REVIEW

What we can learn from Big Data about factors influencing perioperative outcome

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Purpose of review
This narrative review will discuss what value Big Data has to offer anesthesiology and aims to highlight recently published articles of large databases exploring factors influencing perioperative outcome. Additionally, the future perspectives of Big Data and its major pitfalls will be discussed.

Recent findings
The potential of Big Data has given an incentive to create nationwide and anesthesia-initiated registries like the MPOG and NACOR. These large databases have contributed in elucidating some of the rare perioperative complications, such as declined cognition after exposure to general anesthesia and epidural hematomas in parturients. Additionally, they are useful in finding patterns such as similar outcome in subtypes of beta-blockers and lower incidence of pneumonia in preoperative influenza vaccinations in the elderly.

Summary
Big Data is becoming increasingly popular with the collaborative collection of registries offering anesthesia a way to explore rare perioperative complications and outcome to encourage further hypotheses testing. Although Big Data has its flaws in security, lack of expertise and methodological concerns, the future potential of analytics combined with genomics, machine learning and real-time decision support looks promising.

Keywords
anesthesiology, large databases, review

INTRODUCTION

Anesthesia has advanced from opening up the possibility for a patient to survive a surgical procedure to being considered safe in the 20th century. Venturing further into the end of the 20th century, we entered the third industrial revolution with analogue data transitioning into digital. The field of anesthesiology was one of the first to evolve from paper documentation to a sophisticated electronic monitoring system, generating and acquiring data from patients during the perioperative period using anesthesia information management systems (AIMS) [1], whereas the rest of the healthcare system followed implementing electronic health records (EHR) systems, opening up the possibility to accumulate vast amounts of patients' data. Currently we have entered the fourth industrial revolution (Fig. 1), in which Big Data will play a key role alongside the Internet of Things and Artificial Intelligence (Table 1), in analyzing and understanding human data in business, commerce, economy and medicine [2]. Google has demonstrated how Big Data analytics can predict people's shopping behavior [3] and was able to estimate influenza outbreaks activity in regions of the United States based on the analysis of millions search engine queries [4]. IBM has developed an Artificial Intelligence, Watson for Oncology, which makes cancer treatment recommendations by acquiring knowledge from reading and learning from literature, protocols and patients' charts [5]. When these technological advances will be fully realized and integrated, healthcare might be transformed in which a patient's health is being monitored by wearables, whereas Artificial Intelligence is predicting adverse events to take place and has already calculated the most optimal treatment solely based on data.

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KEY POINTS

- The collaborative collection of registries offers anesthesia a way to explore rare perioperative outcome through large databases.
- The potential of Big Data in predictive analytics combined with genomics, machine learning and real-time decision support looks promising.
- Big Data has its flaws in cybersecurity, lack of expertise and methodology.

As a specialty dealing with a continuous stream of data from patients, anesthesia offers the opportunity to utilize data to explore and learn more about patients and how it influences perioperative outcome. For this very reason the creation of national, regional health registries and or surveys were multiplied over the last couple of years to collect perioperative large databases for research purposes (Fig. 2).

This narrative review will shortly discuss what value Big Data has to offer anesthesiology and aims to highlight recently published articles, which used large databases analyzing factors influencing perioperative outcome. Additionally, we will discuss its future perspectives and the major pitfalls this type of research presents.

WHAT BIG DATA OFFERS ANESTHESIOLOGY

Although the definition of Big Data varies greatly in healthcare [6▪▪], it is commonly described as digital data, which have become so large and complex, they surpass the capability of traditional techniques and technologies to capture, store, distribute, manage and analyze the data [7]. The core characteristics that define Big Data are the 3 V's: Volume (the quantity of data produced), Velocity (the speed at which the data is generated and processed) and Variety (the type and nature of data, structured, unstructured or semi-structured) [7]. Although the data collected from AIMS and EHR have a lot of variety (lots of different types of physiological data points), the data used within anesthesiology lack in velocity (physiological data only being recorded every minute, instead of milliseconds) and volume (not ranging into terabytes each day), leaving scientists into debate if anesthesia data can be considered Big Data [8–10]. Some claim anesthesiology will only obtain Big Data when registries have collected AIMS' physiological data in waveform data

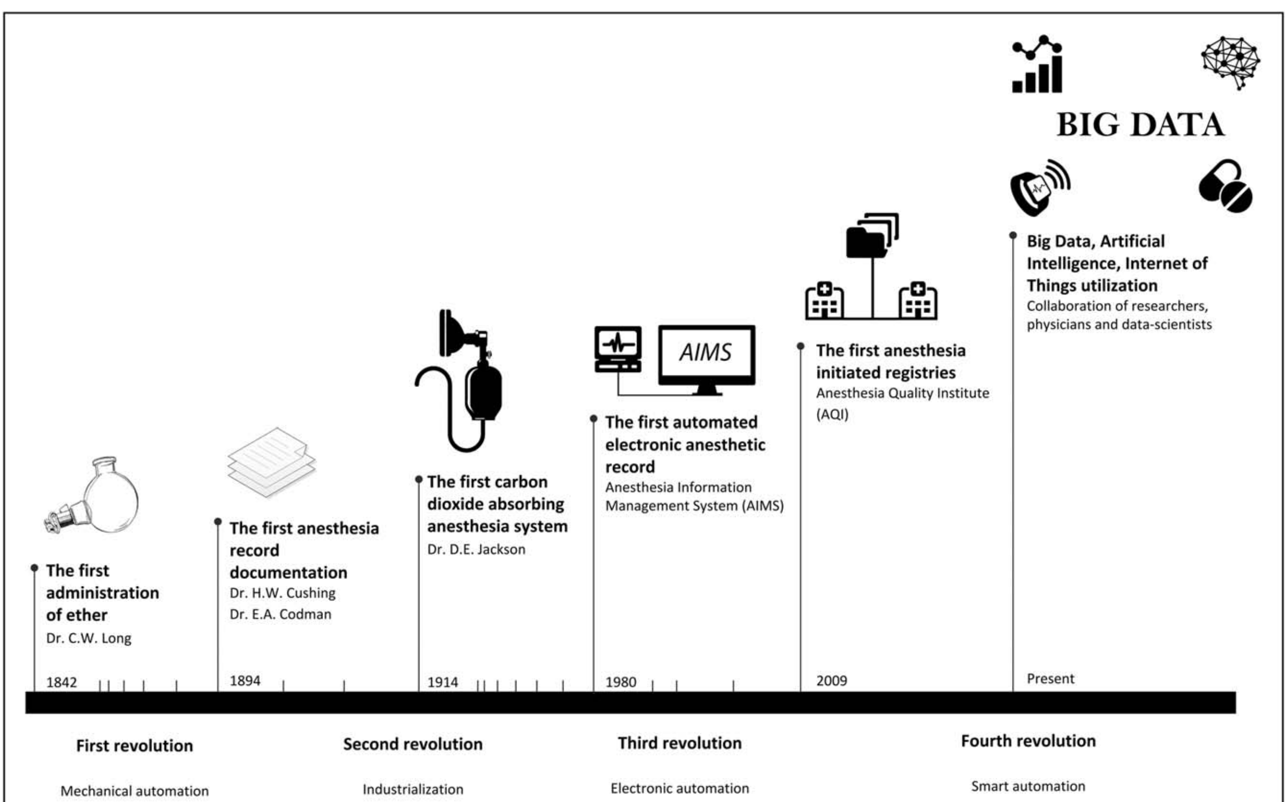

FIGURE 1. Timeline history of anesthesia's documentation to digital.

Table 1. Descriptions of key terms

Terms	Descriptions
Big Data	Digital data sets so large and complex; they are impossible to manage with traditional hardware and/or software, nor are they easily manageable with traditional or common data management tools and methods. The core characteristics of Big Data are Volume, Velocity and Variety. Veracity has also been proposed as another critical feature of Big Data in healthcare.
AIMS	Anesthesia Information Management System, an electronic record keeper to document the patient's intraoperative process by automated and or manual recording of vital signs, events and administration of medication.
MPOG	The Multicenter Perioperative Outcomes Group, a nonprofit academic consortium of more than 50 hospitals across 2 countries aiming to improve patient care by collecting data through EHR and AIMS.
NACOR	The National Anesthesia Clinical Outcomes Registry, founded by the Anesthesia Quality Institute, collects anesthesia cases and outcomes in the USA to improve the quality of clinical practice in anesthesiology. The NACOR collects data from AIMS, billing data, administrative data, comorbidities, outcome and quality reporting.
Hadoop	A software processing tool constructed for Big Data, able to partition, allocate, integrate and aggregate large data sets for analytics. Currently most widely used in healthcare.
Artificial Intelligence	The concept of machines able to perform tasks characterized as human intelligence.
Machine learning	Currently one application of Artificial Intelligence. A method in computer science to construct statistical complex models and algorithms based on previously obtained knowledge of data to produce predictions. Machine learning can then improve predictions of outcomes when new similar data is presented, letting machines learn for themselves.
Deep learning	A type of machine learning using linear and nonlinear computational models composed of numerous layers to learn from raw data. This type of machine learning is less dependable on preprogrammed algorithms, work well with large data and are have greatly improved speech, visual and object recognition.
Data mining	A process to discover new unknown patterns in large data sets.

AIMS, Anesthesia Information Management system; MPOG, Multicenter Perioperative Outcomes Group; NACOR, National Anesthesia Clinical Outcomes Registry.

instead of minute-intervals, yet for this narrative review's purposes, we will mainly discuss all types of large databases.

Conducting randomized controlled trials (RCTs) has proven to be very challenging in the field of anesthesia [11]. Deviating or withholding standard care is not achievable from an ethical point of view and could impose serious risks to patients. Additionally, because of the small incidence of adverse perioperative outcomes, a large sample of patients is needed for a RCT to determine clinically meaningful effect, resulting in calculated expenses far above the restricted budget. Big Data, even though retrospective in nature, offers invaluable insights and possibilities in rare perioperative outcomes within anesthesiology, by acquiring the large number of cases needed for proper analysis.

By monitoring the patient's vital signs diligently, anesthesiologists have access to massive amounts of various data. This automated data has proven to be more structured, accurate, complete and reliable than manual imputation of data, which other fields suffer from, although dealing with artifacts needs to be warranted [12,13]. Exploring the perioperative period and outcome in more detail, opens up the possibility of discovering more trends and generating novel hypotheses to justify setting up clinical trials [14].

LARGE DATABASES

The potential Big Data has to offer to the healthcare system has not gone unnoticed, resulting in an increasing demand of registries on both regional and national level, collecting EHR data to pool in one set. Existing research registries specialized in improving perioperative outcome are the National Surgical Quality Program (NSQIP) [15] and the Society of Thoracic Surgeons Database. Registries specified in the field of anesthesiology and collecting data from AIMS are the Multicenter Perioperative Outcomes Group (MPOG) [16] and the National Anesthesia Clinical Outcomes Registry (NACOR) [17]. Although not meeting the strict definition of Big Data, they have provided valuable insights in understanding rare perioperative outcomes and need to be mentioned.

NATIONWIDE DATABASES

A clear example of the valuable use of nationwide database to validate the risk/side-effects of anesthesia

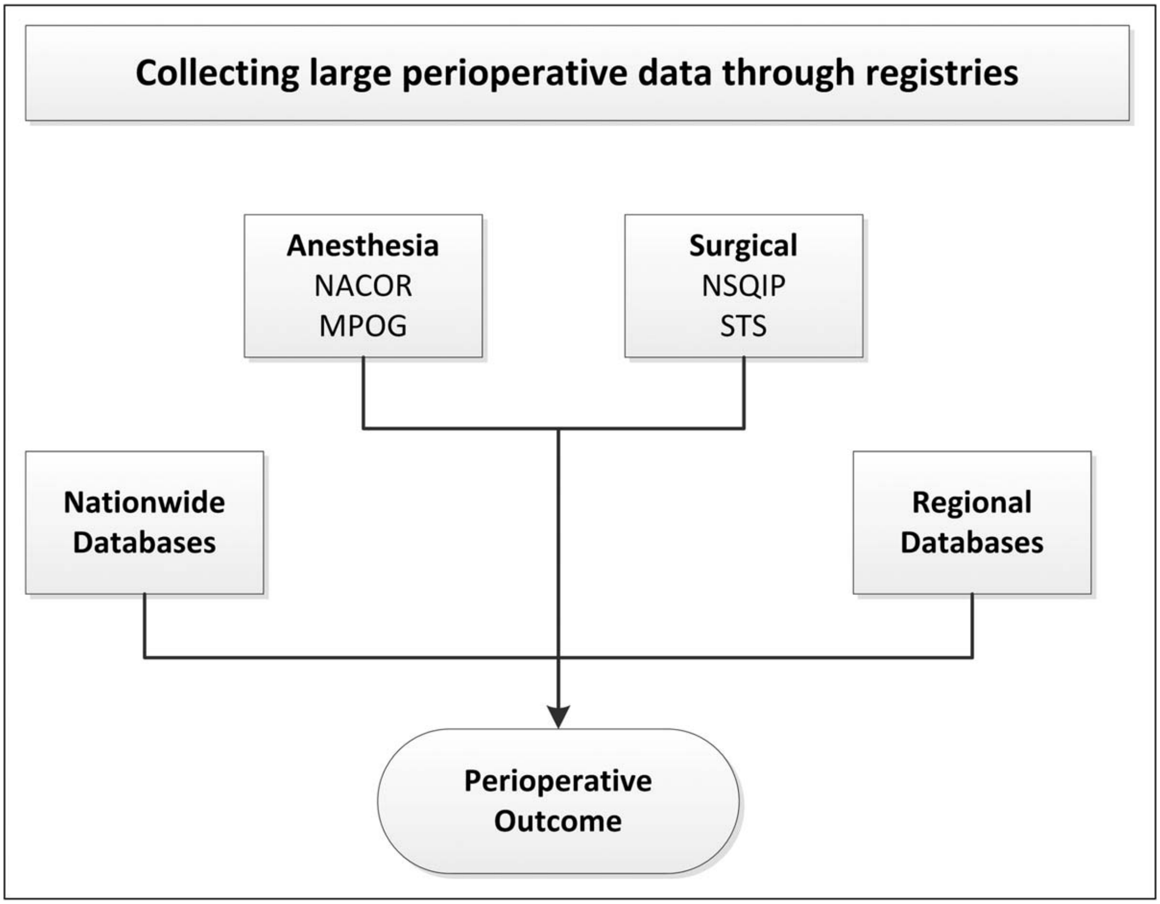

FIGURE 2. Overview of the collection of large perioperative data through registries mentioned in this review. MPOG, Multicenter Perioperative Outcomes Group; NACOR, National Anesthesia Clinical Outcomes Registry; NSQIP, National Surgical Quality Improvement Program; STS, Society of Thoracic Surgeons.

is the use and link of regional and national databases how surgery and general anesthesia might have an effect on brain development in children. A population-based cohort study in 188 557 children in Canada [18] demonstrated children undergoing surgery prior to primary school to be at risk of early development vulnerability by linking provincial health administrative databases to children's developmental outcomes. In the same edition of *Anesthesiology*, Graham *et al.* [19] demonstrated similar results in 18 056 children by linking the Population Health Research Data Repository, constituting of province-wide data from several governmental ministries including health, social services and education in Canada. Additionally Glatz *et al.* [20▪] showed the long-term effects as lower academic and cognitive performance in adolescence in a nationwide population-based cohort study by linking the birth and patient registers with the school grade registers in Sweden.

Similarly the cognitive effects of anesthesia in the elderly have also been explored in a cohort of 219 423 patients from a Korean nationwide cohort database, showing that previous exposure to general anesthesia, the number of exposures, the number of anesthetic agents administered and the cumulative exposure time were associated with an increased risk of dementia [hazard ratio (HR) = 1.29, 95% confidence interval (CI) = 1.26-1.38] in a 12-year follow-up [21▪].

Discovering the effects of already commonly used medications is also being explored. With the plethora of different types of beta-blockers and their controversial benefit in the perioperative setting, many hypothesized whether the varying subtypes of beta-blockers would affect perioperative risk differently. The large Danish Nationwide cohort study of 61 660 patients was able to elucidate on this subject by studying patients whom were treated with a beta-blocker chronically and undergoing noncardiac surgery [22▪▪]. The study showed no increase of risk of 30-day all-cause mortality or 30-day major adverse cardiovascular events between the subtypes of beta-blockers, offering further insights for the debate of beta-blocker usage in the recent guidelines.

On the opposite side of the spectrum is rediscovering already commonly used medication and its beneficial effect on perioperative outcome, for example, influenza vaccinations. Even though they are recommended for the elderly by the World Health Organization, there has been a decline in usage over the past several years. Recently, the Taiwan National Health Insurance Research Database discovered a lowered risk of developing postoperative pneumonia and in-hospital mortality in geriatric patients receiving influenza vaccinations prior to their surgery [23▪].

One of the possible postoperative outcomes, which occurs infrequently, is postoperative opioid overdose. Although considered a rare event, 1 patient in a 1000, it has very detrimental effects such as respiratory depression, hypoxic brain injury and possible death. Using the Nationwide Inpatient Sample database in the United States, Cauley *et al.* [24] were able to collect data of 11 317 958 patients undergoing major elective surgery. Their study showed a four-fold increase of mortality rate and prolonged hospital stay if an event occurred in case of a postoperative opioid overdose. The greatest predictors of postoperative opioid overdose were a history of substance abuse, type of operation, age, sex, race, income status, comorbid diseases and geographic location, providing us a clearer picture of patients at danger in the current opioid epidemic [24].

MULTICENTER PERIOPERATIVE OUTCOMES GROUP

Founded in 2008, the MPOG is a nonprofit collaboration of over 50 academic hospitals and 2 countries to collect EHR and AIMS data primarily for anesthesia research and also allowing any physician from the participating department to apply for permission of the use of the aggregated data. Firstly, through expanding their vastness of data from multiple sources, they aim to improve on the versatility of data in anesthesia, consequently creating sufficient statistical power for even the most rare perioperative outcomes. Secondly, through effective research, the goal is to improve clinical guidelines and anesthesia care based on valuable research [25]. Each institution's different type of AIMS is used to collect and translate the electronic records to a common uniform registry, containing data such as patients' demographics, medical history, information of the anesthesia procedures, fluids, monitors, vital signs and medications.

Their database is already being utilized to either explore normal physiological values or rare anesthesia-related events. In a recent study utilizing the AIMS data from the MPOG, de Graaff *et al.* [26▪]were able to analyze 116 362 cases of American Society of Anesthesiologists (ASA) class 1 or 2 children from 10 centers and determined age-specific and sex-specific noninvasive blood pressure reference values to utilize for children under anesthesia. The authors were able to ascertain reference values in children previously unknown, offering a consistent reference for future pediatric anesthesia, potentially minimizing perioperative risk by adhering to them. Conversely, data is also utilized to investigate whether intraoperative threshold settings are adhered to. Colquhoun *et al.* [27] discovered most patients undergoing one-lung ventilation received Vt-PEEP well above the recommended thresholds. Additionally, anesthesia equipment can also be validated, for example, if alarm settings for intraoperative drug infusions (propofol, norepinephrine and phenylephrine) are triggered at the correct installed percentile rates [28]. In the case of uncommon complications, Aziz *et al.* [29] were able to demonstrate a higher rescue intubation success rate if video laryngoscopy was used instead of other rescue techniques and Lee *et al.* [30▪▪] were able to calculate risks of an epidural hematoma when neuraxial techniques were performed in thrombocytopenic parturient. Thrombocytopenia is considered a relative and or even absolute contraindication to neuraxial techniques, which is why it is rare to record cases of patients receiving an epidural and their outcome. Out of the 149 673 parturients identified in the MPOG database, the authors were able to include 573 patients with a platelet count <100 000/μl and combine them with previous literature to write a systematic review, estimating the risk of an epidural hematoma at 11% when platelet count is 0–49 000/μl , 3% when 50 000–69 000/μl and 0.2% when 70 000–100 000/μl.

NATIONAL ANESTHESIA CLINICAL OUTCOMES REGISTRY

Founded by the Anesthesia Quality Institute (AQI), a nonprofit organization created by the ASA since 2009, the NACOR started collecting anesthesia cases from 2010 with their goal to improve local quality, inter-practice benchmarking and scientific research. Reaching over more than 3700 hospitals and outpatient centers, the NACOR is heavily used for understanding trends in demographics of anesthesia cases. Similar to the MPOG, the NACOR not only collects data from AIMS, but also collect billing data, administrative data, comorbidities, outcome and quality reporting.

Recent examples are the comparison of anesthesia for dental surgery [31], the distribution of common anesthesia procedures being similar during different work hours (i.e. normal, evening and weekend) [32] and demonstrating an increase and demand of non-operating room anesthesia [33]. Additionally, trends are assessed within the quality of anesthetic care, demonstrating a decreased risk of mortality when a board-certified anesthesiologist is present during cardiac surgery [34] and providing inferior care (i.e. less antiemetic administration) in patients with a lower socioeconomic status [35]. Rare anesthetic complications such as unanticipated early postoperative reintubations are also being researched. It was generally accepted to be associated with a high morbidity and mortality rate, but due to the rare occurrence, the incidence was previously unknown. By using millions of cases in the NACOR database, Tillquist *et al.* were able to discover the incidence (0.061%), though also proving a low clinical relevance, and were able to confirm already expected risk factors such as age under 1 year, age 80 years or above, a higher ASA classification, longer procedures and thoracic/vascular surgery [36▪]. However, ascending beyond just assumptions is crucial in evidence-based medicine, which makes these studies critical in identifying which type of individual patients are at most risk of these rare complications during surgery, consequently, providing important first data to improve perioperative management of these high-risk patients.

FUTURE PERSPECTIVES

Although Big Data in anesthesia might already have some results from its analytics, the potential it harbors to change future patient's care is impressive.

REAL-TIME BIG DATA ANALYTICS AND CLINICAL DECISION SUPPORT

Another proposed field within anesthesia, which utilizes Big Data is the use of real-time processing and analysis of intraoperative data [8]. Patients' physiological data will be processed/analyzed in high velocity every milliseconds and will be large in volume to be computationally complex [37]. Studies have already demonstrated how real-time clinical decision support is able to improve administration of perioperative antibiotic prophylaxis [38,39] and prophylactic antiemetics [40] with improved post operative nausia and vomiting (PONV) outcome [41]. Pop-up warnings in AIMS have also proven to improve vital sign monitor management [42,43▪▪], intraoperative glucose management [44▪], improved reduction of low tidal volume when warned of possible acute lung injury [45] and improved high fresh gas flow management [46]. Though it must be noted that the level of evidence is limited because of the current low reproduction of the studies and whereas there is improved adherence to their chosen protocol, it did not always improve perioperative outcome [47▪▪]. It is potentially possible when all physiological parameters in Big Data are used for analytics, we can have a full understanding how to improve on intraoperative monitoring and modification.

GENOMICS

One of the burdens anesthesia carries, is the risk of patients having a potentially life-threatening adverse reaction to one of the drugs, because of an unusual or unpredictable hypersensitivity, allergy or variance in drug metabolism. An area uncommonly applied in anesthesia is Big Data applied in genomics as patient tailored medicine. Currently, a handful of drug pharmacogenetics have been discovered in anesthesia and complications such as malignant hyperthermia, PONV and delayed emergence have been associated with pharmacogenetics of perioperative medications [48]. If we are able to discover more genotypes for drug sensitivity, drug metabolisms, allergies, susceptibility to pain, PONV, thrombosis, hemorrhaging, infections or other perioperative adverse events, the anesthetist will then have a plethora of information of which complications to expect and can prepare accordingly/provide optimal individualized care [49].

MACHINE LEARNING

In order to process all the complex data, systems are required to partition, allocate, integrate and aggregate the large data sets. Currently, the most popular tool used to manage Big Data for analytics is Hadoop, which is an open-source distributing data-processing platform [7]. Although for healthcare not user-friendly, complex and programming intensive, it is able to dissect Big Data into nodes and is currently essential to process Big Data for analytics. However, as the information from research on AIMS, real-time decision support and genomics will inevitably expand so enormous for even the advanced tools to process, data mining and machine learning might be solutions to process such data. Machine learning has already been applied by Lee *et al.* [50▪] in predicting the bispectral index (BIS) of patients under total intravenous anesthesia of target-controlled propofol and remifentanil infusion. Their deep learning approach, based on dosing histories and demographic data, proved to be more accurate in predicting BIS index in patients than the traditional method, giving us a glimpse how machine learning can be utilized in conjunction with Big Data in the future. Indeed, researchers are starting to recognize the potential Artificial Intelligence has to offer perioperative medicine [51,52], subsequently setting up machine learning to analyze patients' history, laboratory values and AIMS (vital signs and medication administration) to develop forecasting algorithms to predict postoperative complications [53▪].

PREDICTIVE ANALYTICS

Genomics and machine learning are still in their nascent stages, but have the potential to radically evolve the current perioperative care and the prevention of adverse outcomes when combined with real-time data-analytics. Ideally, we want to be able to use Big Data analytics on preoperative, intraoperative and postoperative data combined with knowledge how a patient may potentially react based on their genetic code. Simultaneously we want to use Artificial Intelligence to accurately discover patterns, which will advance our understanding of how they affect the patient and anesthesia, which in turn can create a prediction of adverse clinical outcome before they occur. In conjunction with the utility of clinical decision support systems, this may transform perioperative care into proactive support in the prevention and reduction of perioperative outcomes [54].

CHALLENGES OF BIG DATA

Although the potential of Big Data has its strong merits, these are not without challenges clinicians have to face. The use of Big Data in every day care is dependent on specific conditions.

Firstly, Big Data analytics, Hadoop and machine learning require individuals who are specialized in this particular type of skill set, which not every clinician or department has readily available [54]. Experts also need to be well educated within the medical field for proper processing of the unstructured data. Clinicians and researchers whom are working with Big Data should be advised to follow courses or lectures on the subject. Currently, the IT-infrastructure is lacking and investment costs for implementing the technical expertise is also of major concern [6▪▪].

Secondly, although the data from AIMS is perceived as highly accurate and has less human error [55], unstructured data is prone to loss in data quality, data inconsistency and instability [56]. In the case of AIMS, vital parameters have shown to have higher incidences of artifacts [12]. Additionally, data can vary substantially between type of source collection (e.g. administrative claims, clinical registries) [57,58]. Therefore, processing of Big Data needs to be thoroughly cleaned before analysis and preferably needs to be validated [59,60,61▪]. Failure to adhere to these steps will give a misrepresentation of the data and may lead to false predictive analytics. Afterwards, in order for the integration of Big Data analytics in daily anesthesiology practice to be effective, the complex data has to be constructed and filtered into easy to use interfaces, for example, visual analytics tools [62].

Thirdly, although tools as propensity-score matching can be used to control confounding in these large retrospective databases, the threat of selection bias, lack of generalizability and confounding remain present, which could lead to misinterpreting association for causation [60]. Therefore, Big Data analytics need to be interpreted with caution and should primarily be used for hypothesis testing as a basis to conduct clinical trials [14] and to adhere to standardized clinical endpoints to add value as reproducible research [63].

Lastly, data collection on a grand/large scale creates difficulty in keeping patients' data security safe on multiple perspectives [54]. It will be highly debatable whether patients' data will be allowed to access without proper informed consent. By collecting, increasing the patients' data and made readily accessible for multicenter collaboration via the cloud, the patient's information will become increasingly less secure. With improved data-sharing through network-connected devices comes the increasing vulnerability for cyber-attack, especially in healthcare in which cybersecurity is unlikely the priority when acquiring products [64]. These issues will probably be addressed in the near future as the General Data Protection Regulation have come into force since May 2018, which will act as an incentive for healthcare organizations to radically improve cybersecurity. Vulnerabilities in cybersecurity remain of utmost concern and it will take a combined effort from organizations, governments and experts to improve on safety and resilience [65].

CONCLUSION

Big Data is becoming increasingly popular and offers anesthesia a way to explore rare perioperative complications and outcome in a more efficient and less time consuming manner than previously possible. Although it will not replace RCTs, through collaborative collection of registries on national levels, Big Data can discover trends to encourage further hypotheses testing. With the integration of AIMS, the physiological mechanisms of the complex perioperative process and how it effects perioperative outcome will also be further explored. Although not without its flaws of security, expertise and methodological concerns, if Big Data analytics can be combined with genomics, machine learning and real-time decision support, it has the potential to change the perspective of the current perioperative period and how we can modify the supportive care to an active individual patient-tailored process.

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Conflicts of interest

There are no conflicts of interest.

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