Med Pregl 2026; LXXIX(1-2): 45-48. Novi Sad: januar-februar.

SEMINAR FOR PHYSICIANS
SEMINAR ZA LEKARE U PRAKSI

ARTIFICIAL INTELLIGENCE IN *IN VITRO* FERTILIZATION: CURRENT APPLICATIONS, LIMITATIONS AND FUTURE DIRECTIONS

VEŠTAČKA INTELIGENCIJA U PROCESU VANTELESNE OPLODNJE: PRIMENE, OGRANIČENJA I BUDUĆNOST

Daniel BJELICA[1], Tijana STANIVUKOVIĆ[2], Gabriel-Stefan NAĐ[2,3], David STRILIĆ[3] and Artur BJELICA[2,3]

ORCID NUMBER
Daniel Bjelica – 0009-0004-3486-9780
Tijana Stanivuković – 0009-0009-5642-5861
Gabriel-Stefan Nađ – 0000-0002-9938-431X
David Strilić – 0009-0000-1721-904X
Artur Bjelica – 0000-0002-1219-4936

University Clinical Center of Vojvodina, Novi Sad, Radiology Center[1]
Clinic of Gynecology and Obstetrics[2]
University of Novi Sad, Faculty of Medicine Novi Sad[3]

Seminar for physicians
Seminar za lekare u praksi
UDK 618.177-089.888.11:004.8
https://doi.org/10.2298/MPNS2602045B

Abstract

Introduction. Infertility represents a major global health challenge with profound medical, psychological, and social consequences. Despite substantial advances in assisted reproductive techniques, the success rates of *in vitro* fertilization remain limited, largely due to subjectivity in embryo selection and variability in ovarian stimulation management. **Application of artificial intelligence in embryo selection**. Artificial intelligence systems enable the analysis of large and complex datasets, including morphological and morphokinetic embryo characteristics derived from static imaging and continuous developmental monitoring. These approaches enhance the standardization of embryo quality assessment and reduce interobserver variability; however, their performance remains constrained by the quality of training data and the incomplete representation of biological determinants of implantation. **Role of artificial intelligence in ovarian stimulation management**. Algorithms integrating clinical, hormonal, and ultrasonographic parameters facilitate individualized gonadotropin dosing, more accurate determination of final oocyte maturation timing, and reduction of ovarian hyperstimulation risk. Existing studies demonstrate a high level of concordance between algorithm-based recommendations and expert clinical decision-making. **Future directions**. Further advancements are anticipated through the development of multimodal models integrating morphological, clinical, and genetic data, alongside the implementation of explainable systems to enhance transparency and clinical trust. **Conclusion**. Currently, artificial intelligence serves primarily as a decision-support tool rather than a substitute for clinical expertise. Its routine clinical implementation requires robust prospective validation and regulatory approval.

Key words: Artificial Intelligence; Fertilization in Vitro; Reproductive Techniques, Assisted; Embryo Transfer; Infertility; Ovulation Induction; Machine Learning; Decision Support Systems, Clinical

Sažetak

Uvod. Neplodnost predstavlja značajan globalni zdravstveni problem sa dalekosežnim medicinskim, psihološkim i društvenim posledicama. I pored napretka u metodama asistirane reprodukcije, uspešnost postupaka oplodnje van tela i dalje je ograničena, naročito zbog subjektivnosti u selekciji embriona i vođenju ovarijalne stimulacije. **Primena veštačke inteligencije u selekciji embriona**. Savremeni sistemi veštačke inteligencije omogućavaju analizu velikih skupova podataka, uključujući morfološke i morfokinetičke karakteristike embriona dobijene statičkim snimanjem i kontinuiranim praćenjem razvoja. Ovi sistemi doprinose standardizaciji procene kvaliteta embriona i smanjenju varijabilnosti među embriolozima, ali su i dalje ograničeni kvalitetom ulaznih podataka i nedovoljnom obuhvaćenošću svih bioloških faktora relevantnih za implantaciju. **Uloga veštačke inteligencije u vođenju ovarijalne stimulacije.** Algoritmi zasnovani na kliničkim, hormonskim i ultrazvučnim parametrima omogućavaju individualizaciju doziranja gonadotropina, preciznije određivanje trenutka indukcije završnog sazrevanja oocita i smanjenje rizika od sindroma ovarijalne hiperstimulacije. Studije pokazuju visok stepen saglasnosti ovih sistema sa kliničkim odlukama iskusnih lekara. **Budući pravci.** Dalji razvoj ide ka multimodalnim modelima koji integrišu morfološke, kliničke i genetske podatke, kao i ka objašnjivim modelima koji bi povećali kliničko poverenje. **Zaključak**. Veštačka inteligencija trenutno predstavlja alat za podršku odlučivanju, a ne zamenu za kliničko iskustvo. Njena rutinska primena zahteva dodatne prospektivne studije i regulatornu validaciju.

Ključne reči: veštačka inteligencija; vantelesna oplodnja; potpomognute reproduktivne tehnike; transfer embriona; neplodnost; stimulacija jajnika; mašinsko učenje; sistemi za kliničku podršku odlučivanju

Introduction

Infertility affects approximately 15% of couples worldwide and imposes substantial psychological, social, and economic burdens [1]. When natural conception is unsuccessful, assisted reproductive technologies (ART) – particularly *in vitro* fertilization (IVF) – are commonly employed. IVF encompasses controlled ovarian stimulation, oocyte retrieval, laboratory fertilization, embryo culture, and embryo transfer [2,3].

Corresponding author: Gabriel-Stefan Nađ, E-mail: gabrielnadj021@gmail.com, gabriel-stefan.nadj@mf.uns.ac.rs

Abbreviations

AFC	– antral follicle count
AI	– artificial intelligence
AMH	– anti-Müllerian hormone
ART	– assisted reproductive technologies
BMI	– body mass index
CNN	– convolutional neural network
DL	– deep learning
E2	– estradiol
FSH	– follicle-stimulating hormone
ICSI	– intracytoplasmic sperm injection
ILETIA	– individualized trigger-to-oocyte pickup interval estimation algorithm
IVF	– *in vitro* fertilization
ML	– machine learning
OHSS	– ovarian hyperstimulation syndrome
P4	– progesterone
PGT-A	– preimplantation genetic testing for aneuploidies
XAI	– explainable artificial intelligence

Despite continuous technological advancements, clinical outcomes – including pregnancy, implantation, and live-birth rates per embryo transfer – remain modest (typically < 30%) and are influenced by factors such as maternal age, ovarian response, embryo quality, and endometrial receptivity [3,4].

Conventional embryo selection relies on morphological assessment at predefined time points, with embryologists evaluating blastomere symmetry, fragmentation, and blastocyst morphology to guide transfer decisions [4,5]. However, this approach is inherently subjective and prone to interobserver variability, and morphologically normal embryos may still harbor chromosomal or functional abnormalities that comprise implantation potential [4,5]. Time-lapse incubation systems provide continuous morphokinetic data – such as cleavage timing, compaction, and blastulation – while maintaining stable culture conditions. Nevertheless, interpretation of these data largely remains dependent on human judgment [5,6].

Against this backdrop, artificial intelligence (AI), including machine learning (ML) and deep learning (DL), has emerged as a powerful tool for analyzing large, heterogeneous datasets encompassing imaging, time-lapse recordings, hormonal profiles, ultrasonographic parameters, and clinical variables [2,7]. AI facilitates the identification of complex patterns beyond human perception, offering the potential to standardize embryo assessment and enable personalized decision-making through the IVF process. Several studies have demonstrated improved predictive performance of AI models compared to conventional morphological evaluation in selected datasets [4]. The clinical relevance of IVF outcomes at our institution has previously been documented, providing a baseline for longitudinal outcome assessment [8].

AI in embryo selection

AI-based embryo assessment models range from traditional ML classifiers to DL architectures, particularly convolutional neural networks (CNNs), trained on static images and time-lapse sequences. Deep learning extracts hierarchical visual features – including inner cell mass quality, trophectoderm structure, blastocoel expansion, and compaction dynamics – and integrates them with morphokinetic parameters to predict outcomes such as blastocyst development, implantation potential, and euploidy [4,5,9–11]. The incorporation of time-lapse imaging enhances temporal resolution, enabling the identification of kinetic markers (e.g., timing of early cleavages) that are not discernible from static images alone [5,11].

Key advantages of AI include improved reproducibility, scalability, and reduced variability associated with operator fatigue. Several retrospective and prospective studies suggest that AI-based classifiers may outperform conventional manual grading systems in predicting implantation and clinical pregnancy rates within specific cohorts [4,10]. Additionally, AI systems can systematically rank embryos and provide a valuable second opinion to support embryologist decision-making.

However, significant limitations persist. Many AI models rely on "ground truth" labels from embryologist assessments or clinical outcomes, rendering them susceptible to bias inherent in the training data. Consequently, AI systems may inadvertently perpetuate or amplify existing interobserver variability and clinic-specific practices rather than mitigate them [7]. Furthermore, image-based models fail to account for non-morphological determinants of implantation, such as endometrial receptivity, immunological factors, and sub-microscopic chromosomal abnormalities, unless such variables are explicitly incorporated [5]. Another major challenge is the limited interpretability of DL models, often characterized as "black boxes", which complicates clinical validation, regulatory approval, and user trust [5,7,12,13].

Given these constraints, current AI applications are best regarded as decision-support tools that enhance standardization and assist in embryo prioritization, while final clinical decisions remain under the responsibility of experienced embryologists [4,7].

AI in ovarian stimulation management

Ovarian stimulation protocols – including regimen selection, initial follicle-stimulating hormone (FSH) dosing, dose adjustments, timing of ovarian trigger, and prevention of ovarian hyperstimulation syndrome (OHSS) – significantly affect oocyte yield and cycle safety. Traditionally guided by ultrasonographic findings, estradiol levels, and clinician expertise, this process is subject of considerable inter-physician variability.

AI models trained on large clinical datasets offer the potential to standardize and optimize these decisions. Relevant inputs variables include patient age, body mass index (BMI), anti-Müllerian hormone (AMH) levels, antral follicle count (AFC), baseline hormonal profiles, and dynamic follicular and estradiol measurements. For example, Letterie et al. developed a decision-support system trained on 2,603 IVF cycles (validated on 556 cycles), capable of recommending daily clinical actions - such as continuation or cessation of stimulation, dose adjustment, trigger timing, or cycle cancellation – with 92-96% concordance with clinician teams [14]. Similarly, prospective multicentre studies (e.g., Canon et al.) have demonstrated reduced cumulative FSH consumption without compromising the number of mature (MII) oocytes when AI-assisted recommendations are applied [15]. Real-world data further suggest improved stimulation efficiency without adverse effects on clinical outcomes [16].

Explainable AI (XAI) approaches applied to large datasets (e.g., 19,082 cycles in Hanassab et al.) have identified intermediate-sized follicles (13–18 mm) as strong predictors of mature oocytes and high-quality blastocysts, whereas a predominance of follicles > 18-mm is associated with progesterone elevation and suboptimal outcomes. These findings indicate that ovulation trigger timing should account for the overall follicular distribution rather than solely the leading follicle [17]. Emerging algorithms, such as ILETIA, aim to individualize the interval between ovulation trigger and oocyte retrieval, thereby optimizing MII oocyte yield through patient-specific timing adjustments [18].

The principle advantages of AI in this domain include improved standardization, individualized treatment strategies, reduced gonadotropin consumption, and optimized synchronization of follicular maturation [14–19]. Nonetheless, limitations parallel those observed in embryo selection, including dependence on retrospective datasets, limited external validation, potential bias inheritance, and a scarcity of randomized controlled trials with live birth as primary endpoint [2,14–19]. Additionally, challenges related to interpretability and regulatory approval continue to impede clinical adoption [12,13].

Future directions

Future developments in AI-assisted IVF are expected to focus on multimodal integration, combining embryo imaging/time-lapse, and morphokinetics with hormonal profiles (E2, P4, AMH), follicular dynamics, endometrial parameters, and genetic testing data (PGT-A) to improve prediction of implantation and live–birth outcomes [10,11]. Integration of imaging data with molecular and gene-expression profiles from the trophectoderm may enable simultaneous assessment of morphological, functional, and genetic embryo competence [20].

In parallel, robotic systems incorporating AI-guided image recognition are being developed assistance for micromanipulation such as intracytoplasmic sperm injection (ICSI). These systems demonstrate technical feasibility in experimental settings, enabling precise identification of cellular structures and stabilization of micromanipulation instruments; however, they remain investigational and lack regulatory approval for routine clinical use [21,22]. The concept of an integrated "AI embryologist assistant" – capable of monitoring ovarian stimulation, optimizing dosing strategies, ranking embryos, and supporting procedural tasks – holds considerable promise. However, its realization will require standardized datasets, robust explainability, clear regulatory frameworks, and high-quality randomized evidence demonstrating improvements in live-birth outcomes [14,23–25].

Conclusion

Artificial intelligence provides objective and reproducible support across critical stages of *in vitro* fertilization, particularly in embryo selection and ovarian stimulation management. At present, it serves to augment – rather than replace – clinical expertise. Key barriers to broader implementation include heterogeneity of training data, limited external validation, scarcity lack of randomized controlled trials with live birth as the primary endpoint, and challenges related to model interpretability. Future progress will depend on the development of multimodal, explainable artificial intelligence systems, rigorous clinical validation, and robust regulatory oversight to ensure patient safety and maintain clinical accountability.

References

1. Wang R, Pan W, Jin L, Li Y, Geng Y, Gao C, et al. Artificial intelligence in reproductive medicine. Reproduction 2019;158(4): R139-54.

2. Wu S, Wang X, Liu Y, Ren Y, Zhao M, Song H, et al. Predictive models for live birth outcomes following fresh embryo transfer in assisted reproductive technologies using machine learning. J Transl Med 2025;23(1):1004.

3. Mina A, Younesi M, Doohandeh T, Darzi S, Ardehjani NA, Sheibani S, et al. Predicting pregnancy outcomes in IVF cycles: a systematic review and diagnostic meta-analysis of artificial intelligence in embryo assessment. Contracept Reprod Med 2025;10(1):59.

4. Papamentzelopoulou MS, Prifti IN, Mavrogianni D, Tseva T, Soyhan N, Athanasiou A, et al. Assessment of artificial intelligence model and manual morphokinetic annotation system as embryo grading methods for successful live birth prediction: a retrospective monocentric study. Reprod Biol Endocrinol 2024;22(1):27.

5. AlSaad R, Abusarhan L, Odeh N, Abd-alrazaq A, Choucair F, Zegour R, et al. Deep learning applications for human embryo assessment using time-lapse imaging: scoping review. Front Reprod Health 2025;7:1549642.

6. Ouyang X, Wei J. Multi-Modal Artificial Intelligence of Embryo Grading and Pregnancy Prediction in Assisted Reproductive Technology: A Review [Internet]. arXiv; 2025 [cited 2025 Nov 2]. Available from: https://arxiv.org/abs/2505.20306

7. Allahbadia GN, Allahbadia SG, Gupta A. In Contemporary Reproductive Medicine Human Beings are Not Yet Dispensable. J Obstet Gynecol India 2023;73(4):295-300.

8. Kostić S, Bjelica A, Kopitović V, Starčević M, Trninić-Pjević A. Rezultati i iskustva nakon hiljadu ciklusa vantelesne oplodnje na Klinici za ginekologiju i akušerstvo u Novom Sadu. Med Pregl 2011;64(11-12):565-70.

9. Khan HL, Khan S, Bhatti S, Abbas S. Role of Artificial Intelligence in Quality Assurance in ART: A Review. FandR 2023;05 (01):1-7.

10. Khosravi P, Kazemi E, Zhan Q, Malmsten JE, Toschi M, Zisimopoulos P, et al. Deep learning enables robust assessment and selection of human blastocysts after in vitro fertilization. NPJ Digit Med 2019;2(1):21.

11. Tran D, Cooke S, Illingworth PJ, Gardner DK. Deep learning as a predictive tool for fetal heart pregnancy following time-lapse incubation and blastocyst transfer. Hum Reprod 2019;34(6): 1011-8.

12. Fanton M, Nutting V, Rothman A, Maeder-York P, Hariton E, Barash O, et al. An interpretable machine learning model for individualized gonadotrophin starting dose selection during ovarian stimulation. Reprod BioMed Online 2022;45(6):1152-9.

13. Chan B. Black-box assisted medical decisions: AI power vs. ethical physician care. Med Health Care Philos 2023;26(3):285-92.

14. Letterie G, Mac Donald A. Artificial intelligence in in vitro fertilization: a computer decision support system for day-to-day management of ovarian stimulation during in vitro fertilization. Fertil Steril 2020;114(5):1026-31.

15. Canon C, Leibner L, Fanton M, Chang Z, Suraj V, Lee JA, et al. Optimizing oocyte yield utilizing a machine learning model for dose and trigger decisions, a multi-center, prospective study. Sci Rep 2024;14(1):18721.

16. Bixby CJ, Miller B. Real-world use of an artificial intelligence-powered clinical decision support tool for ovarian stimulation. F&S Reports 2025;6(2):140-6.

17. Hanassab S, Nelson SM, Akbarov A, Yeung AC, Hramyka A, Alhamwi T, et al. Explainable artificial intelligence to identify follicles that optimize clinical outcomes during assisted conception. Nat Commun 2025;16(1):296.

18. Wu B, Li Q, Kuang Z, Gao H, Liu X, Guo H, et al. ILETIA: An AI-enhanced method for individualized trigger-oocyte pickup interval estimation of progestin-primed ovarian stimulation protocol [Internet]. arXiv; 2025 [cited 2025 Nov 2]. Available from: https://arxiv.org/abs/2501.16386

19. 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;120(1):8-16.

20. More A, Chimurkar V, Mahajan S, Dakre S, Anjankar N, More D. The Integration of Artificial Intelligence in In Vitro Fertilization: A Comprehensive Narrative Review. J Pharm Bioall Sci 2025;17(Suppl 1):S155-8.

21. Jiang VS, Bormann CL. Artificial intelligence in the in vitro fertilization laboratory: a review of advancements over the last decade. Fertil Steril 2023;120(1):17-23.

22. Sadeghi MR. Will Artificial Intelligence Change the Future of IVF? JRI [Internet]. 2022 [cited 2025 Nov 2]. Available from: https://publish.kne-publishing.com/index.php/JRI/article/view/10003

23. Kakkar P, Gupta S, Paschopoulou KI, Paschopoulos I, Paschopoulos I, Siafaka V, et al. The integration of artificial intelligence in assisted reproduction: a comprehensive review. Front Reprod Health 2025;7:1520919.

24. European Society of Human Reproduction and Embryology. Guideline on Ovarian Stimulation for IVF/ICSI [Internet]. Grimbergen (BE): ESHRE; 2019 [cited 2025 Nov 3]. Available from: https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Ovarian-Stimulation-in-IVF-ICS

25. Practice Committee of the American Society for Reproductive Medicine. Comprehensive guidance for human embryology, andrology, and endocrinology laboratories: management and operations: a committee opinion [Internet]. Birmingham (AL, US): ASRM; 2022 [cited 2025 Nov 3]. Available from: https://www.asrm.org/practice-guidance/practice-committee-documents/comprehensive-guidance-for-human-embryology-andrology-and-endocrinology-laboratories-management-and-operations-a-committee-opinion-2022/

Rad je primljen 21. I 2026.
Recenziran 20. III 2026.
Prihvaćen za štampu 20. III 2026.
BIBLID.0025-8105:(2026):LXXIX:1-2:45-48.