

Effects of endometrial thickness and echogenic pattern on assisted reproductive treatment outcome

A. Çorbacioğlu, B. Baysal

Department of Obstetrics and Gynecology, Istanbul Medical Faculty, Istanbul (Turkey)

Summary

Purpose: To assess the effects of endometrial thickness and echogenicity on pregnancy and implantation rates in cases using assisted reproductive technology (ART). **Methods:** We retrospectively analyzed the data of 241 ART cycles performed at Istanbul Medical Faculty, Reproductive Endocrinology Unit. The cycles were classified into three groups according to ultrasonographic endometrial thickness measurements on the day of hCG application; 51 cases (group 1) ≤ 8 mm, 182 cases (group 2) between 8-14 mm, and eight cases (group 3) ≥ 14 mm. Also the cycles were grouped according to endometrial echogenicity as trilaminar, isoechogenic and hyperechogenic pattern. **Results:** There was no significant difference in pregnancy rates between the three endometrial thickness groups and echogenic patterns. When conception and non-conception cycles were compared, no significant difference in endometrial thickness was observed (9.88 ± 1.83 mm vs 9.84 ± 1.89 mm). **Conclusion:** Ultrasonographic evaluation of endometrial thickness and pattern is not useful in predicting implantation and conception rates in ART cycles.

Key words: Endometrial thickness; Endometrial pattern; Pregnancy outcomes; ART.

Introduction

Endometrial receptivity is one of the most important factors in the implantation process. However the optimal method for endometrial receptivity has not been found yet. Although ultrasound (US) has allowed endometrial thickness and echogenic pattern to be evaluated during controlled ovarian hyperstimulation, their effects on predicting implantation remain controversial. Several studies have shown that endometrial thickness lower or higher than a definite range affects pregnancy rates negatively [1, 2]. Others, on the contrary, have failed to find any relation between endometrial thickness and implantation rates [3, 4]. Furthermore, some studies have suggested that a trilaminar pattern is a good prognostic factor for achieving pregnancy [5]. However, other authors do not accept endometrial echogenicity as a predictive factor for implantation [6]. The clinical significance of sonographic features remains unclear.

Materials and Methods

We have retrospectively analyzed the data of 241 cases using assisted reproductive technology (ART) performed at the Reproductive Endocrinology Unit of Istanbul Medical Faculty, during the period from February 2005 to February 2007. Long and antagonist protocols were performed for the controlled ovarian hyperstimulation according to the patient's age, ovarian reserve and previous response to ovarian stimulation. In the long protocol with GnRH agonist, 1 mg of leuprolide acetate (Lucrin) s.c. was started on the 21st day of the previous cycle.

After the baseline ultrasonographic evaluation of the endometrium and ovaries on the third day of the cycle, either recombinant FSH (Puregon, follitropin beta or Gonal-F - follitropin alfa) or human menopausal gonadotrophin (hMG) was started for ovarian stimulation with an appropriate dosage; GnRH agonist dosage was reduced to 0.5 mg daily. In the antagonist protocol, ovarian stimulation was started on the third day of the cycle and GnRH antagonist of 0.25 mg cetrorelix (Cetrotide) s.c. was applied when the leading follicle became 13-14 mm in diameter throughout the stimulation. The response to treatment was monitored daily by transvaginal ultrasound (TVS) measurements of endometrial thickness – the greatest anteroposterior dimension in a longitudinal section – and follicular diameters. Human chorionic gonadotropin (10000 IU; Profasi or Pregnyl) was administered IM when there were two or more follicles > 18 mm and several follicles ≥ 14 mm. Oocyte retrieval was performed approximately 36 hours after hCG administration by TVS-guided follicular aspiration. Three days after oocyte retrieval usually three but occasionally one or two embryos of grade 1 and 2 were replaced. Pregnancy was diagnosed by serum concentration of β -hCG on the 12th day of embryo transfer.

The cycles were classified into three groups according to ultrasonographic endometrial thickness measurements on the day of hCG application; 51 cases (group 1) ≤ 8 mm, 182 cases (group 2) between 8-14 mm, 8 cases (group 3) ≥ 14 mm. The cycles were grouped according to echogenicity as trilaminar (central and outer echogenic lines with hypoechogenic areas between them), isoechogenic (same reflectivity compared to myometrium) and hyperechogenic (increased reflectivity compared to myometrium) pattern. The pregnancy rates of these groups were compared. Conception and non-conception cycles were compared according to treatment characteristics and ovarian response.

Data were analyzed with the Statistics Package for Social Sciences (SPSS). The level of statistical significance was defined as $p < 0.05$. Statistical tests included χ^2 , one-way ANOVA and Student's t test as appropriate.

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Results

The demographic characteristics of patients are summarized in Table 1. Among the 241 ART-embryo transfer cycles the total pregnancy rate was 26.6% (64 cycles).

Table 1. — Summary of demographic data (values are mean \pm SD).

Total number of ART cycles	241
Age (years)	31.3 \pm 5.4
Duration of infertility (years)	7.3 \pm 4.5
Diagnosis (%)	
Male factor	45.6
Tuboperitoneal factor	17
Ovarian factor	5
Endometriosis	2.5
Unexplained	26.1
Multiple	3.7
Number of ART attempts	1.5 \pm 1
Stimulation protocols (%)	
Long protocol	61
Antagonist protocol	39

Endometrial thickness measurements ranged from 6.5 to 16 mm with a mean of 9.85 mm. Table 2 shows the comparisons of the three groups according to the age, the day of hCG application, the total dose of gonadotrophin, number of oocytes retrieved and the number of embryos per transfer. None was significantly different. Pregnancy rates were 29.4% (15 cycles), 26.4% (48 cycles), 12.5% (1 cycle) respectively.

Table 2. — Comparisons of variables between the groups according to endometrial thickness (values are mean \pm SD).

Variables	Group 1 (n = 51)	Group 2 (n = 182)	Group 3 (n = 8)	<i>p</i>
Age (years)	31.3 \pm 5.4	31.3 \pm 5.5	31.5 \pm 5.8	n.s.
Day of hCG application	12.1 \pm 1.8	12.6 \pm 1.3	12.6 \pm 1.4	n.s.
Total dose of gonadotrophins (IU)	3025.3 \pm 1379.5	3308.5 \pm 1329.4	3309.3 \pm 2031.3	n.s.
Oocyte number	13.4 \pm 7.8	12.7 \pm 7	12 \pm 8.7	n.s.
Embryo/transfer	2.7 \pm 0.6	2.8 \pm 0.5	2.6 \pm 0.5	n.s.
Pregnancy rate (%)	29.4	26.4	12.5	n.s.

n.s. = not significant.

The trilaminar pattern was detected in 184 cycles, the isoechogenic pattern in 24 cycles and the hyperechogenic pattern in 33 cycles (Table 3). The pregnancy rates were 26.6% (49 cycles), 20.8% (5 cycles), 30.3% (10 cycles) respectively. There were statistically significant differences between the average ages ($p = 0.01$), the number of oocytes retrieved ($p = 0.01$) and embryos per transfer ($p = 0.05$).

The age distribution of patients was significantly different between conception and non-conception cycles (30.1 \pm 5.1 vs 31.8 \pm 5.5, $p = 0.05$). Day 3 E₂ levels, day 3 FSH levels, day of hCG application, total dose of gonadotrophin and number of oocytes retrieved were not significantly different in conception and non-conception cycles (Table 4). However the number of embryos per transfer was 2.9 \pm 0.2 vs 2.7 \pm 0.5 ($p < 0.005$). For those who conceived the mean thickness was 9.88 \pm 1.8 mm as compared to 9.84 \pm 1.8 mm for those that did not conceive.

Table 3. — Comparisons of variables between the groups according to endometrial echogenicity (values are mean \pm SD).

	Trilaminar n = 184	Isoechogen n = 24	Hyperechogen n = 33	<i>p</i>
Age (years)	30.82 \pm 5.33	33.04 \pm 5.46	33.27 \pm 5.57	< 0.05
Total dose of gonadotropin	3133.32	3469.79	3731.06	< 0.05
Endometrial thickness (mm)	9.79 \pm 1.73	9.52 \pm 2.07	10.45 \pm 2.32	n.s.
Oocyte number	13.54 \pm 7.37	11.79 \pm 5.62	9.70 \pm 6.72	< 0.05
Embryo/transfer	2.81 \pm 0.49	2.83 \pm 0.48	2.55 \pm 0.71	< 0.05
Pregnancy rate (%)	49 (26.6%)	5 (20.8%)	10 (30.3%)	n.s.

n.s. = not significant.

Table 4. — Comparisons of variables between the conception and non-conception cycles (values are mean \pm SD).

Variable	Conception (n = 64)	Non-conception (n = 177)	<i>p</i>
Age (years)	30.1 \pm 5.1	31.8 \pm 5.5	< 0.05
Day 3 FSH levels (IU/l)	6.5 \pm 1.9	7.1 \pm 2.7	n.s.
Day 3 E ₂ levels (pg/ml)	49.1 \pm 26.2	49.1 \pm 29.6	n.s.
Day of hCG application	12.5 \pm 1.5	12.5 \pm 1.4	n.s.
Total dose of gonadotrophin(IU)	3092.5 \pm 1206	3305.1 \pm 1417	n.s.
Oocyte number	13 \pm 6	12.7 \pm 7.6	n.s.
Embryos/transfer	2.9 \pm 0.2	2.7 \pm 0.5	< 0.005
Endometrial thickness (mm)	9.88 \pm 1.8	9.84 \pm 1.8	n.s.

n.s. = not significant.

Discussion

As a result of non-invasive and easy evaluation of the endometrium by TVS, endometrial thickness and pattern have been one of the most commonly investigated issues as a prognostic factor of ART cycles. In the past many authors suggested that a favorable endometrial thickness can be used as an indicator of conception. However, recently most studies conclude that endometrial thickness at the time of hCG has only marginal prognostic value when extremes of poor growth are seen [7, 8].

This study indicates that there is no relationship between pregnancy rates and endometrial sonographic features. The absence of marginal values of endometrial thickness may be one of the reasons for this result. Although the pregnancy rate of group 3 was as low as 12.5%, the number of cycles was not sufficiently high enough to cause a significant difference. In contrast other to studies, the hyperechogenic pattern had a higher pregnancy rate despite the poor prognostic factors like older age, low number of oocytes retrieved and embryos per transfer. This may be because of the limited number of cycles with the hyperechogenic pattern which is only 33, since most of the cycles appeared to cluster in a trilaminar pattern.

The endometrium can be evaluated on the day of oocyte retrieval or embryo transfer as well as the day of hCG application. Since high levels of progesterone in the luteal phase have some effect on the endometrium, the day of evaluation may change the results of studies. In our study we preferred to measure the endometrium on the day of hCG application. Early evaluation also gives us the opportunity to cryopreserve embryos or postpone hCG in case of an unfavorable endometrium.

In summary, the study presented here shows that endometrial sonographic features have no significant effect on predicting pregnancy rates. On the contrary, age and number of embryos per transfer are the major prognostic factors for ART cycles.

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Address reprint requests to:
A. CORBACIOGLU, M.D.
Besni Hospital
Bensi, 2300
Adiyaman (Turkey)
e-mail: draytul@yahoo.com