

Effect of maximal endometrial thickness on outcome after frozen embryo transfer

The largest study to date on the association of endometrial thickness and subsequent pregnancy rates following frozen embryo transfer with the endometrium prepared by estrogen and progesterone found no improved or adverse outcome if the endometrial thickness was ≥ 2 standard deviations above the mean. Neither was there a trend noted for thin endometria. (Fertil Steril® 2004;81:1399–400. ©2004 by American Society for Reproductive Medicine.)

There have been many published studies with various conclusions about the effect of minimal endometrial thickness at the time of hCG or oocyte retrieval and subsequent pregnancy rates (PRs) after controlled ovarian hyperstimulation (COH) and IVF–embryo transfer. There are fewer studies evaluating the effect of a maximum endometrial thickness at these times on pregnancy outcome after IVF–embryo transfer (1–6). An extensive review of the literature failed to find any studies of maximum endometrial thickness on pregnancy and implantation rates after frozen embryo transfer where graduated estrogen (E) followed by P is given instead of COH. We thus decided to retrospectively review a large number of frozen embryo transfer cycles to evaluate the effect of endometrial thickness on subsequent outcome.

The first frozen embryo transfer cycle of all patients <40 years of age from January 1, 1997 to June 30, 2001, was retrospectively reviewed. This starting date was chosen because various changes, for example, embryo growth medias and type of transfer catheter, were made at this time. During this time period, laboratory conditions and protocols were uniform. The cryopreservation technique used a simplified method in which a slow cooling program is started at the seeding temperature of -6°C in an alcohol bath controlled-rate freezer. 1,2 Propanediol was used as the cryoprotectant. A one-step fast thawing procedure at room temperature was used and the cryoprotectant was removed from the embryos in one step (7).

Frozen embryo transfer was performed on E₂/P-treated cycles. Oral E₂ was initiated beginning on day 2 at 2 mg for 5 days then increased by 2 mg every 5 days. If the endometrial thickness was ≥ 9 mm on the 14th or 15th day of oral E₂, P vaginal suppositories at 200 mg b.i.d. and P in oil 100 mg/day i.m. were added. If despite the use of E₂ the ovulation was not inhibited, 0.5 mg of leuprolide acetate (LA) was added on the seventh day of spontaneous increase of P and continued through the next cycle until P was suppressed, and E₂ was started on day 2 of the next cycle. Embryo transfer was performed on the fourth day of P.

If the endometrium did not attain a 9-mm endometrium by day 16, the dosage was increased to 8 mg p.o. or sometimes the 2-mg E₂ tablets were placed intravaginally. If the endometrium did not attain a 9-mm endometrium by day 22, the cycle was usually cancelled and another one initiated after induced menses usually starting at a higher dosage of E₂ including vaginal administration. If despite the attempts to increase endometrial thickness the goal was not accomplished, the patients were given the option of transferring the frozen-thawed embryos despite a thickness that in the past was considered insufficient for fresh embryo transfer.

The two most common endometrial thicknesses were 9 mm (22.1%) and 10 mm (23.4%). Clinical pregnancies were observed in patients with endometrial thickness as thin as 5 mm and as thick as 18 mm. The mean thickness for frozen embryo transfer in nonrecipients was 10.23 ± 1.93 mm and was 10.04 ± 2.25 mm for oocyte recipients. Using the criteria that values more than two standard deviations from the mean are unusual, the cycles were classified as either normal thickness (<14.5 mm) or unusually thick (>14.5 mm).

During the period of study the overall clinical PR per frozen embryo transfer for women having prior oocyte retrievals was 40.3% (408/1,013) and for oocyte recipients, 41.3% (88/213).

A comparison of clinical and delivered PRs and implantation rates is seen in Table 1 and showed no difference in outcome between normal thickness and excessively thick endometria within each patient type (viable/delivered PR: 33.9% for normal thickness of lining and 34.3% for thick endometrial lining, standard patients, 37.3% and 44.9% for recipients). Although there were only 10 women with an endometrium measuring 16–18 mm, there were six (60%) clinical pregnancies. There were insufficient number of thin endometrias to evaluate two standard deviations below the mean. However, the clinical PRs for all women with endometria ≤ 8 mm was 36.4% (83/228) vs. 36.7% (397/1,135) for women whose endometria ranged from 9–14 mm, therefore there did not appear to be any trend for lower PRs with thin endometria after frozen embryo transfer either.

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Comparison of pregnancy rates by midcycle endometrial thickness.

	Standard frozen ET		Recipient frozen ET	
	Normal thickness (≤ 14.5 mm)	Thick thickness (> 14.5 mm)	Normal thickness (≤ 14.5 mm)	Thick thickness (> 14.5 mm)
Clinical PR	40.2% (393/978)	42.9% (15/35)	41.2% (84/204)	44.9% (4/9)
Delivered PR	33.9% (332/978)	34.3% (12/35)	37.3% (76/204)	44.9% (4/9)
Implantation rate	17.2% (583/3,387)	19.0% (22/116)	16.6% (122/735)	20.6% (7/34)

P = not significant.

Check. Maximal endometrial thickness effect on outcome after frozen ET. *Fertil Steril* 2004.

The dosage and length of E₂ supplementation varied. To assess what effect this regimen had on PRs and thickness, patients were compared by the days of E₂ taken until the P was started and the maximum dosage administered. If LA was used these cycles were included. There were no significant differences in clinical or delivered PRs or endometrial thickness according to whether the E₂ was taken for the usual 13–15 days or longer than 15 days. Furthermore, no differences were seen in delivered PRs according to the maximal daily dosage of E₂. However, the maximal endometrial thickness decreased in those women taking higher dosages of E₂ reflecting their resistance to endometrial growth.

These data suggest that, at least with frozen embryo transfer, using E/P replacement there is no association of lower PRs with too thick of an endometrium. Although there were insufficient number of endometria to evaluate two standard deviations below the mean, and thus perform χ^2 analysis, for thin endometria, there was not an observed trend suggesting lower PRs either. We believe this to be the largest study of the association of endometrial thickness and pregnancy outcome after frozen embryo transfer, if not the only one.

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