Defining the high-risk patient

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Abstract: As the volume of surgery continues to grow worldwide, the identification of high-risk patients is an important goal to guide clinical decision making in the perioperative period. Risk stratification evolved over the last decade from simple risk stratification tools, still used widely in the clinical arena to more sophisticated risk prediction models based on machine learning and latent class analysis, which can be incorporated into a well-developed electronic patient record or critical care clinical information system. As the debate about which patients will benefit most from critical care admission and interventions is still ongoing, the identification of the high-risk patient is a continuing challenge. In this review we will summarise the latest developments in the use of these risk stratification tools and risk prediction models, which can be utilised to identify the high-risk surgical candidate.

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Introduction

As the volume of surgery continues to grow worldwide, the identification of high-risk patients is an important goal to guide clinical decision making in the perioperative period. Recent advances in anaesthesia and surgical techniques have led to reduced morbidity and mortality in the developed world, with postoperative complications clustering in the "high-risk" patient group and those undergoing certain emergency surgeries (1). Early recognition of such patients can facilitate prehabilitation, tailored intra and postoperative management and may lead to better outcomes (2,3).

Risk stratification evolved over the last decade from simple risk stratification tools, still used widely in the clinical arena to more sophisticated risk prediction models based on machine learning and latent class analysis, which can be incorporated into a well-developed electronic patient record or critical care clinical information system. As the debate about which patients will benefit most from critical care admission and interventions is still ongoing, the identification of the high-risk patient is a continuing challenge. In this review we will summarise the latest developments in the use of these risk stratification tools and risk prediction models, which can be utilised to identify the high-risk surgical candidate.

Risk stratification tools

Due to the heterogenous nature of patient populations, post-operative mortality and morbidity is not evenly distributed. Thus, the development of individualised care to minimise adverse peri- and post-operative events is paramount. In an attempt to reduce these events much has been made to identify the high-risk individual prior to their surgery. Primitive methods to identify these groups relied much on clinical judgement, leading to a great amount of variability due to clinician experience and the nature of the surgery itself. Risk assessment tools employ fixed clinical variables to create a prognosis based on a score or modelling of these factors. Risk stratification tools have been further developed in recent years due to multiple quality improvement initiatives and national audits undertaken by the likes of the UK based National Emergency Laparotomy Audit and the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) to name but two, these have been undertaken in recognition of the high mortality associated with emergency laparotomy surgery (4,5). Risk stratification tools not only allow for more patient-centric care and rationalisation of critical care resources, but also lead to more informed decision making between clinicians, patients and relatives.

American Society of Anesthesiologists' Physical Status (ASA-PS) classification, Revised Cardiac Risk Index (RCRI) and American College of Surgeons' National Surgical Quality Improvement Program Risk Calculators (ACS-NSQIP), Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) and its modification P-POSSUM score are commonly used peri-operative scoring systems.

The American Society of Anesthesiologists Physical Status classification (ASA-PA) is a long-standing, simple scoring system, now employed as part of the WHO surgical check list. It is based on the patients physical status as determined by the clinicians assessment and assigns them to class I-VI. Due to this, there is wide subjectivity to the classification between clinicians, particularly between different specialties. Surgery type does not influence the ASA classification and so its utilisation in emergency or 'high-risk' procedures is limited, however in elective procedures, there is good correlation between higher ASA status and peri-operative outcomes and post-operative mortality (6,7).

The Revised Cardiac Risk Index (RCRI) is a predictor for peri-operative cardiac adverse events, or major adverse cardiovascular events (MACE), in patients undergoing non-cardiac surgery. It quantifies this risk through the presence or lack of, six major cardiovascular risk factors, including a history of diabetes mellitus requiring insulin, congestive cardiac failure, cerebrovascular disease, ischaemic heart disease, pre-operative renal disease and high-risk surgery. These factors are then combined to give a total score that in turn correlates to a percentage risk of undergoing a MACE. The RCRI is an easy to use, bedside test that correlates well with its intended outcomes. It does not, identify patients at high risk of developing non-cardiac post-operative complications. It's use, when combined with other scoring tools will enable an informed risk decision to be undertaken (8,9).

The ACS NSQIP Surgical Risk Calculator (SRC) is a clinical tool produced by the American College of Surgeons commonly used for evaluating postoperative risk after acute surgical care. It comprises 21 patient specific variable data points incorporating ASA status and procedure-specific estimations of post-operative risk. Reviews of outcomes compared with the ACS NSQIP risk calculator found it performed well at identifying serious risks, though there was large variability between all procedures. It should also be noted that this tool is validated only in the American population and requires internet access for its use, which for some, could prove prohibitive (10,11).

Further risk models have been developed and validated in risk-prediction for surgical patients. The P-Possum (Physiological and Operative Severity Score for the enUmeration of Morbidity and Mortality) risk calculator utilises individual patient specific data points and intra-operative findings to develop a post-operative outcome score. P-POSSUM is well validated internationally. Developed in 1998, it comprises 12 physiological variables and 6 surgical variables; these were identified by multivariate logistic regression and found to have the most significant predictive value for 30-day mortality and morbidity. It has been found to over-estimate mortality and morbidity in the low-risk and extremes of age (12,13).

The UK based National Emergency Laparotomy Audit group was developed to investigate and improve the significant variability in mortality risk between hospital Trusts treating high-risk emergency general surgery patients. They have utilised and extrapolated the P-POSSUM calculator by incorporating ASA, Creatinine and age as a continuous variable. More variables in NELA calculations have been changed to continuous so as to reflect smaller differences that will exist, compared with the P-POSSUM calculator. No direct studies have, as yet, compared the two risk predictor models, though NELA would appear to be designed and therefore more appropriate to use in emergency cases and P-POSSUM in elective procedures (14-16).

Risk prediction models focus on the individual risk, based on population derived variables. These tools can look attractive alternatives for the simpler risk-stratification scores, however they also have their own issues. Recently the use of advanced statistical methods such as latent class analysis and supervised machine learning produced interesting and potentially useful models to predict unfavourable outcome from baseline patient and care process factors. Latent class analysis (LCA) is a statistical modeling technique used to identify the groups of subjects that are similar with respect to a set of observed characteristics and represents a novel approach to assess the risk based on the entirety of a patient's comorbidities and risk factors. Kim *et al.* has recently shown variable discriminatory power of the nine latent classes to predict postoperative outcomes, both mortality and morbidity. They found that during their LCA analysis of 466,177 observations in patients undergoing intraabdominal surgery the risk classes stratified patients with regard to 30-day mortality, with a 133-fold difference in mortality between the lowest and highest risk classes, after adjusting for procedure. Similar wide discrimination was found for postoperative morbidity. In both occasions adding the simple and widely used ASA-PS score to the LCA model has significantly increased the predictive ability of the models. With conventional approaches to risk stratification, every patient is evaluated and classified into categories based on established criteria, such as age, sex etc. Contrary to this, LCA employs an empirical approach to identify groups of patients with similar characteristics without prior established constrains. The recognition of the patterns of comorbidities and risk factors in the LCA analysis enables categorising actual patients presenting for various surgical procedures.

A key advantage to the use of latent variable models is that they provide an effective way to reduce the dimensionality of data, that is, to reduce the complex interrelationships among many variables into a smaller number of factors. The attraction of this approach is that the patients are classified into clinically recognisable classes, based on the baseline variables. These approaches could be incorporated into a well-functioning Electronic Health Records (EHRs) and could be used in everyday decision making and informed consent of the patients (17,18).

The availability and functionality of EHRs is increasing and together with the rise of well defined—omics data (i.e., 'big data') could be exploited for risk prediction. Using these new tools requires researchers and clinicians to rethink risk modelling: for analysts, new statistical techniques may be needed; for clinicians, clinical decision tools may evolve beyond simple scoring algorithms to ones that require computational assistance through computer applications. Machine learning models are an attractive proposition to integrate multiple variables, each of which do not have a linear relationship with the outcome (mortality or postoperative complications) and many of which are codependent on each other. Unlike regression models, machine-learning models do not estimate an easily interpretable quantity that relates the predictor variables to the outcome. Since the relationship that machine-learning models fit is more complex than regression models, it is generally not straightforward to summarize the relationship into any single parameter. The machine learning algorithm also allows for evaluation of far more clinical variables than would be present in traditional modeling approaches, contributing to its superior performance. In addition, the model can be updated either in real-time or periodically as new data is acquired, reflecting a key component of the push toward a self-learning healthcare system (19). Recently a model has been introduced to the clinical workstream: Bihorac *et al.* developed and validated an algorithm called *MySurgeryRisk* in a large single-center cohort of surgical patients, using existing clinical data in electronic health records to predict the risk for major complications and death after surgery with high sensitivity and high specificity (20). This machine learning model will be deployed as a part of a prospective clinical trial embedded into the clinical workflow (21). The model is based entirely on routinely available data before surgery, may be applied to any surgical context and any type of surgery, offers exportability to other EHR systems, and the ability to handle any data type in EHR (such as semistructured data, missing or sparse data). The algorithm takes into account patient (such as deprivation status of patients' residence) and physician-specific characteristics (surgical performance metrics on similar population and complexity of procedure), provides consistency of interpretation (a machine makes the same prediction on a specific set of data every time), gives predictions with high sensitivity and specificity, and has the potential for near instantaneous reporting of results. In addition, because an algorithm produces a precise probability of the risk, the thresholds for high-risk group can be set at different operating points so that sensitivity and specificity can be tuned to match the requirements for specific clinical settings, such as high sensitivity for a screening setting.

As with any new development in risk prediction models, further external validation will be necessary to determine the feasibility of applying this algorithm in a real-time clinical setting outside of the US healthcare system (22).

Functional testing

Risk models and stratifications, patient examination and static tests can be utilised to give an overall indicator of a patients peri-operative risk. Functional testing looks at the patients ability to meet the increased metabolic demand needed when surgery is undertaken. A patient needs to be able to perform >4 METS (One metabolic equivalent (MET) represents the oxygen consumption of an adult at rest ~3.5 mL/kg/min) or at least climb a flight of stairs to consider undertaking major surgery. Patients often give inaccurate estimations of their functional capacity, therefore cardiopulmonary exercise testing (CPET) can be undertaken to gain a reliable and validated functional capacity assessment (23). It is important to note that there are contraindications to undertaking CPET testing and patient consent needs to be thoroughly gained prior to undertaking a test.

Two clinicians, safety and resuscitative equipment are present at all times for CPET assessments. A static cycle is connected to an ECG, pulse oximeter and gas analyser for breath-by-breath measurement of oxygen consumption (VO_2) and carbon dioxide production (VCO_2). Baseline measurements are taken with no load on the bicycle and the patient coached into maintaining 50–60 revolutions per minute. Load or resistance is then sequentially added with the aim of reaching a true exercise limit.

The anaerobic threshold (AT) is an indicator of the efficiency of the lungs, heart and circulatory system. The VO_2 or oxygen consumption and VCO_2, carbon dioxide production, are continuously measured along with the Respiratory Exchange Ratio (RER). As exercise progresses, oxygen demand will increase. During some point of exercise anaerobic production of ATP will begin, resulting in the by product of lactic acid and ultimately increased CO_2 production. The VO_2 measurement at the point of this increase in VCO_2 is known as the anaerobic threshold. This can be derived graphically through examination of the curves of the VO_2, VCO_2 and the point at which the RER increases above 1.

Many subjects can continue to exercise past the point of AT with encouragement, however AT itself will not be affected and so this provides an excellent patient-specific piece of data to assess functional capacity. An AT of <11 mL/kg/min benefit from postoperative critical care, or indeed, a delay in surgery and prehabilitation to try to improve their AT results.

The Perioperative Exercise Testing and Training Society (POETTS) have recently produced guidelines recommending the standardisation of CPET testing and interpretation of results due to an increase in institutions using this as part of their pre-operative assessment and risk assessment (24-26).

Conclusions

Risk stratification for the surgical patient has improved recently, both based on physiological data derived from functional testing and new mathematical models. With the advent of electronic health records there are multiple studies aimed at developing and validating risk stratification tools, based on various patient subgroups. There are many recommendations to use risk stratification tools in a day-to-day practice. Crucially, there is lack of evidence to suggest this approach has significant effects on clinician behavior, patient outcome, and resource utilization. Randomized, controlled trials to evaluate impact of both functional testing and epidemiology based mathematical approaches are required for further validation of existing models across multiple healthcare systems. Collaboration between multiple specialties including surgeons, anaesthetists, perioperative care providers, critical care physicians and basic scientists should help us to define the high-risk surgical patient in the 21st century.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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