Three different endometrial receptivity profiles can be defined in patients with previous failed embryo transfer

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STUDY QUESTION

What are the different profiles of the implantation window (IW) in patients with previous failed transfer under hormonal replacement therapy (HRT) cycle?

SUMMARY ANSWER

Three distinct profiles were observed.

WHAT IS KNOWN ALREADY?

Although the many advancements in ART technologies, implantation remains a limiting step for the success of IVF. Embryo implantation is a complex event that requires synchronicity between the embryo development and the endometrium maturation. The endometrium is only optimally receptive to the implanting blastocyst during a short period of time refer as the implantation window (IW). Recent studies have revealed that the timing and the length of this receptive stage is patient dependant. The Win-Test (Window Implantation Test) is a molecular diagnostic tool that determines the receptivity status by analyzing the expression level of specific and predictive genes in the endometrial biopsies using quantitative RT-PCR.

STUDY DESIGN SIZE AND DURATION

We analyzed the results from patients that underwent an endometrial receptivity test at **clinique ovo** between June 2016 and February 2019 and had signed the research consent form. This retrospective study includes 126 endometrial biopsies from 55 patients with at least one previously failed transfer (mean of 3.1 failed embryo transfer).

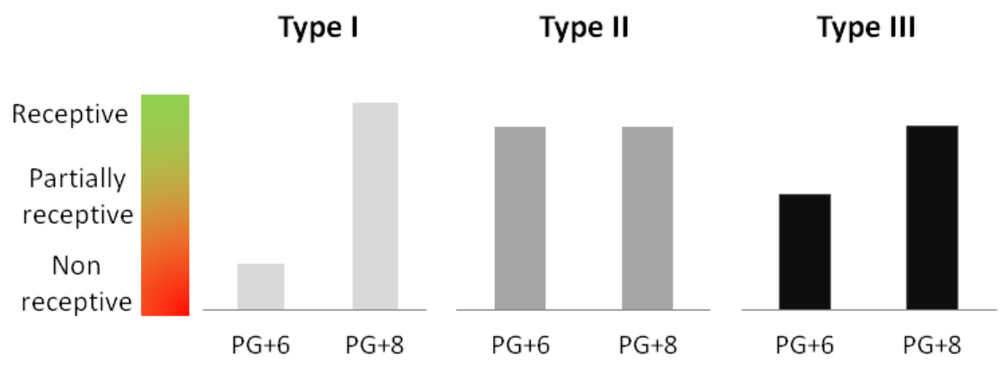
PATICIPANTS/MATERIALS, SETTING AND METHODS

During a HRT cycle, endometrial biopsies were collected at progesterone (PG)+6 days and PG+8. Additional biopsies (PG+7, +9) were retrieved in a subsequent HRT cycle if the initial samples were non or partially receptive. The mRNA expression level of 11 genes was quantified by qRT-PCR for the receptivity prediction at **ovo labo**. Using an algorithm, the Win-Test team in Montpellier (France), classified samples as receptive, non-receptive or partially-receptive and the optimal frozen embryo transfer (FET) day was recommended. Personalized FET (pFET) were completed in a identical HRT cycle.

MAIN RESULTS AND ROLE OF CHANCE

The expression levels of specific biomarkers of human endometrial receptivity was analyzed for 126 endometrial biopsies. 110 endometrial biopsies from 55 patients were retrieved at PG+6 and PG+8. Additionally, for 8 patients, 2 other biopsies were retrieved in a subsequent mock HRT cycle at PG+7 and +9 (n=16).

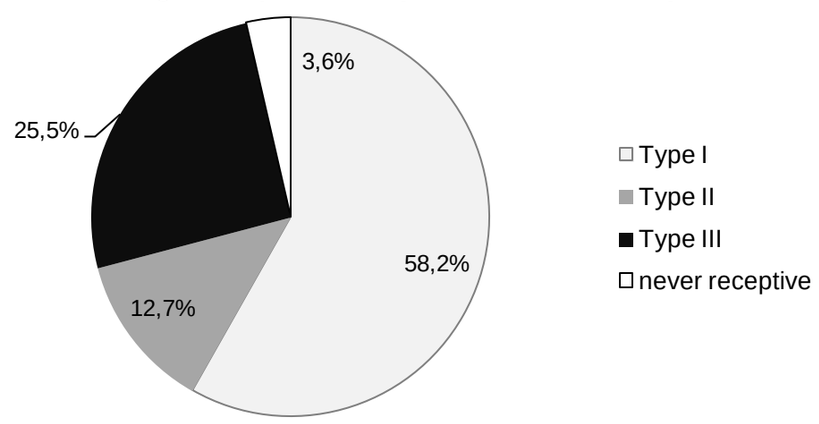
Fig. 1 Endometrial receptivity profiles



By examining the different receptivity status of the 55 patients, 3 profiles emerged: Type I- non-receptive endometrium in one sample and receptive endometrium in the other sample collected at 48h interval, Type II- both samples (PG+6, +8) being receptive, therefore their IW lasted over 48h and Type III- partially-receptive endometrium and then a receptive endometrium 48 to 72h later. Examples profiles are shown in Figure 1.

A majority of the patients, 58.2% (n=32), had a Type I profile. One patient had a very delayed and short IW: the only receptive sample was measured at PG+9. Few patient, 12.7% (n=7), had a Type II profile. Whereas, 25.5% of the patients (n=14) had a Type III profile. For 2 patients (3.6%), their endometrium was never found receptive after the analysis of 4 biopsies. The results are shown in Figure 2.

Fig 2. Proportion of patients in each IW profiles



Recommendations for pFET were given following the analysis of the expression of the endometrial biomarkers. A blastocyst (day 5 or 6) was transferred during the receptive phase and cleaved day 3 embryo was transferred 48h before the observed receptive phase. Thirty-six patients had a pFET at **clinique ovo**, for a total of 55 FET. The standard protocol at **clinique ovo** is that a blastocyst is transfer at PG+6, 88.7%.of the pFET did not follow this protocol.

Twenty-three of the patients with Type I profile had a pFET resulting in 21.7% clinical pregnancy rate after a first trial and 21.6% pregnancy rate per FET. Four patients with a Type II profile had a pFET, resulting in a 75% clinical pregnancy rate on the first trial and 80% pregnancy rate per FET. No pregnancy was achieved in the Type III group (n=8) (Table 1). More investigation has to be complete for this profile.

Tb 1. Patients characteristics and pregnancies outcomes following FET

	Type I	Type II	Type III
Number of patient	23	4	8
Number of failed previous FET	3	3,8	3
Mean age	35,7	35,5	33,8
Number of FET	37	5	13
Clinical pregnancy (%), per FET	**21,6**	**80**	**0**

LIMITATION, REASONS FOR CAUTION

These data were collected in a single IVF center. A multi-centric study with an increased sample size would give a better understanding of the endometrial receptivity profiles of patients with previous failed transfer under HRT cycle.

WIDER IMPLICATIONS OF THE FINDINGS

This study demonstrates the variability in endometrial receptivity profiles and thus the importance of detecting the IW in patients with previous failed transfer in order to offer personalized FET.