

## Difficult or repeated sequential embryo transfers do not adversely affect in-vitro fertilization pregnancy rates or outcome

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**In order to assist the medical team in the decision-making process and in adequate counselling of patients when encountering technical difficulties at the time of embryo transfer, we investigated the effect of difficult embryo transfer, with or without the need for cervical dilatation or repeated sequential attempts because of retained embryos in the catheter system, on in-vitro fertilization (IVF) pregnancy rates and outcome. A total of 854 consecutive embryo transfer procedures were prospectively categorized as (i) easy (smooth, unforced), (ii) difficult (requiring uterine manipulation or increased force or cervical grasping and/or accompanied by trauma), (iii) requiring cervical dilatation, or (iv) multiple (two or three) sequential attempts because of embryos retained in the catheter system. Embryo transfer was easy in 734 cases (85.9%). It was difficult in 72 (8.4%), cervical dilatation was required in 21 (2.5%), and one or two repeated attempts were needed in 27 cases (3.2%). Pregnancy rates for the different categories of embryo transfer were 23.3, 23.6, 23.8 and 29.6% respectively. There were no significant differences in the percentage of the ongoing/delivered pregnancies for the different categories of embryo transfer (69, 64.6, 60 and 62.5% respectively). There were no significant differences in the distribution of embryo transfer types among the six infertility specialists who performed the procedures. To conclude, embryo transfers that are difficult to perform or that require cervical dilatation or repeated attempts do not adversely affect pregnancy rates and outcome following IVF. Cervical dilatation, if needed for patients with cervical stenosis, should be performed at the time of the embryo transfer and not earlier. Surgical transmyometrial embryo transfer or rescheduling patients for delayed embryo transfer could be avoided in most patients. This information is important for patient management and counselling in cases of embryo transfer that are not easy to perform.**

**Key words:** cervical dilatation/cervical stenosis/embryo transfer/IVF/transcervical catheterization

### Introduction

Embryo transfer is a short but crucial step in the lengthy process of in-vitro fertilization (IVF) treatment. Most embryo transfers proceed smoothly and do not require the use of force. However, the procedure is sometimes difficult to perform, requiring increased force, uterine manipulation or cervical grasping or even cervical dilatation, and may be accompanied by trauma. Embryos retained in the transfer catheter or its sleeve require repeat transfers.

Technical difficulties at the time of embryo transfer are frustrating for both the patient and the medical team. Furthermore, it has been shown significantly to reduce the chances of successful transfer and implantation (Leeton *et al.*, 1982; Visser *et al.*, 1993). Thus, surgical transabdominal, perurethral, or transvaginal transmyometrial embryo transfer has been suggested to overcome difficult embryo transfer because of cervical stenosis (Lenz and Leeton, 1987; Parsons *et al.*, 1987; Kato *et al.*, 1993), or rescheduling patients for delayed embryo transfer while using laminaria tents for cervical dilatation (Glatstein *et al.*, 1997). Rescheduling patients for delayed embryo transfer rather than repeated sequential attempts because of retained embryos in the catheter system has also been suggested (Visser *et al.*, 1993).

Other studies, however, have shown that embryo transfers which were not easy to perform resulted nevertheless in pregnancy rates comparable to those of easy embryo transfer (Wood *et al.*, 1985; Wisanto *et al.*, 1989; Nabi *et al.*, 1997). All the technical difficulties at the time of embryo transfer have not yet been evaluated together in one study. In order to assist the medical team in the decision-making process when problems arise during embryo transfer, as well as in proper counselling of patients, and to avoid surgical embryo transfer or rescheduling patients for delayed embryo transfer, we investigated the effects of all these difficulties during embryo transfer on IVF outcome in a large cohort of patients.

### Materials and methods

The results of all 854 embryo transfer procedures carried out at our IVF Unit between November 1994 and June 1996 were analysed. The transfers were performed by six infertility specialists experienced in IVF and embryo transfer techniques. Each procedure was carried out with the patient in the lithotomy position and without anaesthesia. General anaesthesia was never used even in cases of difficult embryo transfer or when cervical dilatation was performed. Edwards–Wallace embryo replacement catheters (Simcare, Lancing, West Sussex, UK) were used. This catheter system has a rigid outer Teflon<sup>®</sup> sleeve and a soft silicone open-ended inner catheter. The sleeve is passed through the cervical canal and is used as an introducer.

After cleaning the cervix with a sterile swab soaked with saline

**Table I.** Pregnancy rates and outcomes for the different categories of embryo transfer

Pregnancy outcome	Easy (%)	Difficult (%)	Cervical dilatation (%)	Multiple (%)	Total (%)
Ongoing or delivered	118/171 (69)	11/17 (64.6)	3/5 (60)	5/8 (62.5)	137/201 (68.2)
Ectopic	0	2/17 (11.8)	0	0	2/201 (1)
Missed abortion	26/171 (15.2)	2/17 (11.8)	2/5 (40)	3/8 (37.5)	33/201 (16.4)
Chemical	27/171 (15.8)	2/17 (11.8)	0	0	29/201 (14.4)
Total (%)	171/734 (23.3)	17/72 (23.6)	5/21 (23.8)	8/27 (29.6)	201/854 (23.5)

and dry swab, the transfer catheter was loaded and presented by the IVF embryologist to the gynaecologist performing the procedure. The uterine length was not measured. The tip of the inner catheter was placed about 1 cm from the uterine fundus (6–6.5 cm from the external cervical os), and the embryos were injected into the uterine cavity. After withdrawal, the catheters were immediately checked for the presence of retained embryos. If embryos were found, they were immediately reloaded and retransferred with the same catheter.

Embryo transfer procedures were defined as follows: (i) easy (smooth, unforced); (ii) difficult (requiring uterine manipulation or increased force or cervical grasping, and/or accompanied by trauma); (iii) requiring gentle cervical dilatation with Hegar dilators (to enable the catheter to pass through the internal os); and (iv) multiple sequential attempts (two or three entries into the uterine cavity to transfer all embryos). The grading of 'easy' or 'difficult' embryo transfer was determined prospectively by three embryologists who all have at least 8 years of experience in the IVF laboratory.

IVF pregnancy outcome was classified as ongoing/delivered, ectopic pregnancy, missed abortion, or chemical pregnancy.

$\chi^2$  and Fisher's exact tests were used for statistical analysis where appropriate.

## Results

The 854 embryo transfers performed during the study period resulted in 201 pregnancies (a pregnancy rate of 23.5%), of which 170 proved to be clinical pregnancies (a clinical pregnancy rate of 19.9%). Table I records the pregnancy rate and outcomes for the different categories of embryo transfer. Of the embryo transfers, 85.9% (734) were graded as easy and resulted in a pregnancy rate of 23.3% and 8.4% (72) as difficult with a pregnancy rate of 23.6%. Cervical dilatation was required in 2.5% (21) of cases (pregnancy rate = 23.8%), and in 3.2% (27) of cases the procedure was repeated once or twice for retained embryos (pregnancy rate = 29.6%). There were no significant differences in pregnancy rate for the different categories of embryo transfer. There were no significant differences in the percentage of the ongoing/delivered pregnancies for the different categories of embryo transfer. Because of the above and the small numbers in the subgroups of non-favourable pregnancy outcomes (ectopic pregnancy, missed abortion, or chemical pregnancy) for the non-easy embryo transfers, no further statistical analysis was performed (Table I). The distribution of the various transfer categories did not differ significantly among the six infertility specialists who performed the transfers.

## Discussion

This study demonstrates that technical difficulties experienced during embryo transfer do not adversely affect IVF pregnancy rates or outcome. Uterine manipulations, cervical dilatation and one or two repeated sequential transfers because of embryos retained in the catheter may be safely performed, when required, at the time of embryo transfer. This is the only study to investigate it while including all types of the non-easy embryo transfers at once [categories (ii), (iii) and (iv)]. In order to be able to compare our results with those from other studies we differentiated repeated transfers because of retained embryos in the catheter or its sleeve from repeated transfers because of difficulties experienced in inserting the catheter into the uterus [categories (iv) and (ii) respectively; Table II]. The distribution of the different categories of embryo transfer in our study is in line with the findings of others (Leeton *et al.*, 1982; Wood *et al.*, 1985; Diedrich *et al.*, 1989; Wisanto *et al.*, 1989; Visser *et al.*, 1993; Nabi *et al.*, 1997).

Published pregnancy rate for the different categories of embryo transfer (Leeton *et al.*, 1982; Wood *et al.*, 1985; Wisanto *et al.*, 1989; Visser *et al.*, 1993; Nabi *et al.*, 1997) and the results of this study are summarized in Table II. Easy embryo transfers resulted in a pregnancy rate of 21.5% (670 pregnancies out of 3118 embryo transfers, all studies in Table II). This is not significantly higher than the pregnancy rate of 18.7% (45 of 241) obtained after difficult embryo transfers, or the 13.3% (15 of 113) obtained after embryo transfer with cervical dilatation, or the pregnancy rate of 19.2% (25 of 130) obtained with multiple sequential embryo transfers (Table II).

The most problematic embryo transfers are those in which cervical dilatation is required. Cervical dilatation is mandatory only when the gynaecologist or the nurse (Barber *et al.*, 1996) cannot introduce the catheter into the uterine cavity after the use of increased force and repeated attempts with uterine manipulation with or without grasping of the cervix with a tenaculum. Even the use of ultrasound guidance (Woolcott and Stanger, 1997) in cases of difficult embryo transfer is not always effective and resulted in performing cervical dilatation in 3.3% of such cases (three of 92) (Wisanto *et al.*, 1989). Visser *et al.* (1993) achieved no pregnancies when cervical dilatation was performed under general anaesthesia 2–3 days before the embryo transfer, during the laparoscopic aspiration of oocytes. In contrast, our group, as well as others (Wood

**Table II.** Summary of pregnancy rates for the different categories of embryo transfer.**A.** Comparison of pregnancy rates after easy or difficult embryo transfer

Study	Easy (%)	Difficult (%)	P value
Leeton <i>et al.</i> , 1982 <sup>a</sup>	34/159 (21)	0/28 (0)	0.002
Wood <i>et al.</i> , 1985 <sup>a</sup>	102/659 (15.5)	28/169 (16.6)	NS
Tur-Kaspa <i>et al.</i> , 1998 <sup>b</sup>	171/734 (23.3)	17/72 (23.6)	NS
Total <sup>a</sup>	273/1393 (19.6)	45/241 (18.7)	NS

**B.** Comparison of pregnancy rates after easy embryo transfer or transfer requiring cervical dilatation

Study	Easy (%)	Cervical dilatation (%)	P value
Wood <i>et al.</i> , 1985	102/659 (15.5)	1/28 (3.6)	NS
Wisanto <i>et al.</i> , 1989	69/345 (20)	9/46 (19.5)	NS
Visser <i>et al.</i> , 1993 (Figure 2)	48/245 (19.8)	0/8 (0)	0.0001
Tur-Kaspa <i>et al.</i> , 1998 <sup>b</sup>	171/734 (23.3)	5/21 (23.8)	NS
Total	390/1983 (19.7)	15/113 (13.3)	NS

**C.** Comparison of pregnancy rates after easy embryo transfer or after multiple sequential transfers because of retained embryos

Study	Easy (%)	Multiple embryo transfers (%)	P value
Visser <i>et al.</i> , 1993 (Figure 1)	60/296 (20.3)	1/34 (3)	0.0015
Nabi <i>et al.</i> , 1997	280/1135 (24.7)	16/69 (23.2)	NS
Tur-Kaspa <i>et al.</i> , 1998 <sup>b</sup>	171/734 (23.3)	8/27 (29.6)	NS
Total	511/2165 (23.6)	25/130 (19.2)	NS

<sup>a</sup>Data of Leeton *et al.* (1982) are included in Wood *et al.* (1985) and, therefore, are not summed within the total.

<sup>b</sup>This study.

*et al.*, 1985; Wisanto *et al.*, 1989), demonstrated similar pregnancy rates to those achieved after easy embryo transfer when cervical dilatation was performed at the time of embryo transfer (Table IIB). We therefore recommend that if required during the IVF treatment cycle, cervical dilatation for cervical stenosis can be and should be performed only at the time of embryo transfer. The recent prospective randomized study (Groutz *et al.*, 1997) that failed to demonstrate a benefit of surgical transmyometrial embryo transfer over transcervical embryo transfer in patients with previously failed IVF cycles who were known to have cervical stenosis supports our conclusion. Furthermore, performing cervical dilatation may prevent the complication of intramural pregnancy which probably resulted from false cervical passage following difficult embryo transfer (Khalifa *et al.*, 1994).

The need to check the catheters for retained embryos following transfer has been consistently stressed since the embryo transfer technique used in the first IVF live birth was described by Steptoe *et al.* (1980). Retained embryos can be handled in three ways: freezing the embryos and transferring them during a later cycle, repeating the embryo transfer the next day (Visser *et al.*, 1993), and performing immediate repeated sequential embryo transfers. Freezing–thawing cycles result in lower pregnancy rates than those obtained when fresh embryos are used (SART and ASRM, 1996). Visser *et al.* (1993) experienced significantly lower pregnancy rates in multiple sequential transfers for retained embryos than in single

transfers (Table IIC). They therefore suggested postponing the transfer of retained embryos to the following day. Our experience, similar to that of Nabi *et al.* (1997), shows that immediate repeated sequential embryo transfers resulted in pregnancy rate similar to those of single embryo transfers (Tables I and IIC). This is supported by the finding of Caspi *et al.* (1989) that dividing of embryos between two sequential embryo transfers 24 h apart has no advantage over single embryo transfers. Nabi *et al.* (1997) demonstrated that embryos were significantly more likely to be retained when the embryo transfer was difficult to perform or when the catheter was contaminated with mucus or blood. Nevertheless, since it did not affect the pregnancy rate, we, like Nabi *et al.* (1997), do not aspirate the cervical mucus prior to the embryo transfer.

There were no significant differences in the percentage of the ongoing/delivered pregnancies for the different categories of embryo transfer. Because of that, and the small numbers in the subgroups of non-favourable pregnancy outcomes (ectopic pregnancy, missed abortion, or chemical pregnancy) for the non-easy embryo transfers, no conclusions could be reached about a possible association between them (Table I).

In summary, difficult or sequentially repeated embryo transfers do not adversely affect IVF pregnancy rates or outcome. This important information may assist the medical team in the decision-making process and in adequate counselling of patients when encountering technical difficulties at the time of embryo transfer. In cases of embryo transfer that are not easy to perform, we suggest trying to complete the procedure at that time even if cervical dilatation or repeated sequential transfers are required. In this way, surgical transmyometrial embryo transfers or rescheduling patients for delayed embryo transfer can be avoided in most patients.

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