

The added value of three-dimensional ultrasonography in uterine pathology

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Abstract. The rapid development achieved over the last decades in volume rendering of ultrasound data, known as three-dimensional (3D) ultrasound technique, leads to new opportunities for refining the diagnosis in many gynaecologic conditions. The aim of the present study was to evaluate the advantages of 3D ultrasound over two-dimensional (2D) ultrasound in uterine pathology and to establish the optimal time point during the menstrual cycle to perform 3D ultrasound examination in order to achieve the maximum of useful information. A cross-sectional study on 200 patients who underwent gynaecologic 2D and 3D ultrasound examinations was performed. The addition of 3D examination to 2D ultrasound in uterine pathology provided the most useful information concerning: Congenital uterine anomalies, intrauterine devices (IUDs), adenomyosis, and submucous myomas. The findings showed that the 3D ultrasound scan is a useful tool in gynaecology, especially in cases with congenital uterine anomalies, myoma, and IUD. Although initially it was used for research purposes only, recent findings suggest its usefulness in routine ultrasound scan and the possibility of witnessing its introduction as a recommended examination procedure in the foreseeable future. Further research should be conducted in order to establish the sensitivity of 3D ultrasound in the detection of minor endometrial conditions, by correlating the imaging findings with the hysteroscopic results.

Introduction

In the last few decades, significant progress has been made in the quality of imaging techniques in gynaecology that has

consistently contributed to the improvement and refining of diagnoses. Despite competition from magnetic resonance imaging (MRI) and computer tomography (CT), ultrasound remains the first-line modality for gynaecologic applications. The introduction of three-dimensional (3D) ultrasound in the early 1990s was an important step, and numerous studies have been conducted to determine the impact of 3D ultrasound (1). Currently, 3D is widely accepted in the diagnosis of foetal abnormalities and in the assessment of the main complications of pregnancy (2,3). Few studies have been published in the field of gynaecologic applications of 3D ultrasound, rendering the present study a vital one.

The aim of the present study was to evaluate the advantages of 3D ultrasound over two-dimensional (2D) ultrasound in uterine pathology and to establish the optimal time point, with regards to the menstrual cycle, to perform 3D ultrasound examination in order to attain the maximum of useful information.

Patients and methods

Patient details. A cross-sectional study was performed in which 200 patients [age range, 19-76 years; mean, 40.38 years; inclusion and exclusion criteria provided in Table I] underwent gynaecologic and ultrasound examinations at Medis Medical Centre Iasi, Romania, between November 2019 and October 2020, comprising standard 2D followed by 3D ultrasound. For both examinations, a 3D endo-vaginal ultrasound probe [4-8 megahertz (MHz), Voluson E8; GE Healthcare] was used. The ultrasound examination began with a conventional 2D scan in order to establish the uterus position and its dimensions (longitudinal and antero-posterior diameters and the width of the corpus). Endometrial thickness was measured in the longitudinal plane, including the two layers at the level of its maximum thickness. Any pathological findings were recorded. The adnexal region was then scanned in order to identify the ovaries, the fallopian tube and a possible adnexal pathology. After the 2D ultrasound examination and Doppler assessment a diagnosis was established. The same sonographer, longitudinally along the length of the uterus, obtained the 3D volume. The coronal plane was obtained and then volume contrast imaging was gently applied (4). Both 2D images and

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3D volumes were saved on the ultrasound machine's hard drive. The findings observed by 2D and 3D ultrasound were analysed by sonographers and compared. In cases with endometrial pathology, in order to confirm the diagnosis, a hysteroscopy (considered gold standard) was performed.

A comparison was made between the patients who benefitted from the reconstructed coronal view of the uterus vs. those who did not, based on the indication for scanning, and sonographic findings on the 2D ultrasonography.

Ethics. Each patient was properly informed regarding the conditions of the study and provided informed consent. Ethics approval was obtained from the Institutional Board of the 'Medis' Medical Centre (Iasi, Romania).

Statistical analysis. Data were analysed using the statistical package SPSS 26 (IBM Corp.) and JASP 0.13 (University of Amsterdam). The statistical tests used were: Chi Square, Shapiro-Wilk, Kruskal-Wallis, Levene and binomial test. The cut-off value of $P < 0.05$ was considered to indicate a statistically significant difference. The confidence interval was designated at 95%.

Results

The age of the patients ranged between 19 and 76 years with a mean of 40.38 years (SD, 9.133). The indications for scanning for the 200 patients are presented in Table I.

In 71 cases (35.5%) (CI 28.9-42.6%) the ultrasound scan (both, 2D and 3D) revealed no uterine abnormalities. In 129 cases, different conditions were encountered. The results are presented in Table II.

The 3D ultrasound changed the diagnosis established by 2D ultrasound in 6 cases (3.0%) (CI 1.1-6.7%): Four cases with uterine congenital anomalies and two cases with IUD malposition in the uterine cavity.

In 53 cases (26.5%) (CI 20.5-33.2%), although the diagnosis was not changed it was completed by adding 3D and coronal plane examination. In cases with uterine myoma, the 3D ultrasound proved to be useful when myoma was situated intracavitary (total or partial) by showing the type of myoma (G0, 1 or 2 type), (Fig. 1A-C).

Uterine anomalies, classified as per the ESHRE/ESGE criteria (5) suspected by 2D, but completely diagnosed by 3D ultrasound were as follows: Arcuate uterus, 3 cases; septate uterus, 4 cases (Fig. 2A-C); bicorn uterus, 1 case and unicorn uterus, 1 case.

In two cases with IUD, the diagnosis of misplaced or incongruence between IUD and uterine cavity was missed by 2D ultrasound (Fig. 3A-C).

High level of agreement was found between 2D and 3D in cases of uterine myoma and adenomyosis, a κ value of 0.8 and 0.74, respectively. A moderate level of agreement was observed in cases of polyps (κ -0.67) and a low one in IUD (κ -0.44).

In order to establish the optimal time point for performing a 3D scan with regards to menstrual cycle, results were compared in relation to the endometrial thickness. The quality of 3D images was favorable in 149 cases (74.5%) (CI, 67.9-80.4%) and inadequate in 51 cases (25.5%) (CI: 19.6-32.1%). The quality of the image was quantified by the possibility of obtaining a clear

picture of the uterine cavity and endometrio-myometrial junction (EMJ). The mean endometrial thickness was 7.86 mm (SD, 2.903) with values between 2 and 19 mm. A significant statistical relationship existed between the quality of the image obtained and the thickness of the endometrium ($P=0.622$). A thin endometrium was associated with a poor 3D image. The present study showed a high probability to achieve a good image if the endometrium was ≥ 7.38 mm (value calculated using the Kruskal-Wallis non-parametric test).

Discussion

Ultrasonography is the most frequently used imaging technique in the assessment of the female genital tract. Usually the uterus and ovaries are evaluated using a 2D endovaginal ultrasonography. The main disadvantage of the 2D ultrasound scan consists in the difficulty of obtaining the coronal plane of the uterus. Adding a 3D ultrasound scan to the conventional examination may be beneficial as the coronal plane of the uterus can be obtained easily using the reconstruction 3D technique.

The present study revealed that from a total number of 200 examinations, 3D examination changed the diagnosis in 6 cases (3.0%) (CI: 1.1- 6.7%) and added useful information or reinforced the diagnosis in 53 cases (26.5%) (CI: 20.5- 33.2%).

The most useful information was obtained in patients referred to for ultrasonic scan for the following indications: Infertility, uterine haemorrhage and IUD placement follow-up. Concerning the accuracy of the final diagnosis, the most useful information was obtained in patients with uterine pathology: Uterine congenital anomalies, IUD misplacement, adenomyosis, and submucous myomas. Neither 3D nor volume contrast imaging (VCI) were useful in cases with normal uterus.

Although conventional 2D ultrasound has a good accuracy in diagnosing congenital uterine anomalies, it is highly dependent on the expertise of the examiner and is limited by the difficulty in obtaining the coronal plane of the uterus. Several studies have demonstrated the advantages of 3D ultrasound in diagnosing uterine anomalies (6-8). Comparing 3D ultrasound to laparoscopy and hysteroscopy, Mohamed *et al* recorded a sensitivity of 97%, specificity of 96%, positive predictive value of 92% and negative predictive value of 99% in the diagnosis of uterine anomalies (9). Ghi *et al* reported both a sensitivity and a specificity of 100% in the diagnosis of uterine malformations and 96% concordance between ultrasound and endoscopy with respect to the type of anomaly diagnosed (10). In this study, 3D was mandatory for the final diagnosis in all cases with uterine congenital anomalies. As the coronal plane enables the visualization of not only the endometrial cavity, but also of the uterine fundus, 3D scan was necessary for the differential diagnosis between bicornuate and septate uterus. Moreover, in these cases, 3D proved to be superior to hysteroscopy. Hysteroscopy is able to confirm an anomaly of the uterine cavity but is not able to provide any information regarding the external contour of the uterus. In addition, in the coronal plane of the uterus obtained with 3D ultrasound it is possible to measure the size of the septum and classify the anomaly according to the ESHRE/ESGE classification system of female genital anomalies (5). Although MRI is considered the gold standard for congenital uterine anomalies,

Table I. Indications for the ultrasound scan (N=200).

Indication	Data	
	No. of patients	Percentage
On demand at a routine gynaecological consult	51	25.5
IUD control	10	5.0
Abdominal pain, dysmenorrhea	38	19.0
Menorrhagia	33	16.5
Infertility	39	19.5
Menstrual disorders	13	6.5
Myoma, cyst	16	8.0
Total	200	100

IUD- intrauterine device.

Table II. The results provided by the ultrasound scan (N=200).

Diagnosis	Data	
	No. of patients	Percentage
No uterine abnormalities	71	35.5
Uterine myoma/myomas	52	26
Uterine congenital anomalies	10	5.0
IUD displacement - Cooper IUD	1	0.5
IUD displacement - levonorgestrel IUD	2	1
Endometrial polyps	17	8.5
Isthmocele	15	7.5
Adenomyosis	22	11
Endometrial hyperplasia	10	5
Total	200	100

IUD, intrauterine device.

3D can provide the same type of information (11). However, in doubtful or complex cases, MRI should be performed, particularly for the assessment of the cervix and vagina (12). Thus, 3D ultrasound may be associated with 2D ultrasound in the diagnosis of uterine malformations.

Analysing the IUD cases from the current study, 3D was useful for both types: Copper IUD and levonorgestrel (LNG IUD). VCI proved to be particularly useful especially in cases with LNG IUD. Observations of this study confirm those of several studies performed in order to assess the role of 3D ultrasound in patients with IUD (13-16). These studies agree that the coronal view shows the entire device and its position within the uterus, in this way helping to identify the cause of pelvic pain and (or) bleeding in patients with an embedded IUD (14). Hösli *et al* demonstrated that 3D ultrasound offers the advantage of a better visualisation of LNG IUD and at the same time the assessment of uterine anomalies (13). The coronal plane is useful not only to detect the exact position of the IUD, but also to measure the uterine cavity and thus to establish the proper size of the IUD to be inserted in the uterus (17).

One interesting issue in gynaecology is the assessment of submucous myomas. It is important when diagnosing a myoma to know its level of extension in the uterine cavity. Moreover, before planning a hysteroscopic resection of a submucous myoma, it is necessary to know the type of myoma (G0, 1 or 2 type). Salim *et al* demonstrated that three-dimensional sonohysterography (3D-SIS) had a similar accuracy as hysteroscopy in classifying submucous fibroids (18). Lee *et al* demonstrated that 3D-SIS is reproducible among different observers for quantification of the percentage of a submucous fibroid protruding into the uterine cavity (19). Mavrellos *et al* demonstrated that 3D-SIS may be useful in predicting complete hysteroscopic resection of submucous myomas (20). Although findings of the present study show a high level of agreement between 2D and 3D ultrasound in the diagnosis of myoma ($\kappa=0.8$), reconstructed coronal plane added useful information for planning the surgical management of the case.

Regarding adenomyosis, 2D ultrasound was useful in establishing the diagnosis by revealing the classical ultrasound signs including: Anechoic foci, heterogeneous myometrium,

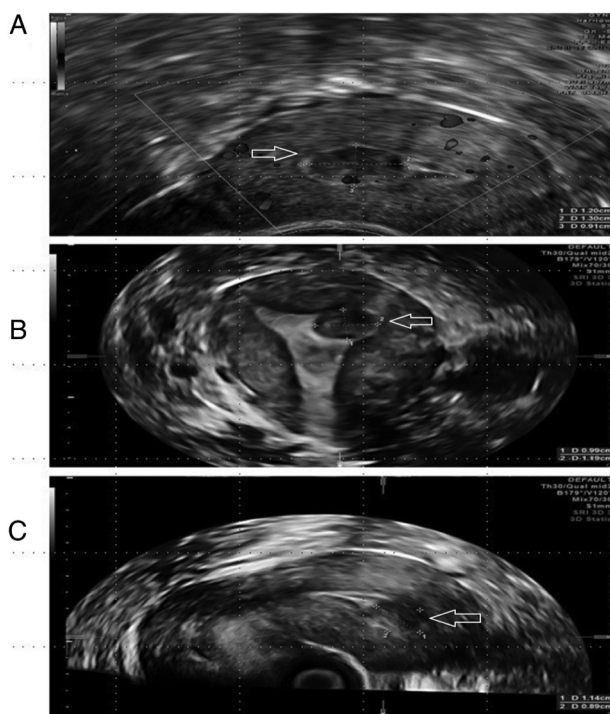


Figure 1. Submucous myoma (arrow). (A) 2D transversal plane of the uterus. (B) 2D ultrasound longitudinal plane of the uterus. (C) 3D ultrasound, coronal plane of the uterus. 2D, two dimensional; 3D, three dimensional.

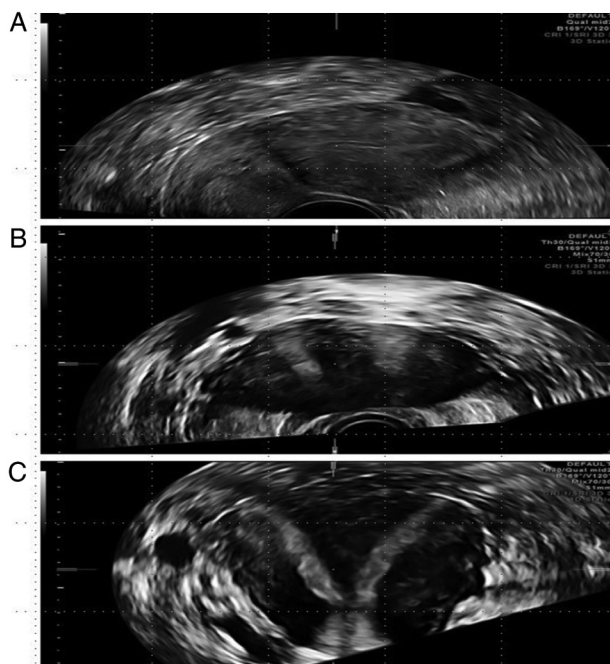


Figure 2. Septate uterus. (A) 2D ultrasound longitudinal plane of the uterus. (B) 2D transversal plane of the uterus. (C) 3D ultrasound, coronal plane of the uterus. 2D, two dimensional; 3D, three dimensional.

asymmetrical uterine wall, uterine enlargement and hyper-echogenic striations (21). However, 2D ultrasound cannot provide information regarding the endometro-myometrial junction (EMJ). The changes in EMJ are considered a key element in diagnosing adenomyosis and traditionally the assessment of the EMJ has been part of the MRI evaluation

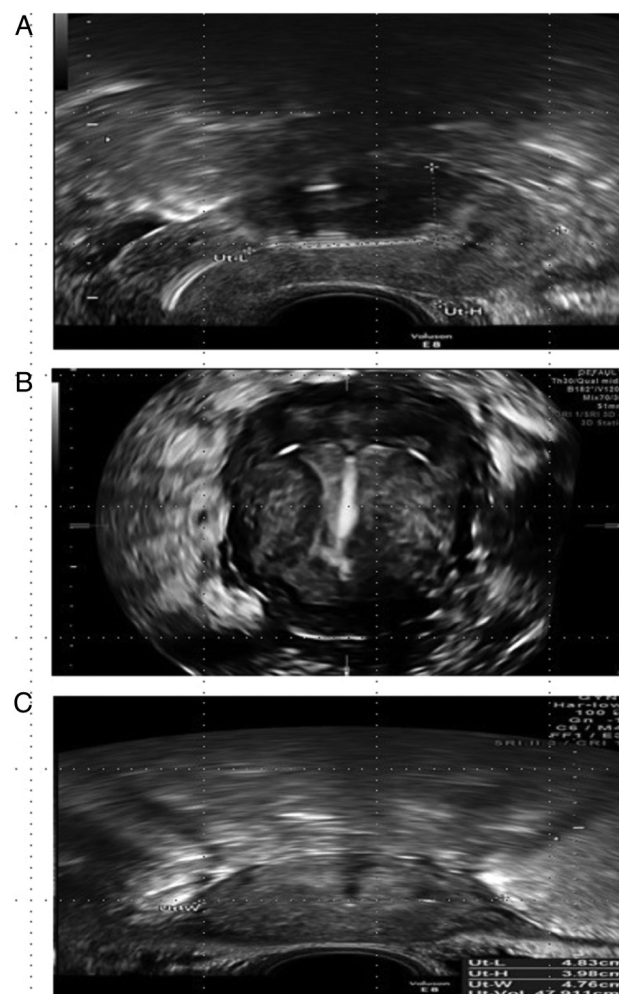


Figure 3. Intracavitary IUD. (A and B) 2D ultrasound longitudinal plane and transversal plane showing a normal position of the IUD in the cavity. (C) 3D ultrasound with coronal plane showing the IUD embedded in the myometrium. 2D, two dimensional; 3D, three dimensional; IUD, intra-uterine device.

of the uterus (21). 3D US enables visualisation of the coronal plane of the uterus and consequently provides a clear image of the EMJ. Due to the possibility of visualising the EMJ, 3D ultrasound opens up new horizons in the diagnosis of adenomyosis. Adding VCI to the coronal plane provides a clearer view of the EMJ. 3D ultrasound allows visualisation of the lateral and fundal EMJ, which is almost impossible to observe only with 2D imaging. Thanks to the clearer view provided by the VCI, this procedure is considered as the best in analysing and measuring the junctional zone (22). In our cases, 3D and VCI identified changes in EMJ as different size of the EMJ in different parts of the cavity and the penetration of the endometrium into the myometrium. There is some supposition that adenomyosis began with EMJ alteration and therefore 3D and VCI would be useful for an early diagnosis of the disease (23).

In the present study, the 2D ultrasound scan diagnosed endometrial polyps in 17 cases (8.5%). In all cases the diagnosis was suspected by 2D ultrasound and confirmed by 3D and VCI. During the 2D ultrasound scan, a search for the pedicle artery sign was conducted in order to detect the

position of the stalk of the polyp (24). 3D and VCI proved to be useful in 2 of 17 cases by providing a clearer image regarding the topography of the polyps. At the same time, the coronal plane was useful in the patient's understanding of the disease. Identical size of the polyps using 2D and 3D scans was obtained. Based on longitudinal and coronal plane and using Doppler mode we localised the base of the polyps and the place of its stalk. In all cases of polyps, hysteroscopy confirmed the diagnosis. 3D scan seems not to be superior to 2D in diagnosing endometrial polyps, but it helps in reinforcing the diagnosis and is very useful for the patient's understanding of the disease.

Another important issue concerns the question if there is a specific time frame regarding the endometrial cycle to perform a 3D ultrasound scan for obtaining the ideal image of the coronal plane. In relation to the size of the endometrium, the coronal plane was difficult to obtain if the size was <7.38 mm. Difficulties in obtaining a proper image of the uterine cavity have been noted in cases with endometrium thickness <7.38 mm or in cases with multiple uterine myomas or adenomyosis. Benaceraff *et al* reported in a study on 66 patients that the coronal view is helpful in patients with an endometrium greater than or equal to 5 mm (14). Therefore, we recommend, in order to obtain a good 3D reconstructed image, that the sonography should be carried late in the follicular or in the secretory phase. In menopausal women, because the endometrial thickness is usually <5 mm, 3D is not helpful.

Another advantage of 3D ultrasound that should be considered is the capability of storing volumes, ensuring a further process of the information. In this way, it is possible to follow-up the patients for a long period of time and if a uterine pathology will appear in the future, a reassessment of the previously rendered volumes would possibly bring useful information regarding the pathogenesis of the disease.

The main limitation of this study is represented by the fact that hysteroscopy was not performed in cases where 2D and 3D findings were normal; thus, it was possible to overlook some minor pathologic findings.

As a conclusion, we can state that the 3D ultrasound scan is an extremely useful tool in gynaecology, especially in cases with congenital uterine anomalies, submucous myomas and the assessment of IUD placement. Although initially it was used for research purposes only, currently it has been proven to be useful in the routine ultrasound scan and there is a possibility of witnessing its introduction as a mandatory examination procedure in the foreseeable future.

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Availability of data and materials

All data generated or analysed during this study are included in this published article.

Authors' contributions

MG, RP, LMH and RM designed the study. MG, LMH, ISS and RP collected, analyzed and interpreted the patient data. MG, RM, MO, BFT, and AMG were responsible for discussion and interpretation of the data. BFT, AMG and ISS had major contributors in the writing of the manuscript. MG, RM, LMH and MO supervised and visualised the final form. All authors have read and agreed to the published version of the manuscript. MG and RP confirms the authenticity of all raw data assessed in the manuscript.

Ethics approval and consent to participate

The present study was conducted in accordance with the World Medical Association Declaration of Helsinki and was approved by the Institutional Board of the 'Medis' Medical Centre Iasi, Romania (approval no. 12/18.09/2019). Informed consent was obtained from the patients.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that there are no competing interests.

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