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Preoperative Cardiac Risk Assessment

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Abstract

Major adverse cardiac events are common causes of perioperative mortality and major morbidity. Preventing these complications requires thorough preoperative risk assessment and postoperative monitoring of at-risk patients. Major guidelines recommend assessment based on a validated risk calculator that incorporates patient- and procedure-specific factors. American and European guidelines define when stress testing is needed on the basis of functional capacity assessment. Favoring cost-effectiveness, Canadian guidelines instead recommend obtaining brain natriuretic peptide or N-terminal prohormone of brain natriuretic peptide levels to guide postoperative screening for myocardial injury or infarction. When conditions such as acute coronary syndrome, severe pulmonary hypertension, and decompensated heart failure are identified, nonemergent surgery should be postponed until the condition is appropriately managed. There is an evolving role of biomarkers and myocardial injury after noncardiac surgery to enhance risk stratification, but the effect of interventions guided by these strategies is unclear.

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Major adverse cardiac events (MACEs), defined as death or myocardial infarction (MI), are common causes of perioperative mortality and major morbidity.[1] Multiple guidelines provide recommendations to guide cardiac preoperative evaluations. These guidelines are written by the American College of Cardiology/American Heart Association (ACC/AHA), the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA), and the Canadian Cardiovascular Society (CCS).[1-3] While similarities exist between these guidelines, there are differences that can lead to confusion for the clinical practitioner. We aim to synthesize each guideline, discuss where differences arise in the major guidelines and why, present a systematic approach to the preoperative cardiovascular evaluation, and share the approach we use to characterize cardiac risk prior to noncardiac surgery.

PREOPERATIVE RISK STRATIFICATION

Major perioperative cardiac guidelines all recommend beginning preoperative cardiac risk assessment with a focused history and physical exam to identify unstable or undiagnosed cardiac conditions, estimate the risk of MACE and determine who may benefit from additional testing or revascularization prior to surgery. Our approach has been outlined in a previous article in this series, and it is similar to recommendations from the 2014 ACC/AHA guideline. The ACC/AHA guideline outlined a multistep algorithm for patients with risk factors for, or known, coronary artery disease (CAD). Components of the algorithm include an assessment of surgical urgency, clinical assessment for acute coronary syndrome, and estimation of combined medical and surgical cardiac risk using a validated instrument such as the Revised Cardiac Risk Index (RCRI), the Gupta Myocardial Infarction and Cardiac Arrest (MICA) calculator or the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) surgical risk calculator.[1] Patients with an estimated risk of MACE < 1% (low risk) can proceed to surgery without further testing. The assessment of functional capacity in metabolic equivalents (METs) is recommended for patients with an estimated cardiac risk of greater than or equal to 1% (elevated risk).[1] Patients with elevated cardiac risk who have a poor or unknown functional capacity (<4 METs) can be further risk

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5α-reductase inhibitors, gonadotropin-releasing hormone agonists) and nonhormonal (gabapentin, baclofen, digoxin, and phosphodiesterase type 5 inhibitors) therapies. Hormonal agents for priapism can suppress serum testosterone and its effects—antiandrogens block binding to androgen receptors while gonadotropin-releasing hormone agonists down-regulate the release of gonadotropins from the pituitary gland—and should not be used in men who are trying to conceive or in younger patients who have not reached sexual maturation.[2]

In this case, the patient was treated successfully with ketoconazole using a previously published protocol of 200 mg 3 times a day for 2 weeks with subsequent taper to 200 mg nightly to complete 6 months of therapy.[8] Ketoconazole, an antifungal agent, inhibits androgen synthesis in the adrenal cortex and testicular Leydig cells.[11] It has a rapid onset of action and a short half-life. Thus, nighttime dosing has been postulated to prevent nocturnal tumescence while preserving libido and sexual function. Prednisone is generally coadministered with prolonged, high-dose ketoconazole use due to the risk of developing adrenal insufficiency.[2] Data regarding the success rate of ketoconazole have been limited to small case series. In the largest study thus far, 16 of 17 patients (94%) with recurrent ischemic priapism had resolution of symptoms while receiving ketoconazole therapy.[8] Eleven patients continued to have ameliorated symptoms after ketoconazole was discontinued, for a mean follow-up period of 36.7 months. Additional outcome studies are needed to more clearly define treatment for recurrent ischemic priapism.

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CORRECT ANSWERS: 1. a. 2. d. 3. c. 4. b. 5. e

stratified with pharmacologic stress testing, if the results would change perioperative management. Management changes might include changes in operative plans, changes in pharmacotherapy, or rarely, coronary revascularization. Patients with a normal stress test can proceed to surgery, whereas those with an abnormal stress test should be managed according to existing clinical practice guidelines.[1]

The ESC/ESA also issued guidelines in 2014 that incorporated a stepwise approach to preoperative cardiac evaluation.[2] The initial step is an assessment of surgical urgency, with a recommendation to proceed to surgery if the need is urgent. Patients undergoing elective surgery should be assessed for active or unstable cardiac conditions, with stabilization according to clinical practice guidelines. The surgical risk is then assessed according to low (<1%), intermediate (1%-5%), and high (>5%) risk categories (Table 1). Patients undergoing low-risk surgical procedures can proceed to surgery without additional testing, whereas patients undergoing intermediate or high-risk surgeries should have their functional capacity in METs assessed. Patients with a functional capacity greater than 4 METs can proceed to surgery. If the functional capacity is less than 4 METs, or cannot be determined, clinical risk can be assessed using the RCRI (Gupta MICA calculator can also be used, but the authors do not indicate how this fits in the algorithm). If the RCRI is greater than 2, then stress testing could be considered if the results would change management. The authors provide some nuance to suggest that stress testing might also be considered in patients with an RCRI score of 1 to 2 in some cases. However, a class I recommendation is given to consideration of stress testing in patients undergoing high-risk surgery with RCRI greater than 2 and poor functional capacity.[1,2]

The CCS issued guidelines in 2017 for patients undergoing noncardiac surgery, requiring at least overnight hospital admission, who are 45 years or older or 18 to 44 years old with known significant cardiovascular disease (CAD; e.g., cerebral vascular disease, peripheral artery disease, congestive heart failure [CHF], or severe pulmonary hypertension [PH], which was defined as pulmonary artery pressure greater than 70 mmHg, or severe valvular heart disease [VHD]). The surgical urgency should be evaluated first, as there are distinct pathways for emergent, urgent, semiurgent, and elective surgery. Patients with emergent surgical needs should proceed to surgery without further cardiac assessment.[3]

ARTICLE HIGHLIGHTS

- Different guidelines have different recommendations regarding cardiac risk stratification and testing. This article summarizes and synthesizes these recommendations.
- Myocardial injury after noncardiac surgery is a recognized risk factor for postoperative mortality. There is no consensus on what should be done and there is no current recommended intervention.
- Indications for postponing surgery for additional evaluation are discussed.

TABLE 1. Surgical Risk Stratification by Surgery Type

Low risk (<1%)	Intermediate risk (1%-5%)	High risk (>5%)
• Breast	• Carotid (symptomatic)	• Aortic and major vascular surgery
• Carotid (asymptomatic)	• Endovascular aneurysm repair	• Adrenal resection
• Dental	• Head and neck surgery	• Pneumonectomy
• Eye	• Hip surgery	• Pulmonary or liver transplant
• Other minor or superficial procedures	• Intraperitoneal	• Repair of perforated bowel
	• Intrathoracic (nonmajor)	• Revascularization or thromboembolectomy of lower limbs
	• Renal transplant	
	• Spine surgery	

Postoperative monitoring with troponins and electrocardiography and comanagement by a medical specialist is recommended if the patient is older than 64 years or has known significant cardiovascular disease. Patients with urgent or semiurgent surgical need should proceed to surgery, with preoperative cardiac assessment only if there is an unstable cardiac condition, suspicion of severe VHD, or evidence of severe PH. Postoperative monitoring can be implemented as described in emergency surgery. Patients undergoing elective surgery should undergo risk stratification with calculation of an RCRI score.[3] The version of the RCRI calculator is different than the version used in the ACC/AHA and the ESC/ESA guidelines (this will be discussed in more detail in a subsequent paragraph). Patients who are age 65 years or older, are 45 to 64 years old with significant cardiovascular disease, or have an RCRI score of 1 or greater are recommended to have brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (NT-proBNP) testing to further stratify risk. If the BNP is greater than 92 ng/L, NT-proBNP is greater than 300 ng/L, or the patient would have qualified for natriuretic peptide measurement but the results are not available, then patients are determined to be higher risk and postoperative monitoring as described above is recommended. Postoperative monitoring is not recommended for patients with normal preoperative natriuretic peptide levels. In this guideline, there is no indication for preoperative stress testing.[3]

There are multiple similarities in the approach to preoperative cardiac risk assessment among the major guidelines. All recommend a stepwise approach assessing surgical urgency, surgery specific risk, patient-specific risk, and consideration of additional risk stratification in patients with an elevated combined medical and surgical risk. The RCRI risk calculator is recommended by each of the guidelines, and no preoperative testing is recommended for low-risk patients undergoing low-risk surgeries. Several important differences also exist, and they are summarized in Table 2.[1-3] A major point of difference relates to stress testing and functional capacity assessment. Both the ACC/AHA and ESC/ESA recommend considering stress testing for patients with elevated risk (>1%) and poor functional capacity (<4 METs).[1,2] The CCS deviates and makes no formal recommendation on assessing functional capacity or preoperative cardiac stress testing. Instead, they define populations for which natriuretic peptide levels should be checked. If BNP levels are elevated, postoperative troponin monitoring, rather than preoperative stress testing, is recommended.[3] The

TABLE 2. Summary of Guidelines for Preoperative Cardiac Risk Assessment

Cardiac evaluation	ACC/AHA 2014 guidelines	ESC/ESA 2014 guidelines	CCS 2017 guidelines
Whom to evaluate	Patients with known CVD or risk factors for CVD planning to undergo a noncardiac surgery	All patients planning to undergo a noncardiac surgery	Patients undergoing surgery requiring an overnight stay with pre-existing CVD or who are ≥45 years old
Categorizing risk of MACE	Combined patient-specific and surgical risk: • Low risk (<1%) • Elevated (≥1%)	Surgical risk • Low risk (<1%) • Intermediate risk (1%-5%) • High risk (>5%)	Low risk (<5%) Elevated risk (≥5%)
Risk calculator	RCRI (Lee 1999),[6] MICA, ACS NSQIP	RCRI (Lee 1999),[6] MICA	RCRI (Lee 1999)[6]
Functional capacity goal	>4 METs subjectively or objectively (DASI)	>4 METs subjectively	No recommendation

ACC = American College of Cardiology; ACS = American College of Surgeons; AHA = American Heart Association; CCS = Canadian Cardiovascular Society; CVD = Cardiovascular Disease; DASI = Duke Activity Status Index; ESC = European Society of Cardiology; ESA = European Society of Anaesthesiology; MACE = major adverse cardiac event; MICA = myocardial infarction and cardiac arrest; NSQIP = National Surgical Quality Improvement Program; RCRI = Revised Cardiac Risk Index.

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TABLE 3. Summary of Guidelines for Preoperative Cardiac Testing[a]

Test	ACC/AHA 2014 guidelines	ESC/ESA 2014 guidelines	CCS 2017 guidelines
Electrocardiogram	• Used in patients with known CVD (except in low-risk surgery) • Used to establish baseline and discover underlying CVD in asymptomatic individuals (except in low-risk surgery) • Used postoperatively in those with signs or symptoms of MI	• Used in those who have CVD risk factors or are undergoing high-risk (>5%) surgery • Used postoperatively in those with signs or symptoms of MI	Used postoperatively in the PACU for those who are at high risk
Echocardiogram	Used in those who have unexplained dyspnea, a history of heart failure with a change in clinical status or no assessment in the last year, or are undergoing high-risk surgery (> 1%)	Used in those who have unexplained dyspnea, a history of heart failure with a change in clinical status or no assessment in the last year, or are undergoing high risk surgery (>5%)	Not recommended
Stress testing	Considered in those who are undergoing elevated-risk surgery (≥1%) and unknown or low functional capacity (<4 METs)	Considered in those who have unknown or low functional capacity (<4 METs) and RCRI > 1 who are undergoing intermediate or high risk surgery[b]	Not recommended
Angiogram	Same uses as nonoperative indications	Same uses as nonoperative indications	Same uses as nonoperative indications
BNP or NT-proBNP	Used for diagnosing heart failure or assessing optimization of heart failure patients	Used as additional independent prognostic information for perioperative and late cardiac events in high-risk patients (RCRI >1 for vascular surgery, RCRI >2 for other surgeries)[b]	Strongly recommend before noncardiac surgery (that will require at least one overnight stay in the hospital) in patients who are >65 years old, are 45-64 years old with significant CVD, or have RCRI score ≥1[b]
Troponin	Used postoperatively in those with signs or symptoms of MI	Used in high-risk patients both before and 48-72 hours after major surgery	Used in patients >65 years old or age 18-64 with significant CVD or a positive BNP or NT-proBNP or in those who would have qualified for BNP or NT-proBNP but were unable to have the test performed

[a]ACC = American College of Cardiology; AHA = American Heart Association; BNP = brain natriuretic peptide; CCS = Canadian Cardiovascular Society; CVD = cardiovascular disease; ESC = European Society of Cardiology; ESA = European Society of Anaesthesiology; MET = metabolic equivalent; MI = myocardial infarction; NT-proBNP = N-terminal pro-brain natriuretic peptide; PACU = postanesthesia care unit; RCRI = Revised Cardiac Risk Index.

[b]RCRI risk factors: high-risk type of surgery, history of ischemic heart disease, history of congestive heart failure, history of cerebrovascular disease, preoperative treatment with insulin, and preoperative serum creatinine >2.0 mg/dL.

ESC/ESA and CCS algorithms specifically discuss evaluating patients for low-prevalence, yet high-risk, conditions such as severe VHD, symptomatic arrhythmias, decompensated CHF, or severe PH.[2,3] The ACC/AHA guidelines discuss management of noncoronary cardiac conditions, which increase perioperative risk, separately from the algorithm.[1] All guidelines support delaying nonemergent surgery to optimize medical therapies for these conditions if they are decompensated; this is discussed in greater detail later.[1-3]

Another important difference between the guidelines is how cardiovascular risk is defined. The ESC/ESA guideline uses low (<1%), intermediate (1%-5%) and high (>5%) surgical risk categories and uses the RCRI and MICA risk calculators to determine patient-specific risk (see Table 2).[1-3] The

ACC/AHA guideline uses a combined patient- and surgery-specific risk, with 2 risk categories: low (<1%) and elevated (≥1%) risk.[1] The CCS guideline identifies specific-patient risk populations.[3] For example, patients age 45 years and older, or patients with known cardiovascular disease, have a 1% or greater risk of perioperative MACE. The CCS guideline recommends BNP or NT-proBNP testing for this group. In addition, the choice of populations qualifying for postoperative troponin monitoring (see Table 3)[1-3] was based on an estimated risk of greater than 5%.[3] However, the data used to create these risk estimates were weighted differently by the various guideline committees. Different from the ACC/AHA and the ESC/EHA guidelines, the CCS guideline committee emphasized data on postoperative MACE outcomes that were much higher than were reported in other studies, because all patients (symptomatic and asymptomatic) were universally screened for postoperative MI or myocardial injury. The universal screening studies have identified that the majority of patients with postoperative ischemia were asymptomatic (65%). Because many studies did not use universal screening for postoperative outcomes, a significant number of asymptomatic patients might not have been identified as having postoperative MI. There were also a number of patients that had elevated biomarkers postoperatively, but did not meet the definition of MI. These patients were defined as having myocardial injury after noncardiac surgery (MINS).[4] This places a greater emphasis on studies such as Vascular Events In Noncardiac Surgery Patients Cohort than on data derived from the NSQIP database, which does not require routine screening for asymptomatic MI.[5] Current American and European practice guidelines do not address MINS systematically but do recognize the association with increased mortality.[1,2] Canadian guidelines are specifically structured to screen for MINS.[3] MINS is discussed in greater detail later.

The ordering of risk assessment components also differs between guidelines. The ACC/AHA recommends using an absolute estimate of combined medical and surgical risk, as is reported by the RCRI, Gupta MICA, or ACS Surgical Risk calculators, followed by functional capacity assessment for elevated-risk patients (≥1%).[1] The ESC/ESA recommends using only surgical risk for baseline assessment and next proceeding to functional capacity assessment. The RCRI or Gupta MICA calculators are used as modifiers to the elevated surgical risk, but only in patients with poor functional capacity.[2] The CCS guideline again specifies populations based on a combination of surgical risk (required overnight hospital stay) and medical risk (age, risk factors, cardiac comorbidities, RCRI score).[3]

CARDIAC RISK CALCULATORS

Risk calculators are an essential component of preoperative cardiac evaluation; however, they are a significant cause of confusion for the clinician. The calculators recommended by current guidelines use patient and procedural factors to estimate the risk of MACE after surgery. Each calculator has differences related to input variables, the derivation population, and outcome definitions resulting in variability in risk estimates depending on which calculator is used. This can result in confusion because the calculated risk of MACE for the same patient might differ significantly according to which calculator is chosen. Each calculator has limitations that are important to understand to help with interpreting the scores. Complicating things even further, over the years since it was initially validated, and there have been modifications and different versions of the RCRI used; however, they have not been as widely validated. Changes in medical practice over time have created issues with using older cardiac risk calculators. Some of these changes include the use of troponin to diagnose MI, advancements in surgical technique, and improvements in anesthesia. Although the RCRI has been re-evaluated in these modern settings, older risk calculators, such as the Eagle cardiac risk criteria, Detsky index, and Goldman Cardiac Risk Index, have not; this limits their applicability to modern clinical practice. A major limitation of risk calculation tools is the exclusion

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of low-prevalence, yet high-risk, conditions such as severe VHD, symptomatic arrhythmias, decompensated CHF, and severe PH. Screening for these conditions should be performed on a clinical basis, with further diagnostic testing as would be indicated in non-perioperative setting. We recommend using the RCRI, Gupta MICA, or the ACS NSQIP surgical risk calculators to assess the risk of adverse cardiac outcome in the patient contemplating noncardiac surgery.

RCRI CALCULATOR

The most widely validated risk prediction tool is the RCRI. It was developed in 1999 on a prospective sample of patients age 50 years and older undergoing nonemergent inpatient surgery during 1989-1994 and who had a hospital stay of at least 2 days and assessed for 5 in-hospital major cardiac complications (see Table 4).[5-9] In this version of the RCRI, the variables that determined risk of adverse cardiac outcomes were (1) high-risk surgery, (2) history of ischemic heart disease, (3) history of CHF, (4) creatinine greater than 2 mg/dL, (5) cerebrovascular disease, and (6) diabetes requiring insulin. Patients with increasing numbers of these variables had a higher risk for postoperative adverse cardiac outcomes. The adverse outcomes measured were MI (using creatinine kinase-muscle/brain [CK-MB], as troponin assays were not yet developed), ventricular fibrillation or cardiac arrest, complete heart block or pulmonary edema. Postoperative MI definition depended on the type of CK-MB assay. "When the ion-exchange chromatography assay was used, acute MI was diagnosed if the peak CK-MB was greater than 5% of an elevated total CK or if the peak CK-MB was greater than 3% of an elevated total CK in the presence of electrocardiogram (ECG) changes, consistent with ischemia or infarction. When the CK-MB mass assay was used, acute MI was diagnosed if peak CK-MB levels exceeded the normal range (<5 ng/mL) and the ratio of CK-MB to total CK exceeded 0.0278 or, in the setting of ECG changes, 0.0167.[6] Patients with an RCRI score of 0 had a 0.4% risk of postoperative cardiac event, a score of 1 had a 0.9% risk, a score of 2 had a 7% risk, and a score of 3 or greater had an 11% risk. The RCRI has stood the test of time and has been validated in multiple populations, and these risk factors have been recommended for use in the ACC/AHA guidelines since 2007. Since the original publication of the RCRI in 1999, however, subsequent meta-analyses have suggested that the RCRI underestimated risk in vascular surgery procedures.[10] In addition, there have been alternative versions of the RCRI published, reflecting outcomes more consistent with other risk prediction tools (ie, using solely MI and cardiac arrest as adverse postoperative outcomes measured) and reflecting changes in clinical practice (ie, using troponins to diagnose MI, using estimated glomerular filtration rate [GFR] rather than creatinine to define kidney disease). In 2005, adverse cardiac outcome risk estimates that included only MI and cardiac arrest were published using the entire original RCRI cohort (see Table 5). Updates to the RCRI calculator aimed at improving predictive performance have been investigated but not robustly validated.[8,11] Cardiac risk increases when the GFR is less than 60 mL/min and a revision using a GFR-based criterion rather than a creatinine greater than 2 mg/dL had superior performance.[2,11,12] A 5-factor reconstruction of the RCRI eliminating diabetes and using a GFR less than 30 mL/min improved net risk reclassification at higher risk scores compared with the original RCRI criteria, and performed better than a model using a GFR less than 60 mL/min.[8] This reconstructed version of the RCRI used outcomes of MI, pulmonary edema, and cardiac arrest during hospitalization, excluding the originally included outcomes of ventricular fibrillation and complete heart block because of data collection issues (see Tables 3 and 4).

More recent studies have also validated the RCRI, although significant heterogeneity exists in the timing of outcomes (30-day outcomes verses in-hospital outcomes) and how the outcomes are identified (newer studies have reported higher rates of adverse outcomes because all patients were screened

TABLE 4. Summary of Cardiac Risk Assessment Calculators[a]

Calculator Year	Population	Variables	Outcomes	Outcome timing	Advantages	Limitations
RCRI, 1999[6]	Nonemergent inpatient surgery with 2 day stay, age ≥ 50; derivation n=2893; validation n=1422	• Ischemic heart disease[b] • Congestive heart failure[c] • Cerebrovascular disease[d] • Diabetes treated with insulin • Cr>2 mg/dL • High-risk surgery[e]	• Postoperative MI[f] • Ventricular fibrillation or CA • Complete heart block • Pulmonary edema[g]	During hospitalization	• Validated in diverse settings • Easy to calculate	• Emergent surgeries and ambulatory surgeries excluded • Underestimates vascular surgery risk • Overestimates ambulatory surgery risk • Lack of universal serial monitoring for postoperative events (ie, ECG, CK-MB) • Does not predict mortality or 30-day events well
RCRI (MI, CA outcomes only), 2005[7]	Nonemergent inpatient surgery with 2 day stay, age ≥ 50 years (n=4315)	• Ischemic heart disease[b] • Congestive heart failure[c] • Cerebrovascular disease[d] • Diabetes treated with insulin • Cr>2 mg/dL • High-risk surgery[e]	• Postoperative MI[f] • Ventricular fibrillation or CA	During hospitalization	• Less well validated in external populations • Easy to calculate	• Emergent surgeries and ambulatory surgeries excluded • Underestimates vascular surgery risk • Overestimates ambulatory surgery risk • Lack of universal serial monitoring for postoperative events (ie, ECG, CK-MB) • Does not predict mortality or 30-day events well
Reconstructed RCRI, 2013[8]	Elective inpatient surgery with 2 day stay, age ≥ 50 years (n=9519)	• Ischemic heart disease[h] • Congestive heart failure[i] • Cerebrovascular disease[d] • eGFR<30 mL/min[j] • High-risk surgery[e]	• MI[k] • CA • Pulmonary edema	During hospitalization	• Uses more contemporary diagnostic testing for MI and renal function • Excludes variables that were not predictive (diabetes) • Better calibration vs original RCRI	• Not externally validated, • Excluded urgent and emergent surgery • Lack of universal serial monitoring for postoperative events (ie, ECG, troponins) • Risk estimates higher for scores ≥1 vs RCRI
Gupta MICA[9]	Nontrauma, nontransplant surgical patients of the NSQIP participants	Age, surgery type, ASA class, functional status, Cr>1.5 mg/dL	MI, CA	Within 30 days of surgery	Improved prediction for vascular surgery,	Knowledge of NSQIP definitions required, not externally validated,

Continued on next page

TABLE 4. Continued

Calculator Year	Population	Variables	Outcomes	Outcome timing	Advantages	Limitations
					ambulatory surgery vs RCRI	outcomes and variables limited by NSQIP definitions, requires electronic device
ACS NSQIP Surgical Risk Calculator[5]	Nontransplant surgical patients undergoing procedures with CPT codes from the NSQIP database	Procedure (CPT code), age, sex, functional status, emergency case, ASA class, chronic steroid use, ascites, sepsis, ventilator dependent, disseminated cancer, diabetes status, hypertension requiring medication, congestive heart failure, dyspnea, current smoker, severe COPD, dialysis, acute renal failure, BMI	MI, CA	Within 30 days of surgery	Internally validated in diverse population, assesses multiple complications, most procedure specific universal calculator	Knowledge of NSQIP definitions required, not externally validated, outcomes and variables limited by NSQIP, requires electronic device with internet connection, requires CPT code but cannot accommodate more than 1 for complex surgery

[a]ACC = American College of Cardiology; ACS = American College of Surgeons; AHA = American Heart Association; ASA = American Society of Anesthesiologists; BMI = body mass index; CA = cardiac arrest; CCS = Canadian Cardiovascular Society; CK-MB = creatinine kinase-muscle/brain; COPD = chronic obstructive pulmonary disease; CPT = common procedural terminology; Cr = creatinine; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; ECG = electrocardiogram; ESC = European Society of Cardiology; ESA = European Society of Anaesthesiology; MET = metabolic equivalent; MI = myocardial infarction; MICA = myocardial infarction and cardiac arrest; NSQIP = National Surgical Quality Improvement Program; NT-proBNP= N-terminal pro-brain natriuretic peptide; PACU = postanesthesia care unit; RCRI = Revised Cardiac Risk Index.

[b]Ischemic heart disease was defined as history of myocardial infarction, history of a positive exercise test, current complaint of chest pain considered to be secondary to myocardial ischemia, use of nitrate therapy, or ECG with pathologic Q waves. Patients with prior coronary artery bypass graft surgery or percutaneous transluminal coronary angiography were included in this definition only if they had current complaints of chest pain that were presumed to be due to ischemia.

[c]Congestive heart failure was defined as a history of congestive heart failure, pulmonary edema, or paroxysmal nocturnal dyspnea, physical examination showing bilateral rales or S3 gallop, or chest radiograph showing pulmonary vascular redistribution.

[d]Cerebrovascular disease was defined as a history of transient ischemic attack or stroke.

[e]High-risk surgery was defined as intraperitoneal, intrathoracic, or suprainguinal vascular surgeries.

[f]Postoperative MI was defined as CK-MB >5% total CK value or >3% total CK for patients with ECG changes consistent with ischemia or infarction, or CK-MB/CK total ratio >0.028 or >0.017 with ECG changes.

[g]Pulmonary edema diagnosis required a formal reading of the chest radiograph by a radiologist, consistent with this complication in a plausible clinical setting.

[h]Defined as cardiac ischemia, nitrate therapy, or coronary artery disease.

[i]Congestive heart failure was defined as a history of congestive heart failure (it did NOT include pulmonary edema, or paroxysmal nocturnal dyspnea, physical examination showing bilateral rales or S3 gallop, or chest radiograph showing pulmonary vascular redistribution).

[j]eGFR was calculated using the Cockcroft-Gault equation.

[k]Detection of a rise or fall of cardiac troponin with at least one value above the 99th percentile upper reference limit and with at least one of the following: symptoms of ischemia, new or presumed new significant ST-segment—T wave changes or new left bundle branch block, development of pathological Q waves in the ECG, imaging evidence of new loss of viable myocardium or new regional wall motion abnormality, or identification of an intracoronary thrombus by angiography or autopsy.

for postoperative ischemic events, whereas the older studies reported only events that were identified in a much less systematic way).[3,8] The CCS performed an updated meta-analysis as part of their 2017 guideline and included studies that universally screened patients for postoperative MI using troponin assays.[3] Five studies were included in the meta-analysis, which reported overall postoperative cardiac outcome rates that were significantly higher than those reported in the original RCRI cohort (Table 5). There are several significant practice changes likely contributing to this finding, including the use of a more sensitive troponin detection assay, an increase in patient complexity, and a shift toward more outpatient surgery for healthy patients, leaving the sicker patients with comorbidities in the inpatient surgery group. However, several features of the analysis also contributed to the higher rates of postoperative cardiac outcomes. The CCS analysis included a much higher proportion of vascular (39% vs 20%) and aortic (35% vs 5%) surgery patients than the original cohort.[3,6] They also included 30-day outcomes rather than only in-hospital events. This difference in absolute risk is important when using the RCRI as part of the 2014 ACC/AHA algorithm, as using the CCS-derived estimates would not define any patients as having a risk less than 1%. Given the differences in validation cohorts, we recommend that the estimates from the original RCRI cohort be used when applied to the 2014 ACC/AHA algorithm as recommended by that guideline. There is an ongoing effort to update the RCRI validation in a large, diverse population that can provide more accurate cardiac event rates in a modern cohort.[11]

ACS NSQIP SURGICAL RISK CALCULATOR

The ACS published a comprehensive surgical risk calculator in 2013, also derived from NSQIP data. This calculator estimates the risk of multiple complications within 30 days of surgery, using 20 variables and the specific Current Procedural Terminology code of the procedure.[5] Internal validation showed excellent predictive ability, with a C-statistic of 0.895 for predicting cardiovascular complications. Several studies have questioned the accuracy of the calculator for certain urologic, abdominal, head and neck, and neurosurgical procedures, but the findings were not consistent and were confounded by the inclusion of procedure-specific variables in some studies.[13-17] There are several unique limitations with using NSQIP datasets to build risk-prediction models. None of the NSQIP-derived calculators have been robustly externally validated, as the currently published validation studies have had limitations as discussed above.[17-21] The creators of the Gupta MICA have published the equations underpinning the calculations, but the ACS has not done so with their surgical risk calculator. They all require an electronic device to calculate risk, and the ACS calculator requires an Internet connection and the specific Current Procedural Terminology code of the anticipated procedure. The outcomes and prediction variables are limited to those specified by the NSQIP datasets. This limitation creates the possibility of missing a clinically important risk factor or complication. For example, the NSQIP dataset defines postoperative MI as an acute MI, which occurred intraoperatively or within 30 days following surgery as manifested by documentation of ECG changes indicative of acute MI (either ST elevation >1 mm in 2 or more contiguous leads, new left bundle branch, or new Q-wave in 2 of more contiguous leads) or by new elevation in troponin greater than 3 times the upper level of the reference range in the setting of suspected myocardial ischemia. Because we know that most postoperative MIs are asymptomatic and NSTEMIs, it is possible that the NSQIP dataset could significantly underestimate postoperative cardiac outcomes. The ACS calculator is also difficult to validate externally because the ACS calculator is updated annually with additional NSQIP data, and the model might be adjusted;[18,19]; however, this does allow the ACS surgical risk to remain up to date as medical and surgical practices change.

It is important to acknowledge the challenges with comparing risk assessment tools.

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TABLE 5. Outcome Comparisons by RCRI Score[a]

Validation	Outcomes	Postoperative Cardiac Outcome Rate in Percentage by RCRI Score			
		0	1	2	≥3
Lee, 1999; RCRI derivation[6]	In-hospital myocardial infarction, cardiac arrest, ventricular fibrillation, complete heart block, pulmonary edema	0.5	1.3	3.6	9.1
Lee, 1999; RCRI validation[6]	In-hospital myocardial infarction, cardiac arrest, ventricular fibrillation, complete heart block, pulmonary edema	0.4	0.9	6.6	11.0
Devereaux, 2005 Whole RCRI cohort[3]	In-hospital cardiac death, myocardial infarction, nonfatal cardiac arrest	0.4	1.0	2.4	5.4
Duceppe, 2017[3]	30 day myocardial infarction, cardiac arrest or death	3.9	6.0	10.1	15.0

[a]RCRI = Revised Cardiac Risk Index.

The specific outcomes of interest, timeframe over which the outcomes were collected, and surgical populations investigated vary, all which provide significant variability and make it difficult to compare one tool to another. In addition, as mentioned earlier, the RCRI also has different versions. The surgical population is particularly important; the RCRI is best validated in improving discrimination rather than absolute risk estimates, as it lacked the sample size to stratify by surgery type like the Gupta and ACS calculators do.[5,6,9] The RCRI, reconstructed RCRI, Gupta MICA, and ACS NSQIP calculators were recently compared in a retrospective, single-center study of elective inpatient surgical patients.[20] This study found each tool performed similar to the performance in the original validation studies, as long as the outcomes of interest were kept consistent. The RCRI performance degraded significantly when it was applied to 30-day outcomes and restricted to just cardiac arrest and MI (receiver operating characteristic, 0.85 vs 0.55).[20] This creates significant challenges in accurately comparing performance, especially when applied to NSQIP datasets. We view the RCRI as complimentary to the NSQIP-derived tools. Until more robust validations in modern cohorts are available, we recommend using the RCRI for nonemergent inpatient surgery to predict in-hospital events and relying on the NSQIP calculators for assessing other components of the overall 30-day risks.

FUNCTIONAL CAPACITY

Previous studies have shown only moderate correlation with adverse cardiac events at intermediate functional capacity (4 to 10 METs).[21] Poor functional capacity (<4 METs), owing to noncardiac limitations, might have a stronger correlation with noncardiac complications such as prolonged intubation or infection; this might reflect the importance of pulmonary function and general health status on overall perioperative risk.[22] Poor functional capacity owing to cardiac limitations is associated with an increase in cardiac and noncardiac risk.[23] Excellent functional capacity (>10 METs) is associated with a low risk of cardiac complications, even in the setting of major risk factors.[24] There is a role for assessing functional capacity preoperatively, even if its performance for cardiovascular risk stratification is inferior to biomarkers or clinical risk prediction tools.

Functional capacity has historically been subjective, based on information that the patient provides about activities in which they participate. The recent Measurement of Exercise Tolerance before Surgery (METS) study calls the reliance on subjective functional capacity assessment into question.[22] This study examined the incremental predictive value of adding several methods of assessing functional

capacity to the RCRI score when predicting postoperative cardiac complications. Cardiopulmonary exercise testing (CPET), the Duke Activity Status Index (DASI), functional capacity subjectively assessed by a physician, and NT-proBNP testing were compared. Subjective assessments of functional capacity correlated poorly with actual performance on CPET. Subjective assessments generally overestimated patient performance and did not improve prediction of adverse cardiac events beyond what the RCRI provides. The DASI and NT-proBNP both improved prediction of adverse cardiac events and correlated with performance on CPET, though, only the DASI predicted death and MI postoperatively. The optimal cutoffs of DASI score to discriminate risk have not been established, and they might not correlate with the current threshold of 4 METs. Although the METS study suggests that the DASI score might be superior to these other methods of measuring functional capacity, it is important to remember that there were a relatively small number of participants and a relatively small number of adverse cardiac outcomes, which limits the power of this study.

MYOCARDIAL INJURY AFTER NONCARDIAC SURGERY

MINS is an emerging theme in perioperative medicine.[4] It is defined as myocardial injury owing to ischemia occurring within 30 days after noncardiac surgery.[25] The definition of MINS includes postoperative MI in addition to postoperative elevation in cardiac biomarkers in patients with cardiovascular symptoms or evidence of ischemia on ECG.[25,26] The mechanism of MINS likely involves both supply–demand mismatch from CAD and ischemia secondary to obstructive CAD.[27] Other causes of myocardial ischemia after surgery such as sepsis, pulmonary embolism, or cardioversion are not included in the definition of MINS.[25]

MINS is an important marker for mortality after noncardiac surgery.[28] Thirty-day morality increases with increasing values of postoperative high-sensitivity cardiac troponin T (hs-cTnT), from 0.5% for hs-cTnT<20 ng/L to almost 30% for hs-cTnT≥1000 ng/L.[25] This increase in mortality is not limited to 30 days with postoperative elevation of cardiac biomarkers signifying increased mortality after 30 days as well.[29]

Approximately 8% of patients experience MINS after noncardiac surgery, affecting 8 million adults annually.[4] A large proportion of MINS patients are asymptomatic, making diagnosis challenging.[30] Given the challenge in diagnosis, several groups have developed guidelines for screening patients who are at risk for developing MINS. The CCS guidelines recommend measuring a BNP or NT-proBNP in patients who have a baseline risk greater than 5%, defined as patients age 65 years and older, or who are 45 to 64 years old with a history of cardiovascular disease, or who have a RCRI score greater than 1.[3] For the purposes of Canadian guidelines, cardiovascular disease was defined as CAD, history of stroke, peripheral arterial disease, CHF, severe PH, or a severe obstructive cardiovascular abnormality such as aortic stenosis. For patients who have an elevated BNP or NT-proBNP, defined as greater than 300 ng/L, Canadian guidelines recommend obtaining daily hs-cTnT for 48 to 72 hours to help identify patients who develop MINS.[3] Measuring hs-cTnT 48 to 72 hours after noncardiac surgery in patients at high risk for cardiovascular disease is also suggested by the 2014 ESC/ESA perioperative guidelines.[2]

Management of MINS is evolving. For patients who develop an MI postoperatively, management is similar to patients who develop MI in the non-perioperative period, with caution given to the increased bleeding risk in postoperative patients.[31] For patients who have evidence of myocardial injury without MI, management guidelines are less clear. Evidence supports improved outcomes at 12 months in patients who received medical management in accordance with the 2007 ACC/AHA recommendations for chronic stable angina including β-blockers, ACE inhibitors, antiplatelet agents, and statins.[32] In addition, patients who experience MINS had a reduction in 30-day mortality if they received statin and aspirin.[33] Although there is some debate as to the ideal management of these patients, the CCS guidelines recommend at least initiating statin and aspirin in patients who experience

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MINS with appropriate follow-up care in the outpatient setting.[3]

Recent evidence might support the initiation of anticoagulation in the setting of MINS. The Management of Myocardial Injury After Noncardiac Surgery trial showed that dabigatran, when continued for 2 years, reduced the composite outcome of vascular mortality, all-cause mortality, MI, cardiac revascularization, nonhemorrhagic stroke, peripheral arterial thrombosis, amputation, symptomatic venous thromboembolism, and readmission to hospital for vascular reasons (11% vs 15%).[34] It is important to note that only the outcome of nonhemorrhagic stroke was, by itself, statistically significant with the remainder of outcomes in the composite outcome not reaching statistical significance. Although anticoagulation might eventually play a role in the management of MINS, the current evidence is insufficient to warrant therapeutic anticoagulation for treatment of myocardial injury, particularly in the absence of an MI.

PREOPERATIVE CARDIAC TESTING

No cardiac testing is routinely indicated for low-risk, asymptomatic individuals. Cardiac testing should be considered for those who have cardiac symptoms, have a cardiac history, or have elevated cardiac risk (such as those who are undergoing elevated risk procedure or have multiple cardiac risk factors). Table 3 summarizes testing recommendations from the 3 major guidelines.

ELECTROCARDIOGRAM

American guidelines recommend a preoperative resting 12-lead ECG for patients with a known cardiac history (except those undergoing a low-risk procedure). It can also provide some prognostic information regarding underlying cardiovascular disease, such as arrhythmia, left ventricular (LV) hypertrophy, and bundle branch blocks and therefore can be considered in patients without a known cardiac history.[1] European guidelines also recommend a preoperative ECG in those who have cardiac risk factors or are undergoing high-risk surgery.[2] Canadian guidelines do not recommend a preoperative ECG, but would recommend getting one postoperatively in the postanesthesia care unit for those who are at high risk.[3]

ECHOCARDIOGRAM

Echocardiography can be used to assess LV function or in conjunction with stress testing. American and European guidelines find that assessment of LV function is reasonable in those who have unexplained dyspnea, a history of CHF who have had a change in clinical status or have not had assessment in the past year, in those who are undergoing high risk surgery, in those who have VHD, and potentially in those who have a history of PH.[1,2] Canadian guidelines suggest using BNP or NT-proBNP over echocardiography for LV function assessment.[3]

STRESS TESTING

There are a variety of stress testing options, including exercise stress testing (EST), CPET, and pharmacologic stress testing. All guidelines would agree that stress testing is not indicated in patients who have excellent exercise capacity (>10 METs). American and European guidelines recommend considering preoperative stress testing only in patients who have unknown or poor functional capacity (<4 METs).[1,2] Canadian guidelines do not recommend EST or CPET but emphasize the value of BNP or NT-proBNP.[3] We generally do not pursue stress testing in patients with a functional capacity greater than 4 METs. We do pursue stress testing in nonurgent surgeries for patients with low or unknown functional status when test results would change management.

The type of stress testing used should be determined by the patient's clinical status. Those able to exercise should undergo an EST. The standard ECG EST can provide information for risk stratification at low cost and low risk. This test is limited by the ability to interpret the ECG tracing. For patients with abnormal baseline ECGs, such as ST segment abnormalities, left bundle branch block, frequent ectopy, or atrial fibrillation, other modalities should be pursued. Some centers have migrated toward CPET for perioperative risk stratification because it provides more detailed physiologic data and

better predicts both cardiac and pulmonary outcomes.

CPET provides an objective measure of the integrated function of the cardiac, circulatory, respiratory, and muscular systems under physiologic stress.[35] It measures the anaerobic threshold and peak oxygen uptake, which are thought to aid more definitively in risk assessment. The METS trial, which is the most recent high quality study evaluating CPET, found no clear association with cardiac risk, although it did predict overall risk for postoperative complications.[22] The current guidelines would not support CPET as a cardiac-specific risk assessment tool, but there might be a role in predicting noncardiac complications.

For patients who are unable to exercise, pharmacologic stress testing can be used. Different medications can be used in pharmacologic stress testing, each with distinct disadvantages that must be kept in mind. Vasodilators, such as adenosine and dipyridamole, can induce bronchospasm, precipitate hypotension, accentuate sinus node dysfunction and high-degree atrioventricular block, and increase the risk for an ischemic event during testing.[36] Inotropic drugs, such as dobutamine, can result in severe systemic hypertension, ventricular arrhythmias, and rapid ventricular response in atrial fibrillation; they are contraindicated in the setting of a recent MI, unstable angina, aortic dissection, and hemodynamically significant left ventricular outflow tract obstruction.[37] Of note, the dobutamine stress echocardiogram is the only common pharmacologic test that provides an ischemic threshold.[38]

Lastly, there are nuclear stress tests. This category includes single photon emission computed tomography (SPECT) and positron emission tomography (PET). The most common agents used in SPECT imaging are based on technetium-99m. The most common agents used in PET imaging are rubidium-82 and N13-ammonia. SPECT and PET stress testing provide information on cardiac size and function, myocardial perfusion, and viability. They are preferred in the setting of left bundle branch block, as echocardiography has a significant false-positive rate from ventricular dyssynchrony and in patients with obesity or severe lung disease.[39,40]

ANGIOGRAPHY

Indications for preoperative conventional angiography are identical to those in the nonoperative setting; they would include symptoms consistent with acute coronary syndrome and unstable angina. Although coronary computed tomographic angiography is less invasive than angiography, it was found to overestimate risk in the Vascular Events in Noncardiac Surgery Patients Cohort, and it is not recommended for perioperative risk stratification.[1-3,27]

LABORATORY TESTING

BNP or NT-proBNP

American guidelines recommend preoperative NT-proBNP for diagnosing or optimizing heart failure.[1] European guidelines state that BNP and NT-proBNP measurements can be considered to obtain additional independent prognostic information in high-risk patients undergoing surgery.[2] Canadian guidelines strongly recommend measuring BNP or NT-proBNP before noncardiac surgery to enhance perioperative cardiac risk estimation in patients who are 65 years of age or older, are 45-64 years of age with significant cardiovascular disease, or have an RCRI score of 1 or greater.[3] A systematic review and meta-analysis published in 2014 also showed that a postoperative measurement of BNP or NT-proBNP further enhanced risk stratification above just a preoperative measurement, and it was the strongest predictor of mortality and nonfatal MI postoperatively compared with the preoperative value. The other variables analyzed were RCRI of 3 or greater, preoperative elevation of BNP or NT-proBNP, urgent or emergent surgery, vascular surgery, and age.[41] It is worth noting that troponin was not part of the variables analyzed in this study.

We typically use BNP and NT-proBNP in several ways. First, we can use it for enhancing stratification in patients with elevated risk. Second, the BNP and NT-proBNP can be used to determine when

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postoperative testing with troponins will be useful (eg, monitoring for MINS). Lastly, it can be used in patients who, because of surgical urgency, are unable to undergo stress testing as an aid in predicting risk and in forming postoperative monitoring plans.

Troponin

American guidelines suggest obtaining troponin levels postoperatively for signs or symptoms of MI and do not recommend routinely checking troponins.[1] European guidelines recommend obtaining troponins in high-risk patients both before surgery and for 48 to 72 hours after major surgery.[2] Canadian guidelines use a decision tree that recommends daily postoperative troponins for 2 to 3 days in patients older than 65 years or 18 to 64 years old with significant cardiovascular disease or a positive preoperative BNP or NT-proBNP.[3]

HARD STOPS

Patients with severe or symptomatic cardiac disease represent an elevated-risk population that require careful consideration before proceeding with surgery (see Table 5 for a summary of the relevant cardiac diseases). This population requires a careful assessment of the risks of delaying surgery and the potential benefits of cardiac intervention. Elective surgeries can be delayed for cardiac evaluation or intervention, whereas emergent surgery should not be delayed. Management of time-sensitive and urgent surgery should be individualized. Details on management of these conditions will be discussed in a subsequent article in this series.

Any form of symptomatic obstructive coronary disease requires additional evaluation prior surgery. Acute coronary syndrome (defined as ST-segment elevation MI, non–ST-segment elevation MI, and unstable angina) significantly increases perioperative risk of MACE.[42] One study found an almost threefold increase in relative risk for patients who had an MI in the last 180 days.[6] All the major guidelines agree that if patients have signs or symptoms of acute coronary syndrome, surgery should be delayed unless the surgical need is emergent and the risk of delaying surgery outweighs the benefit of revascularization. If acute coronary syndrome is identified, it should be managed as per published practice guidelines. In the case of a recent MI, timing of this event is paramount. Livhits et al[43] found that postoperative MI and mortality continued to decrease as surgery was delayed up to approximately 60 days after the initial event.[43] This would make sense as time allows of healing of the myocardial tissue and stabilization of the inflammatory and coagulation responses in the body. American guidelines recommend that elective surgery should be delayed at least 60 days after MI even in the absence of coronary intervention.[1] However, patients will most frequently undergo treatment. In those circumstances, American and European guidelines specify treatment based on whether the patient has stable CAD or had an acute coronary syndrome and whether the intervention was a bare metal stent or a drug-eluting stent. American guidelines recommend dual antiplatelet therapy (DAPT) for a minimum of 1 month after bare metal stent, a minimum of 3-6 months after drug-eluting stent (with 6 months being preferred), and a minimum of 12 months after an acute coronary syndrome.[42] European guidelines recommend DAPT for a minimum of 1 month regardless of stent type, up to 6 months depending on risk factors (eg, acute coronary syndrome at stent implantation, complex coronary anatomy, chronic kidney disease, diabetes, prior stent thrombosis while receiving antiplatelet therapy).[44] DAPT management perioperatively is complex, especially if an event occurred in the past 6 to 12 months. Consideration should be given to the guidelines, but management will likely need to be individualized.

Heart failure, the presence of VHD, unstable arrhythmias, PH, and recent transient ischemic attack or stroke have also been

recognized as predictors of postoperative MACE. These predictors will be discussed in further detail in a subsequent publication in this series.

CONCLUSION

The ACC/AHA and ESC/ESA perioperative guidelines incorporate elements of contemporary tools for perioperative cardiovascular risk stratification, include current definitions of operative urgency and risk, and provide evidence-based expert consensus on perioperative cardiovascular care.[1,2,6,9] Preoperative cardiac stress testing should be reserved for patients who have elevated risk and poor functional capacity, and they should be considered only when the results would change perioperative management. Postoperative surveillance for MACE is not routinely recommended in the American or European guidelines; however, the European guideline endorses postoperative measurement of troponins and ECGs in patients who are believed to be at high risk (>5%) of MACE. The American guidelines recommend ECG and troponins in patients who have symptoms of MI postoperatively, but do not make clear recommendations as to when or if high-risk patients should have surveillance for ischemia in the absence of symptoms. The CCS guidelines differ in several respects, most prominently by including no formal recommendation for assessment of functional capacity and recommending against preoperative stress testing. Moreover, the CCS guidelines define populations for whom BNP or NT-proBNP level should be checked to guide postoperative surveillance for MINS.

The role of preoperative biomarkers is still evolving as new data emerges, but they do appear to contribute to preoperative cardiac risk assessment. Functional assessment is integral to risk stratification in both the American and European guidelines, and newer techniques provide even more objective assessments of functional capacity. Still, the utility of functional capacity in predicting MACE is still unclear. It is also not clear whether improving functional capacity preoperatively decreases MACE postoperatively.

Abbreviations and Acronyms: **ACC** = American College Cardiology; **ACS** = American College of Surgeons; **AHA** American Heart Association; **BNP** = brain natriuretic pep tide; **CAD** = coronary artery disease; **CCS** = Canadia Cardiovascular Society; **CHF** = congestive heart failure; **CK MB** = creatinine kinase-muscle/brain; **CPET** = cardiopu monary exercise testing; **DAPT** = dual antiplatelet therap **DASI** = Duke Activity Status Index; **ECG** = electrocardio gram; **ESA** = European Society of Anaesthesiology; **ESC** European Society of Cardiology; **EST** = exercise stres testing; **GFR** = glomerular filtration rate; **hs-cTnT** = high sensitivity cardiac troponin T; **LV** = left ventricular; **MACE** major adverse cardiac events; **MET** = metabolic equivalen **MI** = myocardial infarction; **MICA** = myocardial infarctio and cardiac arrest; **MINS** = myocardial injury after noncar diac surgery; **NSQIP** = National Surgical Quality Improve ment Program; **NT-proBNP** = N-terminal pro-brai natriuretic peptide; **PET** = positron emission tomography **PH** = pulmonary hypertension; **RCRI** = Revised Cardiac Risk Index; **SPECT** = single photon emission computed tomog raphy; **VHD** = valvular heart disease

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A Case of Nodal Anthracosis Presenting as PET-Positive Mediastinal and Hilar Lymphadenopathies

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A 78-year-old Nepali female nonsmoker was referred to the pulmonary clinic for evaluation of an incidental 1.1-cm left upper-lobe lung nodule. A positron emission tomography (PET) scan of the chest showed normal metabolic activity in the left upper lobe but revealed fluorodeoxyglucose-avid bilateral hilar and mediastinal lymph nodes, concerning for malignancy (Figure 1). Subsequently, endobronchial ultrasound-guided transbronchial needle aspiration of the paratracheal lymph nodes revealed abundant anthracitic pigment on microscopic examination, consistent with the diagnosis of nodal anthracosis (Figure 2). Later, it was discovered that this patient had significant exposure to biomass fuels used for cooking in Nepal.

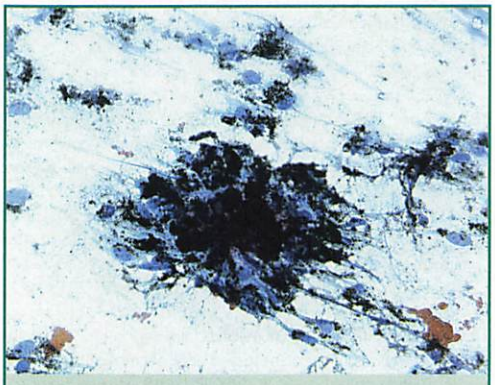

FIGURE 2. Histology of subcarinal lymph node sampled by transbronchial needle demonstrating abundant anthracitic pigment (**coarse black pigment**) within histocytes (Papanicolaou stain at magnification X40).

Anthracosis is an occupational and environment-related lung disease that includes carbon deposition and black pigmentation of the airways and can potentially result in bronchial destruction and obstructive airway disease.[1] The mean age of patients diagnosed with anthracosis is 63 years.[2] The exact prevalence of this disease is difficult to estimate because many people with anthracosis are asymptomatic.[1,2] Hence, many cases of anthracosis are discovered incidentally during bronchoscopy for other reasons (Supplemental Figure; available online at http://www.mayoclinicproceedings.org).

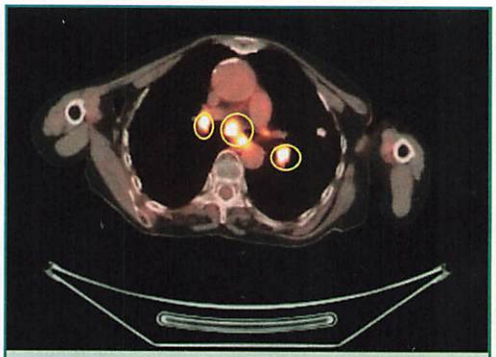

FIGURE 1. F-18-FDG-PET/CT showing increased uptake in the mediastinal and bilateral hilar lymph nodes involving right paratracheal, subcarinal, and bilateral hilar regions (maximum standardized uptake value (SUV) = 14.5).

Patients with anthracosis may develop both physical and radiologic abnormalities of chronic obstructive or fibrotic lung disease due to chronic exposure to smoke and particulates and most often present with dyspnea and cough, as with this patient.[3,4] However, nodal anthracosis with PET-positive mediastinal and hilar lymphadenopathies is considered a rare presentation of this clinical entity that mimics infectious conditions, granulomatous diseases, and

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