European Journal of Obstetrics & Gynecology and Reproductive Biology 215 (2017) 50–54

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Frozen embryo transfer or fresh embryo transfer: Clinical outcomes depend on the number of oocytes retrieved

Bing Xu, Ya-qiong He, Yuan Wang, Yao Lu, Yan Hong, Yao Wang*, Yun Sun*

Shanghai Key Laboratory for Assisted Reproduction and Reproductive Genetics, Center for Reproductive Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

ARTICLE INFO

Article history:
Received 30 October 2016
Received in revised form 11 April 2017
Accepted 25 May 2017
Available online xxx

Keywords:
Fresh embryo transfer
Frozen embryo transfer
Live birth rate
Pregnancy rate
in vitro fertilization

ABSTRACT

Objective: To establish a safe and effective clinical transplantation strategy for determining when to prioritize frozen embryo transfers (FET) or fresh embryo transfers (ET) we conducted a retrospective analysis study, examining several key clinical outcomes.

Study design: In a retrospective cohort study, 1423 patients (age < 40) were categorized into four groups according to the number of oocytes retrieved (15–18, 19–21, 22–24 and ≥25 oocytes). The clinical outcomes of 1423 in vitro fertilization (IVF) cycles (896 fresh ET and 527 FET) were reviewed for each group. Data demonstrated that the clinical pregnancy rates (PR) and live birth rate (LBR) of the FET group was higher than those of the fresh ET group.

Results: Our study further indicates that the clinical benefits of FET become most meaningful when the number of oocytes retrieved ≥19. When the number of oocytes retrieved ≥20,this difference was more significant, with benefits in PR(odds ratio [OR] = 2.46, 95% confidence interval [CI]: 1.74-3.46, P < 0.001) and LBR (OR = 2.27, 95% CI: 1.60–3.22, P < 0.001).

Conclusion: 20 oocytes retrieved may be the optimal cut-off point number for FET in order to achieve both a successful pregnancy and a live birth.

Introduction

The development of assisted reproductive technology has considerably improved the chances for infertile individuals to conceive healthy children. Importantly, especially as the use of assisted reproductive technology becomes more widespread, many of the concerns associated with whole embryo freezing have been dispelled. Using embryo cryopreservation technology, embryo vitrification greatly reduces freezing-induced cell damage, and the embryo recovery rate can reach as high as 95% [1]. With these improvements in vitrification, frozen embryo transfer (FET) may be a viable alternative to fresh embryo transfer (ET) [2,3]. A series of reports pointed out that the implantation and pregnancy rates (PR) of FET are higher than those of fresh ET [4–6], while perinatal outcomes in terms of prematurity, low birth weight, and being small for gestational age are similar or even better [7–9].

Fresh ET is typically the first choice when the number of oocytes retrieved is a fat lot. However, in situations where fresh ET is not appropriate for example, in a scenario where in clinicians want to avoid ovarian hyperstimulation syndrome (OHSS), more and more patients will choose whole embryo freezing [10]. Historically, FET has been performed for patients because they were at high risk for OHSS based on the following criteria: ovary diameter >9 cm; fluid present around the uterus by ultrasound examination; high hematocrit on the day of implantation; complaints of stomach swelling and nausea [11]. FET was also used for patients according to their personal preference or for cases with elevated progesterone or suboptimal endometrial thickness.

To better determine safe and effective clinical transplantation guidelines for prioritizing between FET and fresh ET, a total of 1423 women who were undergoing their IVF treatment cycle at the Reproductive Medical Center from January 2011 to June 2013 were identified and reviewed. This is a large retrospective cohort study; patients were categorized into four groups according to the number of oocytes retrieved (15–18, 19–21, 22–24 and ≥25 oocytes).Clinical outcomes for fresh ET and FET were assessed by group. In particular, the goal of this study is to assess the association between oocyte number and clinical outcome for each embryo transfer method in order to (i) identify an optimal cut-off point of number of oocytes retrieved to maximize the clinical PR and LBR, (ii) to establish a safe and effective clinical transplantation strategy between FET and fresh ET, and (iii) to guide the IVF treatment much more effectively.

* Corresponding authors.
E-mail addresses: drwangyao@163.com (Y. Wang), syun1972@126.com (Y. Sun).

http://dx.doi.org/10.1016/j.ejogrb.2017.05.023
0301-2115/

Table 1
Patient characteristics by group.

Index	ET group	FET group	*P*-value
Number of IVF cycles	896	527	
Age (years old)	29.7 ± 3.9	29.2 ± 3.6	0.03
Baseline FSH (IU/L)	7.27 ± 1.72	7.19 ± 4.5	0.67
Baseline LH(IU/L)	4.78 ± 3.11	5.18 ± 2.85	0.03
Baseline E2(pg/ml)	126.4 ± 77.5	117.5 ± 86.6	0.06
E2 on the day of HCG(pg/ml)	5283.2 ± 2035.1	6905.9 ± 2545.5	<0.001
Number of oocytes retrieved(n)	18.2 ± 3.3	22.4 ± 6.1	<0.001
Ratio of high-quality embryos	0.56 ± 0.29	0.56 ± 0.29	0.93
Number of embryos transferred (n)	2.0 ± 0.27	2.0 ± 0.17	0.84
Endometrial thickness (mm)	10.0 ± 1.86	9.9 ± 2.04	0.38

P<0.05, significant difference.

Materials and methods

Patient data and grouping

In this study, the records of patients who received IVF/intracytoplasmic sperm injection (ICSI) at the Center for Reproductive Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, China from January 2011 to June 2013 were retrospectively identified and reviewed. Patients registered in the analysis were <40 years of age, had ≥15 oocytes retrieved, and had an endometrial thickness on the day of embryo transfer ≥7 mm. Patients were further categorized into four groups based on the number of oocytes retrieved: 15–18, 19–21, 22–24 and ≥25 oocytes. Meanwhile, clinical outcomes for fresh ET and FET were analyzed for each group.

Data collected from the medical records included patient age, baseline hormone levels, estradiol (E2) on the day of human chorionic gonadotrophin (hCG) administration, number of oocytes retrieved, number of high-quality embryos, and endometrial thickness. A series of clinical outcome was also recorded such as PR, LBR, implantation rate and birth weight. This study was subject to approval by the Institutional Review Board of Renji hospital, and the requirement of informed patient consent was waived because of the retrospective nature of the study. All patients provided informed consent for all IVF procedures performed.

IVF and fresh embryo transfer

A conventional ovarian stimulation protocol (agonist protocol) was performed. Gonadotropin stimulation was set up with either recombinant follicle stimulating hormone (rFSH) or urine highly purified FSH (Gonal F; Serono SA, Ivrea, Italy), with or without human menopausal gonadotropin (hMG). The initial dose ranged from 112.5 to 300 IU per day, based on age, antral follicle count, and baseline FSH level. During stimulation, the ovarian response was monitored by E2, progesterone, and luteinizing hormone (LH) levels, and serial transvaginal ultrasound examinations. Gonadotropin doses were adjusted as needed. The administration of hCG with 4000–10,000 IU was applied to induce follicle maturation, defined by the presence of 2 follicles with a mean diameter ≥18 mm or 3 follicles with a mean diameter ≥17 mm. After hCG administration of 36 h, oocytes were harvested by transvaginal ultrasound-guided oocyte aspiration. The IVF/ICSI fertilization method was selected based on semen analysis results, with the types of insemination including IVF, ICSI.

Embryos that reached the 6–8 cell stage with less than 20% fragmentation were defined as good quality embryos. Embryo transfer was employed under ultrasound guidance, usually on day 3 after insemination. The number of embryos transferred complied with the national regulations of China, and conformed to individual patient requests when appropriate. In all cases, no more than 3 embryos were transferred. Starting the day of oocyte retrieval, the luteal phase was supported with 90 mg of intravaginal progesterone gel (Crinone gel 8%; Serono) daily for a minimum of five weeks.

Table 2
Correlation between the outcome of the ET and basic parameters.

Index	OR	95% CI	P-value
Group(ET,FET)	1.75	1.32–2.37	<0.001
Age (years old)	0.99	0.96–1.02	0.42
Baseline FSH (IU/L)	1.05	0.98–1.12	0.16
Baseline LH(IU/L)	0.97	0.93–1.02	0.30
Baseline E2(pg/ml)	1.00	0.99–1.00	0.99
E2 on the day of HCG(pg/ml)	1.00	1.00–1.00	0.81
Number of oocytes retrieved(n)	0.99	0.96–1.03	0.85
Ratio of high-quality embryos	2.58	1.69–3.95	<0.001
Number of embryos transferred(n)	2.13	1.13v4.05	0.02
Endometrial thickness (mm)	1.09	1.02–1.16	0.01

P < 0.05, significant difference.

FET

Vitrification of embryos was carried out on day 3 after oocyte retrieval.The endometrium was prepared for FET by a natural or hormone replacement cycle. Patients who received FET used oral E2 (Progynova; Bayer) 4.0 mg daily for 10 days, and were monitored with serial ultrasonography to determine endometrial thickness. If the endometrial thickness was <7 mm after 10 days, the dose of E2 was increased up to a maximum dose of 8.0 mg daily to achieve a target endometrial thickness of at least 8 mm, or approaching the endometrial thickness in the follicle aspiration cycle. Crinone 8% was then begun once a day (day 0), and ET was performed 3 days after the start of progesterone. The same doses of estrogen and progesterone were continued until 14 days after FET when a serum β-hCG test was performed. If the pregnancy test was positive, hormone replacement was continued for another 2 weeks, and serial ultrasonography was used to determine fetal viability. Patients with ovulatory menstrual cycles were candidates for a natural FET cycle. Starting on day 10 of the menstrual cycle, transvaginal ultrasound was performed to confirm ovulation as well as endometrial development. Examinations were then continued every 1–3 days until ovulation occurred. Supplemental progesterone was provided to all patients (30 mg of oral dydrogesterone daily) at the first day of ovulation, and FET was performed 3 days after the start of progesterone administration. The frozen embryo was thawed rapidly in 2 h before use.

Pregnancy assessment

Pregnancy was confirmed by determining serum hCG concentration 14 days after ET in all patients. When the test results were positive, ultrasound evaluations were performed 28–35 days after transfer, and clinical pregnancy was defined as a gestational sac with fetal heart beat.

Statistical analysis

Data are presented as mean ± standard deviation (SD) for continuous variables, and number and percent for categorical variables. An independent 2-sample *t*-test was used to examine mean differences in characteristics treated as continuous variables between the fresh ET and FET groups, A multiple regression analysis was used to analyze the correlation between outcomes for the1423 patients who received more than 15 oocytes and parameters, while the Chi-square test was used to examine the