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Research Article

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Diagnostic Accuracy of International Endometrial Tumor Analysis Ultrasound Parameters to Differentiate Benign and Malignant Endometrial Pathologies

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ABSTRACT

Purpose: To evaluate the diagnostic accuracy of International Endometrial Tumour Analysis Ultrasound (IETA) parameters in differentiating benign and malignant endometrial pathologies.

Methods: The study comprised 53 women with abnormal uterine bleeding (AUB). IETA parameters were recorded, including endometrial thickness (ET), endometrial echogenicity, midline endometrium, endometrial-myometrial junction (EMJ), intracavitary fluid, Doppler score, and vascular pattern on TVS. The diagnosis was made using these, and a score was calculated with a simple scoring method, which was then correlated with HPE.

Results: The ET was greater in malignancy (22.3 ± 10.3 mm) as compared to 15.4 ± 5.6 mm in benign cases. Heterogeneous endometrial echogenicity and interrupted or not-defined EMJ had a significant correlation with malignancy, with 92.6 % sensitivity. High Doppler score and multifocal vascular patterns showed significant correlation with malignancy (70.4 % & 76.9 % sensitivity, 100 % & 73.1 % specificity, 73.6 % and 86.8 % diagnostic accuracy, respectively). Additionally, a cutoff score of >10 was optimal in predicting malignancy with a sensitivity and specificity of 82% and 92%, respectively.

Conclusion: The evaluation of endometrium using IETA parameters significantly enhances the diagnostic accuracy of endometrial pathologies, correctly stratifying them into benign and malignant; thus, leading to better clinical outcomes.

Keywords: Endometrium, Transvaginal Ultrasound, IETA Parameters, Grey Scale, Doppler, Scoring Method

Introduction

Abnormal uterine bleeding (AUB) is a diagnostic challenge to the radiologist. Many causes of AUB include benign conditions like endometrial polyps, endometrial hyperplasia (EH) and uterine fibroids. It is of importance to rule out endometrial malignancy to enable prompt management [1]. The epidemiological risk factors of endometrial malignancy include uncontrolled estrogen exposure, nulliparity, obesity, early menarche, and late menopause [2]. Endometrial carcinoma (EC) accounts for 20-30% of malignancies of the female genital tract [3]. Age, tumour size, tumour grade, stage, and histological type all affect the prognosis [4].

Histopathological examination (HPE), usually acquired from endometrial sampling and dilation & curettage, is the gold standard for characterising endometrial pathology, but these are invasive procedures, associated with potential morbidity [5,6].

Ultrasound (US) is a more convenient, cost-effective, and non-invasive modality; hence, it is used as the first diagnostic step to screen endometrial pathology and classify low or high risk of malignancy [7]. Transvaginal ultrasound (TVS), being more sensitive than Transabdominal ultrasound (TAS), provides better visualisation and resolution. Magnetic Resonance Imaging (MRI) can also be used to distinguish between benign and malignant endometrial lesions, assess the degree of invasion and stage malignancy. However, it is not the first line imaging

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modality because of being expensive, limited availability, and longer examination time [3].

The International Endometrial Tumor Analysis (IETA) group, which was formed in 2008, provided term, definitions, and standardized technique to describe and measure different US parameters including endometrial thickness (ET), echogenicity of the endometrium, appearance of midline endometrium, endometrial-myometrial junction (EMJ), intracavitary fluid, presence or absence of bright edge, Doppler score, and vascular pattern [7]. In this study, we aim to evaluate the diagnostic accuracy of International Endometrial Tumour Analysis Ultrasound parameters to differentiate benign and malignant endometrial pathologies.

Materials And Methods

This prospective observational cross-sectional study was carried out at the Department of Radiodiagnosis in collaboration with the Departments of Obstetrics & Gynaecology and Pathology for a duration of 18 months. The study protocol received approval from the institutional ethical committee (IEC/VMMC/SJH/Cert./02-2024/285). Written informed consent was obtained from all the patients.

Study Subjects

Adult women who met the inclusion criteria and were willing to participate were included. The inclusion criteria comprised women with AUB having abnormal endometrium on ultrasound, who underwent histopathological evaluation. Women with bleeding due to pregnancy, post-abortion or postpartum situation, evidence of acute PID were excluded from the study.

Data Acquisition

The patient's history, parity, and time since menopause were recorded, along with relevant clinical examination. TVS examination was performed on a Philips Affiniti 70 machine with a C9-4v vaginal probe. Complete sonographic evaluation on grey scale, colour Doppler was done using IETA parameters. The findings recorded included ET, echogenicity of the endometrium, appearance of midline endometrium, EMJ, intrauterine fluid, presence or absence of bright edge, Doppler score, and vascular pattern. The diagnosis was made based on these parameters, and a score was calculated using a simple scoring method based on IETA US parameters given by Lin et al [3]. The diagnosis was finally confirmed with HPE.

Statistical Analysis

Data was coded and recorded in an MS Excel spreadsheet and analysed using SPSS v21 (IBM Corp.). The subjects were segregated into benign and malignant based on HPE to analyse the significance of each IETA parameter. Group comparisons for continuous data were made using the Mann-Whitney U test. The chi-square test was used for categorical data comparisons. Sensitivity, specificity, PPV, NPV, and diagnostic accuracy were calculated. A p-value of <0.05 was considered statistically significant.

Results

A total of 53 women with AUB were included, comprising 26 benign and 27 malignant cases. The average ET was greater in malignant cases, measuring 22.3 ± 10.3 mm, while benign cases had a mean of 15.4 ± 5.6 mm. (Figure 1) This difference was significant (p-value 0.017), highlighting a moderate correlation between increased ET and malignancy. The association of ET was analysed separately in pre- and post-menopausal women. There was a significant difference in ET in post- menopausal women, measuring 24.5 ± 10.6 mm in the malignant group (p value 0.031). However, there was no significant difference among the pre-menopausal women; mean ET 14.93 ± 5.37 mm in benign and 15.74 ± 5.85 mm in malignant cases (p-value 0.755).

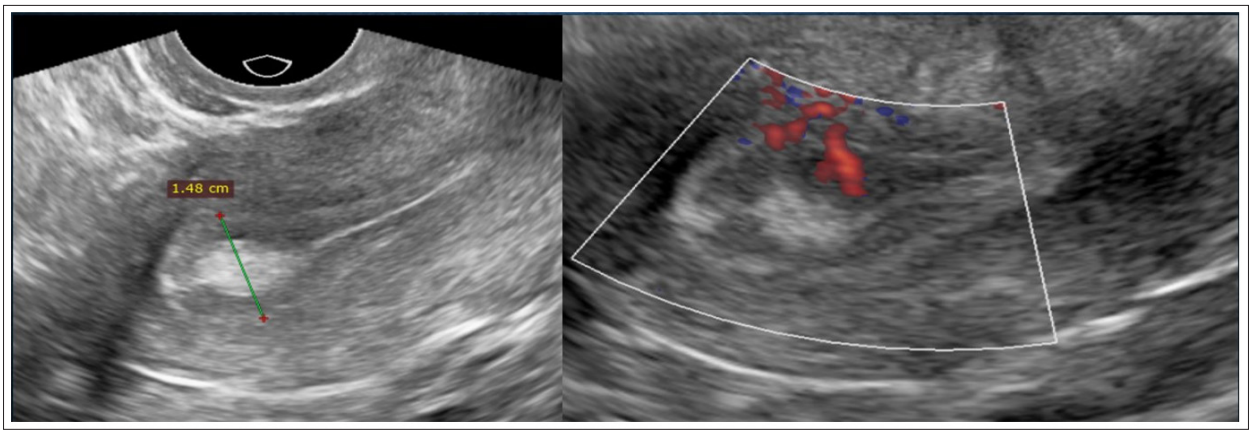

Figure 1: 38-year-old female, P0L0 with irregular bleeding. IETA Parameters on TVS: ET: 14.8 mm, Endometrial echogenicity: uniform, homogenously hyperechoic, Midline endometrium: Linear, Endometrial-myometrial junction: Regular, Intracavitary fluid: No, Bright edge: Yes, Colour score: Minimal, Vascular pattern: Single vessel, Score: 3. HPE: Endometrial Polyp

Heterogeneous endometrial echogenicity, with or without cystic changes, was most associated with EC, with a sensitivity of 92.6%. Only 2 out of 27 patients with EC exhibited homogeneous echogenicity. (Table 1) Irregular, interrupted or undefined EMJ had significant correlation with the malignant pathologies with a sensitivity of 92.6 %. A regular EMJ (90.9%) was predominantly seen in benign cases, while an undefined, interrupted, or irregular EMJ was more frequently observed in the malignant group, with a diagnostic accuracy of 84.9%. There was a significant correlation between interrupted EMJ and EC in the present study. 100 % of the cases with interrupted EMJ were found to have malignancy on HPE. Similarly, higher Doppler score (3 or 4) and complex or

multifocal vascular patterns showed significant correlation with the malignant lesions, with sensitivity and specificity of 70.4 % & 76.9 % and 100 % & 73.1 %, respectively. (Table 2) Additionally, a cutoff score of >10 was optimal in predicting malignancy with sensitivity and specificity of 82% and 92%, respectively.

Table 1: Description of IETA US Parameters for Predicting Malignant vs Benign Endometrial Pathologies

Variable	Category(s) Suggesting Outcome Present	Category(s) Suggesting Outcome Absent	Total Positives	True Positives	True Negatives	False Positives	False Negatives
HPE	Malignant	Benign	27 (50.9%)	-	-	-	-
Endometrium-Myometrium Junction	Irregular, Interrupted, Not Defined	Regular	31 (58.5%)	25 (47.2%)	20 (37.7%)	6 (11.3%)	2 (3.8%)
Endometrial Echogenicity	Heterogeneous without Cysts/ with Regular Cysts, Heterogeneous with Irregular Cysts	Homogeneous	40 (75.5%)	25 (47.2%)	11 (20.8%)	15 (28.3%)	2 (3.8%)
Midline Endometrium	Irregular, Not Defined	Linear	45 (84.9%)	27 (50.9%)	8 (15.1%)	18 (34.0%)	0 (0.0%)
Intra-Uterine Fluid	Ground Glass, Mixed Echogenicity	No Fluid, Anechoic	4 (7.5%)	4 (7.5%)	26 (49.1%)	0 (0.0%)	23 (43.4%)
Bright Edge	Absent	Present	37 (69.8%)	27 (50.9%)	16 (30.2%)	10 (18.9%)	0 (0.0%)
Vascularity	Moderate, Abundant	No Colour, Minimal	25 (47.2%)	19 (35.8%)	20 (37.7%)	6 (11.3%)	8 (15.1%)
Pattern	Multiple Vessels (Focal), Multiple Vessels (Multifocal)	No Flow, Single Vessel	34 (64.2%)	27 (50.9%)	19 (35.8%)	7 (13.2%)	0 (0.0%)
Score (Cutoff: 10 by ROC)	>=10	<10	24 (45.3%)	22 (41.5%)	24 (45.3%)	2 (3.8%)	5 (9.4%)

Table 2: Performance of IETA US Diagnostic Parameters

Variable	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
Endometrium-Myometrium Junction	92.6% (76-99)	76.9% (56-91)	80.6% (63-93)	90.9% (71-99)	84.9% (72-93)
Endometrial Echogenicity	92.6% (76-99)	42.3% (23-63)	62.5% (46-77)	84.6% (55-98)	67.9% (54-80)
Midline Endometrium	100.0% (87-100)	30.8% (14-52)	60.0% (44-74)	100.0% (63-100)	66.0% (52-78)
Intra-Uterine Fluid	14.8% (4-34)	100.0% (87-100)	100.0% (40-100)	53.1% (38-67)	56.6% (42-70)
Bright Edge	100.0% (87-100)	61.5% (41-80)	73.0% (56-86)	100.0% (79-100)	81.1% (68-91)
Vascularity	70.4% (50-86)	76.9% (56-91)	76.0% (55-91)	71.4% (51-87)	73.6% (60-85)
Pattern	100.0% (87-100)	73.1% (52-88)	79.4% (62-91)	100.0% (82-100)	86.8% (75-95)
Score (Cutoff: 10 by ROC)	81.5% (62-94)	92.3% (75-99)	91.7% (73-99)	82.8% (64-94)	86.8% (75-95)

Discussion

Abnormal uterine bleeding (AUB) is a frequent and distressing gynaecological complaint, arising from a spectrum of causes that range from benign structural lesions to endometrial malignancy [8]. In recent years, advancements in TVS have significantly enhanced our ability to accurately identify and manage intrauterine abnormalities. The IETA group, formed in 2008, further contributed by establishing standardised definitions for US findings, thereby improving the diagnosis of endometrial pathologies [7].

The present study was undertaken to evaluate the diagnostic accuracy of IETA US parameters in the assessment of AUB to differentiate benign from malignant endometrial pathologies on grey scale TVS and Doppler imaging, and to correlate with HPE. AH is a recognized precursor to most type 1 EC, sharing clinical, ultrasound, and molecular features that underscore their pathogenic relationship [2]. Hence, AH was included in the malignant group.

In the present study, the malignant group exhibited a higher mean age (57.1 years) as compared to the benign (44.3 years). Also, there was a significant difference in the HPE findings between the pre- and post-menopausal groups. Malignant lesions were far more prevalent in the post-menopausal (74.1%) as compared to only 26.9% of cases in the pre-menopausal group, which had predominantly benign pathologies like polyps and endometrial hyperplasia without atypia. (Figure 2) This is in line with the observation made by Farau et al and Lin et al, who reported EC prevalence in post-menopausal women [2,3]. These age-stratified histopathological distributions emphasise the role of hormonal and menopausal factors in endometrial pathology.

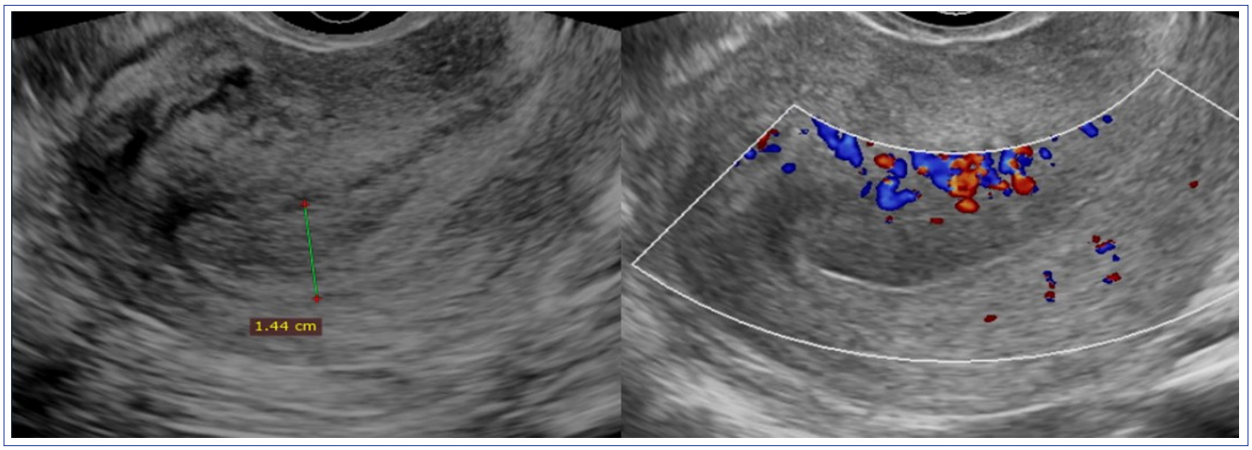

Figure 2: 37-year-old female, P2L2 with heavy menstrual bleeding. IETA Parameters: ET: 14.4 mm, Endometrial echogenicity: Heterogenous, Midline endometrium: Linear, Endometrial-myometrial junction: Regular, Intracavitary fluid: No, Bright edge: No, Colour score: No colour, Vascular pattern: No Flow, Score: 4. HPE: Endometrial Hyperplasia without Atypia

Histopathologically, endometrioid adenocarcinoma accounted for 91.3% of malignant cases in the current study, mirroring Lin et al and Epstein et al, who identified endometrioid as the dominant subtype (81.5% and 86.5%, respectively) [3,4]. Further, the non-endometrioid subtypes (e.g., carcinosarcoma, mixed Müllerian carcinoma) were rare (8.7%), consistent with the predominance of type 1 EC observed in other studies [4].

In the current prospective study, the application of the IETA consensus provided valuable insights into the morphological and vascular characteristics of the endometrial pathologies. Notably, US features such as increased ET, heterogeneous echotexture, interrupted and not-defined EMJ, higher colour score and abnormal complex vascular patterns were more frequently observed in malignant lesions. These findings are consistent with previous literature, which has established the utility of IETA US parameters in improving the detection of endometrial malignancies [2,3,6-9].

The present study demonstrated that the appearance of the EMJ is a significant factor in distinguishing benign and malignant endometrial pathologies. A regular EMJ (90.9%) was predominantly seen in benign cases, while an undefined, interrupted, or irregular EMJ was more frequently observed in the malignant group. These results are consistent with the findings of Farau et al, who reported that 99.3% of EC cases exhibited an irregular or undefined EMJ [2]. Similarly, Madkour et al. found that 80% of malignant cases displayed an ill-defined EMJ [6].

There was a statistically significant correlation between interrupted EMJ and EC in the present study, as all the cases with interrupted EMJ were malignant. Also, there was a significant correlation between multiple complex vascular patterns and EC, with a diagnostic accuracy of 86.8%. These findings are consistent with Dueholm et al. and Stachowicz et al., who developed the REC scoring system incorporating clinical and US features such as an interrupted EMJ, the presence of multiple vessel patterns, and ET > 12 mm to effectively predict the malignancy [1-10]. In concordance, none of the patients in the postmenopausal group with ET < 12 mm had EC or AH, in the present study, further supporting the value of these parameters in identifying high-risk cases.

Endometrial echogenicity was another important parameter assessed in the present study. It was observed that a heterogeneous endometrium, with or without cystic changes, was most associated with EC, demonstrating a sensitivity of 92.6%. (Figure 3) These results were consistent with the findings of Farau et al, who confirmed that an inhomogeneous appearance of the endometrium is frequently present in EC and AH.2 Lin et al, who reported that all cases of EC in their study displayed non-uniform endometrial echogenicity, further support endometrial echogenicity as a reliable ultrasound marker [3].

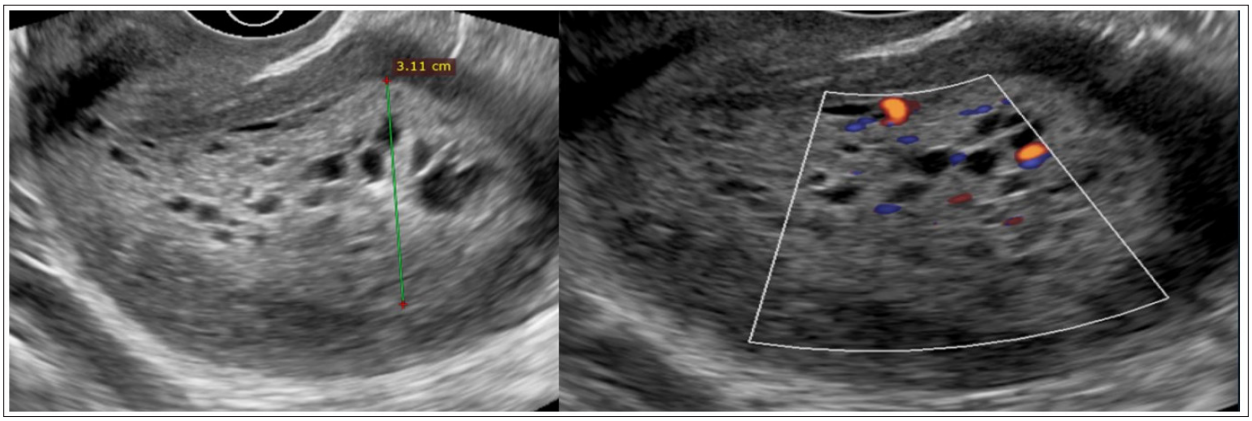

Figure 3: 55 years old postmenopausal female, P4L4 with discharge & spotting PV. IETA Parameters: ET: 31.1 mm, Endometrial echogenicity: heterogeneous with irregular cystic areas, Midline endometrium: Not defined, Endometrial-myometrial junction: Irregular, Intracavitary fluid: No, Bright edge: No, Colour score: Minimal, Vascular pattern: multifocal, Score: 11. HPE: Cystic Endometrial Hyperplasia

The current study demonstrated that higher Doppler scores (3 or 4) were strongly associated with malignant endometrial lesions, achieving a sensitivity of 70.4% and specificity of 76.9%. (Figure 4) This is in line with the findings of Farau et al, who reported that color scores of 3 and 4 were linked to EC, with a relative risk of 2.9 [2]. Similarly, Patil et al found that elevated color scores were significantly associated with malignancy, and Madkour et al, identified a Doppler score greater than 2 as a powerful predictor of EC, with 8 out of 10 malignant cases in their study exhibiting scores above this threshold [6-9].

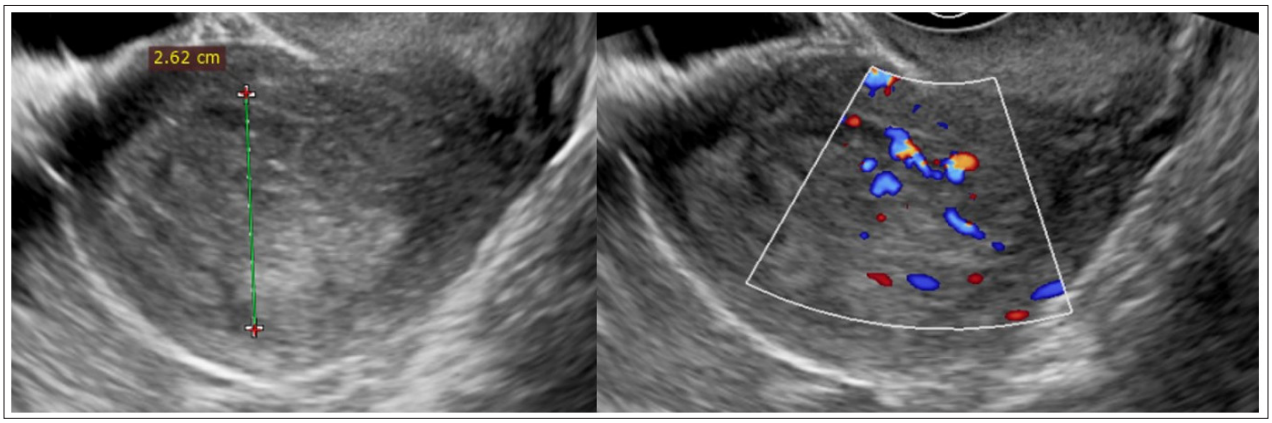

Figure 4: 36-year-old female, P0A1. F/u/c of Mucinous Cystadenocarcinoma with HMB and abdominal pain. IETA Parameters: ET: 26.2 mm. Endometrial echogenicity: Heterogeneous, Midline endometrium: Not defined, Endometrial-myometrial junction: Irregular, Intracavitary fluid: No fluid, Bright edge: No, Colour score: Abundant, Vascular pattern: multifocal, Score: 12. HPE: Atypical Endometrial Hyperplasia

Another parameter which was assessed and revealed a significant association with malignancy was the multiple vessel pattern, particularly with multifocal origin. (Figure 5) Among these, 88.9% were confirmed as malignant, and the overall diagnostic accuracy was 86.8%. These findings align with Lin et al, who reported that 94.4% of EC cases exhibited a dominant multiple vessel pattern on colour Doppler US [3]. Similarly, Kucur et al. demonstrated that multifocal vascular patterns had a sensitivity of 81.25% and specificity of 89.23% for identifying malignancy [11]. Batra et al. also emphasised the strong correlation between multiple irregulars branching vascular patterns and EC [12].

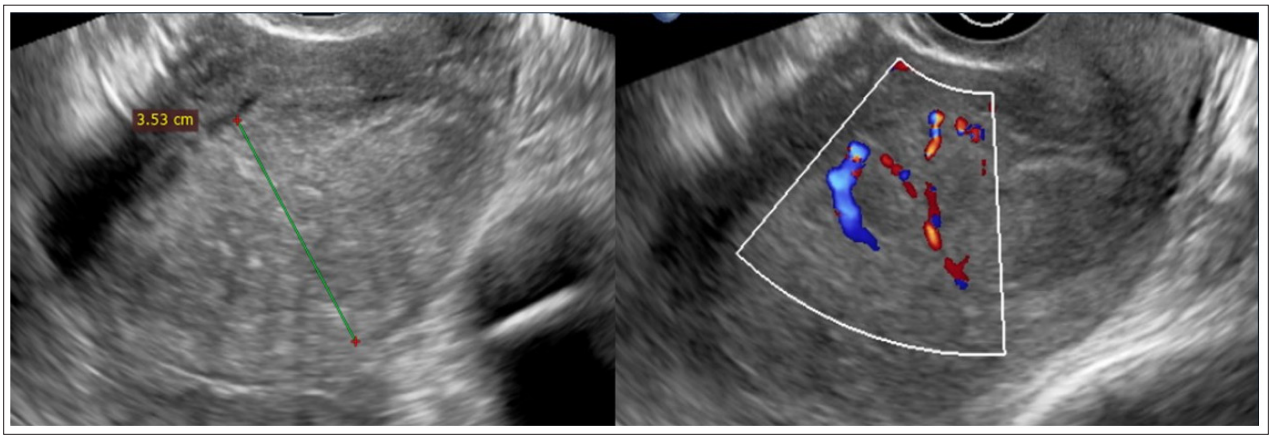

Figure 5: 55-year-old female, P4L4 with postmenopausal bleeding (PMB). IETA Parameters: ET: 35.3 mm, Endometrial echogenicity: heterogeneous, Midline endometrium: Not defined, Endometrial-myometrial junction: Not defined, Intracavitary fluid: Anechoic, Bright edge: No, Colour score: Moderate, Vascular pattern: Multiple vessels multifocal, Score: 14. HPE: Endometroid Cancer FIGO II

Further, to reinforce the fact, Alcazar et al. found that the IETA colour scoring system for assessing endometrial vascularisation with 3D US volume is highly reproducible, regardless of the examiner's level of experience [13]. These results, together with the current data, emphasise the diagnostic value of Doppler assessment within the IETA framework.

In the present study, the average ET was greater in malignant cases, measuring 22.3 ± 10.3 mm, while benign cases had a mean thickness of 15.4 ± 5.6 mm (p-value 0.017), highlighting a moderate correlation between increased ET and malignancy. These findings are consistent with the previous studies done by Kocur et al and Batra et al in which mean ET in the malignant group was 21.10 ± 14.78 and 18.9 ± 8.74, respectively.11, 12 The higher mean ET in the current study might be related to the fact that in a tertiary care centre patients present with advanced stages, which led to thicker mean ET of the study group.

Some easy-to-assess US features were provided by Van Den Bosch et al, i.e. ET <3mm, three-layer pattern, linear mid-line, and single vessel without branching, which makes the possibility of endometrial cancer less likely [14]. The current observations also

found that a single vessel pattern was exclusively associated with benign lesions, particularly endometrial polyps, with 14 out of 15 cases with this vascular pattern being diagnosed as polyps. Additionally, it was observed that the presence of a linear midline endometrium had a sensitivity of 100% for ruling out malignancy, which is consistent with the findings of Van den Bosch et al [14]. The single vessel pattern was also observed by Kocur et al, as a characteristic feature of endometrial polyps with a high specificity of 98.28 %, further supporting the present study results [11].

While there was a statistically significant difference in endometrial midline appearance between benign and malignant lesions, it is noteworthy that an irregular or undefined midline was also present in most benign cases (69.2%) in the present study. Lin et al. demonstrated that 67% of benign endometrial cases exhibited a nonlinear or undefined midline endometrial appearance, while Van den Bosch et al. reported similar findings, with 64% of endometrial polyps and 73% of hyperplasia without atypia showing an undefined midline [3-14]. This overlap poses considerable challenges in reliably distinguishing between benign and malignant lesions based solely on midline appearance. However, notably, this study revealed that a linear midline endometrial appearance had a 100% NPV for excluding EC, underscoring its utility as a reliable marker to rule out malignancy.

The bright edge sign was strongly associated with benign pathologies, as 61% of benign cases exhibited this feature, and all cases showing a bright edge sign were confirmed to be polyps. These findings are consistent with those of Lin et al, who reported that 97.9% of cases displaying the bright edge sign were benign [3]. Similar to the midline endometrial appearance, the presence of a bright edge in the present study also demonstrated a high NPV of 100% for ruling out malignancy. On the contrary, in Van den Bosch et al's study, only 48 % of polyps showed the bright edge sign [14].

According to Farau et al and Patil et al, the presence and characteristics of intrauterine fluid were significant indicators of increased risk for endometrial cancer [2-9]. However, in the current study, we did not observe any significant difference in terms of the presence of intrauterine fluid. This may be explained by the fact that, as a tertiary care centre, our institution tends to receive cases at more advanced stages. In these cases, the endometrial mass is almost completely obliterating the endometrial cavity; consequently, the presence of intrauterine fluid is less common. Thus, the results suggest that endometrial fluid is rarely a sign of malignancy.

Further, we also attempted to calculate a score using IETA US parameters based on a simple scoring method given by Lin et al, who transformed the standardised IETA US parameters into a simple scoring system [3]. For ET, the scoring was stratified by menopausal status: in pre-menopausal women, categories were ≤ 12 mm, 12.1–15 mm, 15.1–20 mm, and > 20.1 mm, while in post-menopausal women, ≤ 5 mm, 5.1–10 mm, 10.1–15 mm, and >15.1 mm. Each category was assigned a score from 0 to 3, reflecting increasing risk. Features typically associated with benign pathology, such as homogeneous endometrial echogenicity, regular EMJ, presence of bright edge, absence of intrauterine fluid, and either no vascular flow or a single-vessel, scattered, or circular vascular pattern, all given 0 points. Conversely, characteristics linked to malignancy, like heterogeneous endometrial echogenicity, an interrupted EMJ, intrauterine fluid, and higher Doppler scores, were assigned higher scores, with the highest score of 4 for vascularity. The appearance of midline endometrium was not assigned any point, as irregular or interrupted midline endometria can be seen in most of the benign cases. The total IETA score was calculated by summing the points assigned to each parameter, providing a method to stratify malignancy risk based on US findings. A cutoff score of 6.5 was provided for predicting malignancy, with a sensitivity of 76.5% and specificity of 96% [3]. In contrast, the current analysis found that a cutoff score greater than 10 was optimal for predicting malignancy, achieving a sensitivity of 82% and a specificity of 92%.

This difference can be attributed to variations in sample size and the distribution of benign and malignant cases between the two studies. Lin et al. included 594 participants, with 475 benign and 119 malignant cases, whereas the present study had a nearly equal number of benign (26) and malignant (27) cases. This more balanced representation of benign and malignant cases has likely contributed to the higher cutoff value in this study.

One of the key strengths of this study is the use of standardised US criteria, as recommended by the IETA group. This approach is fast and effective for diagnosing and classifying benign and malignant pathologies. It minimises inter-observer variability and enhances reproducibility, making the findings more generalizable. Furthermore, the results of the present study suggest that the presence of certain US parameters like ET < 10mm, homogenous echogenicity of endometrium, regular EMJ, linear midline endometrium, presence of bright edge sign, no colour or single vessel pattern on Doppler images can surely suggest the possibility of benign pathology and safely reduce the need for invasive procedures such as D&C in a significant proportion of cases, thereby improving patient comfort and optimizing resource utilization, especially in settings where access to advanced imaging or operative procedures may be limited.

A few limitations of the present study are a relatively small sample size and the fact that all the data were obtained from a single centre, which may limit the ability to generalise and standardise the results. Additionally, most malignant cases in this study were endometrioid EC, with only two cases classified as non-endometrioid EC. Moreover, there was only one patient on hormone replacement therapy (HRT), making it not feasible to assess any association between HRT and endometrial pathologies in this study.

Conclusion

IETA US parameters provide a reliable, non-invasive, standardised approach for distinguishing between benign and malignant endometrial lesions in women presenting with AUB. The US parameters-such as increased ET, heterogeneous endometrial echogenicity, irregular, interrupted or not defined EMJ, higher Doppler score and complex vascularity- are

strongly associated with malignancy. The IETA scoring system enhances diagnostic accuracy and can serve as an effective tool for risk stratification, potentially reducing unnecessary invasive procedures. Incorporating IETA-based US evaluation into routine clinical practice can facilitate early detection and appropriate management of endometrial diseases.

Conflict of Interest
The authors declare that they have no conflict of interest.

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Availability of data and materials
The data supporting this study are available from the corresponding author on request.

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Consent for publication: The authors consented to the submission of the manuscript and publication. They disclosed no competing interests or relevant relationships.

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