

FREEZE-ALL VERSUS FRESH EMBRYO TRANSFER: A CRITICAL COMPARISON IN POOR OVARIAN RESPONDERS

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Introduction: Poor ovarian responders represent a challenging group of patients, characterized by a poor prognosis even in IVF programs^{1,2}. Currently, several studies are exploring whether fresh embryo transfer or freeze-all strategies - by avoiding the detrimental effects of COS on the endometrium - could improve IVF outcomes, though the results remain contradictory.^{3,4}

Objectives: A retrospective cohort study was conducted in a Tertiary IVF Center between January 2019 and July 2024. We included a total of 1283 couples who underwent a controlled ovarian stimulation collecting ≤ 5 oocytes and obtaining at least one good-quality day 3 embryo (> 6 blastomeres and grade 2 according to 'Istanbul consensus'). Freeze-all strategy was performed in case of elevated progesterone ($\geq 1,1$ ng/mL) or endometrial irregularity; otherwise, fresh ET was the first choice. IVF cycles with elective freeze-all (PGD, sperm donation or progesterone level $\geq 1,5$ ng/mL on trigger day) were excluded. We perform a logistic regression analysis adjusted for confounding factors (such as causes of infertility i.e. endometriosis, male factor, tubal factor). The primary outcome of the study was the evaluation of cumulative clinical pregnancy rate CPR (i.e., fetal with cardiac activity on ultrasound).

Results: Of these 1283 couples, 1124 underwent single fresh ET and 159 followed a rescue freeze-all strategy. The number of retrieved oocytes (3.77 ± 1.2 vs 3.09 ± 1.31 , Mean $\pm$ SD, $p < 0.01$) and the number of PN2 oocyte (2.13 ± 1.04 vs 2.65 ± 1.18 , Mean $\pm$ SD) was higher in rescue freeze-all group; nonetheless, cumulative ET numbers ($1,19 \pm 0.05$ vs 1.17 ± 0.87 , Mean $\pm$ SD, respectively for fresh ET and rescue freeze-all) were similar between the two groups. Cumulative outcomes showed a worsening in CPR in rescue freeze-all group (OR 0.67, 95% CI 0.43-1.03), despite not reaching a statistically significant difference. This effect was accentuated when cycles with intermediate progesterone values ($1.1 < P < 1.5$ ng/mL on the trigger day) were excluded, showing a significantly lower cumulative CPR in the rescue freeze-all group (OR 0.53, 95% CI 0.32–0.87, $p = 0.01$). Upon stratifying patients by age, the worsening of CPR with the rescue freeze-all strategy was more pronounced in women aged ≥ 39 years (OR 0.46, 95% CI 0.22–0.98, $p=0.04$). Conversely, in women aged < 39 years, no significant difference was observed (OR 0.85, 95% CI 0.49–1.48, $p=0.57$).

Conclusion: Freeze-all strategy may not be the optimal choice for POR, particularly in women aged ≥ 39 , where a significant reduction in cumulative CPR (clinical pregnancy rate) was observed. Our findings may have broader implications for clinical decision-making, as the freeze-all strategy⁵ could negatively affect IVF outcomes in patients with poor ovarian response, especially in older individuals. Clinicians should carefully consider a patient's age and ovarian reserve when deciding between the rescue freeze-all approach and fresh embryo transfer.

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