



IVF in women with low ovarian reserve or response

Transfer of fresh embryos may be a better option than use of frozen embryos

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In vitro fertilisation (IVF) has revolutionised infertility treatment and offers each year hope to millions of couples worldwide. Embryo freezing has become an increasingly prominent part of the treatment. While initially used for the storing of excess embryos after fresh embryo transfers, the so called freeze-all strategy has now become part of IVF, where no fresh transfer and all suitable embryos are frozen for transfer in subsequent menstrual cycles. In a linked research paper, Wei and colleagues (doi:10.1136/bmj-2024-081474) studied the effectiveness of this strategy in women who have a poor prognosis of IVF treatment success (defined as nine or fewer oocytes retrieved or a poor ovarian reserve).¹

One benefit of the freeze-all method is the ability to reduce the risk of ovarian hyperstimulation syndrome; although, this risk is generally low in women with poor prognosis owing to a low ovarian response. Another rationale for the freeze-all strategy is to improve pregnancy outcomes by avoiding potential negative effects of ovarian stimulation on endometrial receptivity. By postponing embryo transfer to a subsequent cycle without ovarian stimulation, the endometrium is suggested to be more receptive. However, the process of freezing and thawing embryos is not without risks. Damage may occur during cryopreservation, storage, or thawing, and these steps can add substantial financial costs. Furthermore, treatment delays associated with elective freezing may be undesirable for some.

Most studies examining the freeze-all strategy have focused on woman with a good prognosis of IVF treatment success, which showed similar cumulative live birth rates between fresh and frozen embryo transfer.² However, limited evidence exists regarding its benefits for women with a poor prognosis.^{3,4} The study by Wei and colleagues addresses this critical gap. Their multicentre, randomised controlled trial involving 838 participants at nine fertility centres in China compared a fresh versus frozen embryo transfer strategy in women with an antral follicle count lower than five or serum anti-Müllerian hormone <1.2 ng/mL or fewer than nine oocytes in their IVF treatment. The primary outcome was live birth rate per first transfer, while secondary outcomes included cumulative live birth rates within one year of randomisation. The findings showed a lower live birth rate (risk ratio 0.79 (95% confidence interval 0.65 to 0.94)) and a lower cumulative live birth rate in the frozen embryo transfer group (0.86 (0.75 to 0.99)) than in the fresh embryo transfer group.

Concerns remain about potential biases that could have influenced outcomes, such as variations in the day of embryo transfer, differences in the number of double embryo transfers, and a small number of

women who underwent another oocyte retrieval to obtain more embryos. The choice of live birth rate per first transfer as the primary outcome is more often seen in trials in reproductive medicine, but the cumulative live birth rate—which considers all embryo transfers from a single oocyte retrieval cycle—is arguably more relevant from a patient-centred perspective.⁵⁻⁷ Although the study was not powered to assess secondary outcomes, reporting them adds valuable information to the available literature. No differences were observed in obstetrical-neonatal outcomes between the groups, where other studies suggested risks may be increased in the freeze-all group.⁸⁻¹⁰

Previous evidence on the effectiveness of fresh versus frozen embryo transfer in IVF, including a Cochrane review, suggested no clear superiority of one strategy over the other in terms of cumulative live birth rates.² Among the studies included in the review, only one of eight reported lower cumulative ongoing pregnancy or live birth rates for the freeze-all strategy compared with fresh transfer.¹¹ Unlike the other studies, which predominantly included women with a good prognosis of IVF success, that study also included women with a poor prognosis; although, defined as no pregnancy after a period of expectant management. These studies emphasise the importance of providing high level evidence to tailor IVF strategies to meet individual patient characteristics.

Wei and colleagues' trial offers valuable insights for women with a poor prognosis in IVF.¹ The study reported lower live birth rates in the freeze-all group, with no differences in neonatal outcomes, suggesting that fresh embryo transfer may be a better strategy for these patients. These results have broader implications, particularly for centres offering advanced IVF treatments such as [pre-implantation genetic testing for aneuploidy](#) or embryo banking, which involves freezing embryos from multiple IVF cycles before a first transfer. These strategies include freezing of all embryos and are often offered to women with a poor prognosis, such as those of advanced maternal age, to address declining oocyte quality and numbers. However, both approaches remain controversial, with little evidence supporting their efficacy.¹² The findings from the current study suggest that the mandatory freeze-all component in these contexts may not provide benefit to these women.

Rigorous evaluation of these strategies is needed. Any potential advantages must outweigh drawbacks, such as the lower cumulative live birth rates linked to skipping a fresh embryo transfer. Properly assessing the effectiveness of these techniques is

essential for improving outcomes in this challenging patient population.

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