JAMA | Review

Perioperative Cardiovascular Risk Assessment and Management for Noncardiac Surgery
A Review

Nathaniel R. Smilowitz, MD, MS; Jeffrey S. Berger, MD, MS

IMPORTANCE Perioperative cardiovascular complications occur in 3% of hospitalizations for noncardiac surgery in the US. This review summarizes evidence regarding cardiovascular risk assessment prior to noncardiac surgery.

OBSERVATIONS Preoperative cardiovascular risk assessment requires a focused history and physical examination to identify signs and symptoms of ischemic heart disease, heart failure, and severe valvular disease. Risk calculators, such as the Revised Cardiac Risk Index, identify individuals with low risk (<1%) and higher risk (≥1%) for perioperative major adverse cardiovascular events during the surgical hospital admission or within 30 days of surgery. Cardiovascular testing is rarely indicated in patients at low risk for major adverse cardiovascular events. Stress testing may be considered in patients at higher risk (determined by the inability to climb ≥2 flights of stairs, which is <4 metabolic equivalent tasks) if the results from the testing would change the perioperative medical, anesthesia, or surgical approaches. Routine coronary revascularization does not reduce perioperative risk and should not be performed without specific indications independent of planned surgery. Routine perioperative use of low-dose aspirin (100 mg/d) does not decrease cardiovascular events but does increase surgical bleeding. Statins are associated with fewer postoperative cardiovascular complications and lower mortality (1.8% vs 2.3% without statin use; $P < .001$) in observational studies, and should be considered preoperatively in patients with atherosclerotic cardiovascular disease undergoing vascular surgery. High-dose β-blockers (eg, 100 mg of metoprolol succinate) administered 2 to 4 hours prior to surgery are associated with a higher risk of stroke (1.0% vs 0.5% without β-blocker use; $P = .005$) and mortality (3.1% vs 2.3% without β-blocker use; $P = .03$) and should not be routinely used. There is a greater risk of perioperative myocardial infarction and major adverse cardiovascular events in adults aged 75 years or older (9.5% vs 4.8% for younger adults; $P < .001$) and in patients with coronary stents (8.9% vs 1.5% for those without stents; $P < .001$) and these patients warrant careful preoperative consideration.

CONCLUSIONS AND RELEVANCE Comprehensive history, physical examination, and assessment of functional capacity during daily life should be performed prior to noncardiac surgery to assess cardiovascular risk. Cardiovascular testing is rarely indicated in patients with a low risk of major adverse cardiovascular events, but may be useful in patients with poor functional capacity (<4 metabolic equivalent tasks) undergoing high-risk surgery if test results would change therapy independent of the planned surgery. Perioperative medical therapy should be prescribed based on patient-specific risk.

JAMA. 2020;324(3):279-290. doi:10.1001/jama.2020.7840

Author Audio Interview

Supplemental content

CME Quiz at jamacmelookup.com

Author Affiliations: Leon H. Charney Division of Cardiology, Department of Medicine, New York University School of Medicine, New York, New York (Smilowitz, Berger); Division of Cardiology, Department of Medicine, Veterans Affairs New York Harbor Health Care System, New York, New York (Smilowitz); Division of Vascular Surgery, Department of Surgery, New York University School of Medicine, New York, New York (Berger).

Corresponding Author: Jeffrey S. Berger, MD, MS, Center for the Prevention of Cardiovascular Disease, New York University School of Medicine, 530 First Ave, Skirball 9R, New York, NY 10016 (jeffrey.berger@nyumc.org).

Section Editors: Edward Livingston, MD, Deputy Editor, and Mary McGrae McDermott, MD, Deputy Editor.

Approximately 17.2 million surgeries are performed annually in the US.[1] Multiple cardiovascular risk factors such as hypertension and hyperlipidemia are present in 45% of patients aged 45 years or older undergoing noncardiac surgery, and nearly 25% have a history of atherosclerotic cardiovascular disease.[2] The incidence of perioperative cardiovascular events is related to the risk for cardiovascular events in the individual patient before surgery. In a retrospective study[3] of more than 10 million hospitalizations for noncardiac surgery in adults across the US, the combined rate of perioperative death, myocardial infarction, and ischemic stroke was 3.0%. Myocardial injury, defined as an elevated troponin level above the 99th percentile, occurs in up to 20% of patients after noncardiac surgery.[4,5] This review summarizes evidence regarding risk assessment, testing, and optimal medical therapy to reduce perioperative cardiovascular risk prior to noncardiac surgery (**Box 1**).

Methods

We searched the MEDLINE database (using PubMed) and the Cochrane Library for English-language publications from January 1, 1949, through January 27, 2020, related to the evaluation of perioperative cardiovascular risk prior to noncardiac surgery. Clinical practice guidelines, randomized clinical trials, and meta-analyses of observational studies and trials were prioritized for review. Relevant references cited by identified articles were included. Included publications were mutually agreed upon by the authors and selected for clinical importance with consideration of the potential relevance for a general medical readership (eMethods in the Supplement).

Estimating Perioperative Risk

Evaluating perioperative risk begins with a focused history and cardiovascular physical examination. The history should identify cardiovascular conditions associated with perioperative major adverse cardiovascular events (MACE), including history of ischemic heart disease,[6] coronary stent,[7] heart failure,[8-10] arrhythmias,[10] valvular heart disease,[11] systemic hypertension,[12] and pulmonary hypertension.[13,14] Cardiovascular disease risk factors, such as chronic kidney disease and diabetes, are associated with up to a 3-fold increased risk of cardiac events.[6]

Physicians should ask patients whether they can perform workloads of 4 or greater metabolic equivalent tasks (METs) without symptomatic limitation (eTable 1 in the Supplement), consisting of walking up a hill or climbing up 2 or more flights of stairs. Inability

Box 1. Questions Commonly Asked When Evaluating Perioperative Risk

1. Which risk scores provide the best discrimination of perioperative risk?

The 6-component Revised Cardiac Risk Index is relatively simple to use. One point is assigned for each of the following: ischemic heart disease, cerebrovascular disease, heart failure, insulin-dependent diabetes, chronic kidney disease (serum creatinine level ≥2.0 mg/dL), and high-risk surgery (intraperitoneal, intrathoracic, or vascular). The 21-component National Surgical Quality Improvement Program universal surgical risk calculator is more complex but may provide better predictive discrimination.

2. Should preoperative stress testing be routinely performed prior to noncardiac surgery?

Routine cardiac stress testing is not indicated for low-risk patients or for high-risk patients who are able to walk up a hill or climb up 2 or more flights of stairs without difficulty. Testing may be considered for patients with unknown or poor functional capacity who may have high cardiovascular risk. Despite the established risks of coronary artery disease in surgical patients, coronary revascularization prior to surgery did not improve perioperative outcomes in a randomized trial. Thus, stress testing should only be considered if the results would change perioperative medical, anesthesia, or surgical approaches.

3. Can β-blockers and statins prevent cardiovascular complications of noncardiac surgery?

Perioperative use of β-blockers confers some theoretical advantages in reducing mismatch in myocardial oxygen supply and demand. However, high-dose extended-release metoprolol succinate (100 mg/d) initiated immediately prior to surgery is associated with increased perioperative stroke and mortality in randomized trials. Statin therapy administered during hospitalization for surgery is associated with reduced cardiovascular risk in observational data sets. However, randomized trials with 80 mg/d of atorvastatin vs placebo taken within 18 hours before surgery did not clearly demonstrate benefit. Statins should be considered preoperatively in patients with atherosclerotic cardiovascular disease and may be considered in patients with clinical risk factors undergoing higher-risk surgery.

4. Should antithrombotic and anticoagulation therapy be discontinued prior to surgery?

Routine administration of perioperative antiplatelet therapy prior to noncardiac surgery is not recommended because it is not associated with benefit and results in an increased risk of bleeding. Low-dose aspirin may be appropriate for a subset of patients when ischemic risks outweigh the bleeding risks, such as for patients with coronary artery stents. For patients taking warfarin or a direct oral anticoagulant for stroke prevention in atrial fibrillation, perioperative interruption of oral anticoagulation is safe, and bridging with heparin should not be routinely performed. Patients with mechanical mitral valves and those at increased risk for thrombotic events with mechanical aortic valves should receive bridging anticoagulation with heparin prior to noncardiac surgery.

5. How soon after coronary stent implantation may a patient safely undergo noncardiac surgery?

Individuals who require surgery within 1 year after percutaneous coronary intervention are at increased risk of perioperative events compared with those without coronary stents. Ischemic risks are inversely related to the time interval between stent placement and noncardiac surgery. Patients who undergo coronary stent placement should have surgery delayed until the risks associated with delaying surgery outweigh the risks of thrombosis that are associated with cessation of dual antiplatelet therapy. Elective noncardiac surgery should be delayed for at least 30 days after bare metal stent implantation and 12 months after drug-eluting stent placement, although more recent evidence suggests that a delay of 3 to 6 months may be safe.

to do so for any reason is independently associated with a 2-fold increased risk of perioperative complications.[15] Exertional chest pain, dyspnea, orthopnea, palpitations, recent syncope, and physical examination findings, such as murmurs (any diastolic or grade ≥3/6 systolic), gallops, jugular venous distention, or edema, may indicate cardiovascular disease. Ongoing, high-risk cardiac conditions such as acute coronary syndromes or decompensated heart failure are generally contraindications to noncardiac surgery and require additional evaluation (**Box 2**).

Type of surgery is also associated with the degree of risk for MACE (**Box 3**). By expert consensus, noncardiac surgeries with less than a 1% risk for MACE, such as cataract surgery and many types of cosmetic or plastic surgery, are considered low risk.[16] Vascular (7.7%), thoracic (6.5%), transplant (6.2%), and general (3.9%) surgeries are associated with the highest incidence of MACE.[3,6] Use of minimally invasive, laparoscopic, and endovascular techniques may attenuate cardiovascular risk.[17,18] In a randomized trial of open vs endovascular surgical abdominal aortic aneurysm repair, 30-day operative mortality was 4.3% in participants assigned to conventional open surgery vs 1.8% in those assigned to endovascular treatment.[19]

Classification systems and risk scores can help estimate perioperative risk.[6,20-24] The American Society of Anesthesiologists (ASA) Physical Status Classification System, for example, classifies patients into categories according to their overall health status and is independently associated with surgical outcomes. In a prospective study of 6301 patients, healthy patients (ASA class I) had a 0.1% risk of cardiac complications and mortality, whereas patients with "severe systemic disease that is a constant threat to life" (ASA class IV) had an 18% risk.[25] Cardiovascular risk scores commonly used include the Revised Cardiac Risk Index[6,26] and the National Surgical Quality Improvement Program perioperative myocardial infarction and cardiac arrest risk calculator and the universal surgical risk calculator (**Table**).[21,22] These scores provide estimates of cardiovascular risk based on perioperative factors. For example, to calculate the Revised Cardiac Risk Index (range, 0-6; 6 = worst), 1 point is assigned for each of the following: ischemic heart disease, cerebrovascular disease, heart failure, insulin-dependent diabetes, chronic kidney disease (serum creatinine level ≥2.0 mg/dL), and high-risk surgery (intraperitoneal, intrathoracic, or vascular). Patients with a Revised Cardiac Risk Index of 0 have an approximate risk of 0.4% for major cardiovascular complications, whereas those with an index of 3 or greater have an approximate risk of 10%. In a pooled analysis of 24 validation studies, the Revised Cardiac Risk Index had modest risk discrimination for cardiac events in patients undergoing noncardiac surgery (receiver operating characteristic curve, 0.75) and had poorer discrimination in patients undergoing vascular surgery (receiver operating characteristic curve, 0.64).[26] The 21-component National Surgical Quality Improvement Program universal surgical risk calculator may provide superior predictive discrimination.

Preoperative Cardiovascular Testing

An algorithm for perioperative cardiovascular risk stratification appears in **Figure 1**,[16,18] but has not been tested in a randomized clinical trial. Perioperative guideline recommendations from the American Heart Association and the American College of Cardiology (AHA/ACC), the Canadian Cardiovascular Society, and the European Society of Cardiology appear in eTable 2 in the Supplement.

Box 2. High-Risk Cardiac Conditions Considered Contraindications to Noncardiac Surgery

Contraindications to Noncardiac Surgery
- Acute coronary syndrome
- Acute decompensated heart failure
- Tachyarrhythmias or bradyarrhythmias associated with hypotension or requiring urgent medical attention (eg, ventricular tachycardia or high-grade atrioventricular block)
- Symptomatic, severe aortic stenosis (mean gradient >40 mm Hg or peak velocity >4 m/s)

Box 3. Cardiovascular Risk Classification and Examples of Surgery Types[3,6]

Level of Risk for Major Adverse Cardiovascular Events or Death

<1% Risk
Cataract surgery
Cosmetic or plastic surgery

≥1% Risk
Orthopedic surgery
Otolaryngology surgery
Genitourinary surgery

≥3% Risk
General abdominal or intraperitoneal surgery
Neurosurgery

≥5% Risk
Suprainguinal and peripheral vascular surgery
Thoracic surgery
Transplant surgery

12-Lead Electrocardiographic Testing

Preoperative 12-lead electrocardiographic (ECG) testing defines the cardiac rhythm, identifies clinically silent cardiovascular disease such as prior Q-wave myocardial infarction, and provides a baseline for postoperative comparison. Among patients with coronary artery disease (CAD) undergoing major surgery, preoperative ST-segment depressions greater than 0.5 mm are associated with increased risk of postoperative death or myocardial infarction (event rate of 11.2% in patients with ST-segment depressions vs 2.6% in those without such depressions; $P = .001$).[27,28] However, an ECG provides little benefit prior to low-risk surgery such as cataract surgery and cosmetic or plastic surgery.[29-31] Therefore, preoperative 12-lead ECG is reasonable in patients with a history of CAD, arrhythmias, peripheral artery disease, cerebrovascular disease, or structural heart disease scheduled for higher-risk surgery.[16] A 12-lead ECG also is reasonable prior to higher-risk surgeries such as major abdominal or thoracic procedures even among those without symptoms of cardiovascular disease.[16]

Transthoracic Echocardiography

Echocardiography is a noninvasive imaging modality that evaluates left ventricular function and valvular heart disease. In an observational study of 570 patients undergoing noncardiac surgery, elevated aortic valve gradients of 40 mm Hg or greater (odds ratio

Table. Risk Scores and Calculators

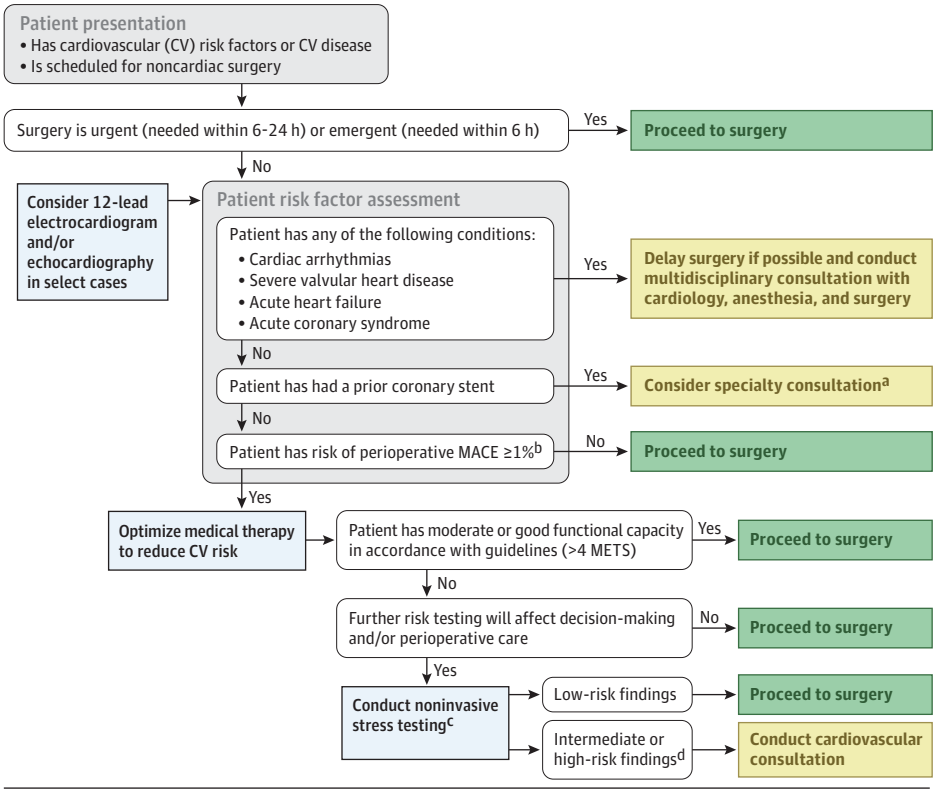
	Goldman Index of Cardiac Risk,[20] 1977	Revised Cardiac Risk Index,[6] 1999	National Surgical Quality Improvement Program Risk calculators		Geriatric-Sensitive Perioperative Cardiac Risk Index,[24] 2017	Cardiovascular Risk Index,[23] 2019
			Perioperative MI and cardiac arrest,[21] 2011	Universal surgical,[22] 2013		
Criteria	• Aged >70 y (5 points) • Had an MI within 6 mo (10 points) • Jugular venous distention or a third heart sound on auscultation (11 points) • ≥5 PVCs/min (7 points) • Nonsinus rhythm or PAC on preoperative ECG (7 points) • Aortic stenosis (3 points) • Intraperitoneal, intrathoracic, or aortic surgery (3 points) • Any emergency surgery (4 points)	• Ischemic heart disease (1 point) • Cerebrovascular disease (1 point) • History of congestive heart failure (1 point) • Insulin therapy for diabetes (1 point) • Serum creatinine level ≥2.0 mg/dL (1 point) • Planned high-risk procedure (intraperitoneal, intrathoracic, or vascular surgery) (1 point)	• Age • ASA class • Preoperative function • Creatinine level • Procedure type: anorectal; aortic; bariatric; brain; breast; cardiac; ear, nose, or throat; foregut or hepatopancreatobiliary; gallbladder, appendix, adrenal, or spleen; intestinal; neck; obstetric or gynecologic; orthopedic; other abdomen; peripheral vascular; skin; spine; thoracic; urological; or vein	• Age group • Sex • ASA class • Functional status • Emergency case • Steroid use for chronic condition • Ascites within 30 d preoperatively • System sepsis within 48 h preoperatively • Required ventilator • Disseminated cancer • Diabetes • Hypertension requiring medication • Prior cardiac event • Congestive heart failure within 30 d preoperatively • Dyspnea • Current smoker within 1 y • History of COPD • Dialysis • Acute kidney failure • BMI • *CPT*-specific linear risk	• Age • Sex • ASA class • High-risk surgery • History of heart failure • Stroke • Required insulin • Diabetes • Dialysis • Medications for hypertension • Current tobacco use • History of COPD • Functional status (partially vs totally dependent) • Creatinine level • Surgical category • Dyspnea • BUN level • Laparoscopic surgery	• Age ≥75 y (1 point) • History of heart disease (1 point) • Symptoms of angina or dyspnea (1 point) • Hemoglobin level <12 mg/dL (1 point) • Vascular surgery (1 point) • Emergency surgery (1 point)
Score range	• Class I: 0-5 points (lowest risk) • Class II: 6-12 points • Class III: 13-25 points • Class IV: ≥26 points (highest risk)	• Class I: 0 points (lowest risk) • Class II: 1 point • Class III: 2 points • Class IV: ≥3 points (highest risk)	0%-100% (0%, lowest risk; 100%, highest risk)	0%-100% (0%, lowest risk; 100%, highest risk)	0%-100% (0%, lowest risk; 100%, highest risk)	• 0 points (lowest risk) • 1 point • 2 points • 3 points • >3 points (highest risk)
Threshold denoting elevated risk	≥Class II (≥6 points)	>1 point	>1%	>1%	>1%	≥2 points
Outcome	Intraoperative or postoperative MI, pulmonary edema, VT, cardiac death	MI, pulmonary edema, ventricular fibrillation, complete heart block, cardiac death	Intraoperative or postoperative MI or cardiac arrest within 30 d	Cardiac arrest, MI, all-cause mortality within 30 d	Cardiac arrest, MI, all-cause mortality within 30 d	Death, MI, or stroke at 30 d
Derivation population	1001	1422	211 410	1 414 006	584 931	3284
Set ROC						
Derivation	0.61	0.76	0.88	0.90 (Cardiac arrest or MI); 0.94 (mortality)		0.90
Validation	0.70	0.81; 0.75[a]	0.87[b]	0.88 (Cardiac arrest or MI); 0.94 (mortality)[b]	0.83 (0.76 in adults aged ≥65 y)[b]	0.82[b]

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; BUN, blood (serum) urea nitrogen; COPD, chronic obstructive pulmonary disease; *CPT*, *Current Procedural Terminology*; ECG, electrocardiogram; MI, myocardial infarction; PAC, premature atrial contraction; PVC, premature ventricular contraction; ROC, receiver operating characteristic curve; VT, ventricular tachycardia.

[a] Pooled validation studies assessing the performance in mixed noncardiac surgery.[26]

[b] Validated using the National Surgical Quality Improvement Program database. The risk calculators are available at https://riskcalculator.facs.org/RiskCalculator/PatientInfo.jsp.

Figure 1. A Proposed Algorithm for Perioperative Cardiovascular Risk Assessment



The algorithm has not been validated. MACE indicates major adverse cardiovascular events; METs metabolic equivalent tasks.

[a] Perioperative considerations during consulation shown in Figure 2.

[b] Risk of perioperative MACE as determined by a clinical risk calculator.

[c] Testing options include: (1) exercise electrocardiographic stress testing without myocardial imaging; or (2) stress testing (exercise or pharmacological) with imaging such as echocardiography, nuclear perfusion via single-photon emission computed tomography, positron emission tomography, or cardiac magnetic resonance imaging.

[d] Intermediate or high-risk findings by stress testing may include moderate to severe myocardial ischemia, ischemia provoked at a low workload, a hypotensive response to exercise, transient ischemic dilatation, and ventricular arrhythmias during stress testing.

[OR], 6.8; 95% CI, 1.3-31.0), left ventricular hypertrophy (OR, 2.1; 95% CI, 1.0-4.5), and any left ventricular systolic dysfunction (OR, 2.0; 95% CI, 1.0-4.1) were independently associated with cardiac events (myocardial infarction, pulmonary edema, ventricular fibrillation or cardiac arrest, and complete heart block in 44 of 570 patients [7.7%]; the absolute event rates corresponding to the ORs were not available).[32] A preoperative echocardiogram with any degree of systolic dysfunction, moderate to severe left ventricular hypertrophy, moderate to severe mitral regurgitation, or an aortic gradient of 20 mm Hg or greater was 80% sensitive for perioperative cardiac events and had a negative predictive value of 97%.[32] A risk model including echocardiographic parameters was more closely associated with perioperative complications than the model including only clinical variables.[32] In other studies, aortic stenosis was associated with increased perioperative death or myocardial infarction (14% vs 2% without aortic stenosis; adjusted OR, 5.2 [95% CI, 1.6-17.0]; $P < .001$).[33] Left ventricular ejection fraction less than 30% was associated with a greater risk of perioperative death, myocardial infarction, and heart failure exacerbation (53.6% vs 26.0% with left ventricular ejection fraction ≥30%; adjusted OR, 4.9 [95% CI, 1.8-14.4]; $P = .008$).[34] However, in a study of 339 men with suspected CAD, echocardiographic measurements did not contribute to the clinical factors associated with perioperative risk.

It is reasonable to consider preoperative echocardiography in patients with moderate or severe valvular disease (stenosis or regurgitation) without echocardiography within the past year, or in those who have new clinical signs or symptoms of severe valvular disease, including dyspnea, angina, edema, or recent syncope.[16] Treatment of severe valvular disease should be considered before noncardiac surgery. Patients with established or suspected hypertrophic cardiomyopathy, in whom hyperdynamic ventricular function may lead to systolic anterior motion of the mitral valve and left ventricular outflow tract obstruction, and high-risk patients undergoing cardiac solid-organ transplantation may benefit from preoperative echocardiographic evaluation.[35-37] Overall, except in special circumstances, routine preoperative evaluation of ventricular function is not recommended.[16,18,32,38,39]

Assessment of Functional Capacity and Stress Testing for Myocardial Ischemia

Poor functional capacity is associated with increased risk of perioperative complications.[15] Patients unable to perform workloads of 4 METs or greater, such as walking up a hill or climbing 2 or more flights of stairs, have a 2-fold increased risk of perioperative cardiovascular complications compared with those who are able (9.6% vs 5.2%, respectively; $P = .04$).[15] Among 1396 patients, the quantitative Duke Activity Status Index, derived from a validated questionnaire assessing functional capacity (range, 0-58.2; higher values indicate greater functionality),[40] was independently associated with death or myocardial infarction in 28 patients (2%) within 30 days of surgery (adjusted OR, 0.91 [95% CI, 0.83-0.99]) for every 3.5 points on the index; however, the absolute event rates corresponding to the ORs were not available).[41]

Exercise ECG stress testing assesses functional capacity and identifies stress-induced myocardial ischemia. Pharmacological stress testing is reserved for patients who are unable to exercise. In a study of 530 patients undergoing dobutamine stress echocardi-

ography prior to noncardiac surgery, ischemia at a low workload (<60% of the maximum predicted heart rate) was associated with increased event rates (23% risk of death or myocardial infarction in patients with ischemia vs 5% without ischemia; adjusted, OR, 7.0 [95% CI, 2.8-17.6]).[42] No MACE occurred in patients without preoperative ischemia, whereas 43% of those with ischemia at low workloads had MACE. In a separate study of 429 participants, dobutamine stress echocardiography had an excellent negative predictive value (98%) for perioperative MACE.[43]

Routine stress testing is not indicated for low-risk patients, which includes those with excellent functional capacity (>10 METs, which is equivalent to playing singles tennis or running at a 10 minute/mile pace) and with moderate to good functional capacity (≥4-10 METs, which is equivalent to playing doubles tennis or cross-country hiking). Cardiopulmonary exercise testing may be considered for patients with unknown functional capacity scheduled for higher-risk surgical procedures (Box 3),[16] but it is not recommended by European guidelines.[18] Canadian guidelines recommend against both preoperative exercise stress testing and cardiopulmonary exercise testing due to limited data supporting testing.[39]

Among patients with poor functional capacity (<4 METs) at higher risk for noncardiac surgery, exercise testing with cardiac imaging or noninvasive pharmacological stress testing (either dobutamine stress echocardiography or vasodilator stress myocardial perfusion imaging) to assess for myocardial ischemia is only reasonable if the results from this testing would change perioperative medical management and decisions regarding coronary revascularization.[16,42-44] European guidelines recommend stress testing with imaging before high-risk surgery in patients with more than 2 clinical risk factors (using the Revised Cardiac Risk Index) and poor functional capacity (<4 METs) and treatment according to clinical indications independent of surgery.[18] In contrast, Canadian guidelines recommend against pharmacological stress echocardiography and radionuclide imaging because the predictive discrimination associated with imaging tests has not been adequately compared with those derived from preoperative risk calculators alone.[39]

Coronary Angiography and Revascularization

Routine preoperative invasive coronary angiography is not recommended before noncardiac surgery.[16] Invasive angiography may be considered in patients with stress tests that indicate myocardial ischemia, but only if the results of angiography would affect perioperative care. The benefit of noninvasive coronary computed tomographic angiography (CCTA) prior to noncardiac surgery is uncertain. In a study of 234 patients undergoing preoperative CCTA, coronary artery diameter stenosis greater than 50% (MACE in 17.2% with obstructive CAD vs 4.3% without obstructive CAD) and multivessel CAD (MACE in 29.7% with multivessel CAD vs 3.7% without multivessel CAD) provided prognostic data in addition to the Revised Cardiac Risk Index.[45] In a meta-analysis of 11 studies evaluating CCTA prior to surgery, severity and extent of CAD were associated with perioperative MACE (specifically, 2.0% in those without CAD; 4.1% in those with nonobstructive CAD; 7.1% in those with 1-vessel obstructive CAD; and 23.1% in those with obstructive multivessel CAD; $P < .001$).[46] However, CCTA-diagnosed CAD may overestimate risks,[47] and it is not currently recommended by clinical practice guidelines for risk stratification prior to noncardiac surgery.[39]

Despite the established risks of CAD, routine coronary revascularization prior to surgery does not improve perioperative outcomes. In the Coronary Artery Revascularization Prophylaxis trial,[48] 510 patients with CAD scheduled for vascular surgery were randomly assigned to coronary artery revascularization before surgery or no coronary revascularization. Postoperative myocardial infarction within 30 days (12% in the revascularization group vs 14% in the no revascularization group; $P = .37$) and long-term mortality at a median follow-up of 2.7 years (22% vs 23%, respectively; $P = .92$) were not different between the groups; however, patients with left main CAD and reduced left ventricular ejection fraction were excluded from the trial.[48] Based on these data, routine coronary revascularization is not recommended before noncardiac surgery to reduce perioperative MACE.[16]

In contrast, European guidelines suggest that prophylactic coronary revascularization may be considered before high-risk surgery if there is substantial stress-induced ischemia.[18] Although preoperative coronary revascularization may be performed for a compelling indication independent of surgery, such as for those with acute coronary syndrome,[16] performing surgery within 12 months after coronary stent placement is associated with increased perioperative risks.[7,49] Nonetheless, despite current guidelines, invasive coronary angiography before noncardiac surgery is common and preoperative revascularization is performed in 24% of these cases.[50]

Biomarker Measurement

Preoperative measurement of biomarkers remains an emerging area of investigation for perioperative risk assessment. Serum levels of B-type natriuretic peptide (BNP), a polypeptide released by cardiomyocytes in response to atrial stretch, or the N-terminal pro-BNP (NT-ProBNP) may be associated with perioperative cardiovascular risk. Based on a meta-analysis[51] of individual patient data from 18 prospective observational studies, preoperative BNP levels greater than 92 pg/mL or NT-ProBNP levels greater than 300 pg/mL were associated with increased risk of death or myocardial infarction at 30 days (21.8% in patients with BNP levels >92 pg/mL or NT-ProBNP levels >300 pg/mL vs 4.9% in patients with natriuretic peptides below these levels). Preoperative natriuretic peptide levels were also associated with improved performance of a risk model that included age, Revised Cardiac Risk Index of 3 or greater, vascular surgery, and urgent surgery for the outcome of 30-day perioperative cardiovascular risk, with a net reclassification index of 18%.[51]

In a prospective cohort study of 10 402 patients undergoing noncardiac surgery, preoperative BNP levels between 100 and 200 pg/mL were associated with a 30-day mortality rate of 0.7%; 200 and 1500 pg/mL, 1.4%; and greater than 1500 pg/mL, 4.0% compared with BNP levels less than 100 pg/mL, which were associated with a 30-day mortality rate of 0.3%.[52] Canadian guidelines recommend measurement of NT-proBNP or BNP levels prior to noncardiac surgery in patients with cardiovascular disease, a Revised Cardiac Risk Index of 1 or greater, or for those who are aged 65 years or older.[39] The AHA/ACC guidelines do not formally endorse a BNP measurement as part of preoperative risk assessment because biomarker-based perioperative management strategies have not been tested to reduce cardiovascular risk.[16]

Cardiac troponin level, a sensitive marker of myocardial injury, should be measured perioperatively when signs or symptoms suggest myocardial ischemia or myocardial infarction.[16] Routine cardiac troponin screening should be avoided in unselected patients without symptoms of myocardial ischemia.[16] The value of postoperative cardiac troponin surveillance in asymptomatic patients at risk for ischemic complications is uncertain because no studies have evaluated the benefits of a testing strategy.[16] However, Canadian guidelines recommend postoperative cardiac troponin surveillance in high-risk individuals (eTable 2 in the Supplement).[39] In the authors' opinion, postoperative surveillance of cardiac troponin level during the first 48 hours after higher-risk surgery is reasonable to detect silent myocardial injury in patients at increased risk of cardiovascular events based on preoperative risk calculators (eg, Revised Cardiac Risk Index >1) if the results of testing would modify clinical management (eg, initiation or intensification of antithrombotic or statin therapy for the prevention of cardiovascular events).

Medical Therapies to Reduce Perioperative Cardiovascular Risk

β-Blockers

Perioperative use of β-blockers confers a number of potentially advantageous effects on perioperative risk. The use of β-blockers decreases myocardial wall stress, prolongs coronary diastolic filling time, and reduces mismatch in myocardial oxygen supply and demand. Despite observational data suggesting an association of perioperative use of β-blockers with improved outcomes in high-risk patients,[53,54] randomized clinical trial results do not support perioperative prescription of β-blockers.[55] In the Perioperative Ischemic Evaluation trial, 8351 patients were randomly assigned to extended-release metoprolol succinate (100 mg/d) or placebo, beginning within 4 hours prior to noncardiac surgery and continuing for 30 days. The participants randomly assigned to metoprolol had fewer perioperative nonfatal cardiovascular events (myocardial infarction, cardiac arrest, and cardiovascular death; 5.8% vs 6.9% among those assigned to placebo; $P = .04$), but increased rates of perioperative stroke (1.0% vs 0.5%, respectively; $P = .005$) and all-cause mortality (3.1% vs 2.3%; $P = .03$).[56]

It is possible that the longer duration of β-blocker administration prior to surgery and lower doses (or titration to heart rate) may be beneficial. In an observational analysis of 940 patients undergoing vascular surgery, fewer cardiovascular events (myocardial infarction or injury, stroke, or mortality) occurred when β-blockers were initiated more than 1 week prior to surgery compared with shorter preoperative durations (15% vs 27%, respectively; $P < .001$).[57] Patients already taking β-blockers should continue treatment during the perioperative period in the absence of bradycardia or hypotension.[16] Initiation of β-blockers before surgery may be warranted in select patients with CAD or with multiple risk factors and at high risk for perioperative myocardial infarction.[16] Although high-dose β-blocker therapy should not be initiated on the day of surgery, it may be reasonable to initiate β-blocker therapy more than 1 week prior to surgery to determine tolerability and safety.

Aspirin

Competing risks of bleeding and thrombosis represent a key challenge during the perioperative period. Aspirin, an irreversible inhibitor of cyclooxygenase-1, reduces platelet aggregation and thrombotic risk by diminishing thromboxane A2 production, with associated increased risks of bleeding. The Perioperative Ischemic Evaluation-2 trial tested the use of routine perioperative aspirin vs placebo in 10 010 patients at risk for cardiovascular complications who were scheduled for noncardiac surgery.[58] Patients assigned to preoperative aspirin did not have significantly lower rates of death or myocardial infarction (7.0% vs 7.1% for those assigned to placebo; $P = .92$), but aspirin was associated with increased rates of major bleeding (4.6% vs 3.8%, respectively; $P = .04$). In this trial, only one-third of patients had established vascular disease, and less than 5% had prior coronary stent placement. Thus, routine perioperative aspirin use prior to noncardiac surgery is not recommended,[16] although aspirin therapy may be appropriate for certain patients if ischemic risks outweigh the risks of bleeding.

Lipid-Lowering Therapy and Statins

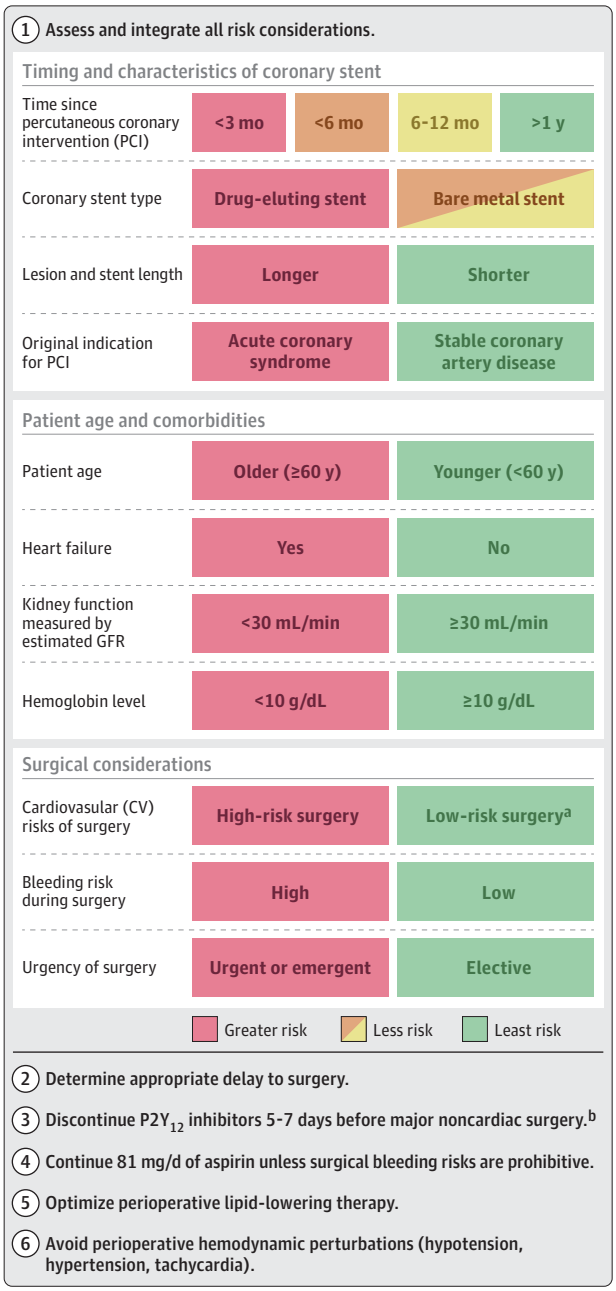
Observational data and small randomized trials suggest that lipid-lowering therapy may be associated with lower perioperative cardiovascular risk. In a retrospective, propensity-matched analysis[59] of 204 885 patients undergoing noncardiac surgery, prescribing lipid-lowering drugs during the surgical hospitalization was associated with lower in-hospital mortality compared with patients who did not receive lipid-lowering therapy (2.1% vs 3.1%, respectively; adjusted OR, 0.62 [95% CI, 0.58-0.67]). Similar results were reported from a Veterans Affairs patient cohort (in-hospital mortality of 1.8% with lipid-lowering therapy vs 2.3% in those without lipid-lowering therapy; relative risk, 0.82 [95% CI, 0.75-0.89]) and from the Vascular Events in Noncardiac Surgery Patients Cohort Evaluation study.[60,61]

The Lowering the Risk of Operative Complications Using Atorvastatin Loading Dose trial[62] randomly assigned 648 statin-naive patients with cardiovascular disease (approximately 25%) or multiple risk factors (approximately 75%) to high-dose atorvastatin or placebo within 18 hours before noncardiac surgery, and continued treatment for 7 days postoperatively. Atorvastatin did not reduce major cardiovascular complications (16.6% vs 18.7% for those assigned to placebo; hazard ratio, 0.87 [95% CI, 0.60-1.26]; $P = .46$).[62] Results from meta-analyses of randomized trials are inconsistent.[63,64] Although randomized trials do not support prescribing statins prior to surgery, the AHA/ACC guidelines suggest that preoperative initiation of statin therapy is reasonable prior to vascular surgery, and the authors' opinion is that statin therapy may be beneficial with few adverse effects in patients with indications for lipid-lowering therapy, such as those with diabetes or atherosclerotic cardiovascular disease who are scheduled for higher-risk surgery.[16]

Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers

The safety of prescribing angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) on the day of surgery is unclear. In a pooled analysis of 3 small randomized trials including 188 participants, perioperative continuation of ACEIs or ARBs was associated with increased rates of intraoperative hypotension (57.8% vs 23.5% in those who discontinued use of ACEIs or ARBs; pooled relative risk, 2.53 [95% CI, 1.08-5.93]).[39,65-67] In a large observational study of 4802 individuals undergoing noncardiac surgery, perioperative discontinuation of ACEIs or ARBs prior to surgery was associated with a lower risk of perioperative hypotension (23.3% vs 28.6% in those with continued use of ACEIs or ARBs;

Figure 2. Perioperative Risk Assessment and Management of Patients With a Coronary Stent



GFR indicates glomerular filtraton rate; MACE, major adverse cardiovascular events; $P2Y_{12}$, group of drugs that includes: clopidogrel, ticlopidine, ticagrelor, prasugrel, and cangrelor.

[a] Expected risk of MACE less than 1%. See also Box 3.

[b] Discontinue clopidogrel and ticagrelor 5 days prior to surgery and discontinue prasugrel 7 days prior to surgery.

adjusted relative risk, 0.80 [95% CI, 0.73-0.88]) and with a lower risk of the composite end point of myocardial injury after noncardiac surgery, stroke, and mortality at 30 days (12.0% vs 12.9%, respectively; adjusted relative risk, 0.82 [95% CI, 0.70-0.96]).[68]

Canadian guidelines recommend discontinuing ACEIs or ARBs for 24 hours prior to noncardiac surgery and resuming ACEI or ARB therapy on the second postoperative day when the patient is hemodynamically stable.[39] European guidelines recommend considering temporary discontinuation of ACEIs or ARBs prior to surgery when prescribed for hypertension, but recommend continuing ACEIs or ARBs in stable patients with heart failure and left ventricular systolic dysfunction.[18] In contrast, the AHA/ACC guidelines indicate that it is reasonable to continue ACEI or ARB therapy, and that if these agents are discontinued, they should be restarted as soon as possible after surgery.[16] Additional investigation is warranted to determine the safety of renin-angiotensin system inhibition during the perioperative period.

Anticoagulation

Oral anticoagulation is frequently indicated for stroke prevention in patients with atrial fibrillation at risk for thromboembolic events and as treatment for patients with venous thromboembolism or valvular heart disease. In patients with atrial fibrillation, anticoagulation is typically interrupted 2 to 5 days prior to noncardiac surgery (based on anticoagulant pharmacokinetics) to reduce the risk of perioperative bleeding. In a trial of 1884 patients with atrial fibrillation randomly assigned to either perioperative bridging therapy with low-molecular-weight heparin (after discontinuing warfarin 5 days before surgery) or placebo, the incidence of arterial thromboembolism was not different between the groups (0.4% vs 0.3% in the placebo group; $P = .01$ for noninferiority), but bridging anticoagulation was associated with more perioperative bleeding (3.2% vs 1.3%, respectively; $P = .005$).[69]

In a study of 3640 patients with atrial fibrillation taking a direct oral anticoagulant, stopping use of the oral anticoagulant 1 to 2 days prior to a procedure with a low bleeding risk (eg, eye surgeries or dental procedures) and 2 to 4 days before a procedure with a high bleeding risk (eg, orthopedic surgeries or vascular surgeries) without perioperative bridging therapy was associated with low rates of arterial thromboembolism (0.33%).[70] Based on the available data, perioperative interruption of oral anticoagulation therapy in patients with atrial fibrillation appears safe and perioperative bridging for patients with atrial fibrillation should not be routinely performed. In contrast, patients with mechanical mitral valves and those at risk for thrombotic events with mechanical aortic valves should receive bridging anticoagulation with heparin prior to noncardiac surgery.

Special Populations

Older Adults

Adults aged 65 years or older account for 37% of all inpatient surgeries in the US, and older age is associated with increased cardiovascular risk.[16,71,72] In the Perioperative Ischemic Evaluation-2 trial, being aged 75 years or older was independently associated with an increased risk of postoperative myocardial infarction (9.5% for aged ≥75 years vs 4.8% for aged <75 years; adjusted hazard ratio, 1.89 [95% CI, 1.60-2.23]; $P < .001$).[58] Age-related changes in cardiovascular physiology, including decreased sympathetic responses to stress, reduced vascular compliance, and impaired baroreceptor responses can lead to labile blood pressure and pulse and enhance susceptibility to perioperative hypotension in older adults.[73,74] Cardiac diastolic dysfunction predisposes to heart failure with small increases in intravascular volume. Aortic stenosis affects 4% of individuals aged 70 to 79 years and 10% of those aged 80 to 89 years,[75] and is associated with higher perioperative risks. Noncardiovascular surgical complications such as infection, respiratory failure, and acute kidney injury are more common in older adults compared with

younger adults (any complication in 26.1% [≥80 years] vs 15.1% [<80 years]; $P < .001$).[74] In a cohort of 30 254 adults aged 65 years or older undergoing noncardiac surgery, 12.1% developed postoperative delirium, 42.9% experienced functional decline (independent vs partially dependent vs totally dependent), and 29.7% required a new postoperative mobility aid.[76]

Compared with younger individuals, less is known about optimal perioperative care of older adults. Older patients are underrepresented in clinical trials and the guidelines provide few cardiovascular care recommendations for this population.[77,78] General principles of perioperative risk stratification should be followed, with an emphasis on assessing baseline functional impairment in older adults.[78,79] Surgical risk prediction models exist for older adults but are not yet widely used. For example, the Geriatric-Sensitive Perioperative Cardiac Risk Index (Table) was recently developed.[24] Additional studies incorporating cognitive function, frailty, and functional status, which are important components of perioperative cardiovascular risk assessment and outcomes in older adults, are needed.[80]

Patients Requiring Urgent or Emergency Surgery

Urgent (required within 6-24 hours) or emergency (required within 6 hours) noncardiac surgeries are independently associated with increased risk of surgical morbidity (13.8% for emergency, 12.3% for urgent, and 6.7% for elective) and mortality (3.7% for emergency, 2.3% for urgent, and 0.4% for elective).[81] Preoperative cardiovascular evaluation must consider the benefits of surgery and also alternatives to surgery in the context of cardiovascular risks. When emergency surgery is lifesaving, a thorough cardiovascular risk assessment may not be possible, particularly if it would be unlikely to affect management. Guideline-recommended cardiovascular evaluation prior to urgent surgery may be appropriate to exclude acute cardiovascular conditions that are contraindications to noncardiac surgery (Box 2). If warranted, involvement of cardiovascular anesthesia specialists and careful intraoperative and postoperative hemodynamic monitoring should be considered. Efforts to avoid perioperative tachycardia, hypertension, hypotension, and anemia are prudent.

Patients With Prior Coronary Stents

Despite recommendations to delay noncardiac surgery after percutaneous coronary intervention (PCI),[16] 3.5% of patients or more undergo noncardiac surgery within 6 months of stent placement.[82,83] Individuals requiring surgery within 1 year after PCI are at increased risk of perioperative events compared with those without coronary stents (8.9% vs 1.5%, respectively; adjusted OR, 2.6 [95% CI, 1.4-4.9]; $P < .001$).[7] Ischemic risks are inversely related to the length of time between stent placement and noncardiac surgery,[7,49,84,85] and are directly related to prothrombotic surgical trauma and early discontinuation of dual antiplatelet therapy (**Figure 2**).[49,85-89] In some cases, clinically significant perioperative stent thrombosis and myocardial infarction can occur.[90]

Patients undergoing coronary stent placement should have surgery delayed until the risks associated with delaying surgery outweigh the thrombotic risks of stopping dual antiplatelet therapy. A Veterans Affairs study of 28 029 patients undergoing 41 989 surgeries within 24 months of PCI reported MACE in 11.6% of surgeries performed within 6 weeks of PCI; in 6.4% of surgeries performed between 6 weeks and 6 months; in 4.2% of surgeries performed between 6 months and 1 year; and in 3.5% of surgeries performed beyond 1 year after PCI. Elective noncardiac surgery should be delayed for at least 2 weeks after balloon angioplasty, 30 days after bare metal stent implantation, and 12 months after drug-eluting stent placement, although evidence suggests that surgery 3 to 6 months after drug-eluting stent PCI or longer may be safe.[16,49,83,91] Elective noncardiac surgery after drug-eluting stent PCI may be considered after 6 months or longer if the risk of further delay is greater than the expected risks of myocardial infarction and stent thrombosis.[16] Shorter delays to surgery after PCI require further study.[91]

After coronary stent placement, continuation of single antiplatelet therapy with aspirin is recommended in the AHA/ACC guidelines,[16] whereas European guidelines favor individualized decisions based on bleeding and thrombotic risks.[18] A post hoc subgroup analysis from the Perioperative Ischemic Evaluation-2 study among 470 patients undergoing noncardiac surgery with a prior coronary stent suggests perioperative aspirin use is associated with a reduction in 30-day death or nonfatal myocardial infarction (6.0% vs 11.5% without aspirin use; hazard ratio, 0.50 [95 CI, 0.26-0.95]).[92] Other factors associated with perioperative risks after coronary stent placement include longer lengths of the treated coronary lesion and a history of acute coronary syndrome as the initial indication for stent placement (Figure 2).[88,89]

Limitations

This review has some limitations. First, a separate systematic literature search was not performed for each subcategory discussed. Therefore, some relevant studies may have been missed.

Second, perioperative care guideline recommendations are limited by the quality and availability of evidence and often rely on expert opinion.

Conclusions

Comprehensive history, physical examination, and assessment of functional capacity during daily life should be performed prior to noncardiac surgery to assess cardiovascular risk. Cardiovascular testing is rarely indicated in patients with a low risk of major adverse cardiovascular events, but may be useful in patients with poor functional capacity (<4 metabolic equivalent tasks) undergoing high-risk surgery if test results would change therapy independent of the planned surgery. Perioperative medical therapy should be prescribed based on patient-specific risk.

ARTICLE INFORMATION

Accepted for Publication: April 27, 2020.

Author Contributions: Drs Smilowitz and Berger had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.
Administrative, technical, or material support: All authors.
Supervision: All authors.

Conflict of Interest Disclosures: Dr Berger reported serving as a consultant to Janssen and Amgen; and receiving grant funding from AstraZeneca and the American Heart Association. No other disclosures were reported.

Funding/Support: Dr Smilowitz was supported in part by a New York University Clinical and

Translational Science Award and grants UL1 TR001445 and KL2 TR001446 from the National Center for Advancing Translational Sciences, National Institutes of Health. Dr Berger was funded in part by grants R01HL139909 and R35HL144993 from the National Heart, Lung, and Blood Institute, National Institutes of Health.

Role of the Funder/Sponsor: The funders/sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Edward Livingston, MD, at Edward.livingston@jamanetwork.org or Mary McGrae McDermott, MD, at mdm608@northwestern.edu.

REFERENCES

1. Steiner CA, Karaca Z, Moore BJ, Imshaug MC, Pickens G. Surgeries in hospital-based ambulatory surgery and hospital inpatient settings, 2014: HCUP statistical brief #223. Accessed June 16, 2020. https://www.ncbi.nlm.nih.gov/books/NBK442035/

2. Smilowitz NR, Gupta N, Guo Y, Beckman JA, Bangalore S, Berger JS. Trends in cardiovascular risk factor and disease prevalence in patients undergoing non-cardiac surgery. *Heart*. 2018;104(14):1180-1186. doi:10.1136/heartjnl-2017-312391

3. Smilowitz NR, Gupta N, Ramakrishna H, Guo Y, Berger JS, Bangalore S. Perioperative major adverse cardiovascular and cerebrovascular events associated with noncardiac surgery. *JAMA Cardiol*. 2017;2(2):181-187. doi:10.1001/jamacardio.2016.4792

4. Smilowitz NR, Redel-Traub G, Hausvater A, et al. Myocardial injury after noncardiac surgery: a systematic review and meta-analysis. *Cardiol Rev*. 2019;27(6):267-273. doi:10.1097/CRD.0000000000000254

5. Devereaux PJ, Biccard BM, Sigamani A, et al; Writing Committee for the VISION Study Investigators. Association of postoperative high-sensitivity troponin levels with myocardial injury and 30-day mortality among patients undergoing noncardiac surgery. *JAMA*. 2017;317(16):1642-1651. doi:10.1001/jama.2017.4360

6. 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(10):1043-1049. doi:10.1161/01.CIR.100.10.1043

7. Mahmoud KD, Sanon S, Habermann EB, et al. Perioperative cardiovascular risk of prior coronary stent implantation among patients undergoing noncardiac surgery. *J Am Coll Cardiol*. 2016;67(9):1038-1049. doi:10.1016/j.jacc.2015.11.063

8. Hernandez AF, Whellan DJ, Stroud S, Sun JL, O'Connor CM, Jollis JG. Outcomes in heart failure patients after major noncardiac surgery. *J Am Coll Cardiol*. 2004;44(7):1446-1453. doi:10.1016/j.jacc.2004.06.059

9. Lerman BJ, Popat RA, Assimes TL, Heidenreich PA, Wren SM. Association of left ventricular ejection fraction and symptoms with mortality after elective noncardiac surgery among patients with heart failure. *JAMA*. 2019;321(6):572-579. doi:10.1001/jama.2019.0156

10. van Diepen S, Bakal JA, McAlister FA, Ezekowitz JA. Mortality and readmission of patients with heart failure, atrial fibrillation, or coronary artery disease undergoing noncardiac surgery: an analysis of 38 047 patients. *Circulation*. 2011;124(3):289-296. doi:10.1161/CIRCULATIONAHA.110.011130

11. Samarendra P, Mangione MP. Aortic stenosis and perioperative risk with noncardiac surgery. *J Am Coll Cardiol*. 2015;65(3):295-302. doi:10.1016/j.jacc.2014.10.051

12. Browner WS, Li J, Mangano DT; Study of Perioperative Ischemia Research Group. In-hospital and long-term mortality in male veterans following noncardiac surgery. *JAMA*. 1992;268(2):228-232. doi:10.1001/jama.1992.03490020076034

13. Ramakrishna G, Sprung J, Ravi BS, Chandrasekaran K, McGoon MD. Impact of pulmonary hypertension on the outcomes of noncardiac surgery: predictors of perioperative morbidity and mortality. *J Am Coll Cardiol*. 2005;45(10):1691-1699. doi:10.1016/j.jacc.2005.02.055

14. Smilowitz NR, Armanious A, Bangalore S, Ramakrishna H, Berger JS. Cardiovascular outcomes of patients with pulmonary hypertension undergoing noncardiac surgery. *Am J Cardiol*. 2019;123(9):1532-1537. doi:10.1016/j.amjcard.2019.02.006

15. Reilly DF, McNeely MJ, Doerner D, et al. Self-reported exercise tolerance and the risk of serious perioperative complications. *Arch Intern Med*. 1999;159(18):2185-2192. doi:10.1001/archinte.159.18.2185

16. Fleisher LA, Fleischmann KE, Auerbach AD, et al; American College of Cardiology; American Heart Association. 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(22):e77-e137. doi:10.1016/j.jacc.2014.07.944

17. Atkinson TM, Giraud GD, Togioka BM, Jones DB, Cigarroa JE. Cardiovascular and ventilatory consequences of laparoscopic surgery. *Circulation*. 2017;135(7):700-710. doi:10.1161/CIRCULATIONAHA.116.023262

18. Kristensen SD, Knuuti J, Saraste A, et al; Authors/Task Force Members. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35(35):2383-2431. doi:10.1093/eurheartj/ehu282

19. Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, Sculpher MJ; United Kingdom EVAR Trial Investigators. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med*. 2010;362(20):1863-1871. doi:10.1056/NEJMoa0909305

20. Goldman L, Caldera DL, Nussbaum SR, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. *N Engl J Med*. 1977;297(16):845-850. doi:10.1056/NEJM197710202971601

21. 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(4):381-387. doi:10.1161/CIRCULATIONAHA.110.015701

22. 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(5):833-42.e1, e3. doi:10.1016/j.jamcollsurg.2013.07.385

23. Dakik HA, Chehab O, Eldirani M, et al. A new index for pre-operative cardiovascular evaluation. *J Am Coll Cardiol*. 2019;73(24):3067-3078. doi:10.1016/j.jacc.2019.04.023

24. Alrezk R, Jackson N, Al Rezk M, et al. Derivation and validation of a geriatric-sensitive perioperative cardiac risk index. *J Am Heart Assoc*. 2017;6(11):e006648. doi:10.1161/JAHA.117.006648

25. Wolters U, Wolf T, Stützer H, Schröder T. ASA classification and perioperative variables as predictors of postoperative outcome. *Br J Anaesth*. 1996;77(2):217-222. doi:10.1093/bja/77.2.217

26. 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(1):26-35. doi:10.7326/0003-4819-152-1-201001050-00007

27. Jeger RV, Probst C, Arsenic R, et al. Long-term prognostic value of the preoperative 12-lead electrocardiogram before major noncardiac surgery in coronary artery disease. *Am Heart J*. 2006;151(2):508-513. doi:10.1016/j.ahj.2005.04.018

28. Landesberg G, Einav S, Christopherson R, et al. Perioperative ischemia and cardiac complications in major vascular surgery: importance of the preoperative twelve-lead electrocardiogram. *J Vasc Surg*. 1997;26(4):570-578. doi:10.1016/S0741-5214(97)70054-5

29. Noordzij PG, Boersma E, Bax JJ, et al. Prognostic value of routine preoperative electrocardiography in patients undergoing noncardiac surgery. *Am J Cardiol*. 2006;97(7):1103-1106. doi:10.1016/j.amjcard.2005.10.058

30. Gold BS, Young ML, Kinman JL, Kitz DS, Berlin J, Schwartz JS. The utility of preoperative electrocardiograms in the ambulatory surgical patient. *Arch Intern Med*. 1992;152(2):301-305. doi:10.1001/archinte.1992.00400140055013

31. van Klei WA, Bryson GL, Yang H, Kalkman CJ, Wells GA, Beattie WS. The value of routine preoperative electrocardiography in predicting myocardial infarction after noncardiac surgery. *Ann Surg*. 2007;246(2):165-170. doi:10.1097/01.sla.0000261737.62514.63

32. Rohde LE, Polanczyk CA, Goldman L, Cook EF, Lee RT, Lee TH. Usefulness of transthoracic echocardiography as a tool for risk stratification of patients undergoing major noncardiac surgery. *Am J Cardiol*. 2001;87(5):505-509. doi:10.1016/S0002-9149(00)01421-1

33. Kertai MD, Bountioukos M, Boersma E, et al. Aortic stenosis: an underestimated risk factor for perioperative complications in patients undergoing noncardiac surgery. *Am J Med*. 2004;116(1):8-13. doi:10.1016/j.amjmed.2003.07.012

34. Healy KO, Waksmonski CA, Altman RK, Stetson PD, Reyentovich A, Maurer MS. 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(2):45-49. doi:10.1111/j.1751-7133.2009.00130.x

35. Hreybe H, Zahid M, Sonel A, Good CB, Shaver J, Saba S. Noncardiac surgery and the risk of death and other cardiovascular events in patients with hypertrophic cardiomyopathy. *Clin Cardiol*. 2006; 29(2):65-68. doi:10.1002/clc.4960290206

36. Thompson RC, Liberthson RR, Lowenstein E. Perioperative anesthetic risk of noncardiac surgery in hypertrophic obstructive cardiomyopathy. *JAMA*. 1985;254(17):2419-2421. doi:10.1001/jama.1985.03360170059031

37. Lentine KL, Costa SP, Weir MR, et al; American Heart Association Council on the Kidney in Cardiovascular Disease and Council on Peripheral Vascular Disease; American Heart Association; American College of Cardiology Foundation. Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific statement from the American Heart Association and the American College of Cardiology Foundation: endorsed by the American Society of Transplant Surgeons, American Society of Transplantation, and National Kidney Foundation. *Circulation*. 2012;126(5):617-663. doi:10.1161/CIR.0b013e31823eb07a

38. Halm EA, Browner WS, Tubau JF, Tateo IM, Mangano DT; Study of Perioperative Ischemia Research Group. Echocardiography for assessing cardiac risk in patients having noncardiac surgery. *Ann Intern Med*. 1996;125(6):433-441. doi:10.7326/0003-4819-125-6-199609150-00001

39. Duceppe E, Parlow J, MacDonald P, et al. Canadian Cardiovascular Society guidelines on perioperative cardiac risk assessment and management for patients who undergo noncardiac surgery. *Can J Cardiol*. 2017;33(1):17-32. doi:10.1016/j.cjca.2016.09.008

40. Hlatky MA, Boineau RE, Higginbotham MB, et al. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol*. 1989;64(10):651-654. doi:10.1016/0002-9149(89)90496-7

41. Wijeysundera DN, Pearse RM, Shulman MA, et al; METS Study Investigators. Assessment of functional capacity before major non-cardiac surgery: an international, prospective cohort study. *Lancet*. 2018;391(10140):2631-2640. doi:10.1016/S0140-6736(18)31131-0

42. Das MK, Pellikka PA, Mahoney DW, et al. Assessment of cardiac risk before nonvascular surgery: dobutamine stress echocardiography in 530 patients. *J Am Coll Cardiol*. 2000;35(6):1647-1653. doi:10.1016/S0735-1097(00)00586-6

43. Labib SB, Goldstein M, Kinnunen PM, Schick EC. Cardiac events in patients with negative maximal versus negative submaximal dobutamine echocardiograms undergoing noncardiac surgery: importance of resting wall motion abnormalities. *J Am Coll Cardiol*. 2004;44(1):82-87. doi:10.1016/j.jacc.2004.03.049

44. Baron JF, Mundler O, Bertrand M, et al. Dipyridamole-thallium scintigraphy and gated radionuclide angiography to assess cardiac risk before abdominal aortic surgery. *N Engl J Med*. 1994;330(10):663-669. doi:10.1056/NEJM199403103301002

45. Ahn JH, Park JR, Min JH, et al. Risk stratification using computed tomography coronary angiography in patients undergoing intermediate-risk noncardiac surgery. *J Am Coll Cardiol*. 2013;61(6):661-668. doi:10.1016/j.jacc.2012.09.060

46. Koshy AN, Ha FJ, Gow PJ, et al. Computed tomographic coronary angiography in risk stratification prior to non-cardiac surgery: a systematic review and meta-analysis. *Heart*. 2019; 105(17):1335-1342. doi:10.1136/heartjnl-2018-314649

47. Sheth T, Chan M, Butler C, et al; Coronary Computed Tomographic Angiography and Vascular Events in Noncardiac Surgery Patients Cohort Evaluation Study Investigators. Prognostic capabilities of coronary computed tomographic angiography before non-cardiac surgery: prospective cohort study. *BMJ*. 2015;350:h1907. doi:10.1136/bmj.h1907

48. McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med*. 2004;351(27): 2795-2804. doi:10.1056/NEJMoa041905

49. Hawn MT, Graham LA, Richman JS, Itani KM, Henderson WG, Maddox TM. Risk of major adverse cardiac events following noncardiac surgery in patients with coronary stents. *JAMA*. 2013;310(14): 1462-1472. doi:10.1001/jama.2013.278787

50. Schulman-Marcus J, Feldman DN, Rao SV, et al. Characteristics of patients undergoing cardiac catheterization before noncardiac surgery: a report from the national cardiovascular data registry CathPCI Registry. *JAMA Intern Med*. 2016;176(5): 611-618. doi:10.1001/jamainternmed.2016.0259

51. Rodseth RN, Biccard BM, Le Manach Y, et al. The prognostic value of pre-operative and post-operative 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(2):170-180. doi:10.1016/j.jacc.2013.08.1630

52. Duceppe E, Patel A, Chan MTV, et al. Preoperative N-terminal pro-B-type natriuretic peptide and cardiovascular events after noncardiac surgery: a cohort study. *Ann Intern Med*. 2020;172 (2):96-104. doi:10.7326/M19-2501

53. Lindenauer PK, Pekow P, Wang K, Mamidi DK, Gutierrez B, Benjamin EM. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. *N Engl J Med*. 2005;353(4): 349-361. doi:10.1056/NEJMoa041895

54. London MJ, Hur K, Schwartz GG, Henderson WG. Association of perioperative β-blockade with mortality and cardiovascular morbidity following major noncardiac surgery. *JAMA*. 2013;309(16):1704-1713. doi:10.1001/jama.2013.4135

55. Wijeysundera DN, Duncan D, Nkonde-Price C, et al. Perioperative beta blockade in noncardiac surgery: a systematic review for the 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(22):2406-2425. doi:10.1016/j.jacc.2014.07.939

56. Devereaux PJ, Yang H, Yusuf S, et al; POISE Study Group. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371(9627):1839-1847. doi:10.1016/S0140-6736(08)60601-7

57. Flu WJ, van Kuijk JP, Chonchol M, et al. Timing of pre-operative beta-blocker treatment in vascular surgery patients: influence on post-operative outcome. *J Am Coll Cardiol*. 2010;56(23):1922-1929. doi:10.1016/j.jacc.2010.05.056

58. Devereaux PJ, Mrkobrada M, Sessler DI, et al; POISE-2 Investigators. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med*. 2014; 370(16):1494-1503. doi:10.1056/NEJMoa1401105

59. Lindenauer PK, Pekow P, Wang K, Gutierrez B, Benjamin EM. Lipid-lowering therapy and in-hospital mortality following major noncardiac surgery. *JAMA*. 2004;291(17):2092-2099. doi:10.1001/jama.291.17.2092

60. London MJ, Schwartz GG, Hur K, Henderson WG. Association of perioperative statin use with mortality and morbidity after major noncardiac surgery. *JAMA Intern Med*. 2017;177(2): 231-242. doi:10.1001/jamainternmed.2016.8005

61. Berwanger O, Le Manach Y, Suzumura EA, et al; VISION Investigators. Association between pre-operative statin use and major cardiovascular complications among patients undergoing non-cardiac surgery: the VISION study. *Eur Heart J*. 2016;37(2):177-185. doi:10.1093/eurheartj/ehv456

62. Berwanger O, de Barros E Silva PG, Barbosa RR, et al; LOAD Investigators. Atorvastatin for high-risk statin-naïve patients undergoing noncardiac surgery: the Lowering the Risk of Operative Complications Using Atorvastatin Loading Dose (LOAD) randomized trial. *Am Heart J*. 2017;184:88-96. doi:10.1016/j.ahj.2016.11.001

63. Sanders RD, Nicholson A, Lewis SR, Smith AF, Alderson P. Perioperative statin therapy for improving outcomes during and after noncardiac vascular surgery. *Cochrane Database Syst Rev*. 2013;7(7):CD009971. doi:10.1002/14651858.CD009971.pub2

64. Putzu A, de Carvalho E Silva CMPD, de Almeida JP, et al. Perioperative statin therapy in cardiac and non-cardiac surgery: a systematic review and meta-analysis of randomized controlled trials. *Ann Intensive Care*. 2018;8(1):95. doi:10.1186/s13613-018-0441-3

65. Coriat P, Richer C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. *Anesthesiology*. 1994;81 (2):299-307. doi:10.1097/00000542-199408000-00006

66. Bertrand M, Godet G, Meersschaert K, Brun L, Salcedo E, Coriat P. Should the angiotensin II antagonists be discontinued before surgery? *Anesth Analg*. 2001;92(1):26-30. doi:10.1097/00000539-200101000-00006

67. Schirmer U, Schürmann W. Preoperative administration of angiotensin-converting enzyme inhibitors. Article in German. *Anaesthesist*. 2007;56 (6):557-561. doi:10.1007/s00101-007-1177-x

68. Roshanov PS, Rochwerg B, Patel A, et al. Withholding versus continuing angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers before noncardiac surgery: an analysis of the vascular events in noncardiac surgery patients cohort evaluation prospective cohort. *Anesthesiology*. 2017;126(1):16-27. doi:10.1097/ALN.0000000000001404

69. Douketis JD, Spyropoulos AC, Kaatz S, et al; BRIDGE Investigators. Perioperative bridging anticoagulation in patients with atrial fibrillation.

N Engl J Med. 2015;373(9):823-833. doi:10.1056/NEJMoa1501035

70. Douketis JD, Spyropoulos AC, Duncan J, et al. Perioperative management of patients with atrial fibrillation receiving a direct oral anticoagulant. *JAMA Intern Med*. 2019. doi:10.1001/jamainternmed.2019.2431

71. Rich MW, Chyun DA, Skolnick AH, et al; American Heart Association Older Populations Committee of the Council on Clinical Cardiology, Council on Cardiovascular and Stroke Nursing, Council on Cardiovascular Surgery and Anesthesia, and Stroke Council; American College of Cardiology; and American Geriatrics Society. Knowledge gaps in cardiovascular care of the older adult population: a scientific statement from the American Heart Association, American College of Cardiology, and American Geriatrics Society. *Circulation*. 2016;133(21):2103-2122. doi:10.1161/CIR.0000000000000380

72. US Centers for Disease Control and Prevention. CDC/NCHS National Hospital Discharge Survey: number of all-listed procedures for discharges from short-stay hospitals, by procedure category and age: United States. Accessed March 26, 2020. https://www.cdc.gov/nchs/data/nhds/4procedures/2010pro4_numberprocedureage.pdf

73. Turrentine FE, Wang H, Simpson VB, Jones RS. Surgical risk factors, morbidity, and mortality in elderly patients. *J Am Coll Surg*. 2006;203(6):865-877. doi:10.1016/j.jamcollsurg.2006.08.026

74. Hamel MB, Henderson WG, Khuri SF, Daley J. Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery. *J Am Geriatr Soc*. 2005;53(3):424-429. doi:10.1111/j.1532-5415.2005.53159.x

75. Eveborn GW, Schirmer H, Heggelund G, Lunde P, Rasmussen K. The evolving epidemiology of valvular aortic stenosis: the Tromsø study. *Heart*. 2013;99(6):396-400. doi:10.1136/heartjnl-2012-302265

76. Berian JR, Zhou L, Hornor MA, et al. Optimizing surgical quality datasets to care for older adults: lessons from the American College of Surgeons NSQIP Geriatric Surgery Pilot. *J Am Coll Surg*. 2017;225(6):702-712.e1. doi:10.1016/j.jamcollsurg.2017.08.012

77. Mohanty S, Rosenthal RA, Russell MM, Neuman MD, Ko CY, Esnaola NF. Optimal perioperative management of the geriatric patient: a best practices guideline from the American College of Surgeons NSQIP and the American Geriatrics Society. *J Am Coll Surg*. 2016;222(5):930-947. doi:10.1016/j.jamcollsurg.2015.12.026

78. Chow WB, Rosenthal RA, Merkow RP, Ko CY, Esnaola NF; American College of Surgeons National Surgical Quality Improvement Program; American Geriatrics Society. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. *J Am Coll Surg*. 2012;215(4):453-466. doi:10.1016/j.jamcollsurg.2012.06.017

79. Gerson MC, Hurst JM, Hertzberg VS, et al. Cardiac prognosis in noncardiac geriatric surgery. *Ann Intern Med*. 1985;103(6 pt 1):832-837. doi:10.7326/0003-4819-103-6-832

80. Rich MW, Chyun DA, Skolnick AH, et al; American Heart Association Older Populations Committee of the Council on Clinical Cardiology, Council on Cardiovascular and Stroke Nursing, Council on Cardiovascular Surgery and Anesthesia, and Stroke Council; American College of Cardiology; and American Geriatrics Society. Knowledge gaps in cardiovascular care of the older adult population: a scientific statement from the American Heart Association, American College of Cardiology, and American Geriatrics Society. *J Am Coll Cardiol*. 2016;67(20):2419-2440. doi:10.1016/j.jacc.2016.03.004

81. Mullen MG, Michaels AD, Mehaffey JH, et al. Risk associated with complications and mortality after urgent surgery vs elective and emergency surgery: implications for defining "quality" and reporting outcomes for urgent surgery. *JAMA Surg*. 2017;152(8):768-774. doi:10.1001/jamasurg.2017.0918

82. Berger PB, Kleiman NS, Pencina MJ, et al; EVENT Investigators. Frequency of major noncardiac surgery and subsequent adverse events in the year after drug-eluting stent placement: results from the EVENT (Evaluation of Drug-Eluting Stents and Ischemic Events) Registry. *JACC Cardiovasc Interv*. 2010;3(9):920-927. doi:10.1016/j.jcin.2010.03.021

83. Smilowitz NR, Lorin J, Berger JS. Risks of noncardiac surgery early after percutaneous coronary intervention. *Am Heart J*. 2019;217:64-71. doi:10.1016/j.ahj.2019.07.010

84. Saia F, Belotti LM, Guastaroba P, et al. Risk of adverse cardiac and bleeding events following cardiac and noncardiac surgery in patients with coronary stent: how important is the interplay between stent type and time from stenting to surgery? *Circ Cardiovasc Qual Outcomes*. 2016;9(1):39-47. doi:10.1161/CIRCOUTCOMES.115.002155

85. Wijeysundera DN, Wijeysundera HC, Yun L, et al. Risk of elective major noncardiac surgery after coronary stent insertion: a population-based study. *Circulation*. 2012;126(11):1355-1362. doi:10.1161/CIRCULATIONAHA.112.102715

86. Rossini R, Musumeci G, Capodanno D, et al. Perioperative management of oral antiplatelet therapy and clinical outcomes in coronary stent patients undergoing surgery: results of a multicentre registry. *Thromb Haemost*. 2015;113(2):272-282. doi:10.1160/TH14-05-0436

87. Albaladejo P, Marret E, Samama CM, et al. Non-cardiac surgery in patients with coronary stents: the RECO study. *Heart*. 2011;97(19):1566-1572. doi:10.1136/hrt.2011.224519

88. Holcomb CN, Hollis RH, Graham LA, et al. Association of coronary stent indication with postoperative outcomes following noncardiac surgery. *JAMA Surg*. 2016;151(5):462-469. doi:10.1001/jamasurg.2015.4545

89. Anwaruddin S, Askari AT, Saudye H, et al. Characterization of post-operative risk associated with prior drug-eluting stent use. *JACC Cardiovasc Interv*. 2009;2(6):542-549. doi:10.1016/j.jcin.2009.03.014

90. Kałuza GL, Joseph J, Lee JR, Raizner ME, Raizner AE. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. *J Am Coll Cardiol*. 2000;35(5):1288-1294. doi:10.1016/S0735-1097(00)00521-0

91. Egholm G, Kristensen SD, Thim T, et al. Risk associated with surgery within 12 months after coronary drug-eluting stent implantation. *J Am Coll Cardiol*. 2016;68(24):2622-2632. doi:10.1016/j.jacc.2016.09.967

92. Graham MM, Sessler DI, Parlow JL, et al. Aspirin in patients with previous percutaneous coronary intervention undergoing noncardiac surgery. *Ann Intern Med*. 2018;168(4):237-244. doi:10.7326/M17-2341