Pregnancy outcomes of the first thawing cycle in "freeze-all" strategy of infertility patients with fever during oocyte recruitment: a matched-pair study

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Abstract

Background: It is currently unknown whether patients with a fever after controlled ovulation during egg retrieval could increase the risk of pelvic infection or not, and fever itself may affect endometrial receptivity or embryo quality with poor pregnancy outcomes. The aim of this study was to analyze the outcomes of patients with fever during oocyte retrieval after the first frozen-thawed embryo transfer (FET) cycle.

Methods: This was a 1:3 retrospective paired study matched for age. In this study, 58 infertility patients (Group 1) had a fever during the control ovulation, and the time of the oocyte retrieval was within 72 hours, they underwent ovum pick up and whole embryo freezing ("freeze-all" strategy). The control subjects (Group 2) are 174 patients matched for age who underwent whole embryo freezing for other reasons. The baseline characteristics, clinical data of ovarian stimulation, and outcomes, such as the clinical pregnancy rate, ongoing clinical pregnancy rate were compared between the two groups in the subsequent FET cycle.

Results: All patients had no pelvic inflammatory disease after oocyte retrieval. Anti-Mullerian hormone (AMH) levels (4.2 *vs.* 2.2, $P < 0.001$) were higher in group 2, and the number of oocytes retrieved, and fertilization rate were lower in group 1 ($P < 0.001$), but the endometrial thickness, the number of embryo transfers, and the type of luteal support supplementation were similar between the two groups. Regarding pregnancy outcomes in the subsequent FET cycle, the implantation rate, clinical pregnancy rate, early spontaneous rate, ectopic pregnancy rate, and ongoing pregnancy rate were all not significantly different. Further regression analyses showed that the clinical pregnancy rate and ongoing pregnancy rate were also not significantly different.

Conclusions: Transvaginal ultrasound-guided follicular puncture for oocyte retrieval is a safe and minimally invasive method for patients with fever. Moreover, the fever had almost no effect on embryo quality.

Keywords: Fever; Oocyte retrieval; Infertility; Pregnancy outcomes

Introduction

Human infertility is defined as the inability of a couple to conceive following at least 12 consecutive months of unprotected sexual intercourse.[1,2] Infertility is a medical distressing chronic condition that is appraised to affect 9% to 30% of reproductive-aged couples worldwide.[3,4] It is well known that assisted reproduction technology (ART) is currently an effective method for treating infertility. Many of them seek to achieve pregnancy via assisted reproductive technologies (ART). Transvaginal ultrasound-guided follicular puncture for oocyte retrieval is a highly efficient and minimally invasive method for assisted reproductive techniques.

ART is complex and costly, and each ART cycle consists of several steps, such as downregulation with agonists or antagonists, ovarian stimulation, ovulation triggering, oocyte retrieval, laboratory phase, and embryo transfer. If one of the steps is incorrectly applied, the conception may not occur and cost a lot. With this in mind, it is important to ensure that each step involved in ART is

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supported by good evidence from well-designed studies,[5] despite the fact that some patients are inevitably recognized as having fever before oocyte retrieval during control ovulation because of infection with viruses, bacteria, or others in every center of the world. To date, there are no consensus guidelines available on the management of infertile women with fever undergoing ART treatment. Thus, we design this study to find the answer of whether the patients with fever during control ovulation and oocyte retrieval by the transvaginal ultrasound-guided follicular puncture would increase the risk of pelvic infection or not, and also want to study if fever itself affect the embryo quality, or induced endometritis and thus caused poor pregnancy outcomes. However, if oocyte retrieval is canceled, the patients might experience economic loss and depression. Meanwhile, the risk of severe ovulation complications might also increase, such as ovarian hyper-stimulation syndrome, thrombus, and ovarian pedicle torsion.

In order to reduce the occurrence of these complications, and the rapid development of the current overall freezing technology, which gradually has a similar to or even better pregnancy outcome than that of the fresh transplantation cycles,[6–9] strictly disinfecting and oral antibiotics were applied for prevention. More importantly, whole embryo freezing ("freeze-all" strategy) was conducted in all the patients for the subsequent frozen-thawed embryo transfer (FET) cycle.

Methods

Ethics approval

The study was approved by the local Ethics Committee of Peking University Third Hospital (No. 2008013). Informed written consent was obtained from all patients before enrollment in this study.

Study design and participants

This study was a retrospective 1:3 matched-pair study, and the data collection protocol was approved by the Ethics Committee of the Medical Center of Peking University Third Hospital (PUTH). Information on infertility patients who underwent whole embryo freezing cycles ("freeze-all" strategy) were collected from 1st Jan 2018 to 31st June 2019 in PUTH. The patients taken "freeze-all" strategy due to having a fever during the oocyte retrieval period before oocyte pick-up within 72 hours were included in the study group (group 1). The control group (group 2) was 1:3 matched with the age of whole embryo freezing cycles because of ovarian hyperstimulation syndrome (OHSS), high progesterone value ($P > 6$ nmol/L), or personal reasons in the same period. All patients underwent oocyte retrieval under strict disinfection and received oral antibiotics for three days to prevent pelvic infection. The available embryos were frozen for subsequent FET. The outcomes of the first thaw cycle between the two groups were compared. The exclusion criteria were as follows: (1) patients with abnormal uterus cavity, such as endometrial polyps, uterus malformation, intrauterine adhesion, and submucosal myoma; (2) endometritis; (3) untreated hydrosalpinx; (4) preimplantation genetic diagnosis cycles; (5) endocrine disorders, such as hyperprolactinemia.

Controlled ovarian stimulation and embryo transfer

The selection of the controlled ovarian stimulation (COS) program should be based on the patient's basic conditions, age, patient's wishes and economic conditions, and the experience of the doctor. All patients received standardized, controlled ovarian stimulation in the cycle. The gonadotropin releasing hormone agonist analogue (GnRHa) long protocol, GnRHa short protocol, GnRHa prolonged protocol, GnRH antagonist protocol, and Mild-stimulation Cycles/Luteal phase stimulation.[10] Human menopausal gonadotropin (Menopur, Ferring; hMG, Lizhu, China) could be added if needed. The doses of the medications were adjusted according to the ovarian response. Recombinant human chorionic gonadotropin (rhCG) at a dose of 4000 to 10,000 IU was administered to induce oocyte maturation when at least two leading follicles achieved 18 mm in diameter (or 17 mm in GnRH antagonist protocol). Oocyte retrieval was performed 36 to 38 hours after recombinant human chorionic gonadotropin (rhCG) injection. All the embryos were *in vitro* fertilization and cultured for three days (D3) or 5 days (D5), all the D3 and D5 embryos were freezing in the group 1 and group 2 for canceling the fresh transfer cycle ("freeze-all" strategy). The pregnancy outcomes of the first FET cycle were analyzed retrospectively.

FET and Luteal supplementation

Performing FET in a monitored natural cycle has the advantage that no medications are used, making such cycles preferable to many women.[11] In the natural cycle FET (NC-FET), the detection of ovulation is a marker for the timing of thawing and transfer. The moment of ovulation can be estimated based on the detection of the luteinizing hormone (LH) surge in either urine or blood (constituting "true" NC-FET) or after triggering ovulation of the dominant follicle using human chorionic gonadotrophin (hCG) ("modified" NC-FET). The luteal support method was 20 mg of oral dydrogesterone, twice a day, until 8 to 10 pregnancy weeks, which is the same in the ovulation induction cycle FET. Artificial cycle FET (AC-FET) mimics the natural menstruation cycle by the administration of consecutive estrogen and progesterone. Otherwise, 90 mg of vaginal progesterone gel daily (Crinone gel 8%, Merck Serono SA, Geneva, Switzerland), they also were provided 6 mg of oral estradiol daily and 20 mg of oral dydrogesterone two times a day and the dose gradually reduce until 12 pregnancy weeks.

Definition of clinical outcomes and follow-up

Clinical pregnancy was defined by the presence of one or more intrauterine gestational sacs. Early miscarriage is defined as pregnancy loss during the first trimester of pregnancy (less than 12 weeks of gestation). Spontaneous abortion rate is expressed per clinical pregnancy cycle. The ectopic pregnancy rate is expressed per clinical pregnancy cycle. The ongoing clinical pregnancy, defined as pregnancy gestational weeks, was more than 20 weeks.

Statistical analysis

Descriptive data for baseline characteristics were compared using the Student's *t* test (normal data distribution) or the Mann-Whitney *U* test (skewed data). One-way ANOVA test, independent *t* test, and two-tailed χ^2 analysis were performed to compare data between the groups. All statistical analysis was performed using the IBM SPSS Statistics Package (IBM SPSS V.20; IBM Corporation Inc., Chicago, USA). A *P* value of 0.05 is used as the cutoff for statistical significance.

Results

Data were extracted from clinical records, including age, duration of infertility, infertility type, basal estradiol (E2), basal follicle-stimulating hormone (FSH), basal LH, the primary cause of infertility, ovulation protocol, total gonadotropin (Gn) dosage, number of oocytes retrieved, number of available embryos (D3 and D5), number of embryos transferred (D3 and D5), and endometrial thickness. Reproductive outcomes included clinical pregnancy rate, early spontaneous abortion rate, and the persistent clinical pregnancy rate.

There were 4312 patients taken the "freeze-all" strategy from 1st January 2018 to 31st June 2019. Based on the exclusion criteria, 2561 patients were included. Fifty-eight patients were included in the study group (group 1) due to fever during oocyte retrieval. All patients had a fever between 37.4°C and 40°C, and upper respiratory tract bacterial infection was the main reason for fever in 53 patients (91.4%), and 5 fever patients for other reasons (such as pneumonia and acute gastroenteritis). With the 1:3 ratio paired of age, 174 patients were enrolled in the control group (Group 2) from the 2503 patients taken "freeze-all" strategy for other reasons (not fever) in the same period. None of the patients had a pelvic inflammatory disease after oocyte retrieval.

The basic characteristics of patients are shown in Table 1. Age was already matched. There were no significant differences in body mass index (BMI), basal FSH, basal LH, basal E2, and infertility type (primary or secondary). However, the anti-mullerian hormone (AMH) levels were higher in the control group compared to the study group (4.2 ng/mL *vs.* 2.2 ng/mL, $P < 0.001$), and the infertility time was longer in the control group (3 years *vs.* 2 years, $P = 0.035$).

Table 2 shows the clinical data after the ovarian stimulation; there were no significant differences in the ovarian stimulation protocol, the usage of Gn (both time and dose), and the intracytoplasmic sperm injection (ICSI) rate between the two groups. The number of oocytes retrieved (10.9 ± 4.6 *vs.* 17.4 ± 5.9) and the fertilization rate (81.0% *vs.* 90.6%) were lower in the study group, with a significant difference ($P < 0.001$), but the two pronucleate (2PN) rate was higher in the study group (66.7% *vs.* 57.4%, $P < 0.001$) and the number of available embryos (D3 and D5) were similar in the two groups ($P > 0.05$).

Regarding pregnancy outcomes, 58 patients in Group 1 had 58 FET cycles with no cycle canceled, and 174 patients in Group 2 had 173 FET cycles with one cycle canceled because of all frozen embryo damage after thawing (Table 3). The endometrial thickness (10.3 ± 2.0 mm *vs.* 9.9 ± 1.5 mm), the number of embryo transfer (D3 or D5), the type of luteal support supplementation was similar between the two groups. The implantation rate (36.4% *vs.* 40.2%), clinical pregnancy rate (48.3% *vs.* 52.0%), early spontaneous rate (17.9% *vs.* 13.3%), ectopic pregnancy rate (3.6% *vs.* 1.1%) and ongoing pregnancy rate (37.9% *vs.* 44.5%) were comparable with no significant difference. After taking into account the effects of age, BMI, AMH, transfer D3 or D5 numbers, endometrial thickness, we performed regression analyses, which are shown in Table 4. Clinical pregnancy and ongoing pregnancy rates were also not significantly different after balance the confounding variables.

The patients with $T \leq 37.2$°C, low fever ($T < 38$°C) and higher fever ($T \geq 38$°C) had no significant difference in clinical pregnancy rate and ongoing pregnancy rate ($P > 0.05$, Table 5).

Table 1: Baseline characteristic of the infertility patients taken whole embryo freezing cycles with fever during oocyte retrieval.

Variables	Group 1 (*n* = 58)	Group 2 (*n* = 174)	*P*
Age (years)	31.4 ± 5.3	31.3 ± 5.2	0.98
Type of infertility			0.88
Primary	58.6 (34/58)	60.9 (106/174)	
Secondary	41.4 (24/58)	39.1 (68/174)	
Duration of infertility (years)	2.00 (1.25, 3.75)	3.00 (2.00, 5.00)	0.04
Nulliparity	86.2 (50/58)	93.1 (162/174)	0.10
BMI (kg/m^2)	23.40 ± 3.60	22.40 ± 3.33	0.06
Basal FSH (IU/L)	6.70 ± 3.64	6.30 ± 2.01	0.40
Basal LH (IU/L)	4.00 ± 2.70	4.80 ± 2.75	0.05
Basal E2 (nmol/L)	181.7 ± 88.06	163.9 ± 62.9	0.16
AMH (ng/mL)	2.20 (1.35, 4.18)	4.20 (2.25, 6.42)	<0.001

Data are presented as % (*n*/*N*), median (range) or mean ± standard deviation. AMH: Anti-mullerian hormone; BMI: Body mass index; E2: Estradiol; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone.

Table 2: Clinical data of the infertility patients after ovarian stimulation.

Clinical data	Group 1 ($n=58$)	Group 2 ($n=174$)	P
Ovarian stimulation protocol			0.92
GnRHa long protocol	25.9 (15/58)	26.4 (46/174)	
GnRHa prolonged protocol	12.1 (7/58)	14.4 (25/174)	
GnRHa short protocol	1.7 (1/58)	4.0 (7/174)	
GnRH antagonist protocol	58.6 (34/58)	54.0 (94/174)	
Mild-stimulation stimulation	1.7 (1/58)	1.1 (2/174)	
Total gonadotrophin dose (IU)	2595 ± 994.1	2399 ± 947.7	0.18
No. days of stimulation (d)	11.1 ± 2.6	11.1 ± 2.1	0.97
Number of oocytes retrieved	10.9 ± 4.6	17.4 ± 5.9	<0.001
ICSI rate	29.3 (17/58)	37.9 (66/174)	0.24
Fertilization rate	81.0 (511/631)	90.6 (2689/2968)	<0.001
2PN rate	66.7 (421/631)	57.4 (1705/2968)	<0.001
Available embryos number			
D3	4 (1, 12)	6 (2, 20)	0.07
D5	2 (1, 8)	2 (1, 12)	0.89

Data are presented as % (*n*/*N*), median (range) or mean ± standard deviation. ICSI: 2PN: Two pro-nucleate; D3: Three days; D5: Five days; GnRHa: Gonadotropin releasing hormone agonist analogue.

Table 3: Outcomes of fist frozen-thawed embryo transfer cycle of the infertility patients.

Outcomes	Group 1 ($n=58$)	Group 2 ($n=174$)	P
Cancelled FET cycles	0	1	
FET cycles	58	173	
Embryos transferred number			
D3	2 (1, 2)	2 (1, 2)	0.14
D5	1 (1, 1)	1 (1, 2)	0.29
Endometrial thickness	10.3 ± 2.0	9.9 ± 1.5	0.16
Luteal support supplementation			0.19
NC-FET cycle	60.3 (35/58)	50.3 (87/173)	
AC-FET cycle	25.9 (15/58)	38.7 (67/173)	
Ovulation induction cycle	13.8 (8/58)	11.0 (19/173)	
Implantation rate	36.4 (32/88)	40.2 (104/259)	0.53
Clinical pregnancy rate	48.3 (28/58)	52.0 (90/173)	0.76
Early spontaneous abortion rate	17.9 (5/28)	13.3 (12/90)	0.77
Ectopic pregnancy rate	3.6 (1/28)	1.1 (1/90)	0.38
Ongoing pregnancy rate	37.9 (22/58)	44.5 (77/173)	0.49

Data are presented as % (*n*/*N*), median (range) or mean ± standard deviation. AC-FET: Artificial cycle rozen-thawed embryo transfer; D3: Three days; D5: Five days; FET: Frozen-thawed embryo transfer; NC-FET: Natural cycle frozen-thawed embryo transfer.

Discussion

The body temperature exceeds the normal body temperature by 0.5°C, which is called fever. In clinical, it is generally considered that T ≥ 37.3°C. According to the armpit temperature, it is divided into low fever (<38°C), medium fever (38–39°C) and high fever (39–40°C), and ultra-high fever (>40°C). In our study, patients had a fever within 72 hours before egg retrieval and lasted from 24 hours to 72 hours. The average duration was 29.4 ± 11.9 hours. The maximum body temperature fluctuated from 37.4°C to 40°C, and the average maximum body temperature was 38.1 ± 0.6°C.

In many studies, recurrent implantation failure was reported to be related to age, BMI, smoking, embryo, and endometriosis,[12] which can be an extremely stressful experience for couples undergoing *in vitro* fertilization (IVF) and embryo transfer (ET) cycles as well as to clinicians. Endometrial receptivity is widely regarded as a key factor in the success of IVF. The current study determined that certain genital tract infection (GTI) may contribute to failure in patients undergoing IVF.[13] Many women who have experienced recurrent implantation failure (RIF) have also been found to have chronic endometritis (CE) from bacterial colonization.[12–14] In fact, Romero *et al*[15] reported that the prevalence rate of CE was as high as 42% in patients with recurrent implantation failure (RIF) underwent *in vitro* fertilization (IVF) cycles. However, we did not know whether having a fever during oocyte retrieval would affect the embryo quality and endometrial receptivity (such as increased chronic endometritis), which may increase implantation failure.

Table 4: Binary logistic regression analysis to account for confounding variables of the infertility patients.

Variables	Clinical pregnancy		Ongoing pregnancy	
	P	OR (95% CI)	*P*	OR (95% CI)
Group	0.81	0.93 (0.49, 1.75)	0.42	0.76 (0.39, 1.48)
Age	0.56	0.98 (0.93, 1.04)	0.74	0.95 (0.89, 1.01)
BMI	0.76	0.93 (0.85, 1.01)	0.02	0.90 (0.83, 0.98)
AMH	0.91	0.99 (0.92, 1.07)	0.98	1.00 (0.93, 1.08)
Transfer D3 number	0.79	1.15 (0.41, 3.25)	0.47	1.48 (0.52, 4.22)
Transfer D5 number	0.72	1.44 (0.21, 10.10)	0.52	1.92 (0.27, 13.70)
Endometrial-thickness	0.51	0.51 (0.89, 1.25)	1.18	1.13 (0.95, 1.35)

AMH: Anti-mullerian hormone; BMI: Body mass index; CI: Confidence interval; OR: Odds ratio.

Table 5: The outcomes of patients with $T \leq 37.2^{\circ}C$, $37.3^{\circ}C \leq T < 38^{\circ}C$ and $T \geq 38^{\circ}C$ group.

Items	$T \leq 37.2^{\circ}C$	$37.3^{\circ}C \leq T < 38^{\circ}C$ ($n = 26$)	$T \geq 38^{\circ}C$ ($n = 32$)	P
Clinical pregnancy rate (%)	52.0 (90/173)	42.3 (11/26)	53.1 (17/32)	0.63
Ongoing pregnancy rate (%)	44.5 (77/173)	30.8 (8/26)	43.8 (14/32)	0.42

Upper respiratory and digestive tract infections accompanied by fever, such as influenza and acute gastroenteritis, can occur in almost any population and are unpredictable. The infertility patients entered in the IVF cycle cannot be completely avoided from them, so doctors should think about how to deal with such patients. Transvaginal ultrasound-guided oocyte retrieval is an essential procedure for ART. It is now considered the gold standard procedure for oocyte retrieval for its simplicity, but the operation must go through the vagina that is not completely sterile. Patients with fever may increase the risk of infection during oocyte retrieval and cause endometritis, decrease in embryo quality, and pelvic inflammatory disease resulting in implantation failure. In our study, none of the patients had a pelvic inflammatory disease after oocyte retrieval using oral antibiotics. It is a relatively straightforward and safe procedure for patients with fever. As shown in Tables 1 and 2, the patients' age, BMI, nulliparity, basal FSH, basal LH, basal E2, infertility type (primary or secondary), ovarian stimulation protocol, usage of Gn, ICSI rate, 2PN rate, and the number of available embryos (D3 and D5) were not significantly different. However, the AMH levels were higher in the control group (4.2 ng/mL *vs*. 2.2 ng/mL, $P < 0.001$). The number of oocytes retrieved (10.9 ± 4.6 *vs*. 17.4 ± 5.9) and the fertilization rate (81.0% *vs*. 90.6%) were lower in the study group. The higher AMH and number of oocytes retrieved in the control group were because of most whole embryos freezing in the control group due to the OHSS. We can see that AMH can more sensitively respond to ovarian function than the hormones FSH, LH, and E2 in predicting the number of oocytes obtained. Fever does not affect the rate of embryo formation.

Great progress has been made in ART in the past few decades. It is more than 30 years since Trounson and Mohr reported the successful cryopreservation and thawing of supernumerary human embryos after IVF or IVF/ICSI treatment, and Zeilmaker reported the first live birth (LB) after FET.[16,17] The technique introduced by these pioneers has had a profound impact on ART; FET performed is associated with good outcomes, and vitrification of embryos obtained better clinical outcomes and did not increase the risks of DNA damage, spindle configuration, embryonic aneuploidy, and genomic imprinting as compared with fresh procedures,[18] therefore, the freeze-all policy can serve as an alternative to fresh embryo transfer to avoid the deleterious effects of COS in embryo-endometrium synchrony.[19,20] Therefore, in our study, we chose the "freeze-all" strategy. All patients underwent FET cycles, which not only reduced the risk of OHSS but also avoided the time of embryo implantation from the patients' inflammatory period. Table 3 shows the endometrial thickness, the number of embryo transfer, and the type of luteal support supplementation were similar during the first FET cycle between the two groups. Regarding pregnancy outcomes in our study, clinical pregnancy rate, ongoing pregnancy rate also were all not significantly different after using regression analyses for balance the confounding variables. Thus, we can conclude that fever cannot affect embryo quality. Moreover, it cannot be concluded that fever might increase endometritis. With this strategy, the entire cohort of embryos is cryopreserved, and delayed FET is performed in an endometrium that is possibly more receptive.[21]

In conclusion, for patients with fever during oocyte retrieval, the transvaginal ultrasound-guided follicular puncture for oocyte retrieval is a safe and minimally invasive method. It is recommended in the "freeze-all" strategy not to cancel the oocyte retrieval cycle, but to cancel the fresh embryo transplantation cycle. FET cycles for embryo transfer would be beneficial for these patients. Although this study was not a randomized controlled trial and the sample size of our study was relatively small, this matched-pair study can be considered to be well designed. More studies should be conducted in this area.

Conflicts of interest

None.

References

1. Van Voorhis BJ. Clinical practice. In vitro fertilization. N Engl J Med 2007;356:379–386. doi: 10.1056/NEJMcp065743.
2. Mascarenhas M, Flaxman S, Ties B, Vanderpoel S, Stevens G. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 Health Surveys. PLoS Med 2012;9: e1001356. doi: 10.1371/journal.pmed.1001356.
3. Inhorn MC, Pasquale P. Infertility around the globe: new thinking on gender, reproductive technologies and global movements in the 21st century. Human Reprod Update 2015;4:411–426. doi: 10.1093/humupd/dmv016.
4. Zelkowitz P, O'Connell MS, Robins SS. An mHealth app designed for fertility patients: from conception to pilot testing. Iproceedings 2019;5:e15236.
5. Farquhar C, Rishworth JR, Brown J, Nelen WL, Marjoribanks J. Assisted reproductive technology: an overview of Cochrane Reviews. Cochrane Database Syst Rev 2013;CD010537. doi:10.1002/14651858.CD010537.
6. Wang X, Wu H, He X, Jiang H, Wu L, Xu Y, *et al*. Retrospective study to compare frozen-thawed embryo transfer with fresh embryo transfer on pregnancy outcome following intracytoplasmic sperm injection for male infertility. Med Sci Monit 2018;24:2668–2674. doi: 10.12659/MSM.907229.
7. Wong KM, van Wely M, Mol F, Repping S, Mastenbroek S. Fresh versus frozen embryo transfers in assisted reproduction. Cochrane Database Syst Rev 2017;3:CD011184. doi: 10.1002/14651858.CD011184.pub2.
8. Maheshwari A, Bhattacharya S, Bowler U, Brison D, Child T, Cole C, *et al*. Study protocol: E-freeze-freezing of embryos in assisted conception: a randomised controlled trial evaluating the clinical and cost effectiveness of a policy of freezing embryos followed by thawed frozen embryo transfer compared with a policy of fresh embryo transfer, in women undergoing in vitro fertilisation. Reprod Health 2019;16:81–181. doi: 10.1186/s12978-019-0737-2.
9. Sik A, Oral S, Aba YA, Ozolcay O, Koc M, Sismanoglu A. Pregnancy results after fresh embryo transfer and selective frozen-thawed embryo transfer: Single-center experience. J Gynecol Obstetr Human Reprod 2020;101707. doi: 10.1016/j.jogoh.2020.101707.
10. Lin-li H, Guo-ning HH, Hai-xiang HS, Li-Qing F, Yun F, Huang S, *et al*. CSRM guideline for the use of ovulation induction drug (2016). J Reprod Med 2017;26:302–307.
11. Ghobara T, Gelbaya TA, Ayeleke RO. Cycle regimens for frozen-thawed embryo transfer. Cochrane Database Syst Rev 2017;7: CD003414. doi: 10.1002/14651858.cd003414.pub3.
12. Bashiri A, Halper KI, Orvieto R. Recurrent Implantation Failure-update overview on etiology, diagnosis, treatment and future directions. Reprod Biol Endocrinol 2018;16:121. doi: 10.1186/s12958-018-04*14-2.
13. Moragianni D, Dryllis G, Andromidas P, Kapeta-Korkouli R, Kouskouni E, Pessach I, *et al*. Genital tract infection and associated factors affect the reproductive outcome in fertile females and females undergoing in vitro fertilization. Biomed Rep 2019;10:231–237. doi: 10.3892/br.2019.1194.
14. Cicinelli E, Matteo M, Tinelli R, Lepera A, Alfonso R, Indraccolo U, *et al*. Prevalence of chronic endometritis in repeated unexplained implantation failure and the IVF success rate after antibiotic therapy. Hum Reprod 2015;30:323–330. doi: 10.1093/humrep/deu292.
15. Romero R, Espinoza J, Mazor M. Can endometrial infection/inflammation explain implantation failure, spontaneous abortion, and preterm birth after in vitro fertilization? Fertil Steril 2004;82:799–804. doi: 10.1016/j.fertn- stert.2004.05.076.
16. Trounson A, Mohr L. Human pregnancy following cryopreservation, thawing and transfer of an eight-cell embryo. Nature 1983;305:707–709. doi: 10.1038/305707a0.
17. Zeilmaker GH, Alberda AT, van Gent I, Rijkmans CM, Drogendijk AC. Two pregnancies following transfer of intact frozen-thawed embryos. Fertil Steril 1984;42:293–296. doi: 10.1016/s0015-0282(16)48029-5.
18. Zhang L, Yan LY, Zhi X, Yan J, Qiao J. Female fertility: is it safe to "freeze?". Chin Med J 2015;128:390–396. doi: 10.4103/0366-6999.150115.
19. Shapiro BS, Daneshmand ST, Garner FC, Aguirre M, Hudson C, Thomas S. Evidence of impaired endometrial receptivity after ovarian stimulation for in vitro fertilization: a prospective randomized trial comparing fresh and frozen-thawed embryo transfer in normal responders. Fertil Steril 2011;96:344–348. doi: 10.1016/j.fertnstert.2011.05.050.
20. Shapiro BS, Daneshmand ST, Garner FC, Aguirre M, Hudson C, Thomas S. Evidence of impaired endometrial receptivity after ovarian stimulation for in vitro fertilization: a prospective randomized trial comparing fresh and frozen-thawed embryo transfers in high responders. Fertil Steril 2011;96:516–518. doi: 10.1016/j.fertnstert.2011.02.059.
21. Weinerman R, Mainigi M. Why we should transfer frozen instead of fresh embryos: the translational rationale. Fertil Steril 2014;102:10–18. doi: 10.1016/j.fertnstert.2014.05.019.

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