Chapter 16
The Role of Artificial Intelligence in Personalized Anesthesiology and Perioperative Medicine

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Introduction

The practice of anesthesiology has evolved over the last two decades from a field focused on the intraoperative and postoperative phases of care, to now encompass an entire perioperative medicine specialty with the goal of continuous optimization of patients from preoperative risk reduction to postoperative recovery and prevention. This transition from a largely reactive to a proactive and preventative perioperative specialty has opened the door to new opportunities for personalized medicine, particularly by leveraging the vast amounts of data generated today in our electronic health record systems, interconnected medical devices and consumer wearables. It is estimated that over 2000 exabytes (1 exabyte = 1 billion gigabytes) of healthcare data will be generated in 2020 (Dimitrov 2016; Ibarra-Esquer et al. 2017; Sheth et al. 2018). Clearly, analyzing all of the available healthcare data today for informed clinical decision-making is beyond the ability of any single clinician. Data science and artificial intelligence are therefore playing increasingly important roles in today's healthcare system, and particularly in the data-intensive field of anesthesiology.

Data science is a rapidly evolving interdisciplinary field of applied mathematics, statistics and computer science that extracts knowledge from increasingly large and

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complex datasets. Artificial intelligence, although often discussed interchangeably with data science, is specifically focused on computer systems which are capable of solving problems that traditionally require human intelligence. Machine learning and deep learning are computational techniques at the intersection of data science and artificial intelligence that are often employed in large healthcare datasets where standard logistic regression and statistical methods are inefficient or impractical. Machine learning uses algorithms such as decision trees, vector machines or Bayesian learning to achieve weak artificial intelligence, while deep learning uses higher-order neural networks and similar algorithms to achieve higher artificial intelligence.

In healthcare, high-volume information assets are ubiquitous, with countless patient records existing in tens of thousands of disparate electronic health record systems. We think of healthcare data in terms of two major buckets—big data (large N to create population level models and hypotheses) and small data (small N or N = 1 to create individual models and hypotheses) (Ofili et al. 2018; Hekler et al. 2019). In healthcare, big data often refers to electronic health records, genetic data, billing records and clinical research data, while small data often includes patient monitor data and patient generated health data from consumer health devices, wearables and mobile applications. While big data practitioners aim to process this vast patient data to model the generalized population and apply systematic hypotheses to individuals, small data practitioners, conversely, use individual digital phenotypes (aka "digital fingerprints") and subject-specific data to inform algorithms and develop individualized models. In simpler terms, while the strength of big data is evidence-based medicine, or applying population-based hypothesis to a patient, the strength of small data is precision or personalized medicine through modeling of the individual.

Murdoch and Detsky theorized in their 2013 JAMA article "The Inevitable Application of Big Data to Health Care" that big data would advance medicine in four main areas: generation of new medical knowledge, dissemination of medical knowledge, translation of personalized medicine initiatives into clinical practice and empowerment of patients with actionable data (Murdoch and Detsky 2013). For the most part, Murdoch and Detsky have been proven right. Advancement of machine learning, deep learning and natural language processing in electronic health records, using tools such as IBM Watson, have increased our medical knowledge base. Clinical decision support tools that integrate AI techniques have also been developed to apply patient data analytics to evidence-based clinical guidelines. However, unlike medical oncology, which has heavily invested in genomics and precision medicine initiatives, anesthesiology and perioperative medicine have lagged behind in the implementation of personalized anesthesiology and perioperative big data technologies.

In the preoperative assessment, anesthesiologists often describe an individual based on a risk stratification score, such as American Society of Anesthesiologists (ASA) class 1–6 or the Revised Cardiac Risk Index (RCRI). While these classifiers are helpful for high-level preoperative risk stratification, in order to personalize a patient's perioperative plan, additional data is needed to understand their specific medical comorbidities, functional capacity, hemodynamic status, nutritional status and mental fitness. Advancements in big data and small data mining and analysis are assisting us in supplementing our existing risk classifiers with the data produced by electronic health records, physiologic monitors, consumer health devices and smartphones for perioperative management. High fidelity patient waveform recordings and machine learning algorithms have also introduced a new dimension to patient analytics, with millisecond-resolution data that allow us to model dynamical physiology and real-time hemodynamic status (Cannesson et al. 2019). Additionally, wearable monitors are producing prehospital patient-generated health data that complement our subjective preoperative exams with new objective and longitudinal metrics, and mobile applications are providing valuable insights into outpatient activity levels, psychological stressors and dietary habits.

Through application of these big and small data tools, preoperative risk stratification, patient monitoring, clinical decision support and perioperative medicine initiatives, such as Enhanced Recovery After Surgery (ERAS), can be advanced beyond empirical protocols to create personalized data-driven algorithms that optimize individual patient outcomes. In this chapter, we review how data science and artificial intelligence is currently playing a role in personalized anesthesiology and perioperative medicine, as well as lay out a vision for the future directions of this growing field.

Big Data and Electronic Health Records

Big data and machine learning algorithms for multivariate modeling have been applied in recent years to predict surgical patient risks, diagnose disease and guide patient management using patient demographics, comorbidities, laboratory results, medications and other patient data found in electronic health records. Many of these algorithms, while still at the exploratory research stage, have outperformed the current standards of care or expert clinicians in comparative studies. Targets of machine learning algorithms in the perioperative environment have included development of dynamic clinical metrics, predictions of surgical outcomes and complications (e.g. perioperative bleeding), mortality predictions and more recently, real-time indicators and predictors of patient hemodynamic status, such as hypotension prediction index (Hatib et al. 2018).

Due to the wide range of outcomes and predictor variables included in existing perioperative machine learning models, there is only limited high quality, randomized controlled data to support implementation of these technologies. However, a 2018 systematic review of neurosurgical machine learning algorithms for a range of outcomes found a median accuracy of machine learning predicted outcomes of 94.5% with an absolute improvement in accuracy of 15% over logistic regression. Input features of the 30 machine learning studies in this systematic review included electronic health record data, such as patient demographics (age, sex, symptoms, signs, disease history, family history, medicine usage), radiological images, EEG

Fig. 16.1 Big data in personalized anesthesiology and perioperative medicine

recordings, microelectrode recordings, pathology reports, surgeon volume and hospital volume (Senders et al. 2018) (Fig. 16.1).

Small Data and Consumer Health Devices

While an enormous amount of patient data exists in electronic health records and other big data repositories, personalized healthcare is also dependent on the digital traces that we don't often collect. Data contained in consumer health products, mobile applications and social media accounts are often ignored by our healthcare system, but contain high volumes of objective and calibrated data about our individual patients. These digital fingerprints, known collectively as "small data", are key components to personalized perioperative medicine.

IBM Watson estimates that each person generates over one million gigabytes of health-related data in their lifetime. This patient-generated health data (PGHD) coming from fitness trackers, heart monitors, wearables and mobile applications is invaluable for modeling individual health status. For high-risk surgical patients, PGHD can be used not only for predictive risk modeling, but can also help guide preoperative optimization, i.e. prehabilitation, and calibrate evidence-based guidelines for improved perioperative outcomes, such as ERAS protocols.

However, there are limitations of our current healthcare system for implementation of systems that integrate small data. In a 2018 review of barriers to the clinical use of PGHD, investigators found data structure, data completeness, reliability, measurement context, information overload, interoperability and workflow to be the most commonly cited barriers (Petersen and DeMuro 2015; Zhu et al. 2016; West et al. 2017; Abdolkhani et al. 2019) (Fig. 16.2).

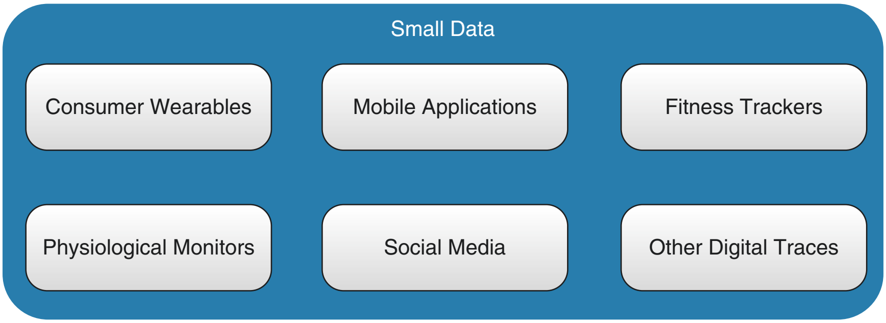

Fig. 16.2 Small data in personalized anesthesia and perioperative medicine

Techniques in AI

Artificial intelligence (AI) is generally taught as containing several subfields, including learning methods (such as machine learning and deep learning), natural language processing, speech and image recognition and expert systems to name a few. In this chapter we will focus on AI learning methods and their application to personalized anesthesiology. Machine learning (ML) was defined by Arthur Samuel in 1959 as the "field of study that gives computers the ability to learn without being explicitly programmed" (Samuel 1959; Connor 2019). Historically, fuzzy set theory and fuzzy logic, in which rule-based algorithms are used with probabilistic categorizations of features, were predecessors to machine learning that required human input to explicitly define rule sets. Instead of explicit rule definitions, machine learning algorithms use input features and data properties to learn how to perform a task through processes known as supervised learning, unsupervised learning or reinforcement learning.

Supervised learning which is found in classical machine learning, is the process of training an algorithm with data features to predict a specified output. Examples of supervised learning algorithms include k-nearest neighbor, naive Bayes, support vector machines, decision trees and neural networks. Conversely, unsupervised learning is used to identify patterns and clusters in data without specifying an output. Some common algorithms for unsupervised learning are self-organizing maps and k-means clustering. Lastly, reinforcement learning algorithms, such as Monte Carlo methods and temporal-difference learning, use a process of trial and error to continually improve on their performance of a task. Supervised learning, unsupervised learning and reinforcement learning are all capable of performing the classification and prediction tasks that are commonly found in healthcare, and the selection of which specific AI technique to use is often determined by the data size and dimensionality, functional complexity, computational bandwidth and operator expertise.

Machine Learning

The most common form of AI used in clinical settings is supervised machine learning. While hundreds of specific machine learning techniques have been developed for optimization of accuracy, performance and fitting, four of the fundamental techniques include linear regression, logistic regression, decision trees and random forests. Linear regression uses a model that predicts a continuous outcome as a weighted sum of the input variables. Conversely, logistic regression is used for classification problems to assign inputs to a discrete set of outcome categories. Decision trees, otherwise known as Classification and Regression Trees (CART), partition input variable data into subsets with homogenous outcome values. Lastly, random forests are ensemble learning methods that fit a plurality of decision trees to subsets of input variable data to achieve improved performance.

Neural Networks and Deep Learning

Artificial neural networks (ANN) are also commonly used in healthcare AI applications. Neural networks mimic the biological interconnectivity of neurons to create a weighted, directed graph of nodes with an input layer, output layer and varying number of hidden layers where computation is performed. In deep learning, neural networks contain several hidden layers, while traditional neural networks may contain up to three (Fig. 16.3).

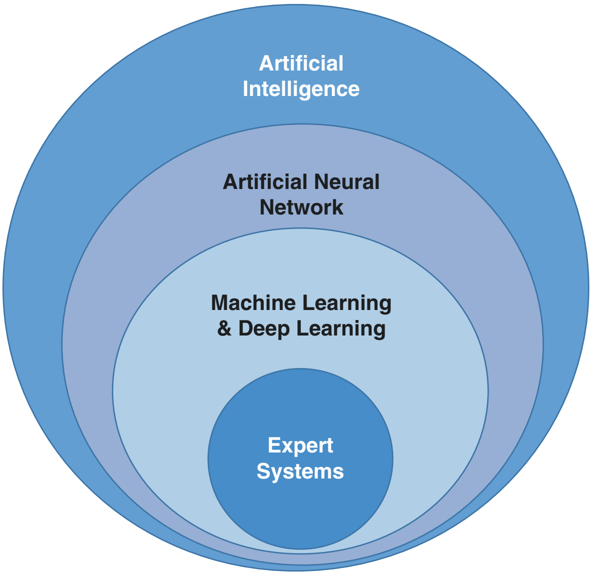

Fig. 16.3 A summary of AI hierarchy; from Rahmatizadeh S, Valizadeh-Haghi S, Dabbagh A. The Role of Artificial Intelligence in Management of Critical COVID-19 Patients. J Cell Mol Anesth. 2020; 5(1): 16–22; with permission (Rahmatizadeh et al. 2020)

Preoperative

Perioperative complications are a major cause of preventable morbidity and mortality after critical illness or surgery but many of the mechanisms continue to be poorly understood. Recent strategies have moved towards characterizing patients' health status preoperatively. There is an increasing possibility to leverage large volumes of unique preoperative data, including patient-generated health data, using artificial intelligence. This requires large-scale, unobtrusive, high quality continuous data collection from the patients' natural environment, and from multiple domains (e.g. heart/motor/brain activity, temperature, circadian/sleep patterns, food intake and physical activity). Put simply, artificial intelligence allows us to use everything about the patient's present state to predict a future state (i.e. perioperative morbidity and mortality). Advancements in health data processing, biosensors, genomics, and proteomics all will help provide a complete picture of a patient which will enable perioperative intelligence. The potential applications are vast, and include prehabilitation and rehabilitation, individualization of perioperative guidelines (ERAS protocols), risk stratification and risk management. These can incorporate not only well established comorbidities relevant to perioperative care, but also unique biomarkers such as circadian/sleep regulation, autonomic function, and genetic risk. All of these interact and are modulated by lifestyle factors.

Artificial intelligence techniques will allow the development of integrative physiological biomarkers that incorporate genetics, circadian biology, physical activity, diet and co-morbidities to predict important postoperative complications. In particular, there is increasing recognition for the link between patients' perioperative outcomes and their prior sleep and circadian health. For example, there is emerging evidence for the potential role of circadian/sleep disturbances in the risk for delirium (Dessap et al. 2015). A fundamental aspect of physiological functions, including sleep, is the adherence to ~24 h cycles, known as circadian rhythms. Circadian/sleep disturbances are more common in the elderly, becoming more pronounced after critical illness (Brainard et al. 2015), and in neurodegenerative diseases such as Alzheimer's disease (AD) (Musiek et al. 2018), groups most vulnerable to delirium. Using wearable technology and actigraphy, personalized machine learning models of sleep-wake states outperform their generalized counterparts in terms of estimating sleep parameters and are indistinguishable from more time-consuming polysomnography labeled sleep-wake states. These personalized machine learning models can be used in actigraphy studies of sleep health, potentially screening for sleep disorders such as insomnia, sleep apnea, narcolepsy or restless leg syndrome known to impact postoperative outcome metrics such as cognition, pain, surgical site infections, and length of recovery or even patient satisfaction.

Preoperative genomics is another area that can leverage artificial intelligence techniques to reveal biological insight into why certain patients experience drastically different postoperative outcomes. Using genetic variability, a way to assess preoperative risk for important responses to perioperative stress is an active area of research. Clinical outcomes include neurocognitive dysfunction, bleeding, myocardial injury, stroke, infections, acute kidney injury and many others. The ability for artificial intelligence to combine genomic advances with circadian/sleep biology, lifestyle factors and existing comorbidities and their multitude of complex interactions, is an exciting prospect.

Intraoperative

In the intraoperative phase of care, there are numerous applications for artificial intelligence that have the potential to improve perioperative outcomes and personalize anesthetics.

Depth of anesthesia monitoring is one application of artificial intelligence that has already shown promise. The majority of depth of anesthesia studies have focused on the use of the BIS (Medtronic, USA) or electroencephalography (EEG). This has borne out of research efforts to reduce the risk of intraoperative awareness and previous literature suggesting that low BIS and burst-suppression on electroencephalography during anesthesia may be associated with poorer outcomes. For example, excess depth may contribute to suppressed intraoperative mean arterial pressure which has been associated with postoperative mortality. Machine learning approaches are well-suited to analyze complex data streams such as EEG. Studies starting in the 1990s described discriminating awake versus anesthetized patients by using neural networks to evaluate EEG power spectra, and in particular, specific frequency bands as a signal seen in commonly used anesthetic drugs. The use of index parameters of depth of anesthesia (e.g. BIS) increased in popularity, such that neural networks and other machine learning approaches were used to analyze EEG data with the goal of approximating BIS through multiple electroencephalography parameters of increasing complexity.

More recent papers have used artificial intelligence techniques and spectral analysis to more directly analyze EEG signals to estimate the depth of anesthesia. Mirsadeghi et al. studied patients and compared the accuracy of their machine learning method of analyzing direct features from EEG signals (e.g., power in different bands [delta, theta, alpha, beta and gamma], total power, spindle score, entropy, etc.) in identifying awake versus anesthetized patients against the BIS index. Their accuracy in using electroencephalography features was 88.4% while BIS index accuracy was 84.2% (Mirsadeghi et al. 2016). Similarly, Shalbaf et al. used multiple features from EEG to classify awake versus anesthetized patients (as four possible states of awake, light, general, or deep anesthesia) during sevoflurane with 92.91% accuracy compared with the response entropy index which had an accuracy of 77.5% (Shalbaf et al. 2013). This same algorithm demonstrated with generalization to Propofol and volatile anesthesia patients with 93% accuracy versus the BIS index's 87% accuracy. Other clinical variables such as heart rate variability have been investigated to approximate sedation level (Nagaraj et al. 2017). These studies highlight the power of artificial intelligence techniques in creating models that can efficiently consider linear and non-linear data simultaneously to generate maximal prediction value.

Related to depth of anesthesia monitoring, there has been increasing interest in the control of automated anesthesia delivery. Control systems using machine learning have also been used to automate the delivery of neuromuscular blockade, where these systems have also incorporated forecasting of drug pharmacokinetics to further improve the control of infusions of paralytics. Other applications include the use of artificial intelligence to achieve control of mechanical ventilation or to automate weaning from mechanical ventilation.

For perioperative care risk prediction, various techniques in machine learning, neural networks, and fuzzy logic have been applied. For example, neural networks used to predict the hypnotic effect (as measured by BIS) of an induction bolus dose of propofol were found to exceed the average estimate of practicing anesthesiologists (Liu et al. 2019). Neural networks have also been used to predict the rate of recovery from neuromuscular blockade and hypotensive episodes post-induction or during spinal anesthesia, while other machine learning approaches have been tested to automatically classify pre-operative patient acuity (i.e., ASA status), define difficult laryngoscopy findings, identify respiratory depression during conscious sedation, and to assist in decision-making for the optimal method of anesthesia in pediatric surgery (Lin et al. 2002). Waveform data from arterial lines has been used to develop models that could predict hypotension before their occurrence on an arterial line waveform (Hatib et al. 2018). Others have used machine learning models to predict morbidity/mortality, sepsis, weaning from ventilation, or readmission.

Imaging guidance has also benefited from using convolutional neural network to identify key vessels e.g. femoral artery/vein during a femoral nerve block, vertebral level, lamina or epidural space during real-time (Hetherington et al. 2017). Pain management may improve with the use of machine learning to measure nociception levels based on photoplethysmograms and skin conductance waveforms or EEG (Hamunen et al. 2012; Pesteie et al. 2018).

Finally, even operating room logistics has benefitted from improved prediction of operation duration, bed usage, recovery throughput and length of recovery using a combination of information on staffing characteristics both anesthesia and surgical, and patient medical history (Gram et al. 2017). In these myriad of potential applications, anesthesiologists should continue to partner with data scientists and engineers to provide their valuable clinical insight into the development of artificial intelligence to ensure its clinical applicability, training data validity, generalizability, and that interpretations of that data are clinically meaningful.

Postoperative

In the postoperative setting, artificial intelligence and telehealth are playing increasingly important roles in disposition and reducing length of stay. Remote monitoring technologies and early warning systems, such as AlertWatch® (Tremper et al. 2018), are transforming postoperative care by reducing ICU admissions and alerting responding clinicians prior to patient decompensation. Postoperative monitors that combine artificial intelligence with plethysmographic and electrocardiographic signals have been developed for noninvasive respiratory and hemodynamic monitoring. Additionally, consumer health wearable devices are providing new sources of patient generated health data for post-discharge monitoring and rehabilitation programs.

Future Directions of AI in Personalized Anesthesiology

As degrees of freedom in a dataset increase, machine learning and deep learning algorithms require larger training datasets to develop accurate models. This means that as our patient datasets become larger and more complex, we'll need more patients to predict outcomes and to leverage all of the available big data and small data resources. Personalized anesthesiology that leverages both electronic health record data and patient-generated health data is on the horizon, but will require collaborative initiatives between academic medical centers to minimize biases and ensure generalizable models. Perioperative data consortiums, such as Multicenter Perioperative Outcomes Group (MPOG), will be critical to the integration of artificial intelligence into the perioperative ecosystem (Kheterpal 2011; Simpao et al. 2015).

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