Accuracy of endometrial 2D ultrasound and power doppler in predicting endometrial pathology among patients with endometrial disease at Dr. Jose Fabella Memorial Hospital*

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ABSTRACT

Background: Transvaginal sonography with Doppler study has helped improve the clinician's ability to diagnose and manage intrauterine abnormalities. Use of International Endometrial Tumor Analysis (IETA) may help predict the risk of endometrial pathologies based on ultrasound appearance.

Objective: To determine the accuracy of 2D ultrasound and power Doppler in the examination of the endometrium using the international endometrial tumor analysis classification in predicting intrauterine disease among patients with endometrial pathology in Dr. Jose Fabella Memorial Hospital.

Study Design: A cross-sectional study was done on patients who were diagnosed with abnormal uterine bleeding and underwent 2D ultrasound and power Doppler studies. Sonographic features were classified using International Endometrial Tumor Analysis group classification and correlated with the histopathologic diagnosis.

Results: Seventy-three patients were included in the study. The age of the subjects was significantly associated with the the histopathologic findings of benignity or malignancy. At 40-49 years old, there was significantly higher proportion of subjects with benign lesions, and 60 years and above had predominance of malignancy. The top three histopathologic diagnoses: endometrial polyp 41 cases (46.2%), proliferative endometrium 9 cases (12.3%), and simple hyperplasia without atypia 8 cases (11.0%). Patients diagnosed with malignancy had significantly thickened endometrium at 2.9 cm. The color content of the endometrium (color score) were statistically significant among different pathologies. Positive predictive value is the same for both, while Doppler showed a higher negative predictive value. Total accuracy was higher for Doppler.

Conclusion: Both greyscale ultrasound and Doppler are 100% accurate in predicting benign lesions but Doppler has a higher accuracy in predicting malignant lesions. The IETA group consensus on descriptive and morphologic nomenclature in describing endometrial findings for power Doppler and on greyscale ultrasound is clinically valuable.

Keywords: Ultrasound, Power Doppler, Terminology, Endometrium

INTRODUCTION

Abnormal uterine bleeding is a common complaint by gynecology patients who consulted at our institution. A gynecological ultrasound examination is preceded by a thorough history taking and physical assessment with speculum and internal examination in diagnosing patients. Use of transvaginal ultrasound plays an important role in the management of these cases especially in detecting nonpalpable intrauterine pathology.

The use of ultrasound in the diagnosis of intracavitary pathology was introduced in the late 1980s and early 1990s.[1-5] Ultrasound is a valuable first-line tool for the evaluation of uterine morphology, though it is difficult to differentiate between various abnormalities affecting the uterine cavity.[6] Hysteroscopy, saline infusion hysterography, dilatation and curettage can be used for confirmation of abnormal endometrial findings on greyscale ultrasound, although patient discomfort and increased cost should be considered, with these procedures. Color and pulsed Doppler are non-invasive tools with which to study the vascular changes that occur in an endometrial pathology.[7] It has been suggested that color Doppler ultrasound examination of uterine and subendometrial arteries can assist in differentiating benign from malignant endometrium.[8-9]

The IETA (International Endometrial Tumor Analysis) statement is a consensus of terms, definitions and measurements that may be used to describe the

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sonographic features of the endometrium and uterine cavity at gray-scale sonography, color flow imaging and sonohysterography.[10] The use of power Doppler is preferred over the color Doppler, since it is superior for the detection of small vessels with slow blood flow velocities.[11]

The objectives of this study are the following: first is to describe the demographic characteristics of the patients with endometrial pathology seen at the Out-patient Department of Dr. Jose Fabella Memorial Hospital, the clinical and sonologic diagnosis ant its concomitant management. Another is to enumerate the different histopathologic diagnosis of the above patients. Also, to determine the accuracy of 2D echo and power Doppler in the diagnosis of endometrial lesions using the IETA (International Endometrial Tumor Analysis) definitions and measurements used to describe the sonographic features of the endometrium and uterus.

METHODOLOGY

A. SETTING

The subjects of this study included all the patients with endometrial pathology who consulted for further uterine evaluation at Dr. Jose Fabella Memorial Hospital.

B. SUBJECTS

To compute for sample size using 5% margin of error for sensitivity and 10% error for specificity, with a 95% confidence interval level. Z=1.96. A total of 44 subjects for those with endometrial malignancy and 41 for those with benign findings. All based on histopathology as needed.

The inclusion criteria consisted of: reproductive and postmenopausal age group of women with endometrial pathology.

The exclusion criteria included the following: pregnancy, use of IUD, use of drugs affecting endometrial vasculature such as hormonal therapy, oral contraceptives or tamoxifen during the last 3 months, pelvic inflammatory disease, polycystic ovarian syndrome and systemic diseases causing abnormal uterine bleeding (e.g. bleeding disorders, thyroid related problems).

C. DATA COLLECTION

All eligible patients signed the informed consent forms prior to examination.

They filled out questionnaires for the demographic data. The patients were examined prospectively by standard B mode Transvaginal sonography and power Doppler sonography by one sonologist accredited by PSUOG to avoid interobserver variability. When a transvaginal scan was considered inappropriate (e.g. virgin), a transrectal ultrasound was used instead. Ultrasound examination was focused on the endometrial cavity with the surrounding myometrium. The machine that was used was Mindray DC-6 with the following settings: frequency of at least 5MHz, pulse repetition frequency 0.3-0.9 kHz, wall filter 30-50 Hz, power Doppler gain was reduced until all color artifacts disappeared, to elicit maximum sensitivity even for low velocity flow.

Initially, all women were scanned on lithotomy position with an empty bladder using 2D Transvaginal ultrasound. The uterus were scanned longitudinally and transversely. The thickness of the endometrium was measured at the thickest portion in the longitudinal plane. It was measured from the highly reflective interface of the junction of the endometrium and myometrium. In the presence of endometrial fluid, composite thickness was measured. Qualitative assessment of the endometrium including the presence of pathological lesions noted, description, location, morphological features, myometrial invasion, and its vascularity on power Doppler interrogation was studied according to the International Endometrial Tumor Analysis (IETA) classification.[10] The power Doppler box included the endometrium with surrounding myometrium, with a pulse repetition frequency of 0.6 kHz. Endometrial vasculature was scored using the International Ovarian Tumor Analysis (IOTA) color score applied to ovarian masses. The color score was a subjective semiquantitative assessment of the amount of blood flow present in the endometrium: a color score of 1 was given when no color flow signal, a score of 2 when only minimal color was detected, a score of 3 when moderate color was present, and a score of 4 when there was abundant color. The classification of the vascular pattern of the endometrium on power doppler was reported according to the International Endometrial Tumor Analysis (IETA) description[10] Ultrasonographic diagnosis was correlated with histopathologic findings in all patients with positive result of endometrial pathology.

Methods of the Study:

Study Design:

This was a cross sectional study, which specifically, determined the accuracy parameters of a test, in this case color Doppler and 2D echo results. Diagnostic statistics such as sensitivity, specificity, PPV, NPV and accuracy was computed. For color Doppler, accuracy parameters such as enumerated above was also computed for the various vascular and color patterns to find the correlation between the ultrasound findings and histopathologic diagnosis. The research population included all patients with endometrial pathology who were eligible with the inclusion criteria, and consulted at Dr. Jose Fabella Memorial Hospital.

Statistical Analysis:

Data were described using frequency counts and percentages. Chi-square was used to determine significant difference in the distribution of discrete variables. Odds ratios and their 95% confidence intervals were computed for variables which showed significance at 95% confidence level.

Accuracy parameters such as sensitivity, specificity, Positive and Negative Predictive Values and their 95% confidence intervals were computed using standard formulas and encoded in Excel and used Stata IC Statistical Software Version 10 (by Stata Corp). A result was judged statistically significant if the P value of each respective test was <0.05.

Significance of the Study:

The study aimed to determine the accuracy of 2D ultrasound and power Doppler in the diagnosis of endometrial lesions using the IETA (INTERNATIONAL ENDOMETRIAL TUMOR ANALYSIS) definitions and measurements used to describe the sonographic features of the endometrium and uterus. If results were proven to be statistically significant, use of IETA (INTERNATIONAL ENDOMETRIAL TUMOR ANALYSIS) would be useful in improving accuracy in diagnosing endometrial pathologies seen in our institution, and help guide the clinicians with their management.

Definition of Terms:

1. 2D ultrasound – radiologic technique wherein structures of the body are visualized by recording the reflections of ultrasonic waves directed into tissues.
2. Doppler Study – measurement and visual recording of reflected sound waves produced by blood flow through blood vessels.
3. Abnormal Uterine Bleeding – episode of heavy bleeding of sufficient quantity to require immediate intervention to prevent further blood loss.
4. Endometrial pathology – abnormality or disease entity seen within the endometrial cavity.

RESULTS

A total of 73 patients diagnosed with abnormal uterine bleeding were scanned and, endometrial curettage was subsequently performed at Dr. Jose Fabella Memorial Hospital.

Table 1 shows the distribution of subjects found with benign and malignant lesions on histopathology, by age and by gravidity and parity. It can be seen that age was significantly associated with findings on histopathology (p 0.0002). The distribution of subjects with benign and malignant findings were essentially similar at <40 yrs of age but was borderline significantly associated, indicating a trend, at 50-59 years. At 40-49 years, there was a significantly higher proportion of subjects found with benign lesions than malignant lesions, with an Odds Ratio of 0.108 meaning those aged 40-49 years are 10.8% less likely to show malignant lesions. At 60 years and above, there was a significantly higher proportion of subjects with malignant lesions, with an Odds Ratio of 18.9, meaning subjects 60 years and above are 18.9 times more likely to show malignant lesions than younger subjects.

Gravidity and Parity did not show significant association with histopathological findings of benign and malignant lesions. (Figure 1)

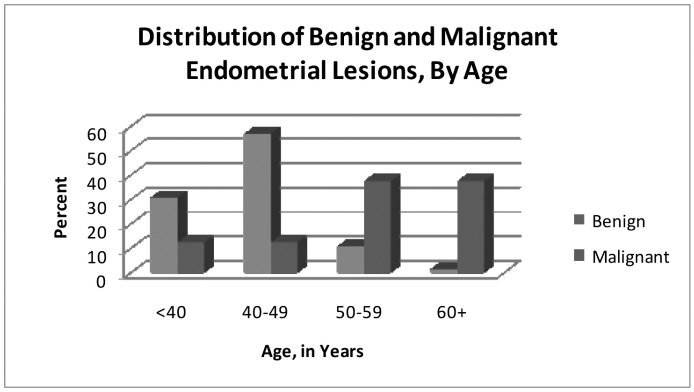

Figure 1

In Table 2, the mean endometrial thickness of the patients with different pathologies were plotted. The mean endometrial thickness in endometrial polyp is 1.37 ± 0.71 cm. In this study, endometrial thickness of 1.0 - 1.15 cm is compatible with normal menstrual phase. Patients with malignancy were significantly noted to have thickened endometrium with a mean of 2.9 ± 2.33 cm., p value of 0.04.

The histopathologic diagnoses were as follows: endometrial polyp, 41 cases (56.2%); proliferative endometrium 9 cases (12.3%), simple hyperplasia without atypia 8 cases (11.0%), malignancy 7 cases (9.6%), secretory endometrium 6 (8.2%), complex hyperplasia 2 (2.7%). (Table 3)

Forty-one patients (55.3%) had no flow, 24 (32%) had minimal flow, 4 (5.5%) had moderate flow and 4 (5.5%) had abundant flow on Doppler assessment of the endometrium. In this study, the color content of the endometrium (color score) were statistically significant among different pathologies (P value 0.1). (Table 4)

Table 5A shows the distribution of the results of 2D Ultrasound and Doppler (Table 5B) arrayed against the gold standard which is Histopathology. It can be seen that 2D ultrasound correctly diagnosed 75% of the truly malignant and 100% of the truly benign, while Power Doppler correctly diagnosed a higher percentage of those

Table 1. Profile of Subjects

	With Benign Findings N=65	With Malignant Findings N=8	P value
AGE, IN YRS			0.0002 (overall)
<40	20 (30.8%)	1 (12.5%)	0.425
40-49	37 (56.9%)	1 (12.5%)	0.024 OR= 0.108 (0.013-0.93)
50-59	7 (10.8%)	3 (37.5%)	0.073
60+	2 (1.5%)	3 (37.5%)	0.008 OR=18.9 (2.5-140.7)
Gravidity			0.930 (overall)
0	11 (16.9%)	1 (12.5%)	
1	10 (15.4%)	1 (12.5%)	
2-3	26 (40%)	4 (50%)	
4-5	13 (20%)	2 (25%)	
6+	4 (7.7%)	0	
Parity			0.661 (overall)
0	11 (16.9%)	1 (12.5%)	
1	16 (24.6%)	2 (25%)	
2-3	26 (40%)	5 (62.5%)	
4-5	11 (16.9%)	0	
6+	1 (1.6%)	0	

Table 2.

Endometrial Thickness	Mean / SD	Median
Endometrial Polyp	1.37± 0.71	1.35
Secretory Endometrium	0.93+49	1.15
Proliferative Endometrium	1.1+0.44	1.00
Malignancy	2.9 ±2.33	2.00
Simple Hyperplasia without atypia	1.7+0.51	1.65
Complex Hyperplasia	1.65+0.5	1.65

p value 0.040

Table 3.

Histopathologic Diagnosis	N=73	Percent
Endometrial Polyp	41	56.2
Secretory Endometrium	6	8.2
Proliferative Endometrium	9	12.3
Malignancy	7	9.6
Simple Hyperplasia without atypia	8	11.0
Complex Hyperplasia	2	2.7

Table 4.

		Endometrial Color Scores			
Histopathologic Diagnosis	**N**	**1**	**2**	**3**	**4**
Endometrial Polyp	41	16 (21%)	24 (32%)	1 (1.4%)	
Secretory Endometrium	6	6 (8.2%)			
Proliferative Endometrium	9	8 (11%)		1 (1.4%)	
Malignancy	7	1 (1.4%)		2 (2.7%)	4 (5.5%)
Simple Hyperplasia without atypia	8	8 (11%)			
Complex Hyperplasia	2	2 (2.7%)			

Table 5A. 2 x 2 Tables for 2D ULTRASOUND

	Malignant (Histopathology)	Benign (Histopathology)	Total
Malignant (2D ULTRASOUND)	6 (75%)	0	6
Benign (2D ULTRASOUND)	2	65 (100%)	67
Total	8	65	73

Table 5B. 2 x 2 Tables for Power Doppler

	Malignant (Histopathology)	Benign (Histopathology)	Total
Malignant (2D ULTRASOUND)	7 (87.5%)	0	7
Benign (2D ULTRASOUND)	1	65 (100%)	66
Total	8	65	73

who had truly malignant lesions - 87.5%, and also correctly diagnosing 100% of those who had truly benign lesions.

Table 6 compares the accuracy parameters of the 2 diagnostic methods. It can be seen that Doppler had a higher sensitivity in diagnosing malignancy, than ultrasound, while both had the same accuracy in predicting benign lesions. Diagnostic yield (PPV) is the same while Doppler showed a higher NPV. Total accuracy was higher for Doppler than ultrasound.

Table 6. Comparison of Accuracy Paremeters of 2D Ultrasound and Power Doppler

	Sensitivity	Specificity	PPV	NPV
2D ULTRASOUND	75 (35.5-95.5)	100 (93-100)	100 (51.7-100)	100 (51.7-100)
Power Doppler	87.5 (46.7-99.3)	100 (93.0-100)	100 (56.1-100)	100 (56.1-100)

Total accuracy 2D Ultrasound = 6+65/73 = 97.3
Total accuracy Power Doppler = 7+65/73 = 72/73 = 98.6

DISCUSSION

Abnormal uterine bleeding is a common symptom presented by patients with intrauterine conditions such as endometrial polyp, submucous myoma, endometritis, endometrial hyperplasia, or malignancy. In this study, subjects with abnormal uterine bleeding were mostly due to endometrial polyp which accounted for 56.2% of cases, followed by proliferative endometrium 12.3%, simple hyperplasia without atypia 11.0%.

Risk factors for uterine intracavitary pathology in general and endometrial cancer in particular include postmenopausal status, advanced age, and estrogen exposure e.g. due to anovulation, obesity, late menopause or unopposed estrogen use.[12-14] In this study, other than the menopausal status and age of patient, the knowledge of patient's history is of little value for predicting presence or absence of intracavitary pathology in women who presented with abnormal uterine bleeding. It was shown in this study that benign intracavitary lesions are present in more than half (56.9%) of premenopausal patients and a tenth (1.5-10.8%) in postmenopausal women with abnormal uterine bleeding. After menopause, endometrial cancer risk increased with advanced age,

which is concordant with previous reports.[15] As shown in this study, patients aged 60 years and above were seen to be 18.9 times more likely to have a malignant lesion.

Transvaginal sonography has been an important diagnostic tool in the evaluation of uterine cavity, since abnormal uterine structures can be seen directly. Also, assessment of endometrial thickness and morphology are good predictors of endometrial diseases. Though, endometrial thickness is a sensitive indicator, it is non specific, thus endometrial biopsy or dilatation and curettage as initial screening methods for diagnosis of endometrial diseases are used but these are blind techniques and inexact.[15] With the advancing high-resolution and technology of transvaginal ultrasound and Doppler, some clinicians consider it an alternative candidate to replace invasive methods.

In the study, it was seen that the use of 2D grey-scale ultrasound had a high percentage of detected benign lesion which was 100%, and correctly diagnosed a truly malignant case which was 75%. Intrauterine pathologies, such as endometrial polyps, fibroids or malignancy may manifest characteristic gray-scale ultrasound morphology but some studies found overlapping ultrasound morphology between benign and malignant endometrial lesions.[16-17] The accuracy of transvaginal ultrasound in detecting endometrial cancer is increased with assessment of endometrial morphology and endometrial border appearance combined with endometrial thickness measurements.[18-19] Uterine curettage or biopsy is still the preferred sampling procedure for diagnosis of endometrial pathology.[20]

With the clinical findings on examination, grey-scale ultrasound morphology of the endometrium, as well as he endomyometrial junction and the vascularization of the endometrium (as evaluated by Doppler ultrasound) are considered in assessing the endometrial thickness when estimating the risk of endometrial malignancy in women with postmenopausal bleeding and a thickened endometrium of 5 mm or more. The following characteristics: irregular echogenicity of the endometrium, irregularly branching vessels, densely packed vessels, or color splashes within the cavity, are found in the endometrium on power Doppler examination increase the risk of malignancy. Also a high color content in the endometrial scan at Doppler examination is a sign of neoplasia.[17,22-23] In line with the study, endometrial malignancy had abundant flow as reflected on endometrial color score. Transvaginal Doppler imaging assesses the vascularity of the endometrium and power Doppler is focused on the amplitude of the Doppler signal, and more sensitive to low-velocity blood flow. Power doppler reflects the number of red blood cells flowing in the vessel, less affected by noise and has better ability to demonstrate tortuous, irregular vessels.[11] With this, detection of blood flow and depiction of vascular architecture of the uterus and endometrium is clear and consistent.[24] The pattern of vascular distribution within a lesion as shown in Doppler ultrasound has been reported to be useful in the diagnosis of malignancy in endometrium, cervix and ovaries.[25]

Based on the results of this study, accuracy of histopathologic diagnosis for malignancy is higher if combined with power Doppler. As seen in this study, with power Doppler interrogation, there was increased accuracy in diagnosing a truly malignant lesion, which was 87.5 %. This showed that addition of power Doppler study to 2d greyscale ultrasound, improved the overall diagnostic performance.

Standardized terms, definitions and measurements was used to describe the ultrasound images of the endometrium and uterine cavity as suggested by the IETA (International Endometrial Tumor Analysis) group. Endometrial thickness was an important predictor of pathology and uniformity in reporting endometrial morphology was useful in the diagnosis of endometrial diseases.[10]

An efficient and non-invasive method that can be used for early detection of endometrial pathology in postmenopausal women is transvaginal ultrasound. Thickened endometrium in postmenopausal women was the most significant ultrasonographic criterion suggestive of its pathology. In the present study, increased endometrial thickness on grey-scale ultrasound is found to be statistically significant in patients with malignancy in line with the literature. Use of transvaginal ultrasound was a sensitive means of diagnosing the cause of postmenopausal bleeding which could aid in planning its appropriate management. Endometrial biopsy was still preferred as the diagnostic test.[26]

Transvaginal ultrasound can be safely used as an initial investigation in the management of abnormal uterine bleeding as it is a noninvasive procedure for detection of intracavitary pathology, as compared to invasive procedures, like dilatation and curettage and hysteroscopy which requires hospitalization and general anesthesia. Ultrasound has good accuracy and positive predictive value in diagnosing benign endometrial lesions, as seen in this study. Because better field of view, Transvaginal sonography can be considered as initial imaging modality in diagnosing submucosal pathologies like polyp over dilatation and curettage which is a blind procedure that can miss the lesions.[28]

CONCLUSION

There were higher odds for malignancy among

subjects 60 years and older. Most common benign histopathologic diagnosis was endometrial polyp. Malignant lesions were found in 9.6% of subjects diagnosed with abnormal uterine bleeding. Both grey-scale ultrasound and Doppler were found to have 100% accuracy in predicting benign lesions but Doppler had a higher accuracy in predicting malignant lesions (87.5%) than greyscale ultrasound (75%). Endometrial color score was found to have clinical value in distinguishing endometrial pathologies in the present study.

RECOMMENDATION

Power Doppler assessment of uterine cavity is completely subjective unless we use standardized terms and definitions to describe findings. With this study, terms to describe endometrial Doppler sonographic features previously reported by the IETA group is clinically valuable and reasonable. This could help in the uniformity of reporting the endometrium to aid clinicians with their diagnosis and management. It will be easier to compare results of different studies in the future on endometrial Doppler ultrasound using IETA. Future research with larger study population is needed to assess reproducibility and inter-intraobserver variability of this nomenclature.

LIMITATION OF THE STUDY

Estimates of accuracy parameters are more robust for benign lesions than malignant lesions because of the small number of cases with malignant lesions. A bigger sample size for malignant lesions should be used in future studies. However, a strength of this study is that all cases underwent histopathological diagnosis. ■

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