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How can we identify the high-risk patient?

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Purpose of review
Accurate and early identification of high-risk surgical patients allows for targeted use of perioperative monitoring and interventions that may improve their outcomes. This review summarizes current evidence on how information from the preoperative, operative, and immediate postoperative periods can help identify such individuals.

Recent findings
Simple risk indices, such as the Revised Cardiac Risk Index or American Society of Anesthesiologists Physical Status scale, and online calculators allow risk to be estimated with moderate accuracy using readily available preoperative clinical information. Both specific specialized tests (i.e., cardiopulmonary exercise testing and cardiac stress testing) and promising novel biomarkers (i.e., troponins and natriuretic peptides) can help refine these risk estimates before surgery. Estimates of perioperative risk can be further informed by information acquired during the operative and immediate postoperative periods, such as risk indices (i.e., surgical Apgar score), individual risk factors (i.e., intraoperative hypotension), or postoperative biomarkers (i.e., troponins and natriuretic peptides).

Summary
Preoperative clinical risk indices and risk calculators estimate surgical risk with moderate accuracy. Although novel biomarkers, specialized preoperative testing, and immediate postoperative risk indices show promise as methods to refine these risk estimates, more research is needed on how best to integrate risk information from these different sources.

Keywords
biomarkers, clinical risk indices, exercise testing, postoperative complications, preoperative risk assessment

INTRODUCTION

Major surgery imposes physiological stresses that can cause significant morbidity and mortality in the perioperative period. This morbidity and mortality tends to occur in a relatively small proportion of surgical patients. For example, the United Kingdom has an overall rate of perioperative mortality of 2%, but 80% of these deaths occur in a small subset of high-risk surgical procedures. This subgroup constitutes only 12% of the surgical population [1].

As perioperative risk appears to be concentrated within a small subgroup of surgical patients, identifying these individuals early through perioperative risk stratification has important value. Nonetheless, there remain several challenges to effectively identify these high-risk patients. First, most perioperative risk stratification methods were designed to predict a certain type of event, typically death or specific complications. The prognostic accuracy of a risk-stratification tool is not necessarily transferable across different postoperative events. For example, the Revised Cardiac Risk Index (RCRI) was designed to predict major cardiac complications after noncardiac surgery [2]. Although it discriminates moderately well between patients with varying risks for cardiac complications, it poorly performs at predicting postoperative mortality [3]. Second, clinicians have to consider prognostic accuracy, simplicity, ease of access, and cost when selecting a particular approach for risk stratification, especially in the case of biomarkers and specialized testing. Even in the case of clinical risk indices, which are the most inexpensive risk stratification approach, an

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KEY POINTS

- Most episodes of postoperative mortality and major morbidity occur within a relatively small subgroup of surgical patients.
- The ASA-PS classification, RCRI, and American College of Surgeons risk calculator facilitate moderately accurate preoperative estimation of surgical risk using readily available clinical information.
- Measurement of natriuretic peptides and cardiac troponins before surgery can further help inform estimates of perioperative risk, as can CPET and cardiac stress testing.
- Immediately after surgery, patients' expected postoperative risks can be further informed using the surgical Apgar score and serial biomarkers (troponins and natriuretic peptides).
- Further research is needed to determine how best to integrate perioperative risk estimates from different sources such as clinical risk indices, biomarkers, and specialized testing.

optimal risk index must be accurate at predicting outcomes, and also simple enough for widespread implementation [4]. Third, the timing of evaluation is crucially important, as information regarding perioperative risk needs to be available early enough to influence clinical decision making.

IDENTIFICATION OF HIGH-RISK PATIENTS PRIOR TO SURGERY

Accurate and timely preoperative identification of high-risk patients provides opportunities to better inform patients about expected risks, make selective referrals to medical specialists before surgery, order further specialized preoperative investigations, initiate preoperative interventions intended to decrease perioperative risk, and arrange for appropriate levels of postoperative care. In select cases wherein a patient is deemed to be at very high risk, consideration might be given to canceling the planned surgery and opting for alternative nonoperative or less-invasive treatments. Importantly, perioperative risk is influenced by both patient-level (e.g., age and comorbidity) and surgery-level risk factors. For example, predictors of postsurgical mortality in the Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION) cohort study included nonelective surgery, select procedures, increased age, and specific comorbidities (Table 1) [5].

Preoperative functional capacity

Evaluation of functional capacity or exercise capacity is highly emphasized in perioperative risk assessment. For example, in the American College of Cardiology and American Heart Association clinical practice guidelines, a patient's estimated functional capacity is a key determinant of whether further specialized preoperative cardiac testing is recommended [6]. This emphasis on functional capacity is likely based on extrapolation from studies of preoperative exercise stress testing or cardiopulmonary exercise testing (CPET). In previous studies, patients performing more than four to six metabolic equivalents (METs) on objective exercise testing had low perioperative risk [7▪,8,9].

By comparison, perioperative physicians typically estimate patients' functional capacity subjectively by enquiring about their activities of daily living. Although a few studies have shown patients' self-reported inability to perform four to five METs to be associated with increased risks of perioperative complications [10,11], the magnitude of this association is weak. For example, poor self-reported functional capacity had a positive likelihood ratio of 1.3 and negative likelihood ratio of 0.62 for predicting complications [10]. By comparison, likelihood ratios greater than 2 or less than 0.5 are recommended for providing even minimal additional information [12]. This weak prognostic accuracy might be explained, in part, by the inherent subjectivity associated with physicians' judgment of patients' functional capacity. Indeed, recent research showed poor agreement between physicians' subjective estimate of preoperative functional capacity and the results of validated objective questionnaires such as the Duke Activity Status Index [13▪]. These data point to the need for more standardized and accurate approaches to assess preoperative functional capacity in usual clinical practice.

Clinical risk indices using preoperative information

Several preoperative scoring systems have been developed to estimate risks of mortality or complications after surgery. A commonly used index is the American Society of Anesthesiologists Physical Status (ASA-PS) classification, which assigns a score of I–V based on a patient's overall health status [14]. Despite its simplicity, the ASA-PS classification scheme has moderately good performance in predicting death [15▪,16] and some complications after surgery [17,18,19▪,20]. The classification scheme also has limitations. Specifically, it has moderate interrater reliability at best [19▪], does not incorporate surgery-specific risks, and has diminished accuracy in settings with high overall mortality rates [15▪].

The RCRI is a simple and widely used index for predicting major cardiac complications after

Table 1. Association of preoperative characteristics with mortality within 30 days after major noncardiac surgery [5]

	Adjusted hazard ratio (95% confidence interval)
Age	
45–64 years	Reference group
74 years to 76 years	1.67 (1.18–2.36)
75 years and older	3.03 (2.20–4.18)
Urgent or emergent surgery	4.62 (3.57–5.98)
Operative procedure	
Major intra-abdominal or head-and-neck surgery	3.25 (1.64–6.45)
Craniotomy or multilevel spine surgery	3.72 (1.68–8.20)
Major vascular surgery	2.38 (1.04–5.47)
Comorbid disease	
Recent high-risk coronary artery disease[a]	3.12 (1.71–5.68)
History of heart failure	1.60 (1.09–2.36)
History of stroke	2.01 (1.42–2.84)
History of peripheral arterial disease	2.13 (1.47–3.10)
Chronic obstructive pulmonary disease	2.15 (1.61–2.89)
Active cancer[b]	2.38 (1.79–3.18)

[a]Acute myocardial infarction, acute coronary syndrome, or severe (Canadian Cardiovascular Society Class 3 or 4) angina within 6 months before surgery.
[b]Active treatment (chemotherapy, radiation, or surgery) for cancer within 6 months before surgery, known metastatic disease, or planned surgery for cancer.

noncardiac surgery. It incorporates six equally weighted components: coronary artery disease, heart failure, cerebrovascular disease, renal insufficiency, diabetes mellitus, and high-risk surgical procedures [2]. Despite being developed in 1999, it still discriminates moderately well between individuals with varying perioperative cardiac risk [3,21▪▪,22]. It also has important limitations. Although the RCRI discriminates between individuals with differing perioperative cardiac risk, it does not accurately predict an individual patient's absolute risk of cardiac complications [23], possibly because of the increased sensitivity of contemporary biochemical tests for postoperative myocardial infarction (MI). In addition, some components of the index, such as diabetes mellitus, may warrant elimination as they provide minimal associated prognostic information [22]. Other components might require modification to better optimize their definitions. For example, renal insufficiency could be better defined using estimated glomerular filtration rate [22], whereas categories of surgical procedure risk could incorporate more levels of operative complexity [24]. Finally, the index may need to incorporate several other prognostically important risk factors including increased age, peripheral arterial disease, and functional capacity [3,24]. Importantly, any future changes to the RCRI must ensure that the index retains the inherent simplicity that led to its widespread uptake into clinical practice.

More recently, online web-based risk calculators have facilitated implementation of more complex risk prediction tools into clinical practice while minimizing the need for additional cumbersome bedside calculations. The key example of this emerging group of indices is the American College of Surgeons risk calculator (http://riskcalculator.facs.org) [25]. This risk calculator implements a series of clinical prediction models developed using the National Surgical Quality Improvement Program (NSQIP) registry. These models have moderate-to-good accuracy at predicting a range of postoperative events, such as death, cardiac complications, pneumonia, and acute kidney injury [25]. The NSQIP risk calculators also have limitations. Although the prediction models were derived in a very large multicenter observational dataset, they have yet to undergo external validation, especially in settings outside the United States. In addition, some prediction models are limited by the manner in which the NSQIP registry ascertains the relevant outcomes. For example, routine postoperative troponin surveillance was not implemented in all participating sites [26], thereby leading to potentially significant underreporting of postoperative MI rates [27▪▪,28]. Finally, many of the prediction models incorporate the ASA-PS classification, which has limited interrater reliability [19▪].

Preoperative biomarkers

Biomarkers are measurable markers of organ dysfunction that can independently predict postoperative complications or augment prognostic

information from clinical risk indices. Two preoperative biomarkers, in particular, have been extensively examined for predicting perioperative risk. They are cardiac troponins and natriuretic peptides, which include B-type natriuretic peptide (BNP) and N-terminal-pro-BNP (NT pro-BNP).

Natriuretic peptides are secreted by the myocardium into the circulation in response to ischemia [29] and stretching of the atrial or ventricular walls [30]. They are powerful markers of cardiovascular risk in nonsurgical patients, including individuals who are at risk for coronary artery disease, have coronary artery disease, or have heart failure [31]. Several systematic reviews indicate that preoperative BNP and NT pro-BNP are independent predictors of cardiac complications (i.e., nonfatal MI and cardiac death) after noncardiac surgery [32,33]. Furthermore, an individual patient data meta-analysis of preoperative BNP or NT pro-BNP in vascular surgery found the biomarkers to significantly improve risk prediction when combined with the RCRI [34]. Both low and elevated preoperative levels help identify patients with differing postoperative risks (Table 2) [35▪▪].

Another promising, albeit less studied, preoperative biomarker for predicting risk after noncardiac surgery is high-sensitivity cardiac troponin. Measurement of cardiac troponins, which are released in response to myocardial injury, is integral to the rapid diagnosis of MI [36]. High-sensitivity assays now allow for detection of low levels of circulating troponins in individuals without manifestations of acute coronary syndromes. In the nonoperative setting, elevated resting levels of circulating troponins predict the development of coronary artery disease, heart failure, and mortality [37,38]. Emerging research now demonstrates that 20% of patients undergoing major noncardiac surgery have elevated high-sensitivity troponin concentrations before surgery [39]. These findings have major implications for interpretation of any elevated postoperative troponin concentration. Furthermore, elevated preoperative high-sensitivity troponin concentrations are associated with increased risks of postoperative MI or mortality [40,41] and augment the predictive information from the RCRI [41].

Preoperative specialized testing

Additional specialized tests that might be performed before surgery to better inform perioperative risk estimation include resting echocardiograms, cardiac stress tests, and CPET. Preoperative resting echocardiography provides potentially important prognostic on cardiac function, including ventricular systolic dysfunction, ventricular diastolic dysfunction, valvular abnormalities, fixed wall motion abnormalities, and pulmonary hypertension. Limited available data indicate that preoperative systolic dysfunction is associated with elevated risks of perioperative death and cardiac complications [42–44]. Nonetheless, these findings may not improve risk prediction beyond that achieved with routine clinical examination alone [44]. Furthermore, resting ventricular function is not a proxy measure of functional capacity [45,46] in individuals who cannot exercise because of arthritis, obesity, or peripheral arterial disease. Finally, routine preoperative

Table 2. Prediction of 30-day death or nonfatal myocardial infarction after noncardiac surgery based on preoperative and postoperative measurement of natriuretic peptides [34,35▪▪]

Test	Measurement period	Concentration (pg/ml)	Likelihood ratio for death or nonfatal MI
BNP	Before surgery	0–99	0.58
		100–250	1.38
		≥250	3.88
NT pro-BNP	Before surgery	0–300	0.42
		301–900	1.46
		901–3000	2.68
		>3000	4.97
BNP	After surgery	0–250	0.58
		251–400	1.37
		>400	2.58
NT pro-BNP	After surgery	0–300	0.16
		301–900	0.75
		901–3000	1.79
		>3000	3.28

BNP, B-type natriuretic peptide; MI, myocardial infarction; NT pro-BNP, N-terminal pro-B-type natriuretic peptide.

echocardiography has not been associated with improved survival after major elective noncardiac surgery [47], although there may be some benefit for patients with cardiovascular risk factors who are undergoing hip fracture repair [48].

The prognostic value of information from cardiac stress testing has been extensively studied [49–51]. If exercise stress testing is performed, the ability to reach seven or more METs is indicative of low perioperative cardiovascular risk, whereas the failure to reach four METs predicts increased risk [8]. Reversible defects on cardiac stress imaging are indicative of increased perioperative cardiac risk, with greater extents of reversibility being associated with progressively increasing risk [50]. Isolated fixed defects on cardiac stress imaging are not predictive of increased perioperative risk [50].

In some regions, especially England, CPET is increasingly popular as a specialized test for preoperative risk assessment [52]. It provides an objective measure of cardiopulmonary fitness and predicts a range of perioperative complications aside from cardiac events, including pneumonia, respiratory failure, and infection. Several CPET-derived measurements, including the inability to exercise at all, low anaerobic threshold (<11 ml/kg/min), or low peak oxygen uptake (VO_2 peak), are predictive of increased risks of postoperative mortality and complications [7▪,53]. Despite these promising initial data, there remains a need for more robust high-quality research in this area, especially studies that recruit large heterogeneous generalizable samples from multiple sites and ensure that clinicians are blinded to CPET results [9,53,54].

IDENTIFYING HIGH-RISK PATIENTS IN THE INTRAOPERATIVE AND POSTOPERATIVE PERIOD

Despite recognition of the intraoperative and immediate postoperative period as being associated with significant physiologic derangements from both surgery and anesthesia, relatively few studies have evaluated how information from this period can help better identify high-risk surgical patients. Previous research has already pointed to the potential importance of intraoperative and immediate postoperative factors as risk indicators. For example, poor postoperative outcomes are associated with surgical procedures that are nonelective, involve more extensive tissue injury, and are longer in duration [5,16,55]. The duration of intraoperative hypotension (i.e., mean arterial blood pressure <55 mmHg) is also associated with increased risks of myocardial injury and acute kidney injury in a dose-dependent fashion [56].

Clinical risk indices using intraoperative and immediate postoperative information

Although intraoperative and immediate postoperative characteristics (e.g., duration of surgery) have been shown to be associated with postoperative outcomes [55], there has been comparatively little research on incorporating these characteristics into clinical risk indices. Two important examples of risk indices that have done so are the Portsmouth Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (P-POSSUM) score [57] and the surgical Apgar score [58].

The P-POSSUM score incorporates 18 variables, including several intraoperative characteristics (e.g., extent of surgery, total blood loss, and peritoneal soiling), into a complex set of mathematical equations for predicting morbidity and mortality. The tool has important limitations, including its inherent complexity for bedside application, as well as its tendency to overestimate or underestimate mortality and morbidity in some surgical populations. Nonetheless, the P-POSSUM score is one of the few predictive tools with consistent predictive accuracy across multiple validation studies [4].

In contrast, the surgical Apgar score is a very simple 10-point risk index that predicts postoperative morbidity and mortality based on three operative characteristics: tachycardia, hypotension, and estimated blood loss [58]. The score has now been validated across multiple institutions [59] and countries [60]. Although a poor surgical Apgar score does not provide insights into the specific mechanisms whereby a patient is at increased risk for postoperative mortality and morbidity, the index facilitates early postoperative identification of patients who warrant more intensive monitoring. This early identification has important potential value as 75% of patients who die after surgery do not receive any access to critical care resources [16].

Immediate postoperative biomarkers

Inroads are being made into using early postoperative biomarkers to further improve identification of surgical patients at elevated risk. Early postoperative elevations in troponin concentrations are consistently associated with increased mortality in noncardiac surgery [5,61,62▪,63], independent of any preoperative risk factors. Importantly, this association is not just mediated by the occurrence of postoperative MI, which by definition entails an elevated troponin concentration [36]. Postoperative troponin elevations are associated with increased mortality even in the absence of a formal diagnosis of MI [27▪▪], although this association is attenuated

when concomitant renal impairment is present [64▪]. Furthermore, as opposed to being only an indicator of postoperative cardiac events, troponin elevations also predict noncardiac death and complications [5,62▪]. Routine early postoperative monitoring for troponin elevations will undoubtedly lead to increased identification of patients at risk for postoperative mortality, especially as less than 40% of patients with postoperative MI exhibit any typical cardiac symptoms such as chest pain or dyspnea [27▪▪]. Nonetheless, the appropriate clinical management of affected individuals has yet to be defined because the pathophysiological link between isolated postoperative troponin elevations (i.e., no concomitant diagnosis of MI) and mortality remains unclear.

Serial postoperative monitoring of natriuretic peptide levels may also help identify high-risk surgical patients. An individual patient data meta-analysis of 2179 patients in 18 noncardiac surgery studies found that postoperative BNP or NT pro-BNP concentrations improved prediction of death or MI at 30 days after surgery, even after accounting for both preoperative risk factors and preoperative BNP or NT pro-BNP levels [35▪▪]. Both low and elevated postoperative biomarkers levels (Table 2) appear to help identify patients with varying risk profiles after surgery [35▪▪]. An important remaining challenge is to better understand the pathophysiological link between elevated postoperative BNP or NT pro-BNP levels and mortality, which is a prerequisite to selecting appropriate interventions for affected patients.

CONCLUSION

Important progress has been made in preoperative identification of high-risk surgical patients. Long-standing and commonly used simple risk indices, such as the ASA-PS and RCRI, retain moderate predictive accuracy. Simultaneously, novel biomarkers and online risk calculators are allowing for a more rapid, accurate, and complex assessment of perioperative risk. Nonetheless, important challenges remain. More research is needed to improve assessment of preoperative functional capacity, define the appropriate use of specialized preoperative tests (e.g., CPET), and delineate how novel biomarkers should be integrated with conventional clinical risk indices. Future research must also develop methods to update estimates of risk obtained before surgery with information gathered from the operative and immediate postoperative periods, such as intraoperative clinical events (e.g., hypotension) and postoperative biomarkers. Overall, the improved ability to identify high-risk surgical patients will help ensure that limited, and potentially expensive, perioperative monitoring and intervention resources are allocated to the relatively small subgroup of surgical patients who are most likely to benefit.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ▪ of special interest
- ▪▪ of outstanding interest

1. Pearse RM, Harrison DA, James P, *et al.* Identification and characterisation of the high-risk surgical population in the United Kingdom. Crit Care 2006; 10:R81.
2. Lee TH, Marcantonio ER, Mangione CM, *et al.* Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999; 100:1043–1049.
3. Ford MK, Beattie WS, Wijeysundera DN. Systematic review: prediction of perioperative cardiac complications and mortality by the Revised Cardiac Risk Index. Ann Intern Med 2010; 152:26–35.
4. Moonesinghe SR, Mythen MG, Das P, *et al.* Risk stratification tools for predicting morbidity and mortality in adult patients undergoing major surgery: qualitative systematic review. Anesthesiology 2013; 119:959–981.
5. Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION) Study Investigators. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. J Am Med Assoc 2012; 307:2295–2304.
6. Fleisher LA, Fleischmann KE, Auerbach AD, *et al.* 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; 64:e77–e137.
7. ▪ James S, Jhanji S, Smith A, *et al.* Comparison of the prognostic accuracy of scoring systems, cardiopulmonary exercise testing, and plasma biomarkers: a single-centre observational pilot study. Br J Anaesth 2014; 112:491–497.

This pilot study provides important initial data suggesting that preoperative CPET and natriuretic peptides are superior to clinical risk scoring systems for predicting postoperative complications.

8. Sgura FA, Kopecky SL, Grill JP, Gibbons RJ. Supine exercise capacity identifies patients at low risk for perioperative cardiovascular events and predicts long-term survival. Am J Med 2000; 108:334–336.
9. Smith TB, Stonell C, Purkayastha S, Paraskevas P. Cardiopulmonary exercise testing as a risk assessment method in non cardio-pulmonary surgery: a systematic review. Anaesthesia 2009; 64:883–893.
10. Reilly DF, McNeely MJ, Doerner D, *et al.* Self-reported exercise tolerance and the risk of serious perioperative complications. Arch Intern Med 1999; 159:2185–2192.
11. Wiklund RA, Stein HD, Rosenbaum SH. Activities of daily living and cardiovascular complications following elective, noncardiac surgery. Yale J Biol Med 2001; 74:75–87.
12. Jaeschke R, Guyatt GH, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. J Am Med Assoc 1994; 271:703–707.
13. ▪ Melon CC, Eshtiaghi P, Luksun WJ, Wijeysundera DN. Validated questionnaire vs physicians' judgment to estimate preoperative exercise capacity. JAMA Intern Med 2014; 174:1507–1508.

This single center cohort study found poor agreement between preoperative functional capacity as estimated by physicians' subjective judgment as opposed to a validated structured questionnaire.

14. Saklad M. Grading of patients for surgical procedures. Anesthesiology 1941; 2:281–284.

15. ■ Koo CY, Hyder JA, Wanderer JP, *et al.* A meta-analysis of the predictive accuracy of postoperative mortality using the American Society of Anesthesiologists' physical status classification system. World J Surg 2015; 39:88–103.

This systematic review provides a comprehensive assessment of the prognostic accuracy of the ASA-PS for predicting postoperative mortality.

16. Pearse RM, Moreno RP, Bauer P, *et al.* Mortality after surgery in Europe: a 7 day cohort study. Lancet 2012; 380:1059–1065.

17. Cullen DJ, Apolone G, Greenfield S, *et al.* ASA physical status and age predict morbidity after three surgical procedures. Ann Surg 1994; 220:3–9.

18. Hightower CE, Riedel BJ, Feig BW, *et al.* A pilot study evaluating predictors of postoperative outcomes after major abdominal surgery: physiological capacity compared with the ASA physical status classification system. Br J Anaesth 2010; 104:465–471.

19. ■ Sankar A, Johnson SR, Beattie WS, *et al.* Reliability of the American Society of Anesthesiologists physical status scale in clinical practice. Br J Anaesth 2014; 113:424–432.

This single-center study found that the ASA-PS had moderate interrater reliability when employed in actual clinical practice.

20. Wolters U, Wolf T, Stutzer H, Schroder T. ASA classification and perioperative variables as predictors of postoperative outcome. Br J Anaesth 1996; 77:217–222.

21. ■■ Andersson C, Wissenberg M, Jorgensen ME, *et al.* Age-specific performance of the Revised Cardiac Risk Index for predicting cardiovascular risk in elective noncardiac surgery. Circ Cardiovasc Qual Outcomes 2015; 8:103–108.

This population-based study found that the RCRI retained moderate prognostic accuracy for predicting postoperative complications of noncardiac surgery, with some diminishment of accuracy in individuals older than 85 years.

22. Davis C, Tait G, Carroll J, *et al.* The Revised Cardiac Risk Index in the new millennium: a single-centre prospective cohort re-evaluation of the original variables in 9,519 consecutive elective surgical patients. Can J Anaesth 2013; 60:855–863.

23. Devereaux PJ, Bradley D, Chan MT, *et al.* An international prospective cohort study evaluating major vascular complications among patients undergoing noncardiac surgery: the VISION Pilot Study. Open Med 2011; 5:e193–e200.

24. Biccard B. Proposed research plan for the derivation of a new cardiac risk index. Anesth Analg 2015; 120:543–553.

25. Bilimoria KY, Liu Y, Paruch JL, *et al.* Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. J Am Coll Surg 2013; 217:833–842.

26. Gupta PK, Gupta H, Sundaram A, *et al.* Development and validation of a risk calculator for prediction of cardiac risk after surgery. Circulation 2011; 124:381–387.

27. ■■ Botto F, Alonso-Coello P, Chan MT, *et al.* Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. Anesthesiology 2014; 120:564–578.

This large multicenter cohort study assessed the prognostic accuracy of postoperative troponin elevations for predicting 30-day mortality, independent of other postoperative noncardiac complications. The study also defines a proposed novel new postoperative complication, namely, myocardial injury after noncardiac surgery (MINS).

28. Devereaux PJ, Xavier D, Pogue J, *et al.* Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. Ann Intern Med 2011; 154:523–528.

29. Goetze JP, Christoffersen C, Perko M, *et al.* Increased cardiac BNP expression associated with myocardial ischemia. FASEB J 2003; 17:1105–1107.

30. Levin ER, Gardner DG, Samson WK. Natriuretic peptides. N Engl J Med 1998; 339:321–328.

31. Balion C, Santaguida P, Hill S, *et al.* Testing for BNP and NT-proBNP in the diagnosis and prognosis of heart failure. Evidence Report/Technology Assessment No. 142. (Prepared by the McMaster University Evidence-based Practice Center under Contract No. 290-02-0020). AHRQ Publication No. 06-E014. 2006.

32. Karthikeyan G, Moncur RA, Levine O, *et al.* Is a preoperative brain natriuretic peptide or N-terminal pro-B-type natriuretic peptide measurement an independent predictor of adverse cardiovascular outcomes within 30 days of noncardiac surgery? A systematic review and meta-analysis of observational studies. J Am Coll Cardiol 2009; 54:1599–1606.

33. Lurati Buse GA, Koller MT, Burkhart C, *et al.* The predictive value of preoperative natriuretic peptide concentrations in adults undergoing surgery: a systematic review and meta-analysis. Anesth Analg 2011; 112:1019–1033.

34. Rodseth RN, Lurati Buse GA, Bolliger D, *et al.* The predictive ability of preoperative B-type natriuretic peptide in vascular patients for major adverse cardiac events: an individual patient data meta-analysis. J Am Coll Cardiol 2011; 58:522–529.

35. ■■ Rodseth RN, Biccard BM, Le Manach Y, *et al.* The prognostic value of preoperative and postoperative B-type natriuretic peptides in patients undergoing noncardiac surgery: B-type natriuretic peptide and N-terminal fragment of pro-B-type natriuretic peptide: a systematic review and individual patient data meta-analysis. J Am Coll Cardiol 2014; 63:170–180.

This individual patient data meta-analysis evaluated the prognostic accuracy of both preoperative and postoperative natriuretic peptide measurement for predicting death or nonfatal MI after noncardiac surgery.

36. Thygesen K, Alpert JS, Jaffe AS, *et al.* Third universal definition of myocardial infarction. Circulation 2012; 126:2020–2035.

37. de Lemos JA, Drazner MH, Omland T, *et al.* Association of troponin T detected with a highly sensitive assay and cardiac structure and mortality risk in the general population. J Am Med Assoc 2010; 304:2503–2512.

38. deFilippi CR, de Lemos JA, Christenson RH, *et al.* Association of serial measures of cardiac troponin T using a sensitive assay with incident heart failure and cardiovascular mortality in older adults. J Am Med Assoc 2010; 304:2494–2502.

39. Kavsak PA, Walsh M, Srinathan S, *et al.* High sensitivity troponin T concentrations in patients undergoing noncardiac surgery: a prospective cohort study. Clin Biochem 2011; 44:1021–1024.

40. Nagele P, Brown F, Gage BF, *et al.* High-sensitivity cardiac troponin T in prediction and diagnosis of myocardial infarction and long-term mortality after noncardiac surgery. Am Heart J 2013; 166:325–332.

41. Weber M, Luchner A, Seeberger M, *et al.* Incremental value of high-sensitive troponin T in addition to the Revised Cardiac Index for peri-operative risk stratification in noncardiac surgery. Eur Heart J 2013; 34:853–862.

42. Halm EA, Browner WS, Tubau JF, *et al.* Echocardiography for assessing cardiac risk in patients having noncardiac surgery. Ann Intern Med 1996; 125:433–441.

43. Healy KO, Waksmonski CA, Altman RK, *et al.* Perioperative outcome and long-term mortality for heart failure patients undergoing intermediate- and high-risk noncardiac surgery: impact of left ventricular ejection fraction. Congest Heart Fail 2010; 16:45–49.

44. Rohde LE, Polanczyk CA, Goldman L, *et al.* Usefulness of transthoracic echocardiography as a tool for risk stratification of patients undergoing major noncardiac surgery. Am J Cardiol 2001; 87:505–509.

45. Benge W, Litchfield RL, Marcus ML. Exercise capacity in patients with severe left ventricular dysfunction. Circulation 1980; 61:955–959.

46. Franciosa JA, Park M, Levine TB. Lack of correlation between exercise capacity and indexes of resting left ventricular performance in heart failure. Am J Cardiol 1981; 47:33–39.

47. Wijeysundera DN, Beattie WS, Karkouti K, *et al.* Association of echocardiography before major elective noncardiac surgery with postoperative survival and length of hospital stay: population based cohort study. BMJ 2011; 342:d3695.

48. Canty DJ, Royse CF, Kilpatrick D, *et al.* The impact on cardiac diagnosis and mortality of focused transthoracic echocardiography in hip fracture surgery patients with increased risk of cardiac disease: a retrospective cohort study. Anaesthesia 2012; 67:1202–1209.

49. Beattie WS, Abdelnaem E, Wijeysundera DN, Buckley DN. A meta-analytic comparison of preoperative stress echocardiography and nuclear scintigraphy imaging. Anesth Analg 2006; 102:8–16.

50. Etchells E, Meade M, Tomlinson G, Cook D. Semiquantitative dipyridamole myocardial stress perfusion imaging for cardiac risk assessment before noncardiac vascular surgery: a meta-analysis. J Vasc Surg 2002; 36:534–540.

51. Kertai MD, Boersma E, Bax JJ, *et al.* A meta-analysis comparing the prognostic accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. Heart 2003; 89:1327–1334.

52. Huddart S, Young EL, Smith RL, *et al.* Preoperative cardiopulmonary exercise testing in England – a national survey. Perioper Med (Lond) 2013; 2:4.

53. Hennis PJ, Meale PM, Grocott MP. Cardiopulmonary exercise testing for the evaluation of perioperative risk in noncardiopulmonary surgery. Postgrad Med J 2011; 87:550–557.

54. Young EL, Karthikesalingam A, Huddart S, *et al.* A systematic review of the role of cardiopulmonary exercise testing in vascular surgery. Eur J Vasc Endovasc Surg 2012; 44:64–71.

55. Turrentine FE, Wang H, Simpson VB, Jones RS. Surgical risk factors, morbidity, and mortality in elderly patients. J Am Coll Surg 2006; 203:865–877.

56. Walsh M, Devereaux PJ, Garg AX, *et al.* Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. Anesthesiology 2013; 119:507–515.

57. Prytherch DR, Whiteley MS, Higgins B, *et al.* POSSUM and Portsmouth POSSUM for predicting mortality. Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity. Br J Surg 1998; 85:1217–1220.

58. Gawande AA, Kwaan MR, Regenbogen SE, *et al.* An Apgar score for surgery. J Am Coll Surg 2007; 204:201–208.

59. Reynolds PQ, Sanders NW, Schildcrout JS, *et al.* Expansion of the surgical Apgar score across all surgical subspecialties as a means to predict postoperative mortality. Anesthesiology 2011; 114:1305–1312.

60. Haynes AB, Regenbogen SE, Weiser TG, *et al.* Surgical outcome measurement for a global patient population: validation of the surgical Apgar score in 8 countries. Surgery 2011; 149:519–524.

61. Beattie WS, Karkouti K, Tait G, *et al.* Use of clinically based troponin underestimates the cardiac injury in noncardiac surgery: a single-centre cohort study in 51,701 consecutive patients. Can J Anaesth 2012; 59:1013–1022.

62. Noordzij PG, van Geffen O, Dijkstra IM, *et al.* High-sensitive cardiac troponin T ■ measurements in prediction of noncardiac complications after major abdominal surgery. Br J Anaesth 2015; 114:909–918.

This single-center cohort study found that troponin elevations after noncardiac surgery were strong predictors of noncardiac complications, raising questions about the pathophysiological link between these troponin elevations and postoperative outcomes.

63. van Waes JA, Nathoe HM, de Graaff JC, *et al.* Myocardial injury after noncardiac surgery and its association with short-term mortality. Circulation 2013; 127:2264–2271.

64. Walsh M, Wang CY, Ong GS, *et al.* Kidney function alters the relationship ■ between postoperative troponin T level and death. J Am Soc Nephrol 2015. [Epub ahead of print]

This substudy of the VISION cohort study found that the association between postoperative troponin elevations and mortality was significantly attenuated in individuals with moderate preoperative renal insufficiency (defined as an estimated glomerular filtration rate less than 30 ml/min/1.73 m^2).