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#### **ORIGINAL ARTICLE**

# Anatomical causes of difficult embryo transfer during in vitro fertilization

Causes anatomiques des transferts embryonnaires difficiles en FIV

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#### **KEYWORDS**

Embryo transfer; Difficult transfer; In vitro fertilization; Uterocervical assessment; Personalized healthcare

#### Summary

*Objectives.* – Identify, define and validate through statistical analysis the anatomical causes of difficult embryo transfers (ET).

Materials and methods. — This observational study, carried out in 306 IVF candidates, compared the frequency of anatomical anomalies of the uterus and cervix in women who underwent an easy ET with that in women who underwent a difficult ET. Anatomical anomalies were detected during an assessment of the cervix and uterus including transvaginal ultrasound, hysteroscopy and a mock transfer. Ease of ET was determined during the actual transfer procedure.

Results. — An easy ET was achieved in 151 patients, whereas difficulties occurred in 155 patients, among whom 55 patients underwent a "very difficult" ET. The most common anatomical characteristics associated with difficult ET were abnormal crypts in the cervical canal (86%) and tortuosity of the cervical canal (68%). Less frequent causes included: internal os contractions (28%) and pronounced anteversion of the uterus (26%). Very difficult ETs were associated with the presence of several causes.

Conclusions. — ET is the clinical step that has the most effect on IVF outcome. Difficult transfers are associated with a fall in pregnancy rates. The anatomical causes of difficult transfer identified in this study led to major changes in transfer procedure in our department and to the development of more adapted catheters.

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#### MOTS CLÉS

Transfert d'embryons ; Transfert difficile ; Fécondation in vitro ; Bilan cervico-utérin ; Soins personnalisés

#### Résumé

*Objectifs.* — Identifier, définir et valider par une analyse statistique les causes anatomiques des transferts difficiles.

Matériel et méthodes. — Cette étude observationnelle réalisée chez 306 patientes en FIV a comparé la fréquence des anomalies anatomiques de l'utérus et du col utérin en fonction de la facilité du transfert. Ces anomalies anatomiques ont été étudiées lors d'un bilan cervico-utérin comprenant une échographie transvaginale, une hystéroscopie et un transfert d'essai. La facilité du transfert a été déterminée lors de la FIV.

Résultats. — Au total, 151 patientes ont eu un transfert facile, 155 un transfert difficile dont 55 un transfert très difficile. Les anomalies anatomiques les plus fréquentes associées à la difficulté de transfert sont les cryptes du canal cervical (86 %) et la tortuosité du canal cervical (68 %). Les causes moins fréquentes sont : les contractions de l'orifice interne (28 %), l'antéversion prononcée de l'utérus (26 %) et des causes isolées (isthmocele). Les transferts très difficiles sont liés à l'association de plusieurs causes.

Conclusions. — Le transfert embryonnaire est l'étape clinique qui a le plus d'influence sur les résultats de la FIV. Les transferts difficiles sont associés à une baisse des taux de grossesse. Les causes anatomiques des transferts difficiles identifiées dans cette étude ont conduit à des changements majeurs dans la procédure de transfert dans notre unité et à la conception de nouveaux cathéters.

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#### Introduction

Embryo transfer (ET) is now recognized as an important step in the success of in vitro fertilization (IVF) [1] and poor ET technique may account for as much as 30% of all failures of assisted reproduction [2]. Difficult transfers have been found to result in significantly lower implantation and pregnancy rates [3–6]. The causes of difficult transfer may be obvious for trained operators, but no review or comprehensive study on the anatomical causes has been published to date. The only factors identified so far as being associated with an increased likelihood of difficult transfer are cervical stenosis and severe anteflexion/retroflexion of the uterus [7,8].

To improve the outcomes of IVF in our center, we initiated a characterization study of the anatomical causes that could explain difficult transfers using specific definitions. Therefore, we first analyzed the systematic assessments of the cervix and uterus of 50 patients with a history of difficult transfer who were under consultation for a further round of IVF in a pilot study carried out early 2010. The assessments of the cervix and the uterus (transvaginal ultrasound, hysteroscopy and mock transfer) were systematically included as part of the routine evaluation for IVF treatment in our center in 2009 under our quality management system for ISO certification and as proposed by other centers to improve the quality of embryo transfer and implantation. At the end of this study, five anatomical characteristics were considered as potential factors influencing the ease of transfer: position of the uterus, tortuosity of the cervical canal, cervical crypts, internal os contractions and other anomalies of the cervix or uterus. To confirm the relevance of this anatomical classification, we analyzed in a further study the anatomical anomalies of the cervix and the uterus in a larger population of IVF candidates and we compared their frequency in women who had an easy transfer with those who underwent a difficult transfer.

Results of this study led to profound improvements in our transfer technique and to the production of new catheters devised using innovative concepts.

#### Materials and methods

#### Study design and setting

This non-randomized observational study was conducted at the fertility center within the Diaconesses-Croix-Saint-Simon hospital and Drouot Laboratory (Paris, France) between April 2010 and December 2012, in accordance with the ethical principles of the Declaration of Helsinki, the guidelines for Good Clinical Practices (CPMP/ICH/135/95) and European regulations. As data analyzed in this study were part of the routine evaluation for IVF treatment and were collected anonymously, the submission of the protocol to an ethic committee was not required by the European authorities. Informed consent was obtained from all patients prior to inclusion in the study.

#### **Participants**

All patients attending our fertility clinic for IVF treatment between January 2010 and December 2012 were prospectively recruited for the study in chronological order, whether they had history of difficult ET or were candidates for a first round of IVF treatment, with the aim of including around 150 patients per group. As no published study has previously assessed the frequency of the anatomical criteria in association with difficulty of ET, a sufficiently large study population of 300 patients (150 patients in each arm) was empirically chosen in order to fit with the recruitment capacity of the center. Patients with a history of conditions known to affect ease of transfer, i.e., severe endometriosis, pelvic surgery or infection, all of which may lead to alterations in uterine

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