

The Merits of Three-Dimensional Transvaginal Ultrasound in the Evaluation of Premenopausal Women with Abnormal Uterine Bleeding

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Abstract

Background/Aims: Endometrial thickening is a nonspecific finding in women with premenopausal bleeding. Though it is expected in the luteal phase of ovulatory cycle or with anovulatory bleeding, it can be due to hyperplasia, polyps, leiomyomas, or endometrial carcinoma. Three-dimensional ultrasonography is an imaging technique that allows unique ways of assessing uterine and adnexal pathology. The objective of this study was to evaluate the effectiveness of three-dimensional transvaginal ultrasound in uterine cavity assessment in premenopausal women with abnormal uterine bleeding.

Methods: This was a prospective single-blinded cohort study of ninety premenopausal women with abnormal uterine bleeding, referred over three years period to one-stop hysteroscopy clinic at Ain Shams University Hospitals in Cairo, Egypt. All women had three-dimensional transvaginal ultrasound, in their first half of their menstrual cycles, followed by outpatient hysteroscopy, performed by a different operator who was blinded to the sonographic findings. Analysis of data was performed using statistical terms sensitivity, specificity, positive predictive value, and negative predictive value.

Results: In comparison to outpatient hysteroscopy in premenopausal women with abnormal uterine bleeding, the sensitivity of three-dimensional ultrasonography to detect intrauterine pathology was 100%, specificity 91.7%, with positive predictive value of 97%, and negative predictive value of 100%.

Conclusions: Three-dimensional transvaginal ultrasound can predict intra-uterine lesions as accurate as outpatient hysteroscopy in premenopausal women with abnormal uterine bleeding.

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Introduction

Abnormal vaginal bleeding is a common presenting complaint in both pre- and postmenopausal women, and its management differs according to the presence or absence of identifiable uterine abnormalities^[1].

Premalignant and malignant lesions of the endometrium accounts for 19% of the causes of bleeding in premenopausal women^[2]. Endometrial thickening is a non-specific finding that might indicate the presence of pathologic endometrial lesions. This can be either due to hyperplasia, polyps, leiomyomas

(intramural or sub mucous), or endometrial carcinoma^[3]. Diagnostic hysteroscopy, combined with histological examination of an endometrial aspiration or biopsy, is considered the 'gold standard' in the diagnosis of intrauterine abnormalities^[4] and is recommended in women with abnormal uterine bleeding^[5].

However, compared with ultrasound-based diagnostic tools, it is an invasive and costly procedure. It is also associated with risks of uterine perforation and ascending genitor-urinary infection, and for the 50% of women who actually have a normal



uterine cavity, diagnostic hysteroscopy is, retrospectively, unnecessary. In addition, the recorded data cannot be modified, the final diagnosis is determined by the initial findings at the operation, and it is sometimes difficult to perform outpatient hysteroscopy particularly in postmenopausal women with a narrowing of the cervix^[6,7].

Easy and minimally invasive ultrasonography, that can be performed on an outpatient basis, may resolve the above problems. Though two-dimensional transvaginal sonography (2DUS) has been studied as an alternative to hysteroscopy in investigation of abnormal uterine bleeding, it was found to have a significantly lower sensitivity (54%) compared to hysteroscopy (79%) but a comparable specificity in premenopausal patients^[8].

On the other hand, the three-dimensional transvaginal ultrasound (3DUS) has proved to be an imaging technique that allows unique ways for assessing uterine and adnexal pathology^[9]. It allows detailed evaluation of pelvic organs from different angles and in any arbitrary plane, and its information can be digitally stored as a dataset, which may then be analyzed on line^[10]. The three dimensional rendering mode of the uterine cavity also allows distinguishing with much more clarity between atrophic endometrium, polyps, focal hyperplasia, generalized hyperplasia and endometrial carcinomas^[11-13]. In this study we are evaluating the effectiveness of three-dimensional transvaginal ultrasound in the assessment of the uterine cavity, in comparison to outpatient hysteroscopy, in the management of premenopausal women with abnormal uterine bleeding.

Materials and methods

This is a prospective single-blinded cohort study of premenopausal women who were referred to the one-stop hysteroscopy clinic at Ain Shams University Hospitals, a tertiary referral centre in Cairo, Egypt. All women referred had chronic abnormal uterine bleeding. The bleeding was either abnormal in volume, regularity and/or timing, inter menstrual, or postcoital bleeding. There was no evidence of sexually transmitted or pelvic inflammatory diseases, in addition to the absence of local causes of vaginal bleeding (vulval, vaginal and/or cervical). An initial assessment of the women uterine cavity was done using three-dimensional transvaginal ultrasound (3DUS), in the first half of their cycles, followed by outpatient hysteroscopy, by a different operator, who was blinded to the sonographic findings.

Over three years period, ninety premenopausal women with abnormal uterine bleeding were recruited to the study from the one-stop hysteroscopy clinic. All of them gave their informed consent prior to their inclusion in the study. The study was approved by the local ethical committee of Ain Shams University Hospitals.

A detailed 3D US examination of the uterus was carried out for women in the lithotomy position with empty bladder, to detect any endometrial pathology such as uterine polyps, leiomyomas (fibroids) and their relation to the endometrium (Leiomyomas were detected as hypo echoic areas in the myometrium while polyps as echogenic thickening of the endometrium), together with aberrant uterine anatomy as septate or bicornuate uterus. The 3D US (ACCUVIX-XQ MEDISON, Korea) was performed using a S-VDW 5 - 8 B probe which is an electronic sector transducer with frequency range of 5 - 8 MHZ. The scan angle is switchable up to 149 degrees and maximum image

depth of 12 cm.

Outpatient hysteroscopy was performed in all women with a rigid 30° hysteroscope and a 3.5 mm diameter diagnostic sheath. (Storz Endoscopy, Germany). Pipelle endometrial sampling and histopathology examination was done for suspicious uterine cavity and endometrial lesions. Patients were classified according to the recent FIGO classification of abnormal uterine bleeding^[14].

Data was statistically represented in terms of range, mean, median, Standard Deviation (SD) and percentages. Comparison was done using student test comparing parametric data. Accuracy was represented using the terms of sensitivity, specificity, Positive Predictive Value(PPV), Negative Predictive Value(NPV) and overall accuracy. All statistical calculations were done using computer programs Microsoft excel version 7 (Microsoft Corporation, NY, USA) and SPSS (statistical package for the social science) statistical programs (SPSS Inc., Chicago, IL USA).

Results

The age of women recruited to the study ranged from 41 - 55 years old, with mean age of 49.5 ± 4.1 years; the mean age of women with endometrial polyps was 48.5 ± 2.8 years, women with leiomyomas was 51 ± 3.1 years, women with endometrial hyperplasia was 48 ± 2.2 years and women with endometrial carcinoma was 44.6 ± 3.5 years. The parity of the studied group ranged from 1 - 7 with a median of 3. The main presenting symptom was in the form of chronic abnormal uterine bleeding that was present for the majority of the previous six months. The bleeding was either abnormal in volume(30%), regularity and/or timing (46.7%), inter menstrual (16.7%), or postcoital bleeding (6.7%).

Descriptive data of the endometrium recorded by 3D US showed that out of the ninety cases included in the study, 6 cases (6.7%) had normal ultrasound findings, 84 women (93.3%) showed abnormalities (figures 1 & 2); in the form of thickened endometrium (36.7%), thickened endometrium with focal lesions (10%), and focal endometrial lesions as polyps (20%) and fibroids (26.7%; 16 intramural and 8 sub mucous fibroids)-Table (1).

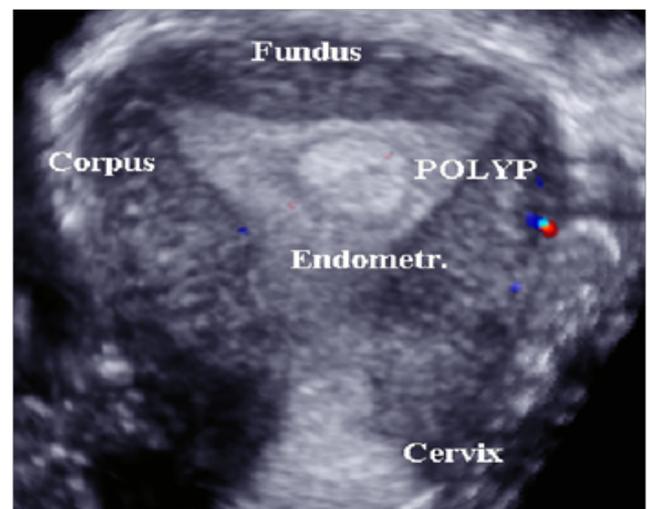


Figure 1: Three- dimensional ultrasound showing endometrial polyp.

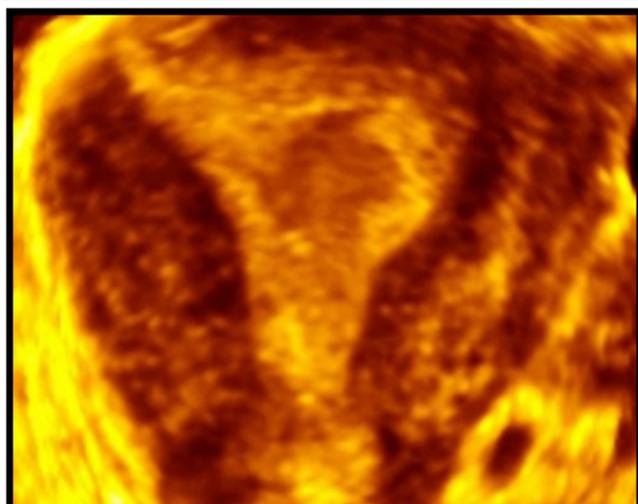


Figure 2: Three- dimensional ultrasound showing endometrial cancer.

Table 1: Summary of 3D-US findings.

	<i>Frequency</i>	<i>Percentage %</i>
Thickened endometrium	33	36.7
Polyps	18	20
Leiomyomas	24	26.7
Thickened endometrium + Focal lesions	9	10
Normal	6	6.7
Total	90	100

Outpatient hysteroscopy was successful in 90 cases with no operative complications recorded in any of them. Only 7 cases needed to be rebooked for diagnostic hysteroscopy under general anaesthesia due to the patient discomfort and significant pains. As the hysteroscopic assessment of the uterine cavity was done in a different day of the cycle, these patients were excluded from the study. Outpatient hysteroscopy and histopathology examination of pipelle endometrial sampling detected 42 (46.7%) women with malignant and premalignant conditions; 33 women (36.7%) with endometrial hyperplasia; 20 with atypical hyperplasia and 13 with simple hyperplasia and nine women (10%) were found to have endometrial carcinoma in the current study. In addition, 18 women (20%) were diagnosed with endometrial polyps, 6 women (6.7%) with leiomyomas, and 24 (26.7%) with proliferative or secretory endometrium (dysfunctional uterine bleeding).-Table (2).

Table 2: Summary of Diagnostic hysteroscopy and histopathology examination.

	<i>Frequency</i>	<i>Percentage %</i>
Malignancy and Premalignant Conditions (AUB-M)	42	46.7
Polyps (AUB-P)	18	20
Leiomyomas (AUB-L)	6	6.7
Normal (AUB-E)	24	26.7
Total	90	100

Using 3D US in this study, the mean endometrial thickness for endometrial carcinoma was 15.3 ± 2.6 mm, for endometrial hyperplasia was 12.66 ± 3.2 mm, and for physiological

endometrial changes (proliferative or secretory) was 8.5 mm. On the other hand, the mean endometrial volume for endometrial carcinoma was 76.6 ± 9.8 ml. Three-dimensional ultrasound (3DUS), when compared to outpatient hysteroscopy and histopathology examination, showed sensitivity of 100%, specificity of 91.7%, PPV 97%, and NPV 100%.

Discussion

This study showed overall agreement between three-dimensional transvaginal ultrasound and outpatient hysteroscopy in the diagnosis and management of premenopausal women with abnormal uterine bleeding. The single-blinded design of the study, where the hysteroscopist was blinded to the sonographic findings, eliminated any source of bias. Also the use of rigid hysteroscopy in the current study make our results more valid. Though the use of flexible hysteroscopy would have helped to visualize deformation of the uterine cavity and curvature of the uterine cervix more easily than a rigid scope, it was reported to have a lower sensitivity of 74% for the diagnosis of endometrial polyps and fibroids when compared with rigid hysteroscopy^[15,16].

We also relied more on the assessment of endometrial and myometrial consistency, and the abnormalities of endometrial morphology rather than the measurements of the endometrial thickness for the assessment of endometrial polyps and fibroids. Ultrasound detection of such uterine lesions in premenopausal women using measurements of endometrial thickness is not very reliable. This is because the normal range of endometrial thickness overlaps with that seen in premenopausal women with endometrial polyps and fibroids^[17]. This may explain why 18 women (20%) in the current study, who had thickened endometrium on 3D-US, were subsequently found to have normal uterine cavity and endometrium (proliferative or secretory) on diagnostic hysteroscopy and endometrial histopathological examination.

Although it is sometimes difficult to provide exact definitions of the outcome variables when performing an agreement study, for the purpose of the current study, we defined the presence of focal lesions of the endometrium as any protrusion or irregularity in the surface of the endometrium. Though we acknowledge that pathological examination is necessary, and invasion of the uterine cavity is ultimately unavoidable if malignant lesion is suspected, we believe that relying on 3D US would help us in choosing the patients where operative hysteroscopy is required, and avoiding the exposure of patients with dysfunctional uterine bleeding and absent endometrial pathology to the risks associated with hysteroscopic procedures.

Our results are in agreement with Kupesic *et al.*^[18], who reported 3D US sensitivity of 100%, specificity of 99%, PPV of 99% and NPV of 100%, in diagnosing endometrial polyps and sub mucous leiomyomas when compared to hysteroscopy with biopsy. However, in their study, only those women with a suspected polyps on 3D US subsequently underwent hysteroscopy and therefore did not include those women with endometrial polyps who had negative 3D US result. This was not the case in the current study because all our women did have the outpatient hysteroscopy by an operator who was blinded to the findings of 3D US.

In 1999, La Torre *et al.*^[19] compared 3DUS to hysteroscopy in diagnosing endometrial focal lesions especially polyps

in 23 patients. They diagnosed 18 endometrial polyps with 3D US with sensitivity of 100%, specificity of 71%, PPV of 89%, NPV of 100%. In the current study, we diagnosed 18 endometrial polyps in 90 patients, with a specificity of 100%. This may be attributed to the higher resolution of the new generation of 3DUS we used in our study compared to what used in La Torre study more than 15 years ago.

The size of endometrial polyps detected by 3DUS ranged from 4 mm to 2 cm in its greatest diameter. These masses were shorter in the other two dimensions and may therefore would be unrecognized on conventional transvaginal ultrasonography due to compression of the mass and resultant flattening, with conformation to the shape of the endometrial cavity. The question has been raised about the clinical significance of these small lesions. However, we believe that any endometrial lesion is of clinically significance if present in women who were experiencing abnormal vaginal bleeding, despite the small size of the mass. Because of the parameters for normal endometrial thickness in the premenopausal women are greater than in the postmenopausal women, masses may be more difficult to define, and more lesions may be missed in the premenopausal women than in the postmenopausal ones. Indeed, it has been shown that intracavitary abnormalities are prevalent in a substantial percentage of peri- and post-menopausal women and not revealed by the conventional transvaginal sonogram^[20,21]. Although several studies has reported the usefulness of two dimensional saline sono-hysterography in visualizing lesions of the uterine cavity, the length of the procedure, the risk of pelvic infection, and the multi planar display provided by the three dimensional ultrasound makes the 3D US the investigation of choice.

The overlap between the endometrial volume in benign and malignant lesions is markedly less than that seen with endometrial thickness. However, it is difficult to determine a cut-off value for normal endometrial thickness and volume in premenopausal women. Obviously, the lower the cut-off value, the higher the sensitivity for detection of uterine abnormalities as endometrial hyperplasia and carcinoma, but that will be at the cost of lower specificity. There was some degree of overlap in this study between women with benign and malignant lesions as regards endometrial thickness. In the current study, 9 premenopausal women (10%) were diagnosed with endometrial cancer. Their mean endometrial thickness was 15.3 ± 2.6 mm and volume 76.6 ± 9.8 ml. In 2006, Andreotti *et al.*,^[22] suggested a cut-off value of 14 mm for exclusion of endometrial carcinoma in premenopausal women. Furthermore, they found that increasing endometrial volume is correlated with myometrial invasion and high tumour grade in patients with endometrial carcinoma; this could not be confirmed in our study since only 9 women were diagnosed with endometrial carcinoma.

The results of our study showed that the three-dimensional transvaginal ultrasound can potentially be a suitable alternative to the use of diagnostic hysteroscopy in women with premenopausal uterine bleeding in the near future. As the 3D US is a non-invasive, less expensive, and is better tolerated by most patients, it could be the investigation of choice in the management of such women. However, the choice of diagnostic method should be based on the condition of the patient, facilities available, and specialist preference and training.

Further research, with relatively larger number of pa-

tients, are needed to show whether the results of our study are reproducible in a different clinical setting, and to determine a cut off endometrial thickness and volume for detection of endometrial carcinoma not only in premenopausal women but also in postmenopausal ones as well.

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