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Progress of Artificial Intelligence in anesthesia and perioperative medicine

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, and anesthesia guarantees smooth operation, comfortable recovery, and long-term good outcome for patients. There is a huge amount of clinical data in anesthesia and perioperative medicine. Because the Artificial intelligence (AI)'s powerful ability of data analysis and evaluation, predicting data based on real clinical big data analysis is a significant advantage of the application of AI in anesthesia and perioperative medicine. Now AI has made some progress in the field of anesthesiology and perioperative medicine. This review is divided into sections dealing with most encountered computerized techniques of AI in anesthesiology, main clinical applications themes of AI in anesthesiology which are divided by perioperative period, and limitations and ethical implications involved in deployment of this technology. The aim of this review of the intersection of AI and anesthesia research is to describe the current state of the research in the field, to discuss the advantages and disadvantages of introducing AI into the medical field, to explore the development direction of anesthesiologists in the future and to inspire scholars' interest in this cross-cutting field.

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

1. 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 (NLP; Figure 1)[1]. In addition to the patient's health data, there are likewise substantial perioperative monitoring data as anesthesia runs through the whole process of the perioperative period, which creates opportunities for the application of AI in the field of anesthesia. Therefore, the characteristics of anesthesiology as a data-intensive discipline make it most likely to benefit from advances in AI[2].

1.1 Machine learning

ML is currently the most mainstream way to achieve artificial intelligence in which a computer generates rules underlying by feeding the 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., BIS), discover associations, generate latent rules, and predict the outcome of continuous learning by computers 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 (kNN) 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 combination of supervised learning and semi-supervised learning where the model is trained with the input eigenvalue and part of the target value.

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

1.2 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 input[3]. The most representative algorithms of deep learning networks are convolutional neural networks (CNNs), which better designed process data with a grid-like structure, such as image data which can be views as two-dimensional grid of pixels (Figure 2). Recurrent neural networks (RNNs) are known as "memory" network of DL, which are sensitive to the sequence of the input. Therefore, RNNs are effective for mining temporal and semantic information from sequential data such as speech[4]. The strength of DL over traditional ML is 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, with simple neuron level processing signal, and then through the weight for parameterization of connections between neurons.

This review aims to identify techniques of AI that are being applied to anesthesia research and describe 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 database of PubMed. 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.

2. AI in pre-operative anesthesia

2.1 Preoperative risk prediction

Risk prediction is the most common AI application in preoperative assessment. Risk stratification is the basis of anesthesia. However, traditional preoperative anesthesia classifications are manually reviewed by clinicians, with certain subjective judgments and limited granularity. Supervised ML methods, specifically random forest split classification, have been tested to automatically generates an ASA PS with finer granularity[5]. This score of preoperative patient acuity may be able to aid anesthesiologist in identifying at-risk patient.

Multiple systems, targeted preoperative risk prediction, have been proposed to ameliorate existing scores such as ASA PS, even defined extra patient-specific risk scores. For example, 51457 patients with different types of major surgery were collected by a famous system called "MySurgeryRisk"[6]. For each patient, 285 preoperative parameters were selected and machine learning was used to establish "MySurgeryRisk" AI system which generate the risk score. Moreover, many scholars have optimized perioperative risk prediction with better algorithms and superior performance. Similarly, Fritz B.A *et al.*[7] developed multipath CNN model from the data of 95907 surgical patients. For each patient, 56 preoperative parameters were selected to predict the risk of death at 30 days. This algorithm has been shown to have better performance with higher AUC value when compared to that of CNN model, random forest model, support vector machine, and logic regression algorithm.

2.2 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 intubation still faces challenges. 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.*[8] developed a CNN algorithm capable of evaluating the difficult intubation with an area under the curve (AUC) of 0.864 by evaluating patients' facial pictures in the supine-side-closed mouth-base position. Matava *et al.*[9] critically assess the current evidence on the use of artificial intelligence and machine learning in the assessment, diagnosis, monitoring, procedure assistance, and predicting outcomes during pediatric airway management.

In addition to AI face recognition analysis techniques that can be used to predict difficult intubation, acoustic features can also predict difficult intubation[10]. Preoperative clinical airway assessment was performed, and acoustic data were collected of 225 patients who underwent orthognathic surgery under tracheal intubation. 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, specificity of 0.582, and sensitivity of 0.772. Acoustic feature shows the potential for predicting difficult intubation among the patients under general anesthesia.

3. AI in intra-operative anesthesia

3.1 Intubation and extubation operation

Intubation is one of the most important anesthetic skills. In 2012, T.M. Hemmerling *et al.*[11] developed a robotic intubation system (Kepler intubation system, KIS) for oral tracheal intubation. 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 was high at 91% for the first human testing of such a 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 artificial intelligence. 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 prevented intubation using KIS.

In the context of coronavirus disease 2019 (COVID-19) pandemic, professor Lu Yi's team 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 can successfully implement tracheal intubation, and the time required is lower than that of traditional laryngoscopy, more importantly reduce the risk of occupational exposure of medical staff.

Robotic endoscope-automated via laryngeal imaging for tracheal intubation (REALITI) has been developed to enable automated tracheal intubation[13]. The robotic device has real-time image recognition and remote automatic positioning. The user can manually control the bending movement of the endoscope tip, and when the image recognition detects the glottal opening, the user can hold down a dedicated button to activate the automatic mode. In automatic mode, the tip of the speculum moved toward the geometric center point of the glottal opening until it entered the trachea. The first automated tracheal device insertion in a manikin has been successfully performed with comparable results in a convenience sample of anaesthetists 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 health care workers to perform tracheal intubation. However, all intubations were performed on the airway trainer mannequin but they are not yet in clinical practice.

Early identification of critically ill patients who will require prolonged mechanical ventilation (PMV) has proven to be difficult. AI can help quantify the risk of extubation to assist in achieving individualized and accurate extubation. In a study, there were 20,262 total hospital stays identified with mechanical ventilation from the Multiparameter Intelligent Monitoring in Intensive Care III (MIMIC- III)[14]. PMV was defined as mechanical ventilation for more than 7 d. 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 trees algorithm for 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 (SOFA) score, cardiac arrhythmia, and the OASIS pre ICU length of stay (LOS). The classifiers for these patients who were admitted to surgical ICU predicted PMV with an AUC of 0.852, which can significantly reduce the probability of reintubation in patients.

3.2 Ultrasound-guided anesthetic techniques

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

In nerve block anesthesia, the performance is different due to the location, image parameters and patient specificity during the actual scanning. Compared with the traditional feature extraction method, deep learning neural network is more stable and accurate. In 2013, the first robotic system, Magellan[15], was invented to perform nerve blocks using a remote control center. The researchers presented the first human testing 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 J *et al.* [16]compared success rates, learning curves, performance times, and inter-subject performance variability of robot-assisted vs manual ultrasound (US)-guided nerve block needle guidance. Linear regression indicated that the average shortening time between two consecutive trials of robot-assisted nerve blocks 1.8 (1.6) seconds was significantly greater than that of manual blocks 0.3 (0.3) seconds. Therefore, this robot allowed beginners to master the operation skills faster and reduces the operator interval differences.

At present, epidural puncture needle placement is mainly manual operation, depending on the hand feel, and the failure rate is very high. 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 the identification of correct point of needle insertion to improve procedural success. Pesteie *et al.*[17] used the hybrid machine learning system to automatically localize the needle target for epidural needle placement and identify anatomical landmarks of epidural space in ultrasound images. Compared with sonographers, the hybrid machine learning system had a transverse and longitudinal error of 1mm and 0.4mm in the 3D-augmented test data plane, which effectively reduced the error and improved the comfort and safety of patients.

Performing subarachnoid or epidural anesthesia in obese patients, especially in obese pregnant women, remains a challenging task, with increased operational difficulty of determining the needle insertion point because of spinal changes induced by obesity and pregnancy. Acting on ultrasound imaging of the lumbar spine, a program based on ML algorithms was developed to automatically identify the needle insertion site[18]. The first attempt success rate for spinal anesthesia was 79.1%, which showed that the automated spinal landmark identification program is able to provide assistance to needle insertion point identification in obese patients.

For practicing UGRA, the tracking of the nerve structure in ultrasound images even for experienced operators is kind of capacity-testing, extremely labor intensive, due to the noise and other artifacts. By using additional information to track nerves and blood vessels, a detection and tracking framework is used in combination with a robotic system to assist in the UGRA. A new and robust tracking technique by using Adaptive Median Binary Pattern (AMBP) was introduced as texture feature for tracking algorithms[19]. This fully automatic nerve tracking method in Ultrasound images achieved best performance with 95% accuracy when it was applied on real data and evaluated in different situations.

Studies of stroke require the acquisition of patient-specific geometry of the carotid artery bifurcation. Although C-mode computed tomography (CT) and magnetic resonance (MR) are effective tests, there are many limitations including but not limited to ionizing radiation, unaffordable expense, and not available for all patients. Ruijter J *et al.*[20] developed an automatic 3D geometry segmentation algorithm for ultrasound images using a 2D US probe. This algorithm is able to segment the common carotid artery (CCA), the internal carotid artery (ICA), and the external carotid artery (ECA) including the carotid bifurcation in transverse B-mode images in both healthy and diseased arteries. The success rate was 89% where this method was tested on 19 healthy volunteers and on 3 patients.

3.3 Depth of anesthesia monitoring

Bispectral index (BIS) and electroencephalogram (EEG) characteristic parameters are usually used to evaluate depth of anesthesia (DoA). However, in anesthesia monitoring, the reliability of the BIS can be affected by numerous other interferences, such as the patient's own factors (basic diseases, etc.), the combination of different anesthetics, muscle relaxants, intraoperative electric coagulation, etc[21]. AI could be used to improve depth of anesthesia (DoA) monitoring. Yu *et al.*[22] proposed an adaptive control scheme that combines BIS and blood pressure to ensure the correct amount of target setting point and drug in the body even if BIS signal is lost intermittently.

ML methods have testified to his competence of processing complex data streams such as EEG. Therefore, a range of EEG-based signals that indicates states of the brain have been analyzed by ML approaches to accurately scale the DoA. In Gu's research, an algorithm based on artificial neural networks (ANNs) and EEG to evaluate DoA was presented. The output results of this algorithm clearly demonstrated a strong linear correlation with BIS[23].

Moreover, machine learning is used to distinguish states of consciousness based on EEG[24]. Three sedation situation was studied with dexmedetomidine i.v., propofol i.v., or natural sleep in this research. Distinct source localised signatures of sensory disconnection and unconsciousness were identified using support vector machine classification. It indicated that occipital delta power differentiated disconnected and unconscious states for dexmedetomidine but not for sleep/propofol. These findings may enable novel monitors of the anaesthetic state that can distinguish sensory disconnection and unconsciousness, and these 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[25,26].

3.4 Intraoperative hypotension and hypoxemia prediction

Intraoperative monitoring of adverse events, such as intraoperative hypotension, which is typically common, is a crucial period of anesthesia execution. Early prediction of adverse events allows physicians to take timely action to significantly reduce patient morbidity and mortality. As mentioned earlier, due to the datafication of clinical information, real analysis based on big data is the advantage of AI applied to predict patterns of intraoperative blood pressure.[27] A model for predicting hypotension based on ML methods analysis of arterial pressure waveforms was established by Hatib F *et al.*[28]. In this real-time dynamic prediction system, the evolution of mean arterial pressure (MAP), the time-to-event interval, is highly consistent with the hypotension prediction index (HPI, the algorithm output).[28]

Similarly, there is a lack of reliable indicators for the prevention of intraoperative hypoxemia. A system, based on ML, was developed to assist anesthesiologist in predicting the occurrence of hypoxemia during anesthesia and delineate the risk factors that contributed to the prediction by visually presenting a weighted function model.[29]

3.5 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 have been summarized in Tables 1.

In 2016, an intravenous anesthesia robot developed by a Beijing company was successfully tested for the first time in Beijing. The system is 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, feedback regulation of drug delivery speed, to automatically complete general anesthesia. At present, the system is in the stage of clinical testing, which opens a precedent for the application of Multiple Input Multiple Output (MIMO) systems[30].

Pattern recognition capabilities of neural networks (NNs) make it possible in automatically classifying breath failures. The performance of many studies related to intelligent anesthesia alarm systems have shown that neural networks have been the technical cornerstone in this field[31]. In 1994, Orr JA *et al.*[32] installed sensors at designated locations to measure respiratory signals such as pressure, flow, and carbon dioxide. 30 descriptive features was extracted for each breath circuit from the breathing signals mentioned above. A neural network system was trained to identify 13 faults. In animal tests, the system detected the problems and reported corrected messages for 95.0% and 86.9% of the failures in controlled and spontaneous respiration, respectively.

Similarly, a hierarchical artificial neural network monitor was developed by Narus SP *et al.*[33] to identify 23 faults in 92% of cases and 21 faults in 83% of cases during controlled and spontaneous breathing, respectively. These days, ANN has been proved be useful in creating intelligent anesthesia alarm systems and already applied to some high-end ventilators or anesthesia machines.

In recent years, closed-loop systems are not 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 (ARDS) patients, Positive End Expiratory Pressure (PEEP) is one of the important parameters following the principles of the open lung concept (OLC)[34]. 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. Artificial intelligence can be used to develop an automatic control system for mechanical ventilation therapy based on the open lung concept (OLC). 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, leads to a significant improvement in oxygenation. The experiment with porcine dynamics demonstrates the feasibility and usefulness of this automatic closed-loop ventilation therapy, with hemodynamic control for severe ARDS.

4. AI in post-operative anesthesia

4.1 Pain medicine

In the field of pain medicine, the use of pain questionnaires is subjective and limited. Thanks to its huge data and complex analyzes, AI is turning out to be valuable. Hu X *et al.*[35] presented an innovative and feasible neuroimaging-based Augmented Reality/Artificial Intelligence (AR/AI) concept that can potentially transform the human brain into an objective target to visualize and precisely measure and localize pain in real time. In this study, the neutral network (NN) with 3 layers achieved an optimal classification accuracy at 80.37% for pain and no pain discrimination, and NN with 6 layers achieved highest classification accuracy at 74.23% for localizing 3 classes of left side pain, right side pain and no-pain states[35].

4.2 Postoperative complication prediction

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

4.2.1 Postoperative in-hospital mortality prediction

Post anesthesia care unit (PACU) evaluation to be performed is the assessment of post-surgical in-hospital mortality. In this context Lee *et al.* [36] have developed a generalized additive model with neural networks (GAM-NNs). It turns out that in terms of performance, it shows a high AUC in predicting mortality in patients with general anesthesia. It has many advantages over simple models such as LR used in previous studies. For example, it can work on nonlinear data, and it has better transparency and higher accuracy with a notable AUC of 0.921.

4.2.2 Perioperative deep venous thrombosis prediction

The formation of deep venous thrombosis (DVT) is an extremely complex pathological process and studies have shown that it is closely related to numerous patient's basic health data and surgical factors[37]. Any single factor is not enough to directly lead to the occurrence of DVT, so predicting DVT based on one or several variables is bound to increase the rate of missed diagnosis[37]. A patient-specific decision system, which had its origin from 35,963 total hip (THA) and knee arthroplasty (TKA) patients, was created to predict the incidence of deep vein thrombosis (DVT), pulmonary emboli (PE) and major bleeding (MBE) after being operated[38].

5. Summary and future directions

The application of AI in medicine is aimed at solving patients' health problems, which is the most original and radical purpose, and has grown rapidly recently. AI is a potentially powerful tool, but it comes with multiple challenges[39]. One objection is that AI, especially neural networks, leads to 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 network. 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 will be coded explicitly or implicitly into the algorithm like similar racial biases. 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[40]. Data from a single source may lead to erroneous conclusions.

The promise of a fiduciary relationship between patients and doctors becomes unclear with AI involved[41]. 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 AI uses to diagnose? Is the responsibility for determining treatment still with the physician?

Doctors traditionally protect patient privacy, but AI requires all aspects of the patient's data, because patients without data cannot benefit from the algorithm. The implementation of AI will therefore require a reimagining of confidentiality and other core tenets of professional ethics[41]. 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 has the potential to foster a deep integration between AI, the medical field, and regulators[42].

Will the anesthetists be replaced by AI and lose their jobs and have to deliver food[43]? Maybe in the future, but not yet. Now we are in the “weak AI”[44] stage, it usually achieves good results in a specific domain, but it is not as universal as people. For example, AlphaGo can only be used in Go, not in chess or military chess. Similarly, the model developed by Lee *et al.*[21]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 trained.

From the perspective of our ordinary people's medical treatment, now AI has invisibly covered various scenes in the medical process. Admittedly, AI is technologically superior to humans in integrating complex, large, structured data sets. But most of the data that doctors collect is based on a trusted doctor-patient relationship, where patients trust their doctors rather than AI[2]. Therefore, physicians should not only make full use of the powerful deep learning ability of AI, but also give full play to the advantages of humans and strive to complement each other between humans and computers.

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