The influence of the depth of embryo replacement into the uterine cavity on implantation rates after IVF: a controlled, ultrasound-guided study

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BACKGROUND: Traditionally, embryo transfer after IVF has been performed blindly and placing the embryos ~1 cm below the fundal endometrial surface. However, it has been suggested that transferring embryos rather lower in the uterine cavity or high in the uterus may improve implantation rates. Nevertheless, there has not yet been a controlled trial to prove this theory. This prospective randomized study investigates the influence of the depth of embryo replacement on the implantation rate after embryo transfer carried out under transabdominal ultrasound guidance. METHODS: A total of 180 consecutive patients undergoing ultrasound-guided embryo transfer were randomized to three study groups according to the distance between the tip of the catheter and the uterine fundus at the moment of the embryo deposition in the lumen of the endometrial cavity: group 1: 10 ± 1.5 mm; group 2: 15 ± 1.5 mm; group 3: 20 ± 1.5 mm. RESULTS: There was equal distribution between all three study groups regarding the main demographic and baseline characteristics of the patients, ovarian response, oocyte retrieval and IVF outcome, as well as the characteristics of embryo transfer and luteal phase support. The position of the catheter tip in relation to the fundal endometrial surface in groups 1 (10.2 ± 0.9 mm), 2 (14.6 ± 0.7 mm) and 3 (19.3 ± 0.8 mm) was significantly different. Implantation rate was significantly higher (P < 0.05) in groups 2 (31.3%) and 3 (33.3%) compared with group 1 (20.6%). CONCLUSIONS: The depth of the embryo replacement into the uterine cavity may influence implantation rates, and thus it should be considered as an additional procedure among factors recently proposed as associated with successful embryo transfer after IVF.

Key words: embryo transfer/implantation rates/IVF/ultrasound-guided embryo transfer

Introduction

Implantation failure following embryo transfer is a major continuing problem in IVF. Thus, it has been disappointing that ~85% of transferred human embryos resulting from IVF fail to implant in the uterus despite the selection of apparently normal embryos for transfer (Edwards, 1995a). The main variables affecting implantation rates are uterine receptivity, embryo quality and transfer efficiency. Embryo transfer is the last and probably least successful step in the IVF treatment procedure. Historically, however, much less effort has been placed on assessing or maximizing embryo transfer procedures compared with the other aspects of IVF, and the technique of embryo transfer has remained largely unchanged since it was first described. Thus, traditionally, embryo transfer has been performed blindly, with no attempt to document the variables which might adversely impact pregnancy rates. In fact, most programmes have relied on ‘feel’ by the clinician placing the transfer catheter and embryos within the uterine cavity at a point ‘near’ the fundus (Salha et al., 2001; Schoolcraft, 2001).

Physicians too often underestimate the importance of embryo transfer technique and are unwilling to modify their own personal habits. The need to revisit embryo transfer technique, however, has recently been highlighted (Kovacs, 1999; Salha et al., 2001). Not touching the endometrium and the uterine fundus with replacement of the embryos in the lumen of the endometrial cavity are considered to be the most important factors for successful embryo transfer by most IVF teams (Kovacs, 1999; Salha et al., 2001). On the other hand, while it has been traditionally accepted that the embryos should be placed ~10 mm below the fundal endometrial surface (Webster, 1986; Brinsden, 1999), some authors have suggested that placing embryos rather lower in the uterine cavity may improve pregnancy rates (Waterstone et al., 1991; Naaktgeboren et al., 1998; Brinsden, 1999). However, as previously stressed...
(Brinsden, 1999), there has not yet been a controlled trial to prove this theory.

Interestingly, blind catheter placement has been shown to result in a malposition of the catheter in >25% of cases, thus indicating that tactile assessment of embryo transfer catheter position is unreliable (Woolcott and Stanger, 1997). Transabdominal ultrasound guidance may represent an important tool in this regard. Unfortunately, most clinicians seem to lack familiarity with this technique (Kovacs, 1999). The rationale for ultrasound-guided embryo transfer includes real-time tracking of the catheter tip and more predictable embryo placement (Salha et al., 2001). In a recent large, prospective, randomized study comparing 182 patients who had an ultrasound-guided embryo transfer with 180 patients who had a clinical touch embryo transfer, we found that the pregnancy rate was significantly higher among the ultrasound-guided group (50%) compared with the clinical touch group (33.7%) (Coroleu et al., 2000).

Therefore, on the above evidence, this prospective, controlled, randomized study was undertaken to investigate the influence of the depth of embryo replacement into the uterine cavity on the implantation rate after embryo transfer carried out under transabdominal ultrasound guidance.

Material and methods

Patients and ovarian stimulation

Between January and March 2000, 180 consecutive patients from the IVF–embryo transfer programme of the Institut Universitari Dexeus' Reproductive Medicine Service underwent ultrasound-guided embryo transfers. They were aged 24–45 years and the main patient indications for IVF/ICSI included male factor, unexplained infertility, tubal infertility, and endometriosis. These patients were randomly assigned to three study groups according to the distance between the tip of the catheter and the uterine fundus at the moment of the embryo deposition in the lumen of the endometrial cavity: group 1: 10 ± 1.5 mm; group 2: 15 ± 1.5 mm; and group 3: 20 ± 1.5 mm. Patients were randomized on the day of embryo transfer, prior to the procedure being carried out, according to a computer-generated randomization table.

As previously reported (Coroleu et al., 2000), in our IVF programme ovarian stimulation is routinely accomplished using gonadotrophin treatment with FSH under pituitary suppression with GnRH agonist. Leuprolide acetate (Procrin; Abbott Laboratories S.A., Madrid, Spain) suppression is started in the mid-luteal phase of the previous cycle at a s.c. daily dose of 1 mg. This dose is reduced to 0.5 mg/day once ovarian arrest has been achieved and is then continued until the administration of HCG. Gonadotrophin stimulation of the ovaries was started when serum estradiol concentrations declined to <50 pg/ml and a vaginal ultrasonographic scan showed an absence of follicles >10 mm in diameter. On days 1–5 of ovarian stimulation, 3 ampoules per day of recombinant FSH (Gonal-F, 75 IU; Serono S.A., Madrid, Spain) were administered s.c. From day 6 onward, FSH was administered on an individual basis according to the ovarian response as assessed by follicular development evidenced by transvaginal ultrasonography and serum estradiol levels determined by radioimmunoassay.

In those patients with a previous poor response and/or basal (cycle day 2–4) FSH serum concentrations >10.5 IU/l which, according to our experience, is associated with poor responsive cycles (Barri et al., 2000), we used a flare-up protocol. Leuprolide acetate (0.5 mg s.c. daily) was begun on day 2 of the menstrual cycle and continued until the day of HCG administration. Follicular stimulation with FSH plus HMG was initiated on day 3 of the menstrual cycle. On days 1–5 of ovarian stimulation, patients received three ampoules of recombinant FSH (Gonal-F; 75 IU; Serono) together with three ampoules of HMG (HMG Lepori; Farma-Lepori, Barcelona, Spain), followed from cycle day 6 onwards by an individual adjustment in the dosage based on daily serum estradiol levels and vaginal ultrasound follicle measurements.

The ovulatory injection of HCG (10 000 IU, Profasi; Serono) was administered when a consistent rise in serum estradiol concentrations was associated with the presence of two or more follicles >18 mm in diameter. Oocyte aspiration was performed by vaginal ultrasonography 35–37 h after HCG administration. IVF procedures, including ICSI, as well as the luteal phase support (additional doses of HCG or vaginal micronized progesterone according to ovarian response) used in our programme have been previously described in detail elsewhere (Calderón et al., 1995; Martinez et al., 2000).

Embryo transfer procedure

Two to three days after oocyte recovery, usually two or three (exceptionally four) embryos per patient were replaced depending upon the age of the patient, the indication for IVF, the number of previous IVF attempts, and the number and quality of embryos available for replacement. Embryo quality was established according to the number and form of blastomeres and the percentage of cytoplasmic fragmentation as suggested (Plachot and Mandelbaum, 1990). For statistical comparison purposes and in order to quantify objectively the embryo quality, those three variables were coded according to fixed criteria and then assigned an arbitrary score of 0, 2 or 4. Embryos having <4 blastomeres on day 2, or <6 blastomeres on day 3, after IVF, were scored 0. In contrast, >4- and >6-cell embryos on days 2 and 3 respectively were scored 2. Irrespective of the day after IVF, symmetrical cells were scored 4 whereas asymmetrical ones were scored 2. Embryos having <15%, >15% to <50% and ≥50% fragmentation were scored 4, 2 and 0 respectively, both on days 2 and 3. Accordingly, an optimal quality embryo would score 10. For the final analysis of results, the embryo score per patient was considered as the mean value of the scores given to each of the transferred embryos.

The preparation for embryo transfer was the same for the three study groups (Coroleu et al., 2000). Patients were placed in the lithotomy position and the cervix was exposed using a bivalve speculum. The exocervix was cleaned with a phosphate-buffered saline (PBS) solution (Dulbecco's PBS solution; Irvine Scientific, Santa Anna, CA, USA) and the endocervical mucus was removed by means of a sterile teflon catheter (Malleable Stylet Wallace; Simcare, Lancing, West Sussex, UK) connected to a syringe. Prior to embryo transfer, the endometrial thickness, the distance from the external cervical os to the fundal endometrial surface, and the point that the tip of the catheter should reach for embryo replacement (10, 15 or 20 mm from the fundal surface of the endometrium depending on the assigned study group) were measured by means of transabdominal and transvesical (with full bladder) ultrasonography [Tosbee (SSA-240A) convex 3.75 MHz; Toshiba Co., Tokyo, Japan]. In order to facilitate this measurement, the speculum was withdrawn, if necessary, so that the external cervical os could be seen. Transfer was performed by the same provider (B.C.) in all patients included in the present study.

The same transfer technique was scrupulously maintained with all patients. The Edwards–Wallace embryo replacement catheter (SIMS Portex Ltd, Kent, UK) connected to an insulin syringe was used for all embryo transfers. This is a soft silicon catheter possessing a stiffer outer sheath that stabilizes the softer inner cannula which carries the

342
embryos and actually enters the endometrial cavity for embryo transfer. The catheter was first loaded with transfer medium [50% synthetic serum substitute (Irvine Scientific) and IVF-50 medium (Scandinavian IVF Science, Gothenburg, Sweden)], taking care to avoid air bubbles. The embryos were loaded in the catheter. Under ultrasound transabdominal guidance, the soft inner catheter was introduced into the cervix and passed through the internal cervical os without using the outer sheath whenever possible. If resistance was met, the inner sheath was withdrawn and the outer sheath of the catheter was then passed through the endocervix and placed into or just through the internal os, not advanced into the uterine cavity. Grasping the cervix with a tenaculum was performed to facilitate this manoeuvre only in difficult cases. The inner catheter was now threaded through the outer sheath and advanced under real-time ultrasound guidance to the pre-selected position. At this point the distance between the catheter tip and the fundal endometrial surface was again measured using ultrasonography and was considered valid if it was found to be within ± 1.5 mm from that assigned to the patient’s experimental group (Figure 1). Otherwise, the inner catheter tip was very gently advanced or withdrawn and thus appropriately relocated keeping its movement to an absolute minimum. This final distance between the catheter tip and the fundus was considered for analysis of the results.

In all transfers, only 30 µl of transfer medium containing the embryos were gently expelled into the uterine cavity under sonographic control, which allowed the visualization of the transfer-associated air bubble (bubble of air between the embryos) into the uterine cavity (Figure 1). The catheter was gently removed immediately after transfer and then checked under a stereomicroscope to ensure that all embryos had been transferred. At the end of the procedure, patients remained resting in bed for 30 min. The ease of each transfer procedure was assessed according to the following criteria: very easy, when the catheter passed smoothly through the cervix; easy, when the rigid outer teflon sheath was required; and difficult, when the use of a tenaculum was necessary in addition to the above.

Pregnancy was diagnosed by increasing serum concentrations of β-HCG after embryo transfer, and the subsequent demonstration of an intrauterine gestational sac by ultrasonography.

**Statistical analysis**

Data are presented as mean ± SD and were analysed by Statistical Package for Social Sciences (SPSS, Chicago, IL, USA). We used the χ²-test to compare qualitative variables, and Student’s t-test to compare quantitative variables. The significance level was set at *P* < 0.05.

**Results**

The results are summarized in Tables I–IV. There was equal distribution between all three study groups regarding the main demographic and baseline characteristics of the patients including age, body mass index, cause and duration of infertility, FSH level in the early follicular phase, number of assisted conceptions and number of patients undergoing ICSI (Table I).

Table II shows the data regarding ovarian response, oocyte retrieval and IVF outcome in the three groups studied. Type of stimulation protocol, the number of follicles punctured, serum concentration of estradiol on the day of HCG injection, the number of oocytes retrieved, the number of embryos suitable for replacement and cryopreservation, the endometrial thickness on the day of embryo transfer, the number of embryos replaced, and the quality of embryos replaced were similar for

![Figure 1](image-url)
Table II. Ovarian stimulation characteristics, oocyte retrieval and IVF outcome in the three groups studied

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 61)</th>
<th>Group 2 (n = 59)</th>
<th>Group 3 (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulation protocol n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long</td>
<td>43 (71.5)</td>
<td>41 (69.5)</td>
<td>39 (65)</td>
</tr>
<tr>
<td>Flare-up</td>
<td>18 (29.5)</td>
<td>18 (30.5)</td>
<td>21 (35)</td>
</tr>
<tr>
<td>No. of &gt;10 mm follicles on HCG day(^b)</td>
<td>12.5 ± 9.1</td>
<td>12.4 ± 6.5</td>
<td>11.9 ± 7.6</td>
</tr>
<tr>
<td>Estradiol (pg/ml) on HCG day(^b)</td>
<td>1645 ± 966</td>
<td>1815 ± 907</td>
<td>1670 ± 1022</td>
</tr>
<tr>
<td>No. of oocytes retrieved(^b)</td>
<td>11.5 ± 9.4</td>
<td>12.3 ± 7.6</td>
<td>11.1 ± 7.8</td>
</tr>
<tr>
<td>No. of embryos/patient(^b)</td>
<td>7.6 ± 6.6</td>
<td>7.7 ± 6</td>
<td>6.4 ± 4.4</td>
</tr>
<tr>
<td>No. of embryos/replacement(^b)</td>
<td>2.5 ± 0.8</td>
<td>2.4 ± 0.7</td>
<td>2.5 ± 0.8</td>
</tr>
<tr>
<td>Mean embryo score/replacement(^b)</td>
<td>8.1 ± 1.8</td>
<td>8.3 ± 1.4</td>
<td>8.4 ± 1.6</td>
</tr>
<tr>
<td>Endometrial thickness (mm) on the day of embryo transfer(^b)</td>
<td>12.1 ± 2.1</td>
<td>11.9 ± 2.4</td>
<td>12.2 ± 2.6</td>
</tr>
</tbody>
</table>

\(^a\)No significant differences between groups.
\(^b\)Values are means ± SD.

Table III. Embryo transfer characteristics and luteal phase support in the three groups studied

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 61)</th>
<th>Group 2 (n = 59)</th>
<th>Group 3 (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day of transfer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td>53 (86.9)</td>
<td>51 (86.4)</td>
<td>53 (88.3)</td>
</tr>
<tr>
<td>Day 3</td>
<td>8 (13.1)</td>
<td>8 (13.6)</td>
<td>7 (11.7)</td>
</tr>
<tr>
<td>Catheter tip–fundus distance (mm)</td>
<td>10.2 ± 0.9(^a,c)</td>
<td>14.6 ± 0.7(^a,b)</td>
<td>19.3 ± 0.8(^b,c)</td>
</tr>
<tr>
<td>Ease of transfer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very easy</td>
<td>41 (67.2)</td>
<td>46 (78)</td>
<td>44 (73.3)</td>
</tr>
<tr>
<td>Easy</td>
<td>18 (29.5)</td>
<td>12 (20.3)</td>
<td>13 (21.7)</td>
</tr>
<tr>
<td>Difficult</td>
<td>2 (3.3)</td>
<td>1 (1.7)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Blood-stained catheter</td>
<td>2 (3.3)</td>
<td>2 (3.4)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Repeated transfer</td>
<td>1 (1.6)</td>
<td>1 (1.7)</td>
<td>2 (3.3)</td>
</tr>
<tr>
<td>Luteal phase support</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCG</td>
<td>22 (36)</td>
<td>25 (42.4)</td>
<td>26 (43.3)</td>
</tr>
<tr>
<td>Progesterone</td>
<td>39 (64)</td>
<td>34 (57.6)</td>
<td>34 (56.7)</td>
</tr>
</tbody>
</table>

Values are n (%) or means ± SD. Values in rows with common superscripts were significantly different: \(^a\)P < 0.05; \(^b\)P < 0.01; \(^c\)P < 0.001.

Table IV. Implantation and pregnancy rates and outcome of gestation in the three groups studied

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 61)</th>
<th>Group 2 (n = 59)</th>
<th>Group 3 (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical pregnancies/embryo transfer</td>
<td>24 (39.3)(^a)</td>
<td>29 (49.2)</td>
<td>36 (60)(^a)</td>
</tr>
<tr>
<td>Single</td>
<td>17 (70.8)</td>
<td>15 (51.7)</td>
<td>25 (69.4)</td>
</tr>
<tr>
<td>Twins</td>
<td>6 (25)</td>
<td>11 (37.9)</td>
<td>11 (30.5)</td>
</tr>
<tr>
<td>Triplets</td>
<td>1 (4.1)</td>
<td>3 (10.3)</td>
<td>1 (2.7)</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>20.6(^b,c)</td>
<td>31.3(^b)</td>
<td>33.3(^c)</td>
</tr>
<tr>
<td>Spontaneous miscarriage</td>
<td>3 (12.5)</td>
<td>3 (10.4)</td>
<td>4 (11.1)</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>1 (4.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are n (%). \(^a,b,c\)Values in rows with common superscripts were significantly different (\(P < 0.05\)).

The three groups of IVF patients. Remarkably, the number of embryos per replacement as well as the mean embryo score per replacement were almost identical in the three groups.

Characteristics of embryo transfer and luteal phase support are presented in Table III. The day of embryo transfer was similar in groups 1, 2 and 3, and no differences were found when technical details of embryo transfer procedure including the ease of transfer, the occurrence of blood-stained catheter, and the number of patients with repeated transfer because of embryo(s) left at the tip of catheter were compared. As expected, the position of the catheter tip in relation to the fundal endometrial surface in groups 1, 2 and 3 was significantly different, which supports the validity of the present investigation. Treatment to support the luteal phase was similar in the three study groups (Table III) but implantation rate was significantly higher (\(P < 0.05\)) in groups 2 (31.3%) and 3 (33.3%) than in group 1 (20.6%) (Table IV). Accordingly, the pregnancy rate per replacement was higher in groups 2 and 3 than in group 1, though the difference was statistically significant only when group 1 was compared with group 3. The outcome of pregnancy was not different in the three groups studied (Table IV).

Interestingly, if we only examined transfers where embryos were deposited \(<10\) mm \((n = 17)\) or \(>20\) mm \((n = 7)\) from the endometrial uterine fundus, both implantation and pregnancy rates were extremely low. In the former group, only one embryo implanted among 49 transferred, giving 2 and 5.8% implantation and pregnancy rates respectively. None of the 18 embryos deposited \(>20\) mm from the uterine fundus
implanted. This is important, considering that in both groups the embryos were deposited at distances within the accepted variation of embryo transfer procedure (8.8 ± 0.2 mm, range 8.5–9.3, and 21.1 ± 0.2 mm, range 20.9–21.5 respectively).

Discussion
The success of IVF–embryo transfer is multifactorial. Previous studies investigating factors that affect the outcome of IVF treatment have established that the possibility of a pregnancy depends on the characteristics of the couple seeking treatment, the ovarian response to gonadotrophin stimulation, and the number and quality of embryos available for replacement (Cohen, 1991; Templeton et al., 1996; Templeton and Morris, 1998; Schieve et al., 1999). Numerous studies have been reported on how to improve ovarian stimulation, oocyte insemination and culture procedures but the physical aspects of embryo transfer have received limited interest (Kovacs, 1999). Thus, there is a marked discrepancy between oocyte retrieval, fertilization and cleavage rates that surpass the 90% range and the pregnancy rate in IVF. Following the high rates of successful oocyte recovery, fertilization and cleavage, rates of implantation following embryo replacement have been traditionally disappointing (Edwards, 1995b) and it is still an enigma why embryo transfer remains the most inefficient step. Clinical approaches to increasing implantation rates have focused mainly on endometrial receptivity and blastocyst culture and transfer (Meldrum, 1991; Edwards, 1995a; Gardner et al., 2000) while embryo transfer has been relatively underrated by most programmes in terms of evaluating changes that might improve clinical pregnancy rates. However, it is now thought that various facets of the embryo transfer practice may be pivotal in improving implantation rates (Kovacs, 1999; Salha et al., 2001).

The influence of the depth of replacement into the uterine cavity has been postulated as being important (Naaktgeboren et al., 1997). Traditionally (empirically), and from the beginning of IVF treatment, most programmes have been placing the embryos 1 cm below the top of the cavity (Webster, 1986; Jones, 1988). Well-designed controlled studies on the subject, however, are lacking (Brinsden, 1999). In fact, while some authors have suggested that the results may be improved by transferring embryos rather lower in the uterine cavity (Waterstone et al., 1991; Naaktgeboren et al., 1998; Brinsden, 1999), others have reported that pregnancy rates may be higher when the embryos are placed ‘high in the uterus’ than when placed in the ‘middle of the uterine cavity’ (Meldrum et al., 1987; Krampl et al., 1995). Finally, other reports have indicated that the depth of replacement has no influence on the implantation rate provided the transfer is in the ‘upper half’ of the uterine cavity (Al-Shawaf et al., 1993; Nazari et al., 1993; Roselund et al., 1996). On the other hand, whilst transfer within 1 cm of the uterine endometrial fundus has been criticized as being associated with a high tubal pregnancy rate (Yovich et al., 1985; Nazari et al., 1993), it has been suggested that, because low fundal implantation is a common finding in pregnancies that eventually abort, lack of consistent high fundal placement of the embryos may be partly responsible for the higher rate of spontaneous abortion generally observed with IVF–embryo transfer and may lead to cervical ectopic pregnancy (Meldrum et al., 1987; Al-Shawaf et al., 1993).

Those previous studies, however, were retrospective observational reports and/or did not use ultrasound guidance at the time of transfer. Tactile assessment of embryo transfer has been assessed as unreliable with marked discrepancies between feel and actual position of the catheter occurring across a number of clinical operators of different levels of experience in embryo transfer (Hurley et al., 1991; Woolcott and Stanger, 1997). In contrast, we and others have recently shown that the accurate positioning of the embryo transfer catheter tip can be confidently achieved with the use of ultrasound scan guidance (Kan et al., 1999; Coroleu et al., 2000; Wood et al., 2000). Thus, a feature of this study is that the embryos could be accurately deposited to the desired level and the depth of replacement into the uterine cavity objectively assessed by means of ultrasound-guided embryo transfer. In addition, randomization of patients was used, thus balancing main confounding variables in IVF such as baseline patient clinical characteristics, treatment cycle characteristics, ovarian response and IVF outcome, which were all similar in the three groups studied. Interestingly, the number and quality of embryos replaced were almost identical in groups 1, 2 and 3. Finally, all transfers were carried out by the same provider, thus avoiding any impact of the ‘physician factor’ on implantation rates (Karande et al., 1999; Hearns-Stokes et al., 2000), and using the most popular embryo transfer catheter (Wood et al., 2000; Salha et al., 2001) according to a strictly standardized protocol. Thus, the three groups studied also had similar embryo transfer characteristics.

All the above adds to the validity of our results, demonstrating that the depth of embryo replacement into the uterine cavity may influence the implantation rate after IVF. According to the present study, embryos should be replaced 15–20 mm from the fundus endometrial surface rather than performing high fundal placement in order to improve implantation rates. Interestingly, the only ectopic pregnancy observed in our study occurred in group 1 where embryo replacement was done within 1 cm of the uterine fundus. This would be in agreement with previous studies reporting an increased risk of the deep fundal transfer in leading to ectopic pregnancies (Yovich et al., 1985; Nazari et al., 1993). Finally, the low rate of spontaneous miscarriage observed in the present study is in contrast with figures expected to be found in pregnancies after assisted reproduction (Society for Assisted Reproductive Technology and American Society for Reproductive Medicine, 2000). It is tempting to speculate that the gentle expulsion of the transfer medium to the site of potential implantation under ultrasound guidance could avoid flowback of the medium containing the embryos, which may favour low implantation and abortion (Leong et al., 1986; Meldrum et al., 1987). A recent report by us (Coroleu et al., 2000), showing that spontaneous abortion was significantly higher in patients undergoing clinical touch embryo transfer as compared with patients having ultrasound-guided replacement, favours this contention.

In conclusion, although embryo transfer appears deceptively simple, the present study and a few other reports in the
literature indicate that various facets of the transfer practice may be pivotal in improving implantation rates. Specifically, our results indicate that the depth of the embryo replacement into the uterine cavity should be considered as an additional procedure among factors recently proposed as associated with successful embryo transfer after IVF (Kovacs, 1999; Salha et al., 2001). The definitive explanation for the higher implantation rate in the midcavity approach, as well as for other physical aspects of embryo transfer reported to be associated with improved success, remains to be elucidated. Thus, further studies are warranted to confirm our results in a similar setting before a definitive recommendation can be made on the procedure of embryo transfer.

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