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Review

Mining of variables from embryo morphokinetics, blastocyst's morphology and patient parameters: an approach to predict the live birth in the assisted reproduction service

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ABSTRACT

Based on growing demand for assisted reproduction technology, improved predictive models are required to optimize *in vitro* fertilization/intracytoplasmatic sperm injection strategies, prioritizing single embryo transfer. There are still several obstacles to overcome for the purpose of improving assisted reproductive success, such as intra- and inter-observer subjectivity in embryonic selection, high occurrence of multiple pregnancies, maternal and neonatal complications. Here, we compare studies that used several variables that impact the success of assisted reproduction, such as blastocyst morphology and morphokinetic aspects of embryo development as well as characteristics of the patients submitted to assisted reproduction, in order to predict embryo quality, implantation or live birth. Thereby, we emphasize the proposal of an artificial intelligence-based platform for a more objective method to predict live birth.

Keywords: assisted reproductive technology, live birth prediction, artificial intelligence

INTRODUCTION

At the end of 1970s, *in vitro* fertilization (IVF) was an experimental process that resulted mostly in abortions or in unsuccessful pregnancies (Steptoe & Edwards, 1976) until, in July 1978, the first successful case obtained through IVF was the birth of Louise Brown (Steptoe & Edwards, 1978). After the introduction of intracytoplasmic sperm injection (ICSI) (Palermo *et al*., 1992), this technique was rapidly integrated into fertility clinics that offer assisted reproductive technology (ART) throughout the world. During the last years, ICSI has become the most frequently used method for fertilization, and in 2004, it was used in nearly 60% of all reported ART cycles in Australia and New Zealand, Europe and the USA (Wang *et al*., 2006; Wright *et al*., 2007; Andersen *et al.,* 2008). In Latin America, in 2012, the largest number of assisted reproduction clinics and ART cycles performed were reported in Brazil, representing 45% of the total; followed by Argentina with 23% and Mexico with 12% (Zegers-Hochschild *et al*., 2014; 2015).

Although advances in IVF were responsible for refining the technology for the treatment of women with tubal disease, patients with natural or premature ovarian failure had no effective treatment until 1983 (Wang & Sauer, 2006). In the last decades, ART has continued to overcome a number of barriers that have allowed its constant improvement; however, singletons of ART pregnancies still exhibit increased maternal and neonatal complications (Zhu *et al.,* 2016). In order to obtain a higher number of positive outcomes, the correct choice of the embryo to be transferred is fundamental to raise the number of live births (Ledford, 2018; Maheshwari *et al*., 2015). Initially, one of the options to obtain improvement of gestational rate was to transfer a high number of embryos, but it also led to increase in multiple pregnancy rate. To change this scenario, embryo selection by culture until blastocyst stage for the best one, which allows genomic activation and/or better endometrial synchronicity, associated with compaction and cavitation events of the embryonic cells, responsible for giving the blastocyst higher potential to establish a gestation has been performed (Rijnders & Jansen, 1998; Hardarson *et al*., 2012).

Since the selection of the best embryo to be transferred is such a defining milestone for gestational success, embryonic classification systems have been developed and improved over time. Among the analyzed morphological aspects are the number of cells, degree of compaction, fragmentation and size of the blastomeres (Lundin & Ahlström, 2015). The main morphological parameters analyzed are based on blastocyst stage and, currently, the most wide classification system used is based on morphological parameters graded by Gardner & Schoolcraft (1999), which involves expansion and hatching (EH) stage, from 1 (the least grade of expansion) to 6 (totally hatched); inner cell mass (ICM) grades, classified from A (many tightly packed cells) to C (very few cells) and trophectoderm (TE) grades, classified from A (many cells forming cohesive epithelium) to C (large and scarce cells). Despite the constant improvement of embryo selection systems, morphological evaluation observed through light microscopy remains the most used in assisted reproduction clinics worldwide (Alpha & ESHRE, 2011; Nasiri & Eftekhari-Yazdi, 2015; Puga-Torres *et al*., 2017).

As pointed by Alfarawati *et al*. (2011), most of the morphologic assessment criteria that are used to evaluate the embryo are only weakly correlated with IVF outcome. Embryo morphology is not always an absolute indicator for implantation potential once the best-looking blastocyst can fail to generate pregnancy or a morphologically suboptimal embryo can evolve into a healthy baby (Pribenszky *et al*., 2017). Furthermore, the nature of these evaluations and decisions made by embryologists is subjective, due to the existence of intra- and inter-observer variability (Sundvall *et al*., 2013), confounding (laboratory) factors such as differences in culture media and culture environment, beyond different handling of oocytes and embryos in the laboratory. Moreover, the quality of these assessments depends on the experience and attention to details, factor that is influenced by mood and fatigue at the moment of evaluation (Lundin & Ahlström, 2015; Rocha *et al*., 2016). Thereby, novel embryo selection technologies have emerged either to replace morphology-based embryo selection or to enhance conventional morphology-based embryo selection (Sengul *et al*., 2015).

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The time-lapse system (TLS) allows embryo development monitoring without its remotion from the incubator, through a coupled camera and an appropriate software that produces a video recording of its evolution (Kovacs, 2014; Perkel *et al*., 2015). In addition, frames obtained by means of TLS allow the acquisition of morphological and kinetic information besides asymmetry of the cleavages in a non-invasive way (Wong *et al*., 2010; Chen *et al*., 2013; Milewski & Ajduk, 2017). The meticulous analysis of TLS images may also be used to detect potential embryo splitting signals, as detected in a monochorionic triamniotic pregnancy case, whereby there was elective single embryo transfer at the hatching blastocyst stage; thus, TLS can be a valuable tool to avoid the occurrence of multiple pregnancy (Sutherland *et al*., 2019).

Currently, there are many types of TLS available in the market. Some of them offer all items integrated in only one device, such as EmbryoScope® (Vitrolife), Geri (Genea Biomedx) and Miri® TL (Esco Medical). In contrast, other systems have the option of introducing a microscope into a regular incubator, *e.g.* Primo Vision® (Vitrolife) and the Eeva™ Test (Merck-Serono) (Aparicio-Ruiz *et al*., 2018; Basile *et al*., 2019).

The ultimate purpose of TLS is selecting the embryo that has the best probability of resulting in live birth. Information obtained through TLS gives us knowledge about the morphological changes, kinetic and abnormalities on embryo that undergoes *in vitro* (Pribenszky *et al*., 2017). Therefore, the analysis of events that occur during embryonic development - the morphokinetic parameters - can be evaluated and, from this, algorithms may be produced to try to predict clinical outcomes of the embryo (Milewski & Ajduk, 2017).

Morphokinetic parameters can be evaluated for their capability to predict the quality of blastocyst (day 5). Table 1 depicts the main morphokinetic timings and their respective definitions. According to Storr *et al*. (2015), eight morphokinetic variables were considered predictive of top-quality blastocyst morphology (s3, t6, t7, t8, tM, tSB, tB and tEB). This observation contrasts with the results obtained by Cruz *et al*. (2012), whose morphokinetic parameters that indicated better morphological quality of the blastocyst were defined as t3, t5, s2 and cc2. At present, there are some published algorithms for the selection of embryos based on morphokinetic parameters, however frequently they can present incomplete datasets and/or heterogeneous methods that can result in conflicting results; hence, there is not one that is universally accepted (Barrie *et al*., 2017; Kaser & Racowsky, 2014; Aparicio-Ruiz *et al*., 2018).

Increased knowledge about the variables that influence the chance of success in ART may have a decisive impact on the guidance for using single embryo transfer (SET). Previous treatment of the patient, for instance, and the number of previous successful/failed IVF treatments were demonstrated to be of strong predictive value for live birth after IVF/ICSI (Nelson & Lawlor, 2011; van Loendersloot *et al.,* 2014). Other than that, pre-pregnancy body mass index (BMI) significantly affects pregnancy outcomes, sometimes leading to gestational diabetes mellitus, gestational hypertension, preeclampsia, macrosomia, and caesarean delivery (Vesco *et al.,* 2009; Baeten *et al.,* 2001; Cedergren, 2004; Sebire *et al*., 2001; Bartolacci *et al*., 2019). Additionally, babies of obese mothers are more likely to experience prematurity, stillbirth, and congenital abnormalities (Provost *et al.,* 2016). Currently, models for predicting live births after an IVF/ICSI cycle are under construction, some of them confirming embryo score, previous treatment, ovarian sensitivity, female age, endometrial thickness, infertility cause, and female height as independent predictors (Vaegter *et al.,* 2017).

Table 1. Morphokinetics parameters evaluated for their capacity to identify the quality of blastocyst. Adapted from Storr *et al*. (2015).

Parameter	Definition
Pntl	Time of pronuclei formation
NEBD	Nuclear envelope break down
Cytokinesis	First cytokinesis
t2	Time of cleavage to a two-cell embryo
t3	Time of cleavage to a three-cell embryo
t4	Time of cleavage to a four-cell embryo
t5	Time of cleavage to a five-cell embryo
t6	Time of cleavage to a six-cell embryo
t7	Time of cleavage to a seven-cell embryo
t8	Time of cleavage to a eight-cell embryo
tM	Time to full compaction
tSB	Time to the first signs of blastulation
tB	Time to full blastocyst
tEB	Time to expanded blastocyst
tHB	Time to hatching blastocyst
s1	Time between NEBD and subsequent division to two cells
s2	Time between division to three cells and subsequent division to four cells
s3	Time between division to five cells and subsequent division to eight cells
t4 int	Time between division to four cells and subsequent division to five cells
t5-t2	Time between division to two cells and subsequent division to five cells
cc2	Duration of the second cell cycle
cc3	Duration of the third cell cycle

Although blastocyst formation and implantation rate are important markers of treatment efficacy, neither of them can be used to replace live birth rate or at least ongoing pregnancy (Kovacs, 2014). However, the own definition of live birth is controversial and Table 2 shows there is no consensus about the definition of this term.

The term known implantation data (KID) has been frequently employed in recent time-lapse researches as a developing and/or validating embryo selection algorithm in a dataset that comprehends a substantial number of double embryo transfer (DET) cycles (Liu *et al*., 2018; Basile *et al*., 2015; Liu *et al*., 2016; Meseguer *et al*., 2011). In these studies, embryos can be considered KID+ (positive) when refer to those generated from a SET cycle where a single fetal heartbeat is recognized under ultrasound or a DET cycle where two fetal heartbeats are recognized. On the other hand, KID- (negative) embryos are concerned to those from a cycle (both SET and DET) with a negative outcome unrelated to the number of embryos transferred. Besides that, KID data do not consider embryos from DET cycles with singleton pregnancy outcomes, due to the impossibility of knowing which embryo had implanted (Liu *et al*., 2018).

Despite the large range of information provided by the various international studies on assisted reproduction, a deeper analysis of the parameters that interfere in the

Table 2. Definitions of the term "live birth" according to different publications

Publication	Definition of live birth
Hill *et al*. (2013)	Birth of a live infant after 23 weeks' gestation
Kirkegaard *et al*. (2016)	Birth of a child
Pribenszky *et al*. (2017)	Baby who was born alive
Zhu *et al*. (2018)	Infant born alive after 24 weeks of gestation who survived more than 28 days
World Health Organization (2019a)	Complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any other evidence of life

gestational success and the birth of a healthy baby is still necessary. To that end, the constant evaluation and improvement of prediction models are fundamental, since the policies that encourage or determine the increased use of SET have been expanded in many countries, due to the risk of multiple gestations and maternal and neonatal complications (Karlström & Bergh, 2007). Therefore, our aim is to present several studies that have used morphological, morphokinetic, patient and partner variables submitted to ART and compare their results in order to predict live birth and/or fetal heartbeat. Based on these studies, we will propose an attempt to link the most relevant variables that contribute to the success of live birth in a way that can be reproducible, objective and non-invasive.

EMBRYO MORPHOLOGY AS PREDICTIVE PARAMETER

At the moment of the decision of which embryo to transfer during ART, morphology is still the most common parameter used for blastocyst quality evaluation (Reignier *et al*., 2018; Gardner *et al*., 2015). Therefore, in general, the best grades of the three morphological parameters (EH stage, TE and ICM qualities), will result in higher likelihood of live birth. However, sometimes there are no embryos in the best grades during the analysis and, even so, it is necessary to choose at least one for the transfer.

Thus, supported by studies based on fresh single blastocyst transfer, Ahlström *et al*. (2011) analyzed the independent ability of each morphological parameter to predict live birth, and all three parameters had significant effects on live birth rates, but the TE grade showed better predictive power compared to the other two parameters. Corroborating such results, Hill *et al*. (2013) showed that TE grade had the strongest correlation with live birth. Unlike both studies, Subira *et al*. (2016) found a strong correlation between ICM and live birth rate. In contrast, Du *et al*. (2016) evaluated the grade of expansion and re-expansion of the blastocoel as better ability to predict live birth (fresh cycles) and only the grade of blastocoel re-expansion was correlated with live birth in vitrified/warmed cycles.

EMBRYO MORPHOKINETIC AS PREDICTIVE PARAMETER

From the beginning of the use of TLS, which allows morphokinetic times evaluation, it is expected to be an improvement in embryologist's ability to select the embryo, which is most likely to be implanted, resulting in an improved clinical result (Kovacs, 2014).

Based on this, Goodman *et al*. (2016) evaluated the inclusion of specific kinetic parameters through TLS, in which results showed that the addition of time-lapse morphokinetic data did not significantly improve clinical reproductive outcomes. Besides that, the study indicated that only tSB was predictive of embryo implantation. On the other hand, Pribenszky *et al*. (2017) supported in their meta-analysis that time-lapse application was associated with a higher ongoing pregnancy rate and a significant increase on live birth rate. Reignier *et al*. (2019) analyzed the performance of KIDScore™ Day 5 morphokinetic prediction models and demonstrated a significant association with chances of pregnancy and live birth after blastocyst transfer, even though there may still be improvements.

Fishel *et al*. (2017) combined morphokinetic data in association with patient age and obtained an increase of 19% in the incidence of live births through embryo selection using morphokinetic algorithms for a cohort of patients younger than 38 years (using their own oocytes) and an increase of 37% for donated oocytes over 37 years.

PATIENT AND PARTNER VARIABLES AS PREDICTIVE PARAMETERS

It is widely accepted that fertility begins to decline years before the onset of menopause, even though continued regular ovulatory cycles happens, and that after 35 years, infertility becomes more frequent, a fact that deeply affects the chance of a full term birth of a baby (Van Noord-Zaadstra *et al*., 1991; Practice Committee of the American Society for Reproductive Medicine, 2006).

Several physiological characteristics of patients submitted to IVF are related with gestational success. Based on the analysis of more than 70,000 blastocysts, Acharya *et al*. (2017) found that advanced age, higher incidence of unexplained infertility, and high oocyte production were related to low blastulation rate. In contrast, high rate of blastulation correlated with lower number of oocytes recovered and with higher incidence of tubal factor infertility. These results challenge current knowledge that high oocyte yield leads to a higher number of blastocysts. Also, according to Almagor *et al*. (2015), the early embryos with irregular cleavage are significantly more prevalent in younger women.

Tan *et al*. (2014) reported a decrease of 13.2% in clinical pregnancy for women aged 40-44 years, compared to women less than 30 years. As concluded by Broekmans and Klinkert (2004), Lintsen *et al*. (2007) and Templeton *et al*. (1996), women age is considered the most important predictor of IVF success.

Thus, in a retrospective study conducted with 146 patients aged between 41 years to younger than 44 years who started the first IVF cycle attempt with their own oocytes, cumulative live birth rate was related to a decrease in the probability of live births with increasing age at the beginning of IVF treatment. Overall odds of a live birth rose up to 45% for women who started IVF at age 41, in contrast to 23% when the treatment started at age 43. Moreover, after 6 cycles of IVF, 42 patients (28.8%) gave birth a live infant (85.7% of the total live birth). The average rate of live births per cycle decreased with age in the initial cycle (8.0% at 41 years, 5.8% at 42 years and 4.1% at 43 years). In this study, patient age, smoking status and mean number of fertilized oocytes were considered as the major factors significantly correlated with the probability of a live birth (Lebovitz *et al*., 2018).

Decline in fertility with increasing age is due to the natural biological depletion of the ovarian reserve. The maximum pool of oocytes, approximately 6 to 7 million,

exists during fetal life and undergoes decreasing during the course of pregnancy and drops to about 1-2 million by birth (Speroff, 1994). At puberty, 300,000 to 500,000 oocytes remain, and around the age of 37, when the rate of depletion doubles, it results in an increased rate of follicular loss, remaining only around 25,000 (Simpson, 2000). The number decreases to around 1,000 follicles when women achieves menopause (Navot *et al*., 1991; Loh *et al*., 2005). Also, Tan *et al*. (2014) found a doubling in miscarriage rate, increasing from 15.1% among women less than 30 years to 30.0% among those with 38 years, leading to the conclusion that another factor linked to the lower live birth rate with increasing maternal age are obstetric complications, mainly due to aneuploidy.

Another retrospective study analyzed the influence of BMI on live birth through IVF, considering the BMI criteria of the World Health Organization (2019b), according to Table 3. Low BMI was correlated with decrease in live birth rates and increase in miscarriage rates compared to normal weight, controlling for covariates that influence the treatment outcome; nonetheless, the age of the patients was the most potent confounder variable. Moreover, low BMI had a more profound effect on live birth rates in patients older than 35 years, whereas the effect in younger patients was insignificant (Cai *et al*., 2017). The inverse was also analyzed and demonstrated the declined probability of live birth following IVF in obese patients in comparison to normal weight patients (Sermondade *et al*., 2019).

Although van Swieten *et al*. (2005) reported that obesity is negatively associated with IVF/ICSI outcome, Fedorcsák *et al*. (2004) reported a significant linear association between higher BMI (above 30 kg/m²) and increased dose and longer stimulation with follicle-stimulating hormone (FSH), increased frequency of cycle cancellation, lower number of oocytes retrieved and lower number of embryos transferred. It was also associated with increased incidence of pregnancy loss before the sixth week of gestation, increased miscarriage during 6 to 12 weeks of pregnancy, lower live birth and cumulative live birth rates. Esinler *et al*. (2008) pointed that obese women had a higher risk of cycle cancellation due to poor ovarian response and lower fertilization rates.

Independent of chronological age, ovarian ageing affects both oocyte fecundity and quality and can negatively impact on the outcome of ART (Akande *et al.*, 2002; Alviggi *et al.*, 2009). With ovarian ageing, the diminishing proportion of normal oocytes needs to be compensated for quantitatively by increasing the number of available oocytes through controlled ovarian hyperstimulation. The result is the ovarian response as one of the parameters most commonly studied and reported in clinical research on IVF treatment, *e.g.* aiming to seek measures to optimize live births rate and minimize the risk of an increase in ovarian hyperstimulation syndrome (Li *et al*., 2014; Fiedler & Ezcurra, 2012). Baseline tests, such as serum FSH, inhibin B, estradiol and anti-Müllerian hormone (AMH), clomiphene citrate test and antral follicle count (AFC) correlate with the degree of ovarian response, but with limited accuracy in relation to the prediction of pregnancy (Broekmans *et al*., 2006; Pettersson *et al*., 2010).

AMH is a glycoprotein produced by granulosa cells of small and large preantral and small antral follicles (La Marca *et al*., 2010; Weenen *et al.*, 2004). This hormone is secreted during the early follicular stage by follicles up to 6 mm in diameter and is also relatively independent of gonadotropin and remains relatively constant within and between menstrual cycles (Fanchin *et al*., 2005; Hehenkamp *et al*., 2006; La Marca *et al*., 2006; Tsepelidis *et al*., 2007; Van Disseldorp *et al*., 2010; Rasool & Shah, 2017). AMH levels peak at 25 years and gradually decline thereafter (Garcia-Velasco *et al*., 2005; Grossman *et al*., 2008; Durlinger *et al*., 2001). AMH declines years before the visible increase in FSH levels, thus being a more sensitive biomarker of the ovarian reserve (Freeman *et al*., 2012a; 2012b; Rasool & Shah, 2017). However, a generalized limit of AMH to predict pregnancy outcomes does not exist, since oocyte quality is not accounted for solely by quantitative ovarian reserve markers (Wang *et al*., 2010; Broekmans *et al*., 2006).

Templeton *et al*. (1996), and Nelson & Lawlor (2011), through the analysis of IVF and ICSI cycles, have identified predictors of live birth following IVF, pointing female age, duration of infertility and previous pregnancy as key prognostic factors. Templeton *et al*. (1996) showed a significant reduction in the success rate with the increasing duration of infertility, and a higher live birth rate per embryo transfer on women with unexplained infertility than woman with other causes. For Nelson & Lawlor (2011), the odds of successful live birth also decreased with increasing maternal age, increasing duration of infertility, greater number of previously unsuccessful IVF treatments, when the woman's own oocytes was used, and when this was the second or third treatment cycle, being lower when the cause of infertility was tubal, anovulatory, or cervical disease or when it was due to a male cause.

Among the results obtained by Templeton *et al*. (1996), stands out that the best possibility of success is in the first cycle of IVF treatment and that there is a significant negative effect with increasing number of attempts thereafter. Besides that, results show that the chance of a live birth begins to fall rapidly after 4 previous unsuccessful cycles, suggesting an inverse relationship between the success of IVF and the number of prior unsuccessful attempts (Nelson & Lawlor, 2011; Roberts *et al*., 2010).

Male infertility is also a factor which can influence the live birth rates. According to a study that considered 781 men with average total testosterone (TT) of 411 (318-520) ng/dL, those with TT<264 ng/dL were less likely to have normal morphology sperm and the chances of live birth decreased by 40% in couples whose male partner had low TT. As follows, the study pointed out that low TT in the male partner was associated with abnormal sperm morphology and lower live birth rates (Trussell *et al*., 2019).

Table 3. Nutritional status according to World Health Organization (2019b)

BMI (kg/m²)	Nutritional status
<18.5	Underweight
18.5-24.9	Normal weight
25.0-29.9	Pre-obesity
30.0-34.9	Obesity class 1
35.0-39.9	Obesity class 2
≥40.0	Obesity class 3

FUTURE PERSPECTIVES

A promising tool for predicting embryo quality, gestational success and live birth based on one or more parameters, such as those described above (Table 4), has been highlighted by its powerful predictive potential: the artificial intelligence (AI) techniques; which have already been used, through digital image processing and artificial neural networks, to classify the quality of mammalian embryos based on the morphological aspects of the blastocyst stage (Rocha *et al*., 2016; Matos *et al*., 2014; Rocha *et al*., 2017).

Table 4. Set of variables mined as potentially predictive to the gestational success based on AI approaches			
Morphokinetic	**Blastocyst Morphology**	**Female variables**	**Male variables**
t2	Trophectoderm texture analysis	Age	Total testosterone (ng/dL)
t3	Inner cell mass texture analysis	Number of retrieved oocytes	Spermatic cell count
t4	Expansion grading (by Gardner & Schoolcraft system)	Body Mass Index (BMI)	Male infertility cause
t8	Inner cell mass grading (by Gardner & Schoolcraft system)	Anti-Müllerian Hormone (AMH) and/or Antral Follicle Count (AFC)	
tSB	Trophectoderm grading (by Gardner & Schoolcraft system)	Previous IFV Attempts	
t4-t3		Female infertility cause	

Recent researches involving human embryos and AI can also be highlighted: Miyagi *et al*. (2019a), through machine learning approaches, used 160 blastocyst images that were implanted to develop a method for classifying embryos to predict the probability of reaching live birth, obtaining as result 65% of accuracy. In other study using specifically deep learning techniques, Miyagi *et al*. (2019b) based on blastocyst images to predict the probability of live birth in patients classified by age, used a total of 5,691 blastocyst images and the best accuracies obtained were 81% and 88%, respectively for the ages 40-41 and ≥ 42 years.

Blank *et al*. (2018) also used machine learning approaches to predict implantation potential after single blastocyst transfer, combining morphological characteristics associated with patient variables, *e.g.* parental age, AMH concentration and number of oocytes. Their application resulted in area under the curve (AUC) of 0.74.

Moreover, Khosravi *et al.* (2019) proposed a computational method based in deep learning techniques, to predict the quality of human embryos. Their approach used 10,148 digital images, obtained by TLS, and it could predict the morphological quality of blastocysts with accuracy of 98%. Also, through a deep learning model, Tran *et al.* (2019) predicted the probability of pregnancy with fetal heartbeat from TLS, based on 10,638 human embryos, and obtained an AUC of 0.93.

CONCLUSION

In view of all the variables shown in this review, which have the potential to predict live birth after ART, it is clear that many attempts have been produced to reduce the subjectivity of the conventional morphological embryonic evaluation. However, from the analysis of the previously described studies, it can be noted that in the majority - if not in full - of them, they do not use many of the variables that can predict live birth (Table 4). This observation could be a factor of why some of them have not achieved satisfactory results.

The approach of the AI techniques offers an outlet for this problem, once this tool allows the application of several variables as input to the software and obtain as output the probability of live birth. Nonetheless, to our knowledge, there is still no available software that includes the main variables that influence the success of full-term birth: morphological and morphokinetic embryo parameters, patient and partner clinical characteristics. As pointed by Simopoulou *et al*. (2018), the development of a program that includes such variables depends on the availability of a large database with KID results. Thus, we emphasize the possibility of developing a platform based on AI that includes all these variables as input and can predict the probability of live birth as output, in a way that is objective, accurate and with high reproducibility. Finally, this platform may be integrated in an app that facilitates its clinical use for embryologists and medical professionals in general.

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CONFLICT OF INTERESTS

No conflict of interest has been declared.

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