

Review

# The Role of Artificial Intelligence in Male Infertility: Evaluation and Treatment: A Narrative Review

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**Abstract:** Male infertility has affected an increasingly large population over the past few decades, affecting over 186 million people globally. The advent of assisted reproductive technologies (ARTs) and artificial intelligence (AI) has changed the landscape of diagnosis and treatment of male infertility. Through an extensive literature review encompassing the PubMed, Google Scholar, and Scopus databases, various AI techniques such as machine learning (ML), artificial neural networks (ANNs), deep learning (DL), and natural language processing (NLP) were examined in the context of evaluating seminal quality, predicting fertility potential, and improving semen analysis. Research indicates that AI models can accurately estimate the quality of semen, diagnose problems with sperm, and provide guidance on reproductive health decisions. In addition, developments in smartphone-based semen analyzers and computer-assisted semen analysis (CASA) are indicative of initiatives to improve the price, portability, and accuracy of results. Future directions point to possible uses for AI in ultrasonography assessment, microsurgical testicular sperm extraction (microTESE), and home-based semen analysis. Overall, AI holds significant promise in revolutionizing the diagnosis and treatment of male infertility, offering standardized, objective, and efficient approaches to addressing this global health challenge.

**Keywords:** male infertility; assisted reproductive technologies; artificial neural networks; artificial intelligence; sperm morphology; seminal quality; microsurgical testicular sperm extraction; deep learning; natural language processing



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## 1. Introduction

Infertility is the inability of a couple to conceive after 12 months of unprotected intercourse [1]. Over 186 million people worldwide suffer from infertility, making it a serious global problem [2–4]. Up to 50% of these cases are thought to be caused by male factors, and this number has been rising over previous years [5]. With regard to male infertility, the exact prevalence is unknown since male infertility is severely underreported [3]. The general trend over the last few decades that has been widely seen and reported worldwide is of greater concern. It shows a continual decline in average sperm counts, which were 113 million/mL in 1940, dropped to 66 million/mL in the 1990s, and then fell by 51.6% between 1973 and 2018 [6,7]. Moreover, the rising use of assisted reproductive technologies (ARTs) is another sign of this expanding pandemic of infertility [4].

Infertility is generally worse in developing areas due to limited resources, as well as cultural norms [3]. Moreover, many infertile men are at greater risk (5–8%) of developing testicular cancer [8]. Concerning the COVID-19 pandemic, studies have found reduced fertility as a result of cellular infection and potential side effects from immunological therapies [9]. Male infertility can result from various factors, including endocrinological issues like congenital GnRH deficiency, genetic causes such as mutations in specific genes,

congenital and acquired urogenital abnormalities, immunological factors, anatomical deficiencies such as varicoceles, infections, sexual dysfunction, malignancies, medication use, and exposure to environmental toxins. Additionally, a significant portion of male infertility is categorized as idiopathic, with normal semen parameters but persistent infertility, highlighting the complexity and diverse origins of this condition [1,3].

In the current period, artificial intelligence (AI) is being used more and more in clinical fields, and reproductive health is no exception [10]. Many studies have considered machine learning (ML)-based solutions for detecting male fertility. Finding the male's contributing factors, treating the reversible ones, determining whether he is a candidate for ARTs, and providing counseling for irreversible and incurable diseases are the main goals of screening a man for infertility. The advent of artificial intelligence has allowed providers to treat patients comprehensively and innovatively.

Modalities such as ARTs, image recognition, genetic testing, and predictive algorithms have provided clinicians with many options to assist patients in their reproductive health. The purpose of this review was to review the current landscape of the various technologies in how artificial intelligence is used to evaluate and treat male infertility.

## 2. Methods

Our narrative review collected sources through a general PubMed Database, Google Scholar, and Scopus Medline search. The discovered papers were then cross-referenced with citations. All references cited in the articles that were chosen were also reviewed and analyzed. The authors decided to present the review's findings narratively in light of the volume of material that has been published on the topic as a whole and each of the active ingredients in particular. This paper does not provide a systematic or meta-analytical comparison of varied outcomes in measures, population, and methods.

The research strategy included the following keywords: "artificial intelligence", "assisted reproductive technologies", "infertility and AI", "machine-learning algorithms", "deep learning", "artificial neural networks", "natural language processing", "big data", "legal and ethical consequences", "future directions" accompanied by "male infertility", "sperm morphology", "seminal quality", "azoospermia", and "inability to conceive." Only papers in the English language were included. Randomized-control trials and non-randomized trials were included in the literature review due to the paucity of information available. Moreover, retrospective cohort studies, case-control studies, cross-sectional studies, and prospective cohort studies were also included. We excluded the use of case reports and case series.

## 3. Artificial Intelligence in Reproductive Medicine: Transformative Applications and Potential Impact

According to ISO/IEC TR 24028:2020, AI is described as the "capability of an engineered system to acquire, process, and apply knowledge and skills." Coined by John McCarthy during the Dartmouth Summer Research Project on Artificial Intelligence in 1955, the term AI officially appeared at the Dartmouth conference in 1956 [11]. Since then, it has become a central reference in the ongoing exploration of artificial intelligence, encompassing the use of computers to replicate various human mental processes, including cognition, learning, decision-making, judgment, and language [12].

AI has revolutionized society over the past decade, with its limitless applications spanning all industries. Its applications are endless, including its use in the automotive industry, financial industry, transport mapping, military applications, and many others [5,13–15]. Leveraging AI branches such as machine learning (ML), artificial neural networks (ANNs), deep learning (DL), robotics, and natural language processing (NLP) for big data analysis holds valuable applications in reproductive domains. These applications span sperm classification, oocyte and embryo selection, outcome prediction, robotic surgery, clinical decision systems, cost-effectiveness, and sperm selection [16,17]. Envisioned as pivotal tools, AI-based prediction models and automated semen analysis stand to revolutionize

the diagnosis and treatment of male infertility, elevating the precision of patient care. The automated predictions facilitated by AI promise a paradigm shift, ensuring consistency and efficiency while simultaneously optimizing time and cost aspects in both infertility research and clinical management [18]. AI has the capacity to identify individuals who are at risk for chronic illness; additionally, AI could speed up and improve the efficiency of cost–benefit ratio computations in the healthcare system and support decision-making. Today, radiology, pathology, ophthalmology, and dermatology are among the sectors that are very interested in artificial intelligence due to its widespread use in image-processing analysis and pattern recognition [19].

Machine learning (ML) can be categorized into three primary groups: unsupervised ML, adept at recognizing patterns; supervised ML, equipped with algorithms for classification and prediction based on past examples; and reinforcement learning, which employs a system featuring reward and punishment methods to devise a solution strategy for addressing specific problems [10]. Machine learning has assisted medicine in a variety of ways, including reconstructing diseases, hypothesis testing, recruiting patients, big data, developing diagnostics, improving prognostics, and patient monitoring [20]. With the plethora of information available in big data through electronic medical records (EMRs) and hospital data, using ML to analyze this large amount of information is crucial.

Deep learning (DL) is part of ML and is inspired by neurons in the human brain, and the specific method is called an artificial neural network [21]. An artificial neural network (ANN) can have one or more layers, and it is made up of processing units (nodes or neurons) coupled by a set of weights that can be adjusted to allow signals to pass through the network both sequentially and in parallel [22]. ANNs can be categorized into three distinct layers of neurons: the input layer, which receives information; the hidden layer, tasked with extracting patterns and carrying out the majority of internal processing; and the output layer, responsible for generating and presenting the final network outputs [22]. Moreover, natural language processing (NLP) is a broader machine learning algorithm that allows for the analysis of free text [23]. In medicine specifically, NLP has been implemented to aid in predicting and forecasting patient outcomes, improving hospital triage systems, and creating diagnostic models that identify chronic diseases in their early stages when combined with medical notes [23]. These programs might be especially helpful in critical care, where analyzing patient data is more common and patient death prediction is a regular practice [23].

## 4. Use of Prediction Models for Risk Factors in Infertility Using AI

### 4.1. Sperm Morphology Assessment

Spermatogenesis entails morphological transformations from round to elongated shapes, and the transition from spermatid to spermatozoa, crucial to normal sperm morphology, serves as a primary selection metric in ART due to its association with successful fertilization and favorable pregnancy outcomes [24]. Sperm morphology, evaluated according to WHO criteria, considers samples with  $\geq 4\%$  morphologically normal sperm normal; however, variability in labeled normal samples poses challenges in cases like Intracytoplasmic Sperm Injection (ICSI), lacking natural egg–sperm selection, and stricter criteria emerge due to poor initial associations with clinical outcomes. Desirable sperm morphology characteristics, involving head shape, acrosome coverage, vacuole absence, midpiece parameters, and cytoplasmic residue, are defined. Still, the inherently subjective nature of embryologists in assessing and interpreting these criteria leads to interobserver and interlaboratory variability and inconsistency in sperm selection [25,26].

The morphological assessment of sperm, performed with various staining methods on fixed samples, aims to enhance visualization but leads to differences in measured dimensions and impacts vitality. Noninvasive methods exist, but evidence on the clinical outcomes of morphologically selected sperm for ICSI is conflicting. Manual selection based on morphology is subjective, inconsistent, and time-consuming, highlighting the need for standardization to minimize subjectivity and assessment time, especially considering the

common use of Polyvinylpyrrolidone in ICSI, which may increase sperm DNA fragmentation with prolonged exposure [27–30]. Thus, a better way to assess and standardize this approach needs to be assessed.

In recent years, the development of a partially spatially coherent digital holographic microscope (PSC-DHM) for quantitative phase imaging (QPI) and deep neural networks (DNNs) has provided a more comprehensive sperm morphology assessment [31]. Phase maps of over total of 10,163 sperm cells were reconstructed using a PSC-DHM, which were then classified by DNNs. When validated against a test dataset, the DNNs demonstrated an average sensitivity of 85.5%, a specificity of 94.7%, and an accuracy of 85.6% [31]. The PSC-DHM technique provides a label-free platform with nanometric sensitivity to identify even the smallest subcellular alterations in the sperm cell's head, midpiece, and tail [31].

The artificial intelligence optical microscopic (AIOM)-based technology LensHooke™ X1 PRO (X1 PRO, Bonraybio, Taichung, Taiwan) has also been employed in sperm analysis. It demonstrated a strong correlation with manual methods in measuring sperm concentration, progressive motility, and progressively motile sperm concentration across 135 clinical samples. Additionally, the X1 PRO yielded comparable seminal pH results to the manual method, establishing its reliability as a diagnostic tool and aligning with World Health Organization guidelines [32].

In the context of reproductive technology, the evaluation of sperm morphology, a critical factor in successful ARTs, encounters challenges related to subjectivity and variability. Recent advancements in AI tools, represented by PSC-DHM and the AIOM-based LensHooke™ X1 PRO, offer standardized and reliable approaches to assess sperm morphology, thus addressing these challenges and aligning with global guidelines. These technologies, utilizing DNNs and AI algorithms, demonstrate promising accuracy in characterizing sperm characteristics, marking a significant step toward more objective and consistent assessments in the field of reproductive health. A summary of studies evaluating sperm morphology characteristics can be located in Table 1.

**Table 1.** Overview of studies evaluating sperm morphology using artificial intelligence techniques.

Author	Year	Country	Sample Size	Study Design	Artificial Intelligence Technique	Results/Main Conclusion
Bartoov et al. [24]	2001	France	100 participants	Prospective cohort	Motile Sperm Organelle Morphology Examination (MSOME)	Positively associated with ICSI fertilization rate (AUC—88%)
Bijar et al. [27]	2012	Iran	N/A	Laboratory-based experimental study	Algorithm involved acquiring stained sperm smear images, applying Bayesian classification for segmentation, and utilizing an iterative method based on structural similarity index and local entropy estimation to identify points on sperm's tail.	Accuracy of sperm's head, acrosome, nucleus, and midpiece computed at 94.3%, 92.4%, 95.1%, and 90.2%, respectively.
Butola et al. [31]	2020	India	Phase maps of 10,163 sperm cells	Laboratory-based experimental study	Partially spatial coherent digital holographic method for quantitatively phase imaging to study sperm cells under stress conditions. Phase maps were reconstructed and then fed into seven feedforward DNNs.	When validated against a test dataset, DNN provided an average sensitivity, specificity, and accuracy of 85.5%, 94.8%, and 85.6%, respectively. Useful for improving ICSI procedure in ARTs

Table 1. Cont.

Author	Year	Country	Sample Size	Study Design	Artificial Intelligence Technique	Results/Main Conclusion
Agarwal et al. [32]	2019	USA	131 clinical semen samples	Laboratory-based experimental study	Development of LensHooke X1 pro—an artificial intelligence optical microscopic-based technology meant to quantitatively assess sperm concentration, motility, and seminal pH	High degree of correlation in concentration and motility between LensHook X1 Pro and manual methods.

Abbreviations: ARTs—assisted reproductive technologies; AUC—area under the curve; DNNs—deep neural networks; ICSI—Intracytoplasmic Sperm Injection.

#### 4.2. Using ANN and DL to Predict Seminal Quality

An analysis of a dataset containing environmental and lifestyle parameters using a datamining method utilizing five different artificial intelligence techniques—multilayer perception, decision tree, naïve Bayes, support vector machine, and support vector machine + particle swarm optimization—showed that semen quality could be predicted with a high degree of accuracy [33]. These AI techniques have been widely used in various fields and have recently been implemented in the field of reproduction. ANNs in particular are machine learning algorithms that can be used to determine the quality of semen because of their high and consistent accuracy, as well as their capacity to show the nonlinear relationship between input and output parameters. Moreover, AI tools such as multilayer perceptrons (MLPs) can be used. Briefly, MLPs are a type of ANN that consists of multiple layers of nodes (neurons), and each node is connected. MLPs are capable of learning in a nonlinear fashion. Naïve Bayes is a probabilistic classification based on Bayes' Theorem, with a "naïve" assumption of independence between features. Decision trees are non-parametric learning methods for classification tasks, and SVMs are another type of learning model that is effective in high-dimensional spaces for performing classification and regression tasks [34,35].

Gil et al. were the first to examine the prediction accuracy of three distinct AI techniques: decision trees (DTs); support vector machines (SVMs); and MLPs used to identify which decision support systems (DSSs) are most effective in assisting with the assessment of male fertility potential [34]. They found that the accuracies of SVMs and MLPs in detecting sperm concentration and morphology were 86% and 69%, respectively. Bidgaoli et al. chose four AI tools for their study, namely, an optimized multilayer perceptron (MLP), naïve Bayes (NB), a decision tree (DT), and a support vector machine (SVMs) [35]. Among these, the optimized MLP demonstrated the highest performance, achieving an impressive outcome of 93.3% [35].

Girela et al. looked at the semen samples of 123 volunteers and found that, by using MLP, 90% and 82% accuracies could be achieved for sperm concentration and sperm motility, respectively [36]. The researchers used two ANNs for the analysis of seminal parameters, focusing on sperm concentration and motility [36]. In the study conducted by Soltanzadeh et al., the researchers evaluated various models including NB, neural networks, logistic regression (LR), and fuzzy C-means [37]. Among these, the most promising results were obtained with NB, which demonstrated the highest performance, yielding an impressive AUC of 0.779 [37]. Studies have also used methods such as fuzzy radial basis functional neural networks (FRBFNNs), which have an accuracy of 90% when compared with other processes, such as MLPs, SVPs, and DTs [38].

Studies have also used the naïve Bayes and artificial neural network classifiers for the characterization of seminal quality to characterize seminal quality, with a reported accuracy of over 97% in the training phase [39]. Engy et al. introduced a novel method of predicting reproductive health, combining the Sperm Whale Optimization algorithm (SWA) with artificial neural networks (ANN-SWA) [40]. This approach, consisting of four phases,

effectively addresses optimization challenges in fertility data, achieving an accuracy of over 99.96%, surpassing existing algorithms in convergence rate and classification accuracy [40].

Other techniques, such as the evolutionary safe-level synthetic minority over-sampling technique (ESLSMOTE) are used to improve the accuracy of back-propagation neural networks, adaptive boosting, and support vector machines [41]. Using the ESLSMOTE model, researchers found an over 97.2% ROC rating for predicting seminal quality [41]. Ghoshroy et al. used the extreme gradient boost (XGB) AI tool with ESLSMOTE modeling to obtain a 93.22% mean accuracy and a 0.98 AUC [42]. Models such as the feed-forward neural network (FFNN) have been compared with common machine learning algorithms such as MLPs and SVMs and have a high predictive accuracy [43]. Various studies have explored the use of artificial intelligence in assessing male fertility, showing promising accuracies in detecting sperm issues and predicting reproductive health.

ANNs can also be used to predict seminal quality through the composition of semen. The discharge known as seminal fluid from many glands is made up of both organic and inorganic substances, such as proteins; fructose; glucosidase; zinc; and other scavenging elements, including Mg(2+), Ca(2+), K(+), and Na(+)[38–40]. Using a back-propagation neural network, biological factors are needed in ART centers to correctly diagnose male infertility [44].

Lastly, in nonobstructive azoospermia patients (a condition that affects 15% of infertile men), the use of microsurgical testicular sperm extraction (microTESE) has been largely used to detect scarce human sperm [45]. However, there can be significant inaccuracy with this technique due to an inability to find scarce sperm among millions of cells analyzed [46]. A technique that uses a convolutional neural network to accomplish pixel-based sperm cell recognition and counting in bright-field images was recently reported by researchers [6]. Using fluorescently marked donor cells from testicular biopsy samples from individuals with non-obstructive azoospermia (NOA), the algorithm was trained to provide a probability map of possible sperm cell-containing pixels. The system’s 86.1% sensitivity rate in identifying uncommon sperm from bright-field pictures was demonstrated by the data that were provided [46].

In conclusion, the application of AI techniques, including multilayer perception, decision trees, naïve Bayes, support vector machines, and others, has demonstrated high accuracy in predicting semen quality. These techniques, ranging from decision support systems to novel methods like the Sperm Whale Optimization algorithm, have shown impressive results in assessing male fertility potential, detecting sperm issues, and predicting reproductive health. The versatility of AI, particularly artificial neural networks (ANNs), in capturing complex relationships between input and output parameters suggests their valuable role in enhancing the evaluation of seminal parameters and diagnosing male infertility. However, several investigations have found only a poor association between manual semen analysis and AI analysis performed by similar instruments [47]. In addition, the use of tiny datasets and imprecise evaluation processes are further constraints on the field of assisted reproduction and sperm motility prediction [48]. A summary of studies evaluating seminal quality can be located in Table 2.

**Table 2.** Overview of studies using artificial neural networks and deep learning for assessing seminal quality.

Author	Year	Country	Sample Size	Study Design	Artificial Neural Networks/Deep Learning Modalities	Accuracy/Results in Comparison to Published Methods
Gil et al. [34]	2012	USA	100 volunteers	Cross-sectional study	DT, MLP, and SVMs to evaluate performance in the prediction of seminal quality	Prediction accuracy values of 86% for seminal quality parameters, useful in predicting seminal profile of an individual

Table 2. Cont.

Author	Year	Country	Sample Size	Study Design	Artificial Neural Networks/Deep Learning Modalities	Accuracy/Results in Comparison to Published Methods
Bidgaoli et al. [35]	2015	USA	n/a	Laboratory experiment	MLP, SVM, NB, and DT	93.86% accuracy
Girela et al. [36]	2013	Spain	123 volunteers	Prospective study	MLP	90% and 82% accuracies were achieved for sperm concentration and sperm motility, respectively
Soltanzadeh et al. [37]	2016	Tehran	n/a	Laboratory experiment	NB, logistic regression, and fuzzy C-means	AUC of 0.779
Candemir [38]	2018	USA	n/a	Laboratory experiment	MLP, SVP, and DT	90% accuracy
Simfukwe et al. [39]	2015	Zambia	100 volunteers	Laboratory experiment	NB	97% accuracy
El-Shafeiy et al. [40]	2018	Egypt	n/a	Laboratory experiment	Sperm Whale Optimization Algorithm	99.6% accuracy
Ma et al. [41]	2021	China	n/a	Laboratory experiment	Evolutionary safe-level synthetic minority over-sampling technique	97.2% accuracy
GhoshRoy et al. [42]	2022	India	n/a	Laboratory experiment	SVM, adaptive boosting, conventional extreme gradient boost, and random forest	AUC of 0.98

Abbreviations: DTs—decision trees; MLP—multilayer perceptron; NB—naïve Bayes; SVMs—support vector machines.

#### 4.3. Computer- and AI-Based Algorithms for Semen Analysis

Over the last 25 years, computer-assisted semen analysis (CASA) has emerged as a viable alternative to traditional semen analysis, offering more dependable and objective outcomes [49,50]. However, the limitations of CASA include requiring manual input and large amounts of oversight to be accurate. CASA systems are automated devices that assess data from microscopic evaluations using cameras and software to produce results for semen parameters [51].

In response to the aforementioned problem, the development of SpermQ (National Institutes of Health, Bethesda, MN, USA) has addressed this need. SpermQ is a novel program designed to analyze flagellar beats in detail, compatible with simple imaging techniques like dark-field and epifluorescence microscopy [52,53]. Notably, it can also handle DIC and phase-contrast images with additional pre-processing. Adhering to the Nyquist–Shannon sampling theorem during image recording ensures an accurate determination of flagellar beat frequency [52,53]. SpermQ reveals various head and flagellar parameters, including frequency analysis, and its automated features facilitate large dataset analysis, reducing user-dependent bias [53]. Suited for labs lacking technical expertise, this program is applicable to tracking both tethered and freely swimming sperm. Beyond its practical applications, SpermQ is expected to advance the study of molecular mechanisms by guiding sperm navigation, encompassing chemotaxis, haptotaxis, thermotaxis, and rheotaxis [53]. By providing default settings, SpermQ aims to enhance analysis ease, comparability, and accessibility, contributing to a deeper understanding of sperm navigation mechanisms [53].

Other methodologies include the research by Kanakasabapathy et al., who validated a smartphone-based semen analyzer with automation features to quantitatively assess sperm concentration and motility for on-the-spot screening of male infertility [54]. Through the examination of 350 clinical semen samples obtained from a fertility clinic, the study demonstrated that this system is capable of analyzing an unprocessed, liquefied semen

sample in less than 5 s on average. Furthermore, it offers users a semen quality assessment in alignment with World Health Organization (WHO) guidelines, achieving an accuracy rate of approximately 98% [54]. One significant limitation of this technology lies in its inability to precisely assess samples characterized by the elevated presence of non-sperm cells [54]. Other forms of DL technology include Mojo AISA, an AI microscopy system that ensures accurate and reliable semen analysis results, enhancing objectivity and reducing human error. In a study involving 64 men over the last nine months, Mojo AISA's performance was compared with the manual microscopy method. The results demonstrated comparable semen parameters, with no significant differences in concentration and motility measurements. Mojo AISA delivered results in just 4 min per sample, saving 50% of the time per procedure compared with manual methods [55].

#### *4.4. Anatomical Variations and AI: Implications for Male Infertility and Testosterone Deficiency Syndrome*

Anatomical variations such as varicocele, an enlargement of the testicular veins, have long been known to cause infertility issues in males in the long term [56]. The etiology of these defects has yet to be fully elucidated; however, they can have a variety of adverse effects on spermatogenesis due to elevated testicular temperature, heightened pressure within the testes, reduced oxygen levels resulting from decreased blood circulation, the backflow of harmful metabolites from the adrenal glands, and irregularities in hormonal levels [57,58]. Moreover, the toxic accumulation of metabolites due to the chronic reflux of the venous plexus has been shown to disrupt spermatogenic equilibrium, further contributing to the development of infertility [59]. Although treatments include surgical modalities, there has recently been development in the use of AI for the prevention and treatment of varicoceles. Bernabó et al. identified a significant downregulation of vanilloid expression in varicocele-affected testes, correlating with fertility, and developed an artificial neural network model predicting varicocele's impact on fertility with high accuracy, offering potential diagnostic insights [60]. Moreover, machine learning models utilizing pre-operative hormonal, clinical, and semen laboratory data have been used to forecast clinically significant post-varicocelectomy sperm characteristics [18]. However, the need for AI models to predict the development of varicoceles and use machine learning algorithms to affect patient care is increasingly necessary.

Another important problem in development that affects 15% of subfertile men is low testosterone [61]. Studies have found that low-testosterone males have lower semen volume and sperm cell counts in comparison with patients with normal levels of testosterone [61]. Moreover, many patients are diagnosed with testosterone deficiency syndrome (TDS) and can experience primary and secondary hypogonadism [62]. Studies have used ensemble-based classifiers within the domain of machine learning to predict TDS at an earlier stage [62]. Ensemble classifiers, particularly the Weighted Average Ensemble Classifier (wAvg), have outperformed single classifiers, with XGBoost being the best among them [62]. Moreover, calibration techniques improve predictions and feature importance analysis highlighting the significance of abdominal circumference, triglycerides, diabetes, and high-density lipoprotein in TDS prediction [62].

### **5. Future Directions**

In terms of CASA, the potential for advancements in result accuracy and improved portability is an avenue for AI to be involved in, which will hopefully decrease inter- and intra-operative errors [32]. The financial aspect of CASA also becomes a barrier of entry for many patients looking for solutions for their male infertility, so further efforts to reduce costs and increase affordability are warranted [63]. Another avenue for semen analysis that needs to be further explored is performing semen analyses in the comfort of the home. Frequently, patients express dissatisfaction with the necessity of providing ejaculated samples in clinical or laboratory settings. These public semen collection environments can be notably uncomfortable, potentially leading to delayed care. Studies have found

that the sperm concentration, total sperm count, rapid progressive motility, and total count of progressive motility are all statistically substantially higher in home-collected samples in comparison with clinic-collected samples [64]. Thus, it is important to develop a way to analyze sperm from the comfort of consumers' homes. The first video-based smartphone platform for home sperm testing to receive FDA clearance (K161493) was the YO Home Sperm Test (Medical Electronics Systems, Los Angeles, California, USA), which recently made its debut on the consumer market [65]. When compared with SQA-vision, a laboratory semen analysis system, the YO Home Sperm Test smartphone device has a high level of accuracy and precision [65]. However, the limitations of these systems include only being able to assess sperm concentration or motility parameters [65].

Moreover, future applications in Micro-TESE have the potential to be automated and thus maximize the identification of scarce sperm from TESE samples [66]. Potential avenues include using a patient's follicle-stimulating hormone (FSH) and testes to predict sperm extraction successfully [67]. In addition, in sperm selection, AI may be used to advance algorithms capable of simultaneously analyzing various sperm traits at the individual cell level in real time [66]. There is ongoing research on single-cell resolution through individual sperm trapping, which may assess the single-cell selection of fertilization [68].

The creation of AI models for the diagnosis of male accessory gland infection (MAGI) and the ultrasonography evaluation of the male genital tract (testes, epididymis, vas deferens, prostate, ejaculatory ducts, and seminal vesicles) present a future challenge [69,70]. Ultrasound evaluation in over 500 MAGI patients revealed specific criteria associated with severe urinary symptoms, spontaneous or post-ejaculate pain, and sexual dysfunction. The study suggests the potential for personalized therapeutic choices based on a correlation between symptoms and specific ultrasound signs in MAGI patients [69,70]. In terms of anatomical deficits, the use of AI in certain pathologies, such as cryptorchidism, Kinfelter's syndrome, and others, is a potential avenue of exploration for combatting the development of male infertility.

Patients with low testosterone may benefit from treatments using AI-driven algorithms to consider other comorbidities such as age, race, socioeconomic status, diet, lifestyle factors, and genetic predisposition, among other things, to individually tailor a regimented plan.

To sum up, the application of AI has enormous potential to transform the diagnosis and treatment of male infertility. Technological developments in CASA present prospects for enhanced precision and mobility in results, mitigating cost obstacles and potentially facilitating on-site semen analysis. Future efforts involve developing AI models for identifying MAGI and ultrasonography evaluation, improving sperm selection algorithms, and automating micro-TESE operations. While AI offers great opportunities for more individualized treatment and better results, ethical issues and further study are necessary to guarantee its appropriate and successful application in reproductive medicine.

## 6. Legal and Ethical Concerns

The advent of AI in medicine has long been a topic of controversy due to ethical and legal concerns. Innovative techniques in AI are frequently met with backlash, as their major potential to profoundly change the lives of many outpace the traditional core ethical and legal standards of society. Specifically, in reproductive medicine, the backlash has already been met with many practices such as heterologous fertilization [71].

In research ethics, the potential risks of the application of AI in reproductive medicine include navigating challenges in adequately informing patients/study participants, managing long-term monitoring feasibility, addressing unrealistic hopes, and grappling with the moral status of the human embryo [72]. Another potential avenue of discussion is the autonomy of the offspring that is affected—as these patients can be inevitably affected by the risks of experiments/treatments without having consented to the procedure. In a similar vein, it might take several years before the long-term impacts of an experimental technique utilized during assisted reproduction become completely clear to the offspring [72]. Reproductive autonomy, the freedom of individuals to make informed decisions about their

reproduction, underscores the importance of ensuring access to advanced reproductive technologies like AI for those desiring children. However, careful consideration of the risks and ethical concerns is essential to safeguard patients' autonomy in this evolving field.

## 7. Conclusions

Male infertility is a growing global health concern and has significant financial and emotional implications for those who are affected. The advent of AI in reproductive medicine is revolutionizing the treatment and evaluation of male infertility by enhancing diagnostic accuracy and personalizing treatment strategies. Artificial intelligence approaches, including machine learning, artificial neural networks, and deep learning, show remarkable accuracy and promise in improving patient outcomes, from predicting seminal quality to guiding decisions on reproductive health.

The increasingly technological advancements in computer-assisted semen analysis systems provide future avenues to enhance accuracy, portability, and affordability in semen analysis. Moreover, microsurgical testicular sperm extractions provide opportunities for efficient and personalized healthcare delivery. Clinicians can improve outcomes for individuals and couples experiencing infertility by optimizing treatment regimens, improving diagnostic accuracy, and leveraging AI technologies.

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