JRME

Journal of Reproductive Medicine and Embryology

Exploring AI-Driven Predictive Models for Ovulation Trigger Timing in ICSI: A Novel Hypothetical Framework for Enhanced Clinical Decision-Making Without Real-World Data

Ashraf Abo Ali[1,2], Karim mekhimer[1,3], Omar Abo Ali[1,2], Aya elsayed[1,3] ,Omar zakaria[1,3], Hassan Maghraby[2,3]

[1]Madina Fertility Center Madina Women Hospital, Alexandria, Egypt.
[2]Egyptian Foundation of Reproductive Medicine and Embryology (EFRE), Alexandria, Egypt.
[3]Obstetrics and Gynecology Department, Faculty of Medicine, Alexandria University, Egypt.

Dr. Ashraf Abo Ali Consultant Reproductive Medicine Director Madina Fertility Centre CEO Madina Women's Hospital Director Madina endocare IVF & Laparoscopy Centre EFRE treasurer and founder.

Abstract

The timing of ovulation trigger administration is a critical challenge in assisted reproductive technologies (ART), where improper timing can lead to suboptimal oocyte retrieval and fertilization outcomes. Despite its significance, there is no standardized approach to determine the optimal timing, leading to clinical variability. This study aims to develop a predictive model using Meta AI to determine the optimal timing for ovulation trigger administration, with the goal of maximizing oocyte yield and the number of mature metaphase II (MII) oocytes retrieved on the day of oocyte pick-up (OPU). By incorporating a comprehensive set of clinical variables, this model seeks to guide clinicians and patients in making evidence-based decisions regarding ovulation induction, even in the absence of real-world data, ultimately improving the efficiency and outcomes of in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) procedures.

A literature review identified key factors influencing ovulation trigger timing, including patient demographics, ovarian reserve markers (AMH, AFC), stimulation parameters, and hormonal levels. Logistic regression was selected as the model due to its simplicity and interpretability. The model was evaluated using performance metrics such as accuracy, precision, recall, F1 score, and area under the curve (AUC).

Three predictive approaches were proposed: a Follicle-Based Trigger Model (FBTM), a refined FBTM integrating AMH and AFC, and a Trigger Day Predictive Score (TDPS) model. Hypothetical results suggest these models could improve ovulation trigger timing and ART outcomes. Further empirical validation is required for clinical application.

Keywords: Ovulation trigger; predictive model; Meta AI; ICSI; machine learning.

Introduction

Timing of the trigger

The temporal aspect of the trigger constitutes a pivotal factor in determining the efficacy of an assisted reproductive technology (ART) cycle. It is meticulously optimized to enhance the retrieval of mature and developmentally proficient oocytes from the existing follicular cohort (1).

JRME® Volume. 2, Issue no 1, May 2025
JRME-2401-1002© 2024 The Author(s). Published by EKB ASRT Journals on behalf of the Egyptian Foundation of Reproductive Medicine and Embryology. This is an **open-access** article https://jrme.journals.ekb.eg/article_421869.html

Narrative Review

An efficacious trigger must guarantee adequate LH exposure to promote meiotic resumption, cytoplasmic maturation, and the attainment of oocyte competence while preserving alignment with endometrial receptivity (2-4).

Optimal triggering is characterized by a substantial yield of mature oocytes accompanied by minimal or no complications (5).

The timing of the trigger in intracytoplasmic sperm injection (ICSI) cycles is instrumental in affecting both oocyte competence and endometrial receptivity (6). Numerous factors have been explored to ascertain the optimal timing for trigger administration in ICSI cycles, which include: 1- follicular diameter 2- serum estradiol (E2) and progesterone concentrations, peak E2 levels per follicle 3- and the individual's previous response to controlled ovarian stimulation (COS).

Timing of the trigger and Follicular Diameter:

The timing of the trigger has been, for over three decades, contingent upon the presence of at least three follicles with a diameter of 17 mm or greater (7-10). Nonetheless, a universal consensus regarding the minimum follicular size requisite for procuring a competent oocyte remains elusive. The threshold for obtaining a mature M2 oocyte is posited to be 16 mm from one perspective (10), while follicles smaller than 12 mm yield oocytes at various stages of immaturity (8,11,12). Follicles exceeding 22 mm frequently harbor "post-mature" oocytes that exhibit diminished fertilization rates and compromised developmental competence (10,13).

Empirical studies have indicated that follicles measuring between 16–23 mm at the time of oocyte retrieval demonstrate superior fertilization rates compared to those surpassing 23 mm (9,10). However, the proportion of oocytes with high-quality scores escalates from 55.4% in the 16–23 mm follicle cohort to 64.6% in follicles exceeding 23 mm. Consequently, the recommendations from the European Society of Human Reproduction and Embryology (ESHRE) 2020 regarding the timing of the trigger are articulated as follows: "Most frequently, final oocyte maturation is triggered at sizes of several of the leading follicles between 16–22 mm as data on specific follicle sizes that are most likely to yield a mature oocyte have predominantly been generated on the day of oocyte retrieval, at which point follicles of 16 to 22 mm are perceived to be most likely to yield oocytes." (14)

Timing of the trigger and E2 and progesterone concentrations

There exists no discernible correlation between E2 levels at the day of trigger and the outcomes of ICSI. Thus, the ESHRE 2020 guidelines for ovarian stimulation in IVF/ICSI do not advocate for the employment of either serum estradiol level or estradiol/follicle ratio as the exclusive criterion for determining the timing of the trigger in IVF/ICSI cycles (15). In terms of serum progesterone levels, the evidence remains insufficient to endorse the utilization of serum progesterone for ascertaining the timing of trigger administration. Furthermore, there are no unequivocal cut-off values delineating normal and elevated progesterone levels.

Timing of the trigger and various stimulation protocols

Postponing the administration of the HCG trigger (by 1–2 days) in agonist ICSI cycles is associated with enhanced oocyte yield, which may consequently exert a favorable influence on both the quantity of embryos produced and the rates of successful pregnancies; nonetheless, this delay could correlate with an elevated frequency of pre-ovulatory progesterone surges. (15,16)

Within the framework of antagonist protocols, it appears that the initiation of oocyte maturation should be executed with greater precision (and typically at an earlier time point) than in agonist cycles; the optimal timing for triggering should occur when a minimum of three follicles have reached a diameter of 17–18 mm (17-21), while the majority of the remaining cohort of follicles should also exhibit a considerable size (≥14 mm), taking into account the requisite serum estradiol level (100–400 pg/mL per oocyte).

Timing of the trigger and differing ovarian reserves

Women exhibiting normal ovarian reserve and those classified as poor responders should not be evaluated by the same parameters during ovarian stimulation, as factors such as early follicular recruitment, the rate of follicular development, endometrial receptivity, and the duration of stimulation significantly differ. A judicious duration of FSH stimulation, in conjunction with criteria based on follicular size, as well as serum estradiol and progesterone concentrations, are critical determinants in establishing trigger timing that effectively balances oocyte maturation with endometrial receptivity. In the context of PCOS,

whether utilizing a GnRH agonist long protocol or a GnRH antagonist protocol, it is imperative to find an equilibrium between the risk of ovarian hyper-stimulation syndrome (OHSS) and the likelihood of clinical pregnancy when determining the timing of the trigger.

Timing of the triggers and artificial intelligence

Recognizing the paramount importance of accurately ascertaining the optimal timing for the trigger, artificial intelligence-driven models are being developed to enhance trigger timing by amalgamating pre-stimulation characteristics with real-time ovarian response metrics, such as follicle count and size, aimed at optimizing oocyte yield and improving procedural efficacy.

Serum estradiol concentrations and three-dimensional assessments of follicular volume via ultrasound have been utilized to ascertain the ideal trigger day and to predict the number of oocytes to be retrieved, with a focus on synchronizing this process with the peak representation of metaphase II (MII) oocytes.

Contemporary predictive models predominantly emphasize the optimization of trigger timing; however, forthcoming advancements are anticipated to incorporate additional variables, including the type and dosage of trigger, in order to further individualize and enhance ovarian stimulation protocols (22,23).

Objective of the Study

The objective of this study is to develop a robust predictive model utilizing Meta AI to determine the optimal timing for the administration of the ovulation trigger, with the aim of maximizing both the total number of oocytes retrieved on the day of oocyte pick-up (OPU) and the quantity of mature metaphase II (MII) oocytes. By incorporating a comprehensive set of clinical variables into the AI framework, this study endeavors to generate a decision-support tool that will assist clinicians and patients in making evidence-based decisions regarding the timing of ovulation induction without real-world data. Ultimately, this model aspires to enhance the efficiency and outcomes of in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) procedures.

Methodology

Problem Definition

This study addresses a critical challenge encountered in the context of intracytoplasmic sperm injection (ICSI) - the optimization of ovulation trigger timing. The objective is to develop a predictive model that accurately forecasts the optimal timing for ovulation trigger administration to enhance the outcomes of oocyte retrieval, including maximizing the total number of oocytes and the number of mature metaphase II (MII) oocytes.

Literature Review

A comprehensive literature review was conducted to assess existing predictive models and to identify factors influencing the timing of ovulation trigger administration. Relevant studies were systematically reviewed, and data on various predictive factors were extracted. These included patient demographics (age and body mass index [BMI]), ovarian reserve markers (anti-Müllerian hormone [AMH] levels and antral follicle count [AFC]), gonadotropin dosing regimens, ovarian response characteristics, the number of follicles, the size of the leading follicle, stimulation duration, and hormonal parameters such as estradiol and serum progesterone levels.

Model Selection

Several machine learning algorithms were considered for model development, including logistic regression, decision trees, random forests, and neural networks. After a careful evaluation of the advantages and limitations of each method, logistic regression was chosen as the initial model due to its simplicity, interpretability, and efficacy in clinical prediction settings (24,25).

Model Development

The predictive model was developed using Meta AI and logistic regression methodology. This theoretical framework was applied in the absence of real-world patient data, facilitating the construction of a robust predictive tool for ovulation trigger timing. The model incorporated key predictive factors identified during the literature review, including age, BMI, ovarian reserve markers (AMH and AFC), gonadotropin dose, ovarian response, follicular count, the size of the leading follicle, stimulation duration, and hormonal levels (estradiol and progesterone).

Model Inputs

The input variables included in the model were:

- Female age
- Body mass index (BMI)
- Anti-Müllerian hormone (AMH) levels
- Antral follicle count (AFC)
- Gonadotropin dosage
- Number of follicles
- Size of the leading follicle
- Duration of ovarian stimulation
- Estradiol levels
- Progesterone levels

Model Outputs

The primary output of the predictive model was the estimated optimal day for ovulation trigger administration, aimed at maximizing the total oocyte yield and the number of mature MII oocytes retrieved.

Model Evaluation

The performance of the predictive model was evaluated through a series of theoretical scenarios, given the absence of real-world patient data. Model evaluation was based on a range of performance metrics, including accuracy, precision, recall, F1 score, and area under the curve (AUC). These metrics were employed to assess the model's ability to accurately predict the optimal day for ovulation trigger administration, in relation to the outcomes of controlled ovarian stimulation.

Statistical Analysis

No statistical analysis was conducted, as the model was developed using a theoretical framework and was not tested on actual patient data. Consequently, the model's evaluation is based on hypothetical data derived from simulated scenarios.

Model Evaluation Results

The model's performance was assessed using theoretical scenarios, with the following results presented for key evaluation metrics (table 1):

Table 1: Key evaluation metrics.

Metric	Value
Accuracy	0.85
Precision	0.80
Recall	0.90
F1 Score	0.85
AUC	0.92

It is important to note that these results are hypothetical and are based on theoretical scenarios, as the model has not been validated with real-world patient data.

Evaluation Metrics

Accuracy: Accuracy represents the proportion of correct predictions made by the model, and is calculated as:

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}$$

where:

- **TP =** True Positives (correctly predicted optimal trigger day)
- **TN =** True Negatives (correctly predicted non-optimal trigger day)
- **FP =** False Positives (incorrectly predicted optimal trigger day)
- **FN =** False Negatives (incorrectly predicted non-optimal trigger day)

Precision: Precision measures the proportion of true positives out of all positive predictions, and is calculated as:

$$\text{Precision} = \frac{TP}{TP + FP}$$

Recall: Recall evaluates the proportion of true positives out of all actual optimal trigger days, and is calculated as:

$$\text{Recall} = \frac{TP}{TP + FN}$$

F1 Score: The F1 score is the harmonic mean of precision and recall, calculated as:

$$\text{F1 Score} = 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}}$$

Area Under the Curve (AUC): The AUC is derived from the Receiver Operating Characteristic (ROC) curve, which plots the true positive rate (sensitivity) against the false positive rate (1-specificity) at various thresholds. AUC quantifies the model's ability to distinguish between optimal and non-optimal trigger days, with higher values indicating better discrimination.

Model Interpretation

The interpretation of the predictive model's results was conducted, focusing on the estimated optimal day for ovulation trigger administration. Additionally,

the relative importance of each predictive factor was analyzed to understand its contribution to the model's performance. The clinical implications of

the model's predictions were explored, including potential applications in reproductive medicine to enhance decision-making processes related to ovulation timing and optimize IVF and ICSI outcomes.

Results

This study demonstrates three distinct approaches for determining the optimal timing of ovulation trigger using Follicle-Based Trigger Models (FBTM). These models integrate multiple parameters, including days of stimulation, estradiol levels, progesterone concentrations, anti-Müllerian hormone (AMH) levels, and antral follicle count (AFC), with the aim of improving the accuracy and timing of ovulation trigger during controlled ovarian hyperstimulation cycles.

For normal responders, we propose the first structured AI-derived scoring system that quantitatively assesses follicular and endocrine readiness for ovulation trigger, independent of endometrial receptivity or overall reproductive prognosis. This model assigns a composite score out of 100 points, integrating four core domains: lead follicle size (LFS), subsidiary cohort size (SCS), stimulation duration (SD), and serum estradiol (E2) concentration (Table 2).

LFS (30 points) is computed as the average diameter of the two to three largest follicles, with peak scores assigned to follicles between 19–21 mm, correlating with optimal oocyte maturity. Sizes >21 mm incur a slight deduction due to concerns of post-maturity. SCS (30 points) evaluates the broader follicular cohort >10 mm in diameter; a majority >17 mm scores highest, while mid-range (15–17 mm) and immature (<15 mm) cohorts are assigned progressively lower points.

Stimulation duration (20 points) reflects temporal maturation kinetics. Extended durations (>11 days) receive full points with clinical caveats, while abbreviated stimulations (<7 days) are scored lowest. Serum E2 (20 points) is interpreted as a surrogate of granulosa cell activity and follicular mass, with >2500 pg/mL scoring highest but prompting OHSS risk mitigation. Intermediate (1000–2500 pg/mL) and low (<1000 pg/mL) values are scored accordingly.

Total scores ≥75 support immediate trigger with optional adjuncts (e.g., GnRH agonist trigger, freeze-all strategy) in high E2 contexts. Scores between 50–74 reflect transitional readiness; a 24-hour delay may optimize cohort maturation. Scores <50 denote insufficient development, warranting continued stimulation or possible cancellation. This model offers a reproducible, physiology-aligned tool for optimizing trigger timing in normo-responders within ART cycles (Table 3).

Table 2: First model - Trigger time predictive model for normal responders.

Category	Criteria	Points
Lead Follicle Size (LFS)	> 16mm	10
	16-18.9 mm	15
	19-21 mm	30
	> 21 mm	25
Subsidiary Cohort Size (SCS)	Most follicles < 15 mm	5
	Most follicles 15 - 17 mm	20
	Most follicles > 17 mm	30
Stimulation Duration (SD)	<7 Day	5
	8-11 Day	15
	> 11 Day	20
Estradiol (E2) Level	< 1000	5
	1000 - 2500	15
	> 2500	20

Table 3: Trigger Decision Guidelines (maximum score 100 points)

Total Score	Recommended Action
≥ 75 points	Trigger Today
50–74 points	Consider Trigger Tomorrow
< 50 points	Rescan Tomorrow

A parallel model was developed for low responders, particularly those categorized under POSEIDON Group 4 (women ≥35 years with AFC <5 and AMH <1.2 ng/mL). This population presents unique challenges—including a narrow follicular window, heightened risk of premature luteinization, and diminished yield—necessitating a distinct strategy focused on maximizing mature oocyte retrieval within biological constraints. The model yields a composite score of 34 points across six parameters: lead follicle size, follicular cohort synchrony, stimulation duration hormonal profile (E2, P4 and LH) (Table 4).

As the most direct indicators of follicular maturity, the number of leading follicles ≥16 mm is assigned the highest weight. Even a single dominant follicle in this size range is considered clinically meaningful in low responders, with progressively higher scores for two or more follicles. The presence of multiple large follicles reflects advanced folliculogenesis and is a strong independent signal to proceed with trigger.

Cohort follicles capture the broader follicular recruitment beyond the lead cohort. While less mature than ≥16 mm follicles, a higher number of ≥13 mm follicles suggests imminent maturity with continued stimulation. Scores increase with the number of cohort follicles, reflecting their potential to contribute to oocyte yield if sufficient growth is achieved over the next 24–48 hours.

The total number of stimulation days is contextualized within the low responder population. Extended stimulation (>9 days) receives the highest score, based on the premise that slow-developing follicles may still yield competent oocytes. Typical durations (7–9 days) are scored moderately, while short protocols (<7 days) are given minimal positive weight, assuming that other criteria justify early consideration for trigger.

The estradiol-to-follicle ratio serves as a proxy for granulosa cell activity and follicular health. Values between 70–110 pg/mL/follicle are considered optimal and are assigned a moderate positive score. Higher values (>110 pg/mL/follicle) receive the greatest weight, reflecting robust endocrine output and strong follicular function. Lower ratios (40–70 pg/mL/follicle) still contribute positively, as they may indicate incomplete maturation.

Unlike traditional scoring systems that penalize elevated P4, this user-modified model assigns a higher score to P4 levels >1.2 ng/mL. This reflects a clinical approach that prioritizes follicular readiness over endometrial receptivity, particularly in contexts where freeze-all or embryo pooling is planned. Lower P4 values (<1.2 ng/mL) also receive a positive score, consistent with their association with better fresh transfer potential.

LH contributes to final follicular maturation and oocyte competence. Day 7 levels >1.2 IU/L are scored positively, indicating a supportive endocrine environment for continued stimulation or immediate trigger. LH <1.2 IU/L receives no points, reflecting possible insufficiency in luteotropic support, although not necessarily a contraindication for continued stimulation.

Table 4: Trigger Decision Guidelines (maximum score 34 points)

Category	Criteria	Points
Leading Follicles ≥16 mm	0	0
	1	5
	2	10
	+3	15
Cohort Follicles ≥13 mm	0	0
	1	2
	2	4
	+3	6
Stimulation Duration (Total)	<7 days	1
	7-9 days	2
	>9 days	3
E2 per Follicle >13 mm (pg/mL)	40-70	1
	70-110	3
	>110	4
Progesterone (P4) (ng/mL)	≤1.2	3
	>1.2	4
Luteinizing Hormone (LH) (IU/L)	≤1.2	0
	>1.2	2

Total scores may range from approximately 5 to 34 (Table 5). A score >22 suggests optimal readiness for trigger and supports proceeding without delay. Scores between 14–22 indicate nearing readiness, where an additional day of stimulation may improve maturity and oocyte yield. Scores of 7–13 reflect insufficient development, warranting continued stimulation and re-evaluation, while scores <7 suggest minimal follicular activity and may prompt consideration of cycle cancellation or alternative management strategies. This scoring model offers a structured, individualized tool for low responder management and requires prospective validation to assess its predictive value for clinical outcomes.

Table 5: Trigger Decision Guidelines (maximum score 34 points)

Total Score	Recommended Action
> 22 points	Trigger Today
14 to 22	Trigger Tomorrow
7 to 13	Rescan Tomorrow
< 7	Patient May Not Be Responding Properly / Consider Cycle Cancellation Discussion

For high responders undergoing antagonist protocols with a planned freeze-all strategy, we introduce a scoring model tailored to optimize GnRH agonist (GnRHa) trigger timing while mitigating OHSS risk and preventing endometrial asynchrony. This system quantifies trigger readiness via five domains: follicular cohort assessment, serum estradiol, serum progesterone, stimulation duration, and baseline LH, with a cumulative maximum of 100 points (Table 6).

The follicular cohort (50 points) carries the greatest weight, with optimal scores assigned when ≥3 follicles are ≥18 mm and >60% of the cohort falls within the 15–21 mm range. Reduced synchrony or suboptimal follicular sizes result in proportionate score reduction. E2 (20 points) is interpreted in light of OHSS risk and yield prediction; ideal levels range between 3000–6000 pg/mL with a stable rise. Sharp spikes (>50%) or very high levels (>6000 pg/mL) reduce the score due to hyperstimulation risk.

Serum P4 (15 points) reflects endometrial dissociation. P4 ≤1.0 ng/mL scores highest, though elevation does not preclude trigger in freeze-all contexts. Stimulation duration (10 points) is optimal at 9–11 days, in line with expected follicular kinetics; deviations are penalized. Baseline LH (5 points) serves as a secondary modifier; levels ≥1.0 mIU/mL are considered adequate for inducing a reliable GnRHa surge.

Total scores >80 justify immediate trigger, denoting favorable maturity, synchrony, and hormonal profile. Intermediate scores (60–80) support triggering the following day. Scores <60 indicate immaturity or excessive risk, warranting continued monitoring (Table 7). This model offers a structured, data-driven framework to harmonize safety and efficacy in high-responder management, reinforcing precision medicine principles in AR.

Table 6: Third model: Trigger time predictive for high responders

Category	Criteria	Points
Follicular Cohort Assessment	≥3 follicles ≥18mm AND >60% of follicles ≥12mm are within 15-21mm range	50
	≥2 follicles ≥17mm AND 40-60% of follicles ≥12mm are within 15-21mm range	40
	≥2 follicles ≥17mm BUT <40% of follicles ≥12mm are within 15-21mm range	25
	≥2 follicles ≥16mm (but 40% of follicles ≥12mm are within 14-19mm range	15
	<2 follicles ≥16mm OR Majority of cohort <14mm	0

Serum Estradiol (E2) Level	**3000 - 6000 pg/mL (Stable or moderate rise)**	**20**
	>6000 pg/mL OR Rapid Rise (>50% increase in 24h)	**10**
	<3000 pg/mL (If classified high responder by follicles only)	**5**
Serum Progesterone (P4) Level	**≤1.0 ng/mL**	**15**
	1.01 - 1.5 ng/mL	**10**
	>1.5 ng/mL	**5**
Stimulation Duration	**9 - 11 days**	**10**
	8 days OR 12 days	**5**
	<8 days OR >12 days	**0**
Baseline LH Level	**≥1.0 mIU/mL**	**5**
	0.5 - 0.99 mIU/mL	**3**
	<0.5 mIU/mL	**0**

Table 7: Trigger Day Prediction Based on Total Score (out of 100)

Score Range	Trigger Decision Guide for High Responders
> 80 points	Trigger Today
60–80 points	Trigger Tomorrow
< 60 points	Rescan Tomorrow

Discussion

It is important to note that this section deviates from the conventional approach typically found in research papers, where the collection and analysis of real-world data are central components. In contrast, the models presented in this study was developed within a theoretical framework, with no real-world patient data utilized.

This study serves as a hypothetical example, illustrating the process of model development in reproductive medicine. The actual creation and validation of a predictive model would necessitate access to real-world clinical data, as well as specialized expertise in both machine learning and reproductive medicine. Consequently, while this theoretical model serves as a conceptual foundation, the practical implementation and refinement of such models would require empirical data to ensure their accuracy and applicability in clinical practice.

Limitations

The limitations of the predictive model were carefully considered, including the absence of real-world validation, which restricts its generalizability and applicability to clinical practice. Additionally, the potential for bias in the model's predictions, arising from the reliance on a theoretical framework rather than empirical data, must be acknowledged. These factors highlight the need for further validation and refinement to enhance the model's accuracy and clinical utility.

Future directions

Future research should focus on the collection and analysis of real-world clinical data to rigorously validate and refine the predictive model. Additionally, further investigation into alternative machine learning algorithms and advanced computational techniques may provide opportunities for enhancing the model's accuracy and robustness. Expanding these efforts will be crucial for ensuring the model's clinical relevance

and effectiveness in guiding ovulation trigger decisions.

Conclusion

In conclusion, our study serves as a proof of concept, proposing a novel approach to integrating AI-driven predictive models for ovulation trigger timing in ICSI. This framework not only potentially enhances clinical decision-making and improves treatment outcomes but also offers a time- and resource-efficient educational tool. Moreover, it could represent a paradigm shift in validation, enabling retrospective analysis of existing ICSI cycles to assess concordance between expert decisions and AI predictions, and evaluating the impact on pregnancy outcomes in both concordant and discordant cases. While theoretical and requiring validation through real-world data and clinical trials, it highlights the promising potential of AI in reproductive medicine. Future research should focus on developing and refining these predictive models, ultimately aiming to personalize and optimize ICSI treatment protocols for improved patient care and success rates.

References

1. Dosouto C, Haahr T, Humaidan P. Advances in ovulation trigger strategies. Panminerva Med. 2019 Mar;61(1):42–51.
2. Voronina E, Wessel GM. The regulation of oocyte maturation. Curr Top Dev Biol. 2003;58:53–110.
3. Palomba S, Santagni S, La Sala GB. Progesterone administration for luteal phase deficiency in human reproduction: an old or new issue? J Ovarian Res. 2015 Nov 19;8:77.
4. 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 Aug;96(2):344–8.
5. Skorupskaite K, George JT, Anderson RA. The kisspeptin-GnRH pathway in human reproductive health and disease. Hum Reprod Update. 2014 Aug;20(4):485–500.
6. Hu X, Luo Y, Huang K, Li Y, Xu Y, Zhou C, et al. New Perspectives on Criteria for the Determination of HCG Trigger Timing in GnRH Antagonist Cycles. Medicine (Baltimore). 2016 May;95(20):e3691.
7. Simonetti S, Veeck LL, Jones HWJ. Correlation of follicular fluid volume with oocyte morphology from follicles stimulated by human menopausal gonadotropin. Fertil Steril. 1985 Aug;44(2):177–80.
8. Scott RT, Hofmann GE, Muasher SJ, Acosta AA, Kreiner DK, Rosenwaks Z. Correlation of follicular diameter with oocyte recovery and maturity at the time of transvaginal follicular aspiration. J Vitro Fertil Embryo Transf IVF. 1989 Apr;6(2):73–5.
9. Dubey AK, Wang HA, Duffy P, Penzias AS. The correlation between follicular measurements, oocyte morphology, and fertilization rates in an in vitro fertilization program. Fertil Steril. 1995 Oct;64(4):787–90.
10. Ectors FJ, Vanderzwalmen P, Van Hoeck J, Nijs M, Verhaegen G, Delvigne A, et al. Relationship of human follicular diameter with oocyte fertilization and development after in-vitro fertilization or intracytoplasmic sperm injection. Hum Reprod Oxf Engl. 1997 Sep;12(9):2002–5.
11. Bergh C, Broden H, Lundin K, Hamberger L. Comparison of fertilization, cleavage and pregnancy rates of oocytes from large and small follicles. Hum Reprod Oxf Engl. 1998 Jul;13(7):1912–5.
12. Rosen MP, Shen S, Dobson AT, Rinaudo PF, McCulloch CE, Cedars MI. A quantitative assessment of follicle size on oocyte developmental competence. Fertil Steril. 2008 Sep;90(3):684–90.
13. Clark L, Stanger J, Brinsmead M. Prolonged follicle stimulation decreases pregnancy rates after in vitro fertilization. Fertil Steril. 1991 Jun;55(6):1192–4.
14. Inaudi P, Germond M, Senn A, De Grandi P. Timing of hCG administration in cycles stimulated for in vitro fertilization: specific impact of heterogeneous follicle sizes and steroid concentrations in plasma and follicle fluid on decision procedures. Gynecol Endocrinol Off J Int Soc Gynecol Endocrinol. 1995 Sep;9(3):201–8.
15. Ovarian Stimulation TEGGO, Bosch E, Broer S, Griesinger G, Grynberg M, Humaidan P, et al. ESHRE guideline: ovarian stimulation for IVF/ICSI(†). Hum Reprod Open. 2020;2020(2):hoaa009.
16. Dimitry ES, Oskarsson T, Conaghan J, Margara R, Winston RM. Beneficial effects of a 24 h delay in human chorionic gonadotrophin administration during in-vitro fertilization

treatment cycles. Hum Reprod Oxf Engl. 1991 Aug;6(7):944–6.
17. Comparable clinical outcome using the GnRH antagonist ganirelix or a long protocol of the GnRH agonist triptorelin for the prevention of premature LH surges in women undergoing ovarian stimulation. Hum Reprod Oxf Engl. 2001 Apr;16(4):644–51.
18. Borm G, Mannaerts B. Treatment with the gonadotrophin-releasing hormone antagonist ganirelix in women undergoing ovarian stimulation with recombinant follicle stimulating hormone is effective, safe and convenient: results of a controlled, randomized, multicentre trial. The European Orgalutran Study Group. Hum Reprod Oxf Engl. 2000 Jul;15(7):1490–8.
19. Fluker M, Grifo J, Leader A, Levy M, Meldrum D, Muasher SJ, et al. Efficacy and safety of ganirelix acetate versus leuprolide acetate in women undergoing controlled ovarian hyperstimulation. Fertil Steril. 2001 Jan;75(1):38–45.
20. Kolibianakis EM, Albano C, Kahn J, Camus M, Tournaye H, Van Steirteghem AC, et al. Exposure to high levels of luteinizing hormone and estradiol in the early follicular phase of gonadotropin-releasing hormone antagonist cycles is associated with a reduced chance of pregnancy. Fertil Steril. 2003 Apr;79(4):873–80.
21. Garcia-Velasco JA, Isaza V, Vidal C, Landazábal A, Remohí J, Simón C, et al. Human ovarian steroid secretion in vivo: effects of GnRH agonist versus antagonist (cetrorelix). Hum Reprod Oxf Engl. 2001 Dec;16(12):2533–9.
22. Letterie G. Artificial intelligence and assisted reproductive technologies: 2023. Ready for prime time? Or not. Fertil Steril. 2023 Jul;120(1):32–7.
23. Hariton E, Pavlovic Z, Fanton M, Jiang VS. Applications of artificial intelligence in ovarian stimulation: a tool for improving efficiency and outcomes. Fertil Steril. 2023 Jul;120(1):8–16.
24. Maghraby, H., Gaafar, S., Abo Ali, A., Elmahdy, M., Adel, N., Hassan, H., Fawzy, R. EFRE 40: An AI-generated predictive algorithm for IVF success in AMA. *Journal of Reproductive Medicine and Embryology*, 2025; 1(4): 276-285. doi: 10.21608/jrme.2025.369219.1035.
25. Maghraby, H., Elmahdy, M., Gaafar, S., Aboali, A., Adel, N., ElKassar, Y., Hassan, H. EFRE IVF 40; AI model for personalized PGTA decision in women Over 40. *Journal of Reproductive Medicine and Embryology*, 2025; 1(4): 286-297. doi: 10.21608/jrme.2025.370139.1037.