Artificial intelligence and anesthesia: A narrative review

ABSTRACT

Rapid advances in Artificial Intelligence (AI) have led to diagnostic, therapeutic, and intervention-based applications in the field of medicine. Today, there is a deep chasm between AI-based research articles and their translation to clinical anesthesia, which needs to be addressed. Machine learning (ML), the most widely applied arm of AI in medicine, confers the ability to analyze large volumes of data, find associations, and predict outcomes with ongoing learning by the computer. It involves algorithm creation, testing and analyses with the ability to perform cognitive functions including association between variables, pattern recognition, and prediction of outcomes. AI-supported closed loops have been designed for pharmacological maintenance of anesthesia and hemodynamic management. Mechanical robots can perform dexterity and skill-based tasks such as intubation and regional blocks with precision, whereas clinical-decision support systems in crisis situations may augment the role of the clinician. The possibilities are boundless, yet widespread adoption of AI is still far from the ground reality. Patient-related "Big Data" collection, validation, transfer, and testing are under ethical scrutiny. For this narrative review, we conducted a PubMed search in 2020-21 and retrieved articles related to AI and anesthesia. After careful consideration of the content, we prepared the review to highlight the growing importance of AI in anesthesia. Awareness and understanding of the basics of AI are the first steps to be undertaken by clinicians. In this narrative review, we have discussed salient features of ongoing AI research related to anesthesia and perioperative care.

Key words: Advances in anesthesia, artificial intelligence, machine learning

Introduction

Artificial intelligence (AI) is defined as the broad concept of machines designed to understand and perform tasks on their own in a "smart" manner. Early attempts at automation in medicine relied on hand-crafted algorithms based on rigid rules and therefore they failed in complex clinical situations. The growing human resource crisis in healthcare today may be an ideal setting for using technology to fill in the gaps; starting with telemedicine, digital health platforms and progressing to the adoption of AI.

So, what exactly is AI? It can be thought of as the programming of computers to simulate cognitive functions of the human mind, such as pattern recognition and problem solving. One important feature of AI is the ability to learn; that is, modification of actions based on previous experience. One of the simpler ways in which a computer can be used in anesthesia is to design a servo system, for instance, to maintain Bi-spectral Index (BIS) within a specified range by continuous assessment and adjustment of the infusion rate of the anesthetic agent(s). If the program is designed so that it can learn from its experience, this would come

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under machine learning. The various subsets of AI include machine learning, neural network, deep learning, robotics, and computer vision. This narrative review aims to discuss the principles and current advances in AI that are likely to impact clinical anesthesia in the near future. A literature search was conducted in the year 2020-21 using the keywords "artificial intelligence, machine learning, and anesthesia" in the database of MEDLINE/PubMed. This review is divided into sections dealing with machine learning, use of robots in anesthesia, implications of AI in anaesthetic management and the ethics involved in deployment of this technology.

Machine Learning (ML)

ML is now regarded as a mature technology and is employed in various industries across the world for quality control, error detection, and product recommendations. It involves collection and analysis of data by the computer, with a focus on model development and pattern detection to make intelligent predictions. Where humans can be overwhelmed by voluminous and complex data, machine learning models have the intrinsic capacity to provide valuable insights based on extensive analysis and computation. Broadly classifying ML into supervised, unsupervised, and reinforcement learning is useful to understand applications.[1] While pattern recognition is unsupervised, supervised applications include training and testing data sets. Reinforcement learning relies on continual feedback for algorithm modification. The ultimate goal of AI-based systems in anesthesia is to give the computer access to real-time patient data as well as information from medical publications; and from these, the system would integrate the various types of data and "learn" the various relationships producing actionable information. The main challenges are firstly, incompatibility between data from different electronic health record (EHR) systems and secondly, the cost of development. A detailed understanding of basic AI concepts in medicine including fuzzy logic, neural networks, deep learning process, and Bayesian method is available in a recent review by Hashimoto and colleagues.[1]

Various ML models have been developed to answer single relevant clinical questions by using representative data, such as using perioperative data to predict postoperative mortality and postinduction hypotension by analyzing preoperative and induction data.[2,3] The reliability of these models depends on the quality and methodology of the studies on which they are based. Another issue is the difficulty clinicians face in understanding the mechanism by which prediction is done. This is especially seen in high accuracy models, which

are often complex and may not provide adequate insight into the "why" of a recommendation in a clinical scenario. It is important to combine accuracy with explanations in healthcare settings; and even more so in anesthesiology, where understanding of mechanisms is critical and consequences of incorrect prediction can be serious.[4]

According to a recent editorial, there is a large discrepancy between the number of ML articles published in technical versus medical journals, highlighting the fact that translation into clinical practice is still fraught with multiple hurdles.[5] The suggested areas for AI application today include risk assessment and clinical treatment strategies. Computers are set to become indispensable tools not only for delivery of anesthetics but also for providing help in day-to-day clinical care and decision-making in anesthesia.

Robots in Anesthesia

A robot is any mechanical system capable of interacting with the environment according to directed interventions. In medicine, the precise and reproducible interventions possible with robots make their role in complex surgery and anesthesia especially attractive. They free the anesthesiologist from repetitive technical tasks, allowing them to concentrate on overall assessment and decision-making. Robots are designed to support clinicians by automating tasks and offer pertinent recommendations based on the clinical scenario to aid decision-making.[6]

Pharmacological robots

Target controlled infusion (TCI) systems can be considered the first-generation open-loop pharmacological robots. Their software has built-in pharmacokinetic models of different drugs, based on which they deliver loading doses to achieve specific plasma drug levels rapidly and then maintain a steady state. They display estimated (not measured) plasma and effect-site concentrations, which may differ from the actual concentrations, especially in patients who display extreme anthropomorphic features or in patients with different racial characteristics.[7,8]

In closed-loop systems, a "goal" for a measured variable is set by the operator and drug delivery is adjusted to make the gap between the set goal and actual variable as small as possible. In the newer versions, refinements in the algorithms such as reinforcement learning, neural network, and fuzzy logic minimize fluctuations from the set target. The initial models were single input single output (SISO) systems, recent advances have led to multiple input multiple output (MIMO) robots, addressing hypnosis,

analgesia, and muscle relaxation simultaneously. Anesthesia parameters targeted by the SISO systems initially included hypnosis (BIS-guided) or muscle relaxation (nerve-stimulator guided) as feedback for drug delivery.[9-12] Subsequently, the "Analgoscore" was described for measuring pain during general anesthesia, calculated from the deviation of the patient's target values for heart rate and mean arterial pressure.[13] Hemodynamic parameters used in SISO closed loop systems include blood pressure, stroke volume, and stroke volume variation.[14-18]

BIS-guided autonomous systems have shown to be consistently superior to manually controlled propofol infusions in a number of trials.[19-22] Reinforcement learning is now used to rapidly achieve steady state based on a wide range of clinical parameters.[23] A recent meta-analysis suggested that BIS-guided closed loop systems provide better clinical performance than manual control of drug delivery for intravenous anesthesia.[24] BIS, respiratory rate, and oximetry have been combined to develop a hybrid sedation system (HSS) and has been shown to outperform manual administration.[25]

Liu et al.[26] were the first to use a dual closed loop system to control propofol and remifentanil infusions, but this was not truly a MIMO, as BIS was the only input guiding propofol infusion, whereas remifentanil infusion rate was linked to that of propofol. In 2013, Hemmerling and colleagues developed the McSleepy for automated closed-loop delivery of propofol, remifentanil, and rocuronium; targeting BIS, analgoscore, and train of four ratio for muscle relaxation.[27] The efficacy of this system has been demonstrated in multiple scenarios including complex cardiac procedures and telemedicine, where a team of anesthesiologists based in Montreal remotely controlled TIVA in 20 patients located in Pisa.[28,29]

Closed loop control of hemodynamic parameters was first demonstrated by Ngan Kee et al.,[14] who used a simple on–off algorithm to control a phenylephrine infusion based on noninvasive blood pressure to manage postspinal hypotension. They further refined their system using a proportional algorithm and demonstrated its performance in a randomized controlled trial comparing it to manual control of the infusion.[15] A novel closed loop vasopressor controller was developed by Rinehart et al.[16] and was shown to maintain the mean arterial pressure within 5 mmHg of baseline in cases lasting over 2 hours.[17] Joosten and colleagues have developed a closed-loop-assisted goal-directed fluid therapy system, which is guided by stroke volume and stroke volume variation.

Automated anesthesia delivery was combined with closed-loop fluid management in the ultimate MIMO system, where two independent CL systems were used for hypnosis, analgesia, and fluid management during major vascular surgery.[30] Investigators are looking into the feasibility of combining fluid administration along with appropriate vasopressor use in a single automated system for guiding perioperative care.[31] The advances in robot guided delivery of anesthetics have been summarized in Tables 1 and 2.

Mechanical robots

The specialty of anesthesia includes cognitive as well as dexterity-based tasks; and robots have been designed to address both aspects. The first robotic intubation was done using the Da Vinci surgical system. Simulated fiber-optic-assisted oral and nasal intubations of a manikin were successful but technically difficult because of the sub-optimal robotic interface, with multiple arms.[32] The Kepler intubation system consists of a single robotic arm controlled by a joystick to guide endotracheal intubation remotely. Successful intubation within 40–60 seconds was demonstrated in 90 simulated cases.[33] For regional anesthesia, the Magellan system has been developed with a block needle mounted on a robotic arm. It also incorporates custom software for ultrasound-guided nerve recognition. The system was found to decrease variability among operators in the time taken for correct needle placement.[34]

Clinical decision support system

Clinical decision support system (CDSS) may be knowledge-based with built-in algorithms or alternatively, nonknowledge based. Essentially designed to provide cognitive aids to the anesthetist, they are not autonomous in execution. Detailed understanding of cognitive robots and their role for clinical decision-making can be obtained in a narrative review by Nair et al.[35]

Preoperative cognitive robots are used for the detection of abnormal laboratory findings, ensuring drug compliance, and conduct of checklists. Intraoperative robots have been used for accurate identification of appropriate prophylactic antibiotics with latest recommendations and dosing schedules, smart alarms, efficient gas delivery, and billing. Multiple components of the closed-loop system may lead to software failure, whereas incorrect data entry may lead to system failure. Safety checks, possibility to override the system, and then return to fully automated mode are important safety considerations. Edge cases are defined as scenarios wherein artificial intelligence is unable to perform in an expected manner, typically in a rare case. In this situation, humans are able to navigate smoothly even in a complex case; hence, physicians must be able to

Table 1: Pharmacological robots for anesthesia and sedation

	Reference	Parameter	Infusion	Study population	Findings
SISO systems	Struys et al.[10]	BIS	Propofol	20 adults, gynec-laparoscopy	A closed-loop system clinically acceptable during general anesthesia
	Absolam et al.[11]	BIS	Propofol	Orthopedic surgery, GA + RA	Clinically adequate anesthesia in 9 of 10 patients
	Liu et al.[19]	BIS	Propofol	RCT, 164 adults having elective surgery	Proportional-integral-differential algorithm. Automated CL delivery of propofol reduced BIS overshoot and propofol consumption compared to TCI.
	Puri et al.[20]	BIS	Propofol	RCT 40 adults, noncardiac surgery	Closed-loop system more effective and efficient than open
	Madhava et al.[21]	BIS	Propofol and Isoflurane	RCT 40 adults, cardiac surgery	Improved anesthetic agent delivery system (IAADS), a modification of closed-loop anesthesia delivery system (CLADS)
	Neckebroek et al.[22]	BIS	Propofol	36 patients, ICU sedation following cardiac surgery	Tighter control with computer-based control systems
	Pasin et al.[24]	BIS	Propofol	Meta-analysis of RCTs	BIS-guided TIVA reduces propofol requirements during induction, better maintains a target depth of anesthesia, and reduces recovery time.
	Eleveld et al.[12]	TOF	Rocuronium	Controller performance tested on 15 adults	Maintained target TOF count of one or two for 96% of the time
	Zaouter et al.[25]	BIS	Propofol	RCT 150 adults, orthopedic surgery under spinal anesthesia	CL system maintained a BIS of 65 better than humans. RR and SaO$_2$ used as safety net
MIMO systems	Liu et al.[26]	BIS	Propofol, remifentanil	RST 196 surgical patients	Dual closed-loop system - remifentanil infusion linked to propofol. Better maintenance of BIS than manual control
	Hemmerling et al.[27]	BIS Analgoscore TOF	Propofol Remifentanil Rocuronium	RCT, 186 adults, GA >1 h. "McSleepy"	Closed-loop system better at maintaining BIS and Analgoscore than manual administration
	Casas et al.[57]	BIS Analgoscore	Propofol Remifentanil	RCT 150 adults, noncardiac surgery	Closed-loop system was better than open system or TCI. No significant difference in analgoscore
	Joosten et al.[30]	BIS SV, SVV	Propofol, remifentanil Fluid bolus	13 adults, major vascular surgery	This study demonstrates the clinical ability in realistic conditions of dual closed-loop systems to maintain their anesthetic and hemodynamic targets for the majority of the case-time in patients undergoing major vascular surgery.

Table 2: Pharmacological robots for hemodynamic management

	Reference	Parameter	Infusion	Study population	Findings
SISO	Ngan Kee 2007	NIBP every 1 minute	Phenylephrine	53 patients, spinal for elective LSCS	Simple on-off algorithm used. Limitations due to noninvasive BP measurement
	Ngan Kee et al.[15]	NIBP every 1 minute	Phenylephrine	RCT, 212 patients, spinal for elective LSCS	Proportional algorithm used. Better BP control with CL feedback computer-controlled phenylephrine infusion compared to manual control.
	Rineheart et al.[16]	Blood pressure	Vasopressor	Simulated stable and unstable blood pressure	Target mean arterial pressure maintained better in the face of random disturbances Uses proportional-integral-derivative (PID) controller
	Joosten et al.[17]	Invasive arterial pressure	Norepinephrine	20 adults, elective surgery lasting 154 min	Closed loop vasopressor controller. Maintained MAP±5 mmHg of baseline
	Joosten et al.[18]	SV, SVV	Fluid bolus	104 patients managed with CL-assisted GDFT paired with historical cohort of 104 manual GDFT patients.	Reduction in intraoperative net fluid balance, postoperative complications and shorter hospital LOS. The system has an adaptive feature where it analyses the patient's previous response to fluid bolus and individualizes further fluid therapy
MIMO	Joosten et al.[30]	BIS SV, SVV	Propofol, remifentanil Fluid bolus	13 adults, major vascular surgery	Anesthetic and hemodynamic targets maintained by dual closed-loop systems for the majority of the case-time in realistic conditions

override automated systems when necessary.[36] CDSS can integrate various physiologic data with preoperative data to produce guidance, which may be accepted or rejected by the anesthesiologist. This human–machine interface has been extensively studied in the aviation industry and may be extrapolated to anesthesia.[37,38]

Current Trends Involving AI in Anesthesia

Prompt adoption of technology has been the hall mark of anesthesia and is responsible for the significant increase in patient safety in this specialty over the last few decades. We need to understand the benefits that AI can bring to clinical

care, as it aims at assisting the clinician and not replacing them.[39] In this section, we have discussed some AI-based advances, which may not have reached clinical use yet but hold promise for future implementation.

AI and Preanaesthetic Evaluation

Traditionally, logistic regression has been the basis of scoring indices widely applied for risk assessment in anesthesia. Today, ML is being studied for risk stratification based on analysis of millions of perioperative data and intervention-based outcomes extracted from EHR of multiple centers. This type of risk prediction is especially useful for counselling, optimization, and planning the anesthetic management of individual cases with rare co-morbidities. Deep neural network (DNN), a branch of AI, has been used for prediction of postsurgical mortality by Lee *et al*.[2] Data related to nearly 60,000 patients was extracted from EHR, with 82 features included for each patient. The algorithm was trained on 80% of data and validated on the remaining 20%. The intrinsic ability to integrate pre, intra and postoperative data seamlessly makes it superior to traditional risk assessment modules.

AI has been employed for airway assessment and encouraging results reported include ability to correctly predict the Cormack–Lehane view on direct laryngoscopy with analysis of face and neck.[40] Preoperative checklists have contributed to increased surgical safety. CDSS for selection of the most appropriate antibiotic and dosing schedule have been developed and widely tested in multicenter trials.[34]

AI and Intraoperative Anesthetic Care

Applications of AI in the operation theater include monitoring and alarm fatigue, administration of anesthesia, hemodynamic management, and clinical decision support. Intraoperative cognitive robots can be integrated into alarm systems for simultaneous analysis of several parameters thereby lowering the rate of false alarms.[41,42]

There is a growing interest in monitoring the target organ of anesthesia, the brain, via the electroencephalogram (EEG) as it may help in measuring the anesthetic effect. Currently, clinical trials are needed to validate any newly developed processed EEG monitor for each anesthetic drug, due to specific differences in drug-induced EEG changes. Research in AI may eliminate the need to perform clinical trials on hypnosis level monitors by the use of deep learning models.[43]

Automated closed loop anesthesia delivery (CLAD) involves hypnosis, analgesia, and muscle relaxant delivery systems incorporating hemodynamic feedback mechanisms being studied with promising results. Advances in noninvasive cardiac output monitoring, cerebral oximetry, EEG processing, and nociception assessment form the basis for CLAD. Intraoperative analgesia-nociception monitors are now available to titrate opioid administration based on changes in the sympathetic and/or parasympathetic systems.[44] The pain indices available include Nociception level Index, Analgesia-nociception index, Surgical plethysmographic index, Pupillometry, and Pupillary pain index, each of which is measured by its respective monitor. Currently, they are being evaluated in various surgical settings; however, there is insufficient data showing clinically significant changes in the outcomes.[45]

Investigators have developed predictive models for intraoperative hypotension after analysis of more than 2 million arterial waveforms.[46] To preempt critical events, investigators have developed "super learner" algorithms specifically trained to predict an acute hypotensive episode 10–30 minutes prior to the event, thereby allowing enough time for intervention. This ML algorithm relies on patient demographics, critical care assessment scores as well as invasive monitoring data, and has been proven to be reliable in critical care settings.[3] "Predictive therapy" refers to prediction of long-term outcomes with the intention to start preemptive therapy for effective use of resources. This concept has been studied and validated in critical care by the use of "Artificial Intelligence Clinician" for lowering mortality rates in sepsis.[47] Rapid technological advances such as three-dimensional ECG imaging as well as analysis of arterial waveforms have been used to provide clues to early detection of coronary insufficiency. Manifold learning, a subtype of AI has been used to study both ECG and ABP waveforms to reflect the underlying cardiovascular status via 3D image visualization.[48] EHR along with real-time monitoring have been studied to predict the onset of reduced ejection fraction in patients undergoing complex surgical procedures. Obviously, confirmatory tests including echocardiography and biomarker assay may be indicated; however, the implications of early suspicion and suitable intervention are vital in decreasing perioperative morbidity and mortality.[49] The ability to predict and investigate these rare but devastating complications may become critical for overall morbidity and mortality reduction.[50]

AI and Postoperative Care

Opioid-induced respiratory depression is traditionally detected by assessment of respiratory rate, pulse oximetry, and mental status. Investigators have studied ataxic or irregular breathing pattern and developed a ML algorithm for quantifying breathing pattern to help with prediction

of respiratory depression in the postoperative period.[51] Advances in telecommunication have led to the development of wireless intelligent patient-controlled analgesia for feedback-enabled pain management in surgical homes.[52] Early discharge and ambulation in patients can be closely monitored via video conferences and effective feedback mechanisms, impacting healthcare costs and patient satisfaction in a positive manner.

Ethics of Artificial Intelligence

Today, the future of AI in medicine, which relies heavily on patient data, cannot progress without sound ethical practices and regulations that place patients and their privacy uppermost. Ethical and humanistic principles remain significant as new interventions relying on AI are developed using medical records by being outsourced to researchers or companies. AI-based medical research needs a strong regulatory body to weigh in all factors for ethical data stewardship. Apart from checking the veracity of the data, there exists the fundamental issue of implicit or explicit bias being integrated into codes written by human beings. Flawed sampling and lack of diversity are major contributors resulting in bias within ML.[53]

ML offers strategies to revolutionize outcomes via computational science in perioperative care by impacting risk assessment, optimization, intra and postoperative interventions, which are backed by best evidence. An ensuing challenge therefore is the evaluation of the methods employed in ML research, which can be explained by the author and understood by the readers. We may expect sophisticated closed loops in anesthesia to become standard of care, yet continual engagement with the clinician is vital for optimal patient care. Guidelines for developing and reporting ML-based predictive models in biomedical research have been developed to ensure ethical research.[54]

Currently available AI solutions focus on providing CDSS and do not replace the physician's judgment. Obviously, the anesthetist needs to take a call in a crisis to follow or ignore AI-based intervention with medicolegal implications. Validation and understanding of the AI systems in clinical care by the clinician is very important to clearly understand strength and flaws of technology. AI-driven healthcare promises better patient outcomes yet risks due to autonomous technology need careful consideration in the healthcare sector where incorrect deductions can be disastrous. Currently, liability of negligence is based on what a reasonable physician would do under similar circumstances. These standards will evolve as technology enters multiple areas of patient care and clinicians need to update and familiarize themselves on a continual basis.[36] While promoting responsible AI, anticipated disruption secondary to loss of jobs is an important consideration.

Conclusions

Only a minority of AI-based studies focus on integration of AI in daily clinical workflow in anesthesia; and just a handful of these have been shown to impact clinical care. Improvement of anesthesia provider's productivity and patient outcome by using "augmented intelligence" based on pooled patient data as well as incorporation of clinical guidelines is the underlying goal for adoption of AI. While this may seem distant to some healthcare workers, there is a raging debate on the socio-economic impact of robots on the human workforce in every field.[55]

In advanced nations, strong collaboration among clinicians, scientists, manufacturers, regulators, and administrators has led to consistent electronic health records amenable to data storage and exchange.[56] In India, we foresee multiple difficulties starting from data viability, standardization of monitoring, acceptance, and validation of basic technological tools. Handwritten medical records continue to be the rule rather than an exception in advanced surgical setups. The timeline may be unpredictable, yet the medical profession cannot steer clear of this eventuality. This review aims to provide a primer on the immense potential of AI and its role in anesthetic care with the objective of stimulating interest and awareness among the anesthesia fraternity.

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