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Title:

The Presence of a Thin Endometrial Stripe in Extremely Low BMI Patients is Not Associated With Lower Implantation Rates

Authors:
L. Sekhon,1,2 K. Shaia,1,2 J. Rodriguez-Purata,1 J. A. Lee,1 L. Grunfeld,1,2 A. B. Copperman1,2

Affiliations:
1. Reproductive Medicine Associates of New York, 635 Madison Ave 10th Floor New York, New York, United States, 10022

2. Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, Klingenstein Pavilion 1176 Fifth Avenue 9th Floor New York, New York, United States, 10029

Objective:
It is well known that high levels of endogenous estrogen mediates endometrial thickening in patients with increased body fat. However, the relative contribution of low/high BMI on the endometrial response to exogenous estrogen supplementation is less understood. This study seeks to assess whether patients with extremely low BMIs are able to achieve adequate endometrial thickness and optimal clinical outcome in response to exogenous endometrium in synthetic ART cycles.

Design:
Retrospective cohort analysis

Materials and Methods:
All patients undergoing endometrial preparation for a euploid embryo transfer (ET) in a synthetic cycle from January 2005 to March 2016 were included. Patients with uterine-factor infertility (ie. history of Asherman's syndrome, submucosal fibroid or uterine septum) were excluded. Patients were stratified by WHO's BMI categories (≤17, 18-19, 20-21, 22-24, ≥25). Maximal endometrial thickness achieved and numbers of days of estrogen supplementation required before ET were analyzed. Clinical outcomes included implantation, clinical pregnancy rate and the rate of early pregnancy loss. Data was analyzed by Kruskal-Wallis, Pearson correlation, linear and binary logistic regression.

Results:
A total of 3858 synthetic cycles were evaluated. Baseline demographics and cycle characteristics are shown in Table 1. Controlling for age, for each unit decrease in BMI there was a 0.06 mm decrease in peak endometrial thickness (r2=0.02, p=0.0005). The strongest correlation between

BMI and endometrial thickness was observed in patients with a BMI of ≤17 (r=0.41, p=0.02). After controlling for both oocyte age and patient age at ET, implantation, clinical pregnancy rate and the rate of early pregnancy loss were not significantly influenced by endometrial thickness (OR 1.07 [95% CI 0.96-1.2], p=0.22; OR 0.86 [95% CI 0.65-1.13], p=0.29; OR 0.91 [95% CI 0.77-1.06], p=0.22); or BMI (OR 0.98 [95% CI 0.96-1.01], p=0.21; OR 0.98 [95% CI 0.95-1.00], p=0.10; OR 1.03 [95% CI 0.99-1.06], p=0.10).

Conclusions:

Patients with extremely low BMI attain lower maximal endometrial thickness compared with normal BMI patients who receive a similar duration of exogenous estrogen supplementation. The hypoestrogenized state of very thin patients may lead to a marked reduction in estrogen receptor induction within the endometrium, limiting the effect of exogenous estrogen. However, these patients and their clinicians can be reassured by the fact that this altered physiology was not seen to adversely impact the probability of achieving clinical pregnancy.

Support:

None.

Table 1:

	<=17	18-19	20-21	22-24	>=25	P value
Euploid FET cycles n=1348	**47**	**224**	**326**	**436**	**315**	
Age at stimulation	32.8 ± 3.8	35.0 ± 4.8	35.2 ± 4.0	35.8 ± 4.0	36.2 ± 4.8	<0.0001
Age at ET	34.6 ± 4.8	36.2 ± 4.5	36.3 ± 4.1	36.7± 4.0	37.4 ± 4.6	<0.0001
Days estrogen supplementation	18.6 ± 4.1	36.2 ± 4.5	36.3 ± 4.1	36.7 ± 4.0	37.4 ± 4.6	NS
E_2 at surge (pg/ml)	871.5 ± 1122.0	510.8 ± 301.9	515.7 ± 381.1	527.9 ± 397.5	536.0 ± 435.3	NS
Endometrial thickness (mm)	8.3 ± 1.6 (6.4-12.0)	8.6 ± 1.4 (5.0-12.0)	8.8 ± 1.5 (6.0-14.0)	9.0 ± 1.5 (6.0-14.0)	9.4 ± 1.7 (6.0-16.0)	0.0012
Correlation with endometrial thickness	r=0.41 P=0.03	r=0.0013 P=0.98	r=-0.05 P=0.33	r=0.05 P=0.29	r=-0.06 P=0.27	
Number of blastocysts transferred	1.2 ± 0.5	1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.3	NS
Implantation rate	59.6% (28/47)	58.4% (131/224)	59.2% (193/326)	60.6% (264/436)	54.9% (173/315)	NS
Clinical pregnancy rate	53.2% (25/47)	54.9% (123/224)	52.7% (172/326)	56.0% (244/436)	48.5% (153/315)	NS
Early pregnancy	29.8%	17.0%	17.5%	22.7%	22.2%	NS

loss rate	(14/47)	(38/224)	(57/326)	(99/436)	(70/315)	