Chapter 1
The Role of Personalized Medicine in Current and Future Clinical Practice of Anesthesiology and Perioperative Medicine: Towards Anesthesiomics

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Introduction

Anesthesia is a medical invention lasting less than 2 centuries. Physicians at that time invented anesthesia due to an inevitable need of physicians who could not proceed a major number of treatments without controlling intolerable pain of their patients. However, during the forthcoming decades, anesthesia grew up; then was transformed from a simple technique application to a branch of medicine often known as "Anesthesiology and Perioperative Medicine" or succinctly as "perioperative medicine". This trend did not stop in the clinical stage; it grew up towards cellular and subcellular aspects of medicine to create a new feature of anesthesiology (Naguib et al. 2012; Dabbagh and Elyassi 2016; Dabbagh 2017; Iravani et al. 2017; Kim et al. 2018; Odell 2018).

In the current era, perioperative medicine has been privileged by domains of care; each including a long list of activities:

- Preoperative care
- Intraoperative care
- Postoperative care

On the other hand, during the last years, especially the last 2 decades, a combination of multiple approaches has revolutionized medicine. The goal of this "novel doctrine in medicine" is to tailor medicine for each human being; simply talking, like fingerprint which is individual-proof. Besides, this is a real and basic shift

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"from reactive medicine to preventive medicine"; taking preventive approaches with a strategic look forward instead of a "wait and watch" approach. However, this approach known as personalized medicine has been mainly granted by the following scientific and/or practical developments:

- genome sequencing and its related techniques
- development of detailed list of cellular and molecular disciplines in medicine; from bench to bedside, creating many—OMICS fields; including but not limited to genomics, epigenomics, transcriptomics, proteomics, metabolomics, interactomics and so on (Topol 2014; Tebani et al. 2016; Donovan et al. 2019; Wolfender et al. 2019; Dabbagh 2020)
- artificial intelligence and big data management (Krittanawong et al. 2017; Schork 2019; Hashimoto et al. 2020)
- involvement of industry in genomics and related sciences (e.g. pharmacogenomics)

Other names have been coined for this medical doctrine; e.g. precision medicine, P4 medicine (predictive, preventative, personalized, participatory) and Theranostics (Flores et al. 2013; Lu et al. 2014). Though they have been used interchangeably, their definition is not necessarily the same. One of the most important applications of personalized medicine is to create and/or optimize the pathways that can predict and plan the health/disease pattern for each person in prevention, diagnosis, treatment, mortality, risk assessment and prognosis based on that person's whole biological data (i.e. —OMICS data) (Topol 2014; Tebani et al. 2016; Donovan et al. 2019; Wolfender et al. 2019; Dabbagh 2020).

In order to review part of the related evidence, a number of clinical applications of personalized perioperative medicine are listed in Table 1.1; the list will be ever increasing with many aspects of the perioperative care being personalized.

In this chapter, a brief overview on the impact of personalized medicine in the main steps of perioperative care is provided; having a general look on the current and future aspects of clinical practice. However, more detailed discussions could be found throughout the book chapters.

Preoperative Care

The main goal for preoperative care is to prepare the patient for tolerating the stress of the surgery or other medical interventions and treatments which are part of the process of controlling the underlying disease; in such a way to optimize the underlying condition and to improve the overall outcome. However, there are always barriers to achieving this goal and the strategy to achieve this goal should be tailored case by case.

Preoperative evaluation is the first step in delivering care by anesthesiologists more than any other time. Not only the medical status of the patient should be optimized but also the psychological, behavioral, economic and societal factors of the

Table 1.1 some clinical applications of personalized perioperative medicine

Preoperative care: • preoperative risk prediction scoring based on personalized models • preoperative prediction of in-hospital and out of hospital mortality and morbidity based on personalized models • preoperative assessments for pharmacologic tailoring (including the anesthetic implications of pharmacogenomics) • management of clinical scenarios with major pharmacological interaction • perioperative acute and chronic pain management; designing a personalized model for pain management • postoperative nausea and vomiting control using a personalized model • perioperative antibiotic choice; perioperative management of septic/infectious complications using a personalized model • intraoperative tailoring of anesthetics, including personalized model of drug selection for hypnosis, amnesia, muscle relaxation and analgesia and also, personalized management of their potential complications/side effects • perioperative protection of organ systems (inflammatory mechanisms, ischemic insults, etc.) • management of vulnerable patient populations (geriatric, infancy, childhood, pregnant mother) • personalized preoperative optimization of patients for the surgery; monitoring patient status using –OMICS markers
Intraoperative care • anesthetic drug choice and dose • intraoperative organ monitoring • intraoperative organ protection • hemodynamic optimization • management of potential intraoperative complications like malignant hyperthermia • intraoperative blood management and transfusion • intraoperative infection control • intraoperative safety management
Postoperative care • postoperative acute and chronic pain management • postoperative nausea and vomiting • hemodynamic management • coagulation and bleeding management • respiratory monitoring and management • management of residual anesthetic drug effects with focus on personalized aspects of anesthetic drug metabolisms • postoperative management of neurologic and psychiatric dilemmas

patient and his/her family should be considered (Fleisher 2018). This process is not just a matter of medical prescription; instead, active participation of the patient side (including the family) has a pivotal role.

However, based on a traditional approach, the first step is to perform an organ system-wide assessment of the patient, mainly focusing on phenotype and the effects of surgery or underlying disease(s) on phenotype of the patient. Besides, clinical history of using any pharmaceutical or other drugs (including any history of drug abuse or smoking) is regularly assessed. A number of patient groups need higher vigilance levels, including the pregnant mother and her fetus, the elderly and children/neonates. Acute and chronic pain management is another integral part of

preoperative care that should be tailored for each patient. In the era of ERAS (Early Recovery After Surgery), preoperative evaluation and optimization have gained much more attention. In the majority of the patients, a battery of preoperative testing is added to the clinical assessment.

Recent studies have suggested the latter traditional assessment is not enough; not only regarding lab tests, but also in order to improve the models of preoperative optimization through personalized medicine approach. In fact, for each patient, his/her individualized path for overcoming the perioperative period and management of its potential complications should be tailored (Dabbagh and Rajaei 2016; Gabriel et al. 2017, 2018, 2020; Aroke and Hicks 2019; Harris et al. 2019; Kaye et al. 2019).

Pharmacogenetics (PGx) or the study of hereditary drug metabolism is one of the key components of personalized medicine. Using Pharmacogenetics data may enable practitioners to target appropriate patient or patients' papulation for the best outcome. PGx is based on the assumption that genetically supported targets are more likely to succeed for treatment. Many studies have been implicated perioperative personalized medication, but the higher quality and more evidence-based studies are needed to make a more pronounced and effective chance in perioperative practice in specific individuals (Saba et al. 2017). A comprehensive and up-to-date resource of our current knowledge about the relation of genetic variation and how our body responds to medication is available in many robust sources like PharmGKB (https://www.pharmgkb.org/) and Pharmacogenetics Research Network (https://www.pgrn.org). Clinical pharmacogenetics implantation consortium publishes guidelines and evidence-based evaluation related to using PGx tests for patient care.

Using Electronic Health Records (EHR) enables recoding of patient's medical and health history longitudinally. EHR has a widespread adoption over the last 15 years in the USA and more than 97% of all hospitals in the USA has adopted *Certified* EHRS in 2014. EHR has generated a vast and continuously growing resource that can enable large scale research. With recent combination of EHR and Genomics Network (*e*MERGE network) has opened another window to personalized medicine. *e*MERGE is a National Institute of Health (NIH)-organized and funded consortium that develops researches combining bioinformatics with EHR for genomic discovery and precision medicine implementation. With eMERGE phase III expansion, a total of 10 websites are involved with developing and validating electronic phenotyping algorithms in order to incorporate large-scale genomic researches in one common source. eMERGE is a great source for EMR and Biorepository Information; while providing sufficient data. The structure of eMERGE includes the following:

- Investigative Sites
- Centralized Sequencing and Genotyping (CSG) Facilities
- Coordinating Center (CC)
- External Scientific Panel

A detailed list of the Participants and Structure of eMERGE could be found at https://www.genome.gov/Funded-Programs-Projects/Electronic-Medical-Records-and-Genomics-Network-eMERGE

Intraoperative Care

This period of care is part the continuum of perioperative medicine with especial considerations. The hallmark of intraoperative care is the relatively exceptional status of the patient; being anesthetized or under anesthesia care and the therapeutic procedure.

Throughout the last decades, there are a number of turning points and/or important events that have affected the intraoperative anesthesia care:

- the increasing trend for monitoring vital organs; especially in the vulnerable patient groups
- the robust evidence in favour of improved outcome due to more sophisticated monitoring of the patients
- much more targeted anesthetic drug designs with fewer side effects and increased efficacy and safety
- preventive strategies to improve the quality of care throughout the surgery (like prevention of organ ischemia, prevention of patient awareness, pre-emptive analgesic approaches, perioperative stress response modification, preventive measures form intraoperative infections and contaminations, etc.)

The trend of improved quality of intraoperative anesthetic care would be undoubtedly thrived using the developments by personalized medicine. Although the price of delivering personalized anesthesia care is still too high to afford, the development in technology during the next years would change the pattern in such a way that these would be affordable in our daily clinical practice (Iravani et al. 2017).

Postoperative Care

Personalized medicine could be a highlighted aspect of care from the entry point of the patient to the postoperative care area (PACU or ICU); starting but not limited to those presented in Table 1.1. The fact is patients undergoing postoperative period do not experience the same; mostly due to the personalized differences in the postoperative effects of anesthesia and surgery. Optimization of patient care through personalized approach would improve the quality of care in postoperative period.

Personalized Anesthesia: A Reality in Daily Practice

As a matter of fact, personalized anesthesia in essence aims to “tailor” medicine for each human being. So, the core concept is not bizarre or far from the goals of treatment so far. However, within the last 2 decades, the revolutionary scientific progress in medicine has made it available to tailor medicine for each human being based on cellular and subcellular mechanisms; i.e. using the —OMICS approach (Gerstein

et al. 2014; Jimenez and Galinkin 2015; Tebani et al. 2016; Iravani et al. 2017; Olivier et al. 2019; Dabbagh 2020).

In fact, the hallmark of this novel school of thought in medicine is adding a point-by-point correlation between genotype and phenotype of each person, both in health and disease. This is not just as simple as previous ones; instead it has created a paradigm shift in many branches of medicine (Tebani et al. 2016; Sezari and Dabbagh 2019). The same is correct for anesthesia and perioperative medicine. Having point of care—OMICS tests in the operating room or before and/or after that is not far from access in near future; while in some aspects, it could be nowadays available. The only remaining things are the matter of time and the expense; both would be resolved within the next couple of years due to inevitable scientific and technical developments. Possibly it is not too far to hear the words "anesthesiomics"or "personalized anesthesia and perioperative medicine" once considered a bit more than a "pipe dream" would be a common clinical word in our day to day practice. Just at a glance! (Bruehl 2015; Stary et al. 2015; Iravani et al. 2017; Knezevic et al. 2017; Kaye et al. 2018; Donovan et al. 2019; Dabbagh 2020).

Personalized Medicine Is Not the Answer for Everything

It is essential to know the personalized medicine pitfalls and restrictions. For instance, the effect of public health interventions such as smoking cessation, although does not fall in any categories of personalized medicine, still is a valid prevention toll in any health system. The relationship between genes and phenotypes are not always clear as environment, exposures, and lifestyle can all influence genetic expression.

In the two medical disciplines that represent the largest cause of morbidity (i.e. oncology and cardiology) personalized therapeutics has yet to show the hoped-for salient changes in clinical outcomes (Dugger et al. 2018). Cost of genetically based research and treatments is another barrier of using precision medicine, especially in the perioperative setting. However, without reservation, personalized medicine has opened a new, real and tangible horizon in the medical field.

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