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Progress of artificial intelligence in anesthesia and perioperative medicine

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Highlights

- This review introduces the core concepts of artificial intelligence (AI) and describes the most commonly encountered computerized functioning of AI in anesthesiology.
- This survey systematically presents the main clinical applications of AI in anesthesia and perioperative medicine according to the perioperative phases.
- The advantages and disadvantages of introducing AI into the medical field are also discussed to explore the career development direction of anesthesiologists in the future.

Abstract

Perioperative medicine is a series of medical activities throughout the perioperative period, including preoperative optimization, intraoperative safety, postoperative rehabilitation, and other activities. Anesthesia is closely integrated with perioperative medicine to guarantee smooth progress of operations, comfortable recovery, and favorable long-term outcome for patients. There are a huge number of clinical data in anesthesia and perioperative medicine, and artificial intelligence (AI) has a powerful ability to analyze and evaluate data; thus, applying AI is a significant advantage in analysis and prediction based on real clinical big data in anesthesia and perioperative medicine. AI has made some progress in the field of anesthesiology and perioperative medicine. This review introduces the most encountered computerized techniques of AI in anesthesiology, main clinical applications themes of AI in anesthesiology, as well as limitations and ethical implications involved in deployment of this technology.

Keywords: Anesthesia, artificial intelligence, machine learning, perioperative medicine

Introduction

Artificial intelligence (AI) is defined as the broad concept of machines designed to imitate the human way of thinking by building a model and finding some rules of the data on their own. The various techniques of AI include machine learning (ML), deep learning (DL), and natural language processing (**Figure 1**) [1]. In addition to the patients' health data, there are likewise substantial perioperative monitoring data as anesthesia runs through the whole perioperative period, which creates opportunities for the application of AI in the field of anesthesia.

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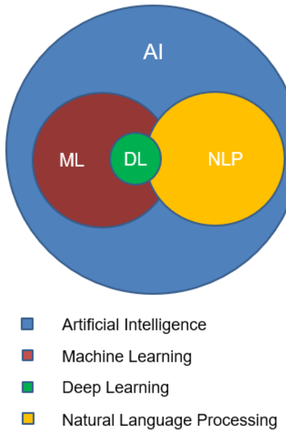

Figure 1. Artificial intelligence. AI, artificial intelligence; DL, deep learning; ML, machine learning; NLP, natural language processing.

Namely, the characteristics of anesthesiology as a data-intensive discipline make it most likely to benefit from the advances in AI [2].

Machine learning

ML is currently the most dominant approach to achieve AI, wherein a computer generates underlying rules by processing raw data and expected answers from the data. ML is an appropriate method for anesthesiology, providing the capability to analyze plentiful clinic data (e.g., Bispectral index (BIS)), discover associations, generate latent rules, and predict the outcomes through continuous learning, which is strikingly similar to the doctor's diagnostic process [3]. Predicting the incidence of postoperative complications caused by clinical factors based on big data analysis is a typical application of ML in anesthesia. According to the learning manner, it includes supervised learning, unsupervised learning, semi-supervised learning, and reinforcement learning.

- Supervised learning is a process by which an algorithm is trained with the input eigenvalue and the target value.

  Decision tree model is a basic classification and regression method that presents a tree structure and classifies instances based on input features.

  The k-nearest neighbor algorithm is another essential classification and regression approach, in which the category of each instance can be represented by the category of its k nearest neighbors (e.g., based on Euclidian distance).

- Unsupervised learning is a ML technique where a model is trained only with the input eigenvalue without the target value.

- Semi-supervised learning is a hybrid approach that combines aspects of both supervised learning and unsupervised learning where the model is trained using input eigenvalue and a subset of the target value.

- Reinforcement learning refers to the process by which an algorithm is asked to attempt a certain task, and it will be given different rewards or punishments according to the completion of the task, then the computer will automatically optimize a criterion based on this reward or punishment, which is also a learning method used by AlphaGo.

Deep learning and neural network

DL is a subset of ML that utilizes multiple layers of connected neural networks, like the human brain, to progressively extract higher-level features from the raw inputs [3]. The most representative algorithms of DL networks are convolutional neural networks (CNNs), which can better process data with a grid-like structure, such as image data that can be viewed as two-dimensional grid of pixels (**Figure 2**). Recurrent neural networks are known as "memory" network of DL, which are sensitive to the sequence of the input. Therefore, recurrent neural networks are effective in mining temporal and semantic information from sequential data such as speech [4]. The strength of DL over traditional ML is that multi-layer mapping of neural networks can automatically learn complex data features, which reduces the workload of feature engineering by a human expert [2]. For example, CNNs are applied to predict difficult airway intubation based on preoperative pictures of patients. These networks utilize a simple neuron-level approach to process signals and then parameterize the connections between neurons by weights.

This review introduces AI techniques currently applied in anesthesia research and describes the current state at the cross-disciplines of AI and anesthesia. A literature search was conducted using the keywords "artificial intelligence", "anesthesia", and "perioperative period" in the PubMed database. This review is divided into sections dealing with most encountered computerized techniques in anesthesiology, main clinical applications of AI in perioperative anesthesiology, and limitations and ethical implications involved in deployment of AI.

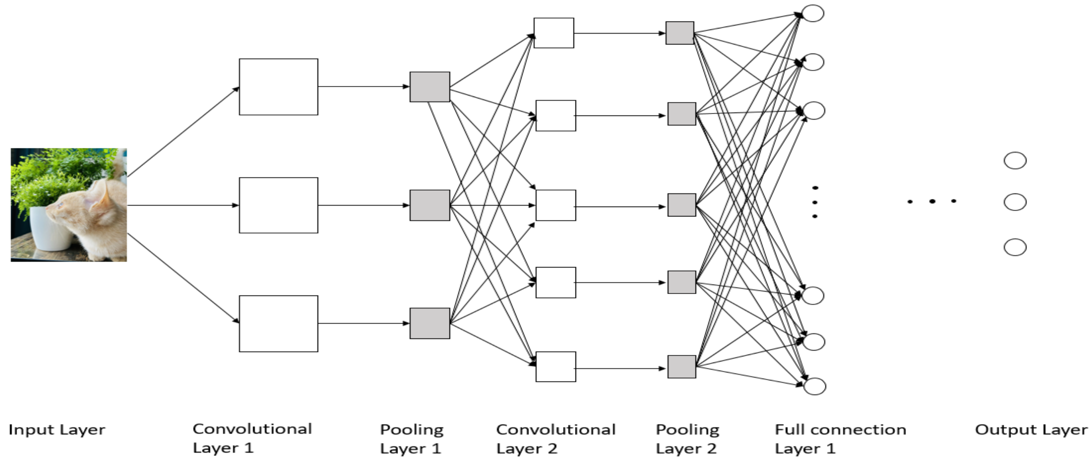

Figure 2. Architecture of convoluted neural networks. The input image is passed through the convolutional neural network model to output the classification result. The box represents the image matrix; the circle represents the neuron; the arrow represents the direction of data movement. Structures associating a convolutional layer and a pooling layer can be used consecutively. Full connection layer can also be used consecutively. The output layer is also referred to as the classification layer since output neurons classify the inputs into one of the output categories.

AI in pre-operative anesthesia

Preoperative risk prediction

Risk stratification is a primary but very important step of anesthesia, and risk prediction is the most common application field of AI in preoperative assessment. However, traditional preoperative anesthesia classifications are manually reviewed by clinicians, with certain subjectivity and limited granularity. Supervised ML methods, specifically random forest split classification, have been tested to automatically generate an American Society of Anesthesiologists Physical Status rating with finer granularity which may be able to aid anesthesiologist in identifying at-risk patient [5].

Multiple systems for preoperative risk prediction have been proposed to improve existing scores such as American Society of Anesthesiologists Physical Status, and some even defined extra patient-specific risk scores. For example, a famous system called "MySurgeryRisk" collected data from 51,457 patients undergoing different types of surgeries, and picked 285 preoperative parameters for each patient to generate a risk score by using ML [6]. Moreover, many scholars have optimized perioperative risk prediction with better algorithms and superior performance. For example, Fritz et al. developed a multipath CNN model from the data of 95,907 surgical patients, and for each patient, 56 preoperative parameters were selected to predict the risk of death within 30 days [7]. This algorithm has been shown to have better performance with higher area under the curve (AUC) value when compared to that of CNN model, random forest model, support vector machine, and logic regression algorithm.

Difficult intubation prediction

Difficult tracheal intubation is the main cause of anesthesia-related morbidity and mortality. Although video laryngoscopy has been widely used in clinical practice, difficult intubations are still frequently encountered. Preoperative airway assessment is an important part of perioperative anesthetic management. Airway examination is another highly operator-dependent assessment. Therefore, an objective method is needed to define the degree of airway difficulty. Hayasaka et al. developed a CNN algorithm capable of evaluating the difficult intubation with an AUC of 0.864 by evaluating patients' facial pictures in the supine-side-closed mouth-base position [8]. Matava et al. critically assessed the use of AI and ML in the assessment, diagnosis, monitoring, procedure assistance, and outcome prediction during pediatric airway management [9].

In addition to AI face recognition analysis techniques that can be used to predict difficult intubation, acoustic features can also predict difficult intubation. The acoustic data of 225 patients who underwent orthognathic surgery under tracheal intubation were collected during preoperative clinical airway assessment, and logistic regression analysis was performed to examine the association between acoustic features and difficult laryngoscopy. The obtained model identified the difficult intubation with an AUC of 0.724, an overall accuracy of 0.632, a specificity of 0.582, and a sensitivity of 0.772 [10]. Acoustic features show the potential for predicting difficult intubation among patients under general anesthesia.

AI-assisted intra-operative anesthesia

Intubation and extubation operation

Intubation is one of the most important anesthetic skills. In 2012, Hemmerling et al. developed a robotic intubation system (Kepler intubation system) for oral tracheal intubation [11]. In this operating system, doctors can remotely use a joystick to control a video laryngoscope and safely insert an endotracheal tube into the patient's trachea. The success rate reached 91% at the first human testing of this system. Although it was the first time to validate and realize the possibility of remote control of tracheal intubation, the system did not strictly reflect AI. Moreover, the system could not quickly identify the trachea to achieve tracheal navigation in difficult airway. In one patient of this study, fogging of the video laryngoscope hindered the intubation using Kepler intubation system.

In the context of coronavirus disease 2019 (COVID-19) pandemic, Wang et al. developed a new tracheal intubation device based on magnetic navigation technology [12]. The new tracheal intubation device was designed by using external magnets to guide corresponding magnets in the body to move towards a preset target area. The tracheal intubation based on magnetic navigation technology is feasible, with high efficiency and easy operation. This magnetic navigation tracheal intubation enables successful tracheal intubation and takes less time than that of traditional laryngoscopy; more importantly, it reduces the risk of occupational exposure of medical staff.

Robotic endoscope-automated via laryngeal imaging for tracheal intubation has been developed to enable automated tracheal intubation [13]. The robotic device has real-time image recognition and remote automatic positioning function. The user can manually control the bending and movement of the endoscope tip; when the image recognition detects the glottal opening, the user can press a dedicated button to activate the automatic mode. In automatic mode, the tip of the speculum moves toward the geometric center point of the glottal opening until it entered the trachea. The robotic endoscope-automated via laryngeal imaging for tracheal intubation was successfully performed for the first time on a manikin and obtained comparable results in a convenience sample of anesthetists and lay participants with no medical training. This study suggests that the time required for non-trained participants to master the skill is similar to that of an experienced anesthesiologist, which may help inexperienced healthcare workers to perform tracheal intubation. However, all the intubations were performed on the airway trainer mannequin, not yet in clinical practice.

Prolonged mechanical ventilation (PMV) is commonly defined as more than 21 days; however, substantial variation exists in the terminology and definitional criteria for PMV [14]. Early identification of critically ill patients requiring PMV has proven to be difficult. AI can help quantify the risk of extubation, thus helping to personalize and achieve accurate extubation. In a study that defined the duration of ventilation with >7 days as PMV, 20,262 total hospital stays with mechanical ventilation were identified from the Multiparameter Intelligent Monitoring in Intensive Care III [15]. Patients requiring tracheostomy placement were identified by the presence of ICD-9-CM procedure codes (31.1, 31.29). Machine-learning classifiers were created using a gradient-boosted decision tree algorithm based on the outcomes of PMV and tracheostomy placement. It showed that variables with the higher importance for predicting PMV and tracheostomy were the logistic organ dysfunction score (pulmonary component), the sepsis-related organ failure assessment score, cardiac arrhythmia, the Oxford acute severity of illness score before ICU stay. The classifiers predicted PMV for these patients who were admitted to surgical ICU with an AUC of 0.852, significantly reducing the probability of reintubation in patients.

Ultrasound-guided anesthetic techniques

For ultrasound-guided anesthetic techniques, artifacts, noise, and anatomic structure variability all affect the accuracy of nerve tracking and needle positioning. AI could be used to assist ultrasound-guided local anesthetic operations.

In nerve block anesthesia, the block performance varies due to the location, image parameters and patient specificity during the actual scanning. Compared with the traditional feature extraction method, DL neural network is more stable and accurate. In 2013, the first robotic system, Magellan, was invented to perform nerve blocks using a remote-control center [16]. The researchers presented the first human test of a robotic ultrasound-guided nerve block system, and the success rate was 100%.

Right after that, to prove whether this newly invented system can shorten the operator learning curve, Morse et al. compared success rates, learning curves, performance times, and inter-subject performance variability between robot-assisted and manual ultrasound-guided nerve block [17]. Analysis of variance indicated that there were significant differences in performance times for performing the manual blocks; no statistical difference for the robot-assisted blocks and linear regression indicated that the average shortening time between two consecutive trials of robot-assisted nerve blocks was significantly longer than that of manual blocks [(1.8 ± 1.6) seconds vs (0.3 ± 0.3) seconds]. Therefore, this robot-assisted model can help beginners master the operation skills faster and reduce the operator interval differences [17].

At present, epidural puncture needle placement is mainly performed manually that largely depending on the hand feel with a very high failure rate. Moreover, improper placement of the epidural needle can lead to inadequate anesthesia, post-puncture headaches and other potential complications. Ultrasonography for neuraxial anesthesia is increasingly being used to identify spinal structures and localize correct point of needle insertion to improve procedural success. Pesteie et al. used the hybrid ML system to automatically localize the insertion point of epidural needle placement and identify anatomical landmarks of epidural space in ultrasound images [18]. Compared with sonographers, the hybrid machine ML has a transverse and longitudinal error of 1 mm and 0.4 mm in the 3D-augmented test data plane, which effectively reduces the error and improves the comfort and safety of patients.

Performing subarachnoid or epidural anesthesia in obese patients, especially in obese pregnant women, remains a challenging task, as obesity and pregnancy may cause spinal changes, which in turn increases operational difficulty of determining the needle insertion point. Acting on ultrasound imaging of the lumbar spine, a program based on ML algorithms was developed to automatically identify the needle insertion site, and the first attempt success rate for spinal anesthesia was 79.1% [19]. This shows that the automated spinal landmark identification program is able to provide assistance to needle insertion point identification in obese patients.

For practicing the ultrasound-guided regional anaesthesia (UGRA), the tracking of the nerve structure in ultrasound images is extremely labor intensive, even for experienced operators, due to the noise and other artifacts. By using additional information to track nerves and blood vessels, the combination of a detection and tracking framework and a robotic system can assist with UGRA. A new and robust tracking technique by using Adaptive Median Binary Pattern was introduced as texture feature for tracking algorithms. This fully automatic nerve tracking method in ultrasound images achieved best performance with 95% accuracy when it was applied in real data and evaluated in different situations [20].

Studies of stroke require the acquisition of patient-specific geometry of the carotid artery bifurcation. Although C-mode CT and magnetic resonance are effective tests, there are many limitations including but not limited to ionizing radiation, unaffordable expense, and not available for all patients. De Ruijter et al. developed an automatic 3D geometry segmentation algorithm for ultrasound images using a 2D ultrasound probe [21]. This algorithm is able to segment the common carotid artery, the internal carotid artery, and the external carotid artery including the carotid bifurcation in transverse B-mode images in both healthy and diseased arteries. The quality metrics of the method performed significantly better than or similar to those proposed in the previous papers, however, this method was tested on limited data, 19 healthy volunteers and 3 patients, which needs further validation [21].

Depth of anesthesia (DoA) monitoring

BIS and electroencephalogram (EEG) characteristic parameters are usually used to evaluate DoA. However, in anesthesia monitoring, the reliability of BIS can be affected by numerous interferences, including patient factors (basic diseases, etc.), different anesthetics, muscle relaxants, intraoperative electric coagulation etc. [22]. AI could be used to refine DoA monitoring. Yu et al. proposed an adaptive control scheme that combines BIS and blood pressure to ensure the proper dosage of drugs to achieve target setting point even if BIS signal is lost intermittently [23].

The competence of processing complex data streams, such as EEG, using ML methods have been testified. A range of EEG-based signals indicating brain states have been analyzed by ML approaches to accurately scale the DoA. In Gu's research, an algorithm based on artificial neural networks and EEG to evaluate DoA was presented, and the output results of this algorithm

Table 1. Anesthesia delivery control system

Name	Control system	Characteristics
Target controlled infusion system	Open-loop system	Based on pharmacokinetic models of drugs to achieve specific plasma drug levels. The concentration of the drug needs to be manually determined and adjusted.
Single input single output system	Closed-loop systems	1. Bispectral index -guided autonomous system. 2. Real-time monitoring of anesthesia parameters (e.g. Bispectral index, blood pressure, and oximetry) as feed back for drug infusion. 3. Algorithms, such as reinforcement learning, neural net work, and fuzzy logic, can improve the performance of the system [3].
Multiple input multiple output system	Closed-loop systems	1. Real-time monitoring hypnosis, analgesia, and muscle relaxation simultaneously as feedbacks for drug infusion. 2. Algorithms, such as reinforcement learning, neural net work, and fuzzy logic, can improve the performance of the system [3].

clearly demonstrated a strong linear correlation with BIS [24].

Moreover, ML is used to distinguish states of consciousness based on EEG [25]. Three sedation situations were studied with dexmedetomidine i.v., propofol i.v., or natural sleep in this research. Distinct source localized signatures of sensory disconnection and unconsciousness were identified using support vector machine classification, indicating that occipital delta power could differentiate disconnected and unconscious states for dexmedetomidine but not for sleep/propofol. These findings may enable novel anesthetic state monitoring to distinguish between sensory disconnection and unconsciousness, and may provide novel insights into the biology of arousal.

With the deepening of DoA investigation, attention has been gradually paid to other clinical signals as well, for example, mid-latency auditory evoked potentials, end-tidal carbon dioxide, blood pressure, and heart rate [26, 27].

Intraoperative hypotension and hypoxemia prediction

Intraoperative monitoring of adverse events, such as intraoperative hypotension, which is commonly encountered, is crucial in anesthesia management. Early prediction of adverse events allows physicians to take timely action to reduce patient morbidity and mortality. As mentioned earlier, due to the datafication of clinical information, real analysis based on big data is an advantage of AI for predicting patterns of intraoperative blood pressure [28]. Hatib et al. established a model for predicting hypotension based on the analysis of arterial pressure waveforms using ML methods [29]. In this real-time dynamic prediction system, the evolution of mean arterial pressure, the time-to-event interval, is highly consistent with the hypotension prediction index (the algorithm output) [29].

Similarly, there is a lack of reliable indicators for the prevention of intraoperative hypoxemia. A ML-based system by visually presenting a weighted function model, was developed to assist anesthesiologist in predicting the occurrence of hypoxemia during anesthesia and delineate the risk factors that contributed to the prediction [30].

Closed loop anesthesia control system

In the field of anesthesiology, how to achieve perioperative precise drug delivery and reduce the workload of anesthesiologists has always been concerned. Therefore, drug delivery robots have been rapidly developed and widely used in clinical practice. These major advances in anesthesia delivery control system are summarized in **Table 1**.

In 2016, an intravenous anesthesia robot developed by a Beijing company was successfully tested for the first time in Beijing and relevant research papers of its mature core technologies have been published before the system came out [31-34]. The system is used to automatically complete general anesthesia mainly through continuous monitoring of the depth of sedation, pain index, muscle relaxation, blood flow and other parameters, and then remote control through cloud computing to adjust the rate of drug delivery with feedback. At present, the system is in the stage of clinical testing, which opens a precedent for the application of Multiple Input Multiple Output systems [35].

Pattern recognition capabilities of neural networks enable the automatic classification of breath failures. Many studies on intelligent anesthesia alarm systems have shown that neural networks are the technical cornerstone in this field [36]. In 1994, Orr et al. installed sensors at designated locations to measure respiratory signals, such as pressure, flow, and carbon dioxide, among which 30 descriptive features were extracted for each breath circuit, and finally, a neural network system was trained to identify 13 faults in an anesthesia breathing circuit [37]. In animal tests, the system detected 95.0% and 86.9% of the introduced failures in controlled ventilation and spontaneous respiration, respectively [37].

Similarly, a hierarchical artificial neural network monitor developed by Narus et al. identified 23 faults in 92% of cases and 21 faults in 83% of cases during controlled and spontaneous breathing, respectively [38]. These days, artificial neural networks have been proven be useful in creating intelligent anesthesia alarm systems and have already been applied to some high-end ventilators or anesthesia machines.

In recent years, closed-loop systems have not been limited to anesthesia, sedation, analgesia, muscle relaxation, etc. In order to further explore the clinical value of closed-loop systems, researchers have also developed closed-loop systems for perioperative fluid infusion and vasoactive drug management. In the treatment of acute respiratory distress syndrome, positive end expiratory pressure (PEEP) is one of the important parameters following the principles of the open lung concept [39]. Application of PEEP can reinflate collapsed alveoli and increase arterial oxygen content, but too high PEEP can lead to hemodynamic instability and reduce oxygen delivery. AI can be used to develop an automatic control system for mechanical ventilation therapy based on the open lung concept. This innovative closed-loop mechanical ventilation system intelligently regulates intraoperative PEEP, end-tidal carbon dioxide, and other parameters, as well as the use of vasoactive drugs, leading to a significant improvement in oxygenation. The experiment with porcine dynamics demonstrated the feasibility and usefulness of this automatic closed-loop ventilation therapy, with hemodynamic control for severe acute respiratory distress syndrome [39].

AI in post-operative anesthesia

Pain treatment

In the field of pain treatment, the use of pain questionnaires is subjective and limited. Thanks to its powerful data analytics, AI is turning out to be valuable. Hu et al. presented an innovative and feasible neuroimaging-based augmented reality/AI concept that can potentially transform the human brain into an objective target to visualize and precisely measure and localize pain in real time [40]. In this study, the neutral network with 3 layers achieved an optimal classification accuracy of 80.37% in discriminating pain and no-pain, and the neural networks with 6 layers achieved the highest classification accuracy of 74.23% for localizing left side pain, right side pain, and no-pain states [40].

Postoperative complication prediction

As described above, postoperative adverse events for hospitalized patients can be better predicted with preoperative risk prediction, intraoperative hypotension prediction, and intraoperative hypoxemia prediction.

Postoperative in-hospital mortality prediction

An important evaluation in post anesthesia care unit is to assess post-surgical in-hospital mortality. In this context, Lee et al. developed a generalized additive model with neural networks [41]. It turns out that in terms of performance, it exhibited a high AUC in predicting the mortality of patients with general anesthesia. Over relatively simple models such as Logistic Regression, it shows better model performance; while over relatively complicated models such as DL, it shows less "black box" features [41]. For example, it can work on nonlinear data, and it has better transparency and higher accuracy with a notable AUC of 0.921.

Perioperative deep venous thrombosis (DVT) prediction

The formation of DVT is an extremely complex pathological process, and studies have shown that it is closely related to numerous basic health data and surgical factors of patients [42]. Any single factor is not enough to directly lead to the occurrence of DVT, so predicting DVT based on one or few variables is bound to increase the rate of missed diagnosis [42]. A patient-specific decision system, which had its origin from 35,963 total hip and knee arthroplasty patients, was created to predict the incidence of DVT, pulmonary emboli and major bleeding after operation [43].

Summary and future directions

The application of AI in medicine is aimed at solving patients' health problems and has grown rapidly in recent years. AI is a potentially powerful tool, but it comes with multiple challenges [44]. One objection is that AI, especially neural networks, has the black box problem. The physician can provide the input and get the prediction (output) through an algorithmic model but cannot examine the logic that produced the decision. In other words, the model cannot give extra details to explain how it works and why the output is produced [2]. Therefore, people pay attention to transparency and interpretability of the AI algorithms. For example, decision tree is an easy to understand and interpretable model, because it not only gives the prediction of the input data, but also provides a series of intermediate decisions that lead to the final prediction, which the researcher can verify or question. However, the accuracy of decision tree prediction is lagging behind that of neural networks. Therefore, combining neural networks with decision trees is a feasible direction to improve their interpretability and maintain their accuracy.

Secondly, AI algorithms are susceptible to bias in data. Whether human biases, like racial biases, will be coded explicitly or implicitly into the algorithms is debatable. People generally believe that ML algorithms, without judgments of human, is free of bias, but in fact bias is horrendously integrated into sample data. The main cause of ML data bias is the lack of diversity of data samples [45]. Data from a single source may lead to erroneous conclusions.

The promise of a fiduciary relationship between patients and doctors becomes unclear with the involvement of AI [46]. At present, with the introduction of AI, there are no laws and regulations to clarify the fiduciary compact. Who is responsible for the errors that generated by AI during its application in diagnoses? Is the responsibility for determining treatment still with the physician?

Doctors are aware of protection of patient privacy, but AI requires all aspects of the patient's data, because patients cannot benefit from the algorithm without data. The implementation of AI will therefore require a redefinition of confidentiality and other core tenets of professional ethics [46]. At the intersection of AI and medicine, a strong regulatory body is urgently needed to weigh all the elements of data ethics management [3]. The use of scientific regulatory concepts holds the potential to foster a deep integration among AI, the medical field, and regulators [47].

Will anesthetists be replaced by AI and lose their jobs and have to deliver food [48]? Maybe in the future, but not yet. Now we are in the "weak AI" stage where AI can achieve good results in a specific domain, but not as universal as people [49]. For example, AlphaGo can only be used in Go, not in chess or military chess. Similarly, the model developed by Lee et al. seems be incapable of predicting outcomes if we double the dose of either propofol or remifentanil, because the training data did not include this case when the neural network was built [22].

Admittedly, AI is technologically superior to humans in integrating complex, large, and structured data sets. But most of the data that doctors collected is based on a trusted doctor-patient relationship, wherein patients place their trust in their healthcare providers rather than AI [2]. Therefore, physicians should not only make full use of the powerful DL capabilities of AI, but also give full play to the advantages of humans, striving for a complementary relationship between humans and computers.

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