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A Quadratic Model to Early Predict the Blastocyst Stage with a Time Lapse Incubator

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Abstract : Introduction: The use of incubator equipped with time-lapse technology in Artificial Reproductive Technology (ART) allows a continuous surveillance. With morphocinetic parameters, algorithms are available to predict the potential outcome of an embryo. However, the different proposed time-lapse algorithms do not take account the missing data, and then some embryos could not be classified. The aim of this work is to construct a predictive model even in the case of missing data. Materials and methods: Patients: A retrospective study was performed, in biology laboratory of reproduction at the hospital 'Femme Mère Enfant' (Lyon, France) between 1 May 2013 and 30 April 2015. Embryos (n= 557) obtained from couples (n=108) were cultured in a time-lapse incubator (Embryoscope®, Vitrolife, Goteborg, Sweden). Time-lapse incubator: The morphocinetic parameters obtained during the three first days of embryo life were used to build the predictive model. Predictive model: A quadratic regression was performed between the number of cells and time. $N = a. T^2 + b. T + c$. N: number of cells at T time (T in hours). The regression coefficients were calculated with Excel software (Microsoft, Redmond, WA, USA), a program with Visual Basic for Application (VBA) (Microsoft) was written for this purpose. The quadratic equation was used to find a value that allows to predict the blastocyst formation: the synthetize value. The area under the curve (AUC) obtained from the ROC curve was used to appreciate the performance of the regression coefficients and the synthetize value. A cut-off value has been calculated for each regression coefficient and for the synthetize value to obtain two groups where the difference of blastocyst formation rate according to the cut-off values was maximal. The data were analyzed with SPSS (IBM, Il, Chicago, USA). Results: Among the 557 embryos, 79.7% had reached the blastocyst stage. The synthetize value corresponds to the value calculated with time value equal to 99, the highest AUC was then obtained. The AUC for regression coefficient 'a' was 0.648 ($p < 0.001$), 0.363 ($p < 0.001$) for the regression coefficient 'b', 0.633 ($p < 0.001$) for the regression coefficient 'c', and 0.659 ($p < 0.001$) for the synthetize value. The results are presented as follow: blastocyst formation rate under cut-off value versus blastocyst rate formation above cut-off value. For the regression coefficient 'a' the optimum cut-off value was -1.14.10-3 (61.3% versus 84.3%, $p < 0.001$), 0.26 for the regression coefficient 'b' (83.9% versus 63.1%, $p < 0.001$), -4.4 for the regression coefficient 'c' (62.2% versus 83.1%, $p < 0.001$) and 8.89 for the synthetize value (58.6% versus 85.0%, $p < 0.001$). Conclusion: This quadratic regression allows to predict the outcome of an embryo even in case of missing data. Three regression coefficients and a synthetize value could represent the identity card of an embryo. 'a' regression coefficient represents the acceleration of cells division, 'b' regression coefficient represents the speed of cell division. We could hypothesize that 'c' regression coefficient could represent the intrinsic potential of an embryo. This intrinsic potential could be dependent from oocyte originating the embryo. These hypotheses should be confirmed by studies analyzing relationship between regression coefficients and ART parameters.

Keywords : ART procedure, blastocyst formation, time-lapse incubator, quadratic model
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