

Preoperative Genetic Testing and Personalized Medicine: Changing the Care Paradigm

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Personalized medicine is the concept of tailoring pharmacotherapy to an individual patient based on their predicted response to that therapy [1, 2]. Its application to perioperative medicine is novel and has much potential for growth. Pharmacogenomics (PGx) is the study of inherited differences in drug metabolism. It is a key component of personalized medicine as a better understanding of the association of an individual's genome and response to therapy may potentially improve outcomes [1, 2]. Over the last decade, several studies have demonstrated an association of genotype with efficacy of various medications applicable to the surgical setting [3–8]. Furthermore, in one recent study when PGx results were integrated into an Enhanced Recovery After Surgery (ERAS) pathway for abdominal surgery, there was an improvement in analgesia and decrease in opioid consumption [9].

Although perioperative PGx testing holds much promise, we have not yet been able to achieve successful implementation across our medical systems and into daily practice. In order to obtain more widespread adoption of perioperative personalized medicine, there needs to be: 1) more substantial evidence that perioperative outcomes improve with PGx; 2)

easy-to-access and -understand information technology interfaces that display the relevant PGx information for a patient; and 3) systems put into place that allow PGx to easily fit into regular clinical workflow.

The first point requires the healthcare researcher community to utilize PGx to create the evidence based from high-quality prospective studies. The second and third points will require adequate institutional informatics support and infrastructure. Several genes have already been implicated in perioperative medication metabolism [1]. Analysis and presentation of the results of individual mutations to these genes can theoretically be long and daunting. One option is to present a list of common perioperative medications that have some prevalence of genetic risk and classify each medication based on the estimated degree of metabolism that patient has for it (i.e. ultra-metabolizer, extensive metabolizer, slow metabolizer, etc) (Fig. 1).

Finally, to facilitate clinical adoption, PGx screening results should be transferred directly into electronic health record (EHR) systems and seamlessly integrated into the patients' anesthesia and postoperative record. Important components of a successfully integrated PGx program into an EHR include: 1) customized report generation unique to each health institution; 2) tailored data analytics; 3) data presentable for research studies; 4) easy-to-use provider-facing interface in the EHR explaining the key salient results (and recommendations) for a patient as well as a separate section with more granular detail; and 5) EHR-integrated real-time alerts warning providers regarding genetic risk to medications.

Ideally, the workflow of PGx screening should start in the surgeon's office or preoperative evaluation clinic, prior to the scheduled surgery. This will allow adequate time for results to become available on the day of the surgery. Upon reviewing the patient's EHR on the day of surgery, the healthcare providers could be alerted to potential genetic risks to specific

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	Ultrarapid Metabolizer	Extensive (normal) Metabolizer	Intermediate Metabolizer	Poor Metabolizer
OPIOIDS				
Morphine				
Fentanyl				
Hydromorphone				
Sufentanil				
Oxycodone				
Tramadol				
NON-OPIOID ANALGESIC				
Ketorolac				
Ibuprofen				
Naprosyn				
Acetaminophen				
Gabapentin				
Pregabalin				
SEDATIVES/ANXIOLYTICS/HYPNOTICS				
Propofol				
Etomidate				
Midazolam				
ANTI-EMETICS				
Ondansetron				
Prochlorperazine				
Droperidol				
Scopolamine				
Metoclopramide				
BETA-BLOCKERS				
Atenolol				
Propranolol				
Metoprolol				
MUSCLE RELAXANTS				
Succinylcholine				
Rocuronium				
Vecuronium				
Cisatracurium				

Fig. 1 Example display of the genetic risk summary to common perioperative medications for a single patient

drugs or drug classes, much like a medication or drug-to-drug interaction alerts. Furthermore, they should be able to easily view the list of genetic risks while simultaneously scanning the medical record for other clinical information. Clinical decision support tools may be integrated into the EHR as well, in which medication recommendations are created based on the patients' PGx profile. These data should be conveniently presented for perioperative providers, including anesthesiologists, nurses and surgeons in pre-, intra- and post-operative setting. Given promising data about ERAS and improved patient outcomes, integration into ERAS pathway protocols would further facilitate more widespread adoption [10, 11].

Personalized medicine holds great promise to improve perioperative outcomes. There is a plethora of possible data, including presence of many single nucleotide polymorphisms in various genes related to metabolism, that one may obtain from PGx screening of a single patient. It is, therefore, important that presentation of the results be well thought-out, strategic, useful, and well integrated into an EHR. PGx services should be adaptable and flexible when it comes to customizing these reports and should be able to work with the facility's

informatics department to ease integration of PGx into regular clinical workflows. The utilization of PGx to drive perioperative systems may ultimately lead to a decrease in adverse events and hospital length of stay following major surgery.

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