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Evaluation of the role of three-dimensional ultrasound and power Doppler in prediction of endometrial receptivity in ICSI patients

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Abstract
Background: The procedures for assisted reproductive technologies (ART) are constantly advancing to improve conception rates, reduce the occurrence of multiple births, and ensure the delivery of healthy children from individuals with genetic conditions. This study set out to assess the parameters of three-dimensional ultrasonography and power Doppler angiography (3D US-PDA). as a possible pregnancy predictors and implantation markers on day of human chorionic gonadotropin (hCG) injection in an intracytoplasmic sperm injection (ICSI) and embryo transfer program.
Methods: 40 patients, ranging in age from 25 to 40, participated in this prospective study, females, with normal basal follicle-stimulating hormone (FSH) level (<10 mUI/mL), good quality embryos and infertility is due to male factor or tubal factor undergoing ICSI. Induction of ovulation [All participants in this trial underwent ovarian stimulation using an oral contraceptive pill regimen consisting of 0.1 mg of Decapeptyl with human menopausal gonadotrophin.] are assed to all patients.
Results: The area under the curve (AUC) for 3D US-PDA parameters was statistically significant; however, their values for predicting endometrial receptivity in ICSI were only suggestive and not conclusive. Patients with endometrial volume (EV) greater than or equal to 5 ml had a group application with 80% sensitivity and 64% specificity; an individual application had a predictive negative value of 84.2% and a predictive positive value of 57.1%. The values of EV, Flow Index (FI), Vascularization index (VI), and Vascularization FI were notably diminished in the group that was not pregnant compared to the group that was expectant.
Conclusions: When evaluating endometrial receptivity in IVF/ICSI and embryo transfer cycles, 3D US-PDA is a helpful test. Pregnancy can be predicted using the EV and 3D power Doppler indexes on the day of hCG injection, particularly if no grade 1 or just one grade 1 embryo is to be transferred.

Keywords: 3D US, power Doppler, endometrial receptivity, Icsi patients

Introduction

The methodologies used in ART have seen significant advancements subsequent to the inaugural successful *in vitro* fertilization (IVF) birth in 1978. Currently, there are tools that facilitate the identification of embryos with superior quality and the evaluation of the condition of the endometrium. In addition, there is ongoing development in ART procedures with the objective of attaining improved rates of conception, reduced instances of multiple births, and the delivery of healthy offspring from genetically compromised individuals. Nevertheless, although these advancements, the rates of pregnancy remain quite modest and have not seen substantial growth over the last decade. This implies that the rates of implantation in cycles that are stimulated continue to be less than ideal [1].

The process of embryo implantation has significant importance in both natural and assisted human reproduction. The process of blastocyst implantation is a complex and dynamic phenomenon that encompasses many key stages, including embryo apposition, attachment to the maternal endometrial epithelium, and penetration into the endometrial stroma [2]. Implantation failure in the context of *in vitro* fertilization (IVF) may arise from several variables, one of which is suboptimal embryo quality. This particular issue has been recognized as a significant contributor to the occurrence of implantation failure [3].

The evaluation of endometrial receptivity may be conducted using many methods, including histological study of an endometrial biopsy, analysis of endometrial proteins in uterine flushes, or the more often used noninvasive ultrasonography assessment of the endometrium [4].

Angiogenesis is a crucial factor in several female reproductive processes, including the maturation of a dominant follicle, the production of the corpus luteum, the expansion of the endometrium, and the process of implantation. Due to this rationale, a considerable amount of research has focused on the examination of ovarian and endometrial vascularization as a means of predicting outcomes in *in vitro* fertilization (IVF) programs [5].

The adequacy of endometrial blood flow is indicative of uterine receptivity due to the fact that the endometrium serves as the location for embryonic implantation [6]. A considerable decrease in the chance of a successful implantation is linked to the absence of colour Doppler imaging in the endometrial and subendometrial areas. Conversely, the likelihood of pregnancy improves when blood vessels can be seen extending into the sub endometrial halo and the endometrium. The assessment of ultrasound parameters related to the endometrium and the examination of blood flow in the uterus and endometrium have been widely regarded as indicators of implantation in *in vitro* fertilization (IVF) and embryo transfer procedures [7].

The use of 3D US-PDA offers the distinct benefit of concurrently evaluating both the blood flow inside the endometrium and the volume of the endometrium (EV) [8].

The aim of this research was to evaluate the potential of 3D US-PDA parameters as predictors of pregnancy and indicators of implantation on the day of hCG injection in the embryo transfer program and *in vitro* fertilization technique known as ICSI.

Materials and Methods

40 patients, ranging in age from 25 to 40, participated in this prospective study, females, with normal basal FSH level (<10 mUI/mL), good quality embryos and infertility is due to male factor or tubal factor undergoing intracytoplasmic sperm injection (ICSI). The research was conducted with the ethical sanction of the Maternity Hospital Ethical Committee of Ain Shams University in Cairo, Egypt. The patient provided written consent that was informed.

Patients older than forty years, those with evident uterine pathology such as endometrial polyps or synechia, those with prior uterine scarring, and those who were smokers were excluded. All patients were subjected to: history taking and induction of ovulation [the ovarian stimulation protocol, used in this study for all patients, was oral contraceptive pills - Decapeptyl, 0.1 mg plus human menopausal gonadotrophin].

Prior to undergoing ovarian stimulation therapy, patients were directed to begin using oral contraceptive pills on day 3 of the previous cycle. Subsequently, a standard regimen of triptorelin, a GnRH agonist (Decapeptyl, 0.1 mg, Fering, Kiel, Germany), was administered subcutaneously at a daily dose of 0.1 mg beginning six days prior to the expiration of the oral contraceptive pills. This dosage was maintained until the day of hCG administration. Subsequently, controlled hyperstimulation with human menopausal gonadotrophin (HMG, 75 IU FSH level (<10 mUI/mL) and 75 luteinizing hormone (LH); Menogon, Ferring, Kiel, Germany) administered intramuscularly beginning on the second day of the stimulated cycle and continuing until more than three follicles reached an 18–22 mm diameter.

Folliculometry and Doppler study: In order to evaluate follicular growth, serial ultrasound examinations were performed on all patients in the ART Unit utilizing a transvaginal probe operating at 7.5 MHz on a Mindray DP 8800 ultrasound machine. All ultrasound examinations and measurements were conducted by the same observer on the day of hCG administration using the ACCUVIX XQ 800 digital platform.

Color voxels dominate the vascularization index (VI) (total voxels minus background voxels).

FI = weighted color voxels divided by the number of color voxels.

VFI is calculated as follows: Weighted color voxels divided by (total voxels minus background voxels).

Oocyte retrieval

The patient presented to the assisted conception unit 34-36 hours after HCG administration on the morning of the procedure. Oocyte retrieval was accomplished using a suction catheter during transvaginal guided aspiration of follicles while under general anesthesia.

Embryo transfer

The process of evaluating fertilized ovaries typically occurs during a timeframe of 2 to 3 days after oocyte extraction, specifically when the oocytes have progressed to a minimum of either a 4-cell or 8-cell stage. The evaluation of embryo quality was conducted based on the identification of nuclear fragments.

Embryo transfer scoring

1. The first symbol (digit) represented the numerical value of the quantity of cells.
2. The second symbol, denoted by a letter, represents the many structural characteristics of blastomeres, including symmetric blastomeres, clearly asymmetric blastomeres, and cytoplasmic defects.
3. The third sign, denoting a number, pertains to the degree of fragmentation seen. This includes categories such as no fragmentation, fragmentation below 20%, fragmentation ranging from 20% to 50%, and fragmentation above 50%.

The procedure of embryo transfer was performed without the administration of anesthesia, while the patient was positioned in lithotomy. A minimum of two high-quality embryos, namely a grade 1 and grade 2, were transferred using the Labotect transfer catheter.

Luteal phase

The use of supported vaginal progesterone, namely Cyclogest manufactured by Cox Pharmaceuticals in Barnstaple, UK, is advocated. On the day of embryo transfer.

A pregnancy test

The procedure was completed 14 days after the transfer of the embryo. In cases where a positive result was obtained, 20 days later, a further ultrasound scan was performed to confirm the intrauterine pregnancy and estimate the number of gestational sacs. Only clinical pregnancies that satisfied the criteria of exhibiting one or more gestational sacs or, in the case of a miscarriage, histological evidence of a gestational product were included in the analysis. The implantation rate refers to the percentage of embryos that were successfully implanted and resulted in the development of an intrauterine gestational sac.

Sample Size Calculation: The Epi Info tool was used to determine the appropriate sample size for a study including forty infertile individuals. The computation was driven by a desired power of the test of 80%, a confidence level of 95%, and an alpha error of 5%.

Statistical analysis: Statistical analysis was performed utilizing SPSS v26, an application created by IBM Inc. headquartered in Chicago, IL, USA. The quantitative variables were represented by the mean and standard deviation (SD), and an unpaired Student's t-test was employed to assess the differences between the two groups with respect to these variables. Qualitative variables were represented using frequency and percentage (%) measures, and their analysis was conducted using the Chi-squared test or Fisher's exact test, as applicable. The estimation of test characteristics was conducted by utilizing the ROC curve. This involved calculating the area under the curve (AUC) and identifying the optimal cutoff value. It was accepted that a two-tailed P value less than 0.05 indicated statistical significance.

Results: Regarding demographic data, the mean age was 29.8±2.9, the mean weight was 30.5±5.8, Regarding past history, 22 (55.0%) patients was laparoscopy, 3 (7.5%) patients was laparotomy.

1 (2.5%) patient was appendectomy, 1 (2.5%) patient had both appendectomy and irrelevant, 13 (32.5%) patients was irrelevant. Regarding Infertility history, the mean duration was 6.4±3.2, it was 1ry in 30 (75.0%) patients, it was 2ry in10 (25.0%) patients, regarding to etiology, it was Tubal in 18 (45.0%) patients, it was due to male in 22 (55.0%) patients, ICSI was presented in 7 (17.5%). Regarding hormonal profile, the mean of E2 was 35.4±11.4, The mean of FSH was 6.3±2.5, The mean of LH was 5.5±3.1, The mean of prolactin was 14.2±6.2. Table 1

Table 1: Hormonal profile, Demographic data and infertility history of studied group

		N=40
Age (years)		29.8±2.9
BMI (kg/m^2)		30.5±5.8
Past history	Laparoscopy	22 (55.0%)
	Laparotomy	3 (7.5%)
	Appendectomy	1 (2.5%)
	D and C	1 (2.5%)
	Irrelevant	13 (32.5%)
Infertility history		
Duration of infertility (years)		6.4±3.2
Type	1ry	30 (75.0%)
	2ry	10 (25.0%)
Etiology	Tubal	18 (45.0%)
	Male	22 (55.0%)
Previous ICSI		7 (17.5%)
Hormonal profile		
E2 (pg/mL) day 3		35.4±11.4
FSH (mIU/mL)		6.3±2.5
LH (mIU/mL)		5.5±3.1
Prolactin (ng/ml)		14.2±6.2

Data are presented as mean ± SD or frequency (%). BMI: Body mass index, ICSI: Intracytoplasmic sperm injection, FSH: Follicle stimulation hormone, LH: luteinizing hormone, E2: Estradiol

3D US-PDA revealed that the mean of EV was 5.3±1.8, the mean of FI was 23.9±2.5, the mean of VI was 18.1±3.2, the mean of vascularization FI was 4.0±2.0. Regarding endometrial pattern, it was triple line in 21 (52.5%) patients, it was non–triple line in 19 (47.5%) patients. Regarding the number of embryos, it was two in 15 (37.5%) patients, it was three in 25 (62.5%) patients. Regarding grade of embryos, it was A1 in 38 (95.0%) patients, it was A2 in 2 (5.0%) patients. Regarding the result of ICSI procedure, it was successful in 15 (37.5%) patients. Table 2

Table 2: Current ICSI procedure, 3D ultrasound and power Doppler angiography parameters and endometrial pattern of the studied sample

		N=40
EV (ml)		5.3±1.8
FI (0-100)		23.9±2.5
VI (%)		18.1±3.2
VFI (0-100)		4.0±2.0
Endometrial pattern	Triple line	21 (52.5%)
	Non–triple line	19 (47.5%)
Current ICSI procedure		
Number of embryos	Two	15 (37.5%)
	Three	25 (62.5%)
Grade of embryos	A1	38 (95.0%)
	A2	2 (5.0%)
Result	Failure	25 (62.5%)
	Success	15 (37.5%)

Data are presented as frequency (%), ICSI: Intracytoplasmic sperm injection, 3D: Three-dimensional, EV: Endometrial volume, FI: Flow Index, VI: Vascularization index, VFI: Vascularization flow index.

In relation to demographic data, infertility history, and levels of FSH, LH, and prolactin, no statistically significant differences were seen between those who were not pregnant and those who were pregnant. The E2 levels were found to be considerably greater in the non-pregnant group compared to the pregnant group. Table 3.

Table 3: Comparison between pregnant and non-pregnant cases as regards infertility history, demographic data and hormonal profile

		Not pregnant (N=25)	Pregnant (N=15)	P
Age (years)		30.2±2.6	29.1±3.2	0.246
BMI (kg/m²)		31.2±5.4	29.5±6.5	0.377
Past History	Laparoscopy	14 (56.0%)	8 (53.3%)	0.343
	Laparotomy	3 (12.0%)	0 (0.0%)	
	Appendectomy	0 (0.0%)	1 (6.7%)	
	D&C	1 (4.0%)	0 (0.0%)	
	Irrelevant	7 (28.0%)	6 (40.0%)	
Infertility history				
Duration of infertility (years)		7.1±3.2	5.3±2.9	0.083
Type	1ry	17 (68.0%)	13 (86.7%)	0.187
	2ry	8 (32.0%)	2 (13.3%)	
Etiology	Tubal	11 (44.0%)	7 (46.7%)	0.870
	Male	14 (56.0%)	8 (53.3%)	
Previous ICSI		3 (12.0%)	4 (26.7%)	0.237
Hormonal profile				
E2 (pg/mL) day 3		38.4±9.6	30.3±12.7	0.027*
FSH (mIU/mL)		6.1±2.8	6.5±1.9	0.635
LH (mIU/mL)		5.0±2.6	6.4±3.7	0.178
Prolactin (ng/ml)		14.4±6.1	13.8±6.4	0.777

Data are presented as mean ± SD or frequency (%). BMI: Body mass index, FSH: Follicle stimulation hormone, LH: luteinizing hormone, E2: Estradiol.

Regarding endometrial pattern, grade of transplanted embryos, and number of transferred embryos, there was actually no significant variations between the non-pregnant and pregnant groups. It was discovered that the non-pregnant group had much lower levels of EV, FI, VI, and Vascularization FI than the pregnant group did. Table 4.

Table 4: Comparison between pregnant and non-pregnant cases as regards Current ICSI procedure, 3D ultrasound and power Doppler angiography parameters and endometrial pattern

		Not pregnant (N=25)	Pregnant (N=15)	P
Number of embryos	Two	10 (40.0%)	5 (33.3%)	0.673
	Three	15 (60.0%)	10 (66.7%)	
Grade of embryos	A1	23 (92.0%)	15 (100.0%)	0.261
	A2	2 (8.0%)	0 (0.0%)	
3D ultrasound and power Doppler angiography parameters				
EV (ml)		4.6±1.4	6.4±1.7	<0.001*
FI (0-100)		23.0±2.1	25.4±2.5	0.002*
VI (%)		17.3±2.9	19.4±3.3	0.040*
VFI (0-100)		3.3±1.6	5.3±2.1	0.002*
Endometrial pattern	Triple line	13 (52.0%)	8 (53.3%)	0.934
	Non–triple line	12 (48.0%)	7 (46.7%)	

Data are presented as mean ± SD or frequency (%), ICSI: Intracytoplasmic sperm injection, 3D: Three-dimensional, EV: Endometrial volume, FI: Flow Index, VI: Vascularization index, VFI: Vascularization flow index.

With 80% sensitivity and 64% specificity, EV ≥5 ml demonstrated the ability to detect uterine receptivity in ICSI patients in a group setting. In an individual setting, it exhibited 57.1% predictive positive value and 84.2% predictive negative value. That means it could be a good way to rule out success. The area under the curve (AUC) for 3D-US-PDA was found to be statistically significant; however, their values were only suggestive and not conclusive in predicting endometrial receptivity in patients undergoing ICSI (i.e., no good diagnostic cutoff points). The only one that did have good value was EV. Figure 1

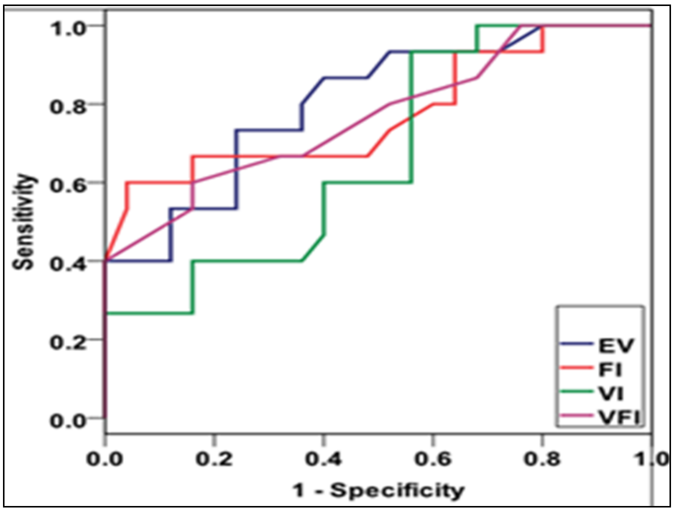

Fig 1: ROC curve for EV, FI, VI and Vascularization FI in prediction of endometrial receptivity in ICSI patients

Discussion

The implantation probability of high-quality embryos in *in vitro* fertilization/embryo transfer (IVF/ET) treatment remains low despite improvements in culture conditions, aided fertilization techniques, and ovarian stimulation regimens. The persistent issue of implantation failure remains an unresolved concern within the domain of reproductive medicine [9]. Effective implantation is predicated on the blastocyst and the receptive endometrium maintaining an intimate conversation. To assess endometrial receptivity, various methodologies have been devised: histologic dating of endometrial biopsies [10], examination of endometrial cytokines in uterine flushing [11], genomic analysis of timed endometrial biopsies, and most frequently, noninvasive ultrasound examination of the endometrium. In comparison to women with lower values, women whose endometrial tissue blood flow was at least 29 mL/min per 100 g of tissue had a considerably higher chance of becoming pregnant (42% versus 15%, respectively, $p<0.05$).

Non-invasive assessment of endometrial blood flow can be achieved through the utilization of two-dimensional (2D) or three-dimensional (3D) ultrasound equipped with color and power Doppler. Power Doppler imaging exhibits enhanced visibility of small vessels due to its greater sensitivity in detecting low velocity flow compared to color Doppler imaging. During the periovulatory phase, Kupesic *et al.* [12] first documented use of transvaginal colour Doppler to evaluate endometrial blood flow. However, there was no correlation between the outcomes and the treatment.

The present study demonstrates that endometrial vascularization, EV, and endometrial morphologic characteristics can be evaluated concurrently using 3D power Doppler indices. It is critical, from a methodological standpoint, to confirm a high degree of interobserver and interobserver reproducibility for every 3D endometrial parameter [13].

Our research findings indicate that the most effective intraclass correlation indices for assessing the EV and endometrial vascularity indexes using the VOCAL software were achieved while operating in the coronal or 'C' plane, with a rotational angle of 9˚. These results align with the findings of Merce *et al.* [14].

We found no evidence of statistically significant differences in endometrial patterns between the non-pregnant and pregnant groups in our investigation.

Even so, the EV was significantly higher among pregnant women. Nevertheless, Previous research has failed to establish a predictive relationship between the EV and pregnancy, which may be attributed to variations in the methodology used for volume computation [15]. The evaluation of the EV was conducted using a non-rotational approach in the studies conducted by Kupesic *et al.* [12] and Wu *et al.* [16].

The thickness of the uterine wall exhibits inter-patient variability. Consequently, if a uniform shell thickness is used, the vessels included inside the sub endometrial zone would exhibit significant variation across patients. This variability undermines the credibility of the obtained findings. In order to objectively define the sub endometrial space, Different percentages would need to be assigned to accommodate for the different uterine wall thicknesses. In contrast, the vascularization of the endometrium is well delineated since it is contained within the boundaries of the Myo endometrial junction.

The findings of the current investigation were consistent with those of a previous study (17) that examined a cohort of eighty women who had *in vitro* fertilization (IVF) cycles. In both studies, the evaluation of the endometrium using three-dimensional ultrasound with power Doppler analysis (3D US-PDA) and the use of VOCAL software yielded similar results. In order to assess the potential of 3D US-PDA measurements of endometrial parameters to predict the outcome of *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI), the findings of this study revealed significant elevations in EV, FI, and VFI among the pregnant group. The findings shown in our study are corroborated by the research conducted by Moustafa *et al.* In their study, they investigated the significance of using 3D power Doppler in predicting pregnancy and implantation outcomes on the day of HCG injection in the context of an intracytoplasmic sperm injection (ICSI) and embryo transfer technique. The researchers observed a significant increase in EV, FI, and VFI among pregnant women in comparison to women who were not pregnant.

In their study, Sini *et al.* [18] conducted an evaluation of the use of three-dimensional power Doppler angiography ultrasonography to forecast the endometrial receptivity in fresh In-Vitro Fertilization (IVF) cycles. The average index of VI (vascularization index) and VFI (vascularization flow index) on the trigger and oocyte retrieval day shown a statistically significant increase in clinically pregnant women compared to non-pregnant women.

The present study observed significant areas under the receiver operating characteristic (ROC) curves for EV (0.803), FI (0.775), and VFI (0.768). However, with regard to VI, no significant difference was observed between the expectant and non-pregnant groups (0.668).

The findings of our study agree with those of Moustafa *et al.* [18], who documented area under the curve (AUC) values of 0.572, 0.562, and 0.904 for EV, FI, and VFI, respectively.

Furthermore, Sini *et al.* [19] provided evidence that the AUC of VFI exhibited a significant predictive capability in predicting receptive endometrium on oocyte retrieval day (0.818) or trigger day (0.813, respectively). In contrast to our findings, they demonstrated that the AUC of VI had a significant predictive value for predicting receptive endometrium on oocyte retrieval day (0.813) or trigger day (0.788).

Furthermore, the findings of the current investigation exhibited partial concurrence with the outcomes reported by Wu *et al.* [16], who assessed the blood flow in the endometrium and sub endometrium on the day after human hCG administration in a cohort of 54 individuals. The pregnant group exhibited a considerably larger endometrial VFI on the day of hCG

administration. However, there were no significant differences in endometrial VI and FI between pregnant and non-pregnant cycles.
The findings of the current study were partially consistent with a previous study, which reported a significant increase in endometrial and sub endometrial flow impedance in pregnant cycles. However, the present study observed no significant differences in endometrial and sub endometrial vascular indices (VI and VFI) between pregnant and non-pregnant patients. These contrasting results contradict the findings of the present study.
Two types of 3D ultrasound were conducted during the study. The first ultrasound was performed after FSH stimulation but prior to hCG administration, while the second ultrasound was conducted on the day of oocyte retrieval, which was 36 hours after hCG administration. In both cycles where conception occurred and cycles where conception did not occur, there was a notable decrease in both endometrial and sub endometrial vascularization between the two ultrasound examinations. This finding aligns with the observations made by Raine-Fenning *et al*. [20] in natural cycles, where they reported a reduction in endometrial vascularity during the periovulatory period. In 525 women undergoing their first IVF cycle, Ng evaluated endometrial and sub endometrial 3D-PDA indices [15]. The results revealed that among several parameters, only the number of embryos replaced and endometrial VI significantly increased the likelihood of conception. However, the predictive value of endometrial VI was only marginal (odds ratio: 0.87, 95% CI: 0.76–0.99).
The incongruity observed in prior published findings may be attributed to various methodological distinctions, most notably concerning the examination period and the VOCAL parameters. Additional factors that may be considered are variations in the study population as well as protocols for embryo transfer and stimulation. The clinical application and interpretation of our results intrigue us, and we await further research to validate our conclusions [17].
Based on our findings, which are consistent with those of [17], we can hypothesize that the 3D ultrasonographic and power Doppler implantation markers have a significant correlation with pregnancy in cases where the quality of the transferred embryos is insufficient or only one embryo of optimal quality can be transferred. When only one high-quality embryo is available for transfer, a healthy endometrial receptivity, as measured by ultrasound markers, appears to be a prerequisite for achieving pregnancy. There is a prevailing recommendation among embryo transfer policies to decrease the quantity of embryos to be transmitted [21, 22]. Additionally, there has been a gradual increase in the number of cycles during which just one embryo is transferred [23].
Our study's recommendations were to confirm the predictive role of EV and 3D power Doppler indexes (FI), (VFI), and (VI) for a large group of infertile patients using 3D US-PDA. The hope was to identify a cutoff point for good characteristics in assessing endometrial receptivity and a normal pregnancy outcome, particularly in cases where the quality of transferred embryos is insufficient or when only one embryo of optimal quality can be transferred.

Conclusions

Although 3D ultrasound has been suggested as a potentially useful method for assessing endometrial receptivity, the findings have generated considerable controversy. This can be accounted for by a variety of methodological distinctions, most notably the examination period and VOCAL parameter values. Additional factors that may be considered are variations in the study population as well as protocols for embryo transfer and stimulation. We are intrigued by the clinical application and interpretation of our results and hope that additional research will validate them. We posit that the novel three-dimensional indicators of endometrial receptivity may prove advantageous in determining which gestational cycle is most conducive to the transfer of a solitary embryo. Power Doppler angiography and 3D ultrasound are valuable diagnostic tools for evaluating endometrial receptivity during IVF/ICSI and embryo transfer cycles. Pregnancy can be predicted using the EV and 3D power Doppler indices on the day of hCG administration, particularly in cases where there is no grade 1 embryo to be transferred or only one degree 1. The practical implications of these findings may extend to programs that adhere to single-embryo transfer policies.

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