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Artificial Intelligence for Smart Procedural Sedation in the Gastrointestinal Endoscopy Suite

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Abstract

Artificial intelligence (AI) is defined as the science of creating intelligent machines. AI has grown exponentially, and its systems have made their way into the anesthesia field. The purpose of this review is to explore how the practice of anesthesiology in the gastrointestinal (GI) endoscopy suite changed with AI. Current AI anesthesia systems in the endoscopy suite include open and closed loop anesthesia delivery systems. The most widely used open loop system is the target-controlled infusion (TCI). During TCI, a drug is given automatically using a pump controlled by a computer. The aim is to achieve a chosen target plasma concentration, based on the hypothesis that the pharmacological effect is proportional to the drug's plasma concentration. Closed loop systems regulate the drug's dosage by checking a controlling parameter such as the patient himself in patient-maintained sedation, or the bispectral index in computer-assisted personalized sedation. As such, the closed loop system regulates the dose according to continuous feedback from the patient. Recent innovations in AI include machine learning and deep learning models that may have future applications in the endoscopy suite. Machine learning models look for patterns in vast amounts of data to draw conclusions. Deep learning models gain the ability to learn new information that they were not "explicitly programmed" to learn and make changes to their function based on that new information. Although the future of AI in anesthesia and the GI endoscopy suite seems bright, one must always keep in mind its shortcomings.

Keywords: Artificial Intelligence; Gastrointestinal Endoscopy Suite; Sedation; Knowledge Acquisition

List of Abbreviations

AI: Artificial Intelligence; GI: Gastrointestinal; TCI: Target-controlled infusion; OL: Open loop; CL: Closed loop; EGD: Esophagogastroduodenoscopy; BIS: Bispectral index; CAPS: Computer-assisted personalized sedation; ERCP: Endoscopic retrograde cholangiopancreatography; FDA: Food and Drug Administration; ASA: American Society of Anesthesiologists; EEG: Electroencephalogram; ML: Machine learning; DL: Deep learning; HIPAA: Health insurance portability and accountability act

Introduction

John McCarthy coined the term "artificial intelligence" (AI) in 1956 and defined it as "the science and engineering of making intelligent machines", with the purpose of making a computer or a robot, think as smart humans

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think. In short, AI is the study of how a human brain thinks, learns, decides, and works when it tries to solve problems and its application to machines. AI has grown exponentially for the past decade, and AI systems have made their way into our daily lives surreptitiously; so much so that we barely even notice their presence anymore. The medical field makes no exception and AI applications have made their way into anesthesia practice. The purpose of this work is to review how the practice of anesthesiology in the gastrointestinal (GI) endoscopy suite changed with intelligent machines and what are possible future applications. Current anesthesia "smart" systems that use AI in the endoscopy suite include open and closed loop anesthesia delivery systems. More advanced AI systems such as machine learning and deep learning systems have started having applications in anesthesia practice that might be applicable to the endoscopy suite in the future.

Search strategy

The search strategy conducted for retrieving relevant literature for this narrative review followed the PICO format. Sources searched included Medline and PubMed. Search terms used: endoscopy, artificial intelligence, machine learning, (gastrointestinal endoscopy) AND (target-controlled infusion). In addition, pertinent papers from the reference lists of the retrieved papers were included.

Open Loop Systems

Open loop (OL) systems are set-ups in which drugs are infused following predefined pharmacokinetic and pharmacodynamic algorithms that estimate the distribution and elimination of the drug; the actual drug effect, however, is usually not measured and there is no automated feedback. These algorithms are based on population studies correlating drug blood concentrations with effect site concentrations. The most widely used OL anesthesia system is the target-controlled infusion (TCI). When using TCI systems, a drug is given intravenously using a pump that is controlled by a computer. The aim is to achieve a target plasma concentration chosen by the user [1], based on the hypothesis that the pharmacological effect is proportional to the plasma concentration of the drug. Parameters to be entered include the selected population pharmacokinetic model, patient physical characteristics, and the desired drug target. Theoretical advantages of use of TCI versus intermittent bolusing would be maintaining a more precise and constant effect site concentration by avoiding multiple peaks and troughs secondary to successive boluses. These small overdosing and underdosing episodes might be responsible for significant cardiovascular and respiratory depression, or awareness and reduced operator and patient satisfaction.

Propofol TCI vs. sedative boluses

Schwilden and Schuttler [1] presented the clinical use of TCI systems in 1990 and the first intravenous drug used in it was propofol [2]. Many studies have looked at the advantages of propofol TCI versus sedative boluses that are traditionally used during procedural sedation for endoscopic procedures. Some showed that there is a reduction in adverse events such as hypoxemia [3, 4] and hemodynamic repercussions such as hypotension and bradycardia [4] when using propofol TCI, while others found both techniques to be equivalent with regards to adverse events [5]. Endoscopist satisfaction was higher when TCI was used in Fanti's work [6] and better sedation quality led to less patient movement in the TCI group during esophagogastroduodenoscopy (EGD) and colonoscopy in Chang's study [7]. Kawano et al. showed that propofol TCI adjusted to depth of anesthesia measured by bispectral index (BIS), combined with a single opioid bolus was an effective and safe anesthetic modality for push enteroscopy with both high patient and endoscopist satisfaction [8].

Propofol TCI vs. propofol infusions

When comparing head-to-head propofol TCI versus traditional propofol infusions Chiang et al. found that TCI use during bidirectional endoscopy was associated with faster recovery times, better hemodynamics, and fewer desaturations as compared to manual infusions [9]. Wang et al. came to the same conclusions as well when sedation for colonoscopy was administered to patients by novice anesthesia residents [10]. Although subtle, a 2008 systemic review looking at TCI vs manually controlled propofol infusions both in general anesthesia and sedation for adults [11] demonstrated that the main advantage of propofol TCI systems versus manual infusion is the reduction in manual interventions needed to maintain anesthesia titrated to clinical required effect. This corresponds to what is expected from AI, smarter machines with a reduced need for human intervention. Nevertheless, this review [11] suggested that there was insufficient evidence to make firm recommendations about the use of TCI versus manually controlled infusions in clinical practice since few clinically significant differences were demonstrated in terms of quality of anesthesia or adverse events.

Propofol and remifentanil TCI combination

Following the clinical success of propofol TCI, algorithms were developed for opioids such as remifentanil and sufentanil [12]. Anesthesia providers tend to shy away from adding opioid boluses or infusions to sedation regimens in the endoscopy suite given the increased risk of encountering adverse events such as respiratory depression, airway obstruction, and desaturation; even though opioids are beneficial for the patient in terms of comfort and immobility. Moerman and colleagues studied 3 groups of patients undergoing colonoscopy [13]. The first group under propofol TCI only, the second under propofol TCI and manually controlled remifentanil infusion and the last group had a

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combination of propofol and remifentanil TCI infusions. The authors noted that patients receiving opioids had better conditions for examination with less movement, cough, or hiccups. Patients receiving remifentanil through TCI had less propofol requirements and less hypopnea and apnea episodes than with manual control infusion. Hemodynamic and recovery parameters did not differ between groups [13]. Going a step further, Gambus et al. modeled the effect of propofol and remifentanil TCI combinations during sedation for ultrasonographic endoscopy and found that the optimal targets to use in order to obtain adequate sedation for these procedures were 1.8 to 2.8 µg/mL for propofol with remifentanil between 0 to 1.5 ng/mL [14].

No matter how popular TCI systems become in the practice of anesthesia, one must remember that their major pitfall is that they do not monitor directly or quantitatively the desired clinical effect in order to titrate the drug accordingly. Furthermore, they do not take into consideration the wide array of possible patient populations or how individual behaviors may vary from that of control populations used to define the initial target-controlled system algorithm.

Closed Loop Systems

In closed loop (CL) systems, drugs are administered automatically, but in contrast to OL, these systems regulate the drug's dosage by checking an appropriate controlling parameter, such as for example the level of consciousness. Whenever the controlling parameter varies, there is automatic feedback and adjustment of the anesthetic drug delivery. The system controls itself continuously to maintain a given anesthetic target without healthcare provider manual input.

When broken down in sections CL anesthesia consists of:

- Administering anesthetic agents through an actuator. In most cases the actuator is a syringe infusion pump.
- Determining the effect of these agents on the patient's body. This effect needs to be precisely measurable in real time such as for example depth of anesthesia as measured by the BIS monitor.
- Analyzing this feedback information by an algorithmic brain in sensible time intervals to adjust the next dose to be given.

In short, a CL system changes the dose according to the information it gets from the patient, similar to an anesthesiologist in his or her everyday practice. This information can be obtained directly from the patient himself such as during patient-maintained sedation and computer-assisted personalized sedation (CAPS) or can be derived from objective patient monitors.

Patient-maintained sedation

In patient-maintained sedation the loop is closed by the patient himself much like patient-controlled analgesia. If the patient feels uncomfortable, he activates the special handset twice within one second and the TCI infusion is increased by a pre-programmed amount. A lockout time and a maximal infusion dose are set as well. If the patient is adequately or overly sedated the handset will not be activated and the target will remain constant. If adequate sedation is not reached after maximal infusion target doses are attained, the system can be manually overridden. Gilham et al. successfully used patient-maintained sedation in a pilot study of 20 patients undergoing endoscopic retrograde cholangiopancreatography (ERCP). The procedure was completed successfully in all but 4 cases. No adverse events were noted. All patient were awake within five minutes of arriving to the recovery room and both patient and endoscopist satisfaction were high [15]. Campbell et al. used the same setup for 20 patients undergoing colonoscopy [16]. The system had to be overridden manually in 4 patients due to perceived oversedation although no hemodynamic or respiratory adverse events were noted. Patients reported being satisfied with the quality of the sedation and were willing to undergo it again [16]. Both these works show that patient-maintained sedation can be used in the GI procedural suite, however the technique never really gained popularity due to the prolonged time required to reach adequate sedation and the necessity to have adequate anesthesia staffing overlooking the process closely.

Computer-assisted personalized sedation (CAPS)

Sedasys (Johnson & Johnson, Los Angeles, California, USA) was the first commercial CL sedation system that was Food and Drug Administration (FDA) approved in 2013. Sedasys was designed for the intravenous administration of propofol intended for the initiation and maintenance of minimal to moderate sedation in American Society of Anesthesiologists (ASA) physical status I and II adult patients undergoing colonoscopy or EGD. The Sedasys protocol involved the administration of fentanyl (25–100 µg), a wait of 3 minutes, followed by the administration of about 0.4 mg/kg of propofol over 3 minutes while continuously monitoring 6 parameters: pulse oximetric oxygen saturation (SpO_2), respiratory rate (RR), heart rate (HR), blood pressure (BP), end-tidal CO_2 ($EtCO_2$), and patient responsiveness. The system detected and responded to signs of oversedation (desaturation and/or low RR/apnea) by stopping or reducing the propofol dosing, by increasing O_2 delivery, and by instructing patients to take a deep breath. Initial assessment of Sedasys showed that achieving minimal to moderate sedation for colonoscopy or EGD procedures was possible, with low intraoperative dosing and quick recovery times [17]. However, in order to secure FDA approval and to ensure patient safety the Sedasys manufacturers had to adopt a highly restrictive dosage strategy which ended up being counterproductive, and it was pulled from the market in 2016 due to minimal

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sales. The main reasons behind this failure were that Sedasys was always programmed to decrease sedation depth, not to increase it, while both the patients and endoscopists expected deep anesthesia. This combined to the inefficient 6-minute wait prior to the start of the infusion resulted in patient and healthcare provider dissatisfaction [18, 19]. Another factor contributing to this failure was its prohibitive cost, indeed there was little to no return on investment given the fact that it was more cost-effective to have an anesthesia provider delivering the anesthetic [20].

Closed loop based on objective criteria

Processed electroencephalogram (EEG): Different apparatuses can be used to monitor objectively depth of anesthesia as an effect site parameter to initiate a feedback loop instead of the traditional scales based on clinical parameters. Numerous studies have successfully used objective data obtained from spontaneous EEG analysis or evoked potentials in CL systems to better titrate hypnotic drugs intraoperatively during surgery, and they outperformed manual administration of hypnotics [21, 22]. When it comes to sedation in the endoscopy suite, Leslie et al. successfully used propofol TCI in an automated closed loop fashion using the BIS monitor. A target BIS value and a minimum target propofol concentration were entered by the operator and the system adjusted the infusion according to BIS value monitored every 5 seconds using a custom-made software algorithm. All 16 patients underwent colonoscopy successfully with a median BIS range of 75 to 85. No adverse events were recorded and both patient and endoscopist satisfaction levels were high [23].

EEG and Analgoscore: McSleepy: Traditionally, anesthesiologists rely solely on objective intraoperative hemodynamic parameters as adequate reflections of pain presence and intensity when the patient is sedated or anesthetized. A novel analgesia score was recently presented called the *Analgoscore™* [24]. This nociception score is calculated based on mean arterial pressure and heart rate and can be used as an effect site parameter. The Analgoscore ranges from -9 (too profound analgesia) to +9 (too superficial analgesia) in increments of 1, with ranges of -3 to +3 representing excellent pain control. This score was successfully used for CL administration of remifentanil during general anesthesia [25], and was combined with EEG analysis as setpoint targets for a novel anesthesia delivery system: McSleepy.

McSleepy is the first completely automated CL anesthesia delivery system that monitors the patient's level of consciousness via EEG analysis, and pain via the Analgoscore throughout general anesthesia, and administers appropriate intravenous doses of anesthetic medications with no manual intervention. The world's 1st totally automated anesthetic took place at McGill university hospital, Canada, in May 2008. The procedure was a partial nephrectomy lasting 3 h 30 min [26]. When compared head to head with manual control, the McSleepy system achieved better control of depth of anesthesia and better analgesia with faster recovery and extubation times [27]. McSleepy was also used successfully in a pilot study of automated anesthesia for cardiopulmonary bypass, where 16 out of the 20 anesthetized patients enrolled did not require any manual intervention from the supervising anesthesiologist [28]. Even though McSleepy is still a research apparatus, this body of work demonstrates that automated administration of anesthesia is feasible and could one day be found in GI endoscopy units for cases requiring general anesthesia or sedation despite the failure of Sedasys.

Machine Learning and Deep Learning: will these applications reach the endoscopy suite?

Recent innovations have greatly improved the potential for future AI successes. These innovations are built on a subtype of AI called machine learning (ML). ML models look for patterns in vast data and try to draw conclusions. The computer is programmed in such a way that it gains the ability to learn new information that it was not "explicitly programmed" to learn and to make changes to its function based on what it has learned. Using the tools of cognitive computing and machine learning, the machine will "learn" the relationships and connections within both the structured and unstructured data. As new data are available, the system will incorporate them, adapt, and respond. This allows analysis and prediction models to be built "de novo" converting raw data to actionable information [29, 30]. One of the most popular methods today for performing work in machine learning is the use of neural networks. They are inspired by biological nervous systems and process signals in layers of computational units (neurons) [31]. Each network consists of an input layer that describes the data, an output layer that yields a result, and in between at least one hidden layer of neurons that conducts different mathematical transformations on the input features.

Recurrent neural network employ feedback such that the output of the system is dependent on both the current input state and the preceding inputs, enabling the network to respond to trends that evolve over time [32]. With continued advances in computational power and with larger data sets, researchers began to develop deep learning (DL) models, a subset of ML. The main difference between ML and DL is that in the former, the model still needs some guidance. If a ML model returns an inaccurate prediction, then the programmer needs to fix that problem explicitly but in the case of DL, the model does so by itself. Predictive analytics derived from ML and DL models become instantaneous clinical support tools for the anesthesiologist.

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One application of ML models related to anesthesia is described by Hatib et al. [33]. In their study the authors suggested that prior to hypotension, there are dynamic changes in arterial waveforms that are not detected. They looked at the arterial waveform and separated it into 5 phases and in each phase, they studied 8 different features; they then developed a ML model that was able to predict hypotension 5 minutes before it happens with a specificity of 87%. Another group of authors [34] showed that a supervised ML program was able to predict post-induction hypotension with a specificity of 76%, a negative predictive value of 19%, and a positive predictive value of 96%. An additional application of ML models resides in the prediction of hypoxemia; Lundberg et al. [35] were able to come up with a ML model that not only predicts hypoxemia ($SpO_2 < 92\%$) in the next 5 minutes at various intraoperative time points but also explains the reasons behind its occurrence. The system, Prescience, was trained on minute-by-minute data from the electronic health record of over 50000 surgeries and made anticipating hypoxemia easier for anesthesiologists. Finally, Syed et al. built a ML model that predicts if a colonoscopy can be successfully completed with moderate sedation (as opposed to deep sedation requiring the presence of an anesthesiologist) based on patient demographics, comorbidities, and medications. This model predicted with 80% accuracy the colonoscopies that could be completed with moderate sedation alone and could therefore be used as a decision support tool for physicians to reduce the number of aborted cases due to inadequate anesthesia [36].

ML and DL are still in their infancy and are not yet used clinically on a wide scale. It looks clear however that they could have applications related to the choice and control of anesthesia, depth of anesthesia monitoring and event and risk prediction [31] and would benefit the subset of critically ill patients presenting to the endoscopy unit. These often frail, elderly, and critically ill patients need to undergo procedures such as ERCPs or control of upper gastrointestinal bleeding.

Limitations of AI

Even though AI applications in the anesthesia field are increasing rapidly, the challenges they are facing are numerous and they should not be considered as the next healthcare panacea without examining their shortcomings. These range from data privacy and security issues to medical liability surrounding the use of the algorithms. In case of improper diagnosis or management, who is ultimately responsible? As potential adverse outcomes could result from machine-human hybrid decisions, or even purely from machine decisions who will bear the medico-legal consequences?

It is also easy to imagine the possibility of having corrupt algorithms that do not change or update with evolving clinical practice or that could be hacked and modified for malicious purposes. How would the healthcare system control or manage such cases? One must also wonder if identifiable data can inadvertently be made available to external sources. How vulnerable will these models be to external unintended or intended malicious influence? In an increasingly digitalized world, how can we make sure we reconcile all these data with the health insurance portability and accountability act (HIPAA) requirements? Lastly, how should we interpret and act upon the information generated by these programs? Should physicians blindly trust their results or take decisions based on their skills, their personal experience, or their sense of anticipation? All these questions remain unanswered to this day.

Table 1: Summary of different types of artificial intelligence for anesthesia in the gastrointestinal endoscopy suite.

Open Loop System	• Drugs are infused automatically following predefined pharmacokinetic and pharmacodynamic algorithms that estimate the elimination and distribution of the drug. • The actual drug effect is usually not measured. • The automatic feedback element is absent.	1. Propofol target-controlled infusion. 2. Remifentanil target-controlled infusion.
Closed Loop System	• Drugs are infused automatically following predefined pharmacokinetic and pharmacodynamic algorithms that estimate the elimination and distribution of the drug. • Regulation of the drug dosage by a controlling parameter that measures the drug effect. • Presence of an automatic feedback loop with adjustment of drug delivery accordingly without any manual input.	1. Patient-maintained sedation. 2. Computer–assisted personalized sedation (Sedasys). 3. Closed loop based on objective criteria: • Processed EEG. • EEG and Analgoscore: McSleepy.
Machine Learning and Deep Learning	Algorithms with the ability to learn from vast amounts of data and make changes to their function based on what was learnt without being explicitly programmed to do so.	• Prediction of hypotension by analyzing arterial wave forms. • Prediction of hypoxemia and the reason behind its occurrence (Prescience). • Decision support tool for physicians to predict which colonoscopies could be done under only moderate anesthesia.

Conclusion

AI for sedation in the endoscopy suite includes open loop, closed loop, and machine learning applications that might help us reach better outcomes, increase satisfaction, and multitask more efficiently (table 1). However, anesthetizing patients independently and successfully requires AI models capable of performing multiple tasks using unitary intelligence similar to humans; and this feat remains, up until now, beyond the scope of available AI technology. Furthermore, machines are easily defeated when it comes to non-technical skills such as providing emotional support and care, the "human touch" factor that helps the patient be reassured and get through the endoscopic procedure safely therefore a continued partnership between healthcare professionals and AI systems seems to be the way of the future.

Declarations

Availability of Data and Materials

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

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