

The Effect of Using Artificial Intelligence and Machine Learning on Parameters of Clinical Trial Involving Anaesthetic Agents

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Received: 25-06-2022 / Revised: 25-07-2022 / Accepted: 30-08-2022

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Conflict of interest: Nil

Abstract

Introduction: Machine Learning and Artificial Intelligence has been in application in several fields including medical field and there is immense untapped opportunity that is yet to be explored in using machine learning models to provide better health care. It may range from pharmacy, medical diagnosis to surgical intervention or support. There have been several occurrence of hypotension post induction of anaesthesia which increases the deaths of the patients undergoing surgery. Therefore, this study has brought forward applicability and analysis of machine learning models in predicting hypotension after induction of general anaesthesia intra-operatively.

Aims and Objectives: To find out the efficacy of performance between USG guided hypotension prediction post-induction and machine learning model by artificial neural networks.

Methods: This retrospective study collected demographic data of the patients underwent cholecystectomy under general anaesthesia from the hospital. The patients were given general anaesthesia, after which each of them was predicted for post-induction hypotension by employing conventional prediction of Inferior Vena Cava (IVC) parameters by ultrasound (USG) guided to determine hypotension post induction and artificial neural network which is a new machine learning model. Evaluation and comparison between the models were done mainly by determining 3 parameters, namely, precision, recall and accuracy.

Results: The study found that ANN is significantly ($p < 0.05$) efficient as compared USG guided prediction by IVC parameters which was conventionally done. The study also pointed out that the age factor is significant in deciding the hypotension after general anaesthesia intra-operatively.

Conclusion: The study has evidently proved the efficiency of machine learning model in this study (ANN) with that of conventionally used USG guided prediction.

Keywords: machine learning, artificial neural network, cholecystectomy, hypotension

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Introduction

The development of robots is usually seen as being the beginning of artificial intelligence (AI). Through the play "R.U.R" (Rossum's Universal Robots,

1921) by Czech playwright Karel Capek, the word "robot" itself was introduced to a wider audience [1]. The term "artificial intelligence," or "AI," refers to all the

methods that give computers the ability to imitate human intelligence. It is built on algorithms that enable computers to think and carry out tasks including problem-solving, word and object recognition, inference of world states, and decision-making [2].

The term "artificial intelligence" (AI) refers to a broad category of computers that are programmed to comprehend and carry out activities independently and in a "smart" way. Early attempts at medical automation relied on manually created algorithms that followed strict regulations, which is why they failed in challenging clinical settings. Today's healthcare industry may be in a perfect position to use technology to close the gaps, starting with telemedicine and digital health platforms and moving on to the use of AI [3].

It can be compared to programming computers to mimic cognitive processes like pattern recognition and problem solving that occur in the human brain. The ability to learn, or the change of actions based on prior experience, is a crucial component of AI. Designing a servo system, for example, to maintain Bispectral Index (BIS) within a specified range by continuous monitoring and adjustment of the infusion rate of the anesthetic agent(s) is one of the easier ways a computer may be used in anesthesia [3].

Machine learning would apply in this case if the program was created with the ability to learn from its past experiences. Machine learning, neural networks, deep learning, robotics, and computer vision are some of the different subdivisions of AI. As an example, postoperative mortality can be predicted using perioperative data, and post-induction hypotension can be predicted using preoperative and induction data by analyzing machine learning models, which have been developed to address specific relevant clinical questions using representative data [4, 5]. The caliber and technique of the studies on

which these models are based determine their dependability. Another problem is the difficulties clinicians have in comprehending the process used to make predictions.

A subset of machine learning (ML), deep learning (DL) makes use of multiple-layered artificial neural networks (ANN). ANN mimics the idea of how the human brain perceives and develops conclusions from information by using numerous layers of calculations. Multiple hidden node layers that learn representations of data by abstracting it in various ways are characteristics of deep learning (DL). The difference between DL and a simple neural network (NN) is that DL has more layers of nodes and a larger total network, which makes it possible to more precisely reflect complicated interrelationships [4].

Every area of medicine, including medical diagnosis, medical treatment, medication development, clinical management, and medical education, is benefiting greatly from AI [6]. For instance, using ML algorithms in patients with osteoporosis and Paget's disease, it was possible to identify the ideal therapeutic combination while minimizing drug-drug interactions, demonstrating the value of AI in lowering costs and saving time [7]. The study of anesthesia is not an exception in this regard. The most often used branch of AI in medicine is machine learning (ML), which gives computers the ability to continuously learn while analyzing massive amounts of data, identifying relationships, and forecasting results. It entails developing, testing, and analyzing algorithms with the capacity to carry out cognitive operations such association between variables, pattern recognition, and outcome prediction [7].

The subfields of anesthesia include anesthesia, intensive care medicine, critical emergency medicine, and pain medicine [8]. Although this area of medicine has a long history of development, the basic idea has remained

constant. The goal is to lessen sensitivity so that surgery can be done. Pre-operative, inter-operative, and post-operative anesthesia influences patient care primarily in three phases [9]. The goal of the preoperative phase is to evaluate the patient's preoperative surgical and anesthetic morbidity and mortality [10]. Inter-operative anesthesia involves managing medication control and patient monitoring during surgery. It necessitates the timely administration of medications in very precise and controlled amounts [11]. Prior to release, post-anesthesia care for patients who have undergone surgery is provided in a post-anesthesia care unit (PACU) [11].

This study intends to find out the efficiency between the conventionally used USG guided prediction of post-induction hypotension by determining the parameters of Inferior Vena Cava with that of machine learning model.

Materials and Methods

Research Design

This retrospective study involved adult patients (more than 18 years) who had cholecystectomy in our hospital. The data and baseline information of the patient including data regarding anaesthesia was obtained from the hospital. The study also considered vital signs and pharmacologic information of the patients including their past history and intra-operative data. In this study, the authors have divided the hypotension induced by anaesthesia into 2 phases, namely, early and late. Early Hypotension is considered from the induction of anaesthesia to tracheal intubation and late Hypotension was considered as the hypotension occurring after tracheal intubation to incision. The primary outcome of this study was to predict the probability of late hypotension by using machine learning data which is obtained during the early stage of anaesthesia induction. The authors considered Systolic Blood Pressure < 90

mmHg or Mean Blood Pressure < 65 mmHg as hypotension. The patients underwent routine monitoring including pulse oximetry, intermittent non-invasive blood pressure, ASA classification, electrocardiography, etc. The patients received general anaesthesia which was a combination of propofol (3–6 µg/mL) and remifentanyl (2–6 ng/mL) was infused by using target controlled pump containing microprocessor. The data related to the pharmacokinetic models of each drug was fed programmatically into the microprocessor.

This study facilitates using two models and making a comparative analysis between them. One of them is conventionally used ultrasound guided measurements of Inferior Vena Cava (IVC) parameters for determination of hypotension and another is machine learning tool ANN.

Collection of Data

Demographic data of the patients were collected. The timing of the anaesthesia induction was considered from the instance when administration of propofol was done via pump. Blood pressure and heart rate were determined in the operating room. The authors of this study obtained these data from the hospital records.

Inclusion and Exclusion Criteria

The patients who were more than 18 years old, underwent cholecystectomy conducted during the period of one year in our hospital were included. The patients who were given general anaesthesia were only considered. The patient who gave consents and cooperated throughout the whole study procedure, were included. The patients who did not complete the whole study procedure and those who could not give complete medical history, were excluded. After applying inclusion and exclusion criteria, the study finally considered 100 patients.

Models used in this study

All the included patients underwent both the prediction processes. One of them is conventional prediction of Inferior Vena Cava (IVC) parameters by ultrasound (USG) guided to determine hypotension post induction. Another is using artificial neural network which is a new machine learning model. In USG guided determination of IVC parameters, the patient is first made to lie in supine position and several parameters of IVC was determined using phased array transducer of USG. M-mode was used to determine the variation in diameter of IVC. In ANN, the complex neuronal connections were used for computation that derives values by using programmed function when information was input in the system.

Evaluation and comparison between the models were done mainly by determining 3 parameters, namely, precision, recall and accuracy.

$$\text{Precision} = \frac{TP}{TP + FP}$$

$$\text{Recall} = \frac{TP}{TP + FN}$$

$$\text{Accuracy} = \frac{TP + TN}{TP + FN + FP + TN}$$

TP = True Positive; FP = False Positive; TN = True Negative; FN = False Negative

Ethical Approval

The study was conducted after obtaining consent from each patient. The patients were made to understand the whole study procedure. The study was approval by the Ethical Committee of the hospital.

Statistical Analysis

The study used SPSS 25 and excel software for effective statistical analysis. The descriptive measurements were expressed as mean±standard deviation. The categorical variables were analyzed by using chi-square tests while for analyzing the performance of the models, ANOVA was used. The level of significance (α) was considered to be 0.05.

Results

The study found that 62 patients had hypotension while 38 patients had no hypotension following intra-operative anaesthesia. Table 1 shows the baseline characteristics of the study population according to the group.

Table 1: Baseline characteristics of the study population who finally had hypotension and had no hypotension

Characteristics	Hypotension N=62	%	No Hypotension N=38	%	p-value*
Age (years)	56.25±3.85		45.55±3.25		$p < 0.05$
<i>Gender</i>					
Male	38		22		$p > 0.05$
Female	7		13		$p > 0.05$
BMI	22.12±3.25		24.58±2.1		$p > 0.05$
<i>ASA classification</i>					
I	15	24.19	13	34.21	$p > 0.05$
II	31	50.00	22	35.48	$p > 0.05$
III	16	25.81	03	4.84	$p > 0.05$
<i>Comorbidities</i>					
<i>Cardiovascular disease</i>					
Hypertension	22	35.48	12	19.35	$p > 0.05$
Atrial fibrillation	2	3.23	1	1.61	$p > 0.05$

Coronary artery disease	1	1.61	1	1.61	$p>0.05$
Angina pectoris	1	1.61	1	1.61	$p>0.05$
Congestive heart failure	2	3.23	0	0.00	$p>0.05$
<i>Respiratory disease</i>					
Asthma	0	0.00	1	1.61	$p>0.05$
Chronic obstructive pulmonary disease	6	9.68	2	3.23	$p>0.05$
<i>Gastrointestinal disease</i>					
Hepatitis	1	1.61	2	3.23	$p>0.05$
Liver cirrhosis	2	3.23	1	1.61	$p>0.05$
Viral carrier	1	1.61	0	0.00	$p>0.05$
Hepatitis B viral infection	2	3.23	0	0.00	$p>0.05$
<i>Renal disease</i>					
Chronic kidney injury	3	4.84	3	4.84	$p>0.05$
<i>Endocrine disease</i>					
Diabetes mellitus	3	4.84	2	3.23	$p>0.05$
Thyroid disease	2	3.23	3	4.84	$p>0.05$
<i>Neurologic disease</i>					
Cerebrovascular disease	2	3.23	1	1.61	$p>0.05$
Cerebral aneurysm	1	1.61	1	1.61	$p>0.05$
<i>Baseline blood pressure—mmHg</i>					
Systolic	131.25±5.5		139.33±5.45		$p>0.05$
Diastolic	76.25±5.2		86.15±3.2		$p<0.05$
<i>Heart rate†—/min</i>					
	76.99±9.1		78.25±8.9		$p>0.05$
<i>Mechanical ventilation data†</i>					
Tidal volume—ml	269.84±5.28		276.1±6.3		$p>0.05$
Minute ventilation—L/min	3.1±0.3		3.2±0.1		$p>0.05$
Respiratory rate—/min	11.2±8.6		11.8±9.4		$p>0.05$
<i>Max positive airway pressure—cmH₂O</i>					
	14.2±3.2		15.3±3.6		$p>0.05$

*compared between the two groups

The study found that ANN is significantly ($p<0.05$) efficient as compared USG guided prediction by IVC parameters which was conventionally done. Table 2 shows the detailed findings.

Table 2: Performance of the two predictors in predicting hypotension post induction

	USG guided IVC parameters	Artificial Neural Network	p -value*
Accuracy	68	86	$p<0.05$
Precision	75	91	$p<0.05$
Recall	69	89	$p<0.05$

*compared between the two groups

Discussion

The characteristic of anesthesia has been quick technological adoption, which has

led to a notable rise in patient safety in this field over the past few decades. Given that AI is intended to support clinicians rather than to replace them, it is important to

comprehend the advantages it can have for clinical treatment [12]. For every anesthetist, preoperative risk assessment is a crucial step. The employment of AI in this situation is producing excellent outcomes. American Society of Anesthesiologists Physical Status is one of the most popular scores (ASA PS). This classification lacks granularity, is subjective, and requires manual physician evaluation to rate.

A system that automatically generates an ASA PS with finer granularity is something Zhang et al. [13] aimed to develop in their study. A model that predicts a patient's ASA PS on a continuous scale using their home meds and comorbidities was developed using supervised ML techniques. Regression models, ordinal models, and classification models were used as three different forms of predictive models. The implementation of the continuous score, according to the authors' findings, may be able to help anesthesiologists identify high-risk patients who would benefit from additional preoperative evaluation.

AKI, delirium, deep vein thrombosis, pulmonary embolism, and pneumonia are five postoperative complications that can be predicted using intraoperative data, only preoperative data, or a combination of both, according to a study by Xue et al. [14]. From frontal facial pictures, Tavolara et al. [15] produced a DL model that outperformed the Mallampati test and thyromental distance to identify patients who were challenging to intubate. Furthermore, the model can operate at low sensitivity and high specificity (0.3684 and 0.9605) or high sensitivity and low specificity (0.9079 and 0.4474), exceeding the low sensitivity thresholds of existing tests. By analyzing patient facial images alone, Hayasaka et al. convolutional neural network (CNN) algorithm [16] was able to assess the difficulty of intubation with an excellent AUC of 0.864, making it a viable

tool for anticipating these failures in guidance.

Electroencephalogram (EEG) monitoring of the brain, the target organ of anesthesia, is becoming more popular as it may aid in determining the anesthetic impact. Due to the unique variances in how each anesthetic drug affects the EEG, clinical trials are now required to validate every newly designed processed EEG monitor. By utilizing deep learning (DL) models, AI research may do away with the necessity for clinical trials on hypnosis level monitors [17]. Predicting long-term results with the purpose to begin preventative therapy for efficient resource usage is referred to as "predictive therapy." The use of "Artificial Intelligence Clinician" to reduce sepsis fatality rates has been researched and validated in critical care [18]. ECG and ABP waveforms have been studied using manifold learning, a sort of AI, to depict the underlying cardiovascular condition through 3D image visualization [19]. For the decrease of total morbidity and mortality, the capacity to anticipate and examine these uncommon but deadly consequences may become essential [20].

While Hetherington et al. [22] used convolutional NN to automatically identify the sacrum, the L1-L5 vertebrae, and the vertebral spaces from US images in real time with up to 95% accuracy; Pesteie et al. [21] used convolutional NN to automate identification of the anterior base of the vertebral lamina. Assessment of respiratory rate, pulse oximetry, and mental state are commonly used to identify opioid-induced respiratory depression. To aid in the prediction of respiratory depression in the postoperative period, researchers have researched ataxic or irregular breathing patterns and generated a machine learning (ML) algorithm for measuring breathing patterns [23].

With many advantages over straightforward models like LR used in previous studies, Lee et al. [24] have

developed a generalized additive model with neural networks (GAM-NNs) that can predict mortality in patients undergoing general anesthesia with a high AUC. For instance, is able to learn nonlinear patterns in the data, which is more clinically intuitive, and it can be interpreted easily with a notable AUC of 0.921. With this in mind, a retrospective single-center study set out to develop a risk predictor tool based on ML; the results shown are promising, with approximately 55% of cases correctly predicted, though the number of cases itself was not very high and further multicenter studies are, in our opinion, necessary before implementation. Acute renal failure after liver transplantation is a serious complication that frequently affects these patients in the postoperative period.

Only a small percentage of AI-based studies are concerned with integrating AI into routine clinical workflow in anesthesia, and only a few of these have been demonstrated to have an influence on clinical care. The fundamental reason for adopting artificial intelligence (AI) is to increase anesthesia providers' productivity and patient outcomes through the use of "augmented intelligence" based on gathered patient data and the incorporation of clinical guidelines.

Conclusion

The study has evidently proved the efficiency of machine learning model in this study (ANN) with that of conventionally used USG guided prediction. All the three performance parameters (Accuracy, Precision and Recall) are significantly better than USG guided IVC parameter prediction model. The study has also shown that the difference in age of the patients who had hypotension and did not have hypotension, was significant. There are several limitations of this study including the number of patients was smaller and it is required to carry out this type of comparative analysis with larger varied

population. Also, there should be studies be conducted with other machine learning models which this study has not considered.

This current research has brought forward an important conclusion and ANN can be considered to be used widely in clinical setting.

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