

Archives of Gynaecology and Women's Health

Review Article

AI Predictive Model for Endometrial Preparation in FET Cycles

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Received Date: 29 September 2025; **Accepted Date:** 21 October 2025; **Published Date:** 24 October 2025

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Abstract

Background: Frozen embryo transfer (FET) involves thawing cryopreserved IVF embryos for uterine transfer, and AI predictive models optimize endometrial preparation by integrating clinical, hormonal, and imaging data to improve implantation success. So, the aim of this minireview was to demonstrate the role of AI predictive model for endometrial preparation in FET cycles.

Methods: We used different researching sites as PubMed, Springer, Frontiersin, ELSEVIER, Scopus, Web of Science, and Google Scholar. Relevant articles published in peer-reviewed journals were identified using a combination of keywords related to artificial intelligence, endometrial preparation, and frozen embryo transfer. The search included studies published in English up to 2025. Peer-reviewed original articles, systematic reviews, and clinical studies relevant to AI applications in reproductive medicine were included. Conference abstracts, non-English publications, and articles without available full text were excluded. Reference lists of selected papers were also screened to identify additional relevant studies.

Findings: The reviewed studies consistently showed that AI models contribute to improved assessment of embryo quality and endometrial receptivity in frozen embryo transfer cycles. Predictive algorithms demonstrated potential in personalizing treatment, reducing failed transfers, and enhancing clinical decision-making. Several reports also highlighted the possible cost-effectiveness of AI tools. However, most studies were limited by small sample sizes and the need for external validation.

Conclusion: AI shows great promise in improving embryo and endometrial assessment, personalizing frozen embryo transfer, and reducing failed cycles. Still, large-scale validation is needed before it can be fully integrated into routine clinical practice.

Keywords: Artificial intelligence, Assisted reproduction technology, Endometrial, Frozen embryo transfer, Predictive model, Reproductive medicine.

Introduction

Frozen embryo transfer (FET) is a widely accepted procedure used for the storage and transfer of excess embryos produced in fresh in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) cycles [1]. Increasing live birth rates resulting from improvements in technology, as well as increasing demand for preimplantation genetics testing and

fertility preservation, has led to a progressive increase in the amount of FET cycles over the past decade [2].

A receptive endometrium and the development of good quality embryos with potential implantation are required for successful implantation [3]. Despite extensive research endeavors, one of the more enigmatic aspects of assisted

reproduction technology (ART) remains the mechanism of embryo implantation [4]. Diverse approaches have been taken in research into embryonic evaluation, encompassing morphological assessments, time-lapse study, blastocyst classifications, chromosome screening and, recently, the integration of artificial intelligence (AI) into clinical settings as a proposed supplementary tool to enhance embryo selection, thereby increasing the likelihood of successful pregnancies [5,6].

Artificial intelligence is an emerging technology aimed at embryo selection, although it may also have alternative aims, such as determining the diagnostic accuracy of PGT [5]. In medical practice, artificial intelligence is becoming more accepted and promises the ability to analyze vast data sets at speeds not possible for humans to compute in the accepted timeframe of preimplantation culture [7]. The advanced mathematics lends itself well to a static image or video analysis of embryo development and can compute and analyses cryptic morphological features [8]. By nature, it is non-invasive and, in due course, may be affordable and more accurate than established approaches, as more data are evaluated and compared between different sources [5]. Embryo grading by conventional morphology evaluation and morpho-kinetic analysis may not be the best or most accurate way to predict implantation potential, but it is standardized and recognized globally [9].

These AI qualities could aid in improving the current embryo grading system used by embryologists, which could be non-reproducible and sub-optimal within the clinical practice [10]. An ideal AI for this purpose should be trained on objective, reproducible parameters such as PGT-a or a pregnancy outcome (implantation, presence of sacs, heartbeat, or live birth), [11]. This way, the AI would learn over a standardized and reproducible procedure, rather than on subjective observations. By this approach, and in addition to relevant clinical data from each patient and cycle, an AI could be comparable or improve on the embryologist's performance [12].

Preparation of the Endometrium for Implantation

From donor-egg cycles in women with no ovarian function, it is obvious that only sequential estrogen and progesterone is required for the endometrium to be receptive to embryo implantation [13]. The methodology for achieving estrogen and progesterone levels adequate for implantation can be quite variable but all appear to be equally effective for pregnancy outcome [14]. During the estrogen phase, the endometrium demonstrates linear growth of endometrial glands and blood vessels resulting in the typical trilaminar appearance of the full-thickness endometrium on ultrasound [15]. The proliferation phase ends 2-3 days after ovulation, but there is continuing growth of endometrial glands and vessels under the influence of progesterone within the endometrium, resulting in

coiling of the glands and vessels and glycogen secretion into the glandular lumen [16]. These changes are accompanied by increased proliferation of T-cells, macrophages, and lymphoid nodules, and all these effects result in a homogeneous hyperechoic pattern on ultrasound associated with increased endometrial density [17].

The importance of growth in endometrial thickness during the estrogen phase is quite clear. A previous publication by [18] demonstrated that optimal clinical and ongoing pregnancy rates after in vitro fertilization occurred with endometrial thickness of R8 mm at the end of the estrogen phase in more than 24,000 fresh embryo transfer cycles and R7 mm in more than 20,000 frozen-thawed embryo transfer (FET) cycles. There was a significant decline in pregnancy rates for each mm decrease of thickness below 8 mm in fresh embryo transfers and below 7 mm in the FETs. Therefore, it appears that any route of administration of estrogen that results in an endometrial thickness of R8 mm with a trilaminar appearance on ultrasound will be optimal for embryo implantation [19].

Assessment of the Window of Implantation

A recent development in assessment of the window of implantation (WOI) is a multigene microarray together with bioinformatics that has been proposed to identify genetic alterations associated with endometrial receptivity in an endometrial biopsy [20]. The endometrial receptivity array (ERA) test examines the expression of 238 genes thought to be involved in implantation [21]. The goal of this test is to enable customized FET based on the determination of a personalized WOI. In a mock cycle, endometrial biopsy is performed on the 7th day after an LH surge or on the 6th day of progesterone during a hormone replacement (HRT) cycle [22]. Results are expressed as perceptive, receptive, or postreceptive. If the result is non-receptive, for example, perceptive, the embryo replacement timing is delayed in a subsequent cycle, thereby enabling personalized embryo transfer [23]. Based on the current understanding of the endometrium and the implantation process, the following are the probable and interrelated five mechanisms regulating a receptive endometrium during the WOI (Figure 1), [20].

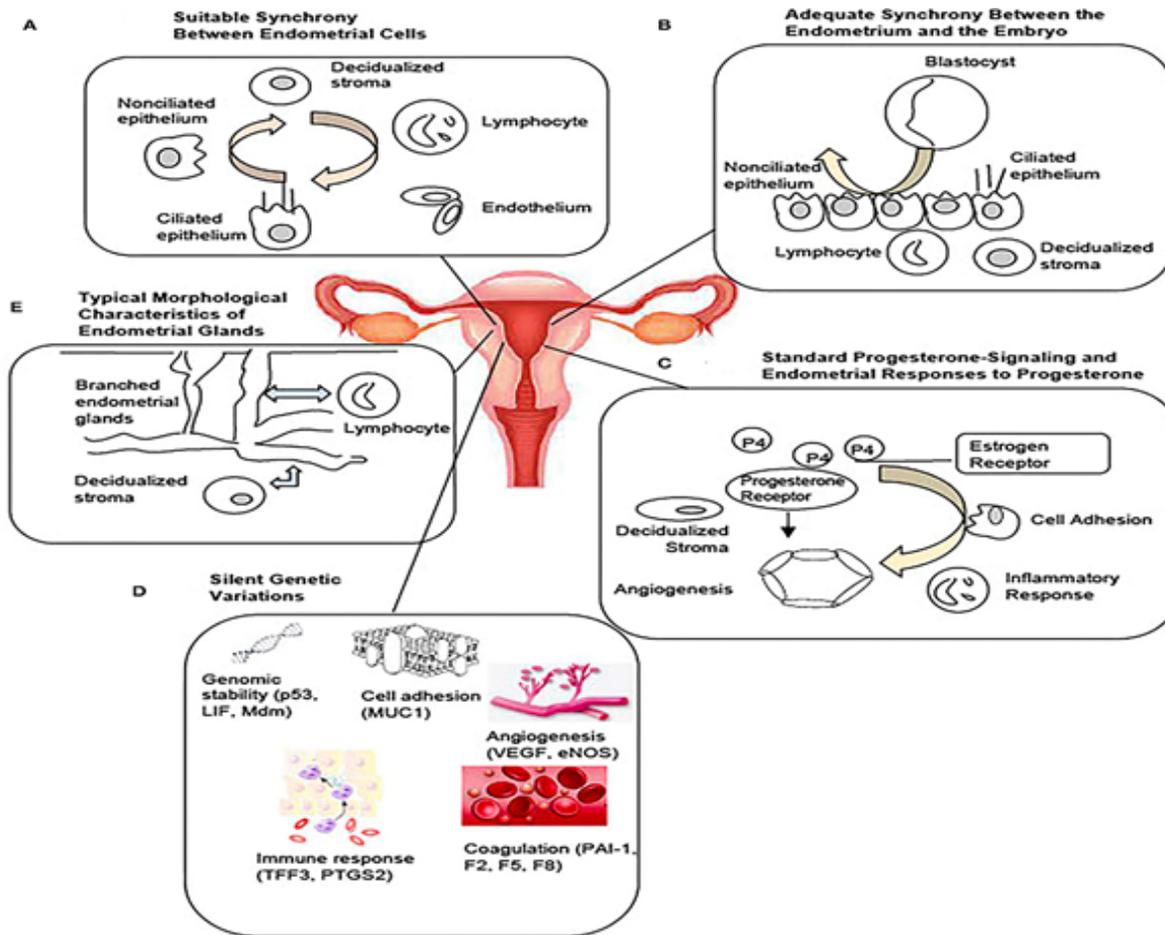


Figure 1: Potential Mechanisms Regulating the Optimal Window of Implantation. Based on current literature, five possible and inter-related mechanisms include: (A) Suitable synchrony between the endometrial cells. (B) Adequate synchrony between the endometrium and the embryo. (C) Standard progesterone-signaling and the endometrial responses to progesterone. (D) Silent genetic variations. (E) Typical morphological characteristics of the endometrial glands may together constitute the molecular basis of a receptive endometrium during the window of implantation [20].

Ultrasound Assessment

The problems with endometrial biopsy tests such as histologic dating, the ERA test, Bcl-6 and SIRT-1 measurement, and the endometrial function test are that they are invasive and the results need to be extrapolated to a subsequent cycle in which the embryo transfer will occur [24,25]. This brings us back to ultrasound, which is non-invasive and can be used in the cycle of interest. There is already evidence that endometrial thickness has good negative predictive ability. That is, an endometrium of < 8 mm thickness on the day of hCG trigger in fresh cycles, or < 7 mm at the end of the estrogen phase in FETs, is associated with an incremental decrease in ongoing pregnancy for each mm decrease in thickness [15]. In contrast, endometrial thickness measured in the progesterone phase before embryo transfer had no significant value in predicting pregnancy outcome [26]. However, the change in endometrial thickness between the day of the hCG trigger and the day of embryo transfer has not been

examined. It was hypothesized that serial ultrasound tests to determine the change in endometrial thickness between the end of the estrogen phase and the time of embryo transfer may be more important to predict pregnancy outcome than the absolute measure of endometrial thickness at either time point alone [27]. Specifically, it was hypothesized that the endometrial thickness should decrease in the natural or artificial luteal phase as the endometrium becomes denser (hyperechoic on ultrasound) because of the secretory changes that are induced by progesterone [28].

Endometrial Preparation Methods

Endometrial preparation protocols prior to FET can generally be divided into three categories: natural cycles, which rely on endogenous hormonal production from a growing follicle; ovulation induction cycles, which use ovulation induction agents to promote follicular growth, primarily in anovulatory

ry women, to mimic a natural cycle; and artificial cycles, in which exogenous estradiol and progesterone are administered. Figure 1 provides a schematic representation of the

endometrial preparation methods and the recommended approaches [29].

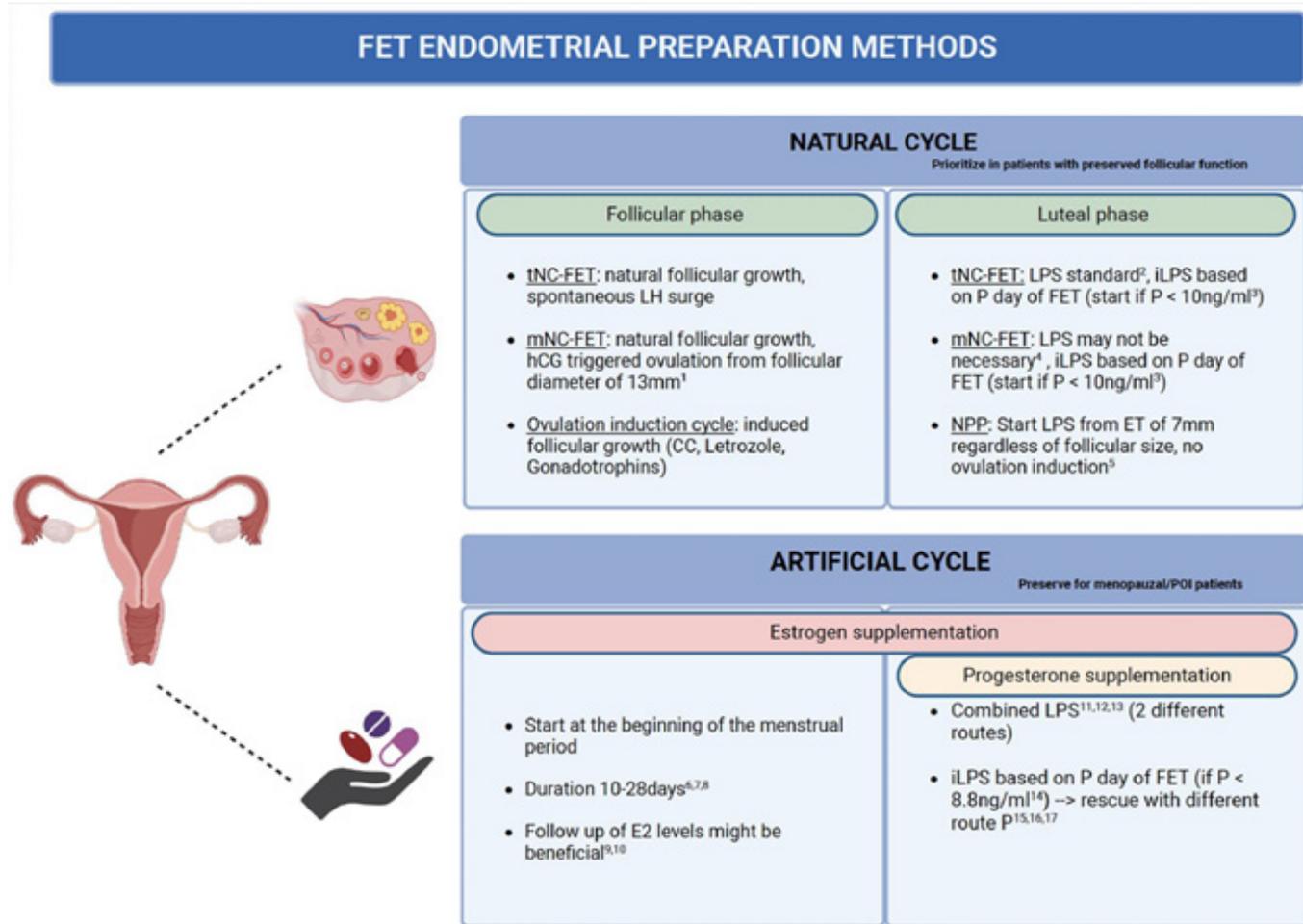


Figure 2: Schematical representation of different endometrial preparation methods prior to frozen embryo transfer (FET). tNC, true natural cycle; mNC, managed natural cycle; CC, clomiphene citrate; NPP, natural proliferative phase; LPS, luteal phase support; iLPS, individualized LPS; P, progesterone; ET, endometrial thickness; E2, oestradiol [29].

Natural Cycle Frozen Embryo Transfer

Endometrial changes and preparation are driven by hormonal production associated with follicular growth, ovulation, and formation of the corpus luteum [30]. This process leads to proliferative changes, followed by secretory transformations of the endometrium, ultimately resulting in a receptive state. During the follicular phase, ultrasonographic evaluation of follicular growth and endometrial thickening is performed to assess an adequate endometrial lining, generally considered sufficient when it exceeds 6.5–7 mm [31]. Hormonal blood sampling may be useful to assess adequate follicular oestradiol production, and to detect premature ovulation characterized by an early progesterone rise, generally considered as more than 1.0 ng/ml [32].

True-NC (t-NC)

For t-NC, transvaginal ultrasonography is performed on day 2 or 3 of menses to rule out any cyst or corpus luteum prevailing from the previous cycle [33]. Cycle cancellation is usually undertaken in cycles with serum P₄ >1.5 ng/ml on day 2 or 3 of menses, even though this practice has been extrapolated from fresh embryo transfer cycles [34]. Transvaginal ultrasonographic monitoring is usually started on day 8-10 and endocrine monitoring is performed, using serum E2, LH and P4 measurements when the leading follicle attains a mean diameter of approximately 15 mm in diameter [35]. Following frequent endocrine and ultrasonographic monitoring, on alternate days or daily, the day of ovulation is precisely doc-

umented to schedule the timing of FET [36].

Modified-NC

For modified-NC, the initial monitoring is the same as in t-NC; however, ovulation is triggered with hCG once the leading follicle reaches a mean diameter of 16-20 mm [37]. In modified-NC, hCG, not only induces ovulation, but also results in increased serum P4 production during the early and mid-luteal phase, thus, the hCG trigger works as an ovulation trigger as well as an early LPS. The place for endocrine monitoring in modified NC is controversial [38,39]. Whether monitoring of serum P4 and LH levels in modified-NC FET cycles has added clinical value needs to be explored [40].

Determination Of Ovulation Onset and Timing of Transfer

Earlier studies yielded conflicting results regarding the efficacy of using a human chorionic gonadotrophin (HCG) trigger in natural cycle frozen embryo transfer (NC-FET) cycles [40,41]. More recent research by Mackens et al. (2020) and Ranisavljevic et al. (2025) [42,43] confirmed that the use of HCG in NC-FET results in comparable pregnancy outcomes, thereby allowing for more flexible planning. FET is typically timed based on either the onset of spontaneous ovulation referred to as 'true NC-FET' (tNC-FET) or by the administration of HCG termed 'modified NC-FET' (mNC-FET), [44]. Preliminary data from a recent RCT involving 604 patients compared pregnancy outcomes following single blastocyst transfers performed either 6 or 7 days after an HCG trigger, and found no significant difference in LBR (33.8% versus 34.5% for day 6 versus day 7 transfers, respectively; adjusted risk ratio 0.98, 95% CI 0.76–1.24), confirming a multiday window for optimal implantation [45]. Similarly, a retrospective cohort study evaluating euploid embryo transfers found higher LBR when transfers were performed 160 ± 4 h post-HCG administration, although LBR remained highly effective within a broader time range [46].

Luteal Phase Support in Natural Cycle Frozen Embryo Transfer

In NC-FET, progesterone production is predominantly regulated by the corpus luteum, a transient endocrine gland formed after ovulation from residual granulosa and theca cells [47]. During the luteal phase, progesterone production by the corpus luteum is driven by LH, and in early pregnancy, this function is sustained by HCG produced by the trophoblast [48]. Progesterone production remains dependent on the corpus luteum until the placenta assumes this role around week 5–7 of gestation. An adequate mid-luteal progesterone concentration near the time of embryo transfer is crucial to achieve successful pregnancy outcomes [49]. A retrospective study by Gaggiotti-Marre et al. (2020) [50] demonstrated significantly higher LBR when the progesterone concentration exceeded 10 ng/ml on the day before blastocyst transfer in tNC-FET. Moreover, 37% of their study population exhib-

ited a low progesterone concentration, indicating that a substantial proportion of patients may experience luteal phase deficiency. A more recent RCT by Wånggren et al. (2022) [51] demonstrated that LPS initiated from the day of transfer in tNC-FET, regardless of progesterone concentration, was associated with improved LBR. In summary, LPS may be unnecessary in mNC-FET due to HCG-stimulated support of the corpus luteum, whereas it may benefit patients undergoing tNC-FET, particularly those with a low progesterone concentration on the day of blastocyst transfer or in cases of inaccurately diagnosed ovulation.

Ovulation Induction Cycles

Ovulation induction cycles are largely comparable with NC-FET, with the primary distinction being that follicular growth is stimulated using ovulation induction agents such as aromatase inhibitors, selective oestrogen receptor modulators, or gonadotrophins [52]. This approach may be particularly advantageous for anovulatory patients, as it preserves natural ovulation and the protective functionality of the corpus luteum [29]. In patients with polycystic ovary syndrome, studies have demonstrated a lower risk of hypertensive disorders of pregnancy in letrozole-induced cycles compared with artificial cycles [53]. Furthermore, research has suggested that letrozole-induced cycles may yield more favourable pregnancy outcomes than artificial or even natural cycles in normo-ovulatory patients [54,55]. Additional investigations are necessary to determine whether letrozole-induced cycles are superior to other preparation methods, and whether the suppression of oestradiol production by letrozole leads to enhanced progesterone production during the luteal phase [29].

Artificial Cycle Frozen Embryo Transfer

In artificial cycle frozen embryo transfer (A-FET), endometrial preparation is achieved through the sequential administration of oestradiol and progesterone to replicate the hormonal changes observed in a natural cycle. The administration of exogenous oestradiol suppresses follicular growth via negative feedback; as a result, most AC-FET are anovulatory [56].

Oestradiol Supplementation

Oestradiol supplementation in AC-FET typically begins at the start of the menstrual cycle and continues for 14 days or longer, consistent with the standard duration of the follicular phase, until an endometrial lining of 6.5–7 mm is achieved [31]. However, prolonged oestradiol administration exceeding 28 days until FET was associated with a decrease in LBR, as shown in an observational cohort study of 1377 cycles [57]. These findings were not confirmed by a larger retrospective study by Rodríguez-Varela (2023) [58], which analyzed more than 7000 cycles and found no association between oestradiol duration and pregnancy rate. Mid-luteal oestradiol concentration measured on the day of blastocyst

transfer may further influence pregnancy outcomes. Concentrations between 292 pg/ml and 409 pg/ml were associated with optimal outcomes, while concentrations outside this range correlated with a reduced pregnancy rate [59].

Progesterone Supplementation

Progesterone supplementation can be administered following adequate oestradiol priming to induce secretory changes in the endometrium, thereby opening the window of implantation [40 & 60]. Individualized LPS has gained attention in AC-FET, largely due to the work of Labarta et al. (2021) [61], who identified reduced pregnancy outcomes when the progesterone concentration fell below 8.8 ng/ml on the day of transfer. Subsequent studies demonstrated that adding subcutaneous progesterone can rescue such cycles, resulting in comparable pregnancy outcomes [62]. Similarly, oral dydrogesterone has also shown potential as a rescue strategy (Mackens et al., 2023; Metello et al., 2024) [63].

Significant intraday variation in serum progesterone concentration has been documented, reflecting the pharmacokinetics of exogenously administered progesterone, as endogenous progesterone is typically absent in AC-FET [64]. Other routes of progesterone administration – such as oral dydrogesterone, and intramuscular and subcutaneous progesterone – are used less commonly but exhibit different pharmacokinetic profiles and corresponding cut-off levels for adequate progesterone during the mid-luteal phase [29]. Combination strategies using different routes of progesterone administration are gaining attention, with several studies demonstrating superiority over monotherapy. These combination approaches may offer a viable alternative when mid-luteal progesterone measurements and subsequent rescue strategies are not feasible [48,65].

Mild-Ovarian Stimulation (Mild-OS)

Mild OS with an oral agent (CC or letrozole) and/or exogenous gonadotropins may be used to prime the endometrium for FET [40]. For this purpose, mild OS is performed with <150 IU urinary/recombinant follicle stimulating hormone (FSH)/day, letrozole at a dose of 2.5 – 5 mg/day or CC at a dose of 50-100 mg/day, starting on the 2nd or 3rd day of the cycle. The follicular response is monitored by frequent vaginal ultrasonography and/or serum endocrine assessment. Human chorionic gonadotropin is administered when the diameter of the leading follicle is greater than 17 mm, endometrial thickness ≥ 7 mm and serum E2 level >150 pg/ml [66]. The timing of the FET is scheduled according to the day of embryo freezing; day-3 embryos are transferred on hCG+5 and day-5/6 embryos are transferred on hCG+7 [67].

The rationale for mild OS in regularly cycling women is to improve subtle defects in folliculogenesis and subsequent luteal phase, resulting in a better endometrial milieu for embryo implantation. In addition, mild-OS avoids the reported risks (e.g. thromboembolic events) associated with exogenous

E2 and P administration in HRT cycles. Letrozole is an aromatase inhibitor; it has a half-life of ~2 days compared to ~2 weeks of CC. Unlike CC, the hypothalamic-pituitary-ovarian axis is intact during letrozole use. Letrozole has no negative effect on the endometrium [35].

Pregnancy Outcomes Between Different Protocols

When comparing pregnancy outcomes between NC-FET and AC-FET, the latest Cochrane review concluded that there is no evidence favoring one method over the other [68]. Additionally, a recent large RCT, which was powered to detect differences in LBR between natural, modified natural and artificial cycles, confirmed these findings, showing no significant differences in LBR in the intention-to-treat analysis (37%, 33% and 34%, respectively). Given that many patients switched from NC-FET or mNC-FET to AC-FET after a cancelled cycle, the per-protocol analysis is important to interpret the outcomes accurately. This analysis yielded similar results (LBR 33.7%, 31.0% and 34.0% for NC-FET, mNC-FET and AC-FET, respectively), [69]. However, a recently published large multicenter cohort study reported that AC-FET was associated with significantly higher rates of pregnancy loss (36.5%, 25.7% and 23.6% for AC-FET, ovulation induction FET and NC-FET, respectively) and lower LBR (16.9%, 18.8% and 19.3% for AC-FET, ovulation induction FET and NC-FET, respectively) compared with ovulation induction or natural cycles [70].

Using transvaginal ultrasonography to measure the endometrial thickness is the most common clinical approach to evaluate endometrial receptivity [71]. A retrospective study compared two regimens of endometrial preparation in 2664 women with PCOS undergoing FET. The results showed that the endometrial thickness on the day of progesterone supplementation and on the day of embryo transfer was significantly thicker in patients receiving mild-OS with letrozole than in those receiving AC [72]. Additionally, after adjusting the related confounding factors, this study demonstrated that LBR was significantly higher, and the early pregnancy loss rate was lower in the letrozole group compared with the AC group [73]. The endometrial thickness was significantly thinner in mild-OS with CC than in AC [68].

Role of Artificial Intelligence in Reproductive Medicine

AI functions today as an augmenting tool that extracts patterns from large, multimodal fertility datasets (images, time-lapse videos, ultrasound, hormone panels, and clinical records) to support diagnosis, prognosis and protocol personalization [74]. In reproductive medicine this has been translated into objective, reproducible assessments (for example of embryo morphology or endometrial features) that reduce inter-observer variability and can surface subtle signals humans miss enabling more data-driven counseling and research hypotheses [75]. It was emphasized that AI enables more objective and personalized fertility care, integrating

multimodal data (imaging, hormonal profiles, patient history) into predictive systems [76].

AI-based Endometrial Analysis as a Predictor of ART Outcomes

A receptive endometrium and the development of good quality embryos with potential implantation are required for successful implantation [77]. Despite extensive research endeavors, one of the more enigmatic aspects of assisted reproduction technology (ART) remains the mechanism of embryo implantation. Diverse approaches have been taken in research into embryonic evaluation, encompassing morphological assessments, time-lapse studies, blastocyst classifications, chromosome screening, and, recently, the integration of artificial intelligence into clinical settings as a proposed supplementary tool to enhance embryo selection, thereby increasing the likelihood of successful pregnancies [5,6,78].

Higher live birth rates with endometrial thickness of 10–12 mm were demonstrated in cycles where a fresh embryo transfer was performed, and in frozen embryo transfer cycles, live birth rates plateaued after 7–10 mm endometrial thickness [31]. The intricate cellular composition of the endometrium has been explored by Greenwald et al. (2022) and Yamaguchi et al. (2021) [79,80] surpassing traditional parameters such as trilaminar patterns and overall thickness measurements in their studies. A novel “rhizome” structure, which is an intricate network of endometrial glands extending

along the myometrium, has been identified in these studies through the utilization of 3D imaging [81]. This discovery provides a novel framework for comprehending the physiology of the endometrium concerning its receptivity to embryos [4]. Notably, AI has been widely used for embryo selection [12]. A recent study introduced a methodology that examines both the absolute and relative dimensions of the external layers of the endometrium. This approach departs significantly from conventional, obsolete and misleading paradigms. AI model was trained based on the findings related to the external layers of the endometrium. It was observed that when the external layers constitute 50% or more of the total endometrial composition in a trilaminar configuration, there is a substantial improvement in pregnancy rates. On the contrary, when the proportion of external layers falls below 50% of the endometrial thickness, a noticeable decline in pregnancy rates occurs [82].

Endometrial Evaluation and Classification System

AI model was trained based on the Asch classification using an ultrasonographic endometrial assessment, as follows: 1) well-defined hyperechoic external layers, 2) thickness of the external layers, 3) echogenic mid line, 4) entirety thickness of the endometrium, 5) hypoechoic intermediate layer positioned between external layers and midline, and 6) the percentage of external layers relative to the total endometrial thickness (equal or greater than 50%, or less than 50%). The resultant classification scheme is summarized in Figure 3 [82].

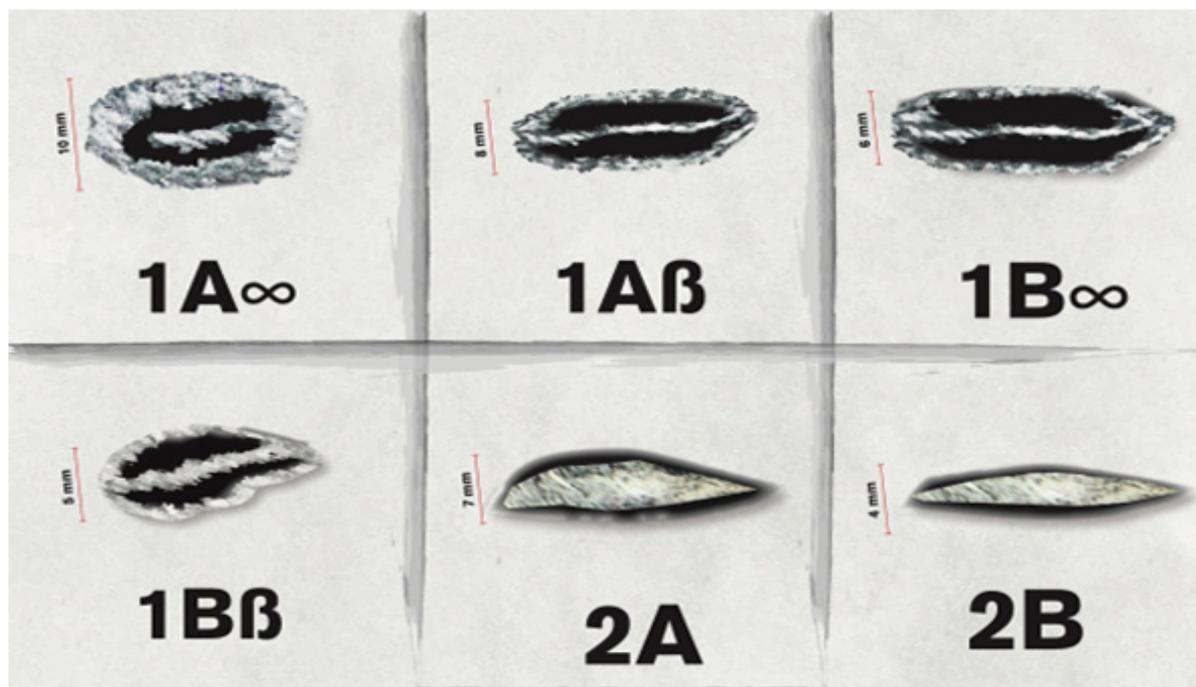


Figure 3: Asch endometrial grading system. Based on the endometrium grading system and the likelihood of pregnancy, the images were categorized into good and bad [82].

AI-Aided Prediction of Endometrial Receptivity

EndoClassify AI model

The development of the AI model involved the de-identification of the images selected for the study, image augmentation processes to train the model with high-quality, diverse, and relevant data, followed by the evaluation and selection of segmentation (Attention U-Net) and classification (Inception GoogLeNet) models with a relatively modest computation cost²² (Figure 4), [83]. A two-tiered AI model (EndoClassify) was implemented using convolutional neural networks. The introduction of the EndoClassify AI model enhances the as-

essment of the endometrium by introducing a new method to evaluate endometrial conditions based on trans vaginal ultrasound images [84]. Image quality is objectively evaluated by this model, and images are categorized as either 'Good' or 'Bad' according to a rigorous set of criteria [85]. Furthermore, valuable insights are provided by quantifying the percentage likelihood of pregnancy for each classification, furnishing clinicians with essential information for decision-making regarding embryo transfer or the postponement of the cycle [4].

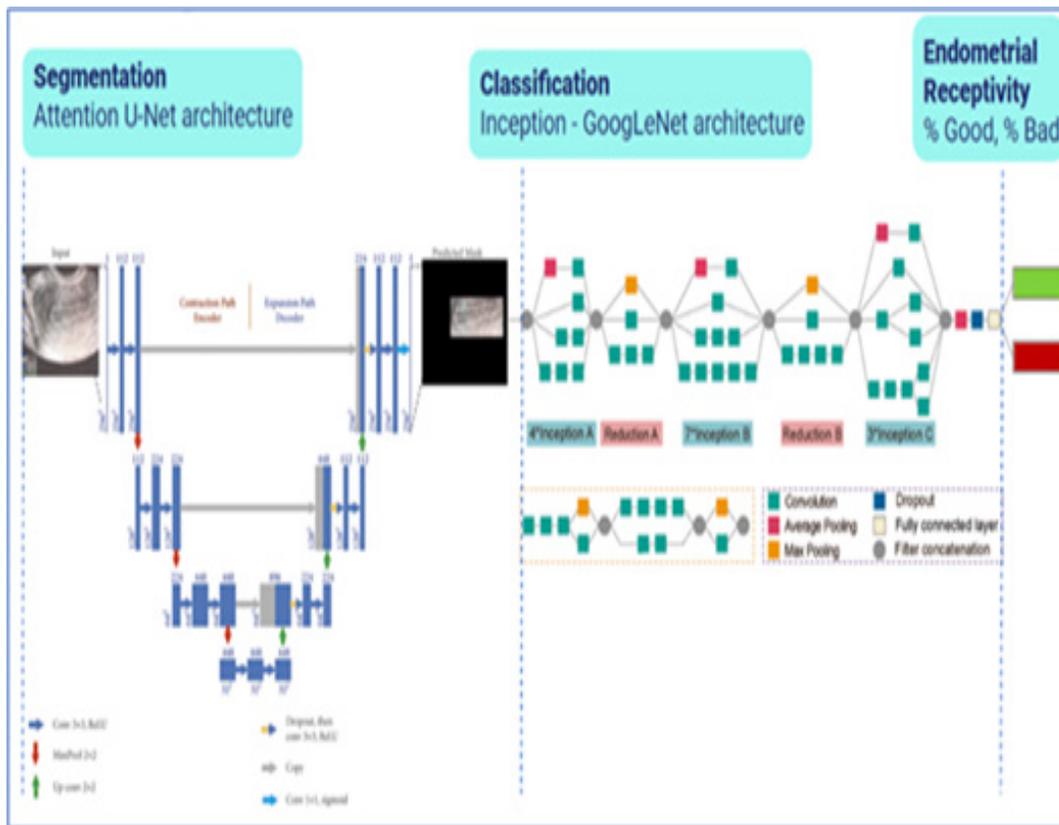


Figure 4: Two-Tiered AI model, segmentation and classification [4].

The decision to employ a two-step process was based on the benefits of applying segmentation before classification. Initially, segmentation was applied to isolate regions of interest (ROI) from the endometrial ultrasound images. Subsequently, classifications were applied to assign labels to de-identified ROIs by allowing features to be captured by the network at multiple scales and resolutions. This label indi-

cated the degree of endometrial receptivity, expressed as a percentage of a good or bad endometrium, as defined by our novel endometrial classification system. Various AI classification models were evaluated to assess final model's accuracy, precision, and ability to avoid false positive predictions (Figure 5), [82].

| Case | Manual Grading System | | | Endoclassify AI automate endometrial prediction to start the IVF cycle | | | | |
|------|-----------------------|---------------------|----------|--|--|----------------|-------|---------------------|
| | ultrasound image | Manual measurements | Category | Segmentation | | Classification | | Recommendation |
| 1 | | 1,02 | 1 A α | | | 0,9% | 99,1% | Start IVF cycle |
| | | 0,29 | | | | | | |
| | | 0,44 | | | | | | |
| 2 | | 1,12 | 1 A β | | | 26,7% | 73,3% | Start IVF cycle |
| | | 0,29 | | | | | | |
| | | 0,25 | | | | | | |
| 3 | | 0,64 | 1 B α | | | 98,1% | 1,9% | Non start IVF cycle |
| | | 0,18 | | | | | | |
| | | 0,17 | | | | | | |
| 4 | | 0,67 | 1 B α | | | 22,8% | 77,2% | Start IVF cycle |
| | | 0,21 | | | | | | |
| | | 0,15 | | | | | | |
| 5 | | 1,23 | 1 A β | | | 89,0% | 11,0% | Non start IVF cycle |
| | | 0,24 | | | | | | |
| | | 0,25 | | | | | | |
| 6 | | 1,32 | 1 A α | | | 1,3% | 98,7% | Start IVF cycle |
| | | 0,36 | | | | | | |
| | | 0,32 | | | | | | |
| 7 | | 1,26 | 2 A | | | 85,2% | 14,8% | Non start IVF cycle |
| | | 0,42 | | | | | | |
| | | 0,43 | | | | | | |

Figure 5: Manual Endometrium Grading System & EndoClassify AI model [82]

Advantages of AI Predictive Models in Clinical Decision-making

AI-based predictive models provide three major advantages. First, personalization: they combine multiple predictors (e.g., age, endometrial thickness, embryo morphology, medical history) into individualized probability estimates, improving treatment tailoring. Second, efficiency and consistency: randomized trials demonstrated that AI embryo selection is comparable to expert embryologists while being significantly faster [86]. Finally, decision support: predictive tools assist clinicians in optimizing transfer timing, endometrial preparation, and patient counseling, which may reduce failed cycles and resource waste [1].

Clinical Implications and Benefits of AI in Frozen Embryo Transfer

Improved Personalization of Treatment

AI models allow clinicians to integrate multiple clinical, hormonal, and imaging parameters to predict the optimal conditions for frozen embryo transfer [87]. By considering variables such as endometrial thickness, hormonal profiles, and embryo characteristics, AI supports truly individualized treatment planning. Recent studies report that AI-based endometrial receptivity analysis improves transfer timing, which can enhance implantation and pregnancy outcomes compared with conventional protocols [1].

Reduction of Failed Cycles

A major challenge in ART is the high proportion of unsuccessful cycles. AI-driven predictive models can identify embryos with higher implantation potential and determine the optimal uterine environment, thereby reducing the likelihood of failed transfers. For example, machine learning approaches applied to time-lapse imaging have shown higher predictive accuracy for implantation compared with traditional morphology assessment, contributing to fewer failed cycles [88].

Potential Cost-Effectiveness

Repeated failed cycles in IVF and FET increase financial and emotional burden for patients [89]. By improving success rates per transfer, AI systems may reduce the number of attempts needed to achieve pregnancy, lowering overall treatment costs. Preliminary cost-effectiveness analyses suggest that AI-guided embryo selection and transfer optimization could make ART more affordable in the long term, especially as models become widely available and require less manual intervention [90].

Conclusion

Frozen embryo transfer success depends on coordinated embryo quality and endometrial receptivity, yet predicting implantation remains a major challenge in assisted reproduction. Recent advances highlight the role of artificial in-

telligence as a non-invasive, data-driven tool that enhances embryo grading, endometrial evaluation, and transfer timing. Predictive models can integrate multiple variables such as embryo morphology, time-lapse imaging, endometrial thickness, and patient clinical data to provide individualized treatment strategies. By improving personalization of treatment, reducing failed cycles, and offering potential cost-effectiveness, AI holds promise as an adjunct in clinical decision-making. However, further validation through large-scale studies is essential before its integration into routine reproductive practice.

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Citation: Sherif Sobhy Menshawy Khalifa, Mohamed Ismail Abdalkareem Abdallatif, Ahmed Ismail Abd El-Karim AbdEllatif. AI Predictive Model for Endometrial Preparation in FET Cycles. *Arch. Gynaecol. Women. Health*. Vol 4, Iss 1. (2025). DOI: 10.58489/2836-497X/033