

Application of Transvaginal Three-Dimensional Ultrasound in Assessing Endometrial Receptivity in Patients with Ovulation Disorder Infertility and the Impact on Subendometrial Vascular Index (VI) and Vascular Flow Index (VFI) Level

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Abstract: *Objective:* To analyze the diagnostic value of transvaginal three-dimensional ultrasound (3D-TVS) in evaluating endometrial receptivity (ER) for ovulation disorder infertility (ODI), and to investigate the impact of subendometrial endometrial vascular index (VI) and endometrial vascular flow index (VFI) levels on ODI. *Methods:* A total of 110 patients diagnosed with ODI admitted between January 2023 and June 2024 were selected. All patients underwent ovulation induction therapy, 3D-TVS examination, and sex hormone testing. Based on pregnancy outcomes, patients were divided into a successful pregnancy group (73 cases) and an unsuccessful pregnancy group (37 cases). ER parameters, sex hormone levels, and endometrial blood flow patterns were compared between the two groups. Receiver operating characteristic (ROC) curves were plotted to evaluate the predictive value of ER for ODI. *Results:* The spiral artery peak systolic velocity (PSV), endometrial volume (EMV), endometrial flow index (FI), and VFI in the successful pregnancy group were significantly higher than those in the unsuccessful pregnancy group ($p < 0.05$). No significant differences were observed in other ER parameters between the two groups ($p > 0.05$). There was no significant difference in sex hormone levels between the two groups on the day of human chorionic gonadotropin (hCG) treatment ($p > 0.05$). Among the endometrial blood flow classifications in the pregnant group, the proportion of Type II was lower than that in the non-pregnant group ($p < 0.05$). The Receiver Operating Characteristic (ROC) curve demonstrated that the area under the curve (AUC) for Endometrial Volume (EMV) in predicting pregnancy after Ovarian Dysfunction Infertility (ODI) treatment was 0.854, with a sensitivity of 92.61% and a specificity of 71.75%. The AUC for Vascularization Index (VI) was 0.771, with a sensitivity of 52.18% and a specificity of 88.70%. The AUC for Vascularization Flow Index (VFI) of the endometrium was 0.887, with a sensitivity of 80.01% and a specificity of 69.20%. *Conclusion:* Three-dimensional transvaginal sonography (3D-TVS) assessment of endometrial receptivity (ER) can effectively detect ODI, and the levels of subendometrial VI and VFI demonstrate superior predictive performance for pregnancy outcomes in this condition, serving as commonly used predictive indicators for the disease.

Keywords: Transvaginal three-dimensional ultrasound; Endometrial receptivity; Ovarian dysfunction infertility; VI; VFI

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1. Introduction

Ovarian dysfunction infertility (ODI) is a type of infertility caused by abnormal ovarian ovulation function, commonly accompanied by manifestations such as amenorrhea and endocrine disorders. It requires standardized ovulation induction therapy to expel mature follicles and enable successful pregnancy in patients ^[1]. Endometrial receptivity (ER) is a primary factor influencing pregnancy outcomes in ODI. It evaluates endometrial morphology and thickness, as well as the characteristics of endometrial blood flow distribution, thereby reflecting the endometrium's ability to accept an embryo ^[2]. At present, transvaginal three-dimensional ultrasound (3D-TVS) is a commonly used method for evaluating endometrial receptivity (ER) status. It offers the advantages of being non-invasive and repeatable, enabling accurate prediction of patients' pregnancy outcomes using ER parameters and demonstrating good diagnostic performance. Based on this, this study selected 110 patients with ovulation disorders and infertility (ODI) to analyze the predictive value of 3D-TVS-assessed ER for pregnancy outcomes.

2. Materials and methods

2.1. General information

A total of 110 patients diagnosed with ODI who were admitted to the hospital between January 2023 and June 2024 were selected for this study. This study was approved by the hospital's ethics committee. The patients were grouped according to their pregnancy status. The pregnancy group consisted of 73 patients, aged between 27 and 37 years, with a mean age of (32.15 ± 2.81) years; the duration of infertility ranged from 1 to 4 years, with a mean of (2.54 ± 0.97) years; the causes of ovulation disorders included 40 cases of polycystic ovary syndrome (PCOS) and 33 cases of premature ovarian failure (POF). The non-pregnancy group consisted of 37 patients, aged between 25 and 39 years, with a mean age of (32.38 ± 2.91) years; the duration of infertility ranged from 1 to 5 years, with a mean of (2.66 ± 0.86) years; the causes of ovulation disorders included 22 cases of PCOS and 15 cases of POF. There were no significant differences in the basic information between the two groups ($p > 0.05$).

2.1.1. Inclusion criteria

Normal sexual activity without contraception, failure to conceive for more than one year; unilateral or single-sided patency shown by hysterosalpingography; meeting the indications for ovulation induction therapy; normal menstrual cycle and volume; presence of dominant follicle development; normal semen analysis of the spouse; consistent ovulation induction protocols among patients; complete basic information; informed consent and agreement to participate in the study.

2.1.2. Exclusion criteria

Use of progestogens or estrogens in the past three months; previous treatment with ODI for symptomatic relief; concurrent uterine pathologies such as fibroids; history of allergy to ovulation induction drugs; developmental abnormalities of the reproductive organs; presence of psychiatric disorders; withdrawal from the study midway.

2.2. Methods

Patients underwent ovulation induction therapy on the 5th day of menstruation, taking oral clomiphene citrate capsules at a dose of 50 mg once daily until the 10th day of menstruation. Color Doppler ultrasound was used to measure endometrial thickness (EMT) in the longitudinal section of the uterus, identifying the point perpendicular to the midline of the uterine cavity between the anterior and posterior myometrium, and assessing the maximum

distance from this point to the endometrial interface, i.e., the maximum perpendicular endometrial distance. Pulse Doppler was employed to measure the peak systolic velocity (PSV) and end-diastolic velocity (EDV) of the spiral arteries at sites with prominent endometrial color flow. In 3D mode, endometrial volume data were evaluated. Simultaneously monitor the uterine blood supply status and follicular development.

When a dominant follicle is identified and its diameter is ≥ 18 mm, collect fasting venous blood (3 mL), centrifuge it for 10 minutes at a speed of 3000 r/min, extract the supernatant, and evaluate the levels of estradiol (E2) and progesterone (P) using the chemiluminescence immunoassay method. On the same day, administer human chorionic gonadotropin for injection via intramuscular injection at a dose of 5000 to 10000 U. After the injection, perform a 3D-TVS examination with a probe frequency of 9 MHz and a scanning angle of 146°. Have the patient assume the lithotomy position, fully expose the external genitalia, apply a sterile protective sheath to the probe, disinfect the sheath with a disinfectant, and slowly insert it into the vagina. Conduct a comprehensive scan in the three-dimensional volume imaging mode, analyze and process the images using the Vocal software provided with the instrument, and automatically obtain ER parameters such as VI.

2.3. Observation indicators

(1) ER parameters

Evaluate parameters such as EMT, spiral artery PSV, and EDV in both groups of patients.

(2) Sex hormone levels

Evaluate the sex hormone levels in both groups on the day of hCG treatment.

(3) Endometrial blood flow classification

According to the Applebaum classification method, Type I is characterized by blood vessels traversing the hypoechoic band on the lateral side of the endometrium without reaching the hyperechoic margin; Type II is characterized by blood vessels traversing the hyperechoic margin of the endometrial region without reaching the hypoechoic area; Type III is characterized by blood vessels traversing the hypoechoic area of the endometrial region.

(4) Predictive efficacy

Draw the ROC curve and calculate the AUC value to evaluate the predictive value of ER parameters for pregnancy status.

2.4. Statistical analysis

Data were processed using SPSS 28.0 statistical software. Count data were expressed as [n/%) and compared using the chi-square (χ^2) test. Measurement data were tested for normal distribution using the Kolmogorov-Smirnov (K-S) test and expressed as ($\bar{x} \pm s$) if they conformed to a normal distribution.

Comparisons between groups were made using the independent samples t -test, while comparisons within groups were made using the paired t -test. The ROC curve was drawn, and the AUC values of each parameter were calculated to evaluate the predictive efficacy. A p -value less than 0.05 was considered statistically significant.

3. Results

3.1. Comparison of ER parameters between the two groups

The peak systolic velocity (PSV), end-diastolic velocity (EMV), flow index (FI), and vascularization flow index

(VFI) of the spiral arteries in the pregnancy group were higher than those in the non-pregnancy group ($p < 0.05$). There were no significant differences in other endometrial receptivity (ER) parameters between the two groups ($p > 0.05$) (refer Table 1).

Table 1. Comparison of ER parameters between the two groups ($\bar{x} \pm s$)

Group	n	EMT (mm)	Spiral artery PSV (cm/s)	Spiral artery EDV (cm/s)	EMV (cm ³)	FI (%)	VI (%)	VFI (%)
Pregnant group	73	9.01 ± 1.78	6.05 ± 1.03	2.67 ± 0.97	3.8 ± 0.9	22.96 ± 1.86	37.51 ± 5.92	5.40 ± 0.61
Non-pregnant group	37	8.69 ± 1.82	5.16 ± 1.05	2.57 ± 0.95	3.1 ± 0.8	21.17 ± 1.90	38.16 ± 5.97	4.62 ± 0.53
<i>t</i>	-	0.884	4.254	0.514	3.996	4.735	0.543	6.612
<i>p</i>	-	0.379	< 0.001	0.608	< 0.001	< 0.001	0.589	< 0.001

3.2. Comparison of sex hormone levels between the two groups

There were no significant differences in sex hormone levels on the day of hCG treatment between the two groups ($p > 0.05$) (refer Table 2).

Table 2. Comparison of sex hormone levels between the two groups ($\bar{x} \pm s$)

Group	n	E2 (pmol/L)	P (nmol/L)
Pregnant group	73	3581.79 ± 305.71	2.85 ± 0.97
Non-pregnant group	37	3625.48 ± 297.84	3.02 ± 0.94
<i>t</i>	-	0.714	0.877
<i>p</i>	-	0.477	0.382

3.3. Comparison of endometrial blood flow patterns between the two groups

The proportion of Type II endometrial blood flow in the pregnancy group was lower than that in the non-pregnancy group ($p < 0.05$) (refer Table 3).

Table 3. Comparison of endometrial blood flow patterns between the two groups [n/%]

Group	n	Type I	Type II	Type III
Pregnant group	73	30 (41.10)	20 (27.40)	23 (31.51)
Non-pregnant group	37	7 (18.92)	21 (56.76)	9 (24.32)
<i>c²</i>	-	9.704		
<i>p</i>	-	0.008		

3.4. Predictive efficacy of ER parameters for pregnancy after ODI treatment

The receiver operating characteristic (ROC) curve showed that the area under the curve (AUC) for EMV in predicting pregnancy after ODI treatment was 0.854, the AUC for endometrial vascularization index (VI) was 0.771, and the AUC for endometrial VFI was 0.887.

Table 4. Predictive efficacy of ER parameters for pregnancy after ODI treatment

Index	AUC	95% CI (AUC)	Cut-off value	Sensitivity (%)	95% CI (Sensitivity)	Specificity (%)	95% CI (Specificity)
Endometrial volume (EMV)	0.854	0.761–0.927	5.2 cm ³	92.61%	85.34–97.05	71.75%	61.54–80.62
Endometrial vascularization index (VI)	0.771	0.664–0.858	7.510%	52.18%	41.55–62.78	88.70%	80.51–94.23
Vascularization-flow index (VFI)	0.887	0.791–0.946	1.990	80.01%	72.64–86.17	69.20%	58.67–72.45

4. Discussion

The etiology of ODI is complex, encompassing hypothalamic-pituitary dysfunction such as excessive anxiety and hyperprolactinemia; ovarian dysfunction such as polycystic ovary syndrome or premature ovarian failure; and endocrine gland disorders such as thyroid dysfunction ^[3,4]. Its symptoms include oligomenorrhea and amenorrhea, making it a common type of infertility. The key factors for successful embryo implantation in ODI patients are the quality of the ovulated follicles and embryos, as well as the embryo implantation environment. ER is an important indicator affecting the uterine environment, manifesting at levels such as EMT or EMV, while also reflecting the blood supply status of the endometrium. Previous studies have indicated that alterations in ER are a prerequisite for embryo implantation, as the endometrium and embryo are in a synchronous developmental state, and EMT and endometrial blood supply directly influence placental development ^[5]. Based on this, improving ER status is necessary when administering assisted reproductive technology treatments to ODI patients to enhance the successful pregnancy rate. Currently, endometrial biopsy is the gold standard for ER evaluation, but it is costly, invasive, and has limited patient acceptance. Therefore, 3D-TVS examination can be conducted to observe uterine structure, blood flow distribution, and vascular characteristics using blood flow energy signals. This method is highly sensitive in detecting low-velocity blood flow and small blood vessels within the uterine cavity, offering high accuracy in ER assessment and the advantage of being non-invasive ^[6].

To fully evaluate the independent predictive value of transvaginal three-dimensional ultrasound parameters for pregnancy outcomes, this study will elaborate on potential confounding factors such as age, BMI, duration of infertility, and ovulation induction protocols in the general information and inclusion/exclusion criteria. After effectively controlling for these factors, relevant research will be conducted. The results revealed that the spiral artery peak systolic velocity (PSV), endometrial motion velocity (EMV), flow index (FI), and vascularization flow index (VFI) were significantly higher in the pregnant group compared to the non-pregnant group ($p < 0.05$). The analysis suggests that following ovulation, the ovaries secrete substantial amounts of progesterone, and successful implantation leads to a marked increase in hCG levels, forming the corpus luteum of pregnancy, which in turn increases estrogen and progesterone secretion. Under these conditions, blood vessels dilate significantly, reducing tension in the uterine spiral arteries and inhibiting vascular resistance, thereby accelerating PSV and increasing blood flow parameters such as FI and VFI ^[7]. High VFI indicates a large volume of endometrial blood perfusion and a dense microvascular network, providing essential nutrients like amino acids and oxygen for embryo implantation, thereby enhancing embryo survival rates. Additionally, high VFI facilitates the clearance of metabolic byproducts such as lactic acid and carbon dioxide from the embryo through high blood flow,

stabilizing the uterine microenvironment, preventing the accumulation of harmful substances, and ultimately improving pregnancy success rates. There were no significant differences in sex hormone levels on the day of hCG treatment between the two groups ($p > 0.05$). The proportion of endometrial blood flow type II was lower in the pregnant group compared to the non-pregnant group ($p < 0.05$). The reasons for the analysis are as follows: Ovulation induction therapy can create a relatively ideal hormonal environment, ensuring the maturity of follicular development. After treatment, the number and size of follicles exhibit standardized characteristics, enabling the sex hormones of patients in both groups to reach similar levels. In contrast, the endometrial blood vessels in the successful pregnancy group often undergo remodeling reactions, which increase blood perfusion and advance blood flow distribution to Type III. Consequently, the proportion of Type II blood flow is relatively low in this group ^[8]. Comparatively, the non-pregnant group exhibits higher vascular resistance, leading to blood stagnation below the endometrium and resulting in Type II blood flow ^[9]. The ROC curve demonstrates that the AUC value of EMV for pregnancy after ODI treatment is 0.854, the AUC value of endometrial VI is 0.771, and the AUC value of endometrial VFI is 0.887. Among the specific indicators, EMV can assess endometrial volume, VI can evaluate endometrial vascular density under three-dimensional ultrasound, and can assess the vascular density distributed within the endometrial volume. VFI can assess the blood flow intensity and specific quantity of endometrial blood vessels, as well as evaluate tissue blood cell density and vascularization. These three indicators can accurately predict changes in ER. Specifically, the higher the levels of EMV, endometrial VI, and VFI, the higher the likelihood of successful pregnancy in patients ^[10]. However, it should be noted that the quality of 3D ultrasound in evaluating ER is influenced by factors such as the operator's expertise and the adjustment of equipment parameters. Therefore, it is necessary to select highly experienced operators and standardize equipment parameter settings to ensure the accuracy of ER parameters. Nevertheless, this study has certain limitations, including a small sample size, a relatively short research duration, and a lack of a control group consisting of normal pregnancies. In future research, it would be beneficial to categorize the etiologies and disease types of patients with this condition more meticulously, expand the sample size, extend the research period, and conduct multi-center studies to fully leverage the diagnostic advantages of 3D-TVS. Additionally, AI technology holds immense potential in imaging analysis. Future studies could incorporate AI algorithms to automatically segment the endometrium, quantitatively extract imaging features, and establish AI learning models based on clinical data, enabling earlier assessment of ER parameters.

5. Conclusion

In summary, 3D-TVS can effectively evaluate ER parameters in patients with ODI and predict pregnancy outcomes in these patients by utilizing EMV, endometrial VI, and VFI levels, demonstrating certain predictive efficacy. It can serve as a preferred predictive indicator for patients with ODI, but its predictive value for other types of ODI patients still requires further validation.

Disclosure statement

The author declares no conflict of interest.

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