ORIGINAL ARTICLE: ASSISTED REPRODUCTION

What is a difficult transfer? Analysis of 7,714 embryo transfers: the impact of maneuvers during embryo transfers on pregnancy rate and a proposal of objective assessment

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Objective: To establish the relationship between the degree of difficulty of ET and pregnancy rate (PR), with a view to proposing an algorithm for the objective assessment of ET.
Design: Retrospective, observational study.
Setting: In vitro fertilization unit.
Patient(s): Women undergoing assisted reproductive technology (ART) with ET after IVF/intracytoplasmic sperm injection, in whom fresh embryo transfer or frozen–thawed embryo transfer was performed.
Intervention(s): None.
Main Outcome Measure(s): Clinical pregnancy rate (CPR).
Result(s): A total of 7,714 ETs were analyzed. The CPR was significantly higher in the cases of easy ET compared with difficult ET (38.2% vs. 27.1%). Each instrumentation needed to successfully deposit the embryos in the fundus involves a progressive reduction in the CPR: use of outer catheter sheath (odds ratio [OR] 0.89; 95% confidence interval [CI] 0.79–1.01), use of Wallace stylet (OR 0.71; 95% CI 0.62–0.81), use of tenaculum (OR 0.54; 95% CI 0.36–0.79). Poor ultrasound visualization significantly diminish the CPR.
Conclusion(s): The CPR decreases progressively with the use of additional maneuvers during ET. An objective classification of the instrumentation applied during ET is proposed. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: Assisted reproductive techniques, clinical pregnancy rate, difficult embryo transfer, embryo transfer technique, IVF

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Despite advances in assisted reproductive technology (ART), implantation rates remain relatively low for universal use of single embryo transfer. Successful implantation requires a viable embryo, a receptive endometrium, and an optimal ET technique.

The ET technique has a major impact on ART outcomes. It has been demonstrated that pregnancy rate (PR) varies significantly between individuals in whom ET is performed in the same IVF program, but when the technique is standardized the results of the ART do not depend on the clinician performing the ET (1). It is estimated that a poor ET technique may be responsible for 30% of all IVF failures (2).

Despite the apparent simplicity of the ET, difficult transfers are frequent and have been shown to significantly decrease PR. Some of the variables that affect ET are the use of ultrasound guidance (3–5), the difficulty of the ET (6–8), type of catheter (9–11), embryo loading technique (12–15), presence of cervical mucus and/or blood (16, 17), retained embryo with repeated ET (18, 19), clinician experience (20, 21), and

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correct replacement of the embryo into the uterine cavity (22–25), among other variables.

There is no universal definition of difficult ET, which makes an accurate comparison of studies even more difficult. Phillips et al. (26) carried out a systematic review and meta-analysis that was eventually limited by such heterogeneity and suggested the need to find a universally accepted definition of difficult ET.

Historically our center has paid special attention to the ET, following a common protocol with systematic records of any additional maneuver or instrumentation needed to perform the procedure and of all the factors that may affect its success (3, 11, 25, 27, 28).

The objective of this study was to establish the relationship between the degree of difficulty of the ET and the PR, with a view to proposing an algorithm for the objective assessment of ET. As a secondary objective we evaluated the impact of other ET-related factors on the PR.

MATERIALS AND METHODS

This was a retrospective, observational study of all ETs performed in the Reproductive Medicine Service of the Hospital Universitario Dexeus between January 2009 and March 2015.

Inclusion and Exclusion Criteria

All patients undergoing ART with ET following IVF/intracytoplasmic sperm injection (ICSI) in whom fresh embryo transfer or frozen–thawed embryo transfer (CT) was performed in the described period were included. Oocyte recipient cycles and cycles involving preimplantation genetic diagnosis were not included. Moreover, patients not undergoing ET because of ovarian stimulation cancellation, no oocyte retrieval, fertilization failure, or because there were no available embryos for transfer were excluded from the analysis.

Controlled Ovarian Stimulation and Cryopreservation

All IVF/ICSI cycles were performed under ovarian stimulation with gonadotropins and pituitary suppression with GnRH analogs (agonists or antagonists) according to established standard protocols (29).

Embryo quality was evaluated according to blastomere number and regularity, degree of fragmentation, and the presence of multinucleation. According to the embryo grading system we used, embryos with a score ≥ 8 on a scale of 1–10 were considered good quality (30).

The remaining embryos were frozen on day 3 or 5 after oocyte retrieval, with the slow-freezing method used from 2009 until mid-2012 (31), and the vitrification method (32) from mid-2012 until the end of the study.

Endometrial Preparation in CT

Endometrial preparation in CT followed the standard protocols described elsewhere by Martínez et al. (33). Briefly, patients underwent treatment with 2 mg/8 h E_2 valerate (Progynova, Schering) for 12–14 days only and then addition of vaginal micronized P treatment at 200 mg/8 h (Utrogestan, Seid) from day 15 until plasma β-hCG determination. In patients with ovarian function the pituitary was suppressed with depot GnRH agonist (triptorelin 3.2 mg).

ET Technique

Embryo transfers were carried out on day 2, 3, or 5 (blastocyst) of development, and between one and three embryos were transferred, depending on patient age, number and quality of embryos available for ET, number of previous IVF attempts, and as per medical indication. The embryos were prepared as described elsewhere (25, 27).

Patients took on the lithotomy position, and after exposure of the cervix with a vaginal speculum the external os was carefully cleaned with a phosphate-buffered saline solution, and the endocervical mucus was removed with cotton swabs. Transabdominal ultrasound was performed by an independent observer, with the bladder full to visualize the angle of the endocervical canal and the endometrial lining (3). A SureView catheter (Wallace/Smiths Medical International) loaded with the embryos was inserted into the cervical os and then through the endocervical canal and into the uterine cavity, and the embryos were deposited in the mid-portion 15–20 mm from the uterine fundus (25). The embryos were gently injected into the uterine cavity by the embryologist, who pushed the plunger of the syringe with a volume of 20 μL of transfer medium, and the catheter was slowly withdrawn after a few seconds (28). The speculum was removed once the catheter had been inspected for retained embryos by means of a microscope. The patient remained in the supine position for 15 minutes.

In some cases, when a difficult ET was suspected, we performed an afterloading ET technique. In those cases, an unloaded catheter was introduced under ultrasound guidance to a point where the inner catheter entered the endometrial cavity. The inner sheath was slowly removed, leaving the outer sheath just beyond the internal os. A second inner sheath was loaded by an embryologist, who then assisted the transfer physician in threading the inner sheath into the catheter, and we continued the ET as described before (34, 35).

If any resistance to negotiating the internal cervical os was encountered, a stepwise approach was used: [1] the use of the outer sheath of the SureView catheter; [2] the use of a Wallace malleable stylet (Simcare); [3] the application of a tenaculum; [4] the insertion of a hysterometer.

All the data related to the ET were systematically recorded in the patient's medical file: the use of an outer catheter sheath, Wallace malleable stylet, tenaculum, or hysterometer; resistance to embryo expulsion; presence of blood and/or mucus in the catheter after withdrawal; repeated ET due to embryo retention in the catheter, involuntary touching of the fundus, and proper visualization by ultrasound, as applicable; position of the uterus, size of the uterine cavity, and endometrial thickness; position of the tip of the catheter with regard to the fundus; number of transferred embryos; and duration of the procedure.

The degree of difficulty of the ET was classified arbitrarily: easy in the case of direct ET or if an outer catheter sheath or Wallace malleable stylet catheter were needed;