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An Innovative Approach To Overcoming Recurring Failures Of Assisted Reproductive Technologies

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Abstract: The introduction of artificial intelligence (AI) in reproductive medicine is one of the most important modern trends in global healthcare. AI technologies allow to significantly improve the diagnostic system, the method of stimulation, the development of new protols stimulation, as well as improve the quality of eggs and embryos to achieve positive results. positive results. Despite the obvious advantages of using AI-based algorithms, there are a number of limitations to the implementation of these programs in reproductive medicine. Among such challenges, the issue of ethical constraints on AI and the responsibility for the decisions that the program is the program is capable of making.To date, the primary goal of research in the Today, the main challenge for AI research should be to improve the accuracy of the program product.

Conclusion: The review considers the main areas of AI application, various machine learning techniques, ethical limitations and prospects for implementation of these programs in clinical practice, including assisted reproductive technologies (ART).

Keywords: Artificial intelligence, ART, Reproductive Medicine.

Introduction: In 1956, American computer scientist John McCarthy first proposed the term "artificial intelligence" (AI), which consisted of the ability of machines to learn. AI was most actively developed in the mid-2000s, when the technological support of computer programs made it possible to analyze a large array of structured and unstructured data [1]. Today, AI is based on machine learning, during which the relationship between objects and responses is established not by explicitly solving a problem, but by identifying patterns based on solving many similar problems [2]. Machine learning can be carried out using several methods: supervised learning, unsupervised learning, and reinforcement learning. The most widespread method is supervised learning, which involves training an algorithm based on a set of labeled input data associated with known output parameters [3]. Unsupervised learning does not assume the presence of a specific outcome and analyzes the relationships and patterns between the objects under study. This technique is most often used to differentiate and classify various images [4]. Reinforcement learning is a special case of supervised learning, but the model itself acts as a teacher, i.e. the system learns by constantly analyzing its own errors. It is worth noting that programs developed using AI do not require defining all the dependencies between the input parameters and the analyzed result [5]. However, the data obtained using machine learning is not always superior in quality and predictive ability to the information obtained during the construction of simpler mathematical models. For example, when solving problems with clear and simple relationships between input parameters, the use of AI-based software may be less accurate [6]. Thus, algorithms using AI are most in demand when solving complex problems in which it is impossible to take into account the full variety of different dependencies and the potential influence of one factor on another. In the field of healthcare, AI is becoming increasingly popular, including in the field of assisted reproductive technologies (ART) [7]. Currently, reproductive medicine is experiencing a rapid narrowing of the gap between science and clinical practice. The accelerated development of scientific and technological progress and the introduction of AI in the field of assisted reproductive technologies (ART) pose a number of new issues for specialists that need to be resolved as soon as possible. In reproductive medicine, along with legal regulation, ethical norms occupy an important place, among which the degree of responsibility of the program for the decision taken should be highlighted. The use of AI-based algorithms, of course, has obvious advantages, allows optimizing the work of a reproductive specialist and embryologist, minimizing the costs of providing medical care and increasing the effectiveness of infertility treatment using ART; however, there are a number of limitations that must be taken into account when integrating these programs into clinical practice.

Use of artificial intelligence in reproductive medicine

• Among the many different areas where AI-based programs are actively used, modern healthcare occupies a special place. AI makes it possible to classify various images obtained using computed tomography, magnetic resonance imaging, ultrasound, as well as histological images, analyzes clinical and anamnestic data of patients, optimizes treatment and diagnostic protocols, determines the relationship between the clinical picture of the disease, laboratory examination indicators and effective therapy [8]. In reproductive medicine, the introduction of programs using machine learning has made it possible to increase the accuracy of ejaculate quality diagnostics and optimize the choice of the most promising sperm for fertilization, predict the effectiveness of ART programs, select the highest quality embryos for transfer into the uterine cavity, determine the most effective ovarian stimulation protocols based on the clinical and anamnestic data of the couple and predict the course of pregnancy in the early stages [6–11]. Machine learning in ART is most often carried out using the following methods:

- Decision tree;
- Random forest;
- Support vector machine, SVM;
- Bayesian network, BN;
- Deep learning;

Each of the methods has its own class of problems, for solving which its use has its advantages. For example, to determine the embryo with the highest implantation potential, it is preferable to use the “decision tree” or “neural network” method compared to the Mann-Whitney test. In 2017, Carrasco B. et al. developed a hierarchical model using “decision tree” algorithms, which included data on the morphological quality and morphokinetic parameters of 800 embryos. The results of the study made it possible to determine the most significant predictors of the implantation capacity of the embryo [12]. It is worth noting that most often, the maximum classification accuracy is achieved using complex models, such as deep learning methods. Considering that deep learning allows you to identify and analyze features not explicitly defined by the data, the resulting models almost always give more accurate results in the case of complex data. Complex data may have features that are unknown to the researcher from previous experience.

"Random forest" is an algorithm that combines decision trees and provides more accurate results due to the fact that, unlike the "decision tree" method, this algorithm corrects the risk of "overfitting" the program. One example of the use of this algorithm is the study by Liao S. et al. In 2020, scientists developed a dynamic infertility assessment scale using clinical and anamnestic parameters of more than 60 thousand patients undergoing ART infertility treatment [13]. The support vector machine is most often used to divide a large data set by creating linear boundaries. For example, the support vector machine makes it possible to classify a large number of embryos into viable and non-viable. In the study by Filho E. et al., they classified embryo images based on the state of the zona pellucida, trophectoderm, and inner cell mass [14]. The resulting system made it possible to further separate embryos of the same quality according to morphological criteria by determining the thickness of the zona pellucida and trophectoderm.

One of the machine learning mechanisms most often used to predict successful embryo implantation in ART programs is the Bayesian classifier or Bayesian network. In the work of Uyar A. et al., the implantation ability of 2453 embryos transferred into the uterine cavity on the 2nd and 3rd day after fertilization by intracytoplasmic sperm injection into the oocyte was retrospectively analyzed. The authors' goal was to identify groups of patients who should be recommended to transfer multiple embryos into the uterine cavity to improve the effectiveness of treatment in ART programs, among which women with a history of unsuccessful IVF attempts, as well as patients who receive low-quality embryos during stimulation should be distinguished [15]. The authors built a predictive model using a Bayesian network based on a combination of embryo morphological parameters, clinical, anamnestic and demographic indicators of the couple and stimulated cycle data. Based on these parameters, Uyar A. et al.

demonstrated that this model can predict the implantation ability of an embryo with 80% accuracy and 63% sensitivity. The study also showed that when multiple embryos are transferred simultaneously, each embryo is most likely to implant separately and is unlikely to have an additional positive effect on the second embryo. Among all possible deep learning mechanisms, the most widely used at the moment are neural networks, which conditionally imitate the neural network of the brain, and deep learning, which uses neural networks with several hidden layers. These mechanisms are most often used to analyze embryo development using time-lapse microscopy. The results of the study by Khan A et al. showed that the rate of embryo development correlates with its quality. In their next work, the authors analyzed about 150,000 images of the studied embryos at different stages of development. Training the program using deep learning made it possible to obtain an algorithm that determines the implantation potential of the embryo with 87% accuracy [16]. Miyagi Y. et al. managed to analyze more than 5,000 images of embryos using deep learning and predict the frequency of live births in patients depending on age. The authors compared the sensitivity and specificity of the model obtained using deep machine learning and a traditional mathematical system. The results of the study showed the advantage of deep machine learning in solving problems involving the analysis of complex structures, in particular embryo images [17]. Thus, AI in ART allows not only to analyze potential connections on a large data sample, but also to create reliable predictive models. The integration of AI into reproductive medicine can provide a number of advantages in the work of the clinic and embryology laboratory, as well as increase the effectiveness of infertility treatment using ART. With the advent of technological capabilities for data analysis, machine learning algorithms have entered a new stage in development. Various machine learning methods, including neural networks, allow for data analysis and classification, and also open up new opportunities in modern healthcare and biomedicine data. However, to integrate data into modern medicine, additional development and improvement of systems for complex analysis and correct interpretation of loaded data is necessary.

Ethical aspects of the use of artificial intelligence in ART.

The implementation of AI in ART differs significantly from other areas of medicine, since IVF programs involve a unique research object, both in terms of scientific discoveries and in terms of ethical issues, namely the human embryo. To discuss the ethical aspects of using AI in ART, one should turn to international experience in regulating the activities of ethical committees (councils). The Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, the Convention on Human Rights and Biomedicine proceed from the fact that any scientific research in the field of biology and medicine is carried out freely, subject to the provisions of this Convention and other legal provisions that ensure the protection of humans. The Convention states that it is mandatory to consider research projects involving humans from an ethical point of view. In addition to the importance of AI in modern reproductive medicine, there are a number of limitations to the use of AI in ART. Among these problems, the issue of responsibility for the decisions that the program is capable of making is acute. Despite the fact that the final decision remains with the specialist, AI can mislead a person [18]. AI, which allows optimizing the selection of the most promising embryo, “manipulates” the behavior of the embryologist, forcing him to make an inaccurate choice. Considering that AI technologies in the field of ART remain imperfect to date, the introduction of such systems may, on the contrary, reduce the effectiveness of ART programs. In this regard, UNESCO has proposed developing a legal act to create an objective ethical basis for the use of AI in various fields, including medicine. An international group of 24 experts appointed by UNESCO prepared a draft “Recommendation on the Ethical Aspects of Artificial Intelligence”, submitted to Member States in 2020 [19]. In 2021, during the twentieth session, the UNESCO General Conference approved the final draft. The approval of this document made it possible to largely regulate many stages of the use of AI [19]. Among the many values described in this document, the fundamental principles included respect for and protection of human rights and freedoms, environmental well-being, safety and security, non-discrimination, the right to privacy, human control, transparency and explainability, responsibility, etc. In addition, the document states that AI will never be able to replace a person as the final subject of responsibility. In ART, this system can only “facilitate” the final decision, reduce the workload of the laboratory technician, reproductive specialist or embryologist, but the specialist must rely on his own experience and knowledge when using AI.

In Uzbekistan, the Decree of the President of the Republic of Uzbekistan dated October 14, 2024 No. PP358 "On approval of the strategy for the development of artificial intelligence technologies until 2030" adopted a regulation on the ethical aspects of the development and use of AI within the framework of the National Strategy for the Development of AI for the period up to 2030 [20]. It is worth noting that the document approved by the UNESCO General Conference indicates general principles without specific provisions. The AI Ethics Resolution contains many more clear and unambiguous provisions.Another limitation of AI in ART is the “black box” principle, when it is impossible to determine how exactly the system came to the conclusions it has reached when determining cause-and-effect relationships between data. For example, when predicting the effectiveness of ART programs using AI for a young married couple who are promising in terms of pregnancy, the system may show a 10% chance of a live birth. How should the results be interpreted correctly and should the couple be informed of such a low chance of a live birth? It seems absolutely necessary to form a consensus opinion on this and similar issues. Family planning, especially in a situation where ART is used, requires the couple to assess their physical and financial capabilities in the long term. The level of trust in these results depends on the clinical applicability of the data obtained, as well as the size of the analyzed sample when building the model used. Of course, to ensure the “ethics” of AI, clinical tasks (required solutions) and requirements for data sets that ensure the impartiality of decisions should be formed by the medical community.Today, AI-based algorithms are widely used in many areas of medicine, healthcare organization, and pharmacy [25]. Among them, it is worth highlighting programs for analyzing medical images (Agfa Radiology Solutions, AQUILAB, etc.), software products for conducting differential diagnostics and assisting in establishing a diagnosis and prescribing the necessary treatment (the Digital Support Project for Doctors, developed by the Department of Information Technology and the Department of Health of the City of Moscow), conducting non-interventional studies on clinical practice data (Real World Data, RWD) to obtain a set of evidence for routine clinical practice (Real World Evidence, RWE), modeling and managing population health [25]. It is worth emphasizing that the inability to explain the decision-making algorithm is not characteristic of all AI methods. For example, linear regression allows you to obtain fully interpretable models. Linear regression reflects the supervised learning method, which is divided into two categories: classification and regression. Another supervised machine learning algorithm is logistic regression. Logistic regression is also used in the construction of a neural network, since each individual neuron can be considered from the point of view of logistic regression. Logistic regression is often sufficient to assess the probability of a particular outcome due to the ease of interpreting the results and the ability to select the most significant features of the data set [25]. An important ethical aspect of the use of AI-based algorithms in reproductive medicine is the creation of software that will analyze new medical information and interpret the results of clinical examination of patients suffering from infertility [25]. Such programs include a medical decision support system [25]. The International Forum of Medical Device Regulators regulates legal approaches to the medical decision support system [24, 25]. According to the Forum's resolution, to date, clear criteria have not been developed for classifying a particular software as a decision support system or a traditional computer program; accordingly, it seems extremely difficult to regulate the activities of various software products within the framework of their use as systems influencing decision making. The main question is to what extent the system can study and interpret clinical data so as not to harm the patient's health. For example, there are systems that help the laboratory technician determine the quality of the sperm sample, and when the morphologically healthy forms of spermatozoa decrease, the algorithm shows a result corresponding to the diagnosis of "teratozoospermia", which is not always confirmed when the spermogram is interpreted by an andrologist. The question of whether such a program should be considered a decision support system that potentially carries a risk of harming the patient's health remains ambiguous [26]. The gradual integration of AI into ART will most likely lead to the automation of a number of processes and the subsequent displacement of medical workers with low and medium qualifications. In addition, the development of AI-based systems will reduce investments in the medical education of embryologists, laboratory technicians and reproductive specialists, which may subsequently become a factor hindering the development of reproductive medicine as a whole. Another important aspect of the use of AI in ART is ensuring the confidentiality of patient data. AI cannot be trained without using a large amount of clinical and anamnestic data of married couples, indicators of the embryological stage and treatment results. Safe storage of data and technical maintenance of AI require additional costs from the clinic, which makes the ART program a more expensive procedure. It is worth noting that when conducting a clinical and economic analysis, no clear advantage was obtained for using AI, compared to simpler programs that have proven themselves in the field of ART [26]. In addition, unregulated use of AI in ART, for example by private clinics, may subordinate the interests of patients to commercial goals or, conversely, to the interests of the state in the area of social control. Among other possible limitations of using AI in modern reproductive medicine, it is necessary to highlight the risk of discrimination against patients of different ethnic groups with low income. Today, AI algorithms are most often implemented in developed countries and become more accessible to patients with a certain socio-economic level [26]. However, the obtained data require mandatory adaptation depending on the characteristics of national healthcare, age, gender, race, ethnicity, sexual orientation and wealth level of patients. The gap between the success of technological demonstrations of AI solutions and the practical benefits of implementing such solutions is called “AI Chasm” [26]. It is worth emphasizing that “AI Chasm” can be observed not only when using data from different demographic and ethnographic groups. The problem of “AI Chasm” also faces solutions developed and implemented in high-income countries. When a system developed on the basis of AI is imported into routine clinical practice, it is not always known what data was used to train the model. In addition, the use of AI in decision making and further recommendations may be limited by incomplete information about the patient data used. Clinicians making AI-based decisions rarely have control over the algorithm used to obtain the final result. Aristidou A. et al. in their review published in 2022 suggested three important steps to overcome the “AI Chasm” problem. First, it is necessary to ensure “transparency” of the data used to initially train the AI-based model. Second, it is necessary to make the features that determine the operation and the algorithm of AI-based decision making more understandable to clinicians. And third, it is necessary to enable treating physicians to “retrain” the AI model if the interests of patients or the clinic require it [26]. The potential of AI in the field of ART will improve the effectiveness of infertility treatment, but most machine learning algorithms require the use of a large array of data for training, which is not always possible. Incorrect model construction and the use of a limited sample of patients will lead to incorrect results and misinterpretation of the analyzed patterns [26].Thus, the current level of AI development in the field of medicine does not allow for data analysis and their safe interpretation in the field of therapy prescription and clinical diagnosis without constant human involvement. However, in the field of ART, the Israeli Medical Center clinic already uses a system for selecting stimulation, drug dosage, puncture day, quantity and quality of eggs, the Fertilane system is used, which does not require human intervention. The software product developed by scientists from Israel allows the reproductive specialist to select the protocol type, drug dosage, stimulation duration, predict the puncture day and how many eggs the reproductive specialist can obtain in terms of quality and quantity, and also predict on what day of the cycle to transfer the embryo to accurately specify the implantation window for a successful ART protocol. Despite the fact that the development and implementation of self-learning programs based on AI seems extremely promising and will probably reduce the workload of a reproductive specialist or embryologist, software products developed using machine learning remain auxiliary tools that do not determine the final solution in implementing the analyzed tasks. The development and improvement of more accurate programs requires further study and research.

CONCLUSION

Currently, various AI-based software products are being actively developed in Uzbekistan. The study of AI-based algorithms is most rapidly occurring in the field of ART, since it is in the ART field that not only large databases are concentrated, but also innovative diagnostic and treatment methods developed on the basis of molecular biological technologies, metabolomic profiling of samples and microscopic analysis. ART is one of the most promising areas for the integration of classification systems, forecasting and support for medical decision-making based on AI-based programs. Today, there are several important ethical issues in the use of AI in medicine. The development of regulatory documents and the ability to follow their provisions facilitates the use of AI in daily clinical practice. It should be emphasized that the operation of AI-based software can be terminated at any stage, as well as questioned by a specialist. The dynamic development of machine learning and the interaction of humans and AI will give rise not only to new risks and challenges for future generations, but will also lead to mutual enrichment in the field of scientific research, treatment and diagnostics.

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