Assessing the developmental competence of atypically pronucleated zygotes

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Introduction

The developmental competence of Atypically Pronucleated Zygotes (APZs) remains a debated topic in assisted reproduction. Although these zygotes are often excluded from clinical use, some studies have reported successful pregnancies resulting from them. With advancements in Artificial Intelligence (AI) and Time-Lapse Monitoring (TLM), it is now possible to analyze their developmental patterns with greater precision, providing new insights into their viability, morphokinetics and morphometrics.

Objectives

This retrospective observational study (2013-2020) analyzed 6052 inseminated oocytes, resulting in 5034 zygotes cultured in Embryoscope from 836 couples (mean maternal age: 39 years, Severe Male Factor [SMF]: 17%), to investigate the developmental competence of APZs compared to normally fertilized embryos. AI-assisted evaluation enabled the classification of different APZ types and the identification of key morphokinetic factors influencing their development. A preliminary morphometric analysis (25 embryos per group) was also conducted to explore potential correlations with the developmental competence of these embryos.

Results

Among the 6052 inseminated oocytes, AI accurately identified ProNuclei (PN) count in 89.6% of cases and corrected 1.2% of embryologists' assessments. Among the 5034 zygotes cultured in Embryoscope, the results revealed that while some APZs reached the blastocyst stage, their success rates varied significantly based on PN count and behavior. Blastulation rates were elevated, as expected, in 2PN zygotes (54%) and reduced in APZs, with the lowest rate in 1.1PN (8%) and the highest in 2.1PN (36%). Odds ratios (ORs) were adjusted for maternal age, type of culture media (continuous vs. sequential), timing of PN appearance (tPNa), timing of PN fading (tPNf)-tPNa, and time to 2-cell stage (t2)-tPNf. APZs exhibited higher arrest rates prior to or around time to 8-cell stage (t8, 60%). tPNa occurred 2-3 hours later in APZs compared to normally fertilized zygotes. At later stages, 1PN and >3PN zygotes were the slowest to reach the expanded blastocyst stage (tEB), while 3PN zygotes reached tEB as the fastest. For each group, analysis of 25 embryos showed similar total zygote area with zona pellucida, but PN area varied across groups at both tPNa and tPNf.

Conclusions

This study highlights the need to increase the sample size for APZs and emphasizes the potential of AI in automating data collection to improve both the quality and quantity of the insights. To fully assess the clinical relevance of APZs, further research should explore additional factors such as early cleavage patterns, blastomere exclusion/extrusion, cytoplasmic strings, blastocyst morphology, chromosomal integrity, and implantation outcomes. By building on previous knowledge of APZs, including 2.1PN and 1.1PN, and leveraging AI technology, this study underscores the value of creating multimodal datasets that can predict when APZ rescue may be clinically applicable. Such data will improve communication between embryologists and clinicians, providing transparent, evidence-based information that can aid in patient counselling and facilitate informed decision-making.

Recommended reading

- *Capalbo A, Cimadomo D, Coticchio G, Ottolini CS. An expert opinion on rescuing atypically pronucleated human zygotes by molecular genetic fertilization checks in IVF. Hum Reprod. 2024;39(9):1869-78.*
- *Capalbo A, Treff N, Cimadomo D, et al. Abnormally fertilized oocytes can result in healthy live births: improved genetic technologies for preimplantation genetic testing can be used to rescue viable embryos in in vitro fertilization cycles. Fertil Steril. 2017;108(6):1007-1015.e3.*
- *Coticchio G et al. Time will tell: time-lapse technology and artificial intelligence to set time cut-offs indicating embryo incompetence. Hum Reprod. 2024;39(12):2663-73.*
- *Ezoe K, Takahashi T, Shimazaki K, et al. Human 1PN and 3PN zygotes recapitulate all morphokinetic events of normal fertilization but reveal novel developmental errors. Hum Reprod. 2022;37(10):2307-19.*