Who is a high-risk surgical patient?

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Purpose of review
Timely identification of high-risk surgical candidates facilitate surgical decision-making and allows appropriate tailoring of perioperative management strategies. This review aims to summarize the recent advances in perioperative risk stratification.

Recent findings
Use of indices which include various combinations of preoperative and postoperative variables remain the most commonly used risk-stratification strategy. Incorporation of biomarkers (troponin and natriuretic peptides), comprehensive objective assessment of functional capacity, and frailty into the current framework enhance perioperative risk estimation. Intraoperative hemodynamic parameters can provide further signals towards identifying patients at risk of adverse postoperative outcomes. Implementation of machine-learning algorithms is showing promising results in real-time forecasting of perioperative outcomes.

Summary
Perioperative risk estimation is multidimensional including validated indices, biomarkers, functional capacity estimation, and intraoperative hemodynamics. Identification and implementation of targeted strategies which mitigate predicted risk remains a greater challenge.

Keywords
high risk, perioperative, postoperative complications, risk estimation, risk indices, risk stratification, surgical

INTRODUCTION

Surgical volume continues to grow globally. An estimated 321.5 million surgical procedures were required to address the needs of the global population in 2010, and this number is expected to increase further with the growth in population worldwide [1]. Advances in anesthetic care have led to significant reduction in perioperative mortality and morbidity in the developed world, despite an increase in baseline risk of patients presenting for surgical procedures [2]. At present, perioperative morbidity and mortality remains largely clustered in a subgroup of high-risk patients [3], which makes prospective recognition of such patients crucial. Early recognition of high-risk patients facilitates surgical decision-making, preoperative optimization, and tailored intraoperative and postoperative management, which can potentially improve outcomes [4,5]. Perioperative risk stratification is complex and depends on interactions between surgical, anesthetic, and patient specific factors [6▪]. In this review, we discuss the various risk-stratification tools which could be utilized to identify surgical candidates at high risk of adverse perioperative outcomes.

RISK-STRATIFICATION TOOLS USING PREOPERATIVE DATA

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) are the most commonly used preoperative scoring systems.

ASA-PS classification is the simplest scoring system and has been in use for over 70 years. It assigns patients a class I–VI with a modifier based on the emergent nature of surgeries. Class assignment is independent of the surgical procedure and is based solely on subjective assessment of a patients' overall health status. This subjectivity leads to inter-rater reliability ranging from fair [7] to moderate [8] at

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KEY POINTS

- Timely identification of high-risk surgical candidates is a key step in mitigating perioperative morbidity and mortality.
- Commonly used indices (ASA PS, RCRI, ACS NSQIP, sAs, and P-POSSUM) complement each other to provide comprehensive perioperative risk assessment.
- Biomarkers (natriuretic peptide and troponin) measured both preoperatively and postoperatively can further enhance estimation of adverse cardiovascular events.
- Subjective assessment of functional capacity has poor sensitivity; instead practitioners should rely on objective measurements (e.g. DASI and CPET) to quantify functional status.
- Identification of effective strategies which reduce adverse outcomes and their successful integration within the perioperative risk estimation framework remains a greater challenge.

best among anesthesia practitioners. Inter-rater reliability is even poorer when compared across different departments within the same institution [9▪]. Despite its limitations, ASA-PS has been shown to have independent associations with postoperative morbidity, mortality [10,11], readmissions [12▪], and postoperative resource utilization [13]. Utility of ASA-PS in predicting postoperative mortality is, however, diminished in higher-risk settings where operative risk likely predominates and addition of a surgical risk modifier has been suggested to enhance its utility in these scenarios [14]. The inherent simplicity of this scoring system lends itself to be a valuable tool, specifically in resource-limited settings.

The RCRI was designed to predict major adverse cardiovascular events (MACE) following noncardiac surgeries [15]. It consists of six independent predictors: high-risk surgery, history of ischemic heart disease, congestive heart failure, cerebrovascular disease, preoperative treatment with insulin, and preoperative serum creatinine above 2 mg/dl. Although the RCRI discriminates moderately well between patients at high and low risk of MACE following noncardiac surgeries, it performs poorly when predicting cardiac events following vascular surgeries or all-cause mortality following noncardiac surgeries [16]. Because RCRI limits itself to predicting MACE, this precludes accurate estimation of overall perioperative morbidity and mortality.

The ACS-NSQIP universal risk calculator was developed using data from 393 hospitals that report to NSQIP [5]. It consists of 21 patient-specific variables including ASA-PS, patient-reported functional capacity, and over 1500 current procedural terminology (CPT) codes that allow procedure-specific estimation of postoperative risk. The inclusion of CPT codes allows detailed procedure-specific modifiers within the risk-estimation model, thereby facilitating informed decision-making during the preoperative phase. This calculator serves not only as a convenient one-stop shop for comprehensive postoperative risk assessment but also includes patient-centered outcome measures such as readmission rates and nonhome discharge [17▪]. Recent American College of Cardiology and American Heart Association guidelines for perioperative cardiovascular evaluation and management for noncardiac surgeries also consider ACS-NSQIP calculators to provide the best estimates of surgery-specific risk of MACE or death [18], although it must be borne in mind that the NSQIP database does not capture important cardiovascular complications like pulmonary edema or complete heart block. Hence, RCRI and ACS-NSQIP should be considered complementary while assessing postoperative cardiovascular risk [19]. Although ACS-NSQIP risk calculator is freely available on the web (https://riskcalculator.facs.org/RiskCalculator/), the requirement of internet connectivity limits its utility in resource-limited settings. The fact that this calculator has not been validated outside the United States does further limit the generalizability of the estimates to non-US centers.

RISK-STRATIFICATION TOOLS USING INTRAOPERATIVE AND POSTOPERATIVE DATA

Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) and its modification P-POSSUM score incorporate 12 preoperative variables and 6 variables at discharge to estimate postoperative morbidity and mortality [20▪]. Although the P-POSSUM overestimates mortality and morbidity in the low-risk patients and at extremes of age death it has been shown to have moderate to high discriminant accuracy and has been validated across three continents [4]. Surgical Apgar Score (sAs) is a 10-point score including intraoperative hemodynamic variables has been validated to discriminate between patients with high and low risk of major complications and death within 30 days of colorectal/general and vascular surgeries [21,22]. Combining the ASA-PS to continuous intraoperative sAs increases the discriminative ability of either ASA-PS or sAs to predict major 30-day postoperative complications. If further developed, this could facilitate real-time risk assessment for patients undergoing surgeries potentially providing actionable data to mitigate risky perioperative states [23].

FUNCTIONAL CAPACITY

Assessment of functional capacity is an important part of perioperative risk assessment [18,19]. Poor functional capacity has been shown to correlate with higher risk of adverse perioperative outcomes in various groups of surgical patients [24–28]. International societies recommend a cut-off below 4 metabolic equivalents (METs) to guide preoperative testing for intermediate to high-risk surgeries [18]. Assessment of functional status can be either subjective or objective. Most commonly, patients are asked to self-report their functional status as part of their preoperative assessment. Subjective assessment of functional capacity has been shown to have poor sensitivity [19.2%, 95% confidence interval (CI) 14·2–25)] in detecting patients who have a functional capacity below 4 METs and often fails to predict major adverse cardiovascular events and is therefore not recommended for preoperative cardiac risk assessment [29▪▪]. Use of objective measures such as the Duke Activity Status Index (DASI) questionnaire, serum N-terminal pro-B-type natriuretic peptide (NT pro-BNP) (detailed below) is preferred over subjective assessment [29▪▪].

Cardiopulmonary exercise testing (CPET) is generally considered the gold standard for assessing functional capacity. Over the course of the last couple of decades, the use of CPET to evaluate the risk of adverse perioperative events in selected high-risk patients has increased significantly in the United Kingdom. Successful integration of this technique into the perioperative workflow is costly and requires the establishment of a structured framework [30▪]. An anaerobic threshold of less than 10 ml O_2/kg/min is commonly recognized to be predictive of perioperative cardiovascular complications, postoperative death, and midterm or late death following major surgeries [18], although choice of this metric to predict adverse cardiovascular events is being challenged [29▪▪]. Overall CPET results have been shown to have various degrees of associations with postoperative mortality [31–33], but there have been no studies which have demonstrated that CPET testing allows enhanced risk stratification over clinical evaluation [34▪▪]. International societies offer different perspectives on the utility of preoperative CPET. While the ACC AHA guidelines suggest CPET in patients undergoing high-risk procedures in patients with unknown functional capacity (class IIb), the Canadian Cardiovascular Society recommend against performing CPET for enhancing cardiac risk estimation (Strong recommendation; Low Quality of Evidence) [18,34▪▪].

FRAILTY

Frailty is defined as a clinically recognizable state of vulnerability arising from age-associated decline in physiological reserve. Assessment of frailty can complement perioperative risk assessment by capturing functional domains which are missed by traditional risk assessment tools [35]. Frailty is being increasingly recognized to be a prognostic indicator of postoperative outcomes and discharge destination [36,37▪▪,38▪,39▪,40,41]. Prognostic value added by frailty assessment can not only lead to effective shared decision-making among patients, family members, and medical teams, but could also limit futile interventions [42]. The common frailty scales used in the perioperative scenario include: Fried frailty phenotype, Rockwood – Canadian Study of Health and Aging – Frailty Index (CSHA – FI), Comprehensive Assessment of Frailty (CAF), Clinical Frailty Scale (CFS), and modified Frailty Index (mFI). At present, there is no gold standard for assessment of frailty [35]. Preoperative and postoperative measures to minimize frailty remain an area of active research.

BIOMARKERS

Biomarkers have emerged as valuable adjuncts to existing risk stratification tools. Natriuretic peptides [B-type natriuretic peptide (BNP), N-terminal pro-BNP) and troponins have shown the most promise in detecting patients at risk of adverse cardiovascular events and postoperative mortality. There is a growing body of evidence which suggests that measurement of natriuretic peptide and troponins substantially enhances risk stratification in both preoperative and postoperative period in a mixed cohort of patients undergoing noncardiac surgeries [43–48]. Preoperative assessment of biomarkers could serve as an effective triaging modality. These tests are noninvasive, accurate, easy to obtain, cheaper-than-conventional workup (stress test/medicine consultation), and could be used to decide which patients might benefit from further specialist workup [49]. Asymptomatic elevations of perioperative troponins, which do not otherwise fulfil universal definition of myocardial infarction (MI), but indicate myocardial injury, have been shown to be associated with increased short (30-day) and intermediate (1-year)-term mortality [50▪▪,51▪▪,52]. In fact, most postoperative MIs are 'silent' and therefore go unnoticed in the absence of surveillance

[47,53▪▪]. Prognosis of postoperative MIs, however, is equally poor, irrespective of symptomatology. Taken in the context of over 10 million cardiac complications which occur annually within 30 days of noncardiac surgeries, this represents a major global health problem. Current evidence base suggests that preoperative and postoperative monitoring of natriuretic peptide and troponin monitoring can substantially improve risk prediction to influence clinical practice [54]. Values at least 300 ng/l of NT-pro-BNP and at least 92 mg/l of BNP are commonly accepted thresholds associated with increased risk of death or nonfatal MI within 30 days of noncardiac surgeries. The Canadian Cardiovascular Society guidelines recommend measurement of NT-pro-BNP or BNP to enhance perioperative cardiac risk estimation in patients aged above 65 years of age, 45 to 64 years with significant cardiac disease, or those with RCRI above 1 (Strong recommendation; Moderate quality evidence) [34▪▪]. The European Society of Cardiology guidelines are, however, more conservative regarding troponins and natriuretic peptide testing in high-risk patients (class IIb, level of evidence: B) [19]. It is, however, at present, unclear if specific therapies directed by these biomarkers can improve perioperative outcomes.

RISK STRATIFICATION USING INTRAOPERATIVE DATA

Intraoperative hemodynamic parameters have been shown to predict postoperative outcomes. Hypotension even for short duration is strongly associated with increased risk of postoperative acute kidney injury, myocardial injury, stroke, and mortality [55▪,56–58]. Absolute thresholds associated with increased 30-day operative mortality include: systolic blood pressure below 70 mmHg for at least 5 min, mean arterial pressure (MAP) below 49 mmHg for at least 5 min, diastolic blood pressure below 30 mmHg for at least 5 min, or MAP decreases at least 50% baseline for at least 5 min [58]. The threshold for myocardial injury is a MAP less than 65 mmHg, whereas that for kidney injury is thought to be near 75 mmHg [59▪▪]. Randomized controlled trials have shown that targeted intraoperative blood pressure management could mitigate postoperative organ dysfunction in high-risk patients [60▪,61▪].

There is conflicting evidence regarding the impact of depth of anesthesia [as measured by Bispectral Index (BIS) and postoperative outcomes] [62–64]. Whether lower BIS values are simply are marker of a sicker patient population or represent a

		Preoperative	Intraoperative	Postoperative
Static Indices	Risk scores	ASA-PS		
		RCRI	Surgical Apgar Score	
		ACS-NSQIP		
		POSSUM	P-POSSUM	
	Functional status	DASI		
		CPET		
		Subjective assessment		
	Frailty	CAF		
		CFS		
		mFI		
		CSHA-FI		
Dynamic Indices	Biomarkers	Tn/NP		Tn/NP
			Intraoperative hemodynamics	
			Low BIS	
		Intelligent Perioperative Systems With Real Time Feedback		
Current framework of perioperative risk stratification				

FIGURE 1. Current framework of perioperative risk stratification. ACS-NSQIP, American College of Surgeons' National Surgical Quality Improvement Program Risk Calculators; ASA-PS, American Society of Anesthesiologists' Physical Status; BIS, Bispectral Index; CAF, comprehensive assessment of frailty; CFS, Clinical Frailty Scale; CPET, cardiopulmonary exercise testing; DASI, Duke Activity Status Index; mFI, modified Frailty Index; NP, natriuretic peptides; POSSUM/P-POSSUM, Physiological and Operative Severity Score for the Enumeration of Mortality and morbidity Score; RCRI, Revised Cardiac Risk Index, Rockwood – Canadian Study of Health and Aging – Frailty Index (CSHA – FI); Tn, troponin.

causal agent in postoperative mortality remains conjectural at this point [65].

Meta-analyses showing association between depth of anesthesia (as measured by BIS) and long-term outcomes have been criticized and it is anticipated that the results of the BALANCED Anesthesia Trial (Australian and Zealand Clinical Trials Registry No. ACTRN12612000632897) would provide a definitive answer [66▪,67▪].

FUTURE DIRECTIONS

The near-universal implementation of electronic health records has expanded into the perioperative sphere leading to the era of 'perioperative big data.' Application of machine-learning algorithms on granular databases is opening up new frontiers in perioperative risk stratification. Machine-learning techniques are being increasingly utilized for surgical risk assessment and forecasting postoperative complications [68,69▪–71▪]. Integration of these machine-learning algorithms to electronic health record system could lead to the development of 'intelligent perioperative systems,' which would provide real-time risk assessment.

This could represent a paradigm shift in perioperative risk assessment which has traditionally relied upon static indices. These algorithms, however, need rigorous validation before integration into current risk assessment framework. Figure 1 summarizes the current framework of perioperative risk stratification.

CONCLUSION

Online universal risk calculators have enhanced our ability to comprehensively quantify the risk of adverse postoperative events. Incorporation of biomarkers, comprehensive assessment of functional status, and frailty into the risk-assessment framework have further refined our ability to identify 'at-risk patients.' Intraoperative predictors of postoperative risk are being identified. Development of machine-learning algorithms holds the promise of dynamic risk estimation throughout the perioperative episode. As work goes on to refine techniques to identify the 'high-risk surgical patients,' the perioperative research agenda should pay greater emphasis on recognition and implementation of targeted interventions, which could mitigate the predicted risk.

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Conflicts of interest

No relevant conflicts of interest.

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▪ of special interest
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