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Antidiastole Value of Three-dimensional Ultrasonography and Power Doppler between Uterine Parenchyma Lumps and Endometrial Cancer: A Retrospective Study*

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Summary: Sometimes endometrial polyps, submucosal myomas, and endometrial cancer show similar findings under ultrasonography. The aim of this study was to assess the antidiastole value of blood flow parameters using three-dimensional (3D) power Doppler ultrasonography angiography (PDA) between endometrial cancer and uterine parenchyma lumps. The data of the blood flow indices in 3D-PDA including the vascularization index (VI), flow index (FI), and vascularization flow index (VFI) in 40 patients with endometrial cancer and 41 patients with uterine parenchyma lumps (endometrial polyps and submucosal myomas) were retrospectively analysed and compared utilizing Virtual Organ Computer-aided AnaLysis (VOCAL) software. The results showed that all the blood flow parameters (VI, FI, VFI) were significantly higher in women with endometrial cancer than in those with uterine parenchyma lumps (P<0.001). The area under the curve of ROC of VI, FI, and VFI was 0.98, 0.84, and 0.97, respectively. Thus, the best predictor of endometrial carcinoma was VI with a sensitivity of 97.0% and a specificity of 91.0%. The optimal cutoff value of VI was 4.06%. Our data demonstrated that all of the blood flow signal parameters (including VI, FI, and VFI) in 3D power Doppler ultrasonography had significant antidiastole values between endometrial cancer and uterine parenchyma lumps to assist clinicians in properly diagnosing patients.

Key words: power Doppler; three-dimensional ultrasound; uterine parenchyma lump; endometrial carcinoma; blood flow signal parameter

As obesity and quality of life risk factors have recently increased, the incidence of endometrial carcinoma has overtaken that of cervical cancer among women, and endometrial carcinoma is now the most common malignant gynecologic tumor[1]. The mean onset age of approximately 7% of women with endometrial cancer is less than 45 years. Postmenopausal vaginal bleeding and abnormal vaginal bleeding of women of child-bearing age should attract concern[2].

Ultrasonography is a simple, widely used, and non-invasive diagnostic tool for women with irregular colporrhagia. In some cases, endometrial polyps, submucosal myomas, and malignant endometrial tumors show similar findings under ultrasonography. Angiogenesis is currently regarded as playing an imperative role in the growth and metastasis of a majority of tumors[3]. Furthermore, more abundant blood flow signals have been found in malignant lesions due to neovascularization than in benign tissues[4]. Hence, because of the limited and less dependable value of two-dimensional (2D) power Doppler for evaluating and quantifying vascularity in lesions, 3D ultrasound and power Doppler angiography (PDA) have become increasingly popular ultrasonic technologies with their own particular merits in differentiating benign and malignant tumors using 3D power Doppler mapping[5–8]. After scanning, clinicians can use Virtual Organ Computer-aided AnaLysis (VOCAL) software to acquire relevant blood flow indices including vascularization index (VI), flow index (FI), and vascularization flow index (VFI)[9].

Although diagnostic dilatation and curettage (D&C) is now identified as the first choice of

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examination for women diagnosed with endometrial cancer, it is an invasive and dangerous method compared to non-invasive ultrasound.

Given the promising results of 3D power Doppler ultrasonography and PDA, our principal objective herein is to assess the antidiastole value of 3D power Doppler angiography for endometrial cancer and uterine parenchyma lumps, including endometrial polyps and submucosal myomas, by analyzing patients' blood flow indices.

1 MATERIALS AND METHODS

This study was approved and supported by the Institutional Ethics Review Board of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (China). The research period was from March 2017 to September 2018. A total of 40 women pathologically diagnosed with endometrial cancer and 41 diagnosed with endometrial polyps or submucosal myomas using postoperative histological examinations were enrolled. Patients who had undergone diagnostic D&C before gynecological surgery were excluded.

The patients underwent transvaginal 3D power Doppler ultrasound (Voluson E10; GE, Zipf, Austria) examinations in the lithotomy position after emptying their bladders. The settings were as follows: a frequency of 5–9 MHz, a pulse repetition frequency of 0.6 kHz, a gain of –5.0, and a wall motion filter of 1. The operator contoured the region of interest and used VOCAL software to analyze the parameters of vascularity using computer algorithms to measure the VI, FI, and VFI (fig. 1 and 2).

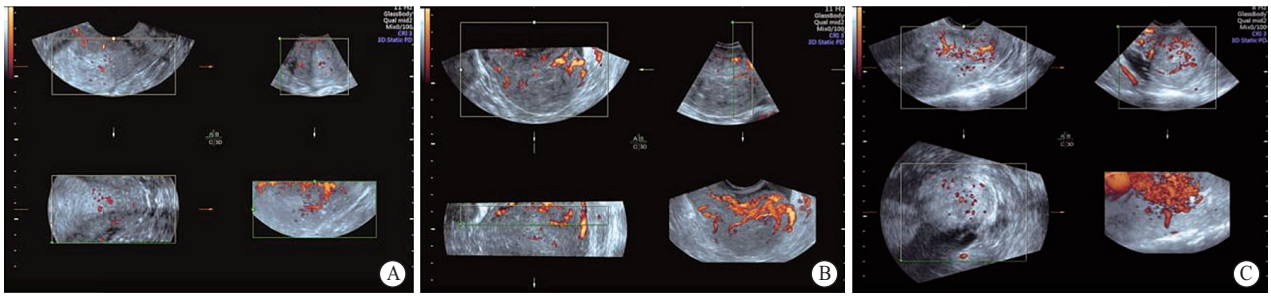

Fig. 1 Images of endometrial polyps (A), submucosal myomas (B), and endometrial cancer (C) using three-dimensional power Doppler ultrasonography
The red area represents abundant blood flow signals of the nidus. Compared to endometrial polyps and submucosal myomas, there were more abundant and conspicuous blood flow signals in the endometrial cancer lesions, whereas there were no obvious differences in the red areas between the endometrial polyps and submucosal myomas.

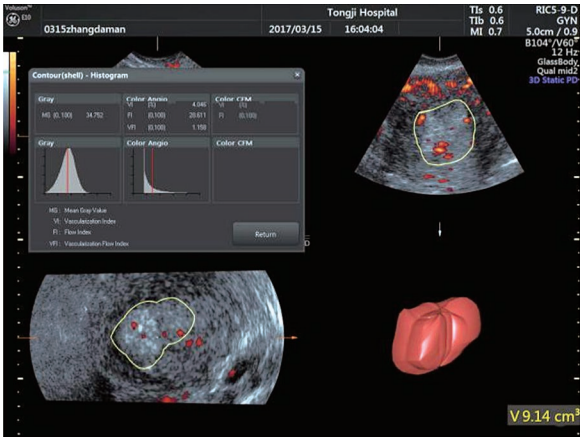

Fig. 2 Analysis of three-dimensional power Doppler indices from the volume acquired in fig. 1
VI: vascularization index; FI: flow index; VFI: vascularization flow index

All of the women were assessed by two ultrasound doctors who were blinded to the measurements. There was no statistically significant difference in the measurements between both sonographers.

The VI is defined as the ratio of the number of color voxels to the total number of voxels (%) and represents the presence of blood vessels (vascularity). The FI represents the average intensity of blood flow. The VFI measures a combination of the vascularity and flow intensity.

The data were represented as mean±standard deviations (SD) or percentages using the independent sample *t* test as assessed by SPSS software version 18.0 (SPSS Inc., USA). The chi-squared test was used to compare the difference in the numbers of patients in the uterine parenchyma lump and endometrial carcinoma groups. Receiver operating characteristic (ROC) curve analysis was conducted to calculate the area under the curve (AUC) and assess the optimal cutoff value of the 3D power Doppler ultrasound markers to differentiate between endometrial cancer and uterine parenchyma lumps. Statistical significance was set up at $P<0.05$.

2 RESULTS

The characteristics of the enrolled women are shown in table 1. A total of 81 patients were included

in our study. Of them, 40 (49.4%) were diagnosed with endometrial cancer and 41 (50.6%) were diagnosed with uterine parenchyma lumps. The average age of patients was 48.27 years. The mean age was significantly older in patients with endometrial cancer than in those with uterine parenchyma lumps (P<0.001). However, there were no significant differences in the average age of menarche (P=0.245), number of pregnancies (P=0.060), and parturitions (P=0.056) between the two groups. Of the 41 women with uterine parenchyma lumps, 3 had hypertension and none had diabetes mellitus. Of the 40 women with endometrial cancer, 10 had hypertension and 5 had diabetes mellitus. Although the ratios of those with hypertension and diabetes mellitus were higher in the endometrial cancer group, there was no significant difference, with P values of 0.052 and 0.102, respectively. Table 2 shows the vascular indices of the two groups. Compared to the women with uterine parenchyma lumps, all of the parameters (VI, FI, and VFI) were significantly increased in those with endometrial cancer (P<0.001). The VI was 1.63% in the parenchyma lump group and 17.11% in the endometrial carcinoma group (P<0.001). The FI was 26.21 in the parenchyma lump group and 37.15 in the endometrial carcinoma group (P<0.001). The VFI was 0.57 in the parenchyma lump group and 6.90 in the endometrial carcinoma group (P<0.001). Table 3 shows the diagnostic performance of the vascular parameters. The areas under the curve of the ROC were 0.98, 0.84, and 0.97 for the VI, FI, and VFI, respectively. Their cutoff values were 4.06%, 29.27, and 1.97, respectively, and sensitivity was 97.0%, 90.6%, and 84.4%, respectively. The specificity was 91.0%, 76.5%, and 94.1%, respectively (table 3). Thus, on the basis of these results, it was reasonably considered that the best predictor for differentiating endometrial carcinoma from uterine parenchyma was the VI, which had a sensitivity of 97.0% and a specificity of 91.0% with an AUC of 0.98 at a cutoff value of 4.06%.

Table 1 The characteristics of participant women

Parameters	Parenchyma lumps Mean (SD)	Endometrial cancer Mean (SD)	P value
No. of women	41	40	0.898
Age	42.27 (9.44)	54.26 (8.5)	<0.001[a]
Age of menarche	13.30 (1.63)	13.93 (1.49)	0.245
No. of pregnancies	2.52 (1.45)	3.45 (1.99)	0.060
No. of parturitions	1.62 (0.82)	2.23 (1.38)	0.056
Hypertension	3	10	0.052
Diabetes mellitus	0	5	0.102

[a]Statistically significant

Table 2 Vascular indices of the two groups

Indices	Parenchyma lumps Mean (SD)	Endometrial cancer Mean (SD)	P value
VI%	1.63 (1.72)	17.11 (11.24)	<0.001[a]
FI	26.21 (8.89)	37.15 (6.46)	<0.001[a]
VFI	0.57 (0.65)	6.90 (5.24)	<0.001[a]

FI: flow index; VI: vascularization index; VFI: vascularization flow index.
[a]Statistically significant

Table 3 Diagnostic performance of the vascular parameters

Parameters	VI (%)	FI	VFI
Cutoff value	4.06	29.27	1.97
AUC	0.98	0.84	0.97
Sensitivity (%)	97.0	90.6	84.4
Specificity (%)	91.0	76.5	94.1

3 DISCUSSION

In accordance with a previous study regarding 3D ultrasound and power Doppler angiography for gynecologic diseases, to the best of our knowledge, this is the first study to assess the clinical value of the lesions dynamic blood flow parameters to discriminate uterine parenchyma lumps (including endometrial polyps and submucosal myomas) from endometrial cancer. In this study, we retrospectively analyzed the blood flow indices of 40 women with endometrial cancer and 41 with uterine parenchyma lumps. Our results indicated that VI, FI, and VFI were significantly higher in the women with endometrial cancer than in those with uterine parenchyma lumps (P<0.001). Furthermore, the AUC values were 0.98, 0.84, and 0.97, respectively, for the VI, FI, and VFI. Thus, the best predictor for discrimination between endometrial carcinoma and uterine parenchyma lumps was the VI (sensitivity of 97.0% and specificity of 91.0%) with an AUC of 0.98 at a cutoff value of 4.06%.

A review of the literature, to a certain extent, parallel with our results, by El-Sharkawy *et al* found that endometrial VI (P<0.001) and VFI (P=0.043) were significantly higher in patients with atypical endometrial hyperplasia and endometrial carcinoma than in those with benign endometrium. The best marker for discrimination between benign and malignant endometrium was the VI with an area under the ROC curve of 0.88 at a cutoff value of 0.81%[10]. Mercé *et al* considered that 3D power Doppler indices were significantly higher in endometrial carcinoma than in endometrial hyperplasia, and the VFI of 2.07 was the best cutoff for predicting endometrial carcinoma, with sensitivity of 76.5% and specificity of 80.8%[11]. Odeh *et al* in a multivariable analysis of the indices (VI, FI, and VFI) between endometrial carcinoma and hyperplasia found that only the endometrial FI was independently associated with endometrial cancer, which differed from our conclusion[12]. Erenel *et al* reported that VOCAL parameters were statistically significantly higher in patients with endometrial cancer

than in those with benign endometrial pathologies with the results of AUC being 0.702, 0.658, 0.706 for VI, FI and VFI respectively[13].

Nevertheless, in contrast to our study, Lieng *et al* did not find differences in 3D power Doppler parameters between women with endometrial cancer and those with endometrial polyps[14].

To the best of our knowledge, when an intrauterine foreign body was found, clinicians preferred to use diagnostic D&C directly. In spite of its comparatively accurate pathological diagnosis, the intrauterine foreign body probably could not be scraped completely because of operational limitations and, more profoundly, the endometrium may be severely and irreversibly damaged during the procedure. In addition, the curettage of malignant tissue causes a risk of massive hemorrhage and cancer metastases. As is well known, the treatments for these two types of diseases completely differ. Both doctors and patients need a secure and reliable method. As a consequence, our study has substantial significance in providing adjuvant evidence and assisting clinicians to properly diagnose patients.

However, there were some limitations to our research. The primary limitation was the relatively little number of recruited patients due to the monocentric nature of this study. Similar to other ultrasound techniques, different operators may achieve varying results. Furthermore, when there is massive necrotic tissue in the cancer nidus, blood flow signals cannot be properly observed, which will unfortunately make this method less valuable. Large and multicenter studies are required to further verify our hypothesis. In summary, 3D power Doppler ultrasound angiography is attracting growing attention as a potential technique to assess substantial antidiastole values between uterine parenchyma lumps and endometrial cancer.

Conflict of Interest Statement

The authors declare there are no conflicts of interest regarding the publication of this paper.

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