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Embryo Analysis
of Culture Environment

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The impact of implementing a non-invasive preimplantation genetic testing for aneuploidies (niPGT-A) embryo culture protocol on embryo viability and clinical outcomes

Objective:

To assess whether modifications in the embryo culture protocol required for non-invasive preimplantation genetic testing for aneuploidies (niPGT-A) impact clinical reproductive outcomes, including blastocyst development and pregnancy outcomes.

Study Design:

- Retrospective, observational, multicenter study with the aim to investigate the concordance between non-invasive PGT-A (cfDNA media analysis) and invasive PGT-A (TE biopsy analysis) across six centers from April 2018 to December 2020 from women aged 20-44 years.
- The clinical outcomes of the study cycles were compared to those of control patients (Figure 1).
- The adherence to the niPGT-A protocol in the study group was not the same between the six participating centers (Clinics A–F).
  - Clinic A, strictly followed the non-invasive protocol (i.e. all their embryos had extended culture up to Day 6).
  - Clinics B–F, deviations from the protocol were registered: 23% of blastocysts were biopsied on Day 5, and no medium was collected.
- In all cases, a frozen single embryo transfer (SET) of a euploid blastocyst (based on the result of the invasive TE biopsy) was performed.
- There was no transfer of mosaic embryos.

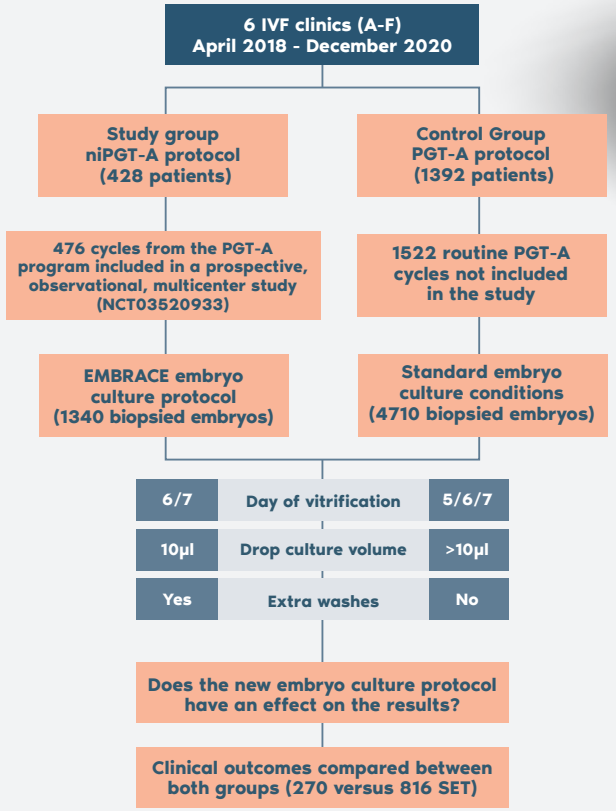

Figure 1. **Scheme of the study design.**

Scan
the paper

Sakkas D, Navarro-Sánchez L, Ardestani G, Barroso G, Bisioli C, Boynukalin K, Cimadomo D, Frantz N, Kopcow L, Mamede Andrade G, Ozturk B, Rienzi L, Weiser A, Valbuena D, Simón C, and Rubio C. Hum Reprod.2024 Sep 1;39(9):1952-1959. doi: 10.1093/humrep/deae156.

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Results:

Patient and cycle characteristics did not differ significantly between the control and study groups, neither for Clinic A nor for the other clinics (Clinics B–F).

The EMBRACE protocol did not negatively impact the total number of biopsied blastocysts, euploidy rates, or informativity rates. No significant differences were observed between the control and study groups, either in Clinic A or the remaining clinics (B–F).

It was evident that allowing embryos to develop one day longer led to higher expansion rates; however, both ICM and TE grades remained unaffected in both Clinic A and Clinics B–F. Overall blastocyst quality was not compromised by changes in culture conditions or the extended culture to Day 6.

Pregnancy outcomes:

- Clinic A showed no significant differences in pregnancy outcomes, including live birth and implantation rates per transfer, regardless of the culture protocol (Table 1).
- For the other clinics (B–F), separate comparisons were made between Day-5 and Day-6 blastocysts, cultured and transferred under the standard and niPGT-A protocols.
- Consistent with Clinic A, no statistically significant differences were found between the control and study groups. The change in culture protocol had no significant impact on pregnancy outcomes (Table 2).

Table 1. Clinical outcomes after single embryo transfer (SET) of euploid embryos comparing standard culture versus non-invasive PGT-A culture conditions in Clinic A.

Clinic A	Control group Day 5, 6, and 7	Control group Day 6 and 7	Study group Day 6 and 7
Number of SET	265	148	64
Number of positve hCG (%)	198 (74.7%)	111 (75.0%)	49 (76.6%)
Number of clinical pregnancies (%)	180 (67.9%)	100 (67.6%)	44 (68.8%)
Number of miscarriages (%)	15 (8.3%)	10 (10.0%)	2 (4.5%)
Number of live births (%)	165 (62.3%)	90 (60.8%)	42 (65.6%)

Differences were not significant when comparing standard versus non-invasive culture.

Table 2. Clinical outcomes after single embryo transfer (SET) of euploid embryos comparing standard culture versus non-invasive PGTA culture conditions in Clinics (B-F)

Rest Clinics B-F	Control group Day 5	Study group Day 5	Control group Day 6	Study group Day 6
Number of SET	284	63	244	129
Number of positive hCG (%)	205 (72.2%)	45 (71.4%)	156 (63.9%)	73 (56.6%)
Number of clinical pregnancies (%)	197 (69.4%)	42 (66.7%)	137 (56.2%)	62 (48.1%)
Number of miscarriages (%)	25 (12.7%)	5 (11.9%)	28 (20.4%)	8 (12.9%)
Number of ongoing pregnancies* (>12 weeks) (%)	172 (60.6%)	37 (58.7%)	109 (44.7%)	54 (41.9%)

Differences were not significant when comparing standard versus non-invasive culture.

*The majority of ongoing pregnancies were followed up to live birth. Only 19 clinical pregnancies were lost to follow up after 12 weeks (15 in control and 4 in the study group).

Main Conclusions:

Neither decreasing the drop culture volume to 10 µl, nor including extra washes on Day 4 affects the number of available embryos or euploidy rates across Clinics A–F.

Furthermore, standardizing the timing of vitrification for all embryos to Day 6 did not negatively impact ongoing pregnancy rates in Clinic A.

This study demonstrates that modifying existing IVF laboratory protocols to implement a non-invasive approach for detecting aneuploidies has no adverse effects on any aspect of reproductive treatment, including the number of blastocysts available for transfer and overall clinical outcomes of transferred embryos.

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