Increased endometrial thickness is associated with improved treatment outcome for selected patients undergoing in vitro fertilization–embryo transfer

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Objective: To examine possible relationships between endometrial thickness and treatment outcome after IVF and embryo transfer, and to explore the role of potential confounding factors that may influence such relationships.
Design: Retrospective study.
Setting: A university-affiliated clinical IVF center.
Patient(s): Patients undergoing IVF–embryo transfer with their own oocytes.
Intervention(s): None.
Main Outcome Measure(s): Endometrial thickness was determined on the day of hCG administration, 2 days before oocyte retrieval. Clinical pregnancy was confirmed by ultrasound observation of fetal heart activity.
Result(s): The study analyzed 897 IVF–embryo transfer cycles. Treatment outcome (clinical pregnancy) after IVF–embryo transfer was positively associated with increased endometrial thickness and peak E_2 concentrations in serum, and negatively associated with advanced age. Endometrial thickness was dependent on peak E_2 concentrations in serum, but was independent of patient age or duration of ovarian stimulation. Thin endometrium reduced PRs in relatively young patients (<38 years old), in patients who required more than 10 days of gonadotropin stimulation, or in patients whose embryo transfers consisted of poor quality embryos.
Conclusion(s): Increased endometrial thickness was associated with improved treatment outcome, but this association was dependant on patient age, duration of ovarian stimulation, and embryo quality. (Fertil Steril® 2005;83:336–40. ©2005 by American Society for Reproductive Medicine.)

Key Words: Endometrial thickness, pregnancy rates, patient age, embryo quality

Endometrial receptivity refers to a physiological state of the endometrium that is optimal for embryo implantation. Endometrial receptivity is brought about primarily by ovarian steroid hormones, and is synchronized with fertilization and embryo development (1). However, the molecular mechanism underlying endometrial receptivity is poorly understood and a reliable molecular indicator of endometrial receptivity remains elusive. Correlating molecular events in the endometrium with its receptivity is even more difficult in the human for both technical and ethical reasons. Measurement of the endometrial thickness under ultrasound is both atraumatic and simple, and has been studied as a possible indicator for endometrial receptivity and predictor for treatment outcome after IVF–embryo transfer procedures (2–5).

However, the findings from these studies were inconclusive largely due to limited sample sizes. The aims of this study were to examine possible relationships between endometrial thickness and treatment outcome after IVF–embryo transfer with a relatively large sample size, and to determine what factors affect such relationships.

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MATERIALS AND METHODS

This study included 897 IVF–embryo transfer cycles performed between January 1999 and June 2002 at the IVF Program of the Feinberg School of Medicine of Northwestern University. Cycles using donor oocytes or cryopreserved embryos were excluded from this study. For patients who underwent more than one IVF–embryo transfer cycle during the period of the study, only the first cycle was included. Endometrial thickness was not used as a criterion for cancellation of oocyte retrieval or embryo transfer. An exempt for patient consent was approved by the Institutional Review Board of Northwestern University.

Procedures for controlled ovarian hyperstimulation, oocyte retrieval, IVF, embryo culture, and embryo transfer have been described elsewhere (6). Embryo transfer was usually performed on day 3, and postponed to day 5 only if more than four good quality embryos (8-cell, little or no fragmentation) were present on day 3. To assess treatment outcome, serum β-hCG levels were measured 13 days after retrieval in all patients and repeated 2 days later if the first result was positive. Clinical pregnancy was confirmed by ultrasound observation of fetal cardiac activity 2–3 weeks after positive hCG tests.

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Endometrial thickness was defined as the maximal distance between the echogenic interfaces of the myometrium and the endometrium measured in the plane through the central longitudinal axis of the uterus. The measurement recorded on the day of hCG injection was used for the analysis in this study. Peak serum E_2 concentration was defined as the value measured on the day of hCG injection.

A step-wise multiple logistical regression analysis was used to assess the impact of age, endometrial thickness, peak E_2 level, and days of stimulation on treatment outcome. The possible dependence of endometrial thickness on patient age, peak serum E_2 concentration, or the number of days of ovarian stimulation before hCG injection was then assessed using a stepwise multiple linear regression analysis. Finally, study cycles were divided into two groups according to patient age at the beginning of the IVF cycle, days of gonadotropin stimulation, the quality of embryos for transfer, or the day of transfer. Each group was subdivided into three endometrial thickness groups (<9 mm, 9–14 mm, and >14 mm), as in earlier studies (5, 7).

A χ^2 test was used to compare differences in pregnancy rates (PR) between the three endometrial thickness groups separately for young (<38 years old) or old patients (≥38 years old), short or long duration of gonadotropin stimulation (<11 days or ≥11 days), transfers consisting of zero or at least one good quality embryo (8-cell stage without fragmentation on day 3, or blastocyst stage with well-defined inner cell mass and trophectoderm on day 5), and transfers performed on day 3 or day 5.

The level of statistical significance was defined as $P<.05$. In addition, the relationship between endometrial thickness and treatment outcome in each of the subgroups was also analyzed by a receiver operator characteristic (ROC) curve, using computer software from Analyse-It Ltd (Leeds, UK).

RESULTS

The age of the patients in this study ranged from 23 to 44 years, averaging 35.6 years. The overall PR per transfer was 43% (Table 1). Other demographic data in this study, including pregnancy history, length of infertility, and diagnosis were comparable to the latest national summary data published by the Centers for Disease Control.

TABLE 1

Summary of demographic data.

Total number of IVF–embryo transfer cycles	897
Age (years)	35.6 +/− 3.7
Months of infertility	30 +/− 24
Diagnosis (%)*	
Male factor	26
Endometriosis/uterine factor	11
Ovarian factor	21
Tubal factor	15
Unexplained/other	36
No. of embryos transferred	2.6 +/− 0.9
Clinical pregnancy rates (%)	43.1

*The sum is greater than 100 because some patients have more than one diagnosis.

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Association of Cycle Characteristics with Treatment Outcome

The relationships between treatment outcome (clinical pregnancy) and patient age, endometrial thickness, peak E_2 levels, and number of days of gonadotropin stimulation are presented in Table 2. Stepwise multiple logistical regression analyses showed that patient age is negatively correlated with treatment outcome, and that increasing endometrial thickness and peak serum E_2 levels are associated with improved PRs. Treatment outcome is independent of the number of days of stimulation.

Factors Influencing Endometrial Thickness and its Effect on Treatment Outcome

Endometrial thickness is positively correlated with peak E_2 concentrations in serum (Fig. 1), but is independent of patient age and the number of days of ovarian stimulation.

When the IVF–embryo transfer cycles were divided according to patient age, cycles with thin endometrium had lower PRs than the medium or thick groups only for the

TABLE 2

Multiple logistical regression analyses.

Independent variables	Patient age	Endometrial thickness	Peak E_2 level	Days of stimulation
R	−0.053	0.062	0.121	0.004
P	0.007	0.011	0.020	0.621

R = Regression coefficient; R is considered statistically significant if $P<.05$.

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