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Evaluation of ovarian function using three dimensional ultrasound in perimenopausal women

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ABSTRACT

To evaluate the feasibility and clinical value of three-dimensional ultrasound in evaluating ovarian function in perimenopausal women. In this prospective cohort study, 102 patients with clinically suspected perimenopause and 90 patients with menopause were enrolled. These patients were classified into three groups according to the level of follicle stimulating hormone (FSH) and estradiol (E2): menopause group, perimenopause group, and normal group. Perimenopause group: There were significant differences in volume, vascularization index (VI), flow index (FI), and vascularization-flow index (VFI) in the ovaries after treatment. Cycle 1 > cycle 0 ($p < .05$) and cycle 3 < cycle 0 ($p < .05$) in FSH. Menopause group: There were significant differences in volume, VI, FI, and VFI of the ovaries after treatment: Cycle 3 > cycle 0 ($p < .05$), and in FSH: cycle 3 < cycle 0 ($p < .05$). Three-dimensional ultrasound in ovarian quantitative measurement can objectively reflect the change in the ovarian function, predicting the effect of drug treatment, and provided an objective information for early intervention to menopausal.

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KEYWORDS

Three dimensional ultrasound; quantitative measurement; ovarian function; perimenopausal

Introduction

Perimenopause refers to the period that when a woman is approaching menopause, the period from the time point of the appearance of menopause-related endocrine, physiology, and clinical features to the time point one year after menopause [1]. The starting point is imprecise, while the terminal is clear. During the span before and after menopause, women exhibit discomfort and symptoms in addition to menstrual disturbances, which seriously affect their quality of life and attract extensive attention [2,3]. Treating perimenopausal women as early as possible has a significant effect on health outcomes. Therefore, determining how to detect this at the early stage and slowdown its occurrence has become a research direction. Perimenopause is a sign of ovarian decline, clinical ovarian function assessment does not have an exact quantitative index, and the quantifiable ovarian blood flow assessment under 3D ultrasound only serves as a reference index for ovarian function assessment [4]. Even so, a preliminary study conducted in our institute revealed that quantitatively measured ovarian parameters have a good correlation with the function of ovary ($p < .05$). This specifically means that volume, vascularization index (VI), flow index (FI), and vascularization-flow index (VFI) have a significant negative correlation with the level of follicle stimulating hormone (FSH). However, no correlation was observed with estradiol (E2), confirming the feasibility of the evaluation of ovarian function with ultrasound [5]. On this basis, further research was conducted to determine the feasibility and clinical value of the quantitative measurement of three-dimensional ultrasound in evaluating the effect of medicine replacement therapy for perimenopausal women, and these were compared with serum hormone changes [6].

Materials and methods

Subjects

The patients treated in our hospital had symptoms such as menstrual disorder, including menstrual irregularities, menostaxis, hypomenorrhea, amenorrhea, and so on, or vasomotor disorders and psychiatric symptoms, but were excluded from gynecological organic diseases and cancers. A total of 102 patients had clinically suspected with perimenopause, and the age of these patients ranged within 40–50 years old, with an average age of 46.87 years old. A total of 90 patients had menopause, and the age of these patients ranged within 45–53 years old, with an average of 50.54 years old. This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of our hospital. All participants provided written informed consent.

Study design

These patients were classified into three groups according to the level of FSH and E2: menopause group, perimenopause group, and normal group. Patients were administered with hormone replacement therapy (HRT): in the perimenopause groups patients took 1 mg/tablet/day of Femoston, 28 day for one cycle; in the menopause group patients took 1 mg/tablet/day of E2 and drospirenone tablets, 28 day for one cycle. The VI, FI, and VFI of the ovary were examined by three-dimensional color power angiography (3D-CPA) during the HRT period. All of these interventions were performed by an associate chief physician who has professional qualifications.

Clinical measurements

An expert color Doppler ultrasonic diagnosis apparatus (GE Voluson 730; GE Healthcare, Chicago, IL) with a volume transducer frequency of 3–9 MHz and the VOCAL software in apparatus were used to conduct the routine 2D transvaginal ultrasonography for patients in these two groups during early follicular phase (amenorrhea time unlimited), and relative information were collected. Then, the power Doppler was activated and the 3D function chosen to emphatically observe the ovary, including 3D gray-scale organization information, and the vascular branches and its distribution in the ovary. The ovary was outlined in manual mode with a rotation angle of 15° on each section for 12 times, in order to obtain a complete profile [3]. The three-dimensional ultrasound volume of the ovary was obtained (Figure 1) and the VI, FI, and VFI were analyzed by three-dimensional energy histogram (Figure 2). These were individually measured twice on each side of the ovary and were averaged. The final value was the average of two sides of the ovaries for each parameter. These parameters are repeatedly detected in cycle 1, 2, and 3 after treatment, and were compared with those before medication.

Laboratory grouping

All blood samples were collected from patients during the early follicular phase (amenorrhea time unlimited). Samples with a FSH level of $>40 \mu\text{L}$ and an E2 level of $<73.2 \text{ pmol}$ were assigned into the menopause group, while samples with a FSH level of $10\text{--}40 \mu\text{L}$, the ratio of FSH/luteinizing hormone (LH) of >3.6 and an E2 level of $<43.9 \text{ pmol}$ were assigned into the perimenopause group. The serum FSH levels of these two groups were detected in cycle 1, 2, and 3 after treatment, and compared with the levels before therapy.

Statistical analysis

Each indicator was presented as mean \pm standard deviation, and all original data were imported into the SPSS version 13.0 software (SPSS Inc., Chicago, IL) for statistical analysis. Pearson's correlation test was applied to analyze the correlation of ovarian volume and blood perfusion parameters with laboratory results. Single-factor ANOVA was performed for parameters between groups. $p < .05$ was considered statistically significant.

Results

Comparison of ovarian volume and blood perfusion parameters with laboratory results before and after medication in the perimenopause group

In the perimenopause group, after treatment, there were significant differences in blood perfusion parameters such as VI, FI, and VFI in the ovary in cycle 1, and FSH in cycle 3, while no evident change was observed in the volume of the ovaries, when compared with those before treatment. The details are presented in Table 1.

Comparison of ovarian volume and blood perfusion parameters with laboratory results before and after medication in the menopause group

In the menopause group, after treatment, there were statistical differences in blood perfusion parameters, such as VI, FI, and VFI in the ovary, as well as FSH in cycle 3, while there was no obvious change observed in the volume of ovaries, when compared with those before treatment. The details are presented in Table 1.

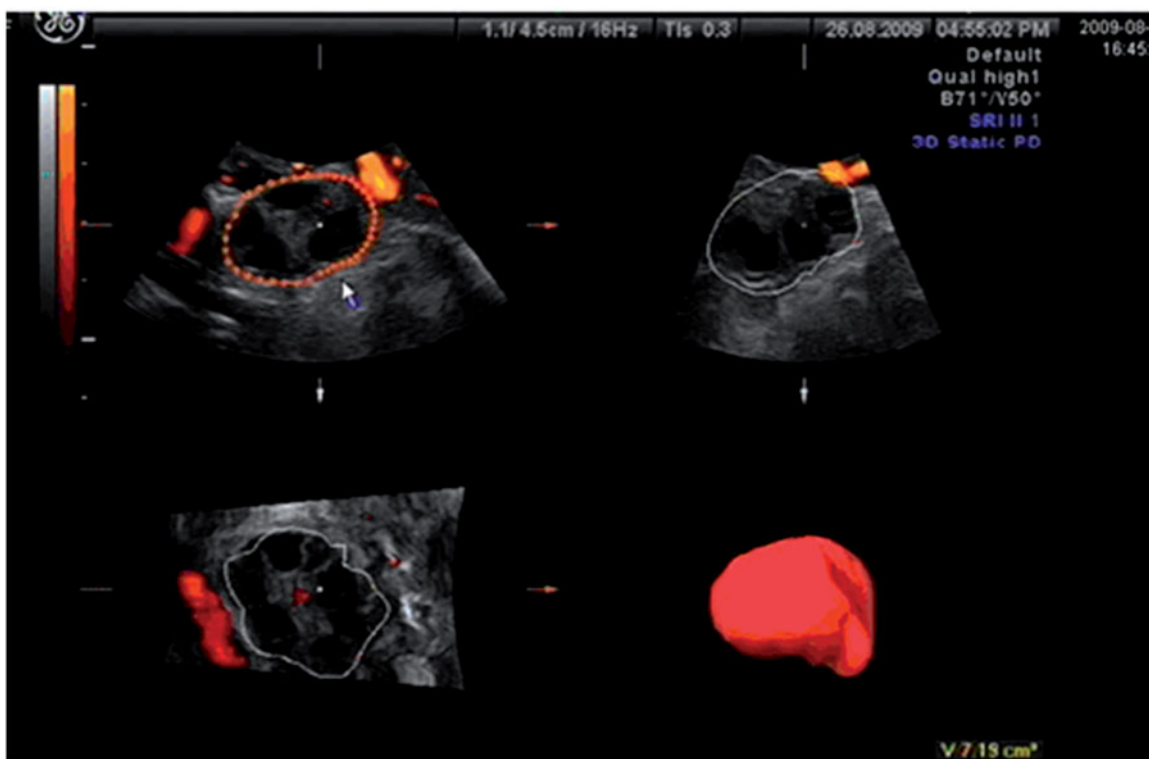


Figure 1. Outline the ovary in manual mode to obtain the 3 D ultrasound volume of ovary.



Figure 2. Vascularization index (VI), flow index (FI), and vascularization-flow index (VFI) of ovarian.

Table 1. Comparison of ovarian volume and blood perfusion parameters with laboratory result before and after medication in perimenopause group and menopause group ($\bar{x} \pm SD$).

Group	Parameters	Before medication	Cycle 1	Cycle 2	Cycle 3
Perimenopause group	VI	1.21 \pm 0.24	1.47 \pm 0.38*	1.66 \pm 0.40*	1.99 \pm 0.42*
	FI	26.60 \pm 3.43	29.00 \pm 2.84*	29.81 \pm 3.26*	30.44 \pm 4.08*
	VFI	0.40 \pm 0.17	0.47 \pm 0.14*	0.57 \pm 0.18*	0.68 \pm 0.21*
	Volume (cm ³)	7.07 \pm 0.42	7.00 \pm 0.58	7.18 \pm 0.52	7.21 \pm 0.54
	FSH (μ L)	23.21 \pm 3.04	22.71 \pm 3.91	22.71 \pm 3.94	21.87 \pm 3.89*
Menopause group	VI	0.76 \pm 0.04	0.76 \pm 0.04	0.77 \pm 0.05	0.80 \pm 0.06*
	FI	20.18 \pm 1.33	20.15 \pm 1.38	20.21 \pm 1.39	20.99 \pm 1.43*
	VFI	0.24 \pm 0.02	0.24 \pm 0.03	0.24 \pm 0.04	0.26 \pm 0.03*
	Volume (cm ³)	3.74 \pm 0.59	3.81 \pm 0.57	3.73 \pm 0.59	3.76 \pm 0.57
	FSH (μ L)	51.67 \pm 4.77	51.43 \pm 4.73	50.92 \pm 5.37	48.36 \pm 6.41*

VI: vascularization index; FI: flow index; VFI: vascularization-flow index.

* $p < .05$, compared with level before medication (single-factor ANOVA).

Discussion

HRT is an irreplaceable therapy for relieving menopausal symptoms, and one of the effective ways to prevent senile chronic disease [7]. At present, there are no effective treatment measures aimed at recovering ovarian function. Therefore, early prevention, identification, and treatment are considerable approaches to slow its progression and relieve clinical symptoms. Perimenopause is in the window period of estrogen application, facilitating the medication in the artificial cycle treatment. This in turn induces a fast effect in significantly improving symptoms, inducing menstruation, preventing genital atrophy, and delaying long-term complications such as osteoporosis, cardiovascular disease, Alzheimer's disease, and so on [8,9].

The starting point of perimenopause is imprecise. Hence, diagnosis is generally made according to the age, ovarian hormone level, and ovarian morphology of the patient. At present, the methods used to detect ovarian reserve function in clinic are

mostly based on the determination of various hormones or the detection of related cytokines, except for the consideration of age factors. In the evaluation of ovarian function, in which laboratory indexes are the gold standard, the most sensitive manifestation is the elevation of serum FSH [10,11]. In fact, some studies have shown that the hemodynamic blood flow of ovaries can reflect the function of ovaries to some extent [2,12], and there is a significant correlation between the blood flow of ovaries and the secretion of sex hormones [13].

With the widespread use of ultrasonographic techniques in the field of assisted reproductive technology (ART), the value of pretesting ovarian reserve function is increasingly reflected [14]. Dogan et al.'s study showed significant differences in ovarian blood flow parameters between ovulating and non-ovulating patients under three-dimensional (3D) ultrasound [15]. Ozdemir et al. and Kamal et al., respectively, use ovarian stromal blood flow indices (VI, FI, and VFI) to evaluate the effects of

laparoscopic ovarian drilling (LOD) and oral contraceptive pill [16,17]. Deb et al.'s study applied 3D ultrasound to quantify the intra cycle variation in markers of ovarian reserve measured by antral follicle counts stratified by size, indicating 3D ultrasound could be an effective way to predict ovarian reserve [18]. A preliminary study in our hospital evaluated the correlation of ovarian volume and the condition of blood perfusion with ovarian function by 3D-CPA combined with VOCAL in 3D ultrasound. It was found that the correlation is relatively close, indicating that ovarian function can be detected and analyzed via three-dimensional ultrasonography.

In conclusion, we advocate the quantitative measurement of ovarian perfusion accompanied with the detection of serum hormone in perimenopause using 3D ultrasound, which is capable of evaluating ovarian function. Meanwhile, ovarian blood detected by 3D ultrasound, which has higher compliance in contrast to the detection of serum hormone levels. It needs more clinical samples to verify this 3D ultrasound method in diagnosing perimenopause, and a systematic clinical evaluation also must be including.

Disclosure statement

The authors of this work have nothing to disclose.

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