### JAMA | Review

## Perioperative Cardiovascular Risk Assessment and Management for Noncardiac Surgery A Review

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**IMPORTANCE** Perioperative cardiovascular complications occur in <u>3%</u> 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 ( $\geq$ 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  $\geq 2$  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  $\beta$ -blocker use; P = .005) and mortality (3.1% vs 2.3% without  $\beta$ -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 <u>functional capacit</u>y during daily life should be performed prior to noncardiac surgery to <u>assess</u> cardiovascular <u>risk</u>. Cardiovascular <u>testing</u> is rarely indicated in patients with a low risk of major adverse cardiovascular events, but <u>may be useful</u> in patients with poor functional capacity (<4 metabolic equivalent tasks) undergoing high-risk surgery<u>if</u> test results would change therapy independent of the <u>planned surgery</u>. Perioperative medical therapy should be prescribed based on patient-specific risk.

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pproximately 17.2 million surgeries are performed annually in the US.<sup>1</sup> 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.<sup>2</sup> The incidence of perioperative cardiovascular events is related to the risk for cardiovascular events in the individual patient before surgery. In a retrospective study<sup>3</sup> 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.<sup>4,5</sup> 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 metaanalyses 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,<sup>6</sup> coronary stent,<sup>7</sup> heart failure,<sup>8-10</sup> arrhythmias,<sup>10</sup> valvular heart disease,<sup>11</sup> systemic hypertension,<sup>12</sup> and pulmonary hypertension.<sup>13,14</sup> Cardiovascular disease risk factors, such as chronic kidney disease and diabetes, are associated with up to a <u>3-fold increased risk of cardiac events.<sup>6</sup></u>

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 <u>climbing up 2 or more flights of stairs</u>. 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 $\beta$ -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 <u>2-fold</u> increased risk of perioperative complications.<sup>15</sup> Exertional chest pain, dyspnea, orthopnea, palpitations, recent syncope, and physical examination findings, such as murmurs (any diastolic or grade  $\geq$ 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.<sup>16</sup> Vascular (7.7%), thoracic (6.5%), transplant (6.2%), and general (3.9%) surgeries are associated with the highest incidence of MACE.<sup>3.6</sup> Use of minimally invasive, laparoscopic, and endovascular techniques may attenuate cardiovascular risk.<sup>17,18</sup> 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.<sup>19</sup>

Classification systems and risk scores can help estimate perioperative risk.<sup>6,20-24</sup> 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.<sup>25</sup> Cardiovascular risk scores commonly used include the Revised Cardiac Risk Index<sup>6,26</sup> and the National Surgical Quality Improvement Program perioperative myocardial infarction and cardiac arrest risk calculator and the universal surgical risk calculator (Table).<sup>21,22</sup> 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  $\geq$  2.0 mg/dL), and high-risk surgery (intraperitoneal, intrathoracic, or vascular). Patients with a Revised Cardiac Risk Index of O 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).<sup>26</sup> 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,<sup>16,18</sup> 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<sup>3.6</sup>

Level of Risk for Major Adverse Cardiovascular Events or Death

Cataract surgery Cosmetic or plastic surgery

≥1% Risk Orthopedic surgery

Otolaryngology surgery Genitourinary surgery

#### ≥3% Risk

General abdominal or intraperitoneal surgery

Neurosurgery 25% 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).<sup>27,28</sup> However, an ECG provides little benefit prior to low-risk surgery such as cataract surgery and cosmetic or plastic surgery.<sup>29-31</sup> 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.<sup>16</sup> 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.<sup>16</sup>

### 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

			National Surgical Quality Improvement Program			
			Risk calculators		Geriatric-Sensitive	
	Goldman Index of Cardiac Risk, <sup>20</sup> 1977	Revised Cardiac Risk Index, <sup>6</sup> 1999	Perioperative MI and cardiac arrest, <sup>21</sup> 2011	Universal surgical, <sup>22</sup> 2013	Perioperative Cardiac Risk Index, <sup>24</sup> 2017	Cardiovascular Risk Index, <sup>23</sup> 2019
Criteria	<ul> <li>Aged &gt;70 y (5 points)</li> <li>Had an MI within 6 mo (10 points)</li> <li>Jugular venous distention or a third heart sound on auscultation (11 points)</li> <li>≥5 PVCs/min (7 points)</li> <li>Nonsinus rhythm or PAC on preoperative ECG (7 points)</li> <li>Aortic stenosis (3 points)</li> <li>Intraperitoneal, intrathoracic, or aortic surgery (3 points)</li> <li>Any emergency surgery (4 points)</li> </ul>	<ul> <li>Ischemic heart disease (1 point)</li> <li>Cerebrovascular disease (1 point)</li> <li>History of congestive heart failure (1 point)</li> <li>Insulin therapy for diabetes (1 point)</li> <li>Serum creatinine level ≥2.0 mg/dL (1 point)</li> <li>Planned high-risk procedure (intraperitoneal, intrathoracic, or vascular surgery) (1 point)</li> </ul>	<ul> <li>Age</li> <li>ASA class</li> <li>Preoperative function</li> <li>Creatinine level</li> <li>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</li> </ul>	<ul> <li>Age group</li> <li>Sex</li> <li>ASA class</li> <li>Functional status</li> <li>Emergency case</li> <li>Steroid use for chronic condition</li> <li>Ascites within 30 d preoperatively</li> <li>System sepsis within 48 h preoperatively</li> <li>Required ventilator</li> <li>Disseminated cancer</li> <li>Diabetes</li> <li>Hypertension requiring medication</li> <li>Prior cardiac event</li> <li>Congestive heart failure within 30 d preoperatively</li> <li>Dyspnea</li> <li>Current smoker within 1 y</li> <li>History of COPD</li> <li>Dialysis</li> <li>Acute kidney failure</li> <li>BMI</li> <li>CPT-specific linear risk</li> </ul>	<ul> <li>Age</li> <li>Sex</li> <li>ASA class</li> <li>High-risk surgery</li> <li>History of heart failure</li> <li>Stroke</li> <li>Required insulin</li> <li>Diabetes</li> <li>Dialysis</li> <li>Medications for hypertension</li> <li>Current tobacco use</li> <li>History of COPD</li> <li>Functional status (partially vs totally dependent)</li> <li>Creatinine level</li> <li>Surgical category</li> <li>Dyspnea</li> <li>BUN level</li> <li>Laparoscopic surgery</li> </ul>	<ul> <li>Age ≥75 y (1 point)</li> <li>History of heart disease (1 point)</li> <li>Symptoms of angina or dyspnea (1 point)</li> <li>Hemoglobin level &lt;12 mg/dL (1 point)</li> <li>Vascular surgery (1 point)</li> <li>Emergency surgery (1 point)</li> </ul>
Score range	<ul> <li>Class I: 0-5 points (lowest risk)</li> <li>Class II: 6-12 points</li> <li>Class III: 13-25 points</li> <li>Class IV: 226 points (highest risk)</li> </ul>	<ul> <li>Class I: 0 points (lowest risk)</li> <li>Class II: 1 point</li> <li>Class III: 2 points</li> <li>Class IV: 23 points (highest risk)</li> </ul>	0%-100% (0%, lowest risk; 100%, highest risk)	0%-100% (0%, lowest risk; 100%, highest risk)	0%-100% (0%, lowest risk; 100%, highest risk)	<ul> <li>0 points (lowest risk)</li> <li>1 point</li> <li>2 points</li> <li>3 points</li> <li>&gt;3 points (highest risk)</li> </ul>
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 <sup>a</sup>	0.87 <sup>b</sup>	0.88 (Cardiac arrest or MI); 0.94 (mortality) <sup>b</sup>	0.83 (0.76 in adults aged ≥65 y) <sup>b</sup>	0.82 <sup>b</sup>

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.

<sup>b</sup> Validated using the National Surgical Quality Improvement Program database. The risk calculators are available

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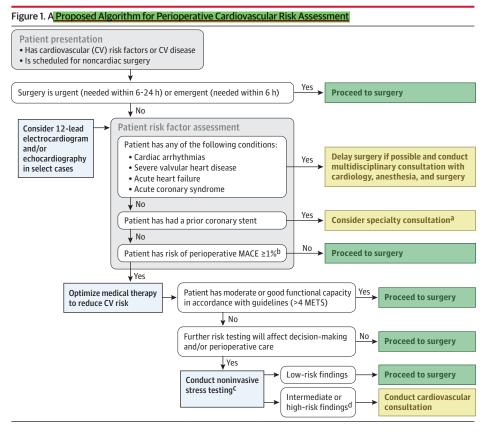
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#### The algorithm has not been validated.

MACE indicates major adverse cardiovascular events; METs metabolic equivalent tasks.

- <sup>a</sup> Perioperative considerations during consulation shown in Figure 2.
- <sup>b</sup> Risk of perioperative MACE as determined by a clinical risk calculator.
- <sup>c</sup> 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, or cardiac magnetic resonance imaging.
- <sup>d</sup> 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).<sup>32</sup> 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%.<sup>32</sup> A risk model including echocardiographic parameters was more closely associated with perioperative complications than the model including only clinical variables.<sup>32</sup> 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).<sup>33</sup> 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  $\geq$  30%; adjusted OR, 4.9 [95% CI, 1.8-14.4]; P = .008).<sup>34</sup> 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.<sup>16</sup> 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.<sup>35-37</sup> Overall, except in special circumstances, <u>routine preoperative evaluation of ventricular</u> function is not recommended.<sup>16,18,32,38,39</sup>

### Assessment of Functional Capacity and Stress Testing for Myocardial Ischemia

Poor functional capacity is associated with increased risk of perioperative complications.<sup>15</sup> 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).<sup>15</sup> 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),<sup>40</sup> 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).<sup>41</sup>

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, <u>ischemia</u> at a low workload (<<u>60%</u> of the <u>maximum predicted heart rate</u>) 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]).<sup>42</sup> 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, <u>dobuta-</u> mine stress echocardiography had an <u>excellent negative predictive</u> value (98%) for perioperative MACE.<sup>48</sup>

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),<sup>16</sup> but it is not recommended by European guidelines.<sup>18</sup> Canadian guidelines recommend against both preoperative exercise stress testing and cardiopulmonary exercise testing due to limited data supporting testing.<sup>39</sup>

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.<sup>16,42-44</sup> 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.<sup>18</sup> 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.<sup>39</sup>

### Coronary Angiography and Revascularization

Routine preoperative invasive coronary angiography is not recommended before noncardiac surgery.<sup>16</sup> 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.<sup>45</sup> 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).<sup>46</sup> However, CCTAdiagnosed CAD may overestimate risks,<sup>47</sup> and it is not currently

recommended by clinical practice guidelines for risk stratification prior to noncardiac surgery.<sup>39</sup>

Despite the established risks of CAD, <u>routine coronary revascu-</u> larization prior to surgery does not improve perioperative out-<u>comes</u>. In the Coronary Artery Revascularization Prophylaxis trial,<sup>48</sup> 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 <u>excluded</u> from the trial.<sup>48</sup> Based on these data, routine coronary revascularization is not recommended before noncardiac surgery to reduce perioperative MACE.<sup>16</sup>

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

### **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<sup>51</sup> 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%.<sup>51</sup>

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%.<sup>52</sup> 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.<sup>39</sup> 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.<sup>16</sup>

Cardiac troponin level, a sensitive marker of myocardial injury, should be measured perioperatively when signs or symptoms suggest myocardial ischemia or myocardial infarction.<sup>16</sup> Routine cardiac troponin screening should be avoided in unselected patients without symptoms of myocardial ischemia.<sup>16</sup> 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.<sup>16</sup> However, Canadian guidelines recommend postoperative cardiac troponin surveillance in high-risk individuals (eTable 2 in the Supplement).<sup>39</sup> 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  $\beta$ -blockers confers a number of potentially advantageous effects on perioperative risk. The use of  $\beta$ -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  $\beta$ -blockers with improved outcomes in high-risk patients, <sup>53,54</sup> randomized clinical trial results do not support perioperative prescription of β-blockers.<sup>55</sup> 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 allcause mortality (3.1% vs 2.3%; P = .03).<sup>56</sup>

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).<sup>57</sup> Patients **already taking** β-blockers should continue treatment during the perioperative period in the absence of bradycardia or hypotension.<sup>16</sup> 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.<sup>16</sup> Although highdose 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 <u>irreversible</u> inhibitor of <u>cyclooxygenase-1</u>, reduces platelet aggregation and thrombotic risk by <u>diminishing thromboxane A2</u> production, with associated increased risks of bleeding. The Perioperative lschemic 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.<sup>58</sup> Patients assigned to preoperative aspirin did <u>not</u> have significantly <u>lower</u> rates of <u>death</u> or myocardial <u>infarction</u> (7.0% vs 7.1% for those assigned to placebo; P = .92), but aspirin was associated with <u>increased rates of major bleeding</u> (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 <u>not recommended</u>.<sup>16</sup> although aspirin therapy may be appropriate for certain patients if ischemic risks <u>outweigh</u> the risks of bleeding.

### Lipid-Lowering Therapy and Statins

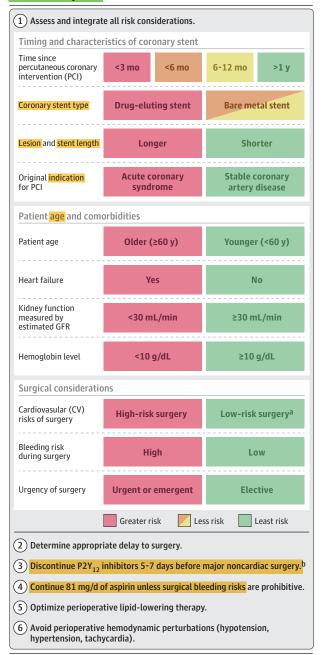
Observational data and small randomized trials suggest that lipidlowering therapy may be associated with lower perioperative cardiovascular risk. In a retrospective, propensity-matched analysis<sup>59</sup> of 204 885 patients undergoing noncardiac surgery, prescribing lipidlowering drugs during the 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 lipidlowering 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.<sup>60,61</sup>

The Lowering the Risk of Operative Complications Using Atorvastatin Loading Dose trial<sup>62</sup> 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).<sup>62</sup> Results from meta-analyses of randomized trials are inconsistent.<sup>63,64</sup> 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.<sup>16</sup>

### 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 <u>unclear</u>. In a pooled analysis of 3 small randomized trials including 188 participants, perioperative <u>continuation</u> 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]).<sup>39,65-67</sup> 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.

<sup>a</sup> Expected risk of MACE less than 1%. See also Box 3.

<sup>b</sup> 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]).<sup>68</sup>

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.<sup>39</sup> 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.<sup>18</sup> 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.<sup>16</sup> 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).

In a study of 3640 patients with atrial fibrillation taking a direct oral anticoagulant, stopping use of the oral anticoagulant <u>1 to 2 days</u> prior to a procedure with a <u>low bleeding risk</u> (eg. eye surgeries or dental procedures) and <u>2 to 4 days</u> before a procedure with a <u>high bleeding risk</u> (eg, orthopedic surgeries or vascular surgeries) <u>without peri-</u> operative <u>bridging therapy</u> was associated with <u>low</u> rates of arterial thromboembolism (0.33%).<sup>70</sup> Based on the available data, perioperative interruption of oral anticoagulation therapy in patients with atrial fibrillation appears safe and perioperative <u>bridging for patients with</u> atrial fibrillation should <u>not</u> be routinely performed. In contrast, patients with <u>mechanical mitral</u> valves and those at risk for thrombotic events with <u>mechanical aortic</u> valves should receive <u>bridging</u> 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.<sup>16,71,72</sup> 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  $\geq$ 75 years vs 4.8% for aged <75 years; adjusted hazard ratio, 1.89 [95% CI, 1.60-2.23]; P < .001).<sup>58</sup> 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.<sup>73,74</sup> 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, <sup>75</sup> 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% [ $\geq$ 80 years] vs 15.1% [<80 years]; P < .001).<sup>74</sup> 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.<sup>76</sup>

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.<sup>77,78</sup> General principles of perioperative risk stratification should be followed, with an emphasis on assessing baseline functional impairment in older adults.<sup>78,79</sup> 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.<sup>24</sup> 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.<sup>80</sup>

### 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).<sup>81</sup> 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), <sup>16</sup> 3.5% of patients or more undergo noncardiac surgery within 6 months of stent placement.<sup>82,83</sup> 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).<sup>7</sup> Ischemic risks are inversely related to the length of time between stent placement and noncardiac surgery, <sup>7,49,84,85</sup> and are directly related to prothrombotic surgical trauma and early discontinuation of dual antiplatelet therapy (Figure 2).<sup>49,85-89</sup> In some cases, clinically significant perioperative stent thrombosis and myocardial infarction can occur.<sup>90</sup>

### 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 drugeluting stent PCI or longer may be safe.<sup>16,49,83,91</sup> 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.<sup>16</sup> Shorter delays to surgery after PCI require further study.<sup>91</sup>

After coronary stent placement, continuation of single antiplatelet therapy with aspirin is recommended in the AHA/ACC guidelines,<sup>16</sup> whereas European guidelines favor individualized decisions based on bleeding and thrombotic risks.<sup>18</sup> 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]).<sup>92</sup> 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).<sup>88,89</sup>

### 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.

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## **Supplementary Online Content**

Smilowitz NR, Berger JS. Perioperative cardiovascular risk assessment and management for noncardiac surgery: a review. *JAMA*. doi:10.1001/jama.2020.7840

eMethods. Search strategy for Medline (using PubMed)
eTable 1. Common activities and corresponding metabolic equivalents (METS)
eTable 2. Comparisons of key American Heart Association (AHA) / American College of Cardiology (ACC), European Society of Cardiology (ESC), and Canadian Cardiovascular Society (CCS) perioperative guideline recommendations

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Common act	tivities and corres	ponding metabolic	equivalents (	(METS)
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Activity	METS
Walking slowly, less than 2 mph	2
Gardening, light effort, using containers	2.3
Cleaning, general house, moderate effort	3.3
Walking briskly, 3 mph	3.3
Bicycling, leisure, 5.5 mph	3.5
Yard work or gardening, moderate effort	4
Climbing stairs, slow pace	4
Bicycling, casual, less than 10 mph	4
Dancing (ballet or modern)	4.8
Snorkeling	5
Mowing the lawn with hand mower	6
Shoveling snow	6
Hiking, cross country	6
Rowing, vigorous effort	6
Tennis, doubles	6
Climbing hills, no load	6.3
Skiing, downhill	7
Carrying groceries upstairs	7.5
Calisthenics, vigorous effort (push ups, sit ups, pull-ups, etc.)	8
Swimming, crawl, slow	8
Bicycling, 12-13.9 mph, leisure, moderate effort	8
Tennis, singles	8
Running, 5 mph (12 min/mile)	8.3
Bicycling, 14-15.9 mph, racing or leisure, fast, vigorous effort	10
Running, 7.5 mph (8 min/mile)	11.5
Running, 10 mph (6 min/mile)	14.5
Running, 12 mph (5 min/mile)	19

Citation: 2011 Compendium of Physical Activities. Med Sci Sports Exerc. 2011 Aug;43(8):1575-81.

eTable 2. Comparisons of key American Heart Association (AHA) / American College of Cardiology (ACC), European Society of Cardiology (ESC), and Canadian Cardiovascular Society (CCS) perioperative guideline recommendations

	2014 ACC/AHA Guidelines *	2014 ESC/ESA Guidelines †	2016 CCS Guidelines §
Risk Prediction Tools	A validated risk-prediction tool can be useful in predicting the risk of perioperative MACE in patients undergoing non-cardiac surgery. (Class IIa; Level of Evidence: B)	Clinical risk indices are recommended to be used for peri- operative risk stratification. The NSQIP model or the Lee risk index are recommended for cardiac peri-operative risk stratification. (Class I, Level of Evidence B).	When evaluating cardiac risk, we suggest clinicians use the RCRI over the other available clinical risk prediction scores (Conditional Recommendation; Low- Quality Evidence).
12-Lead ECG	Preoperative resting 12-lead ECG is reasonable for patients with known coronary heart disease or other significant structural heart disease, except for low-risk surgery. (Class IIa, Level of Evidence B)	Pre-operative ECG is recommended for patients who have risk factors and are scheduled for intermediate or high risk surgery. (Class I, Level of Evidence C)	No Recommendation
	Preoperative resting 12-lead ECG may be considered for asymptomatic patients, except for low-risk surgery (Class IIb, Level of Evidence B)	Pre-operative ECG may be considered for patients who have no risk factors, are above 65 years of age, and are scheduled for intermediate-risk surgery OR have risk factors and are scheduled for low risk surgery. (Class IIb, Level of Evidence C)	
	Routine preoperative resting 12-lead ECG is not useful for asymptomatic patients undergoing low-risk surgical procedures (Class III, Level of Evidence B)	Routine preoperative ECG is not useful for patients who have no risk factors and are scheduled for low-risk surgery (Class III, Level of Evidence B)	
Echocardiography	It is recommended that patients with moderate or severe valvular stenosis or regurgitation undergo preoperative echocardiography if there is (1) no prior echocardiography within 1 year or (2) a significant change in clinical status (Class I, Level of Evidence C)	Rest echocardiography may be considered in patients undergoing high-risk surgery. (Class IIb Level of Evidence C)	No Recommendation
	It is reasonable for patients with dyspnea of unknown origin to undergo preoperative evaluation of LV function (Class IIa, Level of Evidence C)		
	It is reasonable for patients with HF with worsening dyspnea or other change in clinical status to undergo preoperative evaluation of LV function (Class IIa, Level of Evidence C)		
	Reassessment of LV function in clinically stable patients may be considered (Class IIb, Level of Evidence C)		
	Routine preoperative evaluation of LV function is not recommended (Class III, Level of Evidence B)	Routine echocardiography is not recommended in patients undergoing intermediate- or low- risk surgery. (Class III, Level of Evidence C)	We recommend against performing preoperative resting echocardiography to enhance perioperative cardiac risk estimation (Strong Recommendation; Low- Quality Evidence).
Exercise Stress Testing	For patients with elevated risk and excellent functional capacity, it is reasonable to forgo further exercise testing and proceed to surgery (Class IIa, Level of Evidence B)	No Recommendation	We recommend against performing preoperative exercise stress testing to enhance perioperative cardiac risk estimation (Strong Recommendation; Low- Quality Evidence).

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2014 ESC/ESA Cuidalinas #

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	2014 ACC/AHA Guidelines *	2014 ESC/ESA Guidelines †	2016 CCS Guidelines §
	For patients with elevated risk and unknown functional capacity it may be reasonable to perform exercise testing to assess for functional capacity if it will change management. (Class IIb, Level of Evidence B) Cardiopulmonary exercise testing may be considered for patients undergoing elevated risk procedure (Class IIb, Level of Evidence B) For patients with elevated risk and moderate to good functional capacity, it may be reasonable to forgo further exercise testing and proceed to surgery (Class IIb, Level of Evidence B) For patients with elevated risk and poor or unknown functional capacity it may be reasonable to perform exercise testing with cardiac imaging to assess for myocardial ischemia (Class Iib, Level of Evidence C) Routine screening with noninvasive stress testing is not useful for low-risk noncardiac surgery (Class III, Level of Evidence B)		We recommend against performing preoperative CPET to enhance perioperative cardiac risk estimation (Strong Recommendation; Low- Quality Evidence).
Pharmacological stress testing with imaging	It is reasonable for patients at elevated risk for noncardiac surgery with poor functional capacity to undergo either DSE or MPI if it will change management (Class IIa, Level of Evidence B)	Imaging stress testing is recommended before high-risk surgery in patients with more than two clinical risk factors and poor functional capacity (<4 METs). (Class I, Level of Evidence C)	We recommend against performing preoperative pharmacological stress echocardiography to enhance perioperative cardiac risk estimation (Strong Recommendation; Low-Quality Evidence).
		Imaging stress testing may be considered before high- or intermediate-risk surgery in patients with one or two clinical risk factors and poor functional capacity (<4 METs). (Class IIb, Level of Evidence C)	We recommend against performing preoperative pharmacological stress radionuclide imaging to enhance perioperative cardiac risk estimation (Strong Recommendation; Moderate-Quality Evidence).
	Routine screening with noninvasive stress testing is not useful for low-risk noncardiac surgery (Class III, Level of Evidence B)	Imaging stress testing is not recommended before low-risk surgery, regardless of the patient's clinical risk. (Class III, Level of Evidence C)	
Coronary Angiography	Routine preoperative coronary angiography is not recommended	Indications for pre-operative coronary angiography and revascularization are similar to those for the non-surgical setting. (Class I, Level of Evidence C)	No Recommendation
		Pre-operative angiography is not recommended in cardiac- stable patients undergoing low-risk surgery. (Class III Level of Evidence C)	

	2014 ACC/AHA Guidelines *	2014 ESC/ESA Guidelines †	2016 CCS Guidelines §
Coronary CT Angiography	No Recommendation	No Recommendation	We recommend against performing preoperative CCTA to enhance perioperative cardiac risk estimation (Strong Recommendation; Moderate- Quality Evidence).
Coronary Revascularization	Revascularization before noncardiac surgery is recommended when indicated by existing CPGs (Class I, Level of Evidence C)	Performance of myocardial revascularization is recommended according to the applicable guidelines for management in stable coronary artery disease.	No Recommendation
	Coronary revascularization is not recommended before noncardiac surgery exclusively to reduce perioperative cardiac events. (Class III, Level of Evidence B)	Routine prophylactic myocardial revascularization before low and intermediate-risk surgery in patinets with proven IHD is not recommended. (Class III, Level of Evidence B) Prophylactic myocardial revascularization before high-risk surgery may be considered, depending on the extent of a stress- induced perfusion defect. (Class IIb, Level of Evidnece B)	For patients with stable coronary artery disease who undergo noncardiac surgery, we recommend against preoperative prophylactic coronary revascularization (Strong Recommendation; Low-Quality Evidence).
Timing of Surgery after PCI	Elective noncardiac surgery should be delayed 14 days after balloon angioplasty (Class I, Level of Evidence: C) and 30 days after BMS implantation. (Class I, Level of Evidence C)	Consideration should be given to performing non-urgent, non- cardiac surgery in patients with recent BMS implantation after a minimum of 4 weeks and ideally 3 months following the intervention. In patients who have had recent balloon angioplasty, surgeons should consider postponing non-cardiac surgery until at least 2 weeks after the intervention. (Class IIa, Level of Evidence B).	
	Noncardiac surgery should optimally be delayed 365 d after DES implantation. (Class I, Level of Evidence B)	Consideration should be given to performing non-urgent, non- cardiac surgery in patients who have had recent DES implantation no sooner than 12 months following the intervention. This delay may be reduced to 6 months for the new- generation DES. (Class IIa, Level of Evidence B)	
	Elective noncardiac surgery after DES implantation may be considered after 180 days. (Class IIb, Level of Evidence B)	No recommendation	
Biomarker Assessment: BNP	No recommendation	NT-proBNP and BNP measurements may be considered for obtaining independent prognostic information for peri- operative and late cardiac events in high-risk patients (Class IIb, Level of Evidence B)	We recommend measuring NT-proBNP or BNP 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 ≥1 (Strong Recommendation; Moderate-Quality Evidence).
Biomarker Assessment: Troponin	Measurement of troponin levels is recommended in the setting of signs or symptoms suggestive of myocardial ischemia or MI. (Class I, Level of Evidence A)	No recommendation	No recommendation

	2014 ACC/AHA Guidelines *	2014 ESC/ESA Guidelines †	2016 CCS Guidelines §
	The usefulness of postoperative screening with troponin levels in patients at high risk for perioperative MI, but without signs or symptoms suggestive of myocardial ischemia or MI, is uncertain in the absence of established risks and benefits of a defined management strategy. (Class IIb, Level of Evidence B)	Assessment of cardiac troponins in high risk patients both before and 48-72 hours after major surgery may be considered (Class IIb, Level of Evidence B)	We recommend obtaining daily troponin measurements for 48-72 hours after noncardiac surgery in patients with a baseline risk > 5% for cardiovascular death or nonfatal myocardial infarction at 30 days after surgery (Strong Recommendation; Moderate-Quality Evidence).
	Routine postoperative screening with troponin levels in unselected patients without signs or symptoms suggestive of myocardial ischemia or MI is not useful for guiding perioperative management (Class III, Level of Evidence B)	Universal pre-operative routine biomarker sampling for risk statification and to prevent cardiac events is not recommended (Class III, Level of Evidence C)	
Perioperative beta- blocker therapy	Continue beta blockers in patients who are on beta blockers chronically (Class I, Level of Evidence B)	Peri-operative continuation of beta- blockers is recommended in patients currently receiving this medication. (Class I, Level of Evidence B)	Among patients taking a b-blocker chronically, we suggest to continue the b-blocker during the periop- erative period (Conditional Recommendation; Low-Quality Evidence).
	Guide management of beta blockers after surgery by clinical circumstances (Class IIa, Level of Evidence B)	No recommendation	No recommendation
	In patients with intermediate- or high-risk preoperative tests for myocardial ischemia, it may be reasonable to begin beta blockers (Class IIB, Level of Evidence C)	Pre-operative initiation of beta- blockers may be considered in patients who have known IHD or myocardial ischemia. (Class IIb, Level of Evidence B)	
	In patients with ≥3 RCRI factors, it may be reasonable to begin beta blockers before surgery (Class IIB, Level of Evidence B)	Pre-operative initiation of beta- blockers may be considered in patients scheduled for high-risk surgery and who have 2 clinical risk factors or ASA status ≥3. (Class IIb, Level of Evidence B)	
	Initiating beta blockers in the perioperative setting as an approach to reducing perioperative risk is of uncertain benefit in those with a long-term indication but no other RCRI risk factors (Class IIb, Level of Evidence B)	No recommendation	
	iIt may be reasonable to begin perioperative beta blockers long enough in advance to assess safety and tolerability, preferably >1 d before surgery. (Class IIb, Level of Evidence B)		
	No recommendation	Initiation of peri-operative high-dose beta-blockers without titration is not recommended. (Class III, Level of Evidence C)	
		Pre-operative initiation of beta- blockers is not recommended in patients scheduled for low-risk surgery. (Class III, Level of Evidence B)	
	Beta-blocker therapy should not be started on the day of surgery (Class III, Level of Evidence B)	No recommendation	We recommend against b-blocker initiation within 24 hours before noncardiac surgery (Strong Recommendation; High-Quality Evidence).

	2014 ACC/AHA Guidelines *	2014 ESC/ESA Guidelines †	2016 CCS Guidelines §
Statins	Continue statins in patients currently taking statins (class I, LOE B)	Peri-operative continuation of statins is recommended, favouring statins with a long half-life or extended-release formulation. (Class I, Level of Evidence C)	We recommend continuing statin therapy perioper- atively in patients who are receiving chronic statin therapy (Strong Recommendation; Moderate-Quality Evidence).
	Perioperative initiation of statin use is reasonable in patients undergoing vascular surgery (Class IIa, Level of Evidence B)	Pre-operative initiation of statin therapy should be considered in patients undergoing vascular surgery, ideally at least 2 weeks before surgery. (Class IIa, Level of Evidence B)	No recommendation
	Perioperative initiation of statins may be considered in patients with a clinical risk factor who are undergoing elevated-risk procedures (Class IIb, Level of Evidence C)	No recommendation	
ACE inhibitors	Continuation of ACE inhibitors or ARBs is reasonable perioperatively (Class IIa, Level of Evidence B)	Continuation of ACEIs or ARBs, under close monitoring, should be considered during non-cardiac surgery in stable patients with heart failure and LV systolic dysfunction. Initiation of ACEIs or ARBs should be considered at least 1 week before surgery. (Class IIa, Level of Evidence C)	No recommendation
	No Recommendation	Transient discontinuation of ACEIs or ARBs before non- cardiac surgery in hypertensive patients should be considered. (Class IIa, Level of Evidence C)	We recommend withholding ACEI/ARB starting 24 hours before noncardiac surgery in patients treated chronically with an ACEI/ARB (Strong Recommendation; Low-Quality Evidence).
	If ACE inhibitors or ARBs are held before surgery, it is reasonable to restart as soon as clinically feasible postoperatively (Class IIa, Level of Evidence C)	No recommendation	No recommendation
<b>Anti-platelets</b>	Continue DAPT in patients undergoing urgent noncardiac surgery during the first 4 to 6 wk after BMS or DES implantation, unless the risk of bleeding outweighs the benefit of stent thrombosis prevention (Class I, Level of Evidence C)	It is recommended that aspirin be continued for 4 weeks after BMS implantation and for 3–12 months after DES implantation, unless the risk of life-threatening surgical bleeding on aspirin is unacceptably high. (Class I, Level of Evidence C)	No recommendation
		Continuation of P2Y12 inhibitor treatment should be considered for 4 weeks after BMS implantation and for 3–12 months after DES implantation, unless the risk of life- threatening surgical bleeding on this agent is unacceptably high. (Class IIa, Level of Evidence C)	
	In patients with stents undergoing surgery that requires discontinuation of P2Y12 inhibitors, continue aspirin and restart the P2Y12 platelet receptor–inhibitor as soon as possible after surgery. (Class I, Level of Evidence C)	In patients treated with P2Y12 inhibitors, who need to undergo surgery, postponing surgery for at least 5 days after cessation of ticagrelor and clopidogrel—and for 7 days in the case of prasugrel—if clinically feasible, should be considered unless the patient is at high risk of an ischaemic event. (Class IIa, Level of Evidence C)	

2014 ACC/AHA Guidelines *	2014 ESC/ESA Guidelines †	2016 CCS Guidelines §
In patients undergoing nonemergency/nonurgent noncardiac surgery without prior coronary stenting, it may be reasonable to continue aspirin when the risk of increased cardiac events outweighs the risk of increased bleeding (Class IIb, Level of Evidence B) Initiation or continuation of aspirin is not beneficial in patients undergoing elective noncardiac noncarotid surgery who have not had previous coronary stenting. (Class III, Level of Evidence B)	Continuation of aspirin, in patients previously thus treated, may be considered in the peri-operative period, and should be based on an individual decision that depends on the peri- operative bleeding risk, weighed against the risk of thrombotic complications. (Class IIb, Level of Evidence B) No recommendation	We recommend continuation of ASA to prevent perioperative cardiac events in patients with a recent coronary artery stent and patients who undergo carotid endarterectomy (Strong Recommendation; High-Quality Evidence). We recommend against initiation of ASA for the prevention of perioperative cardiac events (Strong Recommendation; High-Quality Evidence).

Strength of Recommendation:

Class I: treatment should be performed (Green)

Class IIa: it is reasonable to perform treatment (Yellow)

Class IIb: treatment may be considered (Orange)

Class III: treatment is not useful and may be harmful (Red)

Level of Evidence

A: Data derived from multiple randomized clinical trials or meta-analyses

B: Data derived from a single randomized trial or non-randomized studies

C: Recommendation based on expert opinion, case studies, or current standard of care) provided

### **Citations:**

\* Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64(22):e77-e137.

† Kristensen SD, Knuuti J, Saraste A, et al. 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.

§ 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.