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Clinical outcomes of natural cycle IVF/M with the different sizes of dominant follicle at the time of hCG triggering

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Abstract

Purpose There is infertility treatment named natural cycle in vitro fertilization (IVF) combined with in vitro maturation (IVM) of immature oocytes (natural IVF/M). The objective of this study is to investigate the clinical outcomes of hCG triggering at the different sizes of dominant follicle during the treatment.

Methods A total of 705 patients with 1,011 natural IVF/M treatment cycles were included in this study. Among these 64 patients had repeated cycles, while 641 patients had only a single cycle. The cycles were divided into 4 groups according to the size of dominant follicle on the day of hCG injection (Group1:≤11.9 mm; Group2:12.0–13.9 mm ** Group3:14.0–15.9 mm ** Group4:≥16.0 mm).Through multivariate logistic regression analysis, candidate factors of number of mature oocytes, available and good quality embryos as well as clinical pregnancy rates were explored.

Results Oocytes maturation, fertilization, cleavage, available and good quality embryo rates ($p > 0.05$) were no difference among 4 groups. The rates for implantation, clinical pregnancy, miscarriage, premature delivery, and live birth were similar among the groups.

Conclusion The presence and different sizes of the dominant follicle in the ovaries during natural cycle IVF/M does not affect clinical outcomes.

Keywords Natural cycle, In vitro fertilization, In vitro maturation, Size of dominant follicle, Clinical outcome

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Introduction

The first live birth after in vitro fertilization (IVF) was produced during the natural pregnancy cycle after transfer of a human embryo [1].With the improvement in IVF technologies, ovarian stimulation IVF gradually replaced natural cycle IVF treatment, owing to the increased number of retrieved oocytes, generation of more embryos, and eventually lead to highly successful pregnancies [2]. However, it also boosted the gonadotrophin-induced side-effects, including the risk of ovarian hyperstimulation syndrome (OHSS) [3]. Alternatively, natural cycle IVF combined with in vitro maturation (IVM) of immature oocytes (natural cycle IVF/M) has been proposed [4], and recently, this technique was emphasized for cancer patients while preserving fertility [5].

Natural cycle IVF/M treatment does not involve controlled ovarian hyperstimulation. This treatment not only avoids the risk of OHSS but also reduces the disadvantage of natural cycle IVF treatment with the high cycle cancellation rate since it introduced the application scope of IVM technology. Natural cycle IVF/M is simple to establish, low cost, and most importantly, and can be implemented every month [6]. Therefore, natural cycle IVF/M has attracted more and more attention [7, 8] and has become an attractive new choice for the treatment of infertility patients [9, 10].

The small follicles as a promising source of oocytes in the natural cycle IVF/M give us a hope [8, 11]for cost-effective and more productive strategy with higher pregnancy rates and healthy offspring in the field of IVF [12, 13]. Before oocyte retrieval, ovarian follicular dominance may occur during natural cycle IVF/M treatment. Human chorionic gonadotropin (hCG), which triggers oocyte maturation in vivo may yield three classes of the oocyte during oocyte retrieval: (1) Metaphase II (M II), (2) Metaphase I (M I), and (3) germinal vesicle (GV) stage of oocytes [14]. It is common believe that the dominant follicle in the ovaries during each menstrual cycle may induce all other subordinate follicles to undergo atresia [15]. Interestingly, it was observed that the oocytes obtained from non-dominant follicles did not start atresia and successfully matured in vitro, resulting in healthy live births [4, 16]. Although the impact of dominant follicle on clinical outcomes was previously demonstrated [8, 17, 18], the correlation between the size of dominant follicles and the quality of oocytes from small follicles is not clear, particularly is not known when hCG triggering should be given during treatment of natural IVF/M cycles.

The aim of this study was to confirm the influence of different sizes of leading or dominant follicles on the day of hCG injection in terms of the numbers of mature oocytes, fertilization, available and good quality embryos as well as clinical outcomes.

Materials and methods

Patients

This study was a retrospective cohort study approved by the Ethics Committee of Seventh Medical Center of PLA General Hospital. Data from natural cycle IVF/M treatments performed in the Center for Reproductive Medicine of the hospital from April 2005 to May 2019 were collected. A total of 705 patients with 1,011 natural IVF/M treatment cycles were included in this study. Among these 64 patients had repeated cycles, while 641 patients had only a single cycle. The ages of these women ranged from 21 to 42 years old, with an average age of 30.85 ± 3.68. All women had normal chromosomal karyotype, normal uterus, and intact ovaries in addition to regular menstrual cycles and the basal serum follicle-stimulating hormone (FSH) level should be < 10 IU/mL on day 3 of the menstrual cycle. The treatment cycle was initiated after a baseline ultrasound scan on day 3 of the menstrual cycle and patients with dominant follicle selected and more than seven antral follicle counts (AFC) present in the ovaries were included in the study.

Collection of mature and immature oocytes

Transvaginal ultrasound scans were started on days 3–5 of the menstrual cycle. A transvaginal ultrasound was repeated every two days to monitor endometrial thickness. When the endometrial thickness reaches 6 mm, a dosage of 10,000 IU hCG was administered. At this time, the follicle with the largest diameter is regarded as the leading follicle or dominant follicle, and the diameter of the leading follicle is recorded. Oocyte collection was performed 36–38 h after the administration of hCG [4, 8, 10, 19].

Oocyte retrieval was performed under the guidance of transvaginal ultrasound as we previously described [8, 10]. The dominant follicles were firstly aspirated using a 17-gauge double-lumen needle (Cook, Eight Mile Plains, Queensland, Australia) with a portable pump connected to the needle at a pressure < 100 mmHg. A 19-gauge single-lumen needle (Cook, Eight Mile Plains, Queensland, Australia) was then used for aspiration of the small follicles. These follicular aspirates were examined for cumulus oocyte complexes (COCs) under a microscope to determine the maturity of oocytes as reported previously [20]. The maturity of oocytes at the time of oocyte retrieval was evaluated under a stereomicroscope with a "sliding" technique. Briefly, as a COC slowly slides from one side to another on the bottom of a tissue culture dish (60 × 15 mm BD Falcon; BD, Franklin Lakes, NI) it is observed under a microscope. The oocyte cytoplasm will be clearly observed to contain (or not) a germinal vesicle (GV) during COC sliding. If an immature oocyte did not contain a GV, the oocyte was defined as GV breakdown. Oocytes with first polar body excretion

in the perivitelline space were considered mature oocytes and were subsequently inseminated 2–3 h later using the method of intracytoplasmic sperm injection (ICSI).

In Vitro Maturation (IVM) and fertilization assessment

The immature oocytes at MI and GV stages were cultured in 1 ml of mature medium (The 1 mL of IVM culture medium is covered with oil. We use a water jacket incubator and use a double-well dish for this culture) supplemented with 30% serum from the patient (inactivated at 56 °C for 30 min), 75mIU/ml human FSH (Gonal-F; Merck Serono, Switzerland), 75 mIU/ml human menopausal gonadotrophin (HMG, Lizhu Pharmacy), and 10 ng/ml recombinant human epidermal growth factor (Invitrogen, Carlsbad, CA, USA) to induce final oocyte maturation at 37 °C, 5% CO2, 5% O2 and 90% N2 with saturated humidity for 24–48 h. After IVM culture, the oocytes were inseminated by ICSI as described previously [8, 10]. Fertilization was assessed 17–19 h later by the appearance of two distinct pronuclei after ICSI after which the fertilized zygotes were further cultured in 20 µl droplets of G1-PLUS medium (Vitrolife, Gothenburg, Sweden) covered with paraffin oil (Vitrolife) and incubated in a tri-gas incubator at 37 °C according to standard procedures for further development.

Endometrial preparation and luteal support

Endometrial preparation was performed by oral administration of 6 mg estradiol valerate (Delpharm Lille SAS, Rue de Toufflers, France) per day starting from the day of oocyte retrieval, and a dosage of 100 mg progesterone was injected (Solvay, Netherlands) starting from the day of ICSI [8]. After assessment of embryonic development, the best quality embryos were selected for transfer. Embryos with at least 3-cells on day 2 and 6-cell on day 3 and < 20% fragments with normal morphology were defined as a good quality embryo. When matured oocyte on the day of oocyte retrieval and its resulting embryo were obtained, embryo transfer (ET) was performed on day 3. If the collected oocytes were all immature on the day of retrieval, ET was performed on day 4. The selected resulting embryos were pooled together and transferred on day 3 or 4 after oocyte retrieval. The Pregnancy status was determined by serum hCG level 14 days after ET, and clinical pregnancy was defined as the presence of an intrauterine gestational sac as detected by ultrasound six weeks after ET.

Group design

Natural cycle IVF/M procedures show us a good pattern and allow us to distinguish oocytes from dominant follicle and small follicles in a same cycle and to characterize different sizes of dominant follicle on the developmental capacity of embryos after dominant follicle selection.

The patients were divided into four groups according to the size of dominant follicle on the day of hCG injection: (1) Group 1: ≤ 11.9 mm in diameter; (2) Group 2: 12.0–13.9 mm in diameter; (3) Group 3: 14.0–15.9 mm in diameter; and (4) Group 4: ≥ 16.0 mm in diameter. The number of retrieved in vivo mature oocytes, in vitro mature oocytes, fertilization, cleavage, and high-quality embryo rates were compared between groups. The clinical and obstetric outcomes also were compared between groups.

Statistical analysis

Statistical analyses were performed using Statistical Package for Social Science (SPSS) software, version 25.0 (IBM, Armonk, New York, USA). Mann-Whitney and chi-square tests were used for comparison of measurement data when appropriate. Comparison of frequency data between groups, such as clinical pregnancy, implantation, live birth, and miscarriage rates were performed by chi-square test. The non-paired t-test and Mann-Whitney test were applied to compare mean numbers. For other quantitative comparisons, analysis of variance (ANOVA) was used. All reported *P*-values were two-tailed, and $p < 0.05$ was established as the level of significance.

Results

As shown in Table 1, group 1 included 176 patients with 191 oocyte retrieval cycles with the size of dominant follicle ≦11.9 mm in diameter. Group 2 with 409 patients with 464 oocyte retrieval cycles had dominant follicles between 12.0 and 13.9 mm in diameter; group 3 with 174 patients with 183 oocyte retrieval cycles had dominant follicles between 14.0 and 15.9 mm in diameter, and group 4 with 165 patients with 173 oocyte retrieval cycles had dominant follicles ≥ 16.0 mm in diameter on the day of hCG injection. No significant differences in maternal age and baseline hormone levels and type of infertility were found. The overall mean patient age was 30.9 ± 3.7 years, and the mean basal FSH was 6.5 ± 2.9 IU/ml.

The number of retrieved oocytes was similar among groups. Nonetheless, the number and percentage of mature oocytes on the day of retrieval differed significantly among the groups ($p < 0.01$). However, the total number of mature oocytes (MII oocyte on the day of retrieval + MII oocyte after IVM) between groups did not reveal any difference ($p > 0.05$). The rates of fertilization, cleavage, and good quality embryos also showed no significant differences between groups (Table 2).

ET was performed over a total of 992 cycles with 187 cycles for group 1, 459 cycles for group 2, 177 cycles for group 3, and 169 cycles for group 4 (Table 2). The mean number of embryos transferred was similar among groups. The rates of clinical pregnancy, implantation,

Table 1 Patient characteristics and embryology information analyzed by the size of the dominant follicle on the day of hCG in natural cycle IVF/M treatment

Variable	diameter of the dominant follicle on the day of hCG injection			
	≤ 11.9 mm	12.0–13.9 mm	14.0–15.9 mm	≥ 16.0 mm
No. of patients	176	409	174	165
No. of oocyte retrieval cycles	191	464	183	173
Age of women (years)	30.77 ± 3.47	30.99 ± 3.75	30.69 ± 3.62	30.74 ± 3.77
Type of infertility				
Primary	105 (59.65%)	232 (56.72%)	104 (59.77%)	110 (66.66%)
Secondary	71 (40.3%)	177 (43.27%)	70 (40.22%)	55 (33.33%)
Infertility factor				
Female	99 (56.25%)	221 (54.03%)	94 (54.02%)	93 (56.36%)
Male	51 (28.97%)	119 (29.09%)	45 (25.86%)	29 (17.57%)
Mix	19 (10.79%)	52 (12.71%)	27 (15.51%)	35 (21.21%)
Unknown	7 (3.97%)	17 (4.15%)	8 (4.59%)	8 (4.84%)
Basal FSH (mIU/ml)	6.66 ± 2.17	6.51 ± 1.66	6.61 ± 2.01	6.74 ± 1.91

Numbers are mean ± SD unless otherwise indicated

Abbreviations:hCG human chorionic gonadotropin, *IVF* invitro fertilization, *No* number, *FSH* follicle-stimulating hormone, *MII* mature metaphase II oocytes

miscarriage, premature delivery, and live births were not statistically different between groups. The rates of single newborns and twins, and the birth weight of single babies and twins also showed no significant differences.

A total of six candidate variables and the size of dominant follicle were subsequently added to a multivariate logistic regression analysis model. It was shown that the size of dominant follicle before oocyte retrieval did not correlate with clinical pregnancy rate ($P = 0.626$; odds ratio [OR] = 0.966; 95% confidence interval [CI]: 0.842–1.109). Among all involved variables, fertilization and good quality embryo rates and mean number of transferred embryos were found to be associated with clinical pregnancy rate ($p < 0.05$, Table 3).

Discussion

The results of the present study demonstrate that the immature oocytes derived from small follicles in the presence of a dominant follicle have a similar developmental potential for pregnancies and live births following IVM culture in nature cycle IVF/M treatment. To our knowledge, this study is the first report with a large number of patients who underwent natural cycle IVF/M when the dominant follicle was different in sizes.

During each menstrual cycle, a batch of follicles was selected from the non-growth follicle pools and allowed to continue to develop. Normally, only one dominant follicle grows to the pre-ovulatory stage and ovulates, while the other small follicles degenerate to atresia [15]. It has been reported that the degenerative changes occur on granulosa cells of nondominant small follicles, but the oocyte inside of follicles can be functioning and capable for > 7 days after follicle selection [21]. In contrary to traditional views for ovarian follicular development, it has been indicated that several waves of follicular growth occur during a normal menstrual cycle, and follicles in the resting phase continuously enter the development phase [22]. Recently, it has been confirmed that women exhibit 2–3 follicular waves with major and minor patterns during a menstrual cycle [23].

Thus, from the results of present study, we can deduce that the oocytes from the small follicles may not necessarily enter atresia immediately after the dominant follicle has developed in the ovaries. Interestingly, studies also have reported that immature oocytes from different stages of menstrual cycle can be recovered and develop to maturity in vitro [24]even from women who underwent a cesarean Sect [25]. or who were in the luteal phase [26].

Our recent study displayed a clear model of dominant follicle at the retrieval time in natural cycle IVF/M cycles and found that the developmental and implantation capacity and the clinical outcomes of immature oocytes retrieved from small follicles were not significantly influenced by the presence or ovulation of dominant follicle at the time of retrieval [8]. These findings may support the observations of different waves of follicular development in the ovaries and the reason why the immature oocytes from the small follicles may not regress when the dominant follicle was selected and have the capability to mature in vitro.

During the menstrual cycle, the dominant follicle occurs naturally in the ovaries. Although the subordinate follicles can mature in the presence of dominant follicle, many centers also avoid this phenomenon by retrieving the immature oocyte before the largest follicle reaches 12 mm in diameter during IVM procedure for women with PCO [27, 28]. It has been suggested that the presence of the dominant follicle will change the small follicular microenvironment and reduce the clinical outcomes compared to the non-dominant follicle group [17]. It also suggested that oocyte collection should be performed when the dominant follicle is < 14 mm in diameter; if the size of dominant follicle is > 14 mm in diameter, it may be detrimental to oocyte quality from the subordinate follicles in natural cycle IVF/M [19].

Lower oocyte maturation rates in vitro were obtained when luteinizing hormone levels were high before oocyte retrieval [6]. Our results indicated that differences in terms of the number of mature oocytes retrieved

Table 2 Comparison of clinical and obstetric outcomes based the size of dominant follicle on the day of hCG injection in natural cycle IVF/M treatment

Variable	diameter of the dominant follicle on the day of hCG injection				*P* Value
	≤ 11.9 mm	12.0–13.9 mm	14.0–15.9 mm	≥ 16.0 mm	
No. of oocyte retrieval cycles	191	464	183	173	
No. of oocytes retrieved	11.19 ± 5.38	10.50 ± 5.08	10.63 ± 5.90	11.32 ± 6.13	0.292
No. of D0 MII	1.94 ± 1.85	1.70 ± 1.61	1.59 ± 1.79	1.09 ± 1.87	<0.01
No. of oocyte for IVM	5.88 ± 3.46	5.46 ± 3.19	5.56 ± 3.47	6.24 ± 4.23	0.397
No. of MII oocytes after IVM	5.35 ± 3.15	5.05 ± 3.04	5.20 ± 3.45	5.98 ± 4.12	0.219
No. of total MII oocytes	7.29 ± 3.54	6.75 ± 3.22	6.79 ± 3.78	7.06 ± 4.39	0.211
Rate of total MII oocyte (%)	67.36 ± 17.05	66.73 ± 17.64	66.38 ± 17.46	63.60 ± 20.38	0.351
Fertilization number	6.07 ± 2.82	5.78 ± 2.95	5.77 ± 3.37	6.00 ± 3.79	0.298
Fertilization rate (%)	85.50 ± 16.15	85.66 ± 16.32	85.45 ± 16.95	85.94 ± 18.73	0.819
No. of cleavages	4.98 ± 2.43	4.76 ± 2.44	4.86 ± 2.90	5.27 ± 3.41	0.461
Cleavage rate (%)	71.68 ± 21.37	72.56 ± 21.86	73.81 ± 23.02	76.32 ± 22.90	0.059
No. of available embryos	2.96 ± 1.16	2.88 ± 1.15	2.80 ± 1.09	2.89 ± 1.35	0.524
Good quality embryo rate (%)	18.02 ± 24.62	18.86 ± 28.10	18.35 ± 26.44	17.31 ± 25.41	0.976
No. of ET cycles	187	459	177	169	
No. of embryos transferred	2.62 ± 0.54	2.55 ± 0.58	2.51 ± 0.59	2.52 ± 0.59	0.285
No. of implantation (%)	79 (16.12)	185 (15.82)	70 (15.73)	69 (16.19)	0.996
No. of clinical pregnancy (%)	64 (34.22)	164 (35.72)	59 (33.33)	57 (33.72)	0.930
No. of live birth (%)	45 (70.31)	108 (65.85)	41 (69.49)	40 (70.17)	0.876
No. of miscarriage (%)	15 (23.44)	36 (21.95)	15 (25.42)	13 (22.80)	0.960
No. of premature delivery (%)	0	2 (0.4)	1 (0.5)	1 (0.5)	
No. of ectopic pregnancy (%)	2 (3.13)	6 (3.65)	2 (3.38)	2 (3.50)	0.998
No. of newborn (%)					
Singleton	39 (60.93%)	93 (56.7%)	35 (59.32%)	34 (59.64%)	0.936
Twins	6 (9.37%)	15 (10.16%)	6 (10.16%)	6 (10.52%)	0.989
Mean birthweight (g)					
Singleton	3367 ± 389	3447 ± 386	3380 ± 421	3411 ± 368	0.618
Twins	2200 ± 386	2433 ± 486	2387 ± 371	2360 ± 509	0.317

Numbers are mean ± standard deviation (SD) unless otherwise indicated. *clinical pregnancy* (%) Percentage of embryo transfer cycles, *Live birth, miscarriage, ectopic pregnancy* (%) Percentage of pregnancies

D0 MII Designates oocytes that had already attained the Metaphase II (MII) stage upon retrieval, requiring no further in vitro maturation, *MII after IVM* Designates oocytes that were retrieved at an immature stage (e.g., Germinal Vesicle or Metaphase I) and successfully progressed to MII through in vitro maturation (IVM) culture

Table 3 Multivariate logistic regression analysis of factors on clinical pregnancy

Variable	β	Wald	*P* value	OR (95% CI)
Dominant follicle size	0.034	0.237	0.626	0.966 [0.842, 1.109]
Rate of total MII oocyte	0.004	1.064	0.302	1.004 [0.996, 1.012]
Fertilization rate	0.020	11.065	0.001	1.020 [1.008, 1.032]
Cleavage rate	0.000	0.003	0.955	1.000 [0.992, 1.008]
Good quality embryo rate	0.009	13.088	<0.001	1.009 [1.004, 1.014]
No. of transferred embryos	0.411	10.402	0.010	1.509 [1.175, 1.938]

β, regression coefficient, *OR* odd ratio

existed (Table 2); however, no difference in the rates of IVM, fertilization, and embryo development in addition to clinical pregnancy and implantation rates in different groups (Table 2) was found, suggesting that the size of dominant follicle does not correlate with clinical outcomes (Table 3). These present results were consistent with another study where no difference in retrieved oocytes, maturation, or fertilization rates from IVM oocytes between luteal phase and follicular phase during the menstrual cycle [29]. However, these were contrary to the observations of Yoldemir et al.[17] where the small follicular microenvironment was observed to be changed and the clinical outcomes were seen to be reduced compared to the non-dominant follicle group. In the study of Yoldemir et al. [17] follicles from dominant or non-dominant were from the controlled ovarian stimulation cycles, where high doses of gonadotropins were administrated, which may be one of the reasons between the IVM cycles and conventional IVF-ET. In our previous literature [30], of 410 cycles, 151 (36.8%) were treated by natural cycle IVF combined with IVM (IVF/M), 63 (15.4%) underwent IVM alone, and 196 (47.8%) underwent COH. With increasing age fewer cycles can be treated by natural cycle IVF/M or IVM. There were no differences in implantation rate and clinical pregnancy rates in the three groups.

Another study also found no difference in retrieved oocytes, maturation, or fertilization rates from IVM oocytes between luteal phase and follicular phase during the menstrual cycle [29]. The present clinical pregnancy (33.3% and 33.7%, respectively) and implantation (15.7% and16.2%, respectively) rates when DF (dominant follicles) diameter was 14.0–15.9 mm and ≥ 16.0 mm were much higher than the rates (17.1% for clinical pregnancy and 4.9% for implantation) when the DF diameter was >14 mm in the study of Son et al.[31]. By defining the pattern of DF at the time of retrieval in our recent results, the developmental and implantation capacity as well as the clinical outcomes of immature oocytes retrieved from small follicles were not significantly influenced by the presence or ovulation of dominant follicle at the time of retrieval [8]. Therefore, we can deduce that the presence of the leading or dominant follicle does not correlate with the oocyte maturation cultured in vitro and subsequent fertilization, embryonic development, and clinical outcomes.

When describing the outcomes of IVM, it has been reported that oocyte maturation rates of the small follicle on retrieval day was 25.4% with 18.3% consisting of good quality embryos, generating 10.5% clinical pregnancy and 8.6% live birth rate (per MII oocyte) while clinical pregnancy rate in the dominant follicles was 24.7% and live birth rate was 19.3% (per MII oocytes) as described by Teramoto et al.[21]. They found that clinical outcomes in the small follicles did not depend on the dominant follicle. Despite the failure of oocyte retrieval or the ovulation of DF when at the retrieval time, our previous results indicated that the immature oocytes were also a promising source in natural cycle IVF treatment produced higher clinical pregnancy [8]than only matured oocytes retrieved from nondominant and dominant follicles [21]. The present data showed that the clinical pregnancy rate of IVM oocytes from the small follicles also did not correlate with the dominant follicle. Thus, we can further deduce that the presence of a dominant follicle does not cause an adverse effect of clinical outcomes on the small follicles.

For the offspring, outcomes are complex and correlated with quality of oocytes, laboratory culture conditions, and parental characteristics. Our results found a similar single baby birth rate and similar birthweights from the oocytes retrieved from the small follicles for IVM at the presence of different sizes of dominant follicles (Table 2). Similar birthweights with IVM oocytes and controlled ovarian stimulation (COS) data were generated by Belva et al.[32], but these data were from patients with PCOS. Our results are also similar to the previous study concerning the outcomes after IVM oocytes demonstrated equal birthweight and preterm birth rates between the IVM oocytes and COS group, but the rate of the hypertensive disorder of pregnancy was higher in the IVM group [33]. The limitation of our study is the retrospective design and not being able to trace the pregnancies after ET in terms of in vivo or in vitro mature oocytes. However, the pregnancies were from the embryos with or without in vivo divided mature oocytes (Supplementary Table).

This study has several limitations that should be considered. Firstly, its retrospective nature may introduce inherent selection bias, although we sought to mitigate this through multivariate regression analysis. Secondly, as a single-center study, the generalizability of our findings to other populations and clinical settings requires further validation. Additionally, we were unable to separately trace the pregnancy outcomes specifically for embryos derived from in vivo matured oocytes versus those from in vitro matured oocytes, which could provide more granular insights into their respective developmental potentials. Despite these limitations, the large sample size and consistent outcomes across all groups strengthen the reliability of our primary conclusion.

In conclusion, our data showed that ovarian follicular dominance during natural cycle IVF/M does not affect embryological and clinical outcomes regardless of the size of dominant follicle. This finding suggests that physicians could trigger hCG as a more cost-effective and more flexible strategy for patients undergoing IVF/M treatment.

Abbreviations

ART	Assisted reproductive technology
IVF	In vitro fertilization
IVM	In vitro oocyte maturation
ICSI	Intracytoplasmic sperm injection
COH	Controlled ovarian hyperstimulation
OHSS	Ovarian hyperstimulation syndrome
COCs	Cumulus-oocyte complexes
M II	Metaphase II
M I	Metaphase I
GV	Germinal vesicle

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13048-025-01914-w.

Supplementary Material 1: Table S1. Clinical pregnancies following transfer of the embryos derived from mature oocytes collected on the day of retrieval according to the size of dominant follicles when hCG injection.

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Disclosures

The authors declare no competing financial, professional or personal interests.

Authors' contributions

SWZ, YZL, and RCQ conceived and designed the study. JHL, JC, JYW, and YX performed the experiments and analyze data. TTJ, YW, and YBC collect the data. JHL, JC, QCCand RCC wrote and revised the manuscript. All authors read and approved the final manuscript.

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Data availability
The data that support the results of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of the Seventh Medical Center of PLA General Hospital (No. 2021-50).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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