Anesthesia 2025

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CHAPTER

Personalized Anesthesia: A Peep at the Future!

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INTRODUCTION

Personalized anesthesia care involves tailoring anesthetic techniques to the unique needs of each patient, while considering factors such as medical history, genetic makeup, and specific physiological conditions. This approach aims to optimize patient outcomes, minimize complications as well as enhance overall surgical experience by (if required) moving away from standardized protocols and providing the perfect human touch.[1]

Personalized anesthesia is a rapidly evolving field with ongoing research exploring the role of genomics, artificial intelligence (AI), and real-time monitoring in enhancing patient care delivery. As technology advances and our understanding of individual responses to anesthesia deepens, personalized anesthesia becomes even more relevant, leading to safer, more effective, and more patient-centered surgical experiences.[1,2]

WHY AND HOW DID PERSONALIZED ANESTHESIA CARE EVOLVE?

Anesthesia began as a modality of pain relief and sedation to allow a painful surgical procedure to be performed and it progressed to advanced perioperative medicine providing perioperative safety for complex surgical procedures. The advent of superior diagnostic techniques, advanced monitoring devices, time-tested standardized protocols, availability of potent medications, intensive postoperative management, and shift in approach of anesthesiologists toward enhanced recovery, early rehabilitation, and patient satisfaction, has made anesthesia safer and more broad-based.

Traditionally, anesthesia care has been guided by generalized protocols, with drug choices and dosages determined by factors such as patient weight, age, and medical history.[3] However, this "one-size-fits-all" approach often overlooks individual variations in drug metabolism and response, leading to unpredictable outcomes.

Anesthesiologists have been providing some form of personalized anesthesia care to patients; thus, targeting a good clinical outcome for them. They have been able to do it by designing anesthesia techniques for the specific requirements of patients, based on their physiological/altered

parameters, existing comorbidities, drug tolerances, surgical requirements, patient psychology, available resources, and their own clinical experiences. However, the concept of personalized anesthesia care and precision medicine with a structured approach, involving knowledge of pharmacogenomics is a recent realization.[3,4]

Various surgery-specific, protocol-based standardized recommendations have been implemented in the past, providing good outcomes to some or most of the patients. In this "one-size-fits-all" approach, there is still a subset of patients that does not benefit from this approach, resulting in an unfavorable outcome and there are always the nonresponders, for whom, the protocolized approach may not work and these patients suffer.[3]

The emphasis of most clinical studies is focused on the comparisons of different anesthetic medications or techniques, while the relationship between cellular mechanisms and outcome is left unexplored.[3] Here, precision medicine offers a promising alternative, aiming to tailor anesthetic care to the unique genetic makeup of each patient. Pharmacogenomics, the study of how genes influence drug response, is central to this personalized approach.[4]

COMPONENTS OF PERSONALIZED ANESTHESIA CARE

Personalized anesthesia care also has the essential components that can be grouped under man, machine, materials, and methods **(Fig. 1)**.

Factors Affecting Personalized Anesthesia Care

Factors affecting personalized anesthesia care involve:

Unique Needs of Patients

No "two patients" requiring anesthesia are the same. Even in the same patient, undergoing same/similar procedure at different times, anesthesia administered and its outcome may vary. The patient-specific anesthesia practice variation becomes even more evident in patients with unique or special needs. For example, anesthesia practice will vary depending on whether the patient is a neonate, infant, child, young adult, or elderly, or a patient with special needs such as preoperative counseling, confidence building, and a different anesthesia technique as happened in our following case study:

Case scenario: A 35-year-old female at 36 weeks of gestation is scheduled for lower segment cesarean section (LSCS). She is a known case of hypothyroidism for last 5 years, on tab thyroxine 50 μg orally daily and has a previous history of lumbar laminectomy and discectomy at L3–4 and L4–5 intervertebral space. There is no other significant history. All investigations done on the perioperative period are within normal limits. However, in view of her previous

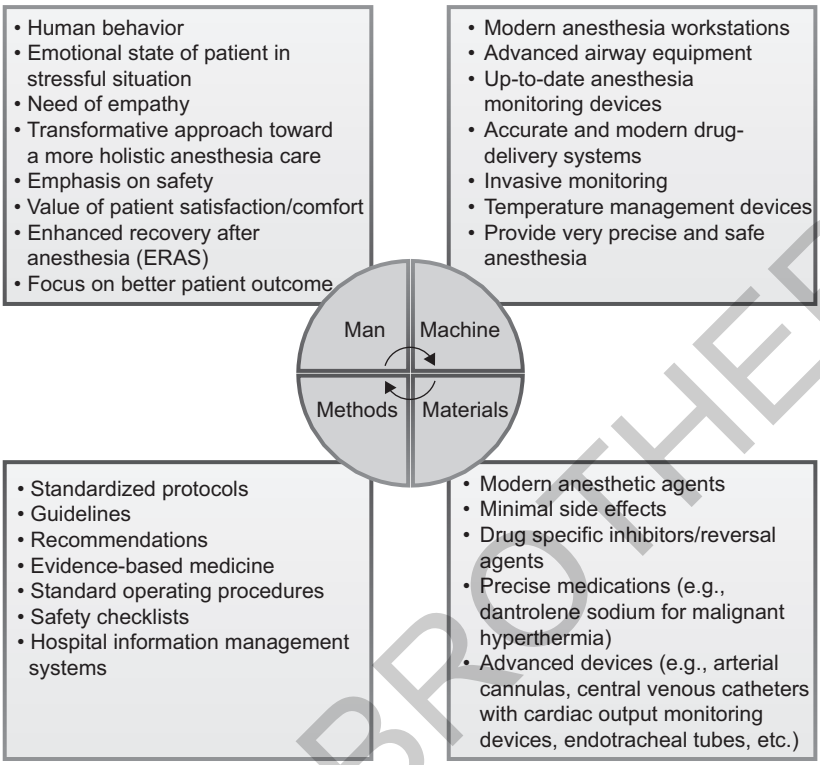

Fig. 1: Components of personalized anesthesia care.

history of pain and surgery, she is apprehensive about the present surgery she is scheduled for.

Management: As per standard practice based on standard protocols, the routine anesthesia plan for a LSCS is administration of subarachnoid block (neuraxial block) or spinal anesthesia. However, as a perioperative physician focused on personalized anesthesia care, one has to consider following specific points in the management of this case:

- She has already undergone lower back surgery (lumbar laminectomy and discectomy at L3–4 and L4–5 intervertebral space).
- She is apprehensive about pain perception.

Most likely, multiple pain management strategies would have been required to alleviate pain before spine surgery. So, she is expected to have a different sensitivity to pain. In view of the previous spine surgery, the alternative plan can be administration of general anesthesia considering the altered anatomy of spine following the previous surgery.

She will need more preoperative counseling and a multimodal analgesia plan in the postoperative period. The added anxiety of delivery and postpartum period along with responsibility of care of a newborn and feeding

may put a lot of stress on the patient. Here, the role of empathy supported by repeated counseling, prompt guidance with postpartum care, and assistance with newborn care will give a better outcome and enhanced satisfaction to the patient.

Genetic Factors

Genetic variability among individuals affects the metabolism of anesthetic drugs and adjuvants and significantly impacts their response to anesthesia. While some patients may have a good outcome, others may not have such a favorable response to the standard medications used. This not only changes the effect of anesthesia but also alters the likelihood of side effects. A knowledge of specific gene variants that affect the processing of anesthetic medications can go a long way in deciding anesthesia drugs to be administered for such a patient. Administering specific anesthetic drugs according to his/her genetics will enhance the patient satisfaction by being efficient in that specific variant. Patients with opioid receptor polymorphism may benefit from use of nonopioid analgesia during the perioperative period.[5]

The opposite can be observed in patients who are administered standard anesthesia, and they happen to be having genetic mutation that metabolizes the drugs too rapidly, and hence, a low satisfaction level. For example, a patient who metabolizes anesthetic agents rapidly may have lighter depths of anesthesia and awareness during surgery. Prior testing of such genetic markers can be of help in selection of appropriate anesthetic medications.[5] A very pertinent application of genomic variants testing is to identify patients who can develop malignant hyperpyrexia.[5]

Pharmacogenomics

Pharmacogenomics is the branch of science studying the genetic makeup of patients and establishing compatibility with pharmacological agents.[6] It helps in predicting drug efficacy and toxicity.[6] This enhances the overall patient satisfaction and long-term prognosis while contributing to reduction of healthcare costs.[6]

The mechanism of an individual metabolizing and consequently responding to the anesthetic medications is governed by the variations and polymorphisms expressed in the genes encoding the enzymes that metabolize these medications.[7] The most notable genetic markers include Cytochrome P450 (CYP) enzyme family, pseudocholinesterase (A and K variants), receptor polymorphisms (opioid and volatile anesthetic agent receptors), and gamma-aminobutyric acid type A (GABAA) receptors. Any polymorphism in these genes can lead to an altered response to the anesthetic medications **(Table 1)**.

TABLE 1: Commonly used anesthetic drugs and genotypes affecting their pharmacological effects.[1]

Class of drug	*Drug*	*Gene*	*Variant*	*Effect*
Opioids	Fentanyl	• CYP3A4 • CYP3A5	CYP3A4*1G	Higher doses of fentanyl required to achieve adequate analgesia
	Tramadol	CYP2D6	• CYP2D6 NM • CYP2D6 IM	Enhanced analgesic efficacy of opioids in postoperative pain
	Codeine		CYP2D6*10	• Reduced codeine-forming morphine • Cmax and AUC of codeine-forming morphine
	Oxycodone		• CYP2D6*4/*4 • CYP2D6*4/*6	Nausea and vomiting
	Hydrocodone		CYP2D6*4/*4	Nausea and vomiting
Intravenous anesthetics	Propofol	CYP2B6	CYP2B6*6	Reduced dose requirements for isoproterenol under general anesthesia
		CYP2C9	• CYP2C9*2 • CYP2C9*3	Increased risk of hemorrhage
	Ketamine	CYP2B6	CYP2B6*6	• Decreased clearance • Increased risk of adverse effects
	Midazolam	CYP3A4	CYP3A4*22	• Reduces enzyme activity • Increased plasma concentrations of midazolam • Increased risk of adverse events
		CYP3A5	CYP3A5*1	Increased metabolism of midazolam
Volatile anesthetics	• Desflurane • Isoflurane • Sevoflurane	CYP2E1	CYP2EI*5	Patients with halothane-induced hepatic inflammation develop autoantibodies specifically against CYP2E1
Antiemetics	Tropisetron Ondansetron	CYP2D6	• Ultrarapid • Phenotype	Reduced antiemetic effect

Unlike inhalational anesthetic agents, which are almost exclusively eliminated by the lungs, intravenous anesthetic agents require metabolism in the liver before being eliminated. For example, a differential response to a commonly used intravenous anesthetic agent "propofol", may be encountered due to polymorphisms in the gene encoding the metabolic enzyme CYP2B6.[6]

Biomarkers

Biomarkers help in predicting infection, assessing response to treatment and affect clinical decision making by serving as a diagnostic and prognostic tool. They also help in designing clinical trials, especially for emerging therapies. Traditionally, perceived only as key indicators of inflammation, various biomarkers also offer valuable insights into the biological basis of disease pathogenesis and outcome **(Table 2)**.[8]

Notable examples are acute respiratory distress syndrome (ARDS), postoperative delirium (POD), and postoperative cognitive dysfunction (POCD). Up-to three sub-phenotypes (of biomarkers) have been identified for ARDS and consequently these sub-phenotypes have been shown to affect the degree of fluid responsiveness in this class of patients.[9]

Postoperative cognitive deficits (postoperative delirium and cognitive dysfunction) are associated with several biomarkers such as IL1β, IgM, β amyloid, S100 β, MMP9, and Tau. Monitoring these biomarkers is a potential area of tailoring Personalized Anesthesia Care regimens in old patients to predict POCD during the postoperative period.[1] In patients prone for POCD, substantial studies have been investigated in the metanalysis describing effects of general anesthesia on POCD.[9] Drugs, such as dexmedetomidine and fentanyl, have been shown to decrease the risk of impaired cognition in comparison to the intravenous and inhalational agents.[1]

Medical History

An individual's medical history as well as comorbidities have a significant effect on the planning and implementation of personalized anesthesia care regimens.[5]

Patients with individual major organ afflictions deserve precision medications which are discussed as follows:

- *Kidney disease:* Muscle relaxants, such as rocuronium and vecuronium, that are excreted through kidneys are retained, and therefore, dose modification is required. Atracurium and cisatracurium undergo Hoffman elimination and are the preferred relaxants in patients with kidney disease.[1]
- *Hepatic dysfunction:* Precision planning for patients with hepatic dysfunction includes the following considerations: Hepatic blood flow is diminished in such patients. Majority of opioids with the exception of

TABLE 2: Biomarkers and anesthesia.[1]

Biomarker(s)	*Biomarker function*	*Result*
IL-1b IL-6, and TNF-α	Inflammatory	Upregulation of levels by surgery and anesthesia can induce central inflammation and POCD
S-100b	Calcium-binding protein	• Relevant in predicting POCD • Overexpression further deteriorates the neuroinflammatory response and neuronal function
MMP9	Inflammatory	Elevated levels seen in patients with POCD
HMGB1	Inflammatory	• High expression observed in and around the hippocampus of the brain of experimental animals in inflammation • Alters peripheral inflammatory signals causing CNS dysfunction—potential in POCD
CRP	Inflammatory	A central inflammatory biomarker; low disease specificity
pNF-H	Neuronal cytoskeletal proteins	Serum pNF-H, a new central damage marker highly correlated with POD, may reflect the occurrence and severity of POD
IgM	Inflammatory	• Low levels in preoperative period may predict POCD • Increasing IgM levels or reducing the endotoxic inflammatory response improves cognitive dysfunction after cardiac surgery
b-amyloid (Ab)	Metabolite	• Excessive deposition of Ab • Cognitive decline • Production and deposition can trigger POCD
Tau	Axon protein	Significantly correlated with the incidence as well as the severity of POD
NfL	Neuronal axonal damage	POD is associated with neuronal axonal damage, and increased NfL predicts POD, supporting that NfL can be used as a biomarker for POD

(CRP: C-reactive protein; CNS: central nervous system; HMGB1: high mobility group box-1 protein; IgM: immunoglobulin M; IL: interleukin; MMP9: matrix metalloprotease 9; NfL: neurofilament light chain; pNF-H: phosphorylated neurofilament heavy chain; POD: postoperative delirium; POCD: postoperative cognitive dysfunction; S-100b: soluble protein-100b; TNF-α: tumor necrosis factor-α)

remifentanil and dexmedetomidine undergo biotransformation in liver necessitating dose modification. Etomidate and thiopentone need to be used with caution in these patients as they reduce hepatic blood flow.[1]

- *Cardiac disease:* Patients with heart disease are prone for dysrhythmias, hemodynamic disturbances, and compromised myocardial blood flow under the effects of anesthetic agents. The side effects need to be anticipated in such patients.[10]

Body Composition

Body composition includes:

- *Advanced age:* Elderly patients have diminished major organ reserves and are susceptible to perioperative cognitive and physical deterioration.[1] A decline in renal function in the elderly delays elimination of anesthetic drugs with a cumulative effect causing increased sedation.[11] In elderly patients, an increased interaction occurs between intravenous anesthetic agents and hypnotic agents. The clearance of benzodiazepines such as midazolam decreases significantly.[1,12]
- *Obesity:* Obesity is associated with hypertension, cardiac hypertrophy, glycemic disturbances, and deranged lipid profiles. Personalized Anesthesia Care for obesity patients should take these factors into account. Anesthetic agents can aggravate effects of obstructive sleep apnea (OSA) that may be already present in these patients.[1] Anesthesia regimens should be tailored with emphasis on rapidly metabolized drugs such as remifentanil and dexmedetomidine. A planned use of noninvasive ventilation strategies in the postoperative period is also desirable.[1] Obesity is also associated with difficult airway as well as complexities in ventilation.[12]

Advanced Monitoring

Near infrared spectroscopy (NIRS), cerebral oximetry, and electroencephalogram (EEG) influence precise and personalized anesthesia care.[1] NIRS-derived indices, which show maximum promise for personalized anesthesia care, include:

- *Cerebral oximetry:* It is a noninvasive method of monitoring that monitors the brain oxygenation and emphasizes that over-oxygenation during anesthesia may be actually deleterious to the brain.[13]
- Near infrared spectroscopy has also been shown to quantify pain perception and cerebral blood flow. Cerebral deoxygenation events (CDE) are NIRS-derived phenomena that have been shown to occur during shoulder arthroscopy in the beach chair position and can serve as potential warning for modifying anesthesia regimens and improving cerebral oxygenation.[14]

Surgery/Procedure Specific Requirements

The outcomes of a particular surgery are different in different patients due to various factors:

Psychological and emotional needs: Surgery is one of the major events of a person's life. It is a period of terrible stress for the patient during the perioperative period and this stress gets aggravated due to the unfamiliar environment and advice of "dos and don'ts" imposed on them. They have to not only understand the medical conditions but also are required to take

important decisions especially in high-risk situations. In a resource limited setting, the financial implications of perioperative care may add to the strain. As perioperative physicians, the anesthesiologists need to be aware of the psychological and emotional status of the patients. A little understanding and empathy can make a remarkable difference in alleviating this stress.

Use of Artificial Intelligence (AI) in Personalized Anesthesia Regimens

The concept of operative precision anesthesia care has become a reality due to advent of AI. The various applications of AI in tailoring perioperative anesthesia care are as follows:

- *Depth of Anesthesia:* NIRS- and EEG-derived indices are advance monitoring indices useful in perioperative anesthesia care. However, use of machine learning AI models in association with EEG data has shown superior efficacy to the conventional BIS algorithm systems.[15] Various authors have developed machine learning-based models of AI to predict depth of anesthesia (DOA) with remarkable success. This paves the way for a more widespread use of AI in predicting DOA.[16]
- *Perioperative ultrasonography (USG):* AI models have also shown promise in improving quality and accuracy of ultrasound images thereby offering perioperative physicians the opportunity to improve delivery of ultrasound-based precise diagnostic and assessment data.[1,16]
- *Predicting difficult Intubation:* An AI model developed by Hayasaka et al. has shown promise to predict difficult intubation.[17]
- *Assessment of cardiac function:* AI has also shown a lot of promise in autonomously measuring cardiac functions such as ejection fraction (EF) and overall cardiac function with matching or even better accuracy and with consistency compared to traditional ultrasound and perception of cardiologists. This will go a long way in planning, optimization, and preoperative management of patients with cardiac perturbations.[18]
- *Identification of anatomical landmarks:* An AI model developed by Hetherington et al showed accurate results to define anatomical landmarks and this helps in performance of central neuraxial blocks and endotracheal intubations.[18,19]
- *Operating room management:* Use of AI driven models has been shown to predict cancellations, surgical duration, postanesthesia care unit outcomes, and optimize operating room usage.[20]

Regional Anesthesia in Precision/Personalized Anesthesia Care

Specific aspects of regional analgesia regimens, that are pertinent to personalized anesthesia regimens include:

- Use of regional anesthesia specific to the site
- Continuous perineural local anesthetic infusion

- The use of early recovery after surgery (ERAS) protocol and increased use of oral anticoagulants have changed the outcome of peripheral nerve blocks with encouraging results.[21]
- Posterior compartment block and adductor canal blocks in patients with total knee arthroplasty (TKA) as well as erector spinae block, transversus abdominis plane block, and rectus sheath block have become popular.[22,23]
- Opioid use during and postoperative period is no longer the choice for its side effects and substance abuse fall-out. It is being replaced with regional anesthesia, ketamine, lignocaine, and gabapentin.
- Use of ultrasound (US) has made anesthesia, especially regional, safer and precise.[24]

Patient factors modulating personalized anesthesia and pain are younger age, anxiety, depression, chronic stress, longstanding pain, and opioid tolerance.[25]

Surgical Procedures Associated with More Pain

Another important factor to consider in curating perioperative analgesia is the consideration that pain in different surgical procedures follows different trajectories, and hence, it is essential to intervene at the right time with right drug, dosage, and frequency. In certain procedures, such as open procedures, TKR, LSCS, limb amputations, and mastectomy, use of adjuvants should be considered during personalized anesthesia care to improve efficacy of blocks.[24,26,27]

Resource Availability to Anesthesiologist

Infrastructure, material, technology, and number and competence of human resources modulate the individual anesthesia care and experience.[25,27]

Involvement and Commitment of Anesthesiologist to Personalized Anesthesia Care

A commonly neglected aspect of anesthesia care is the lack of knowledge of side-effects of anesthesia with almost alarming nonchalance, even among anesthesia providers.[2,25-28]

Anesthesia differs from surgical specialties in terms of *following up* patients; anesthesiologists do not follow-up patients as much as their surgical colleagues do. They also do not get structured feedback on the outcome of anesthesia. This is an area which, if addressed, can improve patient outcome following anaesthesia.[29]

Monitoring pain during the preoperative period is essential for titrating anesthesia during surgery so as to avoid unwanted opioid-related side-effects and under or overdosing. Presence of anesthesiologist in operating room all the time is an essential aspect of care.[2]

Anesthesia Environment

An important aspect of precision-based anesthesia regimen is noise-level monitoring with an effort to minimize patient discomfort and disturbance during surgery. Temperature of operating room, type of conversations, music, and utterances during a complication are all influencers of care delivery.[30,31]

American Society of Anesthesiologists Standard Monitoring

It is pertinent to remember that a combination of hemodynamics, pulse oximetry, temperature, and capnography monitoring is a vital cog in improving patient experience and should be done without fail.[2,32]

Quality Indicators Influencing Personalized Care

Enhanced recovery after abdominal surgery and safe brain initiative are the outcomes of efforts to integrate quality matrices into anesthesia care. The "Safe Brain Initiative" is a recent example of an innovative and cost-effective precision anesthesia algorithm that aims to galvanize perioperative care to avoid postoperative neurological perturbations such as POD and POCD.[33]

Standard reporting of established patient outcomes, integrating data from various sources with the aim of creating a detailed profile, regular review to improve quality matrices, educating and training anesthesia service providers about precise anesthesia care, and collaboration with other specialties are the important components of quality frameworks in anaesthesia.[2,33]

Cost and Quality of Personalized Care

Cost is an important consideration for personalized anesthesia care. Higher cost does not become synonymous with better quality of care.[34] The patient's financial background is an important arbiter of anesthesia care delivery. His paying capacity and delivery of care should be balanced.[35]

CHALLENGES IN IMPLEMENTATION OF PERSONALIZED ANESTHESIA CARE

Cost and access to pharmacogenomic testing, the latter's standardization and interpretation into a decision matrix are perhaps the bigger challenges to implement personalized anesthesia care. AI can be a useful guide for personalized care but it has to sufficiently evolve before it can play a lead role. Clinical trials, formulation of evidence, and incorporation into guidelines are the logical next steps in making personalized anesthesia care a reality.[1]

CONCLUSION

Personalized anesthesia regimen is an exciting concept. The integration of genetics, patient's unique health conditions, pharmacogenomics, and the

advent of technological breakthroughs is going to enable precise and tailored anesthesia care for patients presenting for surgery. There are multiple challenges such as cost, access to technology, lack of proper training in interpreting results, and getting newer efficient formulations. The future of personalized anesthesia care hinges on the commitment of health administrators toward patient-safety and patient satisfaction, seriousness of caregivers toward providing precision, enjoyable anesthesia experience, and affordability to their patients.

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Recent Advances in Anesthesia 2025

Salient Features

- This book aims to bring to the students and the practicing intensivists the very happening, cutting edge of the field of anesthesia
- New pharmacokinetic models for total intravenous anesthesia (TIVA) and target-controlled infusion
- Are worries about anesthesia for the very young justified?
- Can robots be used in anesthesia?
- Hypovolemic phlebotomy for liver surgery
- Perioperative neurocognitive dysfunction in the elderly.

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