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Research article

Feasibility of intelligent drug control in the maintenance phase of general anesthesia based on convolutional neural network

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ABSTRACT

Background: The growth and aging process of the human population has accelerated the increase in surgical procedures. Yet, the demand for increasing operations can be hardly met since the training of anesthesiologists is usually a long-term process. Closed-loop artificial intelligence (AI) model provides the possibility to solve intelligent decision-making for anesthesia auxiliary control and, as such, has allowed breakthroughs in closed-loop control of clinical practices in intensive care units (ICUs). However, applying an open-loop artificial intelligence algorithm to build up personalized medication for anesthesia still needs to be further explored. Currently, anesthesiologists have selected doses of intravenously pumped anesthetic drugs mainly based on the blood pressure and bispectral index (BIS), which can express the depth of anesthesia. Unfortunately, BIS cannot be monitored at some medical centers or operational procedures and only be regulated by blood pressure. As a result, here we aim to inaugurally explore the feasibility of a basic intelligent control system applied to drug delivery in the maintenance phase of general anesthesia, based on a convolutional neural network model with open-loop design, according to AI learning of existing anesthesia protocols.
Methods: A convolutional neural network, combined with both sliding window sampling method and residual learning module, was utilized to establish an "AI anesthesiologist" model for intraoperative dosing of personalized anesthetic drugs (propofol and remifentanil). The fitting degree and difference in pumping dose decision, between the AI anesthesiologist and the clinical anesthesiologist, for these personalized anesthetic drugs were examined during the maintenance phase of anesthesia.
Results: The medication level established by the "AI anesthesiologist" was comparable to that obtained by the clinical anesthesiologist during the maintenance phase of anesthesia.
Conclusion: The application of an open-loop decision-making plan by convolutional neural network showed that intelligent anesthesia control is consistent with the actual anesthesia control, thus providing possibility for further evolution and optimization of auxiliary intelligent control of depth of anesthesia.

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1. Introduction

The depth of anesthesia depends on the applied dose of respective anesthetic drugs, but in most of the cases, individuals have distinct sensitivity to these drugs. The stimuli during operation has also changed continuously, so varying depths of sedation and analgesia are required in distinct maintenance phases of anesthesia, while the anesthetic drugs must be timely controlled. Such drug monitoring persists throughout the anesthesia during the whole operation, thus requiring a distinctive and continuous attention from the involved anesthesiologists. Nevertheless, it is usually challenging for anesthesiologists to keep such a high level of dedication under constantly intensive work. According to a comprehensive cross-sectional survey which focused on the situation of anesthesiology departments, conducted by Chinese Anesthesiology Department Tracking Database (CADTD) in 2018–2019, chinese anesthesiologists were able to accomplish more than 4.6 million anesthetic procedures per year, from 2015 to 2017. Moreover, the annual growth rate of cases requiring anesthesia in operation room was 929%. Therefore, the workload of the Chinese anesthesiologists have increased by at least 10%, while the number of anesthesiologists during the same period rose by 597% (2/3 of the growth rate of anesthesia cases), so the burnout rate of clinical anesthesiologists in some regions had exceeded 68%, a much higher percentage as compared to those in Western countries [1]. Artificial intelligence (AI) can potentially address issues related to inconsistent labor force during clinical anesthesia [2]. Since AI does not reach exhaustion while maintaining a high-density monitoring and control, this approach may offer a more stable chain of anesthetic control and, at the same time, reduce the workload of anesthesiologists. As a result, anesthesiologists can be more focused on coping with complicated emergency procedures, thus maintaining organ function(s) in a more precise manner. Therefore, control systems of anesthesia, designed from reinforcement learning [3, 4] and other machine learning methods [5], may provide a safer and more efficient management of depth for anesthesia [6], as well as better maintenance of mechanical ventilation [7], analgesia [8] and prediction of events and risks [9].

In terms of decision-making systems for medication, specific plans made by the involved anesthesiologist(s) may, in fact, influence the current vital signs of their patients. Since it does not follow fixed rules, the system cannot be based solely on a closed-loop system. However, the greatest advantage of an open-loop decision-making system is that it can simulate and evolve the input of various real scenes, routinely faced by anesthesiologists, to achieve the preventive effects beyond the expectation of fixed rules, thus satisfying the requirements for distinct personalized medication applied at different times. In the process of general anesthesia, appropriate depth of the procedure, stable vital signs and sufficient organ perfus'ion are crucial priorities of anesthesia management [10]. Moreover, the management of anesthetic dose is one of the key factors for anesthesia management, which can be easily neglected by some anesthesiologists. Nevertheless, no personalized decision-making has been realized by open-loop AI algorithms in the context of the dosage of analgesic and sedative drugs, used during the maintenance phase of perioperative anesthesia. In the present work, the "AI anesthesiologist" model was first proposed to create conditions for the personalized management of AI-assisted anesthesia during the maintenance phase of anesthesia as well as some more precise and confident experience in medical anesthesia.

In the following sections, some recent research progress in regard to the application(s) of AI models is disclosed. Thereafter, the sources of major datasets as well as the specific cleaning steps for data preprocessing are provided. Specifically, the decision-making process of anesthetic dose was completed by formalizing AI. Respective algorithms are described in details, while the differences between AI decision-making and the actual clinical decision-making are further discussed and analyzed. Finally, we observed that the medication predicted by the "AI anesthesiologist" could be maintained at the same level as the actual medication recommended by the clinician(s). According to this work, intelligent algorithms might be potentially introduced into the surgical anesthesia management, thus providing innovations in the intelligent management of anesthesia.

1.1. Related research

Benefiting from the rapidly emerging and innovative algorithm models, including the rigorous data processing methods, AI technology has started to be applied into various disciplines of medicine [11]. Specifically, massive positive results of intelligent control of anesthetic medication have been obtained in regard to aspects of patient safety and recovery, reduction of treatment cost, and improvement of medical expertise [12, 13, 14, 15].

The earliest prototype of automated anesthesia was generated by clinical drug-based pharmacokinetics-pharmacodynamics (PK-PD) model and formed by servo-anesthesia theoretical system to the gradual improvement of the electroencephalogram monitoring system for depth of anesthesia. Based on this initial prototype, the indexes and parameters of the depth of anesthesia, such as bispectral index (BIS), have become widely used [16]. Moore and colleagues have demonstrated the validity of closed-loop anesthesia control system with BIS as a controlled variable by clinical research [17]. Padmanabhan and colleagues have developed a closed-loop anesthesia control algorithm, using BIS and mean arterial pressures, and then applied it to closed-loop control of continuous intravenous pumping of sedative drugs for patients in intensive care units (ICUs) [18]. Puri and coworkers have also demonstrated, *via* multi-center experiments, that the closed-loop system of automatic anesthesia delivery is superior to traditional manual control, in such a way that it can overcome the practical differences between anesthesiologists [19]. Shalbaf and colleagues have also applied multiple features of electroencephalogram to intelligent classification of the depth of anesthesia for patients submitted to sevoflurane gas [20].

In the research direction of anesthesia modeling and control, Visioli and coworkers used a proportional-integral-derivative controller to regulate the depth of hypnosis in anesthesia by using propofol administration and bispectral index as control variables [21]. Ionescu and colleagues described a bioimpedance sensor's development and validation for time-frequency analysis of pain phenomena [22]. They later proposed a mathematical framework for drug capture estimation in PK models for estimating optimal drug infusion rates to maintain long-term anesthesia in Covid-19 patients [23]. Struys and colleagues found that brain tumors may alter the pharmacokinetics of propofol [24]. Moreover, in a later study, they compared the bias and inaccuracy of population-based and individualized TCI propofol titrations using Bayesian adaptation [25].

Reinforcement learning (RL) is an AI branch that aims to maximize the expected return of strategies, under complex and uncertain environmental interactions [26]. RL has been extensively used in various fields of engineering and medical sciences. Komorowski and colleagues have developed "AI clinicians" by means of reinforcement learning to provide septic patients with the optimal personalized treatment strategies focused on intravenously injected drugs and vasopressin. Their results have indicated that, compared with human clinicians, the AI model can provide more valuable and reliable treatment strategies, thus effectively improving the prognosis and prolonging patient lifespan [27]. As for automatic pain management and intervention, Lopez-Martinez and coworkers have put forward a decision-making model of opioid dosing, based on deep RL, which help doctors to make appropriate medication decisions in the ICUs by providing personalized measures of pain management [28].

In contrast to existing studies, we have presently investigated a novel AI-based auxiliary anesthetic medication decision-making plan, to offer real-time suggestions and lightweight decision-making assistance for anesthesiologists possibly. At the same time, training and evolution of the "AI anesthesiologist" should be based on real and effective drug delivery in the clinic, thus reducing the risk of decision-making deviation to the patients [29, 30, 31].

2. Material and methods

Blood pressure is one of the most important monitoring indicators for patients undergoing surgery under general anesthesia, thus reflecting the organ perfusion of patients. Excessive high blood pressure not only increases the cardiac afterload as well as the risks of myocardial ischemia and heart failure, but also correlates with other complications such as cerebral vascular accident and bleeding. In contrast, low blood pressure may decrease organ perfusion and induce blood redistribution, possibly leading to anaerobic metabolism, increase on lactic acid accumulation and, ultimately, to organ failure and death. Hence, the maintenance of adequate blood pressure by an anesthesiologist during surgery can be considered as the primary management indicator to ensure patient safety.

As a short-acting intravenous anesthetic (derived from alkyl acids), propofol is often used to induce and maintain general anesthesia. After intravenous injection, this drug can be rapidly distributed across the body and lead to dormancy within 40 s, thus promoting a quick and smooth anesthesia. Remifentanil, an ultrashort-acting opioid analgesic with rapid onset, is capable of reaching an effective concentration within 1 min, so it has been frequently used to maintenance analgesia during general anesthesia. Both drugs

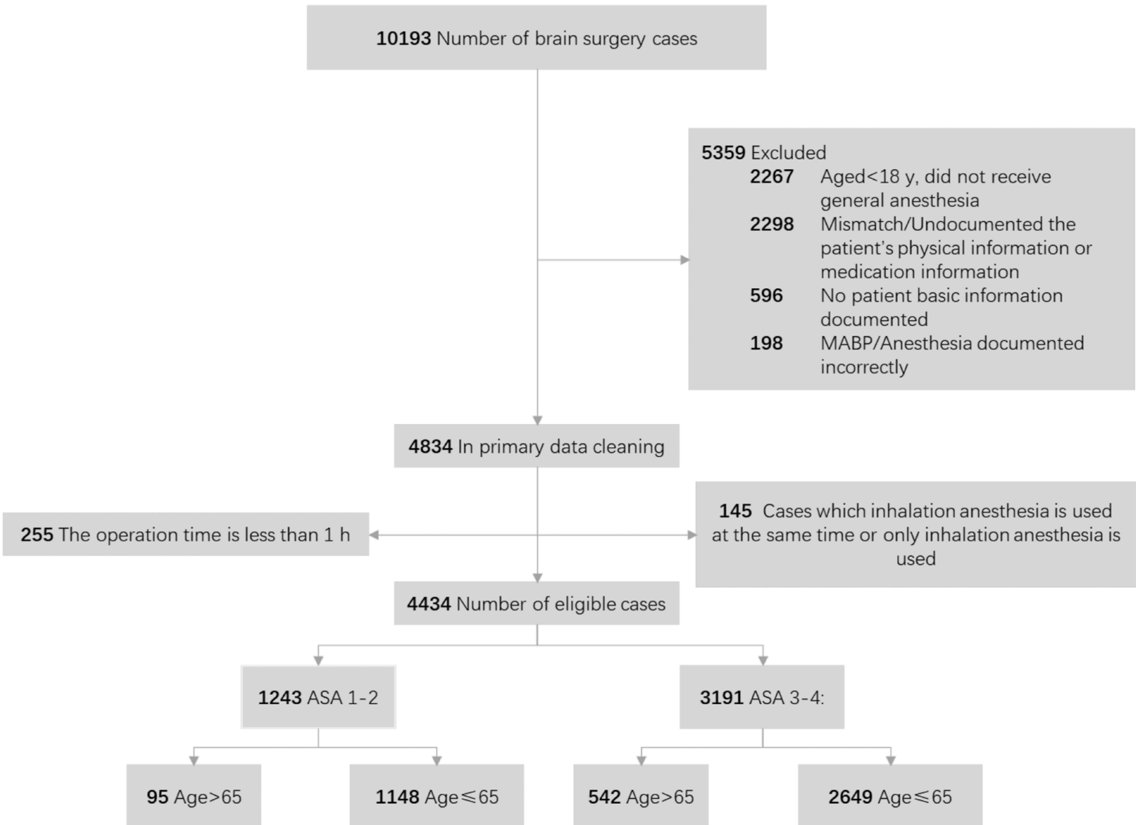

Figure 1. Workflow diagram for patient selection.

may lead to dose-dependent myocardial depression and vasodilatation effects, therefore affecting the blood pressure of patients and the depth of anesthesia. Moreover, the rapid onset and metabolism of these two drugs appear beneficial to control the depth of anesthesia and then facilitate a quick resuscitation. In the present study, propofol and remifentanil were both selected as prototypical drugs for regulating the depth of anesthesia and blood pressure. Hence, the feasibility of intelligent drug control, based on convolutional neural network, during the maintenance phase of general anesthesia was presently investigated.

2.1. Data extraction

Current data were collected from the database of the Information Center of West China Hospital, Sichuan University. All the authors had access to information that could identify individual participants during or after data collection. Real-time signs and medication information of the patients were recorded by the Information Center once every minute according to intraoperative information collecting modules. Information related to intraoperative medication and signs were extracted from 10,193 patients receiving neurosurgical procedures. This study was approved by the Ethical Committees of Sichuan University. All patients provided written informed consent in accordance with the Declaration of Helsinki. For each patient, the age, gender, height, weight, American Society of Anesthesiologists (ASA) grade, mean arterial blood pressure(MABP) and real-time dosage were obtained as representative input terms of feature The workflow diagram for patient selection is shown in Figure 1. Data cleaning rules were further formulated for all cases as the following:

2.1.1. Exclusion criteria

a. Patients with absent or abnormal (outlier) information on basic medication and real-time signs;
b. Patients younger than 18 years old, the blood pressure of minor patients is different from that of adults, and the blood pressure of different age groups is also different;
c. Patients who were not administered with propofol or remifentanil for anesthesia maintenance;
d. Patients submitted to surgery that took less than 1 h;
e. Patients with ASA grade higher than 4.

2.1.2. Data inclusion, stratification and cleaning

a. Data from anesthetic drugs and vital signs (MABP) obtained during the maintenance phase of general anesthesia were included. The starting time of intravenous remifentanil pumping was set as the beginning of the maintenance phase, while the termination time of the pumping for both remifentanil and propofol was defined as the respective endpoint of this phase. Moreover, any time slices where other inhalation-based anesthetics were simultaneously applied were also excluded;
b. The surgical patients were stratified according to the ASA grade and age.

To solve the issue of any eventual loss of local information sampling, a multivariate nearest-neighbor permutation was adopted for the interpolation processing of any missing data, the value of the missing item equal to the value of the valid sample at the nearest subsequent time point, and patient data were then encoded into multi-dimensional discrete time series. After preprocessing, the median time length of a single case was 332 min (interquartile range: 260–441 min). A total of 4,434 perioperative patients met the above criteria after data cleaning. The detailed information obtained from the datasets is shown in Table 1.

Table 1
Description of the datasets.

Description of the datasets	
Hospital	West China hospital
Characteristics of hospital	Teaching tertiary hospital
Operation room	Neurosurgery
Total number of cases	4434
ASA:1–2 [cases, (%)]	1458 (32.88%)
ASA:3–4 [cases, (%)]	2976 (67.12%)
Female gender [cases, (%)]	2468 (55.67%)
Age>65 [cases, (%)]	637 (14.37%)
18 < Age<65 [cases, (%)]	3797 (85.63%)
Age (x ± s, year)	49.58 ± 13.83
Height (x ± s, cm)	161.8 ± 8.59
Weight (x ± s, kg)	62.29 ± 11.12
Duration of anesthesia (P25, P75) minutes	332 (260,441)
Training data [cases, (%)]	3103 (70%)
Testing data [cases, (%)]	886 (20%)
Validation data [cases, (%)]	445 (10%)

2.2. Methodology

The datasets presently analyzed were randomly divided. In this case, complex case datasets were divided into three parts following cleaning, namely (i) training (70%), (ii) validation (10%) and (iii) testing (20%) sets. Specifically, the training set was employed to train the established model to determine the parameters of respective network. The validation set was used to test the convergence of the model during training and whether the training was overfitted. The testing set was applied to measure the fitting degree of decision when comparing the AI model and clinical evaluation. The algorithm framework is displayed in Figure 2.

An Anesthesia-based convolutional neural network (ACNN) model was designed, according to the collected patient information that included (i) ASA grade of operative risk, (ii) age, (iii) height, (iv) weight, (v) gender and (vi) real-time MABP as its input terms. Treatment protocols with personalized anesthetic auxiliary decision-making were generated according to the real-time MABP of the patients. The logical calculation formula was defined as the following:

$$f_t(propofol, remifentanil) = ANN_t(ASA, age, height, weight, gender, ABPMean_t)$$

In order to measure the accuracy of the ACNN model for predicting the dose of personalized drug, the accuracy rate of the cumulative error of respective dose was recorded. Thereafter, the symmetry and dispersion of medication established by the “AI anesthesiologist” were compared, and the distribution interval of medication between the two types of anesthesiologists was presented. Finally, the mean values of propofol and remifentanil used by both AI and clinical anesthesiologists, in different MABP intervals, were fitted separately. The reliability of the AI model to predict recommended medication(s) was judged by comparing the correlation of respective medication curves.

The sliding window method was adopted for data sampling, and the frequency of the time series for the maintenance phase in the perioperative anesthesia was set to 5 min. During the model training, the intraoperative data were sampled at three consecutive time-points each time. The information related to real-time signs and medication applied to the patients were regarded as the input terms of neurons. The decision at each time-point was sampled three times to properly simulate the ways of clinician thinking while taking into account the impact of the previous and/or next decisions on the current evaluation.

After tabulation of the input of structural data according to the model, the size of data segments was obviously smaller than that of non-structural data (i.e. videos and images). When the model was trained with structured input features, the correlation between the

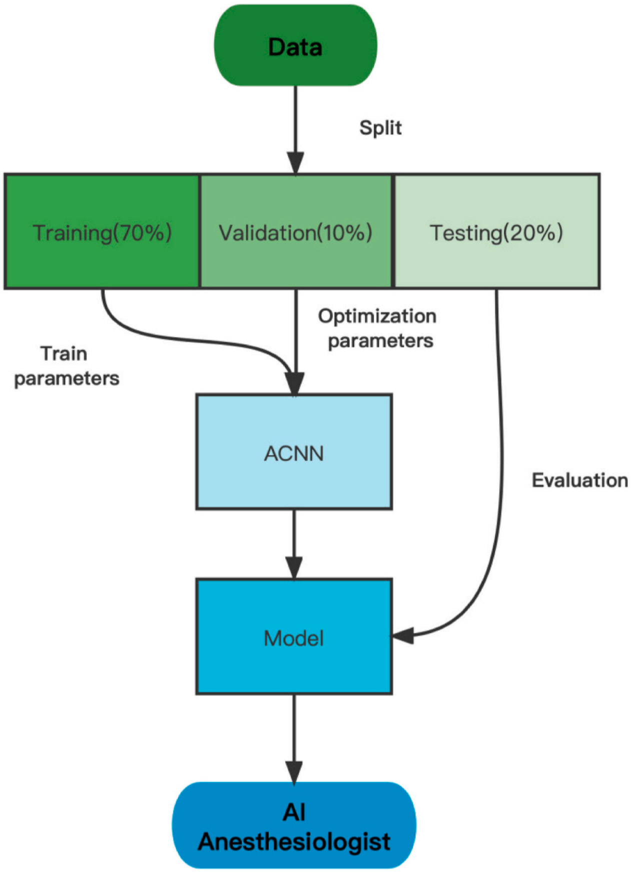

Figure 2. Data flow of AI Clinician.

gradients after several layers of back propagation became gradually weaker due to different linear changes, so the predictive effect of the network model was degraded beyond expectation. Therefore, a residual learning method was added to improve the accuracy of the model *via* the residual module and to optimize the model convergence [32]. The addition of a residual module enabled the identity mapping of the network model, in such a way that the network performance was not reduced by small data slices and increased network layers.

The purpose of The hierarchical structure of the ACNN was established by sliding sampling and residual module, as shown in Table 2 below. The anesthesia convolutional neural network algorithm proposed in this paper comprises five residual modules. The network model and data cleaning codes are designed and built independently based on the Pytorch (1.6) framework and python (3.8). The network uses the Adam optimizer with a learning rate of 0.0001 and a batch size of 256. The weight of the data window connected by each neuron, along different hierarchies, was adequately fixed.

Specifically, a Batch Normalization hierarchy was used for (i) data normalization, (ii) improvement of the generalization ability of the network, and (iii) acceleration of network convergence [33]. Transpose hierarchy was applied to calculate matrix transposition, while the Conv hierarchy was used for convolutional calculation between neurons and respective weights [34]. The LeakyRelu hierarchy was utilized to perform non-linear mapping of the output result of the Conv hierarchy [35], while the Squeeze hierarchy was applied to decrease the number of parameters [36] and improve the accuracy under limited parameters. The Gemm hierarchy was utilized to convert convolution into matrix operation and fill the matrix [37]. The final output neural network was able to predict the medication strategy proposed by the AI Clinician model from the discrete time series. This data is represented by the network framework, as shown in Figure 3.

3. Results

The cumulative proportion of the AI-based anesthetic dose prediction and the clinician-based drug dosing was compared across different ranges to further determine the accuracy of the model. When the cumulative error of propofol reached less than 0.2 mg/kg/h, the precision of the “AI anesthesiologist” was higher than 80% in different classification models. Similarly, the precision of the “AI anesthesiologist” exceeded 90% when the cumulative error of propofol was up to 0.4 mg/kg/h. When the cumulative error of remifentanil was lower than 0.04 and 0.06 μg/kg/h, the precision of the “AI anesthesiologist” in different models of patient classification was higher than 80% and 90%, respectively. In the case of cumulative error lower than 0.02 μg/kg/min, the sampling precision of the model was close to 70% for the average patients, including young and middle-aged subjects, as well as the young and middle-aged patients with ASA grade 3–4. The sampling precision was 70–80% for all remaining patients (Table 3).

The center line of each diagram block refers to the median value, while the bottom and top edges of each respective block represent the 25th and 75th percentiles, respectively. Whiskers extend to 1.5 times the quartile ranges.

Figure 4 displays the box plot distribution of drug dosing used by clinicians as well as the AI-based predicted drug dosing along the collected data, in which the medication symmetry between the AI and the clinical anesthesiologists, as well as the dispersion of medication distribution, was compared. For patients over 65 years old, the drug dose provided by the “AI anesthesiologist” was, in general, slightly higher than that given by the clinical anesthesiologist. For young and middle-aged patients, the “AI anesthesiologist” generally offered a slightly lower drug dose than the clinical anesthesiologist. The median doses of remifentanil used by the clinical and AI anesthesiologists were 0.15 (interquartile range: 0.12–0.2) and 0.15 (interquartile range: 0.13–0.18), respectively. The median doses of propofol used by the clinical and AI anesthesiologists were 4.186 (interquartile range: 3.50–5.00) and 4.10 (interquartile range: 3.60–4.90), respectively. Altogether, the median drug doses provided by the clinical anesthesiologist deviated more from the centers of the upper and lower quartiles when compared with those offered by the “AI anesthesiologist”, thus showing some obvious distribution skewness. In addition, the box data originated by the “AI anesthesiologist” was flatter, suggesting milder fluctuations along the distribution of recommended drug doses.

Table 2
Description of the network structure.

Input:Patient metrics	Network layer	Number of channels	other
Layer 1	Conv LeakyRelu	1→64	Stride = 2 Kernel size = 4
Layer 1	Conv BatchNorm + LeakyRelu	64→128	Stride = 2 Kernel size = 4
Layer 1	Conv BatchNorm + LeakyRelu	128→256	Stride = 2 Kernel size = 4
Layer 1	Conv BatchNorm + LeakyRelu	256→256	Stride = 2 Kernel size = 4
Layer 1	Conv BatchNorm + LeakyRelu	256→512	Stride = 2 Kernel size = 4
Layer 1	Conv BatchNorm + LeakyRelu	512→512	Stride = 2 Kernel size = 4
Layer 1	Conv BatchNorm + LeakyRelu	512→1	
Layer 1	Sigmoid	1→1	
Output: Drug dose prediction results			

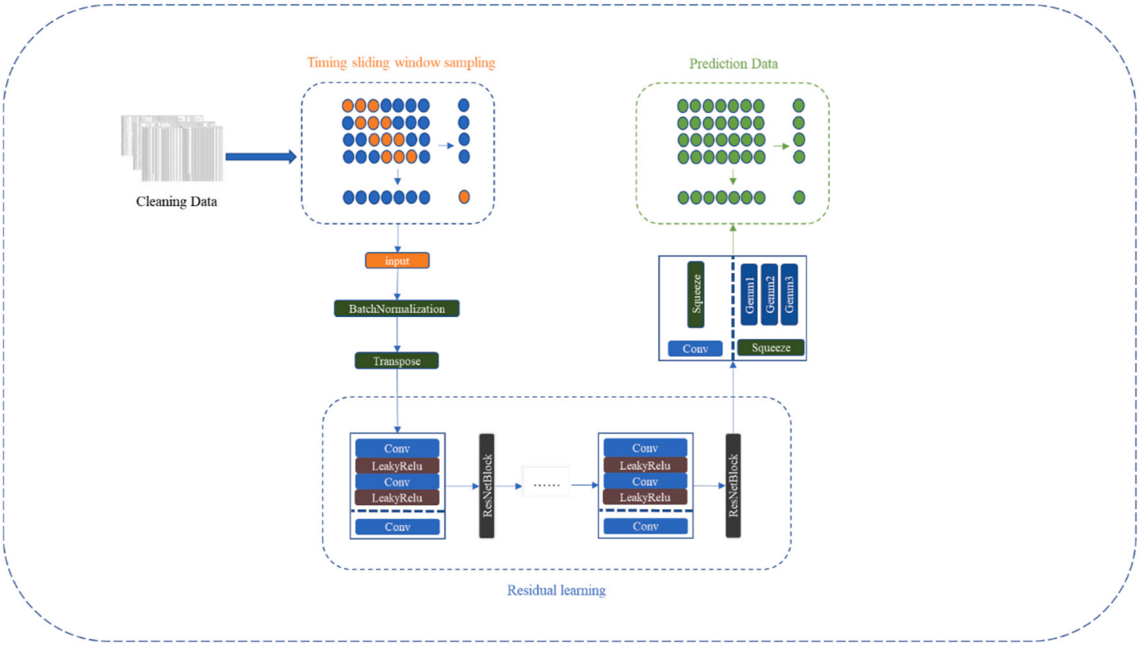

Figure 3. Overall architecture of ACNN. AI-based clinician using timing sliding window sampling, convolution networks and residual learning modules to timely predict the doses of both propofol and remifentanil.

Table 3
Statistics of cumulative error when comparing AI-based predicted dosing and actual dosing of propofol and remifentanil among different patient groups.

Classification		Age > 65		18 ≤ Age ≤ 65		Age > 65	18 ≤ Age ≤ 65	All
		ASA1-2	ASA3-4	ASA1-2	ASA3-4			
Dose deviation	<0.2	86.97%	83.29%	87.46%	81.74%	83.90%	82.69%	82.94%
	<0.4	94.26%	91.42%	93.65%	90.24%	91.90%	90.81%	91.03%
	<0.6	98.75%	95.24%	96.04%	94.87%	95.82%	95.07%	95.22%
	<0.02	80.50%	74.02%	70.36%	67.98%	75.10%	68.38%	69.72%
	<0.04	89.94%	86.65%	83.01%	82.98%	87.20%	82.98%	83.82%
	<0.06	95.88%	95.42%	93.19%	92.73%	95.50%	92.81%	93.35%

a. Cumulative error of propofol dosing, proposed by the "AI anesthesiologist", with three cumulative error thresholds (0.2, 0.4 and 0.6 mg/kg/h). The percentage indicates the hit ratio of the error of propofol dosing between the AI and the clinical anesthesiologists within different thresholds.
b. Cumulative error of remifentanil dosing, proposed by the "AI anesthesiologist", with three cumulative error thresholds (0.02, 0.04 and 0.06 μg/kg/min). The percentage indicates the hit ratio of the error of drug dosing between the AI and the clinical anesthesiologists within different thresholds.

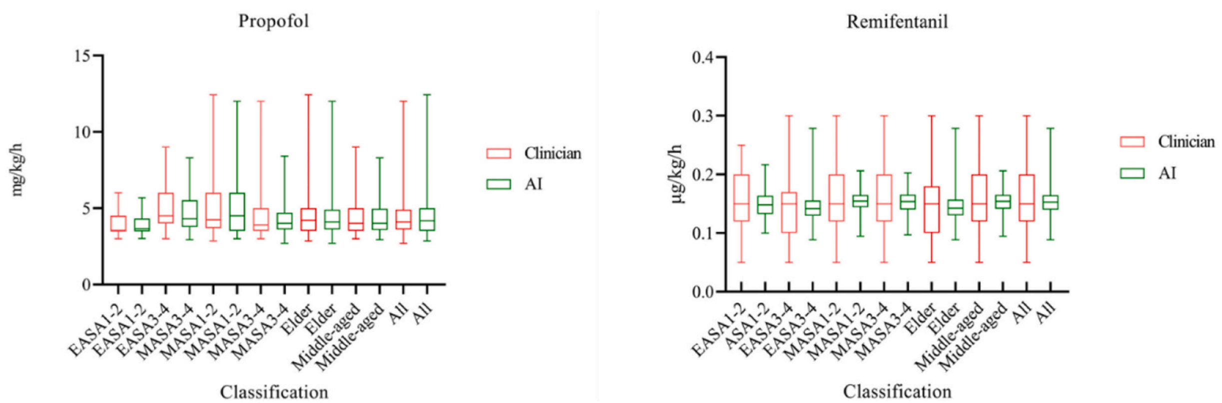

Figure 4. Box plot of dose distribution for remifentanil and propofol.

A heatmap of correlation between medication strategies suggested by clinical and AI-based anesthesiologists was drawn to further compare the dispersion between the actual and the AI-predicted medication (Figure 5), where the logarithm of statistical frequency was generated. It was manifested that the dose of analgesic and sedative drugs, as predicted by the "AI anesthesiologist", exhibited some variable fluctuation tendencies around the actual drug dose. For instance, the recommended dose of propofol predicted by the "AI anesthesiologist" was generally smaller than the actual dose. When the dose of remifentanil provided by the clinical anesthesiologist accounted for low or high values, the "AI anesthesiologist" often selected the dose fluctuating around the numerical value of 0.15.

The three-dimensional (3D) decision distribution was further analyzed to better compare the overall distribution of medication provided by either the AI or the clinical anesthesiologists (Figure 6). In this case, it was observed that the doses of propofol and remifentanil used by the clinical anesthesiologist were slightly higher than those recommended by the "AI anesthesiologist". Besides, the doses provided by the clinical anesthesiologist were excessively concentrated and distributed at 0.1–0.25 μg/kg/min for remifentanil and 3–4.5 mg/kg/h for propofol. However, the dose strategies provided by the "AI anesthesiologist" were distributed more evenly, within the range of 0.1–0.2 μg/kg/min for remifentanil and 3–6.5 mg/kg/h for propofol.

Finally, the similarities between the actual and predicted medication of propofol and remifentanil, at different fluctuation ranges of MABP during surgery, were verified on the testing sets. As shown in Figure 7, the curve of AI-based predicted dose was located farther away from clinician's dose curve, indicating a poorer fitting effect. The linear correlation analysis revealed that the Spearman correlation coefficient between the prediction curve and the actual medication curve for remifentanil was 0.93, while the same Spearman correlation coefficient for propofol was 0.99, thus indicating strong correlations. The "AI anesthesiologist" recommended elevating remifentanil and propofol doses as the MABP intervals increased, basically resulting into the actual doses used by the clinical anesthesiologist.

4. Discussion

The rationale utilized to select a self-constructed ACNN model instead of RL was that the first one is applicable to describing and solving the interaction process between intelligent agent and environment and, ultimately, obtaining long-term maximum benefits through learning as well as improving strategies. The depth of general anesthesia constantly changes during a surgical procedure and, likewise, can be essentially distinctive among individuals. Therefore, it has been challenging to determine the fixed optimal drug dose and formulate uniform evaluation criteria for different drug doses. Unlike the anesthesia control model based on PK-PD and hemodynamic models, using a convolutional neural network, an "AI anesthesiologist" was established to facilitate clinical decision-making *via* automatic treatment guidance rather than replacing the doctors in making decisions during intraoperative treatment.

The data exclusion criteria were designed during preprocessing to not only eliminate noise and ensure the availability of data, but also to exclude the cross influence of inhalation anesthetics. Additionally, the cases whose time of intraoperative anesthesia was lower than 1 h (among the preliminary cleaned adult cases) were subsequently excluded, thus avoiding wrong guidance of intraoperative clinical decision to the "AI anesthesiologist" model, which could affect the precision to predict both propofol and remifentanil doses.

Since BIS can be significantly affected by the basic vital status of patients and restrained by certain medical conditions, MABP was

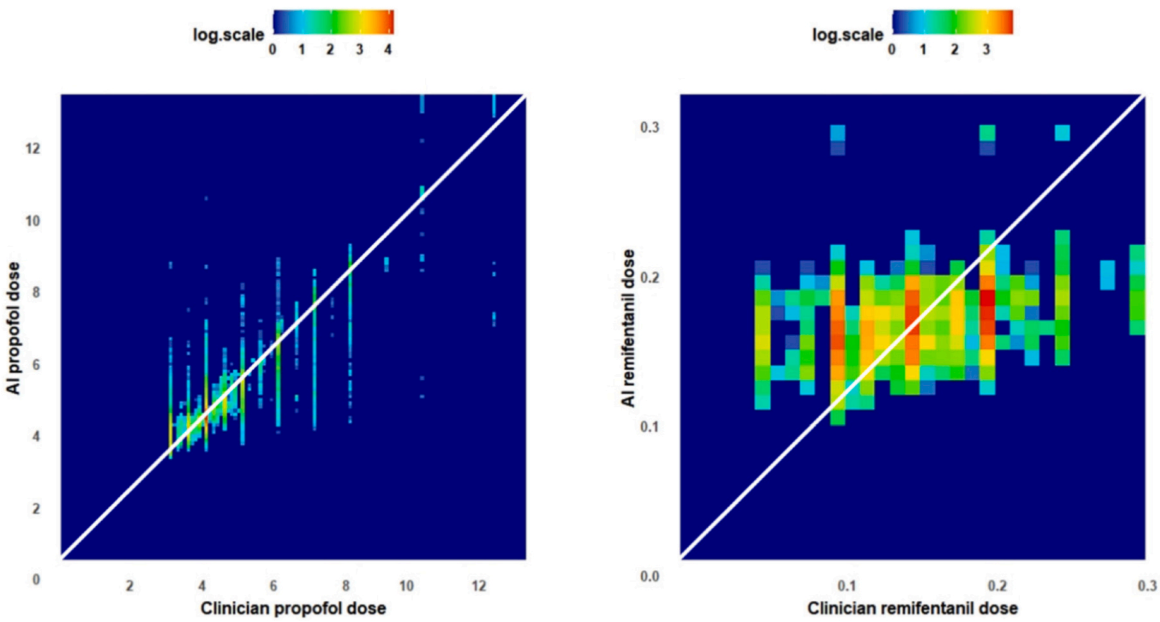

Figure 5. Comparison of medication strategies between clinical and AI-based anesthesiologists.

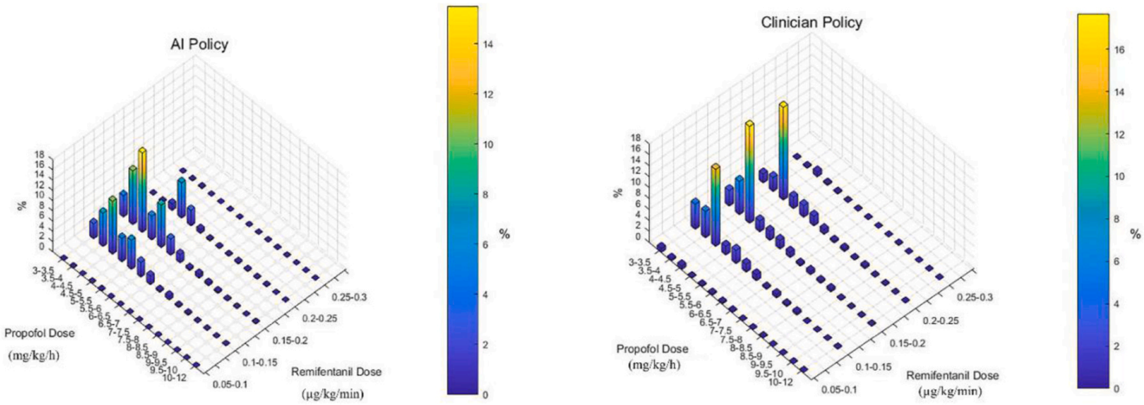

Figure 6. Three-dimensional (3D) decision distribution for clinician- and AI-based policies.

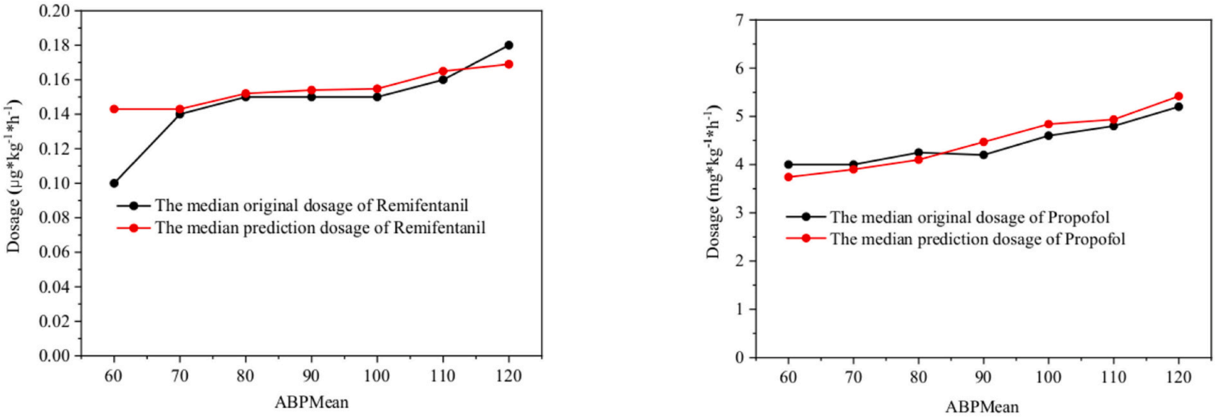

Figure 7. Line charts of anesthetic doses defined according to the MABP intervals.

selected as an input term of the model as well as the learning parameter for the "AI anesthesiologist". For critically ill patients, such as patients suffering from shock or subjected to cardiac and other major operations, clinicians usually choose blood pressure as the primary reference indicator to reflect the depth of anesthesia and vital function of patients, while BIS serves as a secondary reference indicator. Hence, MABP was first adopted in the univariate design of this study. According to our statistical results, the "AI anesthesiologist" could appropriately modulate the doses of propofol and sufentanil according to the MABP fluctuation, thus showing a medication trend which was consistent with that of the clinical anesthesiologist. However, it is undeniable that certain discrepancies on our results were still detectable. These may be attributed to the additional single-point injection of anesthetic drugs by clinicians, which is somewhat acceptable in the clinical practice. Chinese anesthesiologists are used to manually add single-point injection of drugs, at certain intervals during operation (according to the signs of respective subjects. In this case, the analgesic sufentanil has been applied as a conventional drug which may affect the dose of anesthetic drugs during the whole procedure, and frequently leads to a smaller overall dose of remifentanil. For such personalized medication, however, there are some differences in regard to clinician's habits and regions. Therefore, it does not have a universal guiding significance and does not meet the conditions to join the intelligent feedback mechanism. These are also one of the main reasons for the overall preparation of the initial and predicted drug doses, which appear to be relatively small.

Some limitations were also noticed in the present study. It can be seen from the results that the accuracy of the model in predicting anesthesia dose decreases relatively with the increase of the patient's ASA grade. The higher the ASA grade, the more comorbidities in the patient, and some underlying diseases may affect the rate of change in blood pressure. Then, whether it is the rate of blood pressure change or the sensitivity of patients to anesthetic drugs, the differences in patients' intraoperative decision-making will be more prominent. For instance, although the feasibility and reliability of the ACNN algorithm to fit the medication of clinical anesthesiologists were demonstrated by experiments, the capacity of the "AI anesthesiologist" to fully maintain stable vital signs and/or sufficient depth of anesthesia should be further verified in clinical human trials. Furthermore, adequate clinical data were collected in this study, but only a single type of operation was adopted, which could lead to some bias related to a single anesthesia mode during the model training. Therefore, incorporating data from more diversified types of anesthesia operations into training is warranted. So far, the scheme of performing intelligent prediction for intravenous infusion of analgesic and sedative drugs was only preliminarily explored in this study. Thus, inhalation-based anesthesia and other anesthetic techniques, with single-point drug injection, remain to be further investigated.

5. Conclusion

Issues related to anesthetic dosing, recommended by intelligent intravenous infusion, were presently investigated. For the first time, the feasible scheme of using the AI model with open-loop design to achieve intelligent control of drugs in the maintenance phase of general anesthesia was presently explored. The “AI anesthesiologist” was trained by the sliding window sampling method and the convolutional neural network (with residual learning module). As a result, it was verified that the medication distribution predicted by the “AI anesthesiologist” could be equivalent to the actual medication distribution provided by the clinical anesthesiologist, thus creating conditions for achieving AI-assisted anesthesia management during the maintenance phase of anesthesia and, therefore, providing precise and comfortable medical anesthesia experience. Based on this work, we expect to introduce the intelligent algorithm into operation anesthesia management and then innovate the intelligent management of anesthesia. We believe that the “AI anesthesiologist” may gradually increase its supplementary role during anesthesia maintenance and management, by also lowering the burnout rate of anesthesiologists, saving manpower and achieving precise anesthesia manipulation, thereby improving the quality of overall anesthetic procedures.

Declarations

Author contribution statement

1 - RW and CJ conceived and designed the experiments;
2 - RW, CX, YY, FZ, and CJ performed the experiments;
3 - RW, CX, TL, and CJ analyzed and interpreted the data;
4 - RW and CJ contributed reagents, materials, analysis tools or data;
5 - RW and CJ wrote the paper.

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Data availability statement

The authors do not have permission to share data.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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