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Original Article

Utility of three dimensional (3-D) ultrasound and power Doppler in identification of high risk endometrial cancer at a tertiary care hospital in southern India: A preliminary study

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ABSTRACT

Objective: The study was conducted to find the utility of three dimensional (3-D) ultrasound and Doppler sonography in differentiating benign and malignant endometrial lesions and to ascertain the association of sonology parameters with type, grade and stage of endometrial cancer.

Materials and methods: Women attending the gynaecology department of a tertiary care hospital, with a provisional diagnosis of carcinoma endometrium were subjected to three dimensional power Doppler ultrasound evaluation and assessment of vascular patterns. VOCAL (Virtual Organ Computer-aided Analysis) software was used to assess volume, Vascularisation Index (VI), Flow Index (FI) and Vascularisation Flow Index (VFI). Ultrasound parameters were compared with histologic diagnosis to evaluate the diagnostic performance using Receiver Operating Characteristic (ROC) Curve.

Results: Sixty-four women were included in the study, 33 with benign and 31 with malignant endometrial lesions. Larger endometrial volume and higher Doppler indices correlated with malignant lesions. The variables with good discriminatory potential between benign and malignant status were VI and VFI, having a sensitivity of 90.3% and specificity of around 80%. VFI (adjusted odds ratio of 40.4; (95% CI − 8.46–192.88), p value < 0.001) was the only significant variable identified by multivariate logistic regression, when adjusted for age and post-menopausal status. Multiple global and focal vessel pattern was seen predominantly in malignant cases (specificity 93.9%), although the sensitivity was low (61.2%). Higher stages and grades of tumour and non-endometrioid types had higher Doppler indices, and requires further evaluation.

Conclusions: 3-D ultrasound has good discrimination potential between benign and malignant endometrial lesions and could be useful as a screening tool. However, utility of 3-D tool for differentiation between tumour characteristics needs further validation.

Introduction

Women with endometrial cancer mostly present either with postmenopausal bleeding or peri-menopausal abnormal bleeding. A two dimensional (2D) trans-vaginal sonography has long been the first line modality in endometrial evaluation. Three dimensional (3-D) ultrasound is a relatively new advance, which can be used to assess several morphological and vascular parameters of endometrium.

Power Doppler measures endometrial volume and vascular indices such as Vascularisation index (VI), FI (Flow index) and VFI (Vascular flow index) using Virtual Organ Computer-aided Analysis (VOCAL) software. These indices point towards tumor neovascularisation thereby raising the suspicion of malignancy. Besides, studying the vessel patterns provide additional information on the nature of the tumor. Several researchers have reported power doppler to be useful in differentiating malignant endometrial lesions from benign ones, but there is only one report that comprehensively showed correlation between power Doppler indices and endometrial histological types, grade, myometrial and cervical invasion and lymph vascular space invasion [1–4].

In India, endometrial cancers are diagnosed and managed mostly by the general gynaecologists; due to limited availability of gynaeco-oncologists at most centres. In one of the few reports on

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Table 1
Comparison of baseline characteristics of benign and malignant cases.

Baseline characteristics	Benign (n = 33) n (%)	Malignant (n = 31) n (%)	Fisher's exact test p value
Age group (yrs)			0.05
35–44	5 (15.2)	3 (9.7)	
45–54	18 (54.5)	9 (29.0)	
>55	10 (30.3)	19 (61.3)	
BMI (kg/m^2)			0.12
<25	24 (72.7)	16 (51.6)	
>25	9 (27.3)	15 (48.4)	
Family history			0.23
Yes	0	2 (6.5)	
No	33 (100)	29 (93.5)	
Parity			0.11
Nulliparous	4 (12.1)	0	
Parous	29 (87.9)	31 (100)	
Post-Menopausal status			0.01
Yes	17 (51.5)	25 (80.6)	
No	16 (48.5)	6 (19.4)	
Presence of DM/HTN			0.35
Yes	5 (15.2)	8 (25.8)	
No	28 (84.8)	23 (74.2)	

endometrial cancer in India, Mahantshetty et al. observed that endometrial cancers were seen in relatively younger population (mean age 54 years) and the trend was towards incomplete staging when surgery was performed by non-oncologists [5]. Pre-operative identification of the risk status in terms of type, grade (differentiation) and stage of the cancer, aids in effective planning for optimal surgery in consultation with an oncologist. Although endometrial biopsy and Magnetic Resonance Imaging (MRI) could provide this information, a non-invasive sonological evaluation may possibly be an alternative option.

With this background in mind, the present study was designed to find the utility of 3-D and Power Doppler sonography parameters in differentiating benign and malignant endometrial lesions and to find the correlation of 3-D and Power Doppler sonography with the type, grade and stage of endometrial cancer.

Patients and methods

A prospective study among gynaecology out-patient attendees of a tertiary care hospital in South India was conducted over a period of two years. Ethical approval was obtained from the Institutional Ethics Committee (IEC 274/2012) and written informed consent was obtained from all the participants. Women with postmenopausal bleeding and with one or more sonological features (endometrial thickness $\geq$5 mm, indistinct endo-myometrial junction, cystic spaces in endometrium, hyperechoic areas and irregular endometrium) or one or more risk factors (obesity, diabetes, hypertension, nulliparity and family history of gynecologic/breast cancer); and women with perimenopausal abnormal uterine bleeding with risk factors and/or endometrial thickness $\geq$18 mm were eligible to be included in the study.

A total of 70 women were enrolled in the study during the stipulated time frame of two years. Women with inadequate histopathology at biopsy and did not wish to have further evaluation and those who were lost to follow up were excluded from the analysis. All the patients underwent meticulous history taking, clinical examination and a 2D transvaginal ultrasonography to measure endometrial thickness. Patients underwent a detailed trans-vaginal ultrasound examination, using Voluson 730 Expert (GE Healthcare, Milwaukee, WI, USA) which had a multi-frequency vaginal probe (3–9 MHz). All 64 cases were examined by a single consultant (Radiologist with >15 years' experience and having the necessary training and expertise to operate the 3D power Doppler). Grey scale assessment of uterus was done and endometrial thickness was measured in the sagittal plane including both layers at the level of maximum thickness. Volume acquisition was done by manually tracing the endometrium in the coronal, axial and mid sagittal planes. Power Doppler was applied over the endometrial and sub-endometrial area. Uniform settings in power Doppler were used, namely; normal frequency, pulse repetition frequency 0.6 kHz, gain 4.0 and low wall motion filter. Vascular patterns were subjectively interpreted and classified based on the International Endometrial Trial Analysis (IETA) group as, no vessels, single vessel, multiple focal vessels, multiple global vessels and scattered vessels [6].

Endometrium was traced manually in three planes, and VOCAL software was used to manually delineate the endometrial area and to calculate the volume and vascular indices (Vascularisation Index, Flow Index and Vascularization flow index). Vascularisation Index (VI) is a measure of the number of color coded voxels in a given volume and represents the number of vessels in a given volume. Flow Index (FI) is the intensity of the Doppler signal in the color coded voxels and is the average color of all voxels. Vascularization flow index (VFI) is a combination of VI and FI and is expressed as a range from 0 to 100.

The final diagnosis was made based on the histopathological report following endometrial curettage or surgery. In cases of endometrial carcinoma, the histopathology report included the

Table 2
VOCAL software characteristics of benign and malignant cases.

VOCAL software characteristics	Benign Median (IQR)	Malignant Median (IQR)
Endometrial volume (cc)	3.48 (2.15–7.79)	10.3° (4.02–25.23)
Vascular indices		
VI	0.49 (0.23–1.78)	11.92 (3.21–22.9)
FI	23.63 (21.18–28.21)	33.16 (26.68–37.45)
VFI	0.12 (0.05–0.42)	3.65 (1.02–10.76)