One for all or all for one? The evolution of embryo morphokinetics

As embryologists and clinicians, we are scientists and professionals who routinely perform highly technical procedures every day as well as make weighty decisions about conditioning successful cycles. The latter have made our work exciting and challenging, especially because, as of 2009, embryo cinematography truly has become a user-friendly clinical tool. In a relatively short period of time, two stimulating reports appeared (1), one by Wong et al. in 2010, one of the most important research groups in the world, and our own first attempt to develop an algorithm for embryo selection in a clinical setting.

We found the real challenges to be dealing with the surfeit of data and finding an appropriate analysis that would result in a feasible procedure for embryo selection. In hindsight, we can see that almost 10 years ago we were starting to work toward morphokinetics. Since then, many issues have changed in both embryology and in time-lapse cinematography. We would emphasize that this technology has extended worldwide—many clinics around the world now have access to time-lapse incubators. As the number of cycles performed with these new devices have increased exponentially, the information collected has increased accordingly.

Additionally, the evolution of data analysis and the inclusion of statistics specialists in studies by some manufacturers and large clinical groups have allowed better number management and deeper analyses of the collected data. Moreover, together with larger sample sizes and better investigative techniques, new or alternative clinical procedures have appeared in the field; for instance, far more clinics culture their embryos under lower oxygen tension compared with 10 years ago. The culture media have evolved as well in the past few years; new brands, new compositions, and single-step media present alternative strategies to sequential media. Just as important is the increased incidence of aneuploidy screening in our preimplantation genetic screening programs, offering increasingly accurate analyses and a higher frequency of blastocyst-stage (trophectoderm) biopsies.

In this issue of *Fertility and Sterility*, Barrie et al. (2) report on their excellent study to examine the efficacy of six published time-lapse imaging embryo selection algorithms to predict implantation potential with the intention to demonstrate the need for the development of specific, in-house morphokinetic selection algorithms. Although there are some specific morphokinetic markers that are already available for embryo selection, even by a commercial diagnostic test, the authors were in favor of developing their own selection method, which combined alternative parameters to those already published. Ideally, their study would be improved by two strategies.

1. Selecting embryos only by morphology and then relating the different models to implantation (not biased by morphokinetics). At present, this is almost impossible as there are many powerful cinematographic parameters for embryo selection or deselection, which may be unethical to ignore when they are present, such as direct-cleavage embryos (1).
2. Applying consecutively and prospectively the various published models and then relating them to embryo implantation potential. This is an ideal situation, but the logistics of such studies make them, in most of the cases, impossible for many centers to undertake.

A careful examination of the detailed report by Barrie et al. (2) reveals that the implantation rates of the morphokinetic categories vary significantly as previously reported by Basile et al. (3) in 2015. This makes sense, as the Barrie study is the largest yet reported. Basile's algorithm, which was developed and validated in an independent data set, included patients from five different in vitro fertilization (IVF) clinics from the same company, though they worked with diverse culture media and atmosphere conditions (CO_2 and N_2 concentrations). Furthermore, they used a mixture of oocyte donation and standard IVF cycles with the patients' own oocytes for their study (probably the most heterogeneous population ever reported and compared) (1).

Unfortunately, there were some relevant models missed by Barrie et al. (2), such as the algorithm applied in Early Embryo Viability Assessment that has been recently validated in an independent setting with the largest data set reported at this time (4). Furthermore, it would be interesting to test an algorithm based on late parameters (blastocyst related) as that suggested by Motato et al. (5). However, the annotations required for these two algorithms were not routinely recorded at the study site.

Some questions remain to be answered, and we encourage the authors to continue their exciting research and contributions to time-lapse technology in the future. As embryologists and clinicians we are all obligated to increase our efforts to make this field more comprehensive and accessible to all IVF units.

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