

## Influence of endometrial thickness and echo patterns on pregnancy rates during in vitro fertilization

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Pelvic sonography using transvaginal transducers has enabled the detection of changes in endometrial thickness and texture as follicular maturation advances.<sup>1</sup> Similar sonographic patterns have also been recorded during hyperstimulation in preparation for in vitro fertilization-embryo transfer (IVF-ET).<sup>2</sup> The possibility exists that successful implantation may be related to the endometrial thickness at the time of human chorionic gonadotropin (hCG) injection during IVF-ET cycles. In fact, one study of IVF cycles demonstrated a significantly thicker endometrium in pregnant as compared with nonpregnant women who employed a clomiphene citrate (CC)-human menopausal gonadotropin (hMG) hyperstimulation regimen.<sup>3</sup>

The study presented herein also compared endometrial thickness and texture in patients who conceived after IVF versus those who failed to conceive. The hyperstimulation protocol used, however, was leuprolide acetate (LA)-hMG (long protocol). Should the same trend of improved pregnancy rates (PRs) with increased endometrial thickness be found, we wanted to determine the effect of a different hyperstimulation protocol on the endometrial thickness level.

### MATERIALS AND METHODS

Each patient was started on LA, 1 mg beginning on day 21 of the cycle for 10 days, and the dosage was decreased to 0.5 mg on the 11th day. Human menopausal gonadotropin (300 IU/d) was started on the 11th day of LA for 4 days and then reduced to 225 IU. Further changes were made in accordance with the results of serum estradiol (E<sub>2</sub>) levels and number and size of follicles obtained by pelvic sonography using a transvaginal transducer. Human chorionic gonadotropin was given when at least two lead follicles attained an average diameter of 18 mm and the serum E<sub>2</sub> was at least 300 pg/mL per follicle.

On the day of hCG injection, careful endometrial sonographic measurements were made using an ATL Ultramark 4 Unit (Advanced Technology Laboratories, Bothell, WA) equipped with a 5-MHz transvaginal ultrasound transducer. The endometrial patterns visualized sonographically were graded A, B, or C using the following criteria: Pattern A presented as a triple-line pattern or a multilayered endometrium in which hyperechogenic outer lines and a well-defined central echogenic line were visualized with hypoechogenic or black areas seen between these lines; pattern B is an intermediate pattern in which the endometrium had the same echogenicity as the myometrium with a poorly defined central echogenic line; pattern C was an entirely homogeneous, echo-dense endometrium, in comparison with the myometrium in which no central echogenic line could be visualized. All endometrial grading was

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**Table 1** Comparison of IVF Factors by Endometrial Pattern and Endometrial Thickness<sup>a</sup>

Factor	Endometrial pattern <sup>b</sup>			Endometrial thickness <sup>c</sup>		
	A	B	C	7 to 8 mm	9 mm	>10 mm
Age (y)	32.4 ± 4.7	33.1 ± 4.1	33.6 ± 5.1	33.0 ± 5.1	34.0 ± 4.9	33.0 ± 4.9
Cycle day of hCG	11.8 ± 2.8	12.4 ± 4.0	12.1 ± 2.5	11.8 ± 3.4	12.8 ± 3.0	11.8 ± 2.9
E <sub>2</sub> (pg/mL)	1,296.1 ± 557.5	1,229.8 ± 466	1,697.0 ± 1,094.6	1,612.2 ± 1,121.9	1,344.8 ± 574.4	1,300 ± 567.4
No. of follicles > 18 mm	4.59 ± 2.93	5.66 ± 2.0	4.4 ± 2.2	3.6 ± 1.8	5.0 ± 2.2	4.9 ± 2.9
No. of oocytes retrieved	13.9 ± 7.4	13.6 ± 7.3	12.7 ± 6.7	13.1 ± 7.5	14.6 ± 11.6	14.0 ± 7.6
Fertilization rate (%)	56.0 ± 23.9	61.5 ± 28.6	62.2 ± 29.6	54.8 ± 27.0	47.1 ± 26.7	61.3 ± 24.5
No. of embryos transferred	3.98 ± 1.07	3.8 ± 1.26	3.3 ± 1.04	3.5 ± 1.0	3.2 ± 1.5	3.9 ± 1.1
Endometrial thickness (mm)	10.5 ± 2.0	10.6 ± 1.68	10.8 ± 2.1			

<sup>a</sup> Values are means ± SD.<sup>b</sup> No significant differences ( $P > 0.05$ ).<sup>c</sup> No significant differences ( $P > 0.05$ ).

done by one sonographer. Thickness was measured in millimeters by placing electronic calipers on the outer walls of the endometrium in the longitudinal axis of the uterine body.<sup>2,3</sup>

Ninety-four consecutive stimulation cycles for IVF-ET, during a 4-month interval, were evaluated. Because there was no fertilization in 9 cycles, a total of 85 transfers were completed. Comparison of echo patterns and endometrial thickness were made between pregnant versus nonpregnant women. Statistical analysis was performed using Fisher's exact probability test.

Factors pertinent to the IVF procedure, namely age of patient, number of days of stimulation before hCG injection, serum E<sub>2</sub> levels (on day of hCG injection), number of mature follicles, number of oocytes retrieved, fertilization rate, and number of embryos transferred were also calculated and compared by IVF outcome, endometrial thickness, and echo pattern. Statistical analysis was performed using Student's *t*-test and ANOVA respectively.

## RESULTS

Pattern A was found in 55 cycles (64.7%), and patterns B and C were found in 15 cycles (17.6%), respectively. The highest PR per transfer occurred with pattern B (4/15 [26.7%]); pattern A also had a similar PR (12/55 [21.8%]), but there was not one pregnancy in 15 women with pattern C (Fisher's exact test;  $P = 0.02$ , comparing A and B versus C).

The data with endometrial thickness found the following: 7 to 8 mm, no pregnancies in 15 cycles; 9 mm, 1 pregnancy in 14 cycles (7.1%); ≥10 mm, 15

of 56 (26.8%) pregnant (Fisher's test;  $P = 0.006$ , comparing ≥10 mm to <10 mm). Thus in 15/16 (94%) of all pregnancies, endometrial thickness was found to be ≥10 mm.

There were no significant differences in the mean age of patient, day of cycle of hCG injection, serum E<sub>2</sub> levels, number of follicles, number of oocytes retrieved, fertilization rate, and number of embryos transferred between pregnant and nonpregnant women. There were also no significant differences in the means of these factors among women whose endometrial thickness measured 7 to 8 mm, those with endometrial thickness 9 mm, and those women whose endometrium measured 10 mm or more or by endometrial echo pattern (Table 1).

## DISCUSSION

The study by Gonen and Casper<sup>3</sup> reported high PRs only with pattern A and poor results with B and C; their hyperstimulation regimen was CC and hMG. In contrast, our data demonstrated both A and B as having good PRs (using long LA-hMG protocol).

With regard to endometrial thickness, our study also found improved PRs with increased endometrial thickness using the LA-hMG hyperstimulation regimen similar to the CC-hMG technique. However, there were differences noted. The mean endometrium thickness in the Gonen and Casper<sup>3</sup> study for those not conceiving was 7.1 mm and was 8.6 mm for those achieving pregnancies; in contrast, not one pregnancy occurred in our study with an endome-

trium of <9 mm and only one with an endometrium of <10 mm.

Thus, our data corroborate the data of Gonen and Casper<sup>3</sup> that both endometrial thickness and sonographic echo patterns, before oocyte retrieval, do correlate with PRs. The differences in the specific measurements could have been related to the antiestrogen (E) effect of the CC.<sup>4</sup> These findings await further confirmation by larger studies. Evaluating specific endometrial sonographic data for each specific hyperstimulation regimen could prove to be important.

Our data suggest that improved PRs with increased endometrial thickness and specific echo patterns, may not be related merely to cycles in which the anti-E drug CC was used. If poor PRs below a specific minimum endometrial thickness do occur, it will be interesting to note if any therapeutic maneuvers can improve the thickness before hCG, e.g., giving hMG therapy longer. Alternatively, in patients who do not generate an appropriate endometrial thickness, it would also be interesting to determine if the cryopreservation of embryos and subsequent transfer of thawed embryos in another cycle (in which the endometrium has been primed with E and progesterone after down regulation with LA) may result in an increased PR. A randomized study to address these questions has been initiated.

## SUMMARY

Previous data has suggested that improved PRs were seen in women with increased endometrial thickness as determined by sonography before oocyte retrieval. The hyperstimulation protocol used was CC-hMG. The study presented herein was initiated to evaluate if a similar trend was evident in women whose hyperstimulation protocol included the long LA-hMG therapy. We also demonstrated an improved PR in women with greater endometrial thickness, but in general, the endometrium was thicker in the pregnant women treated with the gonadotropin-releasing hormone agonist than in those treated with CC.

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