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CLINICAL ARTICLE

Assessment of endometrial volume and vascularization using transvaginal 3D power Doppler angiography in women with postmenopausal bleeding

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A B S T R A C T

Objective: To compare the usefulness of 3D power Doppler angiography (3D-PDA) and endometrial thickness measurement by 2D Doppler ultrasound in the distinction of benign from malignant disease in postmenopausal women with abnormal uterine bleeding (AUB) and an endometrial thickness greater than 4.5 mm. *Methods:* Forty-eight women with AUB and an endometrial thickness greater than 4.5 mm on 2D ultrasound underwent 3D-PDA. The endometrium and a 5-mm subendometrial "shell" were evaluated at rotation angles of 9° and 30°. Endometrial volume, vascularity index, flow index, and vascularization flow index were obtained. *Results:* The histologic findings were normal or benign for 38 women (79%) and malignant for 10 (21%). All vascular indices were significantly higher in the group with malignancies except for the vascularization flow index. There were no differences in the values obtained using the 9° or the 30° angle. Receiver-operating characteristics curves were traced for all indices. The vascularity index had the best area under the curve (0.78), 77.8% sensitivity, and 82.6% specificity. The areas under the curve were smaller for the shell than for the endometrium. *Conclusion:* 3D-PDA was not found better than 2D ultrasound at distinguishing benign from malignant disease in women with AUB and an endometrial thickness greater than 4.5 mm.

1. Introduction

Endometrial carcinoma is the most common gynecologic malignancy in European countries [1]. Postmenopausal bleeding is usually the first symptom of endometrial cancer, but only 10% to 15% of women seeking gynecologic care for this complaint are actually affected by a malignancy.

The most commonly used technique for detecting endometrial disease in symptomatic women is 2D transvaginal ultrasound [2]. Previous studies have reported a relationship between endometrial thickness assessed by 2D transvaginal ultrasound and the histologic diagnosis of endometrial cancer in postmenopausal women [3–8]. Although the sensitivity of 2D transvaginal ultrasound in detecting endometrial cancer has been considered good, it is associated with a low but concerning false-negative rate, however, and a meta-analysis recently concluded that earlier meta-analyses probably overestimated the diagnostic accuracy of 2D transvaginal ultrasound [9,10].

Conventional 2D power Doppler ultrasound imaging can be used to estimate the color content—defined as the number of pixels in which it is possible to identify the power Doppler signal—and to examine the vascular arrangement in the endometrium being scanned. By permitting to distinguish subjectively between benign and malignant disease, this form of imaging was reported to represents diagnostic improvement over grayscale 2D ultrasound for women with postmenopausal bleeding and an endometrial thickness of 5 mm or greater [11]. However, 2D power Doppler imaging for the evaluation of endometrial vascularization has the limitation of being subjective, whereas 3D power Doppler imaging enables an objective evaluation of endometrial vascularization. Besides, 3D power Doppler imaging depicts endometrial vascularity much more clearly than a single 2D power Doppler scan [12].

A study was conducted in 2008 to calculate endometrial volume in women with postmenopausal bleeding using a 3D power Doppler ultrasound machine. It concluded that 3D power Doppler imaging was more effective than 2D power Doppler imaging in distinguishing benign from malignant endometrial disease [13]. And in theory, assessing endometrial vascularity by 3D power Doppler imaging should indeed be useful. Yet, a 2010 study concluded that none of the vascular indices provided by 3D power Doppler analysis proved superior to a 2D measurement of endometrial thickness [14].

The vascular indices provided by 3D power Doppler analysis (an analysis also called Doppler angiography [3D-PDA]) represent blood flow in part or the whole of the studied endometrium. They are the following: the vascularization index (VI), or ratio (expressed as percentage) of the observed color-coded voxels (or units of volume) to the totality of voxels present in the image of the endometrial volume of interest; the flow index (FI), or mean intensity of flow for all color-coded voxels observed; and the vascularization flow index

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(VFI), which combines VI and FI [15]. The subendometrial (or myometrial) region can also be evaluated by 3D-PDA using what has been called shell-imaging analysis. This method allows the examiner to analyze the vascular indices beneath the endometrium.

The reproducibility of endometrial volume measurements using a 3D power Doppler machine has been considered moderately satisfactory, probably because of measurement plane and rotation step bias [16]. However, another study by several of the same authors published 2 years later found good interobserver reliability for both endometrial volume and vascular measurements with 3D power Doppler imaging, particularly when the endometrial thickness was between 5 and 15 mm, and recommended that the technique be further developed [17].

The aim of the present study was 2-fold. It was to determine whether endometrial volume and the vascular indices obtained from 3D power Doppler imaging are useful for distinguishing benign from malignant endometrial disease in postmenopausal women with abnormal uterine bleeding (AUB) and an endometrial thickness greater than 4.5 mm. It was also to assess the diagnostic performance of 3D-PDA for rotation steps of 9° and 30° using the Virtual Organ Computer-aided Analysis (VOCAL) software imaging program (GE Healthcare, Barrington, IL, USA).

2. Materials and methods

Between February 1 and September 1, 2011, 48 consecutive women with postmenopausal bleeding admitted to the Department of Obstetrics and Gynecology of the University of Udine were enrolled in a pilot observational study.

The inclusion criteria were the following: age older than 45 years; natural menopause, defined as an absence of menstruation for at least 1 year; total (i.e. double-layer) endometrial thickness greater than 4.5 mm on 2D transvaginal ultrasound; and histologic diagnosis of the endometrium from the authors' university hospital. The exclusion criteria were the following: total endometrial thickness less than 4.5 mm; any kind of hormone therapy for menopause symptoms; use of tamoxifen citrate; and histologic diagnosis of the endometrium not from the authors' university hospital.

A detailed medical history was taken and all participants underwent a general and a gynecologic examination, the latter including a transvaginal ultrasound evaluation and endometrial thickness measurement. The ultrasounds were performed according to a scanning protocol by a single operator (A.R.) using a Voluson E8 system (GE Medical Systems, Milwaukee, WI, USA) equipped with a multifrequency (3–9 MHz) endovaginal probe. Briefly, a B-mode ultrasound was first performed to obtain longitudinal and transverse sections of the uterus. The maximal total endometrial thickness was then measured in the longitudinal plane.

After the B-mode assessment of the maximal total endometrial thickness, 2D power Doppler imaging was performed to evaluate endometrial and subendometrial vascularity. The settings used were those determined to achieve maximum sensitivity in the detection of low-velocity flow without noise. The 3D volume acquisition box was activated so that 3D imaging could be performed. With a sweeping angle of 90°, the volume box was placed over the power Doppler window. Since volume acquisitions were made over time intervals of 10 to 20 seconds, the participants were asked to remain as still as possible. Acquisitions were repeated when flash-like artifacts appeared because of intestinal or respiratory movements.

The contour of the endometrium was traced in the coronal plane and the endometrial volume measured using the VOCAL imaging program. The vascular indices for the entire endometrial volume and for a 5-mm subendometrial shell were calculated using the same program.

Endometrial volume can be measured by rotation in the longitudinal plane, the transverse plane, or the coronal plane [17]. With rotation steps of 30°, the 6 obtained endometrial slices provided the outline of the endometrium at the myometrial-endometrial junction, from the uterine fundus to the internal cervical os. With rotation steps of 9°, 20 endometrial slices were obtained from which the VOCAL imaging program calculated the endometrial and subendometrial shell volumes as well as the 3D-PDA indices. All calculated values were included in the analysis.

The 3D volumes were analyzed offline by a single observer (L.F.). In the week that followed the ultrasound measurements, all study participants underwent a hysteroscopic endometrial biopsy. Benign findings included endometrial atrophy, endometrial polyps, and endometrial hyperplasia. Malignant histologic findings consisted endometrial cancer. The participants were then allotted to one of 2 groups: a group with normal histologic findings or findings of endometrial atrophy, polyps, or hyperplasia without atypia (group 1); and another with findings of endometrial carcinoma (group 2).

Qualitative data were reported as number and percentage and quantitative data as mean and standard deviation. The nonparametric Mann–Whitney and Bonferroni tests were used to compare ultrasound indices between the 2 groups, with $P<0.05$ considered significant. In addition, receiver operating characteristic (ROC) curves were traced to obtain sensitivity and specificity. Statistical analysis was performed using SPSS version 15.0 (IBM, Armonk, NY, USA). The study was approved by the local ethics committee, and written informed consent was obtained from all participants.

3. Results

Of the 48 women included, 38 (79%) had benign findings (group 1) and 10 (21%) had malignant findings (group 2). The median age was 61 years in group 1 and 79 years in group 2. The mean body mass index (calculated as weight in kilograms divided by the square of height in meters) was 26 in group 1 and 28 in group 2. The participants in group 2 were older than those in group 1 ($P<0.05$), with a higher body mass index ($P<0.05$) and a thicker endometrium ($P<0.05$). Endometrial thickness was 6.9 mm in group 1 and 11.02 mm in group 2 (Tables 1, 2).

The main ultrasound values calculated for the endometrium and the subendometrial shell using 30° rotation steps are shown in Table 2. Whether they concerned volume or vascular indices, the values were higher in group 2 than in group 1, and the differences were all significant except for VFI in both the endometrium ($P=0.07$) and the subendometrial shell ($P=0.06$). There was no statistical difference between the results obtained using the 9° and those obtained using the 30° rotation angle (Tables 3, 4).

For all measurements ROC curves were traced. The performances of the studied variables are shown in Table 5. The best variables for the distinction between benign and malignant status were VI, FI, and VFI, with an AUC of 0.78, 0.77, and 0.76, respectively. Regarding endometrial thickness, the AUC was 0.76 using a population-based cutoff value of 10 mm for endometrial thickness. With this cut-off value, the sensitivity was 67%, the specificity was 86%, the positive

Table 1
Baseline characteristics of the study participants.[a]

Characteristic	Group 1 (n = 38)	Group 2 (n = 10)	*P* value
Age, y	61 (58–79)	79 (61–79)	0.02
BMI	26 (20–40)	28 (22–43)	0.04
Histologic finding			
Atrophic endometrium	8 (21)		
Polyp	18 (47)		
Myoma	7 (18)		
Hyperplasia without atypia	5 (13)		
Adenocarcinoma		10 (100)	

Abbreviation: BMI, body mass index, calculated as weight in kilograms divided by the square of height in meters).
[a] Data are given as mean (range) or number (percentage).