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Is the Mock Transfer Enough Reliable to Evaluate Hysterometry for Embryo Transfer?

Ana Touré Ecra[1*], Luc Nigué[2], Noumoutié Kourouma[3]

[1]General Hospital of Yopougon Attié, Abidjan, Côte d'Ivoire
[2]Biostatistics Laboratory, Department of Medical Sciences, University Félix Houphouët-Boigny, Abidjan, Côte d'Ivoire
[3]Dominique Ouattara Mother-Child Hospital, Bingerville, Côte d'Ivoire
Email: *anaecra@yahoo.fr

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Abstract

Objectives: The aim of this study was to assess the reliability of the mock transfer during *in vitro* fertilization process **Method:** A case-control study was conducted on 134 patients included in IVF/ICSI cycles. From the hysterometry obtained during the mock transfer, the ideal embryo replacement site, *i.e.* two cm from the uterine fundus has been determined. **Results:** Significant differences were noted between the area estimated from the mock transfer and the area where the embryo was deposited during the actual embryo transfer. In fact, 15.9% of the patients had a difference between four and six cm, and 32% of the patients returning for a subsequent transfer had at least 2 cm of difference between the embryo deposit zones. This difference was significant ($P < 0.00$) **Conclusion:** More than ultrasound guidance, the challenge with embryo transfer is to be able to minimize variations in the length of the uterus. This would make it possible to determine the ideal transfer depot area without multiple manipulations.

Keywords

Mock Transfer, Hysterometry, Ultrasound Guidance, Embryo Transfer

1. Introduction

The assisted reproduction technics (ART), available since the late 70s, solved many infertility problems.

The best success rates vary between 25% and 30%, all ages combined [1].

Each medical team has been constantly looking for ways to optimize *in vitro* fertilization (IVF) success rates.

One of the most decisive steps in these procedures is the embryo transfer; it

must be atraumatic (avoiding trace of blood is capital) and leads to replace embryo in a specific area of the uterus.

In order to perform these objectives, most medical teams in high-resource countries practice ultrasound-guided transfer, which has become a gold standard practice.

The low-resource countries want to be at the forefront of technology, even if the advent of IVF took place there more than a decade later.

IVF specialists are always able to fill all workstations during IVF procedures.

Consequently, many medical teams in developing countries use hysterometry measurement obtained during hysteroscopy or the mock transfer to proceed with embryo transfer. The mock transfer is intended not only to check the patency of the cervical canal, but also to get an idea of the morphology of the cervical canal and the actual size of the uterus; this in order to anticipate difficulties on the day of the transfer, thus minimizing the stress of the transferring doctor and difficult transfers.

Doing mock transfer prior to IVF makes it possible to mobilize a single practitioner from the ultrasouds (US) monitoring to the final stage, which is the embryo transfer.

This study aims not only to help practitioners in their choice between echo-guided embryo transfer and preliminary mock transfer, but also to better face difficulties associated with each embryo transfer method.

2. Methodology

This is a prospective, case-control study, conducted during ART sessions from November 2018 to August 2021.

The *in vitro* fertilization care process is organized in one-week sessions every quarter.

One hundred and thirty-two patients who underwent an IVF/ICSI procedure, were involved in this clinical trial.

All patients had to undergo a mock transfer (MT) before the IVF, and each patient was her own control patient during the actual transfer. A similar catheter was used during the actual embryo transfer.

The catheter had with a removable slider.

Patients are asked to have a full bladder on the day of MT in order to mimic the conditions of the actual transfer.

The patient is supposed to be ready to undergo the MT, when the urge to urinate becomes obvious, taking into account only the patients' feelings; the effectiveness of bladder repletion is not controlled by US.

The patient is then placed in a gynecological position. The vagina is disinfected with povidone iodine and the catheter is introduced through the internal orifice until the pratician feels the catheter abut. The catheter has marked measurements from five up to nine centimeters (cm) with subdivisions in order of 0.5 cm between two measurements. The measurement of the catheter on which the mobile cursor is located at the level of the external orifice is then considered

as the value of the hysterometry. We then deduce the theoretical measurement of the zone of deposit (TZ) of the embryo, by reducing the hysterometry value by two centimeters.

On the day of the actual embryo transfer, patients are asked to have a full bladder, and when they are supposed to be ready, they are transferred to the transfer room.

Bladder fullness is checked using the abdominal probe, placed in a longitudinal position, unrolling the endometrium well from the internal cervical orifice to the uterine fundus.

An assistant operator using the ultrasound cursor identifies the point located two centimeters from the uterine fundus; the doctor performing the embryo transfer introduces the catheter to the point marked by the ultrasound scanner cursor and places the embryos there.

When the catheter reaches the embryo deposition site, the measurement marked on the catheter at the external orifice is noted. This measurement is considered as the real measurement (RM).

For patients coming back for a subsequent session or a thawed embryo transfer, the mock transfer was not made again.

It should be noted that none of these patients experienced any uterine events between the two IVF procedures (pregnancy, childbirth, surgery, symptoms…).

All measurements were noted in centimeters.

The measurements of the TZ are notified in the table one, and RM are reported in table two.

Inclusion Criteria

- All patients included in an IVF or IVF/ICSI process.

Non-Inclusion Criteria

- Patients who didn't proceed to a mock transfer prior to IVF process.

Exclusion Criteria

- Patients for whom a catheter change was performed during the transfer, due to a difficult transfer, this catheter having no graduated measurements.

3. Discussion

This preliminary study aims to participate in the reflection on a question that remains topical: the ideal modalities of embryo transfer during IVF.

Pregnancy outcomes have certainly not been evaluated, but based on the uterine areas of transfer associated with optimal pregnancy rates, practioners may choose one or other of the transfer modalities: ultrasound-guided or not.

3.1. Interest of the Mock Transfer

Since the first pregnancy obtained through *in vitro* fertilization 40 years ago, several aspects of the stages have made remarkable progress. However, the technique of embryo transfer has hardly evolved. The goal of a successful transfer is to deposit the embryos in a strictly atraumatic way at a zone in the uterine cavity where the probability of implantation is maximum.

Embryo transfer is the final step in any *in vitro* fertilization procedure. This step can annihilate the days of hard work of all the medical and biological teams in a fraction of time [2].

The most used technique has been for a long time transabdominal ultrasound guidance.

This final step therefore implied a precise technicality.

In this way, precise anatomical rules have been determined with which the deposit of the embryo must comply.

Mansour demonstrated in 1990 that pregnancy rates were better when a mock transfer had been performed beforehand [3].

The usefulness of ultrasound-guided embryo transfer has been reported since the mid-1980s and its application subsequently described by several authors [4].

Ultrasound guidance was introduced in the hope of reducing the likelihood of endometrial trauma as seen during blind transfers or fundal contact transfers [5].

In addition to this technical advantage, patients seem very satisfied to visualize the final stage of an often long and painful process.

The level of difficulty of the transfer was also a subject of reflection for the American society for reproductive medicine (ARSM) committee of experts; one randomized study demonstrated that ultrasound guidance did not improve transfer rates when a mock transfer had previously been performed without difficulty [6] while another gave the same conclusion provided that cavity measurement uterine examination has been performed before [7].

The limits of ultrasound-guided transfer, according to some authors, are undoubtedly the need for a second operator trained in the use of transabdominal ultrasound, a longer procedure and the need to have the bladder filled, which in addition to a degree of discomfort for the patient, can cause uterine contractions [8].

Bakas doesn't agree with the need of a 2nd operator, as he believes that the embryo transfer can be done with precision by a single operator if the total measurement of the uterus has been determined beforehand with therefore an accurate estimate of the place of embryo deposit [9].

For Revelli, this ultrasound-guided transfer with a single operator requires a certain dexterity because of the number of instruments to be handled [10]; this is why he gives advantage to the prior measurement of the uterine length.

Because of the comfort it provides to patients and the reduced risk of uterine contractions, this transvaginal ultrasound guidance is seen as a method of the future [11].

Cozzolino concludes that ultrasound guidance has not shown evidence of its effectiveness in terms of pregnancy rates [12].

As far as Africa is concerned, IVF arrived there a decade later than in the countries of the North, particularly freezing embryos.

The transfer test was therefore essential because, in addition to the cervical trajectory, it made it possible to detect cervixes blocked by synechiae, frequent complications of clandestine abortions.

In our center, about 50% of patients have had an abortion at least once in their lifetime.

It would therefore have been dramatic for couples in our countries to arrive at the end of the procedure and to be confronted with a non-permeable cervix orifice when there is no freezing; what would be an undesirable event in the high-resource countries would be professional misconduct in our countries.

3.2. Patients Characteristics

78% of patients have the size of their uterus which varies between six and eight cm, which is a normal value. This observation is found during the embryo transfer where most of the patients had a RM between six and eight cm, *i.e.* a uterine size increased by two cm compared to that obtained at the MT (**Table 1** and **Table 2**).

Woolcott demonstrated that tactile assessment of embryo catheter position was unreliable; in fact, in 17% of embryo transfers, the catheter involuntarily bumped into the endometrium; it is true that ultrasound-guided transfer does not prevent this incident, but it has the advantage of identifying the inadequate location of a catheter, and therefore, his repositioning [13].

Sizes of nine to ten cm were found in patients who had already had one or more pregnancies, or in older patients with adenomyosis.

Beyond ten cm, these were patients with strictly interstitial myomas and therefore without cavity repercussions. These patients represented only 2% of the sample (3 patients/132).

This percentage is well below the prevalence rate of myomatosis in the African population in general, and that of the infertile population in particular. Indeed, in the black population, studies show prevalences of 30% in the black population under 30 and up to 50% in women over 50. In fertility centers caring for black women, these rates are obviously increased due to the patient profile. But in our study population, the transfer test is done on patients at the end of the course and who have therefore normally undergone fertility surgery when necessary.

The tests are carried out in the cycle preceding inclusion. ART procedures are done in our center in the form of sessions at the rate of four per year. Uterine sizes of more than 14 WA are patients who had been seen sometimes three months previously; a rapid expansion of a myoma may explain these large uteri. In fact, it was a single patient in this group, in whom a hysteroscopy had been performed immediately, to assess the cavity impact.

3.2.1. The Low Reliability of the Transfer Test

Independently of the unknown factors at the origin of the variation of the uterine size, the conditions of realization could allow an explanation; indeed, during the MT, it is the patient who judges the opportune moment for carrying it out: the fullness of the bladder is estimated by only the patient; it is "objectivized" by the urgency signaled. Ultrasound is not used, because the idea is to evaluate in a very simple way, the TZ. However, the assessment of bladder fullness is

Table 1. Mock transfer measures.

MT (cm)	Patients rate (%)
[5 - 6]	8.4
[6 - 7]	48.5
[7 - 8]	29.5
[8 - 9]	11.4
[9 - 16]	2.2

More than three quarters of the patients had a hysterometry between six and eight cm.

Table 2. Embryo deposit site.

MT (cm)	Patients rate (%)
[5 - 6]	5.7
[6 - 7]	23.4
[7 - 8]	37.2
[8 - 9]	21.4
[9 - 10]	12.3

The differences between the TZ and the RM are provided in **Table 3**.

necessarily subjective. Moreover, stress sometimes gives a feeling of pelvic congestion, which can be mistaken for an urge.

If 90% of patients (120 patients/132) have a uterine size within the norms, that is to say between six and ten cm. Some patients have hysterometries at five cm; taking into account the measurement of the cervix, this would make a cavity length of three up four cm, which is impossible. This size was not found during the real transfer (**Table 1**).

These "false" measurements could be linked to the stoppage of the catheter due to the subendometrial passage of the catheter, or even a sinuous cervical path with closure of the cervico-uterine angle or even a winding of the catheter in the cervix canal; carried out "blindly", the arrest of the progression of the trial catheter is considered as the sign of abutment against the uterine fundus.

The lack of reliability of this mock transfer can maybe explain, how the abutment against the uterine fundus causing uterine contractions, or the passage under the endometrium of the catheter cause to decrease the pregnancy rate.

Mousa *et al.* speculated that clinical experience outweighted the potential benefit of routine use of ultrasound guidance [14].

The aim of Mousa study conducted in 2005 was to use ultrasound guidance to determine the accuracy of the point of trial embryo transfer versus that of the actual transfer.

His work has shown that even in a highly experienced center, if practitioners rely on trial transfer measurements for the actual transfer, more than 19% of embryos will be deposited more than 1.5 cm from the pre-identified location and

approximately 30% to more than 1 cm.

Our patients who had a difference more than 4 cm between RM and MT had a significantly deeper uterine cavity. They were most often multiparous patients or because of myomas; which suggests that they would benefit more from having a mock transfer before their procedure than nulligests.

Miller had in his study demonstrated that the mock transfer not a reliable predictor of the measurement of embryo deposit zone, because after administration of gonadotropins after ovarian stimulation, the depth of the uterine cavity increasedone centimeter or more in 59.7% of patients: the length during the transfer test was significantly less than the actual length during the transfer. The mean difference between the measurement during the transfer test and the actual transfer was 0.94 +/− 0.7 mm; based on this measurement, the positioning of the embryo (6.1 mm +/− 0.7) would be significantly different from where the embryo would be placed during the actual transfer (6.9 mm +/− 0.7) [15].

Our differences are much higher.

3.2.2. Identifying the Ideal Embryo Deposition Zone

The point of embryo deposition is one of the determining factors in the success of IVF attempts [16] [17].

It is therefore quite natural that many authors have been interested in the ideal zone of embryo deposition which would make it possible to obtain an optimal rate of pregnancies.

The studies have made it possible to identify two ways of reflection [2]:

- Deposit at a fixed distance taking into account the uterine fundus.
- Deposition at a variable distance taking into account the length of the uterine cavity.

In the first case, the ideal distance being the one associated with the highest pregnancy rate, the reference distance from the uterine fundus was two centimeters.

In the second case, the appropriate deposit point should be the middle of the uterine cavity.

In our study, we followed the first option: depositing the embryo two cm from the uterine fundus.

The measurement during the transfer shows differences between the deposition measurement according to the mock transfer and the measurement of the actual deposition of up to six cm sometimes, which implies a similar elongation of the uterus (**Table 3**).

Only 3% of the patients had no difference between mock transfer and real transfer measure.

If the correction of the anteversion can explain a uterine elongation of up to four cm, it seems difficult to retain for extreme measurements, such as six cm in our study; this finding, which seems disproportionate, perhaps suggests the possibility of a mechanical obstacle such as partial synechia, or a myoma with a submucosal dome or a passage of the catheter under the endometrium. This lengthening of more than 4 cm concerned 15.9% of patients (21 patients/132).

Table 3. Difference between the measurement of the theoretical deposition and the real deposition zone of the embryo.

MT (cm)	Patients rate (%)
0	3
[0 - 1]	14.4
[1 - 2]	22.7
[2 - 3]	26.5
[3 - 4]	17.4
[4 - 5]	9
[5 - 6]	6.8

P = 0.00. The embryo deposition zone is significantly different between theorical and actual deposition zone. Only 3% of the patients have similar measures between theorical and real deposition zone. The average of this difference is 3.3. The standard deviation is 1.8. Median = 3. Minimum = 0. Max = 6. Twenty-eight of the patients underwent a second embryo transfer: 1) either for a thawed embryo transfer (TET); 2) either during a subsequent session; 3) or for a double embryo transfer during the current session. The differences between the embryo deposition zones during these successive transfers for a same patient are noted in **Table 4**.

Indeed, extreme measurement differences like these were only encountered in myomatous uteri, which confirms our hypothesis of the catheter stumbling over a myoma that has become submucosal or rolled up in the cervix.

The performance of hysteroscopy, which was not compulsory at the beginning, was made compulsory in the face of certain unexplained failures. These hysteroscopies revealed asymptomatic uterine abnormalities.

For supporters of the blind transfer, should we rather retain the values of hysterometry during hysteroscopies? Hysteroscopy cannot totally replace the transfer test, because if it makes it possible to obtain a reliable uterine measurement, it does not make it possible to mimic the cervical path and therefore to apprehend its difficulties.

The gap between the theoretical deposition zone and the actual deposition zone gives at the same time the value of the gap in the 2nd option which is the deposition in the middle of the cavity, and shows that many transfers, based on our measurements during the mock transfer would have been made in the lower part of the uterus, an area where pregnancies have a lower rate.

3.2.3. Variation in the Measurement of Embryo Deposition during Successive Transfers

Twenty-eight patients underwent two transfers two months apart, or for some of them, at 48 hours, on the occasion of a double transfer: generally, on day 3 and day 5.

During these successive transfers, only 25% had the same deposit measurement, and about one third had at least a two cm difference with the first measurement (**Table 4**).

Table 4. Difference between the first embryo transfer zone (t1) and the subsequent embryo transfer zone (t2) measurement.

T1-T2 (cm)	Patients rate (%)
0	25
0.5	17.9
1	25
2	21.4
3	10.7

P = 0.00. The embryo deposition zone is significantly different between two procedures. Only one quarter of the patients have similar measures between two procedures. The average of this difference is 1.1. The standard deviation is 0.98. Median = 1. Minimum = 0. Max = 3.

Since the measure of deposition was two centimeters in our sample, a difference of 0.5 to 1.5 cm does not necessarily compromise the results since some studies have identified the midpoint of the cavity as an acceptable measure of embryo deposition. But from two cm, we pass into the lower part of the uterus which is associated with a lower rate of pregnancy.

This variation between two tests at 48 hours could be explained by the progesterone which permeates more the uterus within two days, and which will therefore increase its relaxation, and perhaps therefore its expansion. But from one session to another, this theory cannot be evoked. It is rather that of the assessment of bladder fullness.

Indeed, whether it is during the same session, or from one session to another, bladder fullness during the actual transfer is judged by the practitioners themselves on ultrasound. Here, the patient's sensation is only taken into account when it corresponds to the visual assessment of bladder fullness on ultrasound.

This assessment of bladder fullness may vary from one practitioner to another depending on the practitioner's experience and habits. The volume of urine during transfers is never objectively quantified because the urine is not collected and measured.

Indeed, it is the volume of urine that would predict the degree of reduction in the anteflexion of the uterus and therefore its lengthening.

To within one or two cc, the bladder still appears full on the ultrasound, without it's able to predict the repercussion on the variation in size.

Another reason mentioned for these changes in the measurement of the uterus by some authors is the uterine anteversion of retroverted uteri, subsequent to the increase of the hyperstimulated ovaries' volume [18] [19].

But Yang points out that anteverted uteri, however, became less frequently retroverted. But the same observation during frozen embryo transfers, in which the ovaries are not stimulated, shows that the mechanisms involved in the change of position remain uncertain.

These unknown mechanisms probably explain that the uterine measurement

changes from one cycle to another in the same woman [20].

These measurement variations make it possible to deduce that a blind transfer is not the most appropriate method since the embryo transfer must be done in a regulatory area.

4. Conclusions

Some practitioners still think that, when done well, the transfer test makes it possible to dispense with the ultrasound-guided transfer, which takes more time and personnel, and which increases the patient's discomfort.

The purpose of this study was neither to judge the advisability or otherwise of ultrasound guidance for embryo transfer, nor to question the experience of practitioners and even less to talk about pregnancy rates; the aim was rather to bring reflection on a factor whose mechanisms remain largely unexplained: the variation in uterine size between successive transfers, whether or not these are distant in time.

Indeed, if the practice of ultrasound guidance is not unanimous, the preferred areas of pregnancy, however, are well described.

Let each practitioner, in the light of his experience, identifies the means of minimizing these variations in uterine size, and he will be certain of always transferring to the preferred areas.

Depending on the means available in terms of human, material and time resources to achieve this, he will be able to choose between ultrasound guidance and the blank test.

Apart from the pregnancy rate, patient comfort must be ensured at each stage of the procedure.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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