CURRENT OPINION

How to better identify patients at high risk of postoperative complications?

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Purpose of review
Preoperative risk assessment and perioperative factors may help identify patients at increased risk of postoperative complications and allow postoperative management strategies that improve patient outcomes. This review summarizes historical and more recent scoring systems for predicting patients with increased morbidity and mortality in the postoperative period.

Recent findings
Most prediction scores predict postoperative mortality with, at best, moderate accuracy. Scores that incorporate surgery-specific and intraoperative covariates may improve the accuracy of traditional scores. Traditional risk factors including increased ASA physical status score, emergent surgery, intraoperative blood loss and hemodynamic instability are consistently associated with increased mortality using most scoring systems.

Summary
Preoperative clinical risk indices and risk calculators estimate surgical risk with moderate accuracy. Surgery-specific risk calculators are helpful in identifying patients at increased risk of 30-day mortality. Particular attention should be paid to intraoperative hemodynamic instability, blood loss, extent of surgical excision and volume of resection.

Keywords
morbidity, mortality, postoperative complications, prediction scores, preoperative risk

INTRODUCTION

Approximately 1 million procedures are performed under anesthesia in the United States each year [1▪▪]. As overall life expectancy continues to increase and technological advances in medical interventions evolve, there is a willingness to offer more complex procedures to patients of advanced age, frailty and comorbidities with inevitable increases in morbidity and mortality. Of the 2 866 141 cases analyzed between 1 January 2010 and 31 May 2014 from the National Anesthesia Clinical Outcomes Registry (NACOR), over 1.7 million were under general anesthesia and almost 0.5 million were under monitored anesthesia care. Nine hundred and forty-four deaths (within 48 h of anesthesia) occurred, giving a crude mortality rate of 33 per 100 000. Factors found to be independently associated with higher perioperative mortality were increasing American Society of Anesthesiologists (ASA) physical status, emergency case status, cases beginning between 4.00 p.m. and 6.59 a.m., and patient age less than 1 year or greater than 64 years. The most common complications reported in patients who died included airway complications (1.7%), resuscitation (2.8%), respiratory complications (8.1%), and hemodynamic instability (35.0%) [1▪▪].

CURRENT PREDICTION TOOLS

Although the ASA physical status score has been shown to predict perioperative morbidity and mortality [2], criticisms of the score include that it is based on baseline risk factors, has limited inter-rater reliability [3] and does not include perioperative factors [4]. Many attempts have been made to

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KEY POINTS

- Most complication prediction scores have at best, moderate accuracy in predicting postoperative complications.
- The Clavien–Dindo classification provides objective clinical grading of postoperative complications, whereas the Comprehensive Complication Index is designed to include patient-centered reporting of complications.
- Increased ASA physical status score, emergent surgery and nonday time operative hours are associated with increased mortality.
- Particular attention should be paid to intraoperative hemodynamic instability, blood loss, extent of surgical excision and volume of resection in prioritizing admission to higher levels of postoperative care.
- More head-to-head comparisons of clinically orientated outcome score with administrative databases should be preformed in surgical subpopulations to enhance our understanding.
- The use of artificial intelligence and machine learning to track patient's perioperative trajectory is an area of ongoing research.

improve on the ASA score using a combination of baseline risk and perioperative risks including patient-specific and surgery-specific variables (Table 1). In 1991, the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM) was proposed and has undergone many modifications over the years [5]. More recent prediction scores include the Risk Stratification Index (RSI) [6], the Risk Quantification Index (RQI) [4], Present-On-Admission Risk (POARisk) score [7] and the Surgical Apgar Score (SAS) [8]. A surrogate of patient preoperative comorbidities quoted in more recent literature is the modified Frailty Index (mFI) [12▪]. This article will discuss the validation of these scores in surgical patients and in specific subpopulations.

The RSI, developed from 35 million Medicare hospitalizations from 2001 to 2006, was constructed using diagnosis and procedure codes associated with each stay [6]. It did not distinguish POA diagnoses from hospital-acquired diagnoses. The POARisk score, published by the same authors assessed POA diagnoses. POARisk is a risk-adjustment model for in-hospital mortality based on preexisting diagnoses, principal procedures, previous procedures, patient age and sex [7]. More recently, the SAS, a 10-point score to rate surgical outcomes, is

Table 1. Postoperative complications prediction scores

Score	Population	Country	Components	Postoperative complication	Predictive performance
POSSUM (Copeland *et al.* [5])	$n=1372$	UK	*Physiological Score* (12 covariates) + *Surgical Severity Score* (5 covariates)	6-week mortality	Sensitivity 52.1% Specificity 92.4%
RSI (*Sessler et al.* [6])	*n = 103324*	USA	Age, sex, race 10 diagnosis codes, 6 procedure codes	30-day mortality	C-statistic 0.84
RQI (Dalton *et al.* [4])	$n=635265$	USA	Age, Sex, ASA score, Procedural Severity Score	30-day mortality	C-statistic 0.915
POARISK (Dalton *et al.* [7])	$n=12.7$ million	USA	Diagnosis present on admission, sex, age, procedure	30-day mortality	C-statistic 0.958
SAS (Gawande *et al.* 2007) [8]	$n=869$	USA	Intraoperative bradycardia, hypotension, blood loss in 102 colectomy patients and 767 vascular patients	30-day morbidity/mortality	C-statistic 0.720
Euroscore II (Nashef *et al.* [9])	$n=22831$	Europe	Cardiac patients across 154 hospitals in 43 countries	Hospital mortality	AUROC = 0.8095
E-PASS (Haga *et al.* [10])	$n=989$	Japan	Elective surgery, PRS + SSS, CRS	Postoperative complications grades 1 – 4 (death)	Spearman's rank correlation test for CRS; $\rho=0.564$
ACS-NSQIP (DeLuzio *et al.* 2016) [11]	$n=8190$	USA	Patients undergoing anatomical lung resection	Prolonged length of stay of more than 14 days	C - statistic = 0.926

ACS-NSQIP, The American College of Surgeons National Surgical Quality Improvement Program; AUROC, area under receiver operative curve; CRS, Comprehensive Risk Score; E-PASS, Estimation of Physiological Ability and Surgical Stress; POARISK, Present On Admission Risk; POSSUM, Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity; PRS, Perioperative Risk Score; RQI, Risk Quantification Index; RSI, Risk Stratification Index; SAS, Surgical Apgar Score; SSS, Surgical Stress Score.

calculated from the estimated blood loss (EBL), heart rate (HR), and mean arterial pressure (MAP) during an operation [8]. Head-to-head comparison of these scores in a single center cohort of 44 835 using bootstrap sampling, showed that RQI outperformed SAS in predicting 30-day mortality [area under receiver operative curve (AUROC) of 0.842 and 0.64, respectively]. The addition of SAS to RQI increased discrimination to 0.853. POARisk also outperformed SAS (AUROC of 0.8608 and 0.63, respectively). Again, the addition of the SAS to the POARisk model only slightly increased model discrimination (AUROC 0.8645) [13▪▪].

LIMITATIONS OF PREDICTION SCORES

A major difficulty in predicting postoperative complications is defining what constitutes a surgical complication and, ergo, perioperative morbidity. A frequently cited classification system of surgical complications, the Clavien–Dindo classification grades complications as I–V [14]. Grades I and II rarely require intervention from the critical care team. Grade III is defined as requiring surgical, endoscopic or radiological intervention, grade IV as life-threatening complications requiring ICU management and grade V as death. Recently, the Comprehensive Complication Index (CCI) has been proposed. The CCI was constructed from a questionnaire of 227 patients and 245 physicians rating the severity of 30 individual complications and scored on a continuous scale of 0–100 [15].

Even if these prediction scores are valid for comparing performance across health systems and trends over time, their transferability to an ‘operating room near you’ is questionable and invokes the problem of ecological fallacy. The pitfall in using any of these scores comes from the fact that they are modeled using heterogeneous populations and as such have less discriminative value in surgical subpopulations [13▪▪]. For this reason, the remainder of this article will focus on risk prediction scores in high-risk surgical subpopulations (Table 2).

CARDIAC SURGERY

Over one million patients undergo cardiac surgery across Europe and the United States each year [21]. There are three established multivariate models used to predict perioperative mortality in the setting of cardiac surgery, the Society of Thoracic Surgeons (STS) score, the Euroscore and the Age, Creatinine, and Ejection Fraction (ACEF) score [16▪]. The STS Risk Calculator estimates a patient’s risk of mortality and other morbidities, such as long length of stay and renal failure from a large self-reporting database (www.riskcalc.sts.org). The Euroscore was developed using prospective risk and outcome data on 22 381 consecutive patients undergoing major cardiac surgery in 154 hospitals in 43 countries over a 12-week period in 2010 [9]. Risk factors for 30-day mortality were NYHA Class III/IV, insulin-dependent diabetes mellitus, increasing age, female sex, extra-cardiac arteriopathy, redo surgery, renal dysfunction, more than moderately poor or worse left ventricular function, pulmonary artery systolic pressure greater than 55 mmHg, urgent/emergent case indication and thoracic aortic surgery. Limitations of the Euroscore II include only 21 (0.093%) of patients were over 90 years of age.

Table 2. Perioperative risk factors for postoperative mortality by surgical subpopulation

Surgical population	Risk factors for perioperative mortality
Cardiac	NYHA III/IV, Insulin-dependent diabetes mellitus, increasing age, female sex, extra-cardiac arteriopathy, redo surgery, renal dysfunction, more than moderately poor left ventricle function, pulmonary artery systolic pressure greater than 55 mmHg, urgent/emergent case indication and thoracic aortic surgery [9,16▪]
TAVR	Increasing age, hemodialysis, NYHA IV, severe chronic lung disease and nonfemoral access site [17▪]
Thoracic	Preoperative risks: severe heart disease, severe pulmonary disease, diabetes mellitus, increased ASA score, poorer performance status index
	Perioperative risks: blood loss/body weight, operation time, extent of skin incision
Hepatobiliary	Preoperative risk: increasing ASA score, smoking status, raised alkaline phosphatase, low albumin and raised activated partial thromboplastin time
	Perioperative risks: extent of hepatectomy, prolonged operative time and transfusion requirements [19]
Liver Transplant	Older age, the presence of NASH, pretransplant diabetes, hypertension, chronic obstructive pulmonary disease preoperative hospitalization, mechanical ventilation, MELD, presence of portal vein thrombosis and cold ischemia time [19]
Vascular	Age 70 years or older, atrial fibrillation, congestive cardiac failure, cigarette smoking, chronic renal failure [20]

ASA, American Society of Anesthesiologist; MELD, Model for End-Stage Liver Disease; NASH, nonalcoholic steatohepatitis; NYHA, New York Heart Association; TAVR, transcatheter aortic valve replacement.

A large meta-analysis, examining 22 eligible studies and 33 comparison groups showed that the Euroscore II and the STS performed similarly (summary AUC difference of 0.0) and out performed ACEF score (summary differences in AUC of 0.10 and 0.08, respectively, $P < 0.05$) in predicting 30-day mortality and in-hospital mortality [16▪]. Recently, a two-stage classification strategy has been proposed. Firstly, a EuroSCORE II/ACEF score was used to predict a mortality risk higher than 25%. Secondly, a high-risk group with pulmonary hypertension, serum creatinine, and anemia was superior to Euroscore II/ACEF score alone for predicting mortality [22▪]. With respect to transcatheter aortic valve replacement (TAVR), risk factors for in-hospital mortality included increasing age, hemodialysis, NYHA Class IV, severe chronic lung disease, and nonfemoral access site [17▪].

THORACIC SURGERY

Thoracic surgeries including lung resection and esophagectomy carry with them high risk of postoperative complications. Knowledge of the underlying pathology and area of the mediastinum being operated upon allows swifter diagnosis of potential complications. Traditionally, perioperative predictors including high ASA score, low serum albumin concentrations, history of smoking, and prolonged operative time have been shown to increase the likelihood of postoperative pneumonia [23].

In 1999, the Estimation of Physiological Ability and Surgical Stress (E-PASS) score was derived in a Japanese cohort receiving gastrointestinal surgery. The derivation model was constructed from 292 patients in a Japanese teaching hospital who underwent a spectrum of elective thoracic gastrointestinal surgeries. The score was then validated in 989 consecutive patients who underwent similar surgeries in another Japanese teaching hospital. E-PASS comprises the preoperative risk score (PRS), the surgical stress score (SSS), and the comprehensive risk score (CRS). Six preoperative factors were found to be significantly associated with postoperative mortality, namely severe heart disease, severe pulmonary disease, diabetes mellitus, increased ASA score, and poorer performance status index.

Three surgical factors found to significantly increase morbidity were blood loss/body weight, operation time, and extent of skin incision. A marked step up in morbidity rates was observed with a CRS of more than 1.0, reaching 86.7% and conferred a more than 20% mortality rate. Since its incarnation, the E-PASS has been shown to predict mortality and morbidity in other surgical populations, [24–30]. Despite this, its practical application to individual cases is questionable. For example, the PRS must be calculated using the regression equation; $\text{PRS} = -0.0686 + 0.00345X1 + 0.323X2 + 0.205X3 + 0.153X4 + 0.148X5 + 0.0666X6$ [$X1$, age; $X2$, presence (1) or absence (0) of severe heart disease; $X3$, presence (1) or absence (0) of severe pulmonary disease; $X4$, presence (1) or absence (0) of diabetes mellitus; $X5$, performance status index (0–4); $X6$, American Society of Anesthesiologists physiological status classification 1-5 [10].

Specific to anatomical lung resection, a model for predicting prolonged postoperative length of stay was developed using 8190 thoracic cases from The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database [11]. Amongst the preoperative variables examined, age more than 70 years, dependent functional status, chronic obstructive airways disease (COPD), serum sodium lower than 135 mmol/l and ASA classification of 3 or greater were significant predictors of prolonged hospital stay. Amongst these, age more than 70 had the lowest odds of morbidity (OR 1.46; 1.18–1.81) and ASA IV and V had the highest odds (OR 2.17; 1.58–2.60). Open thoracotomy was the only intraoperative variable associated with prolonged stay. There was no significant difference in event rates between those who received a lobectomy compared to a pneumonectomy [11].

The SAS was studied in 212 patients post esophagectomy from 2005 to 2014 at Thomas Jefferson University Hospital, Philadelphia, Pennsylvania, USA [30]. Over 50% of patients had minimally invasive esophagectomies (MIE) and 20% had open thoracotomy. Approximately 36% of patients developed respiratory failure or an anastomotic leak, 22% developed an arrhythmia, 9% had pneumonia, and 7% developed sepsis. The mortality rate was 5%. With each one category increase in SAS, there was a significant decrease in Clavien–Dindo classification and mortality, independent of age or type of surgery. A higher SAS was associated with shorter LOS ($P < 0.0001$) [30].

VASCULAR SURGERY

Extra-cardiac vascular surgery is categorized as high-risk surgery by most risk stratifications scores with 30-day mortality from elective procedures as high as 5% [31]. The discriminatory value of several risk stratification scores has been assessed for major vascular surgery, namely open abdominal artery aneurysm repair. Examples of such scores include E-PASS [32], Vascular physiology only Physiological and Operative Severity Score for enUmeration of Mortality (V-POSSUM) [33], the Glasgow Aneurysm Score (GAS) [34], the Revised Cardiac Risk Index

(RCRI) [31] and the Vascular Biochemical and Haematological Outcome Model (VBHOM) [35]. Head-to-head comparison of these scores in 106 open abdominal aneurysm repairs with all-cause mortality and major adverse cardiac events (MACE) as the primary end points, concluded that GAS, VBOM and RCRI performed poorly in predicting outcome. Of the five scores V-POSSUM and E-PASS had only moderate accuracy at predicting MACE (AUC: 0.681 and 0.682, respectively) and all-cause mortality (AUC: 0.780 and 0.703, respectively) [36].

Increasingly, the mFI is being assessed as a surrogate for predicting postoperative complication. The mFI is a 11-point scale consisting of major systemic comorbidities and functional status [37]. In a retrospective review of 379 patients post lower limb amputation, only 2 of 11 variables, COPD and impaired sensorium were significant predictors of 30-day mortality suggesting that the use of mFI in this setting is limited [12▪]. In the carotid entartectomy population, multivariate logistic regression of 120 633 patients derived from the Nationwide Inpatient Sample, age 70 years or older, atrial fibrillation, congestive cardiac failure, cigarette smoking and chronic renal failure were all significantly associated with increased odds of stroke, cardiac complications or in-hospital death [20].

HEPATOBILIARY SURGERY

Hepatobiliary resection, in its many guises, remains a moderate-to-high risk procedure with morbidity and mortality rates for major hepatectomies worldwide at 15 and 1%, respectively [38,39]. Of the 2313 hepatectomies identified in the NSQIP database from 2005 to 2007, the overall 30-day mortality rate was 2.5% and the 30-day major morbidity rate was 19.6%. Multivariate analysis identified five independent preoperative risk factors; increased ASA score, smoking status, raised alkaline phosphatase, low albumin, and raised activated partial thromboplastin time. Perioperative factors, not surprisingly include, extent of hepatectomy, prolonged operative time, and transfusion requirements [18]. E-PASS was examined in a Dutch population of 156 resections of perihepatic cholangiocarcinomas. Liver failure was the most common cause of death. Preoperative cholangitis was associated with increased odds of 30-day mortality. Liver remnant volume below 30% was significantly associated with either sepsis or liver failure-related death (odds ratio, 3.18; 95% CI, 1.15–8.80; $P = 0.03$) [27].

With lower mortality rates over time, major hepatectomies are being combined with pancreatoduodenal resection. A systematic review of combined resections ($n = 289$) revealed a mortality of 3% and a morbidity rate ranging from 26 to 63% [40]. Patients more than 80 years of age have approximately double the risk of 30-day postoperative mortality and 50% increased rate of complications [41]. More specific to liver transplantation, in the largest study to date, 54 697 liver transplant recipients in the Organ Procurement and Transplant Network (OPTN) database from February 2002 to December 2012, the 30-day mortality was 2.9%. Cardiovascular mortality was the leading cause of death (40.2%). The leading underlying cause of early CVD mortality was cardiac arrest (47.9%), and this was followed by stroke (12.5%), heart failure (12.3%), and pulmonary embolism (9.1%). Older age, the presence of NASH, pretransplant diabetes, hypertension, and chronic obstructive pulmonary disease were all more prevalent in recipients with perioperative CVD mortality versus those without early CVD mortality ($P < 0.05$ for all). Other causes of death in the first 30 days were infection (27.9%) and graft failure (12.2%). Covariates significantly associated with all-cause 30-day mortality were age, preoperative hospitalization, mechanical ventilation, MELD, presence of portal vein thrombosis, and cold ischemia time. Of note, the model showed only moderate discrimination (C-statistic 50.66, 95% confidence interval, 50.63–0.68) [19].

ORTHOPEDIC/SPINAL SURGERY

The spinal Risk Assessment Tool (RAT) incorporates procedures, patient and diagnosis elements to predict the likelihood of complications in patients undergoing major spinal procedures. It was developed from 279 145 spinal cases in the United States from 2006 to 2010 [42]. The RAT generates a risk score for adverse events including cardiac, pulmonic, wound infection, and thrombotic, within 30 postoperative days of spine surgery based on nine preoperative factors: age, sex, diagnosis, comorbidity burden, surgical approach, bone morphogenetic protein (BMP) use, fusion status, number of spinal levels operated on, and instrumentation use. In a head-to-head comparison, RAT was equivocal to ACS NSQIP calculator in predicting 30-day morbidity (AUC 0.670 [95% CI, 0.60–0.74] in RAT, 0.669 [95% CI, 0.60–0.74] in NSQIP) [43]. Odds for independent risk factors were not quoted.

E-PASS has been studied in spinal, hip fracture, and all inclusive orthopedic patients [29,45]. In a cohort of 1883 who underwent various inpatient orthopedic procedures for joints, tumors, trauma, and spine, E-PASS predicted nonsurgical site and overall postoperative complications (AUC: 0.794 and 0.777 respectively) [44]. Female sex was associated with higher overall and nonsurgical site complications. Increasing age was associated with higher nonsurgical site complications.

DISCUSSION

Prediction of postoperative complications is difficult. Most prediction scores are constructed from administrative database and scores modeled using heterogeneous populations have less discriminative value in surgical subpopulations [13■■]. Moreover, poor concordance between the predictive accuracy of clinical registries and administrative databases has been shown [45]. From a biostatistical perspective, global prediction models provide at best moderate discriminatory value with most studies reporting a 'C-(concordance) statistic' (Table 1). Subspecialty prediction models often report the area under the receiver operator curve that arguable provide more information. Currently, the Achilles' heel of much of critical care research is heterogeneity and identifying which intervention/predictions tools work best in a predefined cohort. Future research in this area will ultimately require calibration as before, but prospective validation comparing predicted outcomes and actual individual events will be required to overcome the problem of ecological fallacy. Furthermore, subsequent validation, again prospectively will need to be performed across different geo-political sectors to test the external validity of these scores. The ultimate goal of any prediction tool should allow the patient and caring clinicians to preemptively discuss management options, rescue strategies, and end-of-life decisions in an informed manner.

Moving forward, we may see a switch from using predictive scores based on retrospective data to artificial intelligence and machine learning to track a patient's perioperative course based on expected norms and the capability of triggering the clinician's attention to preempt a potential complication. The concepts of 'Big Data', 'Machine-Learning' and 'Visual Analytics' are gaining considerable ground at institutional level [46]. An example of this technology is T3Monitor (Tracking, Trajectory and Triggering; Boston, Massachussets, USA) software that is currently being used in two major pediatric centers in North America. Large anesthesiology-specific databases such as the Multicenter Perioperative Outcomes Group (MPOG; www.mpogresearch.org) , the Anesthesia Quality Institute's (AQI) and National Anesthesia Clinical Outcomes Registry (NACOR; www.aqihq.org) and the Society for Ambulatory Anesthesia database (www.sambahq.org/scor) may provide a fertile ground to roll out large tracking and triggering software to alert us to the potential decline in our patient's perioperative status.

CONCLUSION

Despite only having, at best, moderate discriminatory value, independent risk factors for worse outcomes include increasing age, frailty, poor cardiorespiratory reserve, and chronic renal failure. Intraoperative parameters to include blood loss, hypotension, and bradycardia should heighten our awareness of potential complications in the postoperative course. Surgery-specific parameters to include extent of incision, urgent/emergent indication, and volume of resection may help guide a patient's postoperative course to an environment with a higher level of monitored care. As with many aspects of life, tacit knowledge, and predictability comes with experience in one's chosen subspecialty.

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Conflicts of interest

There are no conflicts of interest.

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■ of special interest
■■ of outstanding interest

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