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ASSISTED REPRODUCTION TECHNOLOGIES

Delayed versus immediate frozen embryo transfer after oocyte retrieval: a systematic review and meta-analysis

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Abstract

Purpose This systematic review and meta-analysis aimed to compare pregnancy outcomes between immediate frozen embryo transfer (FET) performed within the first menstrual cycle after oocyte retrieval and delayed FET following subsequent cycles.

Methods PubMed, EMBASE, and Web of Science were searched for eligible studies through January 2020. The main outcome measures were clinical pregnancy rate (CPR), live birth rate (LBR), and pregnancy loss rate (PLR). The effect size was estimated as risk ratio (RR) with 95% confidence interval (CI) using a random effects model. Inter-study heterogeneity was assessed by the I^2 statistic.

Results Twelve retrospective cohort studies involving 18,230 cycles were included. The pooled results revealed no significant differences between delayed and immediate FET in CPR (RR 0.94, 95% CI 0.87–1.03; $I^2 = 67.9\%$), LBR (RR 0.94, 95% CI 0.85–1.03; $I^2 = 67.5\%$), and PLR (RR 1.05, 95% CI 0.87–1.26; $I^2 = 42.7\%$). Subgroup analyses of freeze-all cycles showed a marginal decrease of CPR in delayed FET (RR 0.93, 95% CI 0.86–1.00; $I^2 = 53.6\%$), but no significant changes were observed regarding LBR (RR 0.93, 95% CI 0.85–1.02; $I^2 = 65.2\%$) and PLR (RR 1.09, 95% CI 0.84–1.41; $I^2 = 59.1\%$). No statistical differences were found in effect estimates among other subgroup analyses by ovarian stimulation protocol, trigger agent, endometrial preparation regimen, and embryo stage.

Conclusion Timing of the first FET after oocyte retrieval was not significantly associated with pregnancy outcomes. This finding refutes the current common practice to delay FET after oocyte retrieval and reassures patients who wish to proceed with FET at their earliest convenience. Due to the high heterogeneity and observational nature of included studies, further randomized controlled trials are needed to confirm the results.

Keywords Frozen embryo transfer · Oocyte retrieval · Pregnancy outcome · Meta-analysis

Introduction

Controlled ovarian stimulation (COS) induces multifollicular development in one cycle and is an essential determinant of in vitro fertilization (IVF) success. In the case of a failed fresh embryo transfer (ET) attempt, cryopreservation of surplus embryos following COS has been widely used as a safe and efficient approach to increase cumulative pregnancy rates per oocyte retrieval [1, 2]. In addition, the practice of a freeze-all strategy is also on a constant increase in recent years [3, 4], which correlates with the improved embryo cryopreservation method by vitrification, incorporation of preimplantation genetic testing for aneuploidy, as well as promising results of preserved or even higher live birth rate and reduced risk of ovarian hyperstimulation syndrome compared to fresh ET [5–10].

One of the debatable issues that arise in daily clinical practice is the optimal time interval between COS and subsequent FET. Some physicians opt to delay the start of FET for at least one menstrual cycle in order to minimize any conceivable residual effect of COS on endometrial receptivity and ovarian function [11, 12]. Contrarily, others choose to perform FET immediately in the first menstrual cycle following oocyte

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retrieval to avoid unnecessary prolongation of time to pregnancy and reduce stress and anxiety of subfertile women who are eager to conceive as soon as possible. Thus far, a number of observational studies have assessed pregnancy outcomes in delayed versus immediate FET after a failed fresh ET or a freeze-all cycle, but the results are varied and inconclusive [13–24].

The aim of the present study is to comprehensively evaluate the effect of FET timing following oocyte retrieval on pregnancy outcomes through a systematic review and meta-analysis.

Materials and methods

This meta-analysis was performed in adherence to the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guideline [25] and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [26].

Search strategy

A systematic database search of PubMed (https://www.ncbi.nlm.nih.gov/pubmed), EMBASE (https://www.embase.com), and Web of Science (https://www.webofknowledge.com) was conducted to identify all relevant literatures published through January 2020. The following terms were applied in our search: "time" or "timing" or "time interval" or "delayed" or "immediate" and "frozen embryo transfer" or "frozen-thawed embryo transfer" or "cryopreserved embryo transfer" or "cryo-thawed embryo transfer" and "oocyte retrieval" or "ovarian stimulation" or "ovum pick-up" or "in vitro fertilization" or "IVF" or "OPU." Study language was limited to English, with no restriction imposed on the year of publication. Moreover, the reference lists of retrieved relevant reports were manually scrutinized for any additional studies.

Study selection

Studies were considered eligible if they satisfied the following four criteria: (i) cohort study design, (ii) the subjects were women undergoing first FET after a failed fresh ET or a freeze-all cycle, (iii) the exposure of interest was the time interval between COS and subsequent FET, and (iv) the outcomes included clinical pregnancy rate (CPR), live birth rate (LBR), or pregnancy loss rate (PLR). Studies were excluded if they (i) compared pregnancy outcomes between delayed and immediate cycles in consecutive fresh IVF/ICSI treatments and (ii) were published as reviews, editorials, commentaries, case reports, conference abstracts, or trial protocols. In the case of duplicate studies with overlapping populations, we retained the most recent version containing a larger sample size.

Studies were selected in a two-step process to ensure the correct identification. Firstly, titles and abstracts of all initially retrieved records were screened by two independent reviewers (J.H. and J.L.). Secondly, a decision on inclusion was made after evaluation of the full manuscripts that were likely to meet the eligible criteria. Any disagreements were resolved by group discussion with a third investigator (Y.K.).

Data extraction and quality assessment

The same two reviewers (J.H. and J.L.) independently performed data extraction with a standardized and pilot-tested form. The following information were recorded for each included study: the first author's name, year of publication, country of origin, cohort design, study duration, population characteristics, definition of immediate/delayed transfer, cycle number, age, ovarian stimulation protocol, trigger agent, endometrial preparation regimen, embryo developmental stage, and outcome parameters. Data from different subgroups in the same study were also extracted for possible synthesis. The corresponding author was contacted by e-mail when information was missing or unclear in the original article.

The methodological quality of eligible studies was evaluated using the Newcastle-Ottawa Scale (NOS) [27]. This scale assigns a maximum of nine points to each study based on the following three broad aspects: the selection of subjects and assessment of exposure (4 points), comparability of study groups (2 points), and outcome ascertainment and follow-up adequacy (3 points). Studies scoring 7–9 points were regarded to have a high quality and a low risk of bias. Each study received a score from one of the two reviewers (J.H. and J.L.), and discrepancies were resolved by consensus with a third investigator (Y.K.).

Statistical analysis

Data for pregnancy outcomes were collected as dichotomous variables, and the results were expressed as risk ratio (RR) with 95% confidence interval (CI). Because the true effect size should not be assumed to be the same across individual studies, meta-analysis was performed using a random effects model to incorporate both within- and between-study variability [28]. The degree of heterogeneity was quantified by the I^2 statistic, and we considered values of < 25%, 25–50% and > 50% to represent low, moderate, and high heterogeneity, respectively [29]. Publication bias was examined by means of funnel plots and Egger's linear regression test, with $P < 0.10$ indicating a statistical significance [30].

Considering the clinical diversity of included studies, we further conducted five subgroup analyses to separately assess the effect of FET timing on pregnancy outcomes as follows: (i) study population (failed fresh ET, freeze-all and mixed), (ii) ovarian stimulation protocol (agonist-based, antagonist-based,

and mixed), (iii) trigger agent (agonist only, hCG included and mixed), (iv) endometrial preparation regimen (artificial, natural, and mixed), and (v) embryo developmental stage (blastocyst, cleavage, and mixed or unclear). The statistical difference of the effects among subgroups was examined by interaction test. A sensitivity analysis by removing one study at a time was also performed to evaluate the stability of results and explore potential sources of heterogeneity.

We used the Stata software (version 16.0; StataCorp LP, College Station, Texas) for all analyses. Statistical significance was set at $P < 0.05$ except where otherwise specified.

Results

Literature search and study characteristics

The initial literature search yielded 3599 records from electronic databases and another two articles through manual search. After removal of duplicates and screening of the titles and/or abstracts, 22 articles were further assessed for eligibility based on full-text review and 12 studies were finally included in the meta-analysis [13–24]. The process of study selection is detailed in Fig. 1.

Table 1 presents the main characteristics of the 12 included studies. These studies were published between 2016 and 2020 and were conducted in 10 different countries. All cohorts were retrospective, with the number of FET cycles varying from 129 to 4994. Seven studies focused on women undergoing first FET after a freeze-all cycle [13, 14, 17, 19, 20, 22, 23], three on women following a failed fresh ET [16, 21, 24], and two on women in both cases [15, 18]. In most studies [13, 14, 17–19, 22, 23], immediate transfer was defined as FET performed within the first menstrual cycle following oocyte retrieval ("cycle 1"), while delayed transfer referred to FET that took place after one or more menstrual cycles ("cycle ≥ 2"). The other five studies used the different time interval from oocyte retrieval to the start of FET (< 22/≥ 22 days) [16, 21], from oocyte retrieval to FET (< 50/≥ 50 days) [24], or from embryo cryopreservation to FET (25–35/50–70 days) [15] for

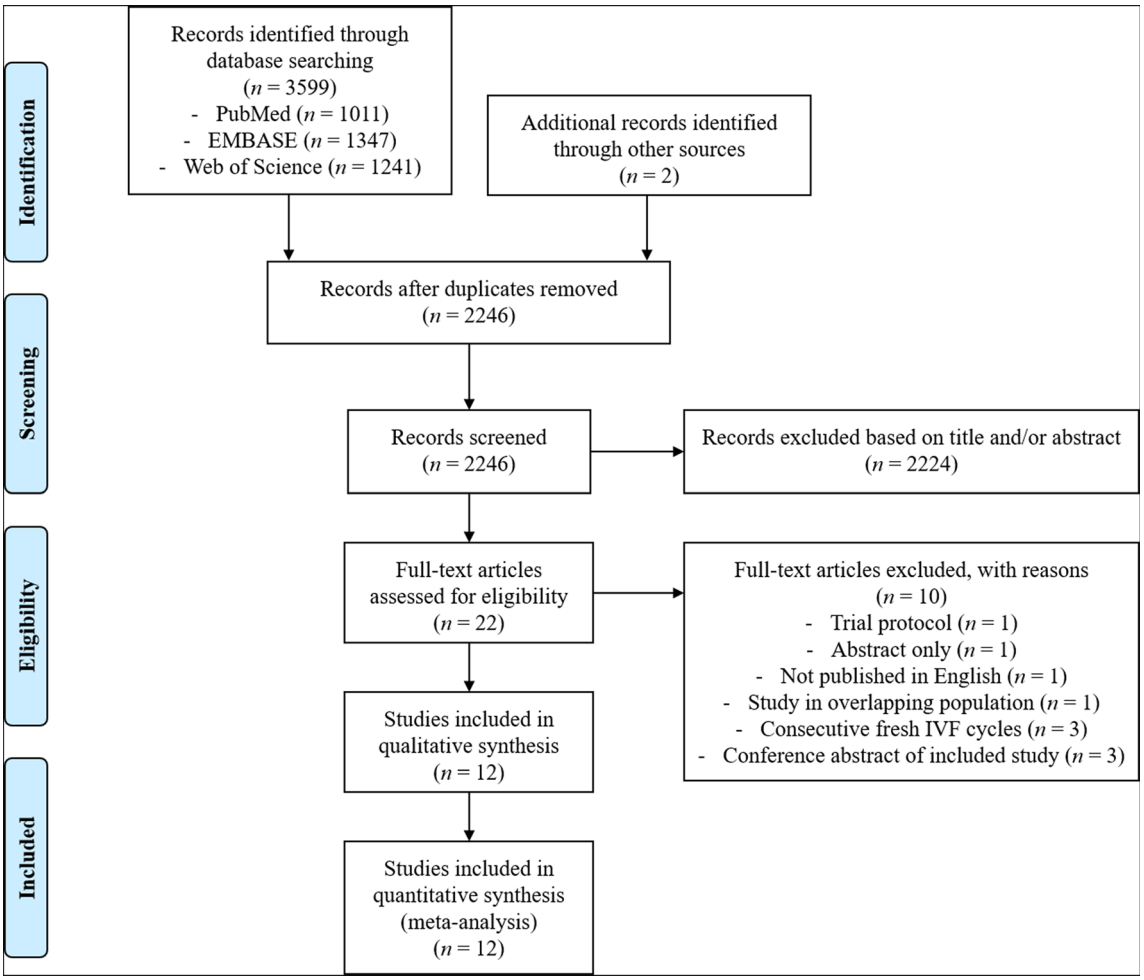

Fig. 1 The flow diagram of study selection. IVF, in vitro fertilization

Table 1 Main characteristics of included studies in the meta-analysis

Study	Country	Cohort design	Duration	Population	Definition of immediate/ delayed transfer	Sample size (cycle)	Age (years)	Ovarian stimulation protocol	Trigger agent	Endometrial preparation	Embryo stage	Outcomes
[13]	France	Retrospective, single-center	2012–2015	Women undergoing first FET after a freeze-all cycle	Within the first menstrual cycle/after one or more menstrual cycles following oocyte retrieval (cycle 1/≥ 2)	474	Mean, immediate, 33.7; delayed, 33.9	GnRH antagonist, long agonist or short agonist	GnRH agonist or hCG	Artificial cycle	Blastocyst	CPR, LBR, PLR
[14]	China	Retrospective, single-center	2014–2017	Women undergoing first FET after a freeze-all cycle	Cycle 1/≥ 2	4404	Mean, immediate, 31.6; delayed, 31.9	GnRH antagonist or long agonist	hCG	Artificial or natural cycle	Cleavage, morula or blastocyst	CPR, LBR, PLR
[15]	Australia	Retrospective, multi-center	2000–2014	Women undergoing first FET after a failed fresh ET or a freeze-all cycle	25–35/50–70 days from embryo cryopreservation to FET	4994	Median, immediate, 36.0; delayed, 35.5	GnRH antagonist, long agonist or short agonist	hCG	Artificial or natural cycle	-	CPR, LBR, PLR
[16]	Israel	Retrospective, single-center	2009–2016	Women undergoing first FET after a failed fresh ET	≤ 22/> 22 days from oocyte retrieval to the start of FET cycle	198	Mean, immediate, 32.8; delayed, 34.1	GnRH antagonist, long agonist or short agonist	hCG	Natural or modified natural cycle	Cleavage or blastocyst	CPR, LBR
[17]	China	Retrospective, single-center	2013–2016	Women undergoing first FET after a freeze-all cycle	Cycle 1/≥ 2	2998	Mean, immediate, 30.6; delayed, 30.9	Short agonist or progestin-primed ovarian stimulation	GnRH agonist, hCG or both	Artificial or modified natural cycle	Cleavage or blastocyst	CPR, LBR, PLR
[18]	USA	Retrospective, single-center	2013–2016	Women undergoing first FET after a failed fresh ET or a freeze-all cycle	Cycle 1/≥ 2	344	Mean, immediate, 33.7; delayed, 33.5	GnRH antagonist or long agonist	GnRH agonist, hCG or both	Artificial or natural cycle	Blastocyst	CPR, LBR, PLR
[19]	Spain	Retrospective, single-center	2012–2014	Women undergoing first FET after a freeze-all cycle	Cycle 1/≥ 2	512	Mean, immediate; 34.7; delayed, 35.3	GnRH antagonist or long agonist	GnRH agonist or hCG	Artificial cycle	Cleavage or morula	CPR, LBR, PLR
[20]	Turkey	Retrospective, single-center	2015–2016	Women undergoing first FET after a freeze-all cycle	32–46/≥47 days from oocyte retrieval to FET	1121	≤ 42	GnRH antagonist	GnRH agonist, hCG or both	Artificial cycle	Blastocyst	LBR
[21]	Belgium	Retrospective, single-center	2010–2014	Women undergoing first FET after a failed fresh ET	≤ 22/> 22 days from oocyte retrieval to the start of FET cycle	1183	Mean, immediate, 32.4; delayed, 32.5	GnRH antagonist	hCG	Artificial, natural or modified	Cleavage or blastocyst	CPR, LBR

Table 1 (continued)

Study	Country	Cohort design	Duration	Population	Definition of immediate/ delayed transfer	Sample size (cycle)	Age (years)	Ovarian stimulation protocol	Trigger agent	Endometrial preparation	Embryo stage	Outcomes
[22]	Belgium/ Vietnam	Retrospective, two-center	2010–2015	Women undergoing first FET after a freeze-all cycle	Cycle 1/≥ 2	333	Mean, immediate, 30.9; delayed, 31.8	GnRH antagonist	GnRH agonist	natural cycle Artificial cycle	Cleavage or blastocyst	CPR, PLR
[23]	China	Retrospective, single-center	2016–2018	Women undergoing first FET after a freeze-all cycle	Cycle 1/≥ 2	1540	Mean, immediate, 31.4; delayed, 31.0	GnRH antagonist, long agonist, ultra-long agonist, short agonist, ultra-short agonist or mild stimulation	GnRH agonist or hCG	Artificial, natural or stimulated cycle	Cleavage	CPR, LBR, PLR
[24]	Israel	Retrospective, single-center	2010–2015	Women undergoing first FET after a failed fresh ET	< 50/≥ 50 days from oocyte retrieval to FET	129	Mean, immediate, 29.9; delayed, 29.6	Long agonist	hCG	Artificial cycle	Cleavage or blastocyst	CPR, LBR, PLR

CPR, clinical pregnancy rate; *ET*, embryo transfer; *FET*, frozen embryo transfer; *GnRH*, gonadotropin-releasing hormone; *hCG*, human chorionic gonadotropin; *LBR*, live birth rate; *PLR*, pregnancy loss rate

classification of immediate and delayed transfer. Overall, the included studies were at low risk of bias with a NOS score of 8 (four studies) or 9 (eight studies) (Table S1).

Meta-analysis of CPR

Eleven studies of 11,709 cycles reported data on the association between FET timing and CPR. In the majority of studies [13–19, 21, 22, 24], clinical pregnancy was clearly defined as the ultrasound visualization of gestational sac with or without cardiac activity at around 7 weeks of gestation, while the study by Song et al. [23] did not provide a detailed description. The pooled results revealed no significant difference in CPR between delayed and immediate FET after oocyte retrieval (RR 0.94, 95% CI 0.87–1.03; $I^2 = 67.9\%$) (Fig. 2a). In subgroup analysis, the combination of the six studies that focused on freeze-all cycles showed a marginally significant decrease of CPR in delayed FET (RR 0.93, 95% CI 0.86–1.00), whereas no such effects were observed in failed fresh ET (RR 1.24, 95% CI 0.77–1.99) and mixed cycles (RR 0.95, 95% CI 0.68–1.33) (Table S2). No significant changes were found in the effect estimates among other subgroup analyses by ovarian stimulation protocol, trigger agent, endometrial preparation regimen, and embryo stage (Table S2).

Meta-analysis of LBR

Eleven studies totaling 17,897 cycles investigated the effect of FET timing on LBR. Live birth was differently described as the delivery of a viable infant beyond 20 [15, 20, 23], 24 [13, 16, 17, 21, 24], or 28 [14] weeks of gestation, and was not defined in detail in two studies [18, 19]. The combination of all these studies showed that FET timing was not significantly associated with LBR (RR 0.94, 95% CI 0.85–1.03; $I^2 = 67.5\%$) (Fig. 2b). This pooled result did not change when subgroup analyses were performed on failed fresh ET (RR 1.21, 95% CI 0.75–1.95), freeze-all (RR 0.93, 95% CI 0.85–1.02), and mixed cycles (RR 0.92, 95% CI 0.64–1.32) (Table S2). Similarly, analyses by ovarian stimulation protocol, trigger agent, endometrial preparation regimen, and embryo stage showed no relevantly differential effect (Table S2).

Meta-analysis of PLR

Nine studies included data on PLR according to the timing of FET after oocyte retrieval, comprising a total of 15,728 transfer cycles. Pregnancy loss was defined as miscarriage occurring before 10 [13], 12 [17], or 20 [18, 19, 24] weeks of gestational age, and was not described in the other four studies [14, 15, 22, 23]. Most studies calculated PLR as the cycle number of pregnancy loss per clinical pregnancy, while Lattes et al. [19] evaluated it on the basis of positive pregnancy test. The pooled RR of PLR for delayed versus immediate

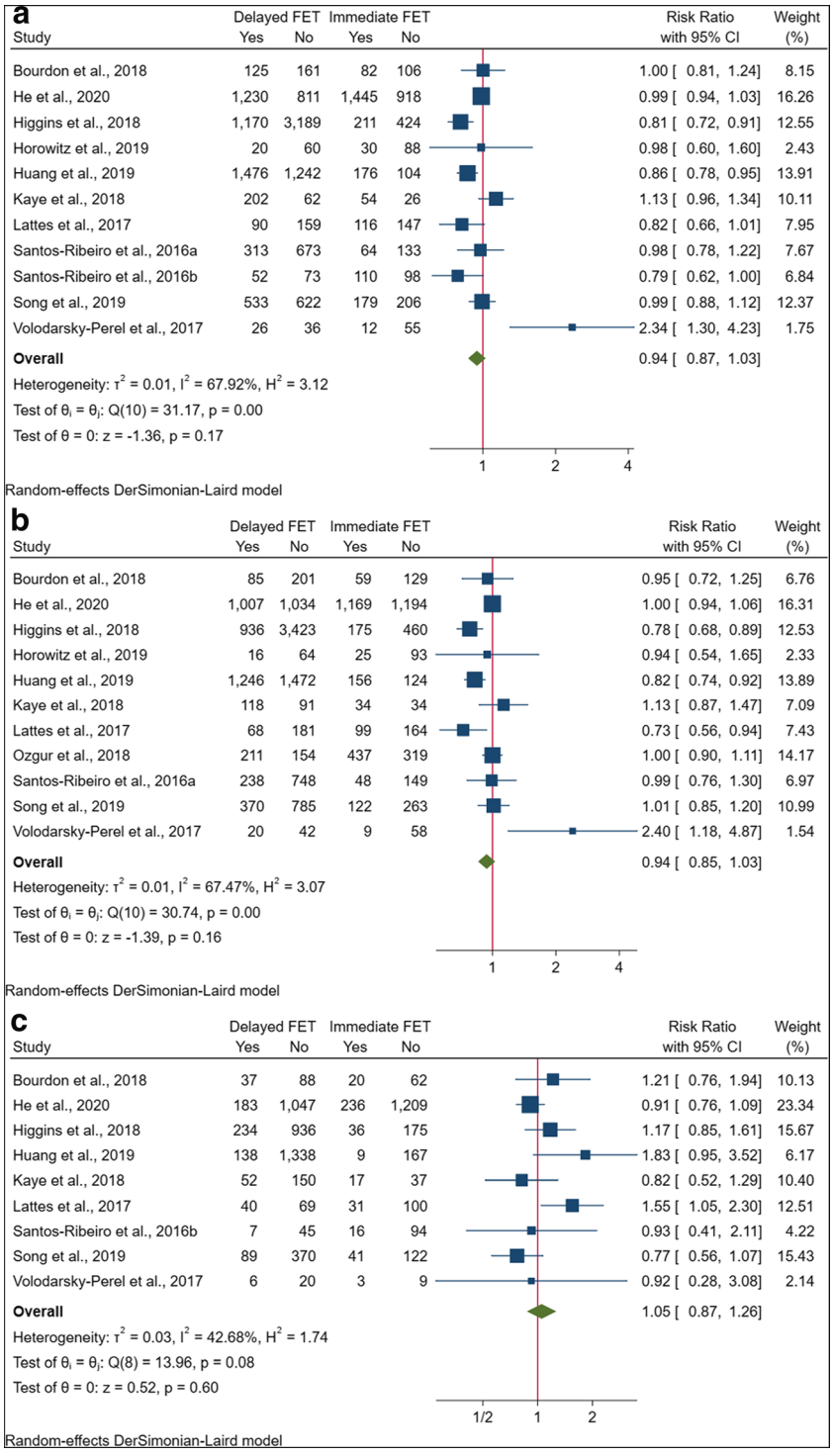

Fig. 2 Forest plots of pregnancy outcomes for delayed versus immediate frozen embryo transfer after oocyte retrieval. **a** Clinical pregnancy rate. **b** Live birth rate. **c** Pregnancy loss rate. CI, confidence interval; FET, frozen embryo transfer

FET was 1.05 (95% CI 0.87–1.26; $I^2 = 42.7\%$) (Fig. 2c). The subgroup analysis of freeze-all cycles presented consistent results (RR 1.09, 95% CI 0.84–1.41) with the combined effects of failed fresh ET (RR 0.92, 95% CI 0.28–3.08) and mixed cycles (RR 1.02, 95% CI 0.72–1.44) (Table S2). Further subgroup analyses by other confounders also showed no significant changes (Table S2).

Sensitivity analysis

On excluding the study by Volodarsky-Perel et al. [24], delayed FET was found to be marginally associated with a decrease in CPR compared with immediate FET (RR 0.93, 95% CI 0.87–1.00) (Fig. S1a), while no significant differences were found in LBR (RR 0.92, 95% CI 0.85–1.00) and PLR

(RR 1.06, 95% CI 0.87–1.28) (Fig. S1 b–c). Removal of any other individual studies did not modify the estimates substantially, with pooled RR of CPR, LBR, and PLR ranging from 0.92 to 0.96, 0.92 to 0.96, and 0.98 to 1.11, respectively (Fig. S1 a–c).

Publication bias

The funnel plot was visually symmetric for each outcome (Fig. S2). In addition, regression-based Egger test did not reach statistical significance ($P = 0.110$, 0.137 and 0.494 for CPR, LBR, and PLR, respectively), indicating no obvious publication bias of included studies.

Discussion

To our knowledge, this is the first meta-analysis to assess the association between timing of FET after oocyte retrieval and pregnancy outcomes. Based on a total of 18,230 cycles from 12 retrospective cohort studies, we found no significant difference in CPR, LBR, and PLR between immediate FET within the first menstrual cycle and delayed FET following subsequent cycles.

In sensitivity analysis, removal of the study by Volodarsky-Perel et al. [24] resulted in a marginal yet significant change of the pooled estimate of CPR. This study supported postponement of first FET after a failed fresh ET using the long agonist protocol, which, from their speculation, may cause deeper suppression on the hypothalamic-pituitary-ovarian axis than the antagonist regimen and could lead to more small sustained lutein cysts with secretory activity in the follicular phase of the immediate FET cycle. However, when introducing the COS protocol for adjustment, several other studies failed to show a significant impact of the GnRH analogue used for stimulation [14, 16, 19]. A further subgroup analysis of agonist- and antagonist-based regimens also presented comparable pregnancy outcomes between delayed and immediate FET. These results suggest that the detrimental influence of COS on endometrial receptivity may end clinically following the first withdrawal bleeding regardless of the stimulation protocol.

Intriguingly, the deferral of FET after oocyte retrieval appears to be marginally associated with a lower CPR in freeze-all cycles, while this relationship is absent in failed fresh ET. One possible explanation for the discrepancy may be the different psychological status in these two situations. Women undergoing IVF treatment are generally desired to get pregnant as soon as possible, yet delayed FET in a freeze-all cycle may add to their anxiety and stress that could pose an adverse influence on pregnancy chance [31–33]. Contrarily, women who had already a failed fresh ET attempt may shoulder a greater psychological burden and thus need a longer time to recover from emotional distress. Nonetheless, it is also reasonable to argue that women undergoing non-elective freeze-all cycles may have decreased stress with their timeline expectations managed through physician communication in advance. Therefore, further research is warranted to examine this explanation since none of the included studies compared the anxiety, depression, and self-motivation level of these women. On the other hand, there could be some differences in the patient and stimulation characteristics of a freeze-all versus a fresh ET cycle, which may possibly influence pregnancy outcomes in later FET cycles. Embryo quality may also differ in FET after freeze-all and failed ET cycles, as embryos of higher quality are often preferentially transferred in a prior fresh cycle. However, as the decrease in CPR barely reached statistical significance and the number of studies in each subgroup was limited with a high heterogeneity, this result may also be coincidental and should be interpreted with caution.

Several included studies have also raised concerns that the effect of FET timing after COS may differ by the ovulation trigger agent and endometrial preparation regimen [13, 16, 18, 19, 22]. Indeed, compared to trigger with hCG that has a prolonged half-life, the luteal phase following agonist trigger is often shortened and disrupted [34] and may thus affect immediate FET in the first menstrual cycle. Patients undergoing natural cycle for FET may also be different from those receiving artificial endometrial preparation [16], in which exogenous steroids are prescribed to overtake or correct ovarian and endometrial function that might be still recovering to pre-stimulation status in an adjacent FET cycle. Nevertheless, both multivariable regression analyses among individual studies and subgroup analyses in this review showed no significant differential effects of these factors, implying further the lack of scientific evidence for deferring FET.

Findings from the present study should provide guidance to both clinical practice and research design. According to a recent web-based survey from 179 IVF centers in 58 countries, over 60% of physicians prefer to delay FET after oocyte retrieval with a failed fresh ET [35]. In randomized controlled trials (RCTs) designed to compare pregnancy outcomes between fresh and frozen embryo transfer, patients in the cryopreservation arm also had to wait for 2 months [36] or one menstrual cycle [8–10] to perform their first FET. Herein, our results refute the current common practice to delay FET in fear of the carryover effect of COS on an adjacent cycle, and reassure physicians and patients who wish to proceed with FET at their earliest convenience.

Several limitations have to be acknowledged of this meta-analysis. Firstly, all included studies were retrospective cohorts, and therefore, the quality of evidence was initially graded as low for the inherent methodological drawbacks. To date, only a two-center RCT was found to be carried out in China [37]. According to the preliminary results presented at the 35th annual meeting of the European Society of Human Reproduction

and Embryology [37], the immediate FET group had a significantly higher ongoing pregnancy rate than the delayed group in both intention to treat analysis (47.0% (170/362) versus 39.2% (142/362)) and per protocol analysis (49.3% (170/345) versus 41.5% (142/342)). However, concern has been raised regarding the adequacy of the randomization process in this study given that important baseline characteristics such as female age varied significantly between the two groups, an event which could limit the validity of the findings of this RCT. Secondly, we observed a high degree of inter-study heterogeneity, which was presumed to be at partially caused by differences in the study population and cycle characteristics. Few studies reported pregnancy outcomes according to the standards by the International Committee for Monitoring Assisted Reproductive Technology (ICMART) [38], and the varied definitions of FET timing in some studies may possibly lead to misclassification of delayed and immediate transfer. In this regard, caution should be taken when generalizing the review finding to individual clinics with various combinations of ovarian stimulation, ovulation trigger, endometrial preparation, and embryo transfer strategies. Finally, bias may have been introduced because studies published as conference abstracts and in languages other than English were excluded from the meta-analysis.

In conclusion, our systematic review and meta-analysis demonstrated comparable pregnancy outcomes for immediate FET performed within the first menstrual cycle after oocyte retrieval versus delayed FET following subsequent cycles. This finding would not only provide reassuring evidence for patients who seek to proceed with their FET after COS without postponement but may also be useful for physicians in future clinical trial design. Due to the limited number, high heterogeneity and observational nature of included studies, further large RCTs are needed to confirm the results.

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Authors' contributions J.H. and Y.K. contributed to the conception of the study. J.H. and J.L. performed the literature search, data extraction, and study quality assessment. J.H., J.L. and X.L. were involved in statistical analysis. J.H., N.S., and R.C. contributed to the interpretation of the results. J.H. was responsible for the manuscript drafting. All authors approved the final manuscript after critical revision for intellectual content.

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Availability of data and materials The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Competing interests The authors declare that they have no competing interests.

Ethical approval Not applicable.

Code availability Not applicable.

References

1. Doody KJ. Cryopreservation and delayed embryo transfer-assisted reproductive technology registry and reporting implications. Fertil Steril. 2014;102(1):27–31.
2. Polyzos NP, Drakopoulos P, Parra J, et al. Cumulative live birth rates according to the number of oocytes retrieved after the first ovarian stimulation for in vitro fertilization/intracytoplasmic sperm injection: a multicenter multinational analysis including approximately 15,000 women. Fertil Steril. 2018;110(4):661–670.e661.
3. Shapiro BS, Daneshmand ST, Garner FC, Aguirre M, Hudson C. Clinical rationale for cryopreservation of entire embryo cohorts in lieu of fresh transfer. Fertil Steril. 2014;102(1):3–9.
4. De Geyter C, Calhaz-Jorge C, Kupka MS, et al. ART in Europe, 2015: results generated from European registries by ESHRE. Hum Reprod Open. 2020;2020(1):hoz038.
5. Blockeel C, Drakopoulos P, Santos-Ribeiro S, Polyzos NP, Tournaye H. A fresh look at the freeze-all protocol: a SWOT analysis. Hum Reprod. 2016;31(3):491–7.
6. Bosch E, De Vos M, Humaidan P. The Future of Cryopreservation in Assisted Reproductive Technologies. Front Endocrinol (Lausanne). 2020;11:67.
7. Zhang W, Xiao X, Zhang J, Wang W, Wu J, Peng L, et al. Clinical outcomes of frozen embryo versus fresh embryo transfer following in vitro fertilization: a meta-analysis of randomized controlled trials. Arch Gynecol Obstet. 2018;298(2):259–72.
8. Chen ZJ, Shi Y, Sun Y, Zhang B, Liang X, Cao Y, et al. Fresh versus frozen embryos for infertility in the polycystic ovary syndrome. N Engl J Med. 2016;375(6):523–33.
9. Shi Y, Sun Y, Hao C, Zhang H, Wei D, Zhang Y, et al. Transfer of fresh versus frozen embryos in ovulatory women. N Engl J Med. 2018;378(2):126–36.
10. Wei D, Liu JY, Sun Y, Shi Y, Zhang B, Liu JQ, et al. Frozen versus fresh single blastocyst transfer in ovulatory women: a multicentre, randomised controlled trial. Lancet. 2019;393(10178):1310–8.
11. 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(2):516–8.
12. 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(2):344–8.
13. Bourdon M, Santulli P, Maignien C, Pocate-Cheriet K, Alwohaibi A, Marcellin L, et al. The interval between oocyte retrieval and frozen-thawed blastocyst transfer does not affect the live birth rate and obstetrical outcomes. PLoS One. 2018;13(10):e0206067.
14. He Y, Zheng H, Du H, et al. Delayed frozen embryo transfer failed to improve live birth rate and neonatal outcomes in patients requiring whole embryo freezing. Reprod Biol Endocrinol. 2020;18(1):1.
15. Higgins C, Healey M, Jatkar S, Vollenhoven B. Interval between IVF stimulation cycle and frozen embryo transfer: is there a benefit

to a delay between cycles? Aust N Z J Obstet Gynaecol. 2018;58(2):217–21.
16. Horowitz E, Mizrachi Y, Farhi J, Shalev A, Raziel A, Weissman A. Modified natural-cycle cryopreserved embryo transfer: is a washout period needed after a failed fresh cycle? Reprod BioMed Online. 2019;39:439–45.
17. Huang J, Lu X, Xie Q, Lin J, Cai R, Kuang Y. Timing of frozen-thawed embryo transfer after controlled ovarian stimulation in a non-elective freeze-all policy. Ann Transl Med. 2019;7(23):752.
18. Kaye L, Marsidi A, Rai P, Thorne J, Nulsen J, Engmann L, et al. Frozen blastocyst transfer outcomes in immediate versus delayed subsequent cycles following GnRH agonist or hCG triggers. J Assist Reprod Genet. 2018;35(4):669–75.
19. Lattes K, Checa MA, Vassena R, Brassesco M, Vernaeve V. There is no evidence that the time from egg retrieval to embryo transfer affects live birth rates in a freeze-all strategy. Hum Reprod. 2017;32(2):368–74.
20. Ozgur K, Bulut H, Berkkanoglu M, Humaidan P, Coetzee K. Frozen embryo transfer can be performed in the cycle immediately following the freeze-all cycle. J Assist Reprod Genet. 2018;35(1):135–42.
21. Santos-Ribeiro S, Siffain J, Polyzos NP, et al. To delay or not to delay a frozen embryo transfer after a failed fresh embryo transfer attempt? Fertil Steril. 2016;105(5):1202–1207.e1201.
22. Santos-Ribeiro S, Polyzos NP, Lan VT, et al. The effect of an immediate frozen embryo transfer following a freeze-all protocol: a retrospective analysis from two centres. Hum Reprod. 2016;31(11):2541–8.
23. Song J, Xiang S, Sun Z. Frozen embryo transfer at the cleavage stage can be performed within the first menstrual cycle following the freeze-all strategy without adversely affecting the live birth rate: a STROBE-compliant retrospective study. Medicine (Baltimore). 2019;98(38):e17329.
24. Volodarsky-Perel A, Eldar-Geva T, Holzer HE, Schonberger O, Reichman O, Gal M. Cryopreserved embryo transfer: adjacent or non-adjacent to failed fresh long GnRH-agonist protocol IVF cycle. Reprod BioMed Online. 2017;34(3):267–73.
25. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of observational studies in epidemiology (MOOSE) group. JAMA. 2000;283(15):2008–12.
26. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700.
27. Wells GA, Shea B, O'Connell D et al The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm. Accessed 14 Jan 2020
28. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to meta-analysis. Chichester: Wiley; 2009.
29. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58.
30. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629–34.
31. An Y, Sun Z, Li L, Zhang Y, Ji H. Relationship between psychological stress and reproductive outcome in women undergoing in vitro fertilization treatment: psychological and neurohormonal assessment. J Assist Reprod Genet. 2013;30(1):35–41.
32. Gameiro S, Boivin J, Domar A. Optimal in vitro fertilization in 2020 should reduce treatment burden and enhance care delivery for patients and staff. Fertil Steril. 2013;100(2):302–9.
33. Cesta CE, Viktorin A, Olsson H, et al. Depression, anxiety, and antidepressant treatment in women: association with in vitro fertilization outcome. Fertil Steril. 2016;105(6):1594–1602.e1593.
34. Humaidan P, Papanikolaou EG, Kyrou D, Alsbjerg B, Polyzos NP, Devroey P, et al. The luteal phase after GnRH-agonist triggering of ovulation: present and future perspectives. Reprod BioMed Online. 2012;24(2):134–41.
35. IVF-Worldwide. Survey results: frozen-thawed embryo transfer. Available at: http://ivf-worldwide.com/survey/frozen-thawed-embryo-transfer/results-frozen-thawed-embryotransfer.html. Assessed 23 June 2019
36. Aflatoonian A, Oskouian H, Ahmadi S, Oskouian L. Can fresh embryo transfers be replaced by cryopreserved-thawed embryo transfers in assisted reproductive cycles? A randomized controlled trial. J Assist Reprod Genet. 2010;27(7):357–63.
37. Li H, Sun X, Yang J, et al. Comparison of the ongoing pregnancy rate of immediate versus delayed frozen-thawed embryo transfer following a stimulated IVF cycle: a prospective randomized controlled trial. Hum Reprod. 2019;34(Supplement_1):i29–31.
38. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, et al. The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary on ART terminology, 2009. Hum Reprod. 2009;24(11):2683–7.