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ORIGINAL ARTICLE *Embryology*

Semi-automated morphometric analysis of human embryos can reveal correlations between total embryo volume and clinical pregnancy

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STUDY QUESTION: Is there a link between morphometric characteristics measured by a computer-assisted scoring system and clinical pregnancy outcome?

SUMMARY ANSWER: The results confirm that computer-assisted assessment of the total embryo volume is associated with clinical pregnancy outcome and can be used to complement current procedures of embryo selection.

WHAT IS KNOWN ALREADY: Morphometric analysis of a large group of embryos has revealed the potential to optimize algorithms for image-analysis systems for the grading of embryos and predicting pregnancy outcomes.

STUDY DESIGN, SIZE, DURATION: Oocytes and embryos were obtained from 458 patients who underwent single embryo transfer on Day 3 after IVF/ICSI, between September 2006 and December 2010 at the Leuven University Fertility Center, Belgium. In total, the data set contained 2796 embryos including 458 embryos that were transferred on Day 3. Ongoing pregnancy was defined as the presence of at least one intrauterine gestational sac at 20 weeks.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Patients included in this study were younger than 36 years, entering their first ($n = 375$) or second ($n = 83$) IVF/ICSI cycle and were only included once. Patients were excluded if the cycle included biopsy for PGD or if donor sperm/donor oocytes were used. Based on the 26 sequential images of the same embryo taken at one time point in different planes, the software calculates the total cytoplasmic volume for each time point, from which any reduction or change in the volume with time can be assessed (which helps interpret the degree of fragmentation) and the size of blastomeres. The diameter of the smallest and largest blastomere and the total volume of each embryo were extracted from the computer-assisted scoring system database and the coefficient of diversity was calculated for Days 1, 2 and 3. A logistic regression analysis was performed to determine the range of embryo volume associated with an increased chance of pregnancy.

MAIN RESULTS AND THE ROLE OF CHANCE: On Day 3, blastomeres of 8-cell stage embryos were less divergent in size than those of 6-, 7-, 9-cell stage embryos. Although, the coefficients of diversity (ratio of the largest:smallest blastomeres) of implanted embryos tended to be lower than for non-implanted embryos, the difference was only significant for 6-cell stage embryos ($P = 0.02$). After logistic regression, an association between total embryo volume and pregnancy was observed which had a quadratic nature: both lower and higher volumes were associated with a lower probability of successful pregnancy. A significant association was identified between total embryo volume and pregnancy rate on both Days 2 ($P = 0.003$) and 3 ($P = 0.0003$). Diagnostic measures (sensitivity, specificity, positive predictive value, accuracy and c-statistics) of the defined volume range were relatively poor. However, results showed a good negative predictive value [76.86% (95% confidence interval 71.03–82.02) on Day 3].

LIMITATIONS, REASONS FOR CAUTION: A general disadvantage of studies evaluating the impact of a characteristic on the implantation potential of an embryo is the fact that the best embryo is chosen for transfer. No comparisons can therefore be made with the other embryos. Moreover, the decision process is currently based on a non-automated, standard scoring system, which means that a 'bias' in the selection process is always present.