivity (100% vs. 73%) and specificity (86.6% vs 63%) and with a much higher specificity by 2 points (88.2%) if we set the specific cut-off at 2.05 cm. Fisherova suggested that in assessing CSI, there are 2 ways[13]: (1) sliding effect is to be done to distinguish simple protrusion [Figure 12 for actual gross sample] from actual invasion; (2) pronounced stromal vascularization on color/power Doppler below the level of uterine arteries in isthmus [Figure 13].[13] A local retrospective study done by Espinosa and Comia[15] (2011) showed that cervical stromal infiltration was determined by the ill-defined borders of neoplastic tissue in the cervical stroma, involving at least the inner third which is congruent with the results in this study [Figure 14].[15]

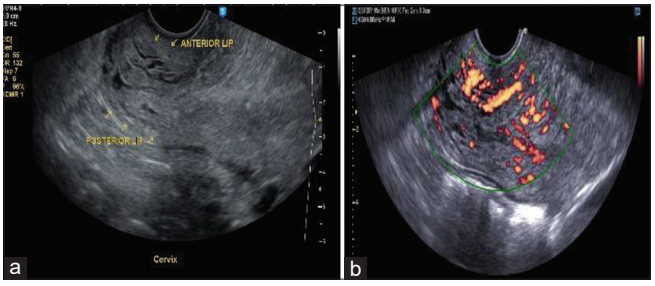

Figure 13: Anteroposterior view of endometrial mass prolapsing into the endocervical canal (a) and power Doppler (b) showing pronounced stromal vascularization at the anterior cervical lip with cervical stromal invasion on final histopathologic examination

Table 13: Diagnostic accuracy of subjective ultrasound assessment of cervical invasion

Author	Year of publication	Number of women	Sensitivity (%)	Specificity (%)
Savelli *et al*.[12]	2003	74	93	92
Akbayir *et al*.[8]	2011	298	77	99
Mascillini *et al*.[4]	2013	144	63	93
Jantarasaengaram *et al*.[9]	2013	60	100	86
Current study		57	80	90.4

Table 14: Comparison of objective measurement distance from the outer cervical os to lower margin of the tumor for prediction of cervical stromal invasion in women with endometrial cancer

Study	Population	Sensitivity (%)	Specificity (%)
Mascilini *et al*. (2013)[4]	*n*=144	73	63
Current study	*n*=57	100	88.2

Dist-OCO cutoff: 2.1 cm. Dist-OCO: Distance from outer cervical os

This is the first study so far to investigate on the use of Dist-ICO, which is the distance of the endometrial mass extending into the endocervical canal, measured from the internal os to the caudal tumor border. There is no established cutoff yet. The measurement included all endometrial masses seen extending to the cervix or prolapsing into the endocervical canal. By plotting the different values altogether and generating the ROC, cutoff at 0.45 cm yielded sensitivity of 60% and specificity of 92% in detecting CSI, with the AUC at 0.731, indicating an excellent diagnostic test. The results were not statistically significant because of only few cases seen with masses extending to the cervix [Tables 9 and 10].

Several studies have shown that deep MI and CSI have higher risk for nodal metastases.[17] There was no significant difference in predicting lymph node metastases in this study due to the small number of cases.

There were only two cases of positive lymph node metastases on final histopathologic examination which were not detected on ultrasound. These nodes where only subcentimeter, which was too small to be detected on ultrasound. The detection of infiltrated lymph nodes, particularly in size, in early stage EC is technically difficult or even impossible. Studies demonstrating the accuracy of ultrasound in detecting infiltrated lymph nodes in EC showed low sensitivity (similar to other imaging modalities) but with high specificity.[13] Results showed that prolapsed endometrial mass significantly had CSI (2/3, 66.7%) and could be of use for future researches, to a larger population. Subjective evaluation done and it was 100% accurate in determining the presence or absence of CSI.

Conclusions

Ultrasound plays a vital role in preoperative planning for EC patients. It is cost-effective, widely available, and noninvasive with excellent imaging in real time. Subjective evaluation by an expert performs better than objective measurement in terms of determining deep MI.

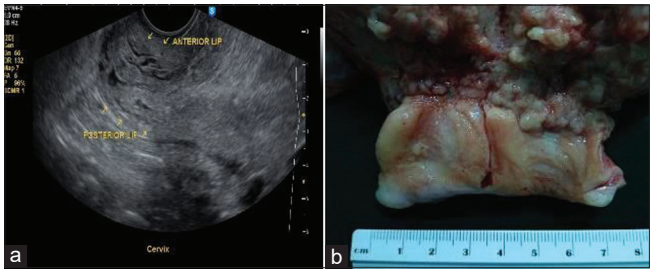

Figure 14: Ultrasound and gross appearance of cervical stromal invasion on ultrasound (a) and gross (b) appearance

Objective measurement of deep MI using TFD of 0.65 cm demonstrated clinically acceptable accuracy. The sensitivity and specificity were almost comparable with subjective evaluation by an expert when the TFD cutoff was lowered to 0.65 cm.

Subjective evaluation of CSI using Dist-OCO is better than objective evaluation. Among the objective measurement techniques, the Dist-OCO was comparable with the subjective assessment with an overall accuracy of 87%.

Dist-ICO or the distance from the internal cervical os to the lowest tumor border was not a good diagnostic test for determining CSI.

This study highlights the validity of TFD and Dist-OCO as objective measurement techniques in assessing deep myometrial and CSI, respectively. It is simple and easy to perform and can be used by any sonologist with varying levels of experience, especially in remote areas where there are few or no sonologists at all.

Recommendations

The study recommends the value of TFD 0.65 cm and Dist-OCO 2.05 cm as auxiliary measurement tools in identifying those patients with EC who are high risk of extensive and progressive disease, lymph node metastases, and recurrence. A prospective validation study to a large population can be done on future researches to determine its value in clinical practice.

Authorship contributions

Dr. Doreen Abria-Ybañez - Involved in the conceptualization, methodology, data curation, writing of the original draft, review and editing.

Dr. Lara Marie David-Bustamante - Involved in conceptualization, methodology, review and editing of the draft.

Dr. Kareen N. Reforma - Involved in conceptualization, methodology, review and editing of the draft.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Laudico AV, Mirasol-Lumague MR, Medina V, Mapua CA, Valenzuela FG, and Pukkala E. 2015 Philippine Cancer Facts and Estimates. Philippine Cancer Society, 2015; p. 79.
2. Society of Gynecologic Oncologists of the Philippines (Foundation) Inc. Clinical Practice Guidelines for the Obstetrician Gynecologist. 3rd ed. Ermita, Manila: Society of Gynecologic Oncologists of the Philippines; 2019. p. 49.
3. Frühauf F, Zikan M, Semeradova I, Dundr P, Nemejcova K, Dusek L, *et al*. The diagnostic accuracy of ultrasound in assessment of myometrial invasion in endometrial cancer: Subjective assessment versus objective techniques. Biomed Res Int 2017;2017. Article ID 1318203. https://doi.org/10.1155/2017/1318203.
4. Mascilini F, Testa AC, Van Holsbeke C, Ameye L, Timmerman D, Epstein E. Evaluating myometrial and cervical invasion in women with endometrial cancer: Comparing subjective assessment with objective measurement techniques. Ultrasound Obstet Gynecol 2013;42:353-8.
5. Navarete H, Bustamante L. Assessing Myometrial Infiltration by Measuring the Tumor Free Distance and Depth of Invasion through 2D Transvaginal Ultrasound Among Patients with Endometrial Cancer. Philippine Journal of Obstetrics and Gynecology; 2018:1-17.
6. Leone FP, Timmerman D, Bourne T, Valentin L, Epstein E, Goldstein SR, *et al*. Terms, definitions and measurements to describe the sonographic features of the endometrium and intrauterine lesions: A consensus opinion from the international endometrial tumor analysis (IETA) group. Ultrasound Obstet Gynecol 2010;35:103-12.
7. Datu MM, David-Bustamante LM. Preoperative Sonographic Evaluation of Myometrial Invasion in Endometrial Cancer: A Comparative Study on the Diagnostic Accuracies of Various Measurement Techniques (Unpublished) 2014.
8. Akbayir O, Corbacioglu A, Numanoglu C, Guleroglu FY, Ulker V, Akyol A, *et al.* Preoperative assessment of myometrial and cervical invasion in endometrial carcinoma by transvaginal ultrasound. Gynecol Oncol 2011;122:600-3.
9. Jantarasaengaram S, Praditphol N, Tansathit T, Vipupinyo C, Vairojanavong K. Three-dimensional ultrasound with volume contrast imaging for preoperative assessment of myometrial invasion and cervical involvement in women with endometrial cancer. Ultrasound Obstet Gynecol 2014;43:569-74. doi: 10.1002/uog.13200.
10. Epstein E, Blomqvist L. Imaging in endometrial cancer. Best Pract Res Clin Obstet Gynaecol 2014;28:721-39.
11. Benavides D, Luna JT, Bustamante LM. The accuracy of ultrasound in preoperative assessment of poor prognostic factors in endometrial carcinoma: A preliminary report. Philipp J Gynecol Oncol 2005;2:1-10.
12. Savelli L, Ceccarini M, Ludovisi M, Fruscella E, De Iaco PA, Salizzoni E, *et al.* Preoperative local staging of endometrial cancer: Transvaginal sonography versus magnetic resonance imaging. Ultrasound Obstet Gynecol 2008;31:560-6.
13. Fischerova D. Ultrasound scanning of the pelvis and abdomen for staging of gynecological tumors: A review. Ultrasound Obstet Gynecol 2011;38:246-66.
14. Alcázar JL, Galván R, Albela S, Martinez S, Pahisa J, Jurado M, *et al.* Assessing myometrial infiltration by endometrial cancer: Uterine virtual navigation with three-dimensional US. Radiology 2009;250:776-83.
15. Espinosa J, Comia L. The accuracy of transvaginal ultrasound in determining depth of myometrial invasion and cervical infiltration among patient preoperatively diagnosed with endometrial cancer: A 5 year retrospective review 2011.
16. Euscher E, Fox P, Bassett R, Al-Ghawi H, Ali-Fehmi R, Barbuto D, *et al.* The pattern of myometrial invasion as a predictor of lymph node metastasis or extrauterine disease in low-grade endometrial carcinoma. Am J Surg Pathol 2013;37:1728-36.
17. Szantho A, Szabo I, Csapo ZS, *et al*. Assessment of myometrial and cervical invasion of endometrial cancer by transvaginal sonography, Eur J Gynaecol Oncol 2001;22:209-12.