经阴道彩色多普勒超声检测卵巢内膜样囊肿患者卵巢间质血流改变的临床价值

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【摘要】 **目的** 探讨经阴道彩色多普勒超声(transvaginal color Doppler ultrasound,TV-CDS)检测卵巢内膜样囊肿患者卵巢间质血流变化的临床价值。**方法** 应用TV-CDS观察60例卵巢内膜样囊肿患者和60例正常妇女卵巢间质动脉血流显像,测定血流动力学参数,进行对比分析。**结果** 卵巢内膜样囊肿卵巢间质动脉血流不丰富,多呈星点状;动脉频谱呈高阻型,阻力指数(resistance index,RI)、搏动指数(pulsatility index,PI)、动脉收缩期峰值流速/舒张末期血流速度值(systolic/diastolic,S/D)均高于正常值,差异有统计学意义($P<0.01$)。病程>1年且囊肿直径≥5 cm是卵巢内膜样囊肿患者卵巢间质动脉血流不易显示的危险因素,其血流显示区域的不同与病程、囊肿直径、囊肿类型(单房或多房)有关($P<0.05$)。**结论** TV-CDS作为一项无创、方便、灵敏的检查方法可用于评价卵巢内膜样囊肿患者的卵巢间质血流变化,提示卵巢内膜样囊肿的病理状态及其对卵巢间质组织的损伤,利于诊治。

【关键词】 彩色多普勒超声; 卵巢内膜样囊肿; 血流动力学

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Clinical value of transvaginal color Doppler ultrasound in the detection of blood flow changes within the ovarian stromal artery in patients with ovarian endometriosis

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【**Abstract**】 **Objective** To explore the clinical value of transvaginal color Doppler ultrasound (TV-CDS) in the detection of blood flow changes within the ovarian stromal artery in patients with ovarian endometriosis. **Methods** Blood flow indices within the ovarian stromal artery were measured by TV-CDS in 60 patients and 60 normal controls. **Results** In ovarian endometriosis group, TV-CDS examination showed the color signal pattern was dot-like with high-resistance ovarian stromal arterial flow which manifested significant higher resistance index (RI), pulsatility index (PI) and systolic/diastolic (S/D) ratio than those in normal group ($P<0.01$). Analysis on clinicopathologic data showed that cystic history and diameter were risk factors affecting the absence of ovarian stromal blood signal, while cystic history, diameter and category were associated with the significant difference of blood flow display area ($P<0.05$). **Conclusions** TV-CDS can be used as a non-invasive, convenient and sensitive method for assessing blood flow changes within the ovarian stromal artery, indicating ovarian interstitial damage as well as pathological conditions of ovarian endometriosis that contributes to clinical diagnosis and treatment.

【**Key words**】 color Doppler ultrasound; ovarian endometriosis; hemodynamics

Ovarian endometriosis, a common and frequent endocrinological disease in women of reproductive age, has recently been the focus of studies for its destruction on ovarian stromal tissues. Clinical diagnosis and

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treatment for the disease turn to be quite difficult as the absence of ideal means to monitor ovarian interstitial damage. Therefore, to search for a safe and non-invasive, quick and easy way to monitor ovarian interstitial damage in ovarian endometriosis is extremely important.

Transvaginal color Doppler ultrasound (TV-CDS), a non-invasive and efficient technique in assessing visualization of small vessels, is a superior way to study blood flow changes in pelvic organs. The investigation of vascular changes assessed by TV-CDS has yield important information on ovaries during the normal menstrual cycle[1] as well as pathological ovarian conditions including polycystic ovary syndrome[2-3], ovarian hyperthecosis[4], hypoestrogenic amenorrhoea[5], ovarian tumors[6-7], *et al*. In addition, it allows the assessment of ovarian endometriosis vascularity. However, there are few published studies on ovarian stromal blood flow changes, especially on ovarian stromal blood flow changes predicting the interstitial damage in ovarian endometriosis[8-9]. Therefore, the aim of our study is to detect ovarian stromal blood flow changes in patients with ovarian endometrioid cysts by using TV-CDS to investigate the changes of ovarian interstitial tissues exerted by ovarian endometriosis, so as to provide evidence for clinical diagnosis and treatment.

Material and Methods

Study group Ovarian endometriosis patients at the age from 26 to 55 years old with cystic history of 1 − 30 months were recruited from those who attended the department of obstetrics and gynecology at the second affiliated hospital of Nantong University from Oct 2008 to Oct 2009. All of them were confirmed by pathology and completed medical records. Exclusion criteria were: (1) smoking; (2) history of any hormonal treatments within the past 3 months; (3) history of any gynecological surgeries; (4) history of endocrine and systemic diseases. Those with ovaries poorly visualized because of abdominal position or an ovarian cyst of 20 mm in diameter on scanning were excluded. Control group was set as healthy women without any history of endocrine diseases and other disorders as well as matched with the age of study subjects.

Informed consent was obtained from all participants after the nature of the procedures had been fully explained to all subjedts. They did not receive any monetary compensation for participation in the study.

TV-CDS examination Philips ultrasound system (Philips IU-22, USA) was equipped with 10 − 15 MHz transvaginal transducer and color imaging as well as pulsed Doppler spectral analysis. In pulsed Doppler mode, the sample volume axial length was set at 1 − 2 mm, and the high pass filter was set at 30 − 50 Hz. A pulsed Doppler range gate was placed across each vessel aiming for an angle of insonation close to 0° between the Doppler beam and the vessel. Spatial peak temporal average intensity was 80 mW/cm^2 on average and pulse repetition frequency was set at 1.5 − 25.0 kHz.

All subjects during their periovulation phase were asked to empty their bladder, normalize blood pressure and pulse rate, and then underwent ultrasound in the lithotomy position between 8:00 and 10:00 am in a quiet and comfortable location. A two-dimensional mode scan was performed to evaluate the shape at first, dimension and morphology of the uterus and ovaries. Then transvaginal color and pulsed Doppler was used to visualize the blood vessels within the ovarian stroma in all subjects, which should be differentiated from vessels adjacent to the follicle or near the ovarian surface. All examinations were performed by the same physician.

Detection items (1) The status of ovarian stromal blood flow imaging were assessed as follows: 0 level indicated the color signal was absent, Ⅰ level indicated the color signal was presented dot-like, Ⅱ level indicated the color signal was belt-like, Ⅲ level indicated the color signal was basket-like. (2) Display area of ovarian stromal blood flow was obtained. (3) After visualization of at least 3 consecutive flow velocity, resistance index (RI) and pulsatility index (PI) were automatically calculated as $RI = (S - D)/S$ and $PI = (S - D)/mean$, in which S was the peak systolic Doppler frequency shift, D was the minimum Doppler frequency shift, and mean was the time-averaged maximum Doppler frequency shift over 1 cardiac cycle. Each sonographic examination and calculations of PI, RI and systolic/diastolic (S/D) ratio lasted approximately 30 minutes. The reproducibility of Doppler measurements was tested in 10 patients by measuring all Doppler parameters for 3 times at 10-minute intervals. The intra-observer coefficients of variation were less than 10% for all of the above-mentioned parameters.

Statistical analysis Data were processed by SPSS 16.0 software. Measurement data and ranked data were compared by Student's *t*-test and Rank sum test, respectively, while numeration data were compared by χ^2 test and Fisher's exact tests when appropriate (expected frequency was less than 5). Unconditional Logistic regression analysis was used for univariate and multivariate data. $P < 0.05$ was considered as statistically significance.

Results

A total of 80 eligible patients and 80 normal woman aged 26－55 years old agreed to participate in the study. They were divided into 3 groups according to their age (group Ⅰ: 26－35 years old; group Ⅱ: 36－45 years old; group Ⅲ: 46－55 years old). Considering the natural decline of stromal flow in normal dominant ovaries (Tab 1), age may be confounding factors in the study of ovarian stromal flow changes caused by ovarian endometriosis. Therefore, subjects in group Ⅲ were excluded from the study. Sixty patients whose average age was (35.5±5.3) years old (26－45 years old) and 60 normal woman whose average age was (35.3±3.1) years old (26－44 years old) were included in the final analysis. No statistical significance was noted in the age between the two groups. According to the ultrasound image, 44 cases had unilateral cysts, 16 cases had bilateral usts, and a total of 76 affected cysts. Among them, 31 cysts were less than 5 cm of diameter, and 10 cysts were polycystic.

Tab 1 Comparison of stromal flow display rate in normal dominant ovaries among different age groups

Group	Normal woman			
	Ovaries (n)	Ovaries		Flow display rate (%)
		With flow	Without flow	
Ⅰ	36	36	0	100
Ⅱ	24	24	0	100
Ⅲ	20	11	9	55(1)(2)

(1) *vs.* groups Ⅰ, $P<0.01$; (2) *vs.* groups Ⅱ, $P<0.01$.

An evident reduction of blood perfusion within ovarian stroma was found in patients compared with controls ($P<0.01$, Tab 2). In ovarian endometriosis patients, dot-like signals (Fig 1A) were registered in 41 affected ovaries and no signal in 25 cases. Whereas in control subjects, color signals were registered in every one with the presence of belt-like or basket-like signals (Fig 1B).

Tab 2 Color Dopper flow imaging of ovarian stromal arteries in the two groups

Group	Affected ovaries (n)	Status of ovarian stromal blood flow (%)				Z	P
		0 level	Ⅰ level	Ⅱ level	Ⅲ level		
Study group	76	25(32.89)	41(53.95)	10(13.16)	0(0.00)	8.81	<0.01
Control group	60	0(0.00)	0(0.00)	16(26.67)	44(73.33)		

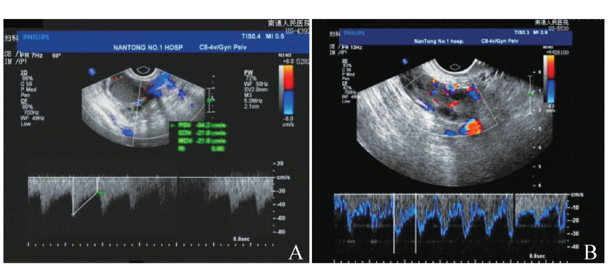

Fig 1 Color Doppler images in the two groups

A: Dot-like color signal image and velocity waveform of the ovarian stromal artery in the ovarian of a patient; B: Basket-like color signal image and velocity waveform of the ovarian stromal artery in the ovary of a normal.

Flow velocity waveforms of ovarian stromal arteries in patients and controls were shown in Fig 1A and 1B, respectively, while vascular indices (Tab 3) manifested significantly higher RI, PI and S/D in patients than those in controls ($P<0.01$).

Statistically significance was occurred in blood flow display rate between the control and ovarian endometriosis groups, in which the display rate was just 67.11% (51/76). Relevant clinicopathologic data were taken for each subject, and parameters (Tab 3) were evaluated: age>35 years old, cystic history>1 year and cystic diameter ≥5 cm were risk factors affecting the absence of ovarian stromal blood signal through forward univariate analysis ($P<0.05$, Tab 4), while cystic history>1 year and cystic diameter≥5 cm were the final significant factors after multivariate analysis of Logistic regression ($P<0.05$, Tab 5), which confirmed age was a confounding factor.

Tab 3 Haemodynamics of ovarian stromal arteries in the two groups ($\bar{x}\pm s$)

Indices	Study group	Control group	t	P
Affected ovaries (n)	51	60		
RI	0.73±0.10	0.59±0.05	8.17	<0.01
PI	1.27±0.25	0.91±0.43	5.27	<0.01
S/D ratio	3.13±0.25	2.56±0.25	11.97	<0.01

Tab 4 Single factorial non-condition Logistic regression analysis in study group

Factors	β(1)	SE(2)	P	OR	95% CI	
					Lower limit	Upper limit
Age (y)	−1.09	0.50	0.03	0.33	0.12	0.89
Cystic history (mo)	−2.53	0.63	<0.01	0.08	0.02	0.27
R-AFS stage						
Ⅲ *vs.* Ⅰ－Ⅱ	−0.97	0.85	0.25	0.38	0.07	1.98
Ⅳ *vs.* Ⅰ－Ⅱ	−1.39	0.87	0.11	0.25	0.05	1.35
Cystic side						
Left side *vs.* right side	−0.42	0.65	0.52	0.66	0.18	2.35
Both sides *vs.* right side	−0.33	0.61	0.58	0.72	0.22	2.35
Cystic diameter (cm)	−1.78	0.61	<0.01	0.17	0.05	0.56
Cystic type	−0.83	0.69	0.23	0.44	0.11	1.67

(1) β: Regression coefficient; (2) SE: Standard error.

Tab 5 Multiple factorial non-condition Logistic regression analysis in study group

Factors	β(1)	SE(2)	Wald	P	OR	95% CI	
						Lower limit	Upper limit
Cystic history (mo)	−3.19	0.75	18.05	<0.01	0.04	0.01	0.18
Cystic diameter (cm)	−2.60	0.77	11.39	<0.01	0.07	0.02	0.34

(1) β: Regression coefficient; (2) SE: Standard error.

Tab 6 shows the significant difference in blood flow display area among 51 affected ovaries with color signals and its relationship with relevant clinicopathologic data. Regarding 0.5 cm adjacent to endometrioid cysts as demarcation line, 15 cases were registered beyond the range (Fig 2A), 25 cases were registered within the range (Fig 2B), and 11 cases were registered at both sites (Fig 2C). The difference was related to cystic history, diameter and polycystic ($P<0.05$).

Tab 6 Blood folw display area and its relationship with relevant clinicaopathologic data

Factors	Affected ovaries (n)	Both(1) (%)	Within the range (%)	Beyond the range (%)	χ^2	P
Age (y)						
≤35	34	10(29.41)	16(47.06)	8(23.53)	4.19	>0.05
>35	17	1(5.88)	9(52.94)	7(41.18)		
Cystic history (mo)						
≤12	36	11(30.56)	21(58.33)	4(11.11)	19.33	<0.01
>12	15	0(0.00)	4(26.67)	11(73.33)		
R-AFS stage						
Ⅰ－Ⅱ	11	5(45.45)	5(45.45)	1(9.09)	5.42	>0.05
Ⅲ	25	4(16.00)	13(52.00)	8(32.00)		
Ⅳ	15	2(13.33)	7(46.67)	6(40.00)		
Cystic side						
Right side	16	4(25.00)	6(37.50)	6(37.50)	8.74	>0.05
Left side	14	0(0.00)	11(78.57)	3(21.43)		
Both sides	21	7(33.33)	8(38.10)	6(28.57)		
Cystic diameter (cm)						
<5	27	11(40.74)	4(14.81)	12(44.44)	29.71	<0.01
≥5	24	0(0.00)	21(87.50)	3(12.50)		
Cystic type						
Monocystic	46	10(21.74)	25(54.35)	11(23.91)	6.89	<0.05
Polycystic	5	1(20.00)	0(0.00)	4(80.00)		

(1) The range of 0.5 cm adjacent to endometrioid was set as demarcation line.

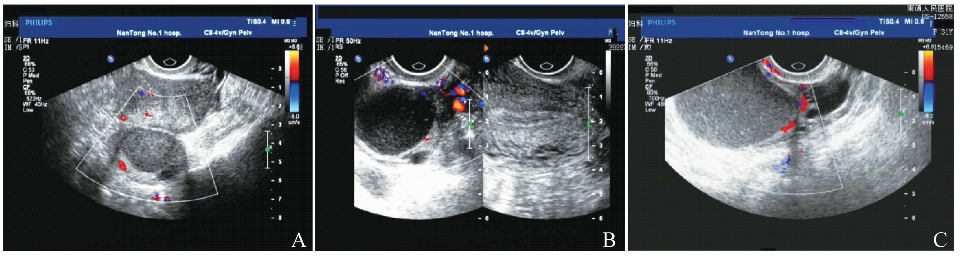

Fig 2 Ovarian stromal blood flow display area in patients with ovarian endometriosis

A:Blood flow signals just registered beyond the area of 0.5 cm adjacent to the ovarian endometrioid cyst; B:Blood flow signals just registered within the area of 0.5 cm adjacent to the ovarian endometrioid cyst; C:Blood flow signals registered beyond and within the area adjacent to the ovarian endometrioid cyst.

Discussion

TV-CDFI, more sensitive to low flow, has been used in clinical practice for several years for the advantage of showing blood flow information, and analyzing blood flow characteristics of small vessels based on traditional gray-scale images. It produces a series of parameters including PI, RI and S/D ratio. Since obtaining an angle between the ultrasound beam and ovarian stromal vessels is difficult, it is possible that blood flow velocities may be inaccurate except for PI, RI and S/D ratio because they are evaluated in terms of the ratio of velocity, the minimization of the dependence on the angle and the increase of the credibility and repeatability. By color Doppler detection, if PI, RI and S/D ratio are low, the flow resistance would also be low, which indicates a good blood perfusion and vice versa. The key of color Doppler detection in this research was to identify ovarian stromal vessels, which should be differentiated from not only vessels adjacent to the follicle or near the ovarian surface but also vessels beyond the ovary including ovarian branches of uterine artery, iliac artery and mesenteric vessels according to their different anatomy and Doppler spectrum waveforms.

The ovarian vascular bed is constituted by two vascular systems: one is the extrinsic system which is represented by the ovarian artery and the uterine-ovarian artery, and the other is the intrinsic system which is formed by the vascular network inside the stroma and supported by double supply both from the ovarian artery and ovarian branch. In addition, two kinds of vascular distribution, unspiral type and spiral type, can be observed in the hilum of an ovary. The former shows one or a few small blood vessels directly enter into the ovaries without hovering or distortion, while the latter manifested an initial hovering before entering into the ovaries. Vascular distribution in the ovarian parenchyma may be different due to different vascular pathophysiology. In patients with ovarian endometriosis, ovarian interstitial fibrosis makes a reduced stromal vascular network as well as a decreased vascular compliance, which contributes to an increased blood flow resistance and a reduced blood perfusion. Besides, an ovarian endometrioid cyst, no matter an invaginated pseudo-sac[10-11] formed by endometrial metaplasia or endometrial tissues planted on the ovarian surface or a cyst deriving from stem cells within endometrial fragments based on theories of origination in recent researches[12-13], has the biological characteristics involving the infiltration into ovarian cortex, the destruction on ovarian tissues and the invasive growth. With the progression of ovarian endometriosis, the endometrioid cyst keeps invading deep seated ovarian tissues and squeezing functional ovarian structure as well as stromal blood vessels, which resultes in a significant low blood flow display.

In our study, outstanding modifications of the color Dopple features and hemodynamic profiles such as inaffluent blood supply, low blood flow display rate and higher RI, PI and S/D ratio actually reflected the pathophysiological changes of ovarian endometriosis, which demonstrated that functional stromal tissues and vessels surrounding ovarian endometrioid cysts had been damaged. It is possible that these changes can be used as markers to monitor the pathological state of ovarian endometriosis, so as to optimize the diagnosis owing to their approximation to histopathologic analysis.

Analysis of relevant clinicopathologic factors showed that cystic history and diameter were risk factors affecting the absence of ovarian stromal blood signal, which can be considered as warnings for ultrasound doctors and clinicians. It suggested that once these risk factors are monitored, early diagnosis and treatment are of great significance. The difference of blood flow display area was detected, and the most significance is that no color signals could be registered within the area of 0. 5 cm adjacent to the cysts in patients with mostly over 1-year history or polycystic cysts, which implies the wide damage of functional tissues and vessels within the 0. 5 cm area as well as the severity of the disease. Accordingly, for patients suffering from ovarian endometrioid cysts, active treatment instead of waiting for a bigger cyst is of great importance to controlling the disease in the early stage. Early treatment is also deserved for patients with polycystic cyst.

TV-CDS is a superior way to detect ovarian endometriosis. At first, it can not only enrich examination items but also improve the diagnostic level by increasing the information of blood flow and detecting hemodynamic parameters on the basis of its morphology. Secondly, it can avoid the interference from obesity, breathing, abdominal gas and blood vessels pulse. In our study, TV-CDS, the combination of transvaginal ultrasound and color Doppler as well as the combination of ultrasound images and traditional pathophysiology, may contribute to a better understanding in the complex pathological changes of this disorder including its interstitial damage, which provides a reliable theoretical basis for early diagnosis and treatment.

In conclusion, TV-CDS is proved to be non-invasive and convenient, and deserves further clinical applications in assessing ovarian stromal blood flow changes in patients with ovarian endometrioid cysts.

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