Prolonged duration of transfer does not affect outcome in cycles with good embryo quality

The objective of investigating the impact of the time that embryos remain in the catheter on the outcome of cycles was assessed by measuring the period between loading the catheter and discharging the embryos in 300 transfer cycles. The pregnancy and implantation rates were similar in cycles with good embryo quality regardless of transfer duration. (Fertil Steril® 2007;87:1218–21. ©2007 by American Society for Reproductive Medicine.)

Embryo transfer is considered to be of utmost importance for the success of assisted reproduction treatment (1). However, although the technology of IVF has developed over the years, the practice of embryo transfer has undergone few alterations. Some modifications that have been suggested to be of importance in improving outcome are visualization of the uterine cavity by ultrasound (2, 3), loading the catheter without air (4), causing minimal trauma (3, 5–8), increasing speed of the procedure (9), and using soft catheters (10).

Although the success of a transfer technique appears to be largely dependent on the skills of the physician (1, 11), the impact of operator variability has been disregarded in many studies; for example, 15 physicians in (7). Embryo quality is another important variable in the assessment (12, 13). Recent studies showed that day 2 embryos displaying four mononucleated blastomeres possessed a higher implantation potential than others (14, 15). Hence, a better prediction of the effect of embryo quality on outcome has been enabled, and evaluation of the impact of the transfer technique after minimizing possible interference of the embryo factor became possible.

Two physicians, each carrying out approximately 2,000 cycles per year, perform embryo transfers in our center. Hence, the situation can be regarded as "minimal impact of operator skills on outcome" compared to those clinics in which many physicians perform the transfers. However, the time that embryos spend in the catheter before they are expelled into the uterus differs among physicians and patients, because of the speed of the manipulation or to other conditions, such as anatomy of the cervical canal, and so on. The outcome may be influenced by the transfer duration, as the microenvironment to which embryos is exposed in the period between loading and discharging the catheter may have a negative impact on their implantation capacity.

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Therefore, the present study investigated the impact of the time that embryos remain in the catheter on the outcome of cycles for a period of three months (October 1, 2005–December 31, 2005). To minimize potential interference on the results of parameters other than the transfer procedure itself, only cycles that met the following criteria were taken into the survey: [1] women of ≤39 years of age, [2] ≤2 previous failed attempts in our unit, [3] no Preimplantation Genetic Diagnosis (PGD) cycles, [4] no thaw cycles, and [5] at least one motile sperm used for insemination. No consent has been obtained from the patients or the ethics committee, because no additional manipulations other than the routine have been applied to gametes and/or embryos.

The procedures for patient preparation and embryo culture have been described elsewhere (16–18). Briefly, embryos were cultured individually in 20 μL of Quinn's Advantage Plus Medium (Sage In-Vitro Fertilization Inc., Trumbull, CT) covered with sterile mineral oil. Zygotes and embryos were evaluated for early cleavage, day 2 and day 3 morphologies. Embryo transfers were performed at days 2 and 3 according to the indications described elsewhere (19). Two physicians (S.T. and A.M.) performed transfers on a weekly basis to patients with full bladder under ultrasound guidance. Two embryologists participated in the study (H.N.C. and O.H.). Only Wallace Embryo Replacement catheters (18 mm or 23 mm, Smiths Medical Int. Ltd., Kent, UK) were used. In none of the transfers was additional equipment (forceps, tenaculum, hysterometer, and so on) needed.

The embryos were drawn into the catheter without air (4). As soon as the catheter was loaded, a digital timer was set. The physician introduced the catheter gently into the cervical canal and expelled embryos smoothly 1 to 2 cm from the fundus. If there were no retained embryos in the catheter, the timer was stopped. Otherwise, the timer was kept running until retained embryos were expelled. Easy transfers were those in which no blood or mucus in the catheter was observed, and there was no reloading or change of catheter. Transfers with other characteristics were described as difficult. Reloading occurred when there

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TABLE 1

The demographics and outcome of cycles in which good and poor quality embryos were transferred.

Embryo quality	Good		Poor	
Transfer	Easy	Difficult	Easy	Difficult
Cycles (N)	187	34	71	8
Mean age of women ±SD (years; range)	31.6 ± 4.3 (18–39)	31.5 ± 4.5 (21–39)	31.6 ± 4.8 (22–39)	30.3 ± 5.9 (23–39)
Mean day 3 FSH ±SD (mIU/mL)	6.9 ± 3.2[c]	5.7 ± 3.7[c]	8.2 ± 3.5	9.9 ± 4.3
Mean peak E_2 ±SD (pg/mL)	2791 ± 1633	3037 ± 1569	1943 ± 1301[d]	1983 ± 1104
Mean thickness of endometrium at transfer ±SD (mm)	10.7 ± 2.3	11.2 ± 2.8	10.5 ± 2.3	11.5 ± 2.7
Mean number of retrieved oocytes ±SD (N)	17.5 ± 10.0 (3,277)	17.9 ± 7.7 (610)	11.7 ± 8.2 (834)[d]	16.6 ± 13.7 (133)
% Mean M2/retrieved oocytes ±SD (N)	81.3 ± 15.5 (2,640)	82.5 ± 9.6 (497)	80.5 ± 15.3 (417)	81.8 ± 15.1 (106)
% Mean 2PN/M2 oocytes ±SD (N)	76.5 ± 16.9 (1,973)[c]	72.9 ± 13.3 (355)	66.7 ± 21.0 (417)	66.5 ± 27.2 (64)
Mean number of good quality embryos[a] ±SD (N)	5.9 ± 4.4 (1,097)[c]	6.6 ± 4.5 (225)[c]	1.2 ± 2.1 (82)	0.9 ± 1.4 (7)
Mean number of embryos transferred ±SD (N)	2.8 ± 0.5 (526)	2.9 ± 0.3 (100)	2.5 ± 0.9 (176)[d]	2.9 ± 0.4 (23)
Mean ET duration ±SD (seconds; range)	86.1 ± 44.6 (38–315)[e]	225.7 ± 108.2 (61–480)	91.5 ± 59.0 (35–340)[e]	253.6 ± 98.7 (130–378)
N positive β-hCG cycles	135	25	41	2
N biochemical pregnancy (% positive cycles)	5 (3.7)	1 (4.0)	12 (29.3)[d]	0
N clinical pregnancy (% ET)	130 (69.5)[bc]	24 (70.6)[c]	29 (40.8)	2 (25.0)
N implantation (%)	194 (36.9)[c]	38 (38.0)[c]	37 (21.0)	2 (8.7)
N ongoing pregnancy (cycles; % ET)	103 (55.1)[c]	20 (58.8)[c]	24 (33.8)	2 (25.0)

Note: The description of difficult and easy transfers are given in the text. ET= embryo transfer.
[a] Embryos with ≤20% fragmentation, four to five cells (day 2 transfers) and seven to nine cells (day 3 transfers).
[b] Four ectopic pregnancies included.
[c] Significantly different from "poor embryo quality" cycles.
[d] Significantly different from "good embryo quality" cycles.
[e] Significantly different from "difficult" transfers.

Ciray. Transfer duration and embryo quality. Fertil Steril 2007.

were any embryo(s) left in the catheter after the initial transfer. Change of catheter was described as a switch from an 18-mm to a 23-mm catheter, as occurred in some transfers for anatomic reasons (deep cervix, and so on).

The definition of outcome measures of the present study has been described elsewhere (20). Briefly, clinical pregnancy was defined as presence of at least one intrauterine gestational sac and ongoing pregnancy rate as presence of viable fetus 20 weeks after transfer. Implantation rate was defined as the ratio of number of sacs to embryos transferred. Statistical analysis was performed by means of Fisher's exact test, and Student's *t* test, where applicable. A *P* value of $<.05$ was considered significant.

A total of 702 fresh embryo transfer cycles were performed in the study period. Of these, 402 were excluded for the following reasons: 177 were 40 years of age and over, 76 had ≥3 failed attempts at our unit, 17 had a PGD cycle, 2 had only immotile sperm injected, and 130 transfers were performed by a third embryologist who did not participated into the study. As a result, 300 cycles were evaluated.

Transfer cycles were assessed in two main groups according to the quality of embryos obtained: [1] cycles with good embryo quality: regardless of the transfer day, these cycles included at least one Grade 1 embryo at day 2, and [2] cycles with poor embryo quality: in these cycles there was no top quality day 2 embryo (Table 1). Each group was subsequently analyzed in two subgroups: easy and difficult transfers (as described in the Materials and Methods section). The results showed that in cycles with good embryo quality, although difficult transfers required longer ($P<.001$) mean duration, the pregnancy and implantation rates were similar to those from easy transfers. Cycles with poor embryo quality, on the other hand, resulted in higher biochemical and lower clinical and ongoing pregnancy and implantation rates ($P<.01$) than easy transfers despite similar mean embryo transfer durations.

The mean embryo transfer duration was similar between cycles with or without a clinical pregnancy. Patients without a clinical pregnancy displayed a higher mean age ($P<.05$) and a higher basal FSH level ($P<.05$) than those with a positive outcome. There were fewer ($P<.05$) fertilized oocytes in the former group and a smaller mean number of good quality embryos ($P<.001$).

The cycles were evaluated in four groups according to the duration of embryo transfer (in seconds): 0–60, 61–120, 121–180, and >181. The demographics of cycles and distribution of good/poor embryos did not differ between groups. Although easy transfer cycles were mostly performed in 120 seconds, the pregnancy rate was similar between groups.

Overall, the results of the present study showed that when good-quality embryos were transferred, the duration of the procedure did not influence the outcome. Embryo transfer duration did not differ between cycles with positive or negative outcome in terms of clinical pregnancy. Furthermore, with prolonged duration of transfer, the outcome