

# Ectopic pregnancy and endometrial thickness in assisted reproduction cycles: is there a link?

S. Mattar<sup>1,2</sup>, L. Lapensée<sup>1,2</sup>, C. Sylvestre<sup>1,2</sup>, A. Eberle<sup>3</sup>, S. Phillips<sup>1,2</sup>, R. Antaki<sup>1,2</sup>

<sup>1</sup> Division of Reproductive Endocrinology & Infertility, Department of Obstetrics and Gynecology, Université de Montréal, Montreal, QC, Canada. <sup>2</sup> Clinique ovo, Montreal, QC, Canada. <sup>3</sup> Faculty of Medicine, Université de Montréal, Montreal, QC, Canada.



Ectopic pregnancy (EP) is more common in pregnancies resulting from assisted reproduction technologies (ART) compared to those from spontaneous conception, with some peculiar risk factors like number and day of embryos transferred, volume and depth of transferred material, among others. However only one study so far assessed the link between endometrial thickness (ET) and EP: Rombauts et al. showed that following IVF, the risk of EP is 4-fold increased in women with an ET of <9 mm compared with women with an ET of >12 mm<sup>1</sup>.

So... **can an ET of > 12 mm measured prior to embryo transfer be considered a protective factor against EP?**

## MATERIALS & METHODS

This is a retrospective case-control study comparing all cases (n=45) of EP (study group) to 119 cases of documented viable intra-uterine pregnancies (control group) between August 2009 and December 2016 at a private fertility clinic (clinique ovo, Montreal, Canada). Pregnancies resulting from both fresh embryo transfer and frozen embryo transfer (FET) were included. The study group consisted of 29 EP in the fresh cycles and 16 in the FET cycles. The control group cases were selected based on a random number generator model on a year-to-year basis. Bivariate analysis was conducted to assess the effect of all collected variables on EP. A multivariate analysis was then used to calculate the odds ratio (OR) for EP with an ET > 12 mm, adjusted for known confounders.

## RESULTS

The two groups did not differ significantly in factors traditionally associated with EP (previous EP, endometriosis, tubal disease, smoking, history of pelvic infection, and abdominal surgery). Patients with EP were more likely to have a thinner endometrium (9.7 vs 10.2 mm, p = 0.009), had day 3 rather than a day 5 transfer (p <0.001), had double rather than a single embryo transfer (p <0.001), and finally were more likely to have had a difficult transfer (p = 0.002), independently of the use of a rigid catheter.

	EP (n=45)	IUP* (n=119)	
	n (%)	n (%)	p value
<b>History of PID</b>	1 (2.2)	3 (2.5)	1.000
<b>Endometriosis</b>	2 (4.4)	6 (5.0)	1.000
<b>Previous EP</b>	2 (4.4)	3 (2.5)	0.616
<b>Tubal disease</b>	2 (4.4)	14 (11.8)	0.239
<b>Major abdominal surgery</b>	1 (2.2)	2 (1.7)	1.000
<b>Smoking</b>	2 (4.4)	14 (11.8)	0.239
<b>Difficult transfer</b>	6 (13.3)	2 (1.7)	<b>0.002</b>
<b>Use of rigid catheter</b>	2 (4.4)	1 (0.8)	0.183
	<b>Median (25th-75th centile)</b>	<b>Median (25th-75th centile)</b>	<b>p value</b>
<b>Age (years)</b>	35 (31-38)	34 (32-38)	0.792
<b>Day of transfer</b>	3 (3-3)	5 (3-5)	<b>&lt;0.001</b>
<b>Number of embryos transferred</b>	1 (1-2)	1 (1-1)	<b>&lt;0.001</b>
<b>ET (mm)</b>	9.7 (8.3-11.3)	10.2 (9.0-12.5)	<b>0.009</b>

\*IUP: intra-uterine pregnancies

In multivariate analysis, ET > 12 mm was found to be a significant protective factor against EP with an OR of 0.32 (95% CI 0.12-0.84). However, difficult transfer and day 3 embryo transfer remained as statistically significant independent risk factors for EP with OR's of 18.04 (95% CI 2.36-137.62) and 7.07 (95% CI 2.62- 19.07) respectively.

	OR	95% CI	p value
<b>Difficult transfer</b>	18.04	2.36- 137.62	<b>0.005</b>
<b>ET &gt; 12 mm</b>	0.32	0.12- 0.84	<b>0.020</b>
<b>Day 3 transfer</b>	7.07	2.62- 19.07	<b>&lt;0.001</b>
<b>Single embryo transfer</b>	0.56	0.23- 1.36	0.200

When analyzed separately, the association between a small ET and EP was preserved in FET cycles (8.9 vs 9.8 mm, p = 0.015) but not in fresh cycles (10.0 vs 10.4 mm, p = 0.116).

**An ET > 12 mm is associated with a 68% decreased chance of EP in ART cycles, namely in FET**

## IMPLICATIONS

It is the first study to show that a higher ET could have a risk-reducing effect on EP, which if confirmed by future prospective observations, can act as a counseling cornerstone by providing reassurance for patients at risk undergoing ART; and also could help developing prevention strategies with estrogen supplementation and delaying FET until adequate thickness is reached.

1 Rombauts L, McMaster R, Mottram C, Fernando S. Risk of ectopic pregnancy is linked to endometrial thickness in a retrospective cohort study of 8120 assisted reproduction technology cycles. Human Reprod (Oxford, England). 2015;30(12):2846-52.