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Suboptimal Mature Oocyte Yield in Antagonist Icsi Cycles: Any Impact of the Ovulation Triggering Agent?

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Abstract

PURPOSE OF RESEARCH: To evaluate the impact of ovulation-triggering agents on suboptimal mature oocyte yield in antagonist ICSI cycles.

DESIGN: We conducted a retrospective cohort study of 2,129 antagonist ICSI cycles at a tertiary university hospital from October 2013 to October 2022. The primary outcome was suboptimal response to triggering, defined as a mature oocyte yield below the 75th percentile. Mature oocyte yield was calculated as the number of mature oocytes retrieved divided by the number of mature follicles (mean diameter ≥ 15 mm) on the trigger day. Prognostic factors for suboptimal response were analyzed using univariate and multivariate methods.

RESULTS: Of the cycles, 909 (42.7%) were triggered with GnRHa, 845 (39.7%) with hCG, and 375 (17.6%) with both. The mean mature follicle count was 7.9 ± 4.3, the average number of mature oocytes was 7.0 ± 5.0, and the mean mature oocyte yield was 92.3 ± 55.2%. The 75th percentile for mature oocyte yield was 117%. Mature oocyte yield was significantly higher with GnRHa versus hCG (96.7 ± 59.1% vs. 87.6 ± 48.8%), with no significant difference compared to dual trigger (92.2 ± 58.0%; p = 0.017). Suboptimal yield was lower with GnRHa (71.6%) than hCG (80%), but not dual trigger (76.8%), p = 0.017. Multivariate analysis showed GnRHa triggering was associated with lower risk of suboptimal yield (p < 0.001).

CONCLUSION: GnRHa triggering is associated with a reduced risk of suboptimal mature oocyte yield compared to hCG

INTRODUCTION

One of the most significant advancements in assisted reproductive technology (ART) over the past few decades has been the use of gonadotropin-releasing hormone agonists (GnRHa) to induce ovulation in antagonist protocols. This development has notably reduced the incidence of ovarian hyperstimulation syndrome (OHSS) [1, 2]. OHSS is an iatrogenic complication associated with controlled ovarian hyperstimulation (COH) in IVF/ICSI cycles, triggered by either exogenous or endogenous human chorionic gonadotropin (hCG). This hormone activates the luteinizing hormone (LH)/hCG receptor in the ovaries, leading to the release of vascular endothelial growth factor (VEGF) and increased capillary permeability [3]. By employing a bolus of GnRHa instead of standard hCG to trigger ovulation, there is a physiological-like surge of endogenous LH, albeit shorter in duration and lower in amplitude [4, 5]. This approach results in the rapid regression of the corpus luteum within a few days, effectively reducing VEGF expression and consequently lowering the risk of OHSS.

Despite the clear safety advantages of using GnRHa over hCG for triggering ovulation, the debate over their clinical efficacy remains unresolved. Some studies indicate that GnRHa leads to improved outcomes, including a higher number of retrieved and mature oocytes, as well as an increased number of embryos [2]. Conversely, other research highlights the risk of suboptimal responses to GnRHa, ranging from suboptimal LH levels post-trigger to insufficient oocyte recovery or even empty follicle syndrome

[6–13]. However, these studies often lack a control group using hCG, making it difficult to differentiate between intrinsic ovarian issues and those related to the triggering method itself.

Given this context of conflicting data, we aimed to compare patients based on their ovulation triggering method to identify clinical factors associated with suboptimal mature oocyte yields in a large cohort undergoing COH for ICSI in a GnRH antagonist protocol.

MATERIALS AND METHODS

Study population and inclusion criteria

We conducted a retrospective cohort study of patients who underwent COH with a GnRH antagonist protocol for ICSI at our university-based reproductive medicine center from October 2013 to October 2022. Inclusion criteria were: (i) age < 43 years at the time of oocyte retrieval; (ii) indication for ICSI, including male factor infertility, previous fertilization failure after conventional IVF, unexplained infertility, and low number of oocytes retrieved [14]; (iii) COH using a GnRH antagonist protocol; and (iv) final COH monitoring conducted on the day of ovulation triggering. Exclusion criteria included: (i) use of other COH protocols, such as long and short agonist protocols or natural cycles; (ii) IVF cycles that did not allow for the assessment of oocyte maturity on retrieval day; (iii) cycles canceled prior to oocyte retrieval; and (iv) oocyte cryopreservation or donation cycles.

General Characteristics

The study analysis was based on a prospectively managed database. Data were collected for each patient prior to ART treatment, encompassing personal history and fertility investigation results. The recorded information included: age at retrieval (years), smoking status (active or non-smoker), body mass index (BMI) calculated as weight (kg)/height (m^2), and country of birth/geographic origin (European, Asian, African-Caribbean) [15]. Additional variables included gravidity, parity, type of infertility (primary or secondary), duration of infertility (years), IVF/ICSI cycle rank, and serum levels of day-3 FSH (IU/mL), estradiol (pg/mL), and LH (IU/mL). Also documented were the antral follicle count (AFC), anti-Müllerian hormone (AMH) levels (ng/mL), ovulation status according to the WHO classification [16], and infertility causes (e.g., male factor, female factor, including ovulatory dysfunction, tubal factor, endometriosis, uterine factor, diminished ovarian reserve/premature ovarian insufficiency, or idiopathic infertility).

ICSI cycles: clinical and laboratory procedures

Before starting COH, a pre-treatment was administered for scheduling purposes, using either antigonadotropic medication (estro-progestin or progestin pill) or estradiol (0.2 mg/day via two simultaneous Vivelledot® 100 systems; Novartis Pharma SA, France). Ovarian stimulation commenced after a wash-out period of five days for antigonadotropic medication and two days for estradiol. COH was conducted using recombinant follicle-stimulating hormone (FSH; Bemfola®; Gedeon Richter,

France) and human menopausal gonadotropin (hMG; Menopur®; Ferring Pharmaceuticals, France), with no adjustments to the gonadotropin dose during stimulation. The initial gonadotropin dose ranged from 150 to 450 IU/day and was determined based on patient age, BMI, AFC, AMH level, and previous responses to gonadotropins. A GnRH antagonist at a daily dose of 0.25 mg was introduced on the 6th day of stimulation. Monitoring of COH occurred every 48–72 hours from the 8th day, involving blood sampling for E2, LH, and progesterone levels, along with transvaginal ultrasonography, according to a standardized protocol at our institution.

Final oocyte maturation was triggered when at least three ovarian follicles measuring 17 mm or larger were visible on ultrasound, and E2 levels were at least 1000 pg/mL. For deferred embryo transfer (ET), final oocyte maturation was achieved with a single injection of 0.2 mg of GnRH agonist (Triptorelin, Decapeptyl®; Ipsen, Boulogne-Billancourt, France). The decision to implement a freeze-all strategy was made either before stimulation or during the stimulation phase, based on specific indications as outlined in previous research by our team [17]. For fresh ET, final oocyte maturation was induced using rhCG (rhCG; Ovitrelle®; Merck Serono, France) or a dual trigger combining rhCG and GnRHa. Oocyte retrieval (OR) was performed by transvaginal aspiration under ultrasound guidance by qualified senior gynecologists [18]. Semen samples were collected through masturbation following a sexual abstinence period of two to five days. Upon receiving the follicular fluid tubes, cumulo-oocyte complexes (COCs) were identified using a binocular magnifying glass. COCs were placed in universal IVF medium® (CooperSurgical) in incubators set at 37°C, with 5.5% CO2 and 5% O2. Between one and two hours after retrieval, the COCs underwent denudation via enzymatic treatment (hyaluronidase 80 UI/ml, Fujifilm Irvine Scientific) and mechanical stripping (Stripper®, Origio). Oocyte maturity was assessed, and mature (MII) oocytes were microinjected with a single spermatozoon.

The precise methods for embryo culture and selection, as well as the vitrification and thawing protocols, have been described in detail previously [19–21]. Briefly, ET was performed on day 2 or at the blastocyst stage, depending on the study period, with exclusive extended embryo culture implemented since 2018. Luteal phase support for fresh and frozen ET was provided according to our institutional protocols [22].

Outcome variables

The primary outcome of the study was the suboptimal response to triggering characterized as a mature oocyte yield below the 75th percentile [13]. The mature oocyte yield was defined as the number of mature oocytes retrieved divided by the number of mature follicles (mean diameter ≥ 15 mm) on the day of triggering [11]. Secondary endpoints included the fertilization rate, calculated as the number of 2PN oocytes divided by the total number of mature oocytes, and the blastocyst formation rate, determined by the number of blastocysts divided by the total number of embryos cultured. Furthermore, the following reproductive outcomes for fresh embryo transfers were recorded: (i) clinical pregnancies [23]; (ii) live births [23]; (iii) early miscarriages [24]; and (iv) ectopic pregnancies [23].

Statistical analysis

Data were compiled into a digital database and analyzed using SPSS version 23.0 software (SPSS Inc., Chicago, Illinois, USA). A p-value < 0.05 was considered statistically significant. Continuous data were presented as means with standard deviation (SD), while categorical data were reported as numbers and percentages.

The characteristics of women and ICSI cycles were compared based on the type of ovulation triggering and mature oocyte yield to identify prognostic factors for suboptimal mature oocyte yield. For univariate statistical analysis, the Pearson χ^2 test was used for qualitative variables, and the Kruskal-Wallis or Mann-Whitney tests were employed for quantitative variables, as appropriate. Variables associated with a suboptimal mature oocyte yield at a threshold of < 0.1 in univariate analysis were subsequently tested in a multiple logistic regression model. The correlation between variables was assessed, and in cases of high correlation, only one variable was retained in the model. For instance, AMH and AFC, as well as mean starting and mean total gonadotropin doses, and LH and E2 levels at triggering were evaluated (Spearman correlations 0.602, 0.87, and 0.403, respectively), with the last parameters excluded from the model. The final model included the following variables: age, cause of infertility, day 3 FSH and LH levels, AMH level, mean starting gonadotropin dose, type of ovulation triggering, and LH level at triggering. The final model was constructed using all selected significant variables via the "Enter" method.

Additionally, a supplementary analysis was conducted in a subgroup of patients with AMH levels ≥ 75th percentile (i.e., 3.8 ng/mL) to evaluate the impact of the type of ovulation triggering on mature oocyte yield in women with high ovarian reserve.

RESULTS

Study population

The cohort selection process is illustrated in Fig. 1. Between October 2013 and October 2022, a total of 2,129 ICSI cycles utilizing a GnRH antagonist protocol were included, with last COH monitoring conducted on the day of ovulation triggering at our tertiary care center. The characteristics of the overall population are summarized in Table 1. The mean age of participants was 35.0 ± 4.1 years, with an average infertility duration of 4.3 ± 2.7 years and a mean ICSI cycle rank of 1.4 ± 0.8. The characteristics and outcomes of the ICSI cycles are detailed in Table 2 and Supplemental Table 1. Among the cycles, 909 (42.7%) were triggered with GnRHa, 845 (39.7%) with hCG, and 375 (17.6%) with both. On average, patients had 7.9 ± 4.3 mature follicles on the day of triggering, resulting in a mean number of mature oocytes of 7.0 ± 5.0, and an average mature oocyte yield of 92.3 ± 55.2%. The 75th percentile for mature oocyte yield was 117%.

Table 1
General characteristics of the study population (n = 2,129)

Characteristics*	Values
Age (years)	35.0 ± 4.1
Body mass index (kg/m^2)	23.8 ± 4.4
Smoking status*	269 (13.1%)
Geographic Origin*	
European	1724 (84.6%)
African-Caribbean	215 (10.5%)
Asian	100 (4.9%)
Gravidity	0.7 ± 1.0
Parity	0.4 ± 0.6
Type of infertility	
Primary	1412 (66.3%)
Secondary	717 (33.7%)
Duration of infertility (years)	4.3 ± 2.7
ICSI cycle rank	1.4 ± 0.8
Ovarian reserve	
Day 3 FSH (IU/L)	7.2 ± 2.4
Day 3 LH (IU/L)	5.4 ± 2.6
Day 3 estradiol (pg/mL)	50.5 ± 36.6
AMH (ng/mL)	3.0 ± 2.8
AFC	17.8 ± 11.7
Ovulation status*	

Note: ICSI = intracytoplasmic sperm injection; FSH = follicle-stimulating hormone; LH = luteinizing hormone; AMH = anti-Müllerian hormone; AFC = antral follicle count; WHO = world health organization ("Agents stimulating gonadal function in the human. Report of a WHO scientific group," 1973); *DOR = diminished ovarian reserve; POI = premature ovarian insufficiency*

** Continuous data are presented as mean ± standard deviation. Categorical data are*

presented as number (percentage). Missing data: smoking status (n = 75), geographic origin (n = 90), ovulation status (n = 58), infertility cause (n = 79)

Characteristics*	Values
Normal ovulation	1861 (89.9%)
WHO I	16 (0.8%)
WHO II	182 (8.8%)
WHO III	12 (0.5%)
Infertility cause*	
Male factors	759 (37.0%)
Female factors	1060 (51.7%)
DOR/POI	228 (21.5%)
Ovulatory dysfunction	147 (13.9%)
Endometriosis	469 (44.2%)
Tubal factor	213 (20.1%)
Uterine factor	3 (0.3%)
Idiopathic	231 (11.3%)

Note: ICSI = intracytoplasmic sperm injection; FSH = follicle-stimulating hormone; LH = luteinizing hormone; AMH = anti-Müllerian hormone; AFC = antral follicle count; WHO = world health organization ("Agents stimulating gonadal function in the human. Report of a WHO scientific group," 1973); *DOR = diminished ovarian reserve; POI = premature ovarian insufficiency*

** Continuous data are presented as mean ± standard deviation. Categorical data are*

presented as number (percentage). Missing data: smoking status (n = 75), geographic origin (n = 90), ovulation status (n = 58), infertility cause (n = 79)

Table 2
ICSI cycle characteristics (n = 2,129)

ICSI cycle characteristics*	Values
Synchronization by OCP	1200 (56.4%)
Mean starting gonadotropin dose (IU)	285.0 ± 86.8
Mean total gonadotropin dose (IU)	2553.8 ± 984.0
Mean cycle duration (days)	9.3 ± 1.5
Type of ovulation triggering	
GnRH agonist	909 (42.7%)
hCG	845 (39.7%)
Dual trigger	375 (17.6%)
Triggering day characteristics	
LH level (IU/L)	1.5 ± 1.6
Estradiol level (pg/mL)	2278.4 ± 1473.6
Progesterone level (ng/mL)	0.76 ± 1.2
Endometrial thickness (mm)	10.0 ± 2.5
Mean mature follicle count (> 15 mm)	7.9 ± 4.3
Mean number of oocytes	9.5 ± 7.1
Mean number of mature oocytes	7.0 ± 5.0
Mean mature oocyte yield (%)$	92.3 ± 55.2
Mean number of fertilized oocytes	4.6 ± 3.8
Mean number of blastocysts	2.4 ± 2.7

Note: ICSI = intracytoplasmic sperm injection; OCP = oral contraceptive pill; GnRH = gonadotropin-releasing hormone; hCG = human chorionic gonadotropin; LH = luteinizing hormone

** Continuous data are presented as mean ± standard deviation and categorical data are presented as number (percentage)*

$ Mature oocyte yield = number of mature oocytes retrieved/number of mature follicles (≥ 15 mm)

Patient and cycle characteristics according to the type of ovulation triggering

The results of the univariate analysis comparing patient and cycle characteristics based on the type of ovulation triggering are presented in Supplemental Table 2. The mean mature oocyte yield was significantly higher in cycles triggered by GnRHa compared to those triggered by hCG, although it did not differ significantly from the dual trigger group (96.7 ± 59.1% vs. 87.6 ± 48.8% vs. 92.2 ± 58.0%, respectively; p = 0.017). Additionally, the rate of suboptimal mature oocyte yield was significantly lower with GnRHa triggering compared to hCG, but not compared to the dual trigger (71.6% vs. 80% vs. 76.8%, respectively; p = 0.017).

Prognostic factors of suboptimal mature oocyte yield

The results of the univariate analysis comparing patients with optimal versus suboptimal mature oocyte yields are detailed in Supplemental Table 3. Women with suboptimal oocyte yields were older (35.1 ± 4.1 vs. 34.7 ± 4.1 years; p = 0.028) and had a higher incidence of female factors as the cause of infertility (52.8% vs. 48.6; p = 0.030). Their ovarian reserve was significantly lower, indicated by higher day 3 FSH levels (7.3 ± 2.5 vs. 6.9 ± 2.2 IU/L; p = 0.008), lower AMH levels (2.8 ± 2.7 vs 3.5 ± 3.1 ng/mL; p < 0.001) and a lower AFC (17.3 ± 11.4 vs. 19.6 ± 12.4; p < 0.001). In terms of ICSI cycle characteristics, women with suboptimal yields required higher mean starting gonadotropin doses (277.2 ± 81.0 vs. 260.0 ± 77.1 IU; p < 0.001), had higher LH levels at triggering (1.6 ± 1.7 vs. 1.4 ± 1.5 IU/L, p = 0.034), and lower E2 levels at triggering (2063.4 ± 1336.1 vs. 2425.4 ± 1727.1 pg/mL; p < 0.001). Furthermore, GnRHa was used less frequently for ovulation triggering in this subgroup (40.3% vs. 50.2%; p < 0.001).

Multivariate analysis revealed that GnRHa triggering was the only factor significantly associated with a reduced risk of suboptimal oocyte yield (OR 0.58, 95% CI (0.44–0.78); p < 0.001), as shown in Table 3.

Table 3

Prognostic factors for suboptimal mature oocyte yield.[α] Multivariate analysis.

Characteristics	OR (95% CI)[a]	P-value
Age	1.01 (0.98–1.04)	0.517
Infertility cause		
Male factor	Reference	
Female factor	1.20 (0.91–1.58)	0.190
Idiopathic	0.98 (0.65–1.48)	0.925
Day-3 FSH	1.02 (0.97–1.09)	0.432
Day-3 LH	0.97 (0.92–1.02)	0.229
AMH	0.97 (0.93–1.02)	0.279
Mean starting gonadotropin dose	1.00 (0.99–1.01)	0.479
Type of ovulation triggering		
hCG	Reference	
GnRH agonist	0.58 (0.44–0.78)	< 0.001
Dual trigger	0.73 (0.52–1.05)	0.087
LH level at triggering	1.03 (0.94–1.12)	0.529

Note: FSH = follicle-stimulating hormone; LH = luteinizing hormone; AMH = anti-Müllerian hormone; hCG = human chorionic gonadotropin; GnRH = gonadotropin-releasing hormone

[a] *Odds Ratio (95% Confidence Interval)*

[α] *Suboptimal mature oocyte yield = mature oocyte yield (number of mature oocytes retrieved/number of mature follicles (≥ 15 mm)) < 75th percentile (< 117%)*

To further investigate the impact of ovarian reserve, a subgroup analysis was conducted focusing on patients with AMH levels ≥ 75th percentile (i.e., 3.8 ng/mL). This analysis confirmed the association between GnRHa triggering and a lower risk of suboptimal mature oocyte yield compared to hCG and dual trigger (66.1% vs. 76.9% vs. 86.0%; p < 0.001) (Supplemental Table 4).

DISCUSSION

This observational cohort study, encompassing 2,129 antagonist ICSI cycles, aimed to investigate the impact of ovulation triggering on oocyte maturity and to analyze risk factors associated with suboptimal outcomes, defined by mature oocyte yield. Our findings indicate that the mean mature oocyte yield was significantly higher in the GnRHa triggering group compared to the hCG group, while the rate of

suboptimal mature oocyte yield (below the 75th percentile) was significantly lower with GnRHa. Multivariate analysis confirmed that GnRHa triggering was the sole significant prognostic factor associated with a reduced risk of suboptimal outcomes in antagonist ICSI cycles.

The strengths of this study include: i) to our knowledge, it is the largest study to date comparing the efficacy of GnRHa and hCG triggering in antagonist ICSI cycles, utilizing a novel and clinically relevant endpoint; ii) all COH protocols adhered to our institutional guidelines, and transvaginal ultrasounds were performed consistently at our ART center, minimizing the risk of comparison bias regarding protocols and mature follicle counts, which could impact oocyte maturity; iii) a comprehensive array of epidemiological and clinical variables was prospectively collected to analyze a broad range of factors potentially associated with suboptimal mature oocyte yield.

The main limitation of this study is its retrospective design, which introduces a risk of confounding bias that cannot be entirely eliminated, despite our efforts through multivariable analysis. Additionally, GnRHa triggering is frequently employed in younger, high-responder patients to mitigate the risk of OHSS, leading to differences in patient characteristics between the GnRHa and hCG groups, particularly concerning age and ovarian reserve. To address this selection bias, we conducted a subgroup analysis of patients with AMH levels ≥ 75th percentile (3.8 ng/mL) and still observed a reduced risk of suboptimal mature oocyte yield with GnRHa. This reinforces the notion that GnRHa positively impacts oocyte maturity, independent of patient profile.

Concerns surrounding the use of GnRHa for ovulation triggering have persisted due to findings from uncontrolled studies utilizing various endpoints [6–9, 12, 13]. Some studies evaluated biological markers such as suboptimal LH or progesterone levels post-triggering [8, 9, 12], which may not accurately reflect oocyte recovery or maturity. Furthermore, these investigations primarily focused on potential suboptimal outcomes following GnRHa triggering without comparing this risk to that of hCG triggering, even though suboptimal outcomes can occur with any triggering method [25]. This publication bias may have contributed to a misleading perception of GnRHa triggering's efficacy.

In our study, we focused on a clinically relevant outcome that directly reflects the efficacy of ovulation triggering by comparing the number of mature oocytes retrieved to the expected number based on the mature follicle count at triggering. This approach differs from the traditional oocyte maturation rate used in previous studies [11, 13], which calculates the maturation rate using the total number of retrieved oocytes. This method can be influenced by how oocyte retrieval is performed, particularly if clinicians aspirates smaller or intermediate follicles containing less mature oocytes [26]. Such practices can lead to a lower maturation rate that does not accurately reflect the effectiveness of the triggering agent.

Our analysis of mature oocyte yield in a large cohort revealed that GnRHa outperformed hCG. This finding is consistent with a recent meta-analysis by Bourdon et al. [2], which reported higher total numbers of retrieved oocytes, mature oocytes, and embryos following GnRHa triggering compared to hCG. The enhanced performance of GnRHa may be attributed to the additional FSH surge it induces, which plays a critical role in final oocyte and follicular maturation in natural cycles. For instance, FSH

facilitates the resumption of meiosis, enhances communication between the oocyte and cumulus cells, promotes cumulus expansion, and stimulates the release of proteolytic enzymes—all vital for successful follicular maturation and ovulation [27–31]. Furthermore, the more physiological LH surge produced by GnRHa may also contribute to its positive effects, as emerging evidence suggests that LH and hCG, despite binding to the same receptor, can activate distinct downstream signaling pathways that may influence the ovulation profile [32].

Given the effectiveness and safety profile of GnRHa triggering, clinicians should consider routinely offering this strategy in antagonist cycles. When a fresh embryo transfer is planned, a dual trigger with hCG can be used to ensure sufficient LH support for the corpora lutea. In our study, we found no significant difference in mature oocyte yield between dual triggering and hCG alone, likely due to the small sample size. However, recent literature has reported favorable outcomes with the dual trigger approach, highlighting improvements in the number of oocytes retrieved, mature oocytes, and blastocysts [33, 34]. Additionally, pregnancy outcomes such as implantation rates, clinical pregnancies, and live births have shown significant enhancement [2, 35, 36], which may be attributed to the positive effects of GnRHa on endometrial receptivity during fresh embryo transfer cycles [37].

In conclusion, our findings indicate that GnRHa triggering is associated with a lower risk of suboptimal mature oocyte yield compared to hCG, suggesting that its systematic use could enhance ART outcomes. This approach may be effective when used alone for deferred embryo transfers or in combination with hCG for fresh transfers. However, further studies are needed to validate these benefits, especially regarding the dual trigger strategy. Caution should be exercised with the dual trigger approach, as the inclusion of hCG poses a risk of OHSS, which is not alleviated by adding GnRHa. Using GnRHa alone mitigates the risk of OHSS, underscoring the importance of carefully assessing OHSS risk at the time of ovulation triggering before implementing this strategy in clinical practice.

Declarations

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

ETHICS APPROVAL

This study received approval for publication from the Ethics Review Committee of Cochin University Hospital (CLEP) (No. AAA-2024-10007). All participants provided written informed consent.

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The authors did not receive support from any organization for the submitted work.

DATA AVAILABILITY

Data will be made available on request.

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Figures

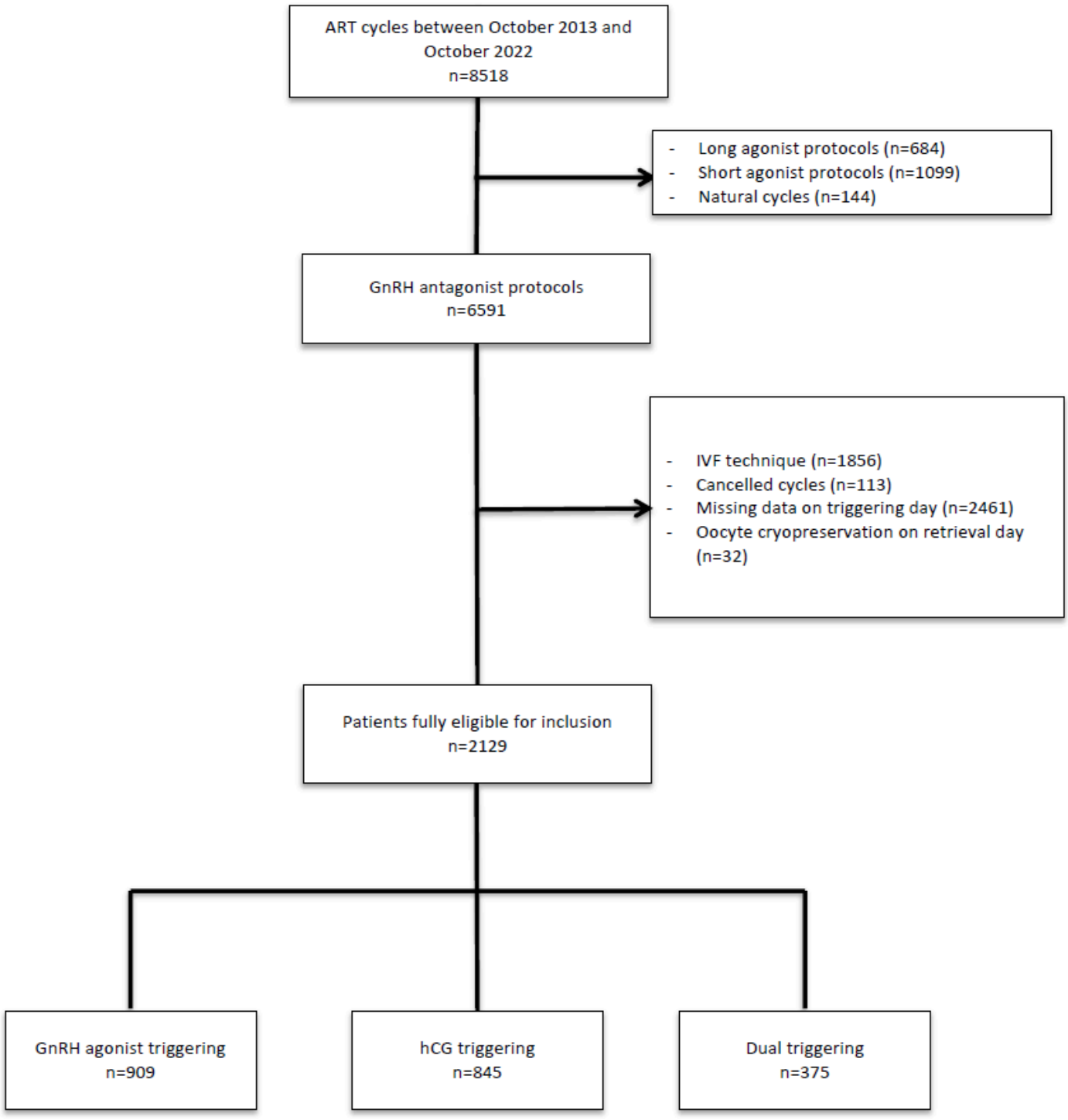


Figure 1

Patient inclusion flowchart

Note: GnRH = gonadotropin-releasing hormone; hCG = human chorionic gonadotropin

Supplementary Files

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