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PREOPERATIVE EVALUATION (BJ SWEITZER, SECTION EDITOR)

Preoperative Cardiac Evaluation of the Patient Undergoing Noncardiac Surgery

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Abstract

Purpose of Review This review summarizes selected recent evidence on cardiovascular evaluation before major noncardiac surgery.

Recent Findings Based on recent studies and advancements in coronary stent technology, guidelines now indicate that major noncardiac surgery may be performed sooner (i.e., 3 to 6 months) after drug eluting stent insertion. In addition, contemporary research has emphasized the importance of heart failure, atrial fibrillation, and recent stroke (i.e., prior 9 months) as determinants of perioperative cardiac risk. Biomarkers are taking on increasing importance in preoperative cardiac risk stratification, with the most promising tests being natriuretic peptides and high-sensitivity troponins. These biomarkers may improve the accuracy of risk prediction beyond that based on clinical risk factors alone. Finally, recent data suggest that temporary preoperative discontinuation of chronic aspirin, angiotensin-converting enzyme inhibitor, or angiotensin receptor blocker therapy is preferred in most patients, while bridging therapy is generally not required when antithrombotic therapy is temporarily discontinued before surgery.

Summary Evidence pertaining to preoperative cardiac evaluation continues to evolve, with increasing emphasis on risk stratification using biomarkers, and more individualized perioperative management of chronic cardiovascular medications.

Keywords Preoperative assessment · Risk stratification · Noncardiac surgery · Cardiac disease · Coronary artery disease · Myocardial infarction

Introduction

Cardiovascular disease accounts for one in seven deaths worldwide, with a higher burden in high income countries, where it accounts for one in three deaths [1]. It is therefore an important contributor to perioperative morbidity and mortality for the 300 million surgeries performed globally each year [2]. If defined as myocardial infarction (MI), cardiac arrest, or death, major adverse cardiac events (MACE) occur in more than 3% of patients having major noncardiac surgery [3•, 4]. These complications are associated with elevated postoperative mortality, duration of hospitalization, and healthcare costs [5]. This review will discuss *selected* recent evidence on cardiovascular evaluation before major noncardiac surgery and will principally focus on elective procedures, where there is sufficient time for interventions and possible preoperative optimization.

This article is part of the Topical Collection on *Preoperative Evaluation*

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Preoperative Evaluation

Thorough preoperative evaluation can help better define perioperative risk, identify the need for further investigations or modification of the surgical plan, facilitate individualized anesthesia management, and specify appropriate postoperative disposition (i.e., need for critical care monitoring). Inadequate preoperative assessment is associated with increased length of stay, perioperative complications, and in-hospital mortality [6, 7].

Coronary Artery Disease

Ascertainment of preexisting coronary artery disease (CAD) is an important component of preoperative evaluation. While CAD afflicts about 6% of American adults [8], its prevalence among surgical patients varies based on the procedure and extent of diagnostic screening. For example, more than 60% of patients having major vascular surgery have significant CAD when assessed using coronary angiography [9, 10]. The importance of identifying CAD largely relates to it being a predictor of postoperative death and myocardial infarction [4, 11, 12]. The two large Vascular Events in Noncardiac Surgery Patients Cohort Evaluation (VISION) prospective cohort studies showed that this association between CAD and postoperative mortality was particularly elevated with recent high-risk CAD, which was defined as a MI, acute coronary syndrome, or Canadian Cardiovascular Society Class III or IV angina within 6 months before surgery [4, 12].

Research also highlights the importance of CAD as a risk factor for a recently described postoperative complication, namely myocardial injury after noncardiac surgery (MINS). This entity has been defined as a prognostically significant postoperative elevation in troponin concentrations with a *presumed* ischemic etiology (i.e., no definitive evidence of a nonischemic cause). Prognostically significant troponin elevation has been defined as a high-sensitivity (i.e., fifth generation) troponin T concentration > 20 ng/L with associated absolute change > 5 ng/L, a high-sensitivity troponin T concentration > 65 ng/L, or a fourth-generation troponin T concentration > 20 ng/L [13••]. Important myocardial injury occurs in at least 12% of patients following noncardiac surgery [4, 12, 14–16]. The two VISION studies [4, 12], as well as several other observational studies [14–16], found an association between increasing postoperative troponin concentrations and elevated mortality. This association persists even in the absence of a formal diagnosis of MI based on consensus-based criteria. Indeed, almost 80% of MINS episodes do not meet current definition for MI, yet remain prognostically important, even when seemingly asymptomatic [14–16]. The underlying mechanisms explaining this association between postoperative troponin elevations and mortality remain to be fully elucidated. While MINS may simply be a marker of unrecognized or under-treated CAD [4], it is noteworthy that deaths due to noncardiac causes appear to occur at least as frequently as cardiac-related deaths following MINS episodes [4, 15].

Timing of Surgery Following Prior MI or Percutaneous Coronary Intervention

Important characteristics of preoperative CAD that impact on the risk of elective noncardiac surgery are the timing of any prior MI and previous percutaneous coronary intervention (PCI) with coronary stent placement. The risk of undergoing noncardiac surgery is inversely related to the length of time since the prior MI or stent placement. The timing of noncardiac surgery after a recent MI was evaluated in a population-based study of 563,842 patients who underwent major noncardiac surgery in California. The data showed that the risks of 30-day postoperative MI and mortality were unacceptably elevated if surgery occurred within one to 30 days (32.8% MI risk, 14.2% mortality risk) or 31 to 60 days (18.7% MI risk, 11.5% mortality risk) after a prior MI [17]. This relationship persisted even after multivariable regression risk adjustment. These data form the basis for the recommendation by the current American College of Cardiology (ACC) and American Heart Association (AHA) perioperative guidelines to delay nonurgent surgery for at least 60 days after a recent MI [18••].

Decision-making is more complicated if a patient has undergone recent PCI with placement of either a bare-metal stent (BMS) or drug-eluting stent (DES). The main clinical implication relates to the requisite minimum duration of dual antiplatelet therapy (DAPT) with aspirin and a $P2Y_{12}$ inhibitor (e.g., clopidogrel). If DAPT is interrupted before adequate re-endothelialization of the stent has occurred, potentially catastrophic stent thrombosis can occur, particularly within the context of the pro-thrombotic state triggered by surgical stress. The recommended minimum duration of DAPT before elective noncardiac surgery continues to evolve. Further, these recommendations are influenced by the type of stent, indications for stent placement, and risk of perioperative bleeding. The recommendations were revised in the 2014 ACC/AHA perioperative cardiovascular management guidelines [18••] and then further modified in the 2016 ACC/AHA focused guideline on DAPT [19••]. Several large cohort studies showed safety with shorter durations of DAPT [20–22], and recent systematic reviews identified important risks with long-term DAPT, specifically increased bleeding events [23–25]. Further, newer generation DES appear to tolerate shorter durations of DAPT. The 2016 ACC/AHA focused guideline on DAPT has used these newer data to inform its recommendations on the minimum duration of DAPT before elective noncardiac surgery [19••]. The 2016 guidelines recommend that elective noncardiac surgery should be delayed for at least 30 days after BMS implantation and *ideally* at least 6 months after DES implantation. When surgery requiring temporary discontinuation of $P2Y_{12}$ inhibitor therapy is performed, patients should maintain aspirin therapy. In some circumstances, elective noncardiac surgery can be performed with temporary discontinuation of $P2Y_{12}$ inhibitor therapy during the window from 3 to 6 months after DES implantation (particularly new generation stents)—provided that the risk of further delaying surgery is judged to be greater than the potential risk of stent thrombosis. The original *indication* for DES implantation

should likely inform judgments on the safety of performing elective noncardiac surgery during this time window. A retrospective cohort study of about 26,600 patients at Veterans Affairs hospitals found that risk of noncardiac surgery early after stent implantation were particularly elevated when PCI had been performed for acute MI, but not when PCI had been performed for unstable angina or nonacute coronary syndrome indications (e.g., stable ischemic heart disease) [26]. Thus, it may be particularly important to delay noncardiac surgery for at least 6 months when DES implantation is performed to treat acute MI. The evidence and recommendations guiding DAPT duration continue to evolve, and appropriate care of a patient on DAPT with coronary stents should involve a multidisciplinary approach.

Heart Failure

Heart failure (HF) is the sequelae of a broad array of underlying pathology. In general, it is classified by the presence of associated signs or symptoms (i.e., compensated versus decompensated), as well as the presence and severity of ventricular systolic dysfunction. Most perioperative research has focused on HF that is symptomatic or associated with systolic dysfunction. *Symptomatic* preexisting HF is a well-established risk factor for mortality and morbidity after noncardiac surgery [27, 28]. For example, a recent matched cohort study of about 10,000 patients in the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database found that new or worsening symptomatic HF within 30 days prior to noncardiac surgery was associated with an increased risk of mortality (RR 2.08) and postoperative complications (OR 1.54) [29]. In addition, a Canadian population-based study found that both ischemic and nonischemic HF were associated with higher risks of postoperative 30-day mortality than CAD [30]. While there is evidence that the risk of noncardiac surgery is increased considerably when the left ventricular ejection fraction (EF) drops below 30% [31], the prognostic significance of *asymptomatic* systolic dysfunction remains uncertain. Accordingly, routine evaluation of left ventricular function in the absence of symptoms or recent change in functional status is discouraged in the 2014 ACC/AHA perioperative cardiovascular evaluation guidelines [18••].

While systolic dysfunction has received most of the focus when classifying HF, there has been increasing recognition of a distinct HF type characterized by *diastolic* dysfunction. The nomenclature continues to evolve, with the current proposed term being HF with preserved ejection fraction (HFpEF) [32], which comprises at least half of all patients with HF [33]. Based on the results of an individual patient meta-analysis, patients with HFpEF have lower risks of mortality than HF patients with systolic dysfunction (adjusted hazard ratio 0.68), but their absolute risk of mortality still remains high [34]. Notably, death from noncardiovascular causes appears to occur more common than in individuals with HFpEF than those with reduced EF [35]. While HFpEF is being recognized as an important clinical entity in the nonoperative setting, it remains to be adequately studied in the perioperative setting. Nonetheless, a recent systematic review of 13 studies (3876 patients) in noncardiac surgery found that diastolic dysfunction identified by preoperative echocardiography was associated with twice the odds of MACE (pooled adjusted odds ratio 2.03) [36•].

Arrhythmias

Historically, atrial arrhythmias have not received much focus in preoperative cardiac risk assessment for noncardiac surgery; however, new evidence challenges this position. In a Canadian population-based cohort study, the unadjusted 30-day mortality after noncardiac surgery was 5.7% for patients with preexisting atrial fibrillation (AF) versus 2.3% for patients with CAD. This association persisted even after risk adjustment (adjusted odds ratio 1.69) or restriction to the subgroup of minor surgical procedures (adjusted odds ratio 1.82) [30]. In the VISION study, preexisting AF was associated with an elevated risk (adjusted odds ratio 1.58) of cardiovascular events (defined as postoperative stroke, cardiovascular death, MINS, HF, or nonfatal cardiac arrest) [37], but not associated with postoperative mortality [4]. Preexisting chronic AF was also associated with a doubling in the risk of perioperative stroke in a population-based cohort study from California [38]. Among patients with preexisting chronic AF, the $CHADS_2$ index, which was specifically designed for estimating nonoperative thromboembolic risk for nonvalvular AF, demonstrated modest discrimination (area under receiver-operating-characteristic curve of 0.67) when predicting perioperative stroke or death [37].

A critical component for perioperative management for patients with chronic AF is the appropriate management of antithrombotic medication, with the goals of minimizing the risk of stroke while mitigating the risk of major perioperative bleeding. Guidelines have been published pertaining to this issue, an example being the evidence-based American College of Chest Physicians (ACCP) guidelines [39•] that recommend bridging anticoagulation with low molecular weight heparin during temporary interruption of vitamin K antagonist therapy (e.g., warfarin) in the perioperative period for high-risk individuals (i.e., $CHADS_2$ index ≥ 5), and intermediate risk individuals when benefit outweighs the risk, but not for low-risk individuals [39•]. Nevertheless, the efficacy of bridging therapy has been challenged by the Bridging Anticoagulation in Patients Who Require Temporary Interruption of Warfarin Therapy for an Elective Invasive Procedure and Surgery (BRIDGE) trial. In this multicenter randomized controlled trial with 1884 participants, placebo was noninferior to bridging therapy with low-

molecular weight heparin during perioperative interruption of warfarin therapy. Further, bridging therapy led to an increased rate of major bleeding [40•]. These findings were replicated in a substudy of the Randomized Evaluation of Long-Term Anticoagulation Therapy trial that compared dabigatran versus warfarin in patients with chronic AF [41]. In this nested cohort substudy of patients requiring temporary interruption of warfarin or dabigatran therapy for surgical procedures, bridging therapy was associated with an increased risk for major bleeding, regardless of whether dabigatran or warfarin was being interrupted. Current guidelines do not yet address whether or how bridging therapy should be applied in patients on newer generation direct oral anticoagulants (DOAC); however, bridging theoretically provides even less benefit for these patients since DOACs all have shorter half-lives. A more in-depth discussion of these issues is presented in a recent review [42].

Cerebrovascular Disease

In patients with CAD, atherosclerosis of other vascular beds, such as cerebrovascular disease (CVD), should always be suspected. CVD is a significant risk for perioperative stroke [43, 44], MACE [11], and death [4] after major noncardiac surgery. Furthermore, timing of surgery after a stroke can influence perioperative risk. A nationwide Danish cohort study showed that the risks of MACE (odds ratio 14) and mortality (odds ratio 3) were highest when elective noncardiac surgery occurred within the first 3 months after an ischemic stroke. This elevated risk appeared to level off after 9 months since the prior stroke [45••]. Not all surgical procedures can be safely delayed several months. Hence, Christiansen et al. investigated the impact of timing of emergency noncardiac surgery following a prior stroke. As with elective surgery, the risks of perioperative mortality and MACE for emergency surgery remained elevated for 9 months after a previous stroke. Nonetheless, patients experienced a lower rate of MACE (21%) when they had emergency surgery performed within 3 days after an ischemic stroke, as compared to within 4 to 14 days (29%, $p = 0.03$) [46•]. The authors hypothesized that impaired cerebral autoregulation was the underlying basis for this increased perioperative vulnerability once 72 h had elapsed after a stroke. Specifically, cerebral autoregulation worsens during the first 5 days after an ischemic stroke, after which recovery occurs over approximately 3 months [47].

Preoperative Physical Examination

Recent research has highlighted the prognostic importance of preoperative heart rate and blood pressure in patients undergoing major noncardiac surgery. In a population-based cohort study of about 250,000 patients having elective noncardiac surgery in the United Kingdom (UK), preoperative ambulatory blood pressure was a predictor of 30-day postoperative mortality. Interestingly, systolic (< 119 mmHg) and diastolic (< 63 mmHg) hypotension was associated with elevated mortality only within the subgroup of patients aged ≥ 65 years. Conversely, diastolic hypertension (> 84 mmHg), but not systolic hypertension, was associated with increased mortality across all age groups [48•]. Furthermore, a substudy of the VISION cohort demonstrated that preoperative pulse pressure, independent of systolic blood pressure, was a predictor of postoperative myocardial injury [49•].

There is also mounting evidence demonstrating that hypotension during noncardiac surgery is associated with increased risk of a range of postoperative complications, including death, myocardial injury, and acute kidney injury [50–55]. Thus, clear documentation of the baseline blood pressure can theoretically guide intraoperative hemodynamic management within the individual patient's normal physiologic equilibrium (i.e., range of autoregulation), with the aim of maintaining adequate end organ perfusion. While there is a sound physiologic basis for the traditional approach of using a threshold for treatment based on a relative change from the baseline blood pressure, this approach has recently been challenged. Several large retrospective studies have demonstrated that an absolute mean arterial blood pressure (MAP) below specific thresholds (< 49–65 mmHg) is a strong predictor of poor outcomes [50, 52–55]. By comparison, Salmasi et al. compared hypotension defined as MAP less than 65 mmHg versus hypotension defined by 20% reduction from baseline blood pressure and found no difference in their strengths of association with myocardial injury or acute kidney injury in a retrospective cohort study of 57,315 patients undergoing noncardiac surgery [50]. Given that these studies were largely retrospective observational studies, caution should be exercised when extrapolating these findings to guide individual patient care.

Certainly, there is a need for randomized trials addressing optimal blood pressure management strategies for intermediate-to-high risk patients undergoing noncardiac surgery. A recent example is a randomized trial that compared intensive blood pressure maintenance to conventional care in 292 patients (≥ 50 years) having major noncardiac surgery and at risk of acute kidney injury [56••]. In the intervention arm, patients received norepinephrine to maintain a systolic blood pressure within 10% of their baseline (preoperative value documented during the preoperative anesthetic consultation), while patients in the control arm received ephedrine (6 mg boluses up to total of 60 mg—after which norepinephrine could be administered) if the systolic blood pressure fell below 80 mmHg or more than 40% from baseline. The treatment arm experienced a statistically and clinically significant reduction (relative risk 0.73, absolute risk difference—14%) in the primary outcome (composite of single organ dysfunction or systemic inflammatory response syndrome) [56••]. While this

trial was relatively small and should therefore be viewed as hypothesis-generating, these results highlight the need for further investigation of the potential benefits of aggressive perioperative blood pressure management.

Recent evidence has also identified an association between preoperative heart rate and increased cardiovascular outcomes. In a secondary analysis of 15,087 patients in the VISION cohort study, a preoperative heart rate > 96 beats/min was associated with elevated risks of postoperative MINS, MI, and mortality [57•]. The study defined preoperative heart rate as the last value prior to induction of anesthesia; thus, this "baseline" heart rate may not be representative of a patient's baseline heart rate in an ambulatory setting such as a preoperative evaluation clinic. Nonetheless, this association between an elevated heart rate and perioperative cardiac risk is consistent with findings in a substudy of the PeriOperative ISchemic Evaluation (POISE) 1 trial [58]. An important unresolved issue pertains to the mechanisms underlying this association between elevated preoperative heart rate and perioperative risk. While traditional teaching has focused on heart rate being a major determinant of the balance between myocardial oxygen demand and supply, recent research suggests that an elevated preoperative heart rate might also be marker for subclinical HF and autonomic dysfunction [59].

Assessment of Overall Perioperative Risk

Accurate identification of the high-risk patient facilitates better communication of risk to the patient and surgeon—which is an essential requirement of informed consent—and may identify circumstances where alternative nonoperative or less invasive interventions should be explored. Furthermore, identification of high-risk surgical patients facilitates targeted use of further investigation, therapeutic interventions, and enhanced postoperative monitoring.

Clinical Predictive Risk Indices

Given the theoretical benefits of accurate estimation of perioperative cardiac risk, a large body of research has focused on developing bedside clinical risk indices, beginning with the publication of the Goldman Cardiac Risk Index in 1977 [60]. These risk indices typically incorporate both patient factors (e.g., age, comorbidity, functional capacity) and procedural factors (i.e., length and complexity of surgery) that relate to perioperative risk. The 2014 ACC/AHA perioperative guidelines recommend the use of either of two clinical risk indices, namely the Revised Cardiac Risk Index (RCRI) and NSQIP risk calculator [18••]. The RCRI is a widely used bedside clinical risk index to estimate the perioperative risk of MACE. It has important advantages, including its relative simplicity and consistent moderate discriminative performance in extensive external validation [61]. Conversely, it estimates risk poorly in patients having vascular surgery [11, 61, 62•] and does not estimate an individual's *absolute* risk well [63]. Furthermore, the predictive performance and definition of two of its components (i.e., renal insufficiency, diabetes mellitus) have been questioned [62•, 64]. In fact, derivation of a further revised index is currently underway [65]. Gupta et al. developed an entirely separate predictive index using the NSQIP database, with the outcomes of interest being MI (defined as ST-segment changes or troponin elevation exceeding three times normal in patients with symptoms of ischemia) or cardiac arrest. This composite outcome of MI or cardiac arrest was termed MICA [62•]. The investigators validated their model in a sequential cohort using the same database and showed excellent discrimination (area under receiver-operating-characteristic curve of 0.87). The NSQIP risk calculator also uses a web-based platform (http://www.surgicalriskcalculator.com/miorcardiacarrest) that allowed for a more complex model to be used. Despite the excellent discrimination of this tool, several weaknesses merit some discussion. First, routine postoperative troponin monitoring was not implemented among patients in the NSQIP database, which means that up to 70% of all postoperative MIs may have been missed [13••]. In addition to underestimating the absolute risk of MI, the absence of routine troponin monitoring may bias the prognostic importance of preoperative factors that influence clinicians' decisions to implement postoperative troponin monitoring. The underestimation of MI rates in the NSQIP database is highlighted by the presence of more postoperative cardiac arrests ($n = 902$) than postoperative MIs ($n = 357$) in the derivation cohort. Second, the derivation dataset included patients undergoing cardiac surgery, albeit only 0.3% of the cohort. Third, the MICA risk calculator has yet to be externally validated. Nonetheless, despite the above limitations, the MICA risk calculator is a relatively simple approach to estimate cardiac risk with excellent discrimination. Further, the risk model has been incorporated into the ACS NSQIP surgical risk calculator that calculates the risks of MICA, mortality, and eight additional serious complications (e.g., surgical site infection, pneumonia) [66].

Functional Capacity Assessment

A key component of the overall assessment of perioperative cardiovascular risk is preoperative cardiopulmonary fitness or functional capacity. Indeed, the ACC/AHA perioperative guidelines recommend that patients proceed directly to major elective noncardiac surgery if they are deemed capable of four or more metabolic equivalents (METs) of activity [18••]. This link between poor functional capacity and perioperative cardiac risk is based on older studies of preoperative exercise testing [67, 68] and more recent studies of preoperative

cardiopulmonary exercise testing (CPET) [69, 70•]. Nonetheless, typical preoperative assessment does not involve objective measurement of functional capacity, but rather physicians making a subjective judgment based on patients' self-reported history. Prior research suggests that subjectively assessed functional capacity has poor agreement with validated measures of functional capacity [71] and relatively poor accuracy when predicting death or complications after surgery [72, 73]. A large international prospective cohort study is currently comparing the utility of several different methods of assessing functional capacity before major noncardiac surgery and should provide further insights in this area [74•].

Specialized Preoperative Investigations

Coronary Artery Imaging

While most previous research on specialized preoperative cardiac testing has focused on stress testing or echocardiography, a recent prospective cohort study evaluated the role of routine preoperative coronary computed tomographic angiography (CTA) for improving prediction of postoperative MACE in patients undergoing major noncardiac surgery. In the Coronary CTA VISION study of 955 patients with known atherosclerotic disease, or risk factors for atherosclerotic disease, having major noncardiac surgery [75••], extensive obstructive coronary disease was present in 15% of participants and associated with elevated risks of postoperative MACE (adjusted odds ratio 3.8). Extensive disease was defined as (i) ≥ 50% stenosis in the proximal left anterior descending artery plus one other coronary artery, (ii) ≥ 50% stenosis in three coronary arteries, or (iii) ≥ 50% stenosis in the left main coronary artery. Nonetheless, routine use of preoperative coronary CTA was five times more likely to result in inappropriate overestimation of risk in patients who did not experience postoperative MACE.

Preoperative Biomarker Testing

The myocardium releases brain natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT pro-BNP) in response to ischemia or stretch [76]. Elevated *preoperative* concentrations of these natriuretic peptides have been shown to predict postoperative cardiovascular complications and death in multiple cohort studies. An individual patient data meta-analysis of 2179 patients from 18 cohort studies showed that elevated preoperative natriuretic peptide concentrations were associated with postoperative death or MI [77••]. Furthermore, the addition of preoperative natriuretic peptide concentrations improved overall risk prediction compared to that based on clinical risk predictors alone (i.e., age, RCRI, surgery type)—in contrast to what was observed with preoperative coronary CTA [75••]. This meta-analysis identified the optimal prognostic threshold as being a BNP concentration < 92 ng/L or NT pro-BNP concentration < 300 ng/L, which screens out patients at lower cardiac risk (negative likelihood ratio 0.42 [77••]. Despite these promising findings, several important study limitations should be considered. For example, the event rate for postoperative death or MI (11%) is high and possibly not generalizable to many surgical populations. Additionally, the definition of MI across the included studies was variable, with two large included studies (516 participants) defining postoperative MI based solely on elevated troponin concentrations [77••, 78]. Based on these initial data, preoperative natriuretic peptide testing has been emphasized in the recent 2017 Canadian Cardiovascular Society (CCS) perioperative cardiovascular management guidelines. The CCS guidelines recommend preoperative natriuretic peptide testing before elective inpatient noncardiac surgery for patients aged ≥ 65 years, patients with RCRI scores ≥1, or patients aged between 45 and 64 years who have significant cardiovascular disease [79•].

In addition to natriuretic peptides, high-sensitivity cardiac troponins have shown promise as preoperative biomarkers that predict postoperative cardiovascular complications. At the minimum, preoperative testing should be conducted whenever postoperative monitoring with high-sensitivity (fourth- or fifth-generation assays) is planned. Specifically, 21% of patients may have *preoperative* high-sensitivity troponin concentrations that exceed the 99th percentile for the assay [80]; hence, testing before surgery is needed to interpret any postoperative troponin measurements. In addition, two prospective cohort studies have shown that elevated preoperative high-sensitivity troponin T concentrations predict mortality and cardiovascular complications after major noncardiac surgery [81•, 82, 83]. Additionally, the addition of preoperative high-sensitivity troponin T testing (threshold cutoff > 14 ng/L) improved risk prediction compared to that based on the RCRI alone [81•, 83], or RCRI plus NT pro-BNP testing [81•].

Preoperative Medication Management

In general, new initiation of cardiovascular medications before surgery has not shown benefits in large randomized trials. For example, acute preoperative initiation (i.e., within 1 day or less before surgery) of beta-blockers is now discouraged [18••] since it leads to increased risks of death and stroke [84•], despite also reducing the risk of perioperative MI [85]. Similarly, the POISE-2 trial found that *new* preoperative initiation of clonidine, an alpha-2 adrenergic agonist, or low-dose aspirin (i.e., 100 mg daily) did not decrease risks of perioperative MI [86•, 87], albeit in a sample with a relatively low prevalence of known CAD (23%). The trial also found the drugs to have important risks, such as perioperative

hypotension with clonidine and major perioperative bleeding with aspirin.

In contrast, patients with cardiovascular disease are typically on a variety of *chronic* cardiovascular medications, such as antihypertensives, antiplatelet agents, and statins. The challenge for the anesthesiologist is to decide whether to continue a medication to maintain its intended therapeutic effects and avoid adverse events related to acute withdrawal or to temporarily interrupt the medication to prevent any direct perioperative adverse effects. Examples of potential perioperative adverse effects include surgical bleeding related to antiplatelet agents or perioperative hypotension related to antihypertensives. Recommendations pertaining to the continuation versus withholding of *chronic* cardiovascular medications continue to evolve as more evidence is accumulating. At present, continuation of chronic beta-blocker therapy is recommended, due to the harmful effects of withdrawal [18••]. Conversely, *routine* continuation of chronic aspirin therapy does not prevent perioperative MI, and leads to increased perioperative bleeding [86••]. A more optimal approach is selective perioperative continuation of aspirin in high-risk patients, including individuals with prior coronary stent insertion, high-risk CAD, or significant CVD.

ACE Inhibitors and Angiotensin Receptor Blockers

Preoperative management of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) has been controversial, with the evidence largely composed of retrospective cohort studies and small randomized trials [88]. The 2014 ACC/AHA perioperative guidelines indicate that either continuation or temporary withdrawal of chronic ACE inhibitors and ARB therapy is reasonable, provided that therapy can be restarted postoperatively as soon a clinically feasible (Class IIa recommendation) [18••]. However, a VISION cohort substudy challenges this approach [89••]. Within the cohort of approximately 4800 patients on chronic ACE inhibitor or ARB therapy, 26% had their medication discontinued 24 h or more prior to surgery. Compared to patients who had their ACE inhibitor or ARB continued, patients who had their therapy held were less likely to experience the composite endpoint of death, stroke, or myocardial injury (adjusted relative risk 0.82), presumably due to a lower risk of hypotension (adjusted relative risk 0.80) [89••].

Conclusion

Cardiovascular disease is prevalent in patients undergoing noncardiac surgery and is a major contributor to perioperative morbidity and mortality. Evidence relevant to this field continues to rapidly evolve, with some important recent changes. First, advancements in stent technology and recent research data now indicate that major noncardiac surgery can be safely performed sooner (i.e., 3 to 6 months) after prior PCI with DES insertion. Second, recent data point to elevated perioperative cardiac risks when elective surgery is performed within 9 months or less after a prior stroke. Third, biomarkers are taking on increasing importance in preoperative cardiac risk stratification, with evidence that both preoperative natriuretic peptide and high-sensitivity troponin concentrations improve the accuracy of risk prediction compared to that based on clinical risk factors alone. Fourth, routine preoperative coronary CTA, while slightly improving discrimination when predicting postoperative MACE, is more likely to result in overestimation of risk in low-risk patients. Fifth, abnormalities in preoperative heart rate and blood pressure have been recognized as prognostic indicators of perioperative cardiovascular complications. The mechanisms underlying this association, as well as appropriate therapeutic interventions, remain to be identified. Finally, recent data suggest that temporary discontinuation of chronic ACEI/ARB therapy is preferred in *most* patients on these medications.

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Compliance with Ethical Standards

Conflict of Interest Dallas Duncan and Duminda N. Wijeysundera declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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