

# A Uterine Ultrasonographic Scoring System as a Method for the Prognosis of Embryo Implantation

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**Purpose:** The objective of the present study was to evaluate an ultrasonographic uterine scoring system as a method for the prognosis of embryo implantation in patients submitted to ICSI.

**Methods:** A total of 562 patients submitted to an ICSI program were prospectively evaluated on the day of hCG administration in terms of the following ultrasonographic uterine parameters: A. Endometrial thickness ( $<7.0$  mm = 0; 7 a 14 mm = 3;  $\geq 14$  mm = 1); B. Endometrial layering (three lines = 2; absence of three lines = 0); C. Myometrial contractions in 2 min ( $<3$  = 0;  $\geq 3$  = 3); D. Uterine artery Doppler flow ( $>3$  = 0; 2.2 a 3 = 2;  $\leq 2.19$  = 3); E. Endometrial power Doppler (The endometrium was divided into four equal quadrants and classified as grade I = 1; II = 2; III = 3; IV = 4, according to the visualization of the power Doppler in the quadrants). The colour Doppler signal was considered to be positive when it reached at least the basal layer of the endometrium; F. Myometrial power Doppler (absent = 0; weakly present = 2; strongly present = 3); G. Myometrial echogenicity (homogeneous = 2; inhomogeneous = 0). The patients were divided into 4 groups according to total score: Group I, score  $<10$ ; Group II, score 10–14, Group III, score 15–17 and Group IV, score 18–20.

**Results:** The uterine parameters using an ultrasonographic scoring system are inversely correlated with patient age ( $p < 0.0001$ ). The number of days of stimulation with FSH did not differ ( $p = 0.10$ ) between groups. The number of follicles measuring  $\geq 16$  mm was different ( $p = 0.01$ ) between groups. The number of metaphase II oocytes also did not differ significantly between groups ( $p = 0.45$ ). The fertilization rate was also similar ( $p = 0.10$ ) for all groups. The number of transferred embryos was different between groups ( $p = 0.02$ ). The rate of embryo implantation did not differ ( $p = 0.60$ ) between groups. Finally, the pregnancy rates did not differ significantly ( $p = 0.93$ ) between groups.

**Conclusions:** The ultrasonographic evaluation of uterine parameters on the day of hCG administration using a scoring system is inversely correlated with patient age. In the present study, the use of this ultrasonographic score method could not identify a population with greater uterine receptivity.

**KEY WORDS:** Embryo implantation; Doppler; ICSI; score; ultrasound.

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## INTRODUCTION

Some investigators have postulated the existence of a correlation between the extent of endometrial development determined by ultrasound and the probability of embryo implantation (1,2), whereas others do not consider the pattern and thickness of the

endometrium to be of fundamental importance for the prediction of embryo implantation (3,4).

Transvaginal Doppler ultrasonography with or without color has been used to assess endometrial receptivity in a noninvasive manner (5,6). These studies have suggested that the impedance of uterine artery blood flow is an important parameter to determine the rates of success in an IVF programme.

The objective of the present study was to evaluate an ultrasonographic uterine scoring system based on the following parameters: endometrial thickness, endometrial layering, myometrial contractions, uterine artery Doppler flow, power Doppler of the endometrium, myometrial power Doppler, and myometrial echogenicity as a method for the prognosis of embryo implantation in patients submitted to ICSI.

## MATERIALS AND METHODS

A total of 562 patients submitted to ovarian stimulation for ICSI were studied on the day of administration of human chorionic gonadotropin (hCG).

Ovarian stimulation before the ICSI procedure consisted of blockade of the second phase with nafarelin acetate at the dose of 400  $\mu\text{g}/\text{day}$  (Synarel, Searle). After 14 days of treatment with the analogue and the establishment of blockade, administration of recombinant FSH (Puregon, Organon) was started at a fixed dose of 150 or 300 IU for a period of 7 days. On the eighth day of ovarian stimulation, we started monitoring follicular development only by vaginal ultrasound and the doses of FSH were adapted to the ovarian response. When at least three follicles measuring  $\geq 17$  mm in diameter were observed, hCG was administered at the dose of 10,000 IU (Day 0).

On Day 0, the patients were prospectively evaluated in terms of the following ultrasonographic uter-

ine parameters: A. Endometrial thickness ( $<7.0$  mm – 0; 7–14 mm – 3;  $\geq 14$  mm – 1); B. Endometrial layering (three lines – 2; absence of three lines – 0); C. Myometrial contractions in 2 min ( $<3$  – 0;  $\geq 3$  – 3); D. Uterine artery Doppler flow ( $>3$  – 0; 2.2–3 – 2;  $\leq 2.19$  – 3); E. Endometrial power Doppler (the endometrium was divided into four equal quadrants and classified as Grade I = 1, II = 2, III = 3, and IV = 4 according to the visualization of the power Doppler in the quadrants). The color Doppler signal was considered to be positive when it reached at least the basal layer of the endometrium; F. Myometrial power Doppler (absent = 0, weakly present = 2, strongly present = 3); G. Myometrial echogenicity (homogeneous = 2; inhomogeneous = 0). The patients were divided into four groups according to total score: Group I, score  $<10$ ; Group II, score 10–14, Group III, score 15–17 and Group IV, score 18–20). These parameters were evaluated with a Synergy ultrasound instrument (Diasonics) equipped with a 7.0 MHz transvaginal probe and high-resolution electronic convection.

Oocytes were collected from the follicles 34–36 h after hCG by transvaginal puncture guided by ultrasound. The ICSI procedure was performed by the method of Svalander *et al.* (7).

Embryo transfer (ET) was routinely performed after 48 h in culture, and supernumerary embryos were cryopreserved at the end of the second day.

Data were analyzed statistically by analysis of variance (ANOVA) and by the chi-square test.

## RESULTS

Table I presents the clinical and laboratory data for the patients, divided according to an ultrasonographic scoring system. The uterine parameters using

**Table I.** Clinical and Laboratory Results According to Ultrasonographic Score

	Group I (score $<10$ )	Group II (score 10–14)	Group III (score 15–17)	Group IV (score 18–20)	<i>p</i>
Cycles	31	301	214	16	
Age (years)	35.7 $\pm$ 4.3	34.8 $\pm$ 4.3	33.2 $\pm$ 4.5	31.7 $\pm$ 4.2	$<0.0001$
Days of stimulation	9.8 $\pm$ 2.0	10.6 $\pm$ 2.2	10.1 $\pm$ 1.9	10.3 $\pm$ 1.4	ns
Number of follicles $\geq 16$ mm	5.5 $\pm$ 3.9	5.9 $\pm$ 3.1	6.7 $\pm$ 3.2	7.0 $\pm$ 3.1	0.01
Oocytes MII	9.0 $\pm$ 7.1	8.4 $\pm$ 5.0	9.0 $\pm$ 4.8	9.5 $\pm$ 4.8	ns
Fertilization rate (%)	69.0 $\pm$ 20	69.3 $\pm$ 20.7	65.0 $\pm$ 22.3	62.2 $\pm$ 22.7	ns
Embryos transferred	2.9 $\pm$ 0.9	2.8 $\pm$ 1.1	2.5 $\pm$ 0.9	2.5 $\pm$ 0.8	0.02
Implantation rate (%)	12.0 (11/91)	16.3 (132/808)	17.6 (90/511)	14.6 (6/41)	ns
Pregnancy rate (%)	29.0 (9/31)	31.5 (95/301)	30.8 (66/214)	25.0 (4/16)	ns
Abortion rate (%)	0	17.3	9.0	0	ns

an ultrasonographic scoring system are inversely correlated with patient age ( $p < 0.0001$ ). Patient age was  $35.7 \pm 4.3$  years for Group I,  $34.8 \pm 4.3$  for Group II,  $33.2 \pm 4.5$  for Group III, and  $31.7 \pm 4.2$  for Group IV.

The number of days of stimulation with FSH also did not differ ( $p = 0.10$ ) between groups:  $9.8 \pm 2.0$  for Group I,  $10.6 \pm 2.2$  for Group II,  $10.1 \pm 1.9$  for Group III, and  $10.3 \pm 1.4$  for Group IV. The number of follicles measuring  $\geq 16$  mm was different ( $p = 0.01$ ) between groups:  $5.5 \pm 3.9$  for Group I,  $5.9 \pm 3.1$  for Group II,  $6.7 \pm 3.2$  for Group III, and  $7.0 \pm 3.1$  for Group IV. The number of metaphase II oocytes also did not differ significantly between groups ( $p = 0.45$ ):  $9.0 \pm 7.1$  for Group I,  $8.4 \pm 5.0$  for Group II,  $9.0 \pm 4.8$  for Group III, and  $9.5 \pm 4.8$  for Group IV.

The fertilization rate was also similar ( $p = 0.10$ ) for all groups:  $(69.0 \pm 20.3)\%$  for Group I,  $(69.3 \pm 20.7)\%$  for Group II,  $(65.0 \pm 22.3)\%$  for Group III, and  $(62.2 \pm 22.7)\%$  for Group IV. The number of transferred embryos was different between groups ( $p = 0.02$ ):  $2.9 \pm 0.9$  for Group I,  $2.8 \pm 1.1$  for Group II,  $2.5 \pm 0.9$  for Group III, and  $2.5 \pm 0.8$  for Group IV.

The rate of embryo implantation did not differ ( $p = 0.60$ ) between groups: 12.0% (11/91) for Group I, 16.3% (132/808) for Group II, 17.6% (90/511) for Group III, and 14.6% (6/41) for Group IV. Finally, the pregnancy rates did not differ significantly ( $p = 0.93$ ) between groups: 29.0% (9/31) for Group I, 31.5% (95/301) for Group II, 30.8% (66/214) for Group III, and 25.0% (4/16) for Group IV.

## DISCUSSION

Our group has studied a correlation between the "degree of endometrial development" evaluated by ultrasound and the probability of embryo implantation since 1993 (3), when the endometrial pattern and thickness were analyzed by ultrasonography in 139 cycles stimulated for IVF on the day of administration of hCG. A semiprogrammed schedule based on the pill + clomiphene citrate + human menopausal gonadotrophin was used in all cycles. Endometrial pattern I (a "triple-line" multilayer) was observed in a total of 105 cycles (76%), and pattern II (fully homogeneous and hyperechogenic in relation to myometrial tissue) in 34 (24%). The incidence of clinical pregnancy did not differ ( $p = 0.52$ ) between the groups with endometrial pattern I (23.8%) and II (29.4%). In addition, the endometrial thickness of the patients who became pregnant ( $8.0 \pm 1.7$  mm) did not differ

( $p = 0.15$ ) from that of women who did not achieve pregnancy ( $8.6 \pm 2.0$  mm).

In another study (4), we evaluated the endometrial pattern and thickness on the day of hCG in a total of 150 patients that were submitted to IVF cycles when ovarian stimulation was performed using a GnRH analogue in combination with gonadotrophins. The pattern I was detected in 129 cycles (86%) and pattern II in 21 cycles (14%). The clinical pregnancy rates per cycle were similar ( $p = 0.79$ ) for pattern I (29.4%) and pattern II (33.3%). There was no significant difference ( $p = 0.40$ ) in the number of miscarriages between patients with pattern I and those with pattern II. The thickness were similar ( $p = 0.14$ ) for pregnant ( $10.8 \pm 2.1$  mm) and nonpregnant ( $10.2 \pm 2.2$  mm), but no pregnancies occurred when thickness was  $< 7.0$  mm.

More recently (8), we used the power Doppler of the endometrium as a parameter for the prognosis of embryo implantation in 185 patients on the day of hCG who underwent ICSI. The power Doppler was performed on a transverse section at the level of the uterine fundus and the endometrium was divided into four equal quadrants and classified as Grade I, II, III, or IV according to the visualization of the power Doppler in the quadrants. The color Doppler signal was considered to be positive when it reached at least the basal layer of the endometrium. The rate of embryo implantation did not differ significantly ( $p = 0.53$ ) among groups: 10% for Grade I, 11.6% for Grade II, 15.4% for Grade III, and 10.5% for Grade IV. The pregnancy rates were 25% for Grade I, 29.7% for Grade II, 37.5% for Grade III, and 23.8% for Grade IV and were also similar ( $p = 0.44$ ).

Despite the improvements of ultrasound equipment and the attempt to evaluate different uterine parameters and their effect on the results of an assisted reproduction programme, literature data continue to be controversial. For this reason, we made an attempt to perform an evaluation based on a score that takes into account several parameters rather than a single one (endometrial thickness, endometrial layering, uterine artery Doppler flow, endometrial power Doppler, myometrial power Doppler, and myometrial echogenicity).

In the present study, the uterine parameters were inversely correlated with patient's age ( $p < 0.0001$ ). Patient's age was  $35.7 \pm 4.3$  years for Group I,  $34.8 \pm 4.3$  for Group II,  $33.2 \pm 4.5$  for Group III, and  $31.7 \pm 4.2$  for Group IV. In addition, the number of follicles measuring  $\geq 16$  mm was different ( $p = 0.01$ ) between groups:  $5.5 \pm 3.9$  for Group I,  $5.9 \pm 3.1$  for Group II,

6.7 ± 3.2 for Group III, and 7.0 ± 3.1 for Group IV; and the number of transferred embryos was also different between groups ( $p = 0.02$ ): 2.9 ± 0.9 for Group I, 2.8 ± 1.1 for Group II, 2.5 ± 0.9 for Group III, and 2.5 ± 0.8 for Group IV. The last two differences observed between groups (number of follicles  $\geq 16$  mm and number of embryos transferred) may be due to the difference observed with respect to patient's age.

However, even when there was a difference in age between groups, with younger patients showing a higher ultrasonographic score, the rate of embryo implantation did not differ ( $p = 0.60$ ) between groups: 12.0% (11/91) for Group I, 16.3% (132/808) for Group II, 17.6% (90/511) for Group III, and 14.6% (6/41) for Group IV; and the pregnancy rates also did not differ significantly ( $p = 0.93$ ) between groups: 29.0% (9/31) for Group I, 31.5% (95/301) for Group II, 30.8% (66/214) for Group III, and 25.0% (4/816) for Group IV.

Ultrasonographic evaluation of uterine parameters (endometrial thickness, endometrial layering, uterine artery Doppler flow, endometrial power Doppler, myometrial power Doppler, and myometrial echogenicity) on the day of hCG administration by using a scoring system is inversely correlated with patient's age. In the present study, the use of this ultrasonographic score method could not identify a population with greater uterine receptivity.

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