Society Guidelines

Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery

Emmanuelle Duceppe, MD,[a,b,c] Joel Parlow, MD, MSc (Co-chair),[d] Paul MacDonald, MD,[e] Kristin Lyons, MDCM,[f] Michael McMullen, MD,[d] Sadeesh Srinathan, MD, MSc,[g] Michelle Graham, MD,[h] Vikas Tandon, MD,[i] Kim Styles, MD,[j] Amal Bessissow, MD, MSc,[k] Daniel I. Sessler, MD,[l] Gregory Bryson, MD, MSc,[m,n] and P.J. Devereaux, MD, PhD (Co-chair)[b,c,i]

[a] Department of Medicine, University of Montreal, Montreal, Quebec, Canada; [b] Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada; [c] Population Health Research Institute, Hamilton Health Sciences and McMaster University, Hamilton, Ontario, Canada; [d] Department of Anesthesiology and Perioperative Medicine, Queen's University, Kingston, Ontario, Canada; [e] Cape Breton Regional Hospital, Cape Breton, Nova Scotia, Canada; [f] Division of Cardiology, University of Calgary, Calgary, Alberta, Canada; [g] Department of Surgery, Section of Thoracic Surgery, University of Manitoba, Winnipeg, Manitoba, Canada; [h] Department of Medicine, University of Alberta, Edmonton, Alberta, Canada; [i] Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [j] Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada; [k] Division of General Internal Medicine, McGill University Health Centre, Montreal, Quebec, Canada; [l] Department of Outcomes Research, Anesthesiology Institute, Cleveland Clinic, Cleveland, Ohio, USA; [m] Department of Anesthesiology and Pain Medicine, University of Ottawa, Ottawa, Ontario, Canada; [n] Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

ABSTRACT

The Canadian Cardiovascular Society Guidelines Committee and key Canadian opinion leaders believed there was a need for up to date guidelines that used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system of evidence assessment for patients who undergo noncardiac surgery. Strong recommendations included: 1) measuring brain natriuretic peptide (BNP) or N-terminal fragment of proBNP (NT-proBNP) before 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 a Revised Cardiac Risk Index score $\geq$ 1; 2) against performing preoperative resting echocardiography, coronary computed tomography angiography, exercise or cardiopulmonary exercise testing, or pharmacological stress echocardiography or radionuclide imaging to enhance perioperative cardiac risk estimation; 3) against the initiation or continuation of acetylsalicylic acid for the prevention of perioperative cardiac events, except in patients with a recent coronary artery stent or who will undergo carotid endarterectomy; 4) against α_2

RÉSUMÉ

Le comité des lignes directrices de la Société canadienne de cardiologie et les principaux leaders d'opinion canadiens ont estimé qu'il y avait un besoin pour des lignes directrices à jour utilisant le système d'évaluation des données probantes GRADE (Grading of Recommendations Assessment, Development, and Evaluation) pour l'évaluation des patients qui subissent une intervention chirurgicale non cardiaque. Les principales recommandations sont les suivantes : 1) la mesure des peptides natriurétiques de type B (BNP) ou le fragment N-terminal du propeptide natriurétique de type B (NT-proBNP) avant l'intervention chirurgicale pour améliorer l'estimation du risque cardiaque périopératoire chez les patients qui ont 65 ans ou plus, ou qui sont âgés de 45 à 64 ans et qui ont une maladie cardiovasculaire importante, ou qui ont un score RCRI (Revised Cardiac Risk Index) $\geq$ 1 ; 2) contre la réalisation de l'échocardiographie de repos préopératoire, l'angiographie cardiaque par tomodensitométrie, l'épreuve à l'effort ou l'épreuve d'effort cardiorespiratoire, ou l'échocardiographie de stress pharmacologique ou l'imagerie isotopique pour améliorer l'estimation

recommendations. These recommendations are aimed to provide a reasonable and practical approach to care for specialists and allied health professionals obliged with the duty of bestowing optimal care to patients and families, and can be subject to change as scientific knowledge and technology advance and as practice patterns evolve. The statement is not intended to be a substitute for physicians using their individual judgement in managing clinical care in consultation with the patient, with appropriate regard to all the individual circumstances of the patient, diagnostic and treatment options available and available resources. Adherence to these recommendations will not necessarily produce successful outcomes in every case.

agonist or β-blocker initiation within 24 hours before surgery; 5) withholding angiotensin-converting enzyme inhibitor and angiotensin II receptor blocker starting 24 hours before surgery; 6) facilitating smoking cessation before surgery; 7) measuring daily troponin for 48 to 72 hours after surgery in patients with an elevated NT-proBNP/BNP measurement before surgery or if there is no NT-proBNP/BNP measurement before surgery, in those who have a Revised Cardiac Risk Index score ≥1, age 45-64 years with significant cardiovascular disease, or age 65 years or older; and 8) initiating of long-term acetylsalicylic acid and statin therapy in patients who suffer myocardial injury/infarction after surgery.

du risque cardiaque périopératoire ; 3) contre l'introduction ou la continuation de l'acide acétylsalicylique pour prévenir les événements cardiaques périopératoires, excepté chez les patients ayant subi l'implantation récente d'une endoprothèse coronarienne ou qui subiront une endartériectomie carotididienne ; 4) contre l'introduction des α2-agonistes ou des β-bloqueurs dans les 24 heures qui précèdent l'intervention chirurgicale ; 5) la suspension des inhibiteurs de l'enzyme de conversion de l'angiotensine et des antagonistes des récepteurs de l'angiotensine II 24 heures avant l'intervention chirurgicale ; 6) la facilitation de l'abandon du tabac avant l'intervention chirurgicale ; 7) la mesure quotidienne de la troponine de 48 à 72 heures après l'intervention chirurgicale chez les patients qui avaient une mesure élevée des NT-proBNP/BNP avant l'intervention chirurgicale ou s'il n'y avait eu aucune mesure des NT-proBNP/BNP avant l'intervention chirurgicale, chez ceux qui ont un score RCRI ≥ 1, ou qui sont âgés de 45 à 64 ans et qui ont une maladie cardiovasculaire importante, ou qui sont âgés de 65 ans ou plus ; 8) l'introduction du traitement par acide acétylsalicylique et statines chez les patients qui souffrent de dommages myocardiques et d'infarctus après l'intervention chirurgicale.

Worldwide 1 in every 30-40 adults has major noncardiac surgery (ie, defined in this report as surgery requiring overnight hospital admission) annually,[1] and > 10 million of the > 200,000,000 patients having surgery will suffer a major cardiac complication (ie, cardiac death, myocardial infarction/injury, cardiac arrest) in the first 30 days after surgery.[2] Moreover, the number of patients who undergo surgery is increasing, as is their mean age and number of cardiac risk factors.[3] Major perioperative cardiac complications are important because they account for at least a third of perioperative deaths,[2] result in substantial morbidity,[2] prolong hospitalization,[4] increase cost,[5] and affect intermediate and long-term prognosis.[6]

Although previous perioperative cardiac risk guidelines exist,[7,8] members of the Canadian Cardiovascular Society (CCS) Guidelines Committee and several Canadian opinion leaders believed there was a need for up-to-date cardiac guidelines for patients who undergo noncardiac surgery using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system of evidence assessment for guidelines.[9] These individuals believed that this process could result in some recommendations divergent from previous perioperative guidelines. The CCS Guidelines Committee appointed co-chairs, a primary panel, and a secondary panel to develop these guidelines. Beyond CCS members, these panels also included a variety of medical specialists who belong to the Canadian Anesthesiologists' Society, Canadian Association of General Surgeons, Canadian Association of Thoracic Surgeons, Canadian Orthopaedic Association, Canadian Society of Internal Medicine, and Canadian Society for Vascular Surgery; members are listed in Appendix 1.

Guidelines Development

The primary panel established the scope of the guidelines (ie, 4 themes: preoperative cardiac risk assessment, perioperative cardiac risk modification, monitoring for perioperative cardiac events, and management of perioperative cardiac

complications), identified topics and working groups, searched the literature, developed the summary of findings and GRADE quality assessment tables, voted on the recommendations, and wrote the guidelines. The secondary panel reviewed the guidelines manuscript and made suggested edits and comments, which the primary panel addressed. Next the guidelines were sent to the CCS Guidelines Committee; they also provided suggested edits and comments that the primary panel addressed before finally submitting the guidelines to the CCS Council.

Because of uncertainty regarding the reliability of data that were published by Dr Don Poldermans,[10] the committee decided to exclude studies for which he was the first or senior author. If a study by Dr Poldermans was included in a meta-analysis, the panel only included the meta-analysis in a summary of findings table if his study had results that were consistent with the results from the other studies.

During an in-person meeting and several conference calls, the primary panel reviewed the summary of findings and GRADE quality assessment tables for each topic. Before discussing any topic all panel members had to declare if they had any financial or intellectual conflicts of interest. If a panel member had a conflict of interest, they were allowed to participate in the discussion but were not allowed to vote on the recommendation. Supplemental Table S1 shows details of all declared conflicts of interest and individual voting results.

The panel used the GRADE recommendation rating system, and recommendations were graded as a strong or conditional recommendation on the basis of high, moderate, low, or very low quality of evidence.[11] Supplemental Table S2 shows, for each GRADE recommendation, the corresponding balance of benefits vs the risks and burdens, the methodological quality of the supporting evidence, and the implications.[11]

Each recommendation required at least two-thirds of the nonconflicted primary panel members to agree during a vote on a GRADE of recommendation rating. If this was not achieved, the primary panel re-evaluated the evidence and another vote
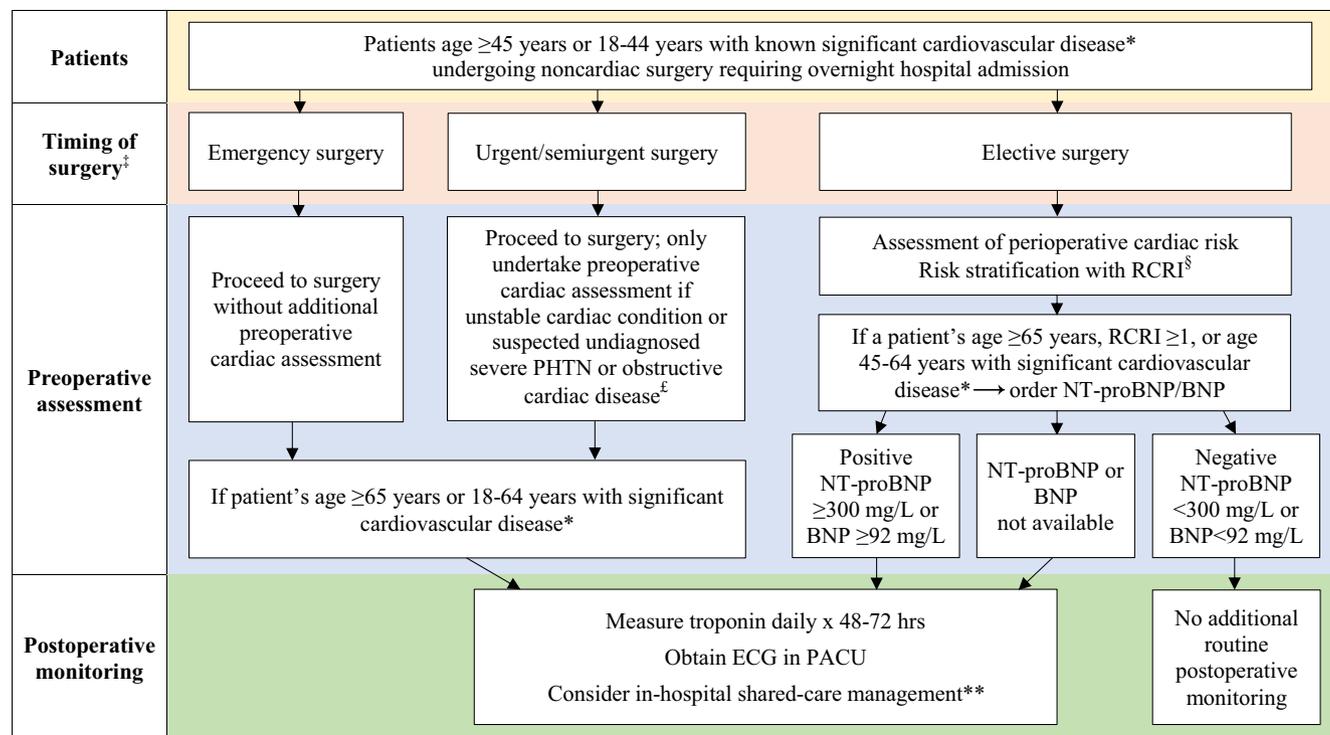
Figure 1. Preoperative risk assessment and postoperative monitoring flow diagram. BNP, brain natriuretic peptide; ECG, electrocardiogram; NT-proBNP, N-terminal pro-brain natriuretic peptide; PACU, postanesthesia care unit; PHTN, pulmonary hypertension; RCRI, Revised Cardiac Risk Index. * Significant cardiovascular disease includes known history of coronary artery disease, cerebral vascular disease, peripheral artery disease, congestive heart failure, severe PHTN or a severe obstructive intracardiac abnormality (eg, severe aortic stenosis, severe mitral stenosis, or severe hypertrophic obstructive cardiomyopathy). ‡ Timing of surgery refers to emergency surgery (eg, severe trauma, ruptured aortic aneurysm), urgent surgery (eg, hip fracture, bowel obstruction), semiurgent surgery (eg, cancer with potential to metastasize), or elective surgery (eg, knee arthroplasty). £ If physical examination suggests there is an unknown severe obstructive intracardiac abnormality (eg, severe aortic stenosis, severe mitral stenosis, or severe hypertrophic obstructive cardiomyopathy) or severe PHTN, then obtain an echocardiogram before surgery to inform the anesthesiologist, surgeon, and medical team of the type and degree of disease. If the history suggests the patient has an unstable cardiac condition (eg, unstable angina) then discussion with the patient and surgical/medical team is required to decide whether to delay, cancel, or proceed with surgery. § RCRI score (each worth 1 point): history of coronary artery disease, cerebrovascular disease, congestive heart failure, preoperative insulin use, preoperative creatinine > 177 μmol/L, and high-risk surgery (ie, intraperitoneal, intrathoracic, or suprainguinal vascular surgery). ** Shared-care management refers to a multidisciplinary approach to inpatient postoperative care; this includes the surgeon and a medical specialist (eg, internist, cardiologist, gerontologist), who will help with perioperative monitoring and management of cardiovascular complications.

was taken, until consensus was achieved. If a panel member still disagreed with the consensus, they were provided the opportunity to discuss their dissension in the text of the guidelines. If two-thirds of the panel members believed the evidence was too weak to support a recommendation, then no recommendation was made. If two-thirds of the panel members believed that a recommendation was indicated only on the basis of values and preferences for a topic with no direct research evidence (eg, communicating to patients their perioperative cardiac risk), then a good practice statement was made.[12]

Preoperative Cardiac Risk Assessment

Accurate preoperative cardiac risk estimation can serve several functions. Valid estimates of the risks and benefits of surgery can facilitate informed decision-making about the appropriateness of surgery. Accurate cardiac risk estimation can also guide management decisions (eg, consideration of endovascular vs open surgical approach) and inform decisions around monitoring (eg, troponin measurements) after surgery.

Which Patients Should Undergo Cardiac Risk Assessment Before Noncardiac Surgery?

Our recommendations only pertain to patients (1) 45 years of age and older or (2) patients 18-44 years of age with known significant cardiovascular disease (ie, coronary artery disease, cerebral vascular disease, peripheral arterial disease, congestive heart failure, severe pulmonary hypertension, or a severe obstructive intracardiac abnormality, such as aortic stenosis, mitral stenosis, hypertrophic obstructive cardiomyopathy), because these patients have, or are at risk of having, an underlying cardiac substrate that puts them at risk of a perioperative cardiac complication.[2,13-16] Moreover, our recommendations apply to noncardiac surgeries that require at least an overnight stay in the hospital after surgery, because of the availability of evidence and these surgeries are most likely to produce sufficient cardiac stressors to put these patients at risk of a cardiac complication.[2,13]

Figure 1 provides an overview of our approach to preoperative cardiac risk assessment and perioperative cardiac monitoring. We divided surgeries into 3 categories on the

basis of the timing of surgery (ie, emergency, urgent/semiurgent, and elective), and these categories influenced our recommendations regarding preoperative cardiac risk assessment.

Regarding whether physicians should undertake a preoperative cardiac risk assessment, our recommendations represent good practice statements. We believe that providing patients with the opportunity to engage in shared decision-making for major health care decisions—including the decision about undergoing elective surgery—irrespective of its effect on other patient-important outcomes, is of value in itself. Providing an accurate risk assessment is a prerequisite for shared decision-making in the perioperative setting. Among patients who undergo elective surgery, patients who are 45 years of age or older or 18-44 years of age with known significant cardiovascular disease have the most to gain from preoperative cardiac risk evaluation—in other elective surgery patients the risk assessment will result in a sufficiently low risk that it is very unlikely to influence decisions regarding surgery.

If a patient requires emergency surgery (ie, an acute life- or limb-threatening condition), we believe the vast majority of patients' values and preferences will favour the benefits of surgery over the risks; therefore, surgery should not be delayed unnecessarily. We believe most patients' values and preferences will favour the benefits of urgent surgery (eg, surgery for an acute bowel obstruction or hip fracture) or semiurgent surgery (ie, surgery for a cancer that has the potential to metastasize) over the risks, unless there is an unstable cardiovascular condition (eg, unstable angina, acute stroke), severe obstructive intracardiac abnormality, or severe pulmonary hypertension. If this is the case, this information might influence the decision around delaying, cancelling, or proceeding with surgery, and the choice of the surgical and anaesthetic techniques.

GOOD PRACTICE STATEMENT

1. In patients who require emergency surgery, we recommend against delaying surgery for a preoperative cardiac risk assessment.
2. In patients who require urgent or semiurgent surgery, we recommend undertaking preoperative cardiac risk assessment only if the patients' history or physical examination suggests there is a potential undiagnosed severe obstructive intracardiac abnormality, severe pulmonary hypertension, or an unstable cardiovascular condition.
3. In patients who undergo elective noncardiac surgery who are 45 years of age or older or 18-44 years of age with known significant cardiovascular disease, we recommend they undergo preoperative cardiac risk assessment.

Practical tip. Preoperative cardiac risk assessments should be undertaken by a physician or surgeon with substantial knowledge in this area (eg, a thorough understanding of these perioperative guidelines) and who is proficient in cardiac clinical evaluation.

Risk communication

There is an ethical requirement to accurately apprise patients about the benefits and risks of surgery.

GOOD PRACTICE STATEMENT

4. We recommend communicating to patients their perioperative cardiac risk.

Supplemental Tables S3 and S4 show the summary of findings and the GRADE quality assessment for communicating perioperative cardiac risk, respectively. A survey of 104 general internists who performed an average of 17 preoperative consults a month showed marked variability in definitions of low, moderate, and high risk.[17] With these results, there is substantial risk of misunderstanding between individuals when they hear subjective terms of risk. A systematic review of high-quality randomized controlled trials (RCTs) in surgical and nonsurgical settings showed that patients have a more accurate perception of risk if probabilistic information is presented as numbers like event rates (natural frequencies), rather than words (ie, subjective terms like low, moderate, or high chance), probabilities, or summarized as effect measures such as relative risk (RR) reduction.[18]

RECOMMENDATION

5. We recommend explicit communication of perioperative cardiac risk on the basis of the expected event rate among 100 patients or the range of risk consistent with the 95% confidence interval (CI) of the risk estimate (Strong Recommendation; Moderate-Quality Evidence).

Practical tip. An example of communicating perioperative cardiac risk quantitatively follows. "Ms Smith, if we had 100 patients with the same underlying conditions that you have who were to undergo the same type of surgery as you, we would expect 8 to 12 of these patients to suffer a heart attack, cardiac arrest, or die within the first 30 days after surgery. This also means we would expect 88 to 92 of these patients to go through surgery without one of these complications."

Methods of preoperative cardiac risk assessment

Researchers have evaluated 3 methods of estimating perioperative cardiac risk (ie, clinical risk indices, cardiac biomarkers, and noninvasive cardiac testing) that can provide the required data for risk communication in addition to routine clinical evaluation.

Clinical risk indices

Supplemental Tables S5 and S6 show the summary of findings and GRADE quality assessment for 3 clinical risk

ARTICLE IN PRESS

Duceppe et al.
Perioperative Cardiac Risk Assessment & Management

5

Table 1. Computation of Revised Cardiac Risk Index score

Variable	Points
History of ischemic heart disease*	1
History of congestive heart failure†	1
History of cerebrovascular disease‡	1
Use of insulin therapy for diabetes	1
Preoperative serum creatinine > 177 μmol/L (> 2.0 mg/dL)	1
High-risk surgery§	1

ECG, electrocardiogram.

*Defined as a history of myocardial infarction, positive exercise test, current complaint of ischemic chest pain or nitrate use, or ECG with pathological Q waves; patients with previous coronary bypass surgery or angioplasty meet criteria if they have such findings after their procedure.

†Defined as a history of heart failure, pulmonary edema, or paroxysmal nocturnal dyspnea; an S3 gallop or bilateral rales on physical examination; or a chest radiograph showing pulmonary vascular resistance.

‡Defined as a stroke or transient ischemic attack.

§Defined as intraperitoneal, intrathoracic, or suprainguinal vascular surgery.

indices, respectively. These risk indices include the most validated clinical risk index (known as the Revised Cardiac Risk Index [RCRI]),[13] and 2 risk indices that were recently developed using data from the National Surgical Quality Improvement Program (NSQIP).[15,19] Although some risk factors (eg, severe aortic stenosis) have important perioperative prognostic implications, a risk factor might not show up in a risk index because few or no patients in the original study had the relevant risk factor or it was not assessed.

The RCRI includes 6 factors, each worth 1 point (ie, history of ischemic heart disease, cerebrovascular disease, congestive heart failure, preoperative insulin use, preoperative creatinine > 177 μmol/L, and high-risk surgery; Table 1).[13] In a systematic review that included 792,740 patients from 24 studies, the RCRI showed moderate discrimination to predict major perioperative cardiac complications.[20]

Table 2 and Supplemental Table S7 show the pooled risk estimates of external validation studies of the RCRI that were published in the past 15 years, systematically monitored perioperative troponin measurements, and reported event rates for the various RCRI scores. The results showed risk estimates for myocardial infarction, cardiac arrest, or death of 3.9% (95% CI, 2.8%-5.4%) for an RCRI score of 0, 6.0% (95% CI, 4.9%-7.4%) for an RCRI score of 1, 10.1% (95% CI, 8.1%-12.6%) for an RCRI score of 2, and 15.0% (95% CI, 11.1%-20.0%) for an RCRI score ≥ 3.[21-25] These values are higher than the risk estimates on the basis of the original data that were used to derive the RCRI.[13,26] The likely explanation for these differences is that the original RCRI

Table 2. Total RCRI score and corresponding risk of myocardial infarction, cardiac arrest, or death at 30 days after noncardiac surgery*

Total RCRI points	Risk estimate, %	95% CI for the risk estimate
0	3.9	2.8%-5.4%
1	6.0	4.9%-7.4%
2	10.1	8.1%-12.6%
≥3	15.0	11.1%-20.0%

CI, confidence interval; RCRI, Revised Cardiac Risk Index.

*On the basis of high-quality external validation studies.

study monitored creatine kinase muscle and brain isoenzyme and excluded emergency surgery patients, whereas the external validation studies monitored troponin measurements that are much more sensitive than creatine kinase muscle and brain isoenzyme, and some studies included emergency surgery patients.

The NSQIP Myocardial Infarction and Cardiac Arrest (MICA) risk index and the American College of Surgeons (ACS) NSQIP risk index have both been developed using large data sets.[15,19] In these studies, these risk indices showed superior discrimination compared with the RCRI; however, it is highly probable that the NSQIP MICA and the ACS NSQIP risk indices underestimated cardiac risk, because patients did not undergo systematic measurements of perioperative troponin levels in these studies. Without cardiac biomarker screening more than half of all perioperative myocardial infarctions go undetected.[27] This likely explains the low number of perioperative myocardial infarctions in these studies that developed the NSQIP MICA and the ACS NSQIP risk indices.[15,19] Moreover, the NSQIP MICA and the ACS NSQIP risk indices have not undergone external validation in a study that has systematically monitored troponin measurements after noncardiac surgery. For these reasons the panel favoured the RCRI for cardiac risk prediction.

RECOMMENDATION

6. When evaluating cardiac risk, we suggest clinicians use the RCRI over the other available clinical risk prediction scores (Conditional Recommendation; Low-Quality Evidence).

Self-reported functional capacity

Some groups have recommended assessing patients' self-reported functional capacity to determine their metabolic equivalents (METs), to guide perioperative cardiac risk assessment.[28] There are, however, limited data to inform this issue.

In 1999, Reilly et al. evaluated 600 consecutive patients who underwent major noncardiac surgery and showed that after adjustment for age, patient self-reported functional capacity (METs) did not predict perioperative cardiovascular complications (adjusted odds ratio [aOR], 1.81; 95% CI, 0.94-3.46).[29] Similarly, Wiklund et al. determined METs in 5939 patients who underwent noncardiac surgery and showed after adjustment for age that patients' METs were not independently predictive of major perioperative cardiac complications.[30] Moreover, the data raised concerns about observer bias in the estimation of patients' METs.

Because of the limitations of the evidence, the primary panel unanimously decided not to make a recommendation on how to use patient self-reported functional capacity to estimate perioperative cardiac risk. A large prospective cohort study (scheduled to report in 2017) that is evaluating the prognostic capabilities of a physicians' assessment of patients' METs vs other measures (eg, cardiopulmonary testing) will

Table 3. Risk of death or myocardial infarction at 30 days after noncardiac surgery, based upon a patient's preoperative NT-proBNP or BNP result

Test result	Risk estimate, %	95% CI for the risk estimate
NT-proBNP < 300 ng/L or BNP < 92 mg/L	4.9	3.9%-6.1%
NT-proBNP value ≥ 300 ng/L or BNP ≥ 92 mg/L	21.8	19.0%-24.8%

BNP, brain natriuretic peptide; CI, confidence interval; NT-proBNP, N-terminal pro-brain natriuretic peptide.

provide more insight into the value of estimating a patients' METs.[31]

Cardiac biomarkers

Brain natriuretic peptides (BNPs) and N-terminal fragment of proBNP (NT-proBNP) are released from the myocardium in response to various stimuli such as myocardial stretch and ischemia.[32-34] Several prospective observational studies have evaluated the prognostic capabilities of NT-proBNP and BNP to predict major cardiovascular events after noncardiac surgery. Supplemental Tables S8 and S9 show the summary of findings and GRADE quality assessment for the prognostic capabilities of NT-proBNP and BNP, respectively.

An individual patient data meta-analysis included 2179 patients from 18 studies and showed that a preoperative NT-proBNP/BNP measurement was independently associated with the primary outcome (ie, death or nonfatal myocardial infarction) at 30 days after noncardiac surgery (aOR, 3.40; 95% CI, 2.57-4.47; $P < 0.001$).[35] Importantly, a preoperative NT-proBNP/BNP measurement before noncardiac surgery improved risk prediction among patients who did and did not suffer the primary outcome. Values ≥ 300 ng/L for NT-proBNP and ≥ 92 mg/L for BNP were identified as significant thresholds associated with an increased risk of the primary outcome. According to these thresholds, 7.6% of patients had an elevated NT-proBNP/BNP measurement before noncardiac surgery. Death or nonfatal myocardial infarction within 30 days after surgery occurred in 4.9% of patients with preoperative NT-proBNP/BNP values below these thresholds compared with 21.8% of patients with NT-proBNP/BNP values at or above these thresholds (Table 3). These findings were consistent with results from previous meta-analyses.[35-39]

RECOMMENDATION

7. 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).

Values and preferences. Cost and accessibility were considered important determinants of biomarker selection. Considering cost, we restricted testing to patient groups that had a baseline clinical risk estimate > 5%. Data from the **V**ascular Events **i**n Noncardiac **S**urgery Pat**i**ents C**o**hort Evaluatio**n** (VISION) Study showed that patients 65 years of age or older or 45-64 years of age with known cardiovascular disease have a baseline risk > 5% for cardiovascular death or nonfatal myocardial infarction at 30 days after surgery, whereas patients without these characteristics have a ≤ 2.0% 30-day event rate.[2] Compared with cardiac imaging and noninvasive cardiac stress testing, NT-proBNP/BNP biomarkers are inexpensive and avoid the need for return visits.

Practical tip. Hospitals that do not analyze NT-proBNP/ BNP in their core laboratory can obtain an instrument to allow clinicians to obtain NT-proBNP as a point of care test in the preoperative setting, offering biomarker information within minutes.

Resting echocardiography

Supplemental Tables S10 and S11 show the summary of findings and GRADE quality assessment for the prognostic capabilities of preoperative resting echocardiography, respectively. Two small studies of 339 and 570 patients suggested that a low ejection fraction was a borderline significant independent predictor of major cardiovascular complications within 30 days after noncardiac surgery.[40,41] The largest study (N = 1923) to assess the prognostic capabilities of preoperative echocardiographic parameters suggested that several parameters (eg, left ventricular ejection fraction < 50%) were independent predictors of major perioperative cardiovascular complications; however, a preoperative NT-proBNP measurement was a much stronger independent predictor.[42] The prognostic capabilities of an RCRI threshold ≥ 2 increased with the addition of an NT-proBNP threshold of ≥ 301 ng/L (ie, an RR of 1.4; 95% CI, 1.0-1.8 went to an RR of 3.7; 95% CI, 2.7-5.0; $P < 0.001$); however, use of echocardiographic parameters in addition did not result in a further increase in the RR.

Because of these data and our recommendation to measure a preoperative NT-proBNP or BNP in patients who undergo noncardiac surgery who are 65 years of age or older, or 45-64 years of age with known cardiovascular disease, the current evidence does not support the use of routine preoperative echocardiography for risk assessment in patients who undergo noncardiac surgery.

RECOMMENDATION

8. We recommend against performing preoperative resting echocardiography to enhance perioperative cardiac risk estimation (Strong Recommendation; Low-Quality Evidence).

Practical tip. Although we recommend against routinely obtaining echocardiography before noncardiac surgery to enhance perioperative cardiac risk estimation, if a patient requires urgent/semiurgent or elective surgery and their clinical examination suggests the patient has an undiagnosed severe obstructive intracardiac abnormality (eg, aortic stenosis, mitral

ARTICLE IN PRESS

Duceppe et al.
Perioperative Cardiac Risk Assessment & Management

7

stenosis, hypertrophic obstructive cardiomyopathy) or severe pulmonary hypertension, then urgent echocardiography should be obtained before surgery to inform the anesthesiologist, surgeon, and medical team of the type and degree of disease. Moreover, if a physician's clinical assessment suggests a patient might have an undiagnosed cardiomyopathy then echocardiography should be performed to facilitate optimization of long-term cardiac health. Physicians should consider the urgency of the surgery when deciding whether echocardiography is obtained before or after surgery.

Coronary computed tomographic angiography

Supplemental Tables S12 and S13 show the summary of findings and GRADE quality assessment for preoperative coronary computed tomographic angiography (CCTA), respectively. Of the preoperative CCTA studies the VISION CCTA study was the highest-quality study.[22] This was a prospective cohort study conducted at 12 centres in 8 countries that evaluated the prognostic capabilities of preoperative CCTA to enhance perioperative risk prediction beyond clinical data in 955 patients. The CCTA results were blinded unless significant left main disease was identified, and patients had daily troponin measurements for 3 days after surgery.[22] The primary outcome of cardiovascular death and nonfatal myocardial infarction occurred in 74 patients (7.7%) within 30 days of surgery.

The study showed, compared with the RCRI alone, that preoperative CCTA findings improved risk estimation (ie, extensive obstructive disease had an adjusted hazard ratio [aHR], 3.76; 95% CI, 1.12-12.62) among patients who suffered the primary outcome, but also overestimated risk among patients who did not suffer the primary outcome. Although CCTA findings can appropriately improve risk estimation among patients who will suffer the primary outcome, CCTA findings are more than 5 times as likely to lead to an inappropriate overestimation of risk among patients who will not suffer a perioperative cardiovascular death or myocardial infarction. The overall absolute net reclassification in a sample of 1000 patients is that CCTA will result in an inappropriate estimate of risk in 81 patients (on the basis of risk categories of < 5%, 5%-15%, and > 15% for the primary outcome).[22]

Overestimating risk can have negative consequences. For example, many patients who have a positive preoperative cardiac stress test have their surgery delayed while they are sent for coronary angiography with a plan for coronary revascularization, which might provide no benefit.[43,44] Overestimating cardiac risk might also result in delays and cancellations of beneficial surgery or inappropriate use of postoperative high-intensity beds, precluding access for patients at greater risk.

> **RECOMMENDATION**
>
> 9. We recommend against performing preoperative CCTA to enhance perioperative cardiac risk estimation (Strong Recommendation; Moderate-Quality Evidence).

Exercise stress testing and cardiopulmonary exercise testing

Supplemental Tables S14 and S15 show the summary of findings and GRADE quality assessment for preoperative exercise stress testing, respectively. Only a few studies have addressed the preoperative value of exercise stress testing to enhance risk prediction of postoperative cardiovascular complications, and the overall number of patients and events were small.[45-48] Results did not show an association between electrocardiogram (ECG) changes during exercise and postoperative outcome.[46-48] Two studies showed that low performance capacity was associated with a higher incidence of postoperative cardiovascular events, but neither study performed a risk-adjusted analysis.[45,48]

Supplemental Tables S16 and S17 show the summary of findings and GRADE quality assessment for preoperative cardiopulmonary exercise testing (CPET), respectively. Few studies have assessed the prognostic capabilities of CPET to independently predict 30-day cardiac outcomes. The largest prospective cohort study included 1725 patients who underwent elective major abdominal or thoracic surgery and showed CPET was a weak independent predictor of long-term postoperative mortality.[49] Other studies showed similar results,[50-53] with various strength of the association between CPET and mortality, but none determined if CPET performance allowed for improved risk reclassification in addition to clinical evaluation. The value of preoperative exercise testing or CPET to enhance perioperative cardiac risk reclassification in addition to clinical evaluation alone remains unclear, is inconvenient for patients, and costs significantly more than NT-proBNP or BNP measurement.

> **RECOMMENDATION**
>
> 10. We recommend against performing preoperative exercise stress testing to enhance perioperative cardiac risk estimation (Strong Recommendation; Low-Quality Evidence).
> 11. We recommend against performing preoperative CPET to enhance perioperative cardiac risk estimation (Strong Recommendation; Low-Quality Evidence).

Pharmacological stress echocardiography and radionuclide imaging

Supplemental Tables S18 and S19 show the summary of findings and GRADE quality assessment for pharmacological stress echocardiography and radionuclide imaging, respectively. Several observational studies have evaluated the predictive value of pharmacological stress echocardiography and radionuclide imaging in patients who undergo noncardiac surgery.[43] All studies had relatively small sample sizes with a limited number of events. Only a few were prospective studies, and few reported risk-adjusted associations. No study

Table 4. Management of interventions targeting the prevention of perioperative cardiac events*

Intervention	Management
Management of medications taken chronically and smoking before noncardiac surgery	
ASA	Withhold at least 3 days before surgery† and restart ASA when the risk of bleeding related to surgery has passed (ie, 8-10 days after major noncardiac surgery)
β-Blocker	Continue the β-blocker during the perioperative period; however, if a patient's systolic blood pressure is low before surgery, physicians should consider decreasing or holding the dose of the β-blocker before surgery
ACEI/ARB	Withhold ACEI/ARB 24 hours before noncardiac surgery and restart ACEI/ARB on day 2 after surgery, if the patient is hemodynamically stable
Statin	Continue the statin during the perioperative period
Smoking	Discuss and facilitate smoking cessation (eg, nicotine replacement therapy), ideally starting ≥ 4 weeks before surgery
Initiation of new medications and coronary revascularization before noncardiac surgery	
ASA	Do not initiate ASA for the prevention of perioperative cardiac events
β-Blocker	Do not initiate a β-blocker within 24 hours before noncardiac surgery
α_2-Agonist	Do not initiate an α_2-agonist for the prevention of perioperative cardiovascular events
Calcium channel blocker	Do not initiate a calcium channel blocker for the prevention of perioperative cardiovascular events
Coronary revascularization	Do not undertake preoperative prophylactic coronary revascularization for patients with stable coronary artery disease

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; ASA, acetylsalicylic acid.

* This applies to patients age 45 years of age or older or 18-44 years of age with known significant cardiovascular disease (ie, history of coronary artery disease, cerebral vascular disease, peripheral vascular disease, congestive heart failure, or a severe obstructive intracardiac abnormality [eg, severe aortic stenosis, severe mitral stenosis, or severe hypertrophic obstructive cardiomyopathy]) undergoing noncardiac surgery requiring hospital admission.

† Except in patients with a recent coronary artery stent and patients undergoing carotid endarterectomy.

adequately assessed the incremental value of these stress tests to well-established perioperative cardiac risk factors (eg, RCRI).

RECOMMENDATION

12. We recommend against performing preoperative pharmacological stress echocardiography to enhance perioperative cardiac risk estimation (Strong Recommendation; Low-Quality Evidence).

13. We recommend against performing preoperative pharmacological stress radionuclide imaging to enhance perioperative cardiac risk estimation (Strong Recommendation; Moderate-Quality Evidence).

Values and preferences. The panel believed that the cost and potential delays associated with these stress tests should be taken into account because of the absence of evidence of an overall absolute net improvement in risk reclassification.

Perioperative Cardiac Risk Modification

Table 4 shows the recommended management of interventions that target perioperative cardiac risk.

Perioperative use of acetylsalicylic acid

Supplemental Tables S20 and S21 show the summary of findings and GRADE quality assessment for perioperative initiation and continuation of acetylsalicylic acid (ASA), respectively. The Pulmonary Embolism Prevention (PEP) trial showed that ASA prevents venous thromboembolism (HR, 0.64; 95% CI, 0.50-0.81) in patients who undergo hip fracture surgery.[54] In PEP, ASA was associated with an increased risk of myocardial infarction (HR, 1.33; 95% CI, 1.00-1.78); however, there was no systematic monitoring of

cardiac biomarkers after surgery, and there were only 184 myocardial infarctions.

The Perioperative Ischemic Evaluation-2 (POISE-2) trial was a large RCT of 10,010 patients who underwent a wide spectrum of in-hospital noncardiac surgeries.[55] Patients who underwent a carotid endarterectomy, had received a bare-metal stent in the 6 weeks before surgery, or had received a drug-eluting stent in the 12 months before surgery were excluded from the trial. Patients had systematic monitoring of cardiac biomarkers or enzymes for the first 3 days after surgery. POISE-2 showed no effect of ASA on myocardial infarction and cardiac or all-cause mortality. POISE-2, similar to PEP, showed perioperative ASA increased the risk of major bleeding. POISE-2 included 5628 patients who were not previously taking ASA and 4382 patients who were taking ASA chronically but had stopped taking it a minimum of 3 days (median of 7 days) before surgery. The results were consistent in these 2 groups of patients. In POISE-2 the risk of bleeding related to surgery had passed 8-10 days after surgery.

RECOMMENDATION

14. We recommend against initiation of ASA for the prevention of perioperative cardiac events (Strong Recommendation; High-Quality Evidence).

15. We recommend against the continuation of ASA to prevent perioperative cardiac events, except in patients with a recent coronary artery stent and patients who undergo carotid endarterectomy (Strong Recommendation; High-Quality Evidence).

Practical tip. The timeline to define "recent" coronary stent varies on the basis of the type of stent but usually refers to 6 weeks for bare-metal stent and between 3 and 12 months for drug-eluting stent, depending on the stent

generation. Physicians should discontinue ASA at least 3 days before noncardiac surgery to reduce the risk of major bleeding.[56] In patients with an indication for chronic ASA, it is important to restart ASA when the risk of bleeding related to surgery has passed (ie, 8-10 days after major noncardiac surgery).[55] Perioperative ASA continuation might be reasonable for some surgical interventions to prevent local thrombosis (eg, free flap, acute limb ischemia). When a patient suffers a myocardial injury or thrombotic event after surgery in the absence of bleeding, there might be a net value to restarting ASA sooner after surgery than 8-10 days.

β-Blockade initiation before noncardiac surgery

Supplemental Tables S22 and S23 show the summary of findings and GRADE quality assessment for perioperative β-blocker initiation, respectively. A recent meta-analysis that included data from > 10,000 patients in 14 trials showed that perioperative β-blockers initiated within 24 hours of noncardiac surgery reduced the risk of nonfatal myocardial infarction but increased the risk of death, nonfatal stroke, hypotension, and bradycardia.[57] This meta-analysis included data from the POISE trial, which randomized 8351 patients with, or at risk of, coronary artery disease to receive extended-release metoprolol or placebo starting 2-4 hours before induction of anesthesia and continued for 30 days.[58] The meta-analysis showed that the increased risk of death and stroke was qualitatively unchanged without the POISE data.

Some authors have advocated for the initiation and titration of β-blockade starting weeks before surgery[59]; however, most patients are seen in preoperative clinics within days to weeks before surgery, making β-blocker dose titration challenging. Moreover, whatever β-blocker dose a patient tolerates before surgery does not necessarily inform a safe perioperative dose because hypotension is common after surgery.[60] Although some authorities advocate beginning β-blockers more than 24 hours before noncardiac surgery, there are no reliable data to support this practice.

RECOMMENDATION

16. We recommend against β-blocker initiation within 24 hours before noncardiac surgery (Strong Recommendation; High-Quality Evidence).

β-Blocker continuation during the perioperative period

Supplemental Tables S24 and S25 show the summary of findings and GRADE quality assessment for perioperative β-blocker continuation, respectively. No RCT informs the risks and benefits of continuing vs holding perioperative β-blockade during the perioperative period in patients chronically taking a β-blocker. Although there are inconsistent results, one large observational study suggested in risk-adjusted analyses that continuing chronic β-blocker usage decreases perioperative mortality, whereas perioperative

withholding of a β-blocker in patients taking a β-blocker chronically increased mortality.[61]

Although POISE evaluated the initiation of a β-blocker in the perioperative setting, the POISE data suggest that hypotension was the likely mechanism regarding how β-blockers increase the risk of mortality and stroke in the perioperative setting.[58]

RECOMMENDATION

17. Among patients taking a β-blocker chronically, we suggest to continue the β-blocker during the perioperative period (Conditional Recommendation; Low-Quality Evidence).

Practical tip. If a patient's systolic blood pressure is low before surgery, physicians should consider decreasing or holding the dose of the β-blocker before surgery.

α_2-Agonist initiation before noncardiac surgery

Supplemental Tables S26 and S27 show the summary of findings and GRADE quality assessment for perioperative initiation of an α_2-agonist, respectively. Researchers have evaluated the potential of α_2-agonists as an alternative means to control the perioperative stress response, which is a major determinant of perioperative cardiac complications. A meta-analysis of small trials suggested α_2-agonists might prevent perioperative cardiovascular complications[62]; however, a large international trial of 10,010 patients that randomized patients to clonidine or placebo showed that clonidine had no effect on myocardial infarction or death.[60] Moreover, clonidine increased the risk of clinically important hypotension and bradycardia and nonfatal cardiac arrest.[60]

RECOMMENDATION

18. We recommend against preoperative initiation of an α_2-agonist for the prevention of perioperative cardiovascular events (Strong Recommendation; High-Quality Evidence).

Calcium channel blocker initiation before noncardiac surgery

Supplemental Tables S28 and S29 show the summary of findings and GRADE quality assessment for perioperative initiation of a calcium channel blocker, respectively. A meta-analysis of several small trials suggested perioperative calcium channel blockers might prevent death or nonfatal myocardial infarction; however, there were only 5 myocardial infarctions and 17 deaths across all the trials, and the meta-analysis suggested implausible large treatment effects.[63] Moreover, the panel was concerned that these small trials with few events

do not provide sufficient confidence to exclude potentially important adverse effects.

RECOMMENDATION

19. We suggest against the initiation of calcium channel blockers for the prevention of perioperative cardiovascular events (Conditional Recommendation; Low-Quality Evidence).

Angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker continuation in the perioperative period

Supplemental Tables S30 and S31 show the summary of findings and GRADE quality assessment for the perioperative withholding of an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB), respectively. Three RCTs (total N = 188 patients) have looked at the effect of preoperative continuing vs withholding an ACEI or ARB around the time of noncardiac surgery.[64-66] All 3 trials showed that preoperative continuation of an ACEI/ARB was associated with an increased risk of intraoperative hypotension (pooled RR 2.53; 95% CI, 1.08-5.93). Only one trial reported on cardiovascular complications, but the number of events was too small to draw any conclusions.[65] In other perioperative studies, clinically important hypotension has been independently associated with an increased risk of death, myocardial infarction, and stroke.[58,60] The highest risk for clinically important hypotension after noncardiac surgery is the day after surgery.[60]

RECOMMENDATION

20. We recommend withholding ACEI/ARB starting 24 hours before noncardiac surgery in patients treated chronically with an ACEI/ARB (Strong Recommendation; Low-Quality Evidence).

Values and preferences. Weight was accorded to the absence of demonstrated benefit and the substantial increase in the risk of intraoperative hypotension associated with perioperative continuation of ACEI/ARB therapy.

Practical tip. Because the risk of hypotension is greatest within 24 hours of surgery, physicians should consider restarting ACEI/ARB on day 2 after surgery in patients receiving chronic ACEI/ARB therapy, if the patient is hemodynamically stable.

Statin initiation before noncardiac surgery

Supplemental Tables S32 and S33 show the summary of findings and GRADE quality assessment for statin initiation before noncardiac surgery, respectively. Sanders et al. reported a systematic review and meta-analysis of 3 trials

(total of 178 patients) that evaluated the cardiovascular effect of initiating a statin in patients who undergo vascular surgery.[67] There were very few events and perioperative administration of a statin had no effect on all-cause mortality (17 outcomes), cardiac mortality (2 outcomes), and nonfatal myocardial infarction (12 outcomes).[67] Panel members believed that the evidence was too weak to support a recommendation.

Statin continuation in the noncardiac surgery setting

Supplemental Tables S34 and S35 show the summary of findings and GRADE quality assessment for statin continuation in the noncardiac surgery setting, respectively. A single RCT included 550 patients who were admitted for an urgent/emergent surgery and had been taking chronic statin therapy.[68] Patients were randomized to receive rosuvastatin 20 mg or placebo 2 hours before surgery. At 30 days 10 patients (3.6%) in the rosuvastatin group and 22 patients (8.0%) in the placebo group suffered a myocardial infarction ($P = 0.03$).

RECOMMENDATION

21. We recommend continuing statin therapy perioperatively in patients who are receiving chronic statin therapy (Strong Recommendation; Moderate-Quality Evidence).

Coronary artery revascularization before noncardiac surgery

Supplemental Tables S36 and S37 show the summary of findings and GRADE quality assessment for coronary artery revascularization before noncardiac surgery, respectively. One trial randomized 216 patients to undergo coronary angiography followed by coronary revascularization, if applicable, followed by carotid endarterectomy, and 210 patients to undergo carotid endarterectomy without undergoing coronary angiography.[69] Among the 216 patients assigned to coronary angiography before carotid endarterectomy, 68 (31%) had significant coronary artery disease on angiography. Sixty-six of these patients underwent percutaneous coronary intervention (PCI), and then while still taking ASA and clopidogrel underwent carotid endarterectomy a mean of 4 days later; 2 patients underwent coronary artery bypass grafting surgery and carotid endarterectomy during one anesthetic period.

Although this trial suggests short- and long-term benefits from a strategy of coronary angiography followed by coronary revascularization—when relevant—before carotid endarterectomy, limitations of the trial include few events, unrealistically large treatment effects, and fixed block sizes that might have compromised concealment of randomization.[69,70] Moreover, it is difficult to know how to translate these results to the broader population of patients who undergo noncardiac surgery, especially because of the very short timelines from coronary revascularization to noncardiac surgery and that all of the PCI patients underwent noncardiac surgery while receiving dual antiplatelet therapy.

ARTICLE IN PRESS

Duceppe et al.
Perioperative Cardiac Risk Assessment & Management

11

The trial that is more broadly applicable to patients who undergo noncardiac surgery is the **C**oronary **A**rtery **R**evascularization **P**rophylaxis (CARP) trial.[71] This trial randomized 510 patients with known significant coronary artery disease to preoperative coronary revascularization vs no coronary revascularization before vascular surgery. At a median of 2.7 years after randomization, mortality was 22% in the coronary revascularization group and 23% in the no-revascularization group (RR, 0.98; 95% CI, 0.70-1.37; $P = 0.92$). Vascular surgery was undertaken a median of 48 days after coronary artery bypass grafting surgery and 41 days after PCI. The CARP trial excluded patients with left main coronary artery disease.

RECOMMENDATION

22. For patients with stable coronary artery disease who undergo noncardiac surgery, we recommend against preoperative prophylactic coronary revascularization (Strong Recommendation; Low-Quality Evidence).

Values and preferences. In the absence of clearly demonstrated benefit, the potential for surgical delays, increase in costs, and risk of bleeding with dual antiplatelet therapy supported a strong recommendation against prophylactic preoperative coronary revascularization.

Practical tip. In patients with CCS class III-IV or unstable angina, obtaining coronary revascularization before noncardiac surgery seems prudent; however, an individual risk-benefit assessment is required in patients who require urgent/semiurgent noncardiac surgery. Patients who receive PCI and a coronary stent should ideally have their noncardiac surgery delayed until the risks of stopping dual antiplatelet therapy are outweighed by the risks associated with delaying noncardiac surgery.[72,73]

Smoking cessation before noncardiac surgery

Supplemental Tables S38 and S39 show the summary of findings and GRADE quality assessment for preoperative smoking cessation interventions, respectively. A meta-analysis of 4 trials that included 653 patients reported no effect of a preoperative smoking cessation intervention compared with standard care on major perioperative cardiovascular complications (RR, 0.58; 95% CI, 0.17-1.96); however, there were only 16 events.

A meta-analysis of 9 trials that included 1251 patients showed that preoperative smoking cessation interventions increase smoking cessation at the time of surgery, and the more intensive interventions increased smoking cessation at 12 month follow-up (RR, 2.96; 95% CI, 1.57-5.55).[74] The more intensive interventions started smoking cessation measures 4 weeks before surgery, and the treatments included smoking cessation counselling and nicotine replacement therapy. The studies were at high risk of bias with high heterogeneity; however, because of the importance of smoking cessation on long-term cardiac outcomes, the panel found the perioperative smoking cessation data compelling.

RECOMMENDATION

23. We recommend discussing and facilitating smoking cessation before noncardiac surgery (Strong Recommendation; Low-Quality Evidence).

Values and preferences. Because even brief counselling on smoking cessation during preoperative evaluation might positively affect smoking cessation, the panel members believe it is important to take advantage of this opportunity to optimize long-term cardiac risk.

Monitoring for Perioperative Cardiac Events

Troponin monitoring

Supplemental Tables S40 and S41 show the summary of findings and GRADE quality assessment for postoperative troponin monitoring, respectively. Most myocardial infarctions occur within 48 hours of noncardiac surgery when patients are receiving analgesic medications that can mask ischemic symptoms.[27] This provides an explanation as to why 65% of patients who suffer a perioperative myocardial infarction do not experience ischemic symptoms, and without perioperative troponin monitoring these myocardial infarctions would go undetected. Asymptomatic myocardial infarctions are associated with an increased risk of 30-day mortality (aOR, 4.00; 95% CI, 2.65-6.06) similar to symptomatic myocardial infarctions (aOR, 4.76; 95% CI, 2.68-8.43).[27] Moreover, asymptomatic perioperative troponin elevation at levels adjudicated as myocardial injuries due to ischemia—that do not fulfil the universal definition of myocardial infarction—are also associated with an increased risk of 30-day mortality (aHR, 3.30; 95% CI, 2.26−4.81).[2]

The largest prospective international cohort study (VISION; N = 15,133) showed that the detection of an elevated troponin T level in the postoperative period was the strongest predictor of 30-day mortality.[75] The prognostic importance of an elevated troponin measurement after surgery was supported by a previous meta-analysis of 14 studies that enrolled 3318 patients.[6] The meta-analysis showed that an elevated troponin level was an independent predictor of all-cause mortality (OR, 6.7; 95% CI, 4.1-10.9) at 1 year after surgery.[6]

Myocardial injury after noncardiac surgery (MINS) was defined as a peak fourth-generation troponin T ≥ 0.03 ng/mL believed to be due to myocardial ischemia.[2] MINS was observed in 8% of patients in the VISION study and was associated with a marked increase in 30-day mortality (9.8% vs 1.1%), and had the largest population attributable risk of all the complications after surgery.[2] Most of these MINS patients (84%) remained asymptomatic and were only detected through the routine surveillance of postoperative troponin levels.[2] The strong association between an elevated troponin level detected during routine postoperative

surveillance and 30-day mortality was confirmed in 2 large cohort studies.[4,76] Moreover, a recent analysis suggests that perioperative troponin surveillance is cost-effective.[77]

Because most patients who suffer a postoperative myocardial infarction or MINS are asymptomatic, routine troponin monitoring can detect patients who are at markedly increased risk of death within 30 days of surgery. Although the optimal management of patients with MINS remains an area of ongoing investigation, we believe that these individuals can benefit from intensification of medical management and close monitoring during their postoperative recovery.

RECOMMENDATION

24. 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 (ie, patients with an elevated NT-proBNP/BNP measurement before surgery or, if there is no NT-proBNP/BNP measurement before surgery, in those who have an RCRI score ≥ 1, age 45-64 years with significant cardiovascular disease, or age 65 years or older) (Strong Recommendation; Moderate-Quality Evidence).

Postoperative ECG

Supplemental Tables S42 and S43 show the summary of findings and GRADE quality assessment for obtaining a postoperative 12-lead ECG. The association between the occurrence of ischemic changes on a postoperative ECG and the occurrence of adverse cardiac events has been shown in several studies.[78,79]

The largest prospective study to address the prognostic value of a postoperative ECG showed that new ischemic findings were an independent predictor of subsequent major cardiac events (aOR, 2.20; 95% CI, 1.1-3.7; $P = 0.009$).[80] Another small study in vascular patients noted that 88% of patients who had ischemic findings on any postoperative ECG had changes detected on the immediate postoperative ECG (15 minutes after surgery); the concordance between ischemia on an ECG and elevation of troponin T level was 85%.[81] The frequent onset of myocardial ischemia during the early postoperative period (< 60 minutes) was also seen in a study using continuous 12-lead ECG recordings after surgery.[82]

RECOMMENDATION

25. We suggest performing a postoperative ECG in the postanesthetic care unit in patients with an elevated NT-proBNP/BNP measurement before surgery or, if there is no NT-proBNP/BNP measurement before surgery, in those who have an RCRI score ≥ 1, age 45-64 years with significant cardiovascular disease, or age 65 years or older (Conditional Recommendation; Low-Quality Evidence).

Postoperative telemetry

Supplemental Tables S44 and S45 show the summary of findings and GRADE quality assessment for postoperative telemetry, respectively. Studies using telemetry after surgery to detect silent ischemia have generally defined ischemia as ≥ 1 mm of horizontal or downsloping ST depression or ≥ 2 mm ST-elevation for ≥ 60 seconds,[78,79,83] with longer durations of ischemia being more predictive of adverse outcomes after surgery.[79,82,84] Investigators have identified ischemia after surgery as a predictor of major cardiac events in patients with, or at high risk of, coronary artery disease[2,6] and in patients who undergo vascular surgery.[83] Because we recommend monitoring troponin in at-risk patients after surgery, the additional benefits of postoperative telemetry monitoring have not been established, and postoperative telemetry is associated with substantial resources and costs, panel members believed that the evidence was too weak to support a recommendation regarding postoperative telemetry monitoring.

Pulmonary artery catheter monitoring

Supplemental Tables S46 and S47 show the summary of findings and GRADE quality assessment for routine pulmonary artery catheter monitoring (PACM) in patients who undergo noncardiac surgery, respectively. Eight RCTs have evaluated the effect of routine PACM in patients who undergo noncardiac surgery. Trials varied in terms of whether or not hemodynamic targets and directed therapies were mandated.

The largest trial included 1994 patients older than the age of 60 years who underwent a high-risk noncardiac surgery. There was no difference in mortality or morbidity, but there was an increase in pulmonary embolism in patients randomized to PACM.[85] All studies were included in a meta-analysis of PACM use, along with an additional 5 studies (2384 patients) that enrolled intensive care unit patients or those with acute heart failure. Overall, the meta-analysis did not support any association between PACM use and improved outcomes.[86]

RECOMMENDATION

26. We recommend against the use of pulmonary artery catheters in patients who undergo noncardiac surgery (Strong Recommendation; Moderate-Quality Evidence).

Postoperative shared-care management

Supplemental Tables S48 and S49 show the summary of findings and GRADE quality assessment for shared-care management of patients who undergo noncardiac surgery, respectively. Surgeons are commonly busy in operating rooms, which limits their ability to rapidly respond to medical complications on surgical floors. For example, among the 5001 patients given placebo in the POISE-2 trial, the median duration of clinically important hypotension during surgery was 15 minutes, whereas on the first postoperative day it was 150 minutes ($P < 0.001$).[60] These data suggest a need for pathways to facilitate more rapid management of cardiovascular compromise on surgical floors.

ARTICLE IN PRESS

Duceppe et al.
Perioperative Cardiac Risk Assessment & Management

13

Shared-care models, between surgeons and medical specialists (eg, anesthesiologist, cardiologist, geriatrician, internist) who are readily available to help with perioperative management of cardiovascular complications, have the potential to improve outcomes. A meta-analysis showed a mortality advantage in patients who had surgery for a hip fracture who were comanaged by surgeons and geriatricians compared with surgeons alone.[87]

RECOMMENDATION

27. We suggest shared-care management of patients with an elevated NT-proBNP/BNP measurement before surgery or if there is no NT-proBNP/BNP measurement before surgery, in those who have an RCRI score $\geq$ 1, age 45-64 years with significant cardiovascular disease, or age 65 years or older (Conditional Recommendation; Low-Quality Evidence).

Management of Postoperative Events

ASA and statin in patients who suffer MINS

Supplemental Tables S50 and S51 show the summary of findings and GRADE quality assessment for ASA and statin in patients who suffer MINS. One prospective cohort study and one retrospective case-control study with propensity score-matching have investigated the question of initiation of ASA and statin therapy in patients who had suffered a myocardial injury or myocardial infarction after noncardiac surgery.[27,88] In the prospective cohort study, among the 415 patients who suffered a myocardial infarction after noncardiac surgery, patients who had started receiving ASA and statin had a significant reduction in 30-day mortality (aOR, 0.54; 95% CI, 0.29-0.99, and aOR, 0.26; 95% CI, 0.13-0.54, respectively).[27]

The retrospective case controlled study by Foucrier et al.[88] comprised a total of 66 patients who suffered a myocardial injury after major vascular surgery. The primary outcome was the occurrence of a major cardiac event (myocardial infarction, coronary revascularization, or pulmonary edema requiring hospitalization) at 1 year. Cardiovascular medication intensification referred to the introduction of at least 1 of 4 cardiovascular medications (ie, antiplatelet, statin, β-blocker, and ACEI). Patients with no modification of their cardiovascular treatment had an HR of 1.77 (95% CI, 1.13-2.42; P = 0.004) for the primary outcome compared with a matched control group. In contrast, patients who received intensification of cardiovascular treatment had an HR of 0.63 (95% CI, 0.10-1.19; P = 0.45) for the primary outcome compared with the matched control group.

RECOMMENDATION

28. We recommend the initiation of long-term ASA in patients who suffer a myocardial injury or myocardial infarction after noncardiac surgery (Strong Recommendation; Moderate-Quality Evidence).

---

29. We recommend the initiation of long-term statin therapy in patients who suffer myocardial injury or myocardial infarction after noncardiac surgery (Strong Recommendation; Moderate-Quality Evidence).

Values and preferences. Although these data are limited to risk-adjusted observational data, the panel believed that the current available data support the use of ASA and a statin in patients who suffer a myocardial injury or myocardial infarction after noncardiac surgery. Panel members also considered the overwhelming evidence of the beneficial effects of ASA and statin after cardiac events in the nonsurgical setting.

Practical tip. Although our recommendations focus on ASA and statin therapy in patients who suffer a myocardial injury or myocardial infarction after noncardiac surgery, these patients should be followed-up by a medical specialist to monitor their status and optimize medications and undertake prognostic tests on the basis of their expert clinical judgement.

Conclusions and Future Research

Throughout the past 2 decades, large clinical trials and prospective observational studies have advanced our understanding of predicting, modifying the risk of, monitoring for, and managing perioperative cardiac complications. Despite these advances, cardiac complications after noncardiac surgery remain a substantial public health problem. There is a need for more large international studies to evaluate promising lines of investigation. Examples include the use of remote, automated, continuous, noninvasive, hemodynamic, and ischemic monitors with alert systems on surgical floors, the prevention or minimization of perioperative bleeding, and management strategies for treating MINS. The evaluation of such lines of investigation holds the potential to substantially improve the safety of noncardiac surgery for the > 200 million adults who annually undergo these procedures.

References

1. Weiser TG, Regenbogen SE, Thompson KD, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. Lancet 2008;372:139-44.

2. Botto F, Alonso-Coello P, Chan MT, et al. Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. Anesthesiology 2014;120:564-78.

3. Siddiqui NF, Coca SG, Devereaux PJ, et al. Secular trends in acute dialysis after elective major surgery—1995 to 2009. CMAJ 2012;184:1237-45.

4. van Waes JA, Nathoe HM, de Graaff JC, et al. Myocardial injury after noncardiac surgery and its association with short-term mortality. Circulation 2013;127:2264-71.

5. Udeh BL, Dalton JE, Hata JS, Udeh CI, Sessler DI. Economic trends from 2003 to 2010 for perioperative myocardial infarction: a retrospective, cohort study. Anesthesiology 2014;121:36-45.

6. Levy M, Heels-Ansdell D, Hiralal R, et al. Prognostic value of troponin and creatine kinase muscle and brain isoenzyme measurement after noncardiac surgery: a systematic review and meta-analysis. Anesthesiology 2011;114:796-806.

7. 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. Circulation 2014;130:e278-333.

8. 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;35:2383-431.

9. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-6.

10. Erasmus MC, Follow-up Investigation Committee. Report on the 2012 follow-up investigation of possible breaches of academic integrity. September 30, 2012.

11. Guyatt GH, Cook DJ, Jaeschke R, Pauker SG, Schunemann HJ. Grades of recommendation for antithrombotic agents: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133:123S-31S.

12. Guyatt GH, Schunemann HJ, Djulbegovic B, Akl EA. Guideline panels should not GRADE good practice statements. J Clin Epidemiol 2015;68:597-600.

13. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999;100:1043-9.

14. Sabate S, Mases A, Guilera N, et al. Incidence and predictors of major perioperative adverse cardiac and cerebrovascular events in non-cardiac surgery. Br J Anaesth 2011;107:879-90.

15. Gupta PK, Gupta H, Sundaram A, et al. Development and validation of a risk calculator for prediction of cardiac risk after surgery. Circulation 2011;124:381-7.

16. Agarwal S, Rajamanickam A, Bajaj NS, et al. Impact of aortic stenosis on postoperative outcomes after noncardiac surgeries. Circ Cardiovasc Qual Outcomes 2013;6:193-200.

17. Taher T, Khan NA, Devereaux PJ, et al. Assessment and reporting of perioperative cardiac risk by Canadian general internists: art or science? J Gen Intern Med 2002;17:933-6.

18. Trevena LJ, Davey HM, Barratt A, Butow P, Caldwell P. A systematic review on communicating with patients about evidence. J Eval Clin Pract 2006;12:13-23.

19. Bilimoria KY, Liu Y, Paruch JL, et al. Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. J Am Coll Surg 2013;217:833-42.

20. Ford MK, Beattie WS, Wijeysundera DN. Systematic review: prediction of perioperative cardiac complications and mortality by the revised cardiac risk index. Ann Intern Med 2010;152:26-35.

21. Devereaux PJ, Bradley D, Chan MT, et al. An international prospective cohort study evaluating major vascular complications among patients undergoing noncardiac surgery: the VISION Pilot Study. Open Med 2011;5:e193-200.

22. Sheth T, Chan M, Butler C, et al. Prognostic capabilities of coronary computed tomographic angiography before non-cardiac surgery: prospective cohort study. BMJ 2015;350:h1907.

23. Ausset S, Auroy Y, Lambert E, et al. Cardiac troponin I release after hip surgery correlates with poor long-term cardiac outcome. Eur J Anaesthesiol 2008;25:158-64.

24. Cuthbertson BH, Amiri AR, Croal BL, et al. Utility of B-type natriuretic peptide in predicting perioperative cardiac events in patients undergoing major non-cardiac surgery. Br J Anaesth 2007;99:170-6.

25. Rajagopalan S, Croal BL, Bachoo P, et al. N-terminal pro B-type natriuretic peptide is an independent predictor of postoperative myocardial injury in patients undergoing major vascular surgery. J Vasc Surg 2008;48:912-7.

26. Devereaux PJ, Goldman L, Cook DJ, et al. Perioperative cardiac events in patients undergoing noncardiac surgery: a review of the magnitude of the problem, the pathophysiology of the events and methods to estimate and communicate risk. CMAJ 2005;173:627-34.

27. Devereaux PJ, Xavier D, Pogue J, et al. Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. Ann Intern Med 2011;154:523-8.

28. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;130:2215-45.

29. Reilly DF, McNeely MJ, Doerner D, et al. Self-reported exercise tolerance and the risk of serious perioperative complications. Arch Intern Med 1999;159:2185-92.

30. Wiklund RA, Stein HD, Rosenbaum SH. Activities of daily living and cardiovascular complications following elective, noncardiac surgery. Yale J Biol Med 2001;74:75-87.

31. Wijeysundera DN, Pearse RM, Shulman MA, et al. Measurement of Exercise Tolerance before Surgery (METS) study: a protocol for an international multicentre prospective cohort study of cardiopulmonary exercise testing prior to major non-cardiac surgery. BMJ Open 2016;6:e010359.

32. Struthers A, Lang C. The potential to improve primary prevention in the future by using BNP/N-BNP as an indicator of silent 'pancardiac' target organ damage: BNP/N-BNP could become for the heart what microalbuminuria is for the kidney. Eur Heart J 2007;28:1678-82.

33. Luchner A, Stevens TL, Borgeson DD, et al. Differential atrial and ventricular expression of myocardial BNP during evolution of heart failure. Am J Physiol 1998;274:H1684-9.

34. Clerico A, Giannoni A, Vittorini S, Passino C. Thirty years of the heart as an endocrine organ: physiological role and clinical utility of cardiac natriuretic hormones. Am J Physiol Heart Circ Physiol 2011;301:H12-20.

35. Rodseth RN, Biccard BM, Le Manach Y, et al. The prognostic value of pre-operative and post-operative B-type natriuretic peptides in patients undergoing noncardiac surgery: B-type natriuretic peptide and N-terminal fragment of pro-B-type natriuretic peptide: a systematic review and individual patient data meta-analysis. J Am Coll Cardiol 2014;63:170-80.

36. Karthikeyan G, Moncur RA, Levine O, et al. Is a pre-operative brain natriuretic peptide or N-terminal pro-B-type natriuretic peptide measurement an independent predictor of adverse cardiovascular outcomes within 30 days of noncardiac surgery? A systematic review and meta-analysis of observational studies. J Am Coll Cardiol 2009;54:1599-606.

37. Ryding AD, Kumar S, Worthington AM, Burgess D. Prognostic value of brain natriuretic peptide in noncardiac surgery: a meta-analysis. Anesthesiology 2009;111:311-9.

38. Rodseth RN, Padayachee L, Biccard BM. A meta-analysis of the utility of pre-operative brain natriuretic peptide in predicting early and intermediate-term mortality and major adverse cardiac events in vascular surgical patients. Anaesthesia 2008;63:1226-33.

39. Young YR, Sheu BF, Li WC, et al. Predictive value of plasma brain natriuretic peptide for postoperative cardiac complications; a systemic review and meta-analysis. J Crit Care 2014;29:696.e1-696.e10.

40. Halm EA, Browner WS, Tubau JF, Tateo IM, Mangano DT. Echocardiography for assessing cardiac risk in patients having noncardiac surgery. Study of Perioperative Ischemia Research Group. Ann Intern Med 1996;125:433-41.

41. Rohde LE, Polanczyk CA, Goldman L, et al. Usefulness of transthoracic echocardiography as a tool for risk stratification of patients undergoing major noncardiac surgery. Am J Cardiol 2001;87:505-9.

42. Park SJ, Choi JH, Cho SJ, et al. Comparison of transthoracic echocardiography with N-terminal pro-brain natriuretic peptide as a tool for risk stratification of patients undergoing major noncardiac surgery. Korean Circ J 2011;41:505-11.

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

44. Etchells E, Meade M, Tomlinson G, Cook D. Semiquantitative dipyridamole myocardial stress perfusion imaging for cardiac risk assessment before noncardiac vascular surgery: a meta-analysis. J Vasc Surg 2002;36:534-40.

45. Kaaja R, Sell H, Erkola O, Harjula A. Predictive value of manual ECG-monitored exercise test before abdominal aortic or peripheral vascular surgery. Angiology 1993;44:11-5.

46. McPhail N, Calvin JE, Shariatmadar A, Barber GG, Scobie TK. The use of preoperative exercise testing to predict cardiac complications after arterial reconstruction. J Vasc Surg 1988;7:60-8.

47. Carliner NH, Fisher ML, Plotnick GD, et al. Routine preoperative exercise testing in patients undergoing major noncardiac surgery. Am J Cardiol 1985;56:51-8.

48. Sgura FA, Kopecky SL, Grill JP, Gibbons RJ. Supine exercise capacity identifies patients at low risk for perioperative cardiovascular events and predicts long-term survival. Am J Med 2000;108:334-6.

49. Colson M, Baglin J, Bolsin S, Grocott MP. Cardiopulmonary exercise testing predicts 5 yr survival after major surgery. Br J Anaesth 2012;109:735-41.

50. Grant SW, Hickey GL, Wisely NA, et al. Cardiopulmonary exercise testing and survival after elective abdominal aortic aneurysm repairdagger. Br J Anaesth 2015;114:430-6.

51. Lai CW, Minto G, Challand CP, et al. Patients' inability to perform a preoperative cardiopulmonary exercise test or demonstrate an anaerobic threshold is associated with inferior outcomes after major colorectal surgery. Br J Anaesth 2013;111:607-11.

52. Hartley RA, Pichel AC, Grant SW, et al. Preoperative cardiopulmonary exercise testing and risk of early mortality following abdominal aortic aneurysm repair. Br J Surg 2012;99:1539-46.

53. Carlisle J, Swart M. Mid-term survival after abdominal aortic aneurysm surgery predicted by cardiopulmonary exercise testing. Br J Surg 2007;94:966-9.

54. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet 2000;355:1295-302.

55. Devereaux PJ, Mrkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery. N Engl J Med 2014;370:1494-503.

56. Devereaux PJ. POISE-2 Investigators. Rationale and design of the PeriOperative ISchemic Evaluation-2 (POISE-2) trial: an international 2 x 2 factorial randomized controlled trial of acetyl-salicylic acid vs. placebo and clonidine vs. placebo in patients undergoing noncardiac surgery. Am Heart J 2014;167:804-809.e4.

57. Wijeysundera DN, Duncan D, Nkonde-Price C, et al. Perioperative beta blockade in noncardiac surgery: a systematic review for the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;130:2246-64.

58. Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. Lancet 2008;371:1839-47.

59. Fleisher LA, Poldermans D. Perioperative beta blockade: where do we go from here? Lancet 2008;371:1813-4.

60. Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing noncardiac surgery. N Engl J Med 2014;370:1504-13.

61. Wallace AW, Au S, Cason BA. Association of the pattern of use of perioperative beta-blockade and postoperative mortality. Anesthesiology 2010;113:794-805.

62. Wijeysundera DN, Bender JS, Beattie WS. Alpha-2 adrenergic agonists for the prevention of cardiac complications among patients undergoing surgery. Cochrane Database Syst Rev 2009:CD004126.

63. Wijeysundera DN, Beattie WS. Calcium channel blockers for reducing cardiac morbidity after noncardiac surgery: a meta-analysis. Anesth Analg 2003;97:634-41.

64. Coriat P, Richer C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. Anesthesiology 1994;81:299-307.

65. Bertrand M, Godet G, Meersschaert K, et al. Should the angiotensin II antagonists be discontinued before surgery? Anesth Analg 2001;92:26-30.

66. Schirmer U, Schurmann W. Preoperative administration of angiotensin-converting enzyme inhibitors [in German]. Anaesthesist 2007;56:557-61.

67. Sanders RD, Nicholson A, Lewis SR, Smith AF, Alderson P. Perioperative statin therapy for improving outcomes during and after noncardiac vascular surgery. Cochrane Database Syst Rev 2013:CD009971.

68. Xia J, Qu Y, Yin C, Xu D. Preoperative rosuvastatin protects patients with coronary artery disease undergoing noncardiac surgery. Cardiology 2015;131:30-7.

69. Illuminati G, Ricco JB, Greco C, et al. Systematic preoperative coronary angiography and stenting improves postoperative results of carotid

endarterectomy in patients with asymptomatic coronary artery disease: a randomised controlled trial. Eur J Vasc Endovasc Surg 2010;39:139-45.

70. Illuminati G, Schneider F, Greco C, et al. Long-term results of a randomized controlled trial analyzing the role of systematic pre-operative coronary angiography before elective carotid endarterectomy in patients with asymptomatic coronary artery disease. Eur J Vasc Endovasc Surg 2015;49:366-74.

71. McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. N Engl J Med 2004;351: 2795-804.

72. Hawn MT, Graham LA, Richman JS, et al. Risk of major adverse cardiac events following noncardiac surgery in patients with coronary stents. JAMA 2013;310:1462-72.

73. Wijeysundera DN, Wijeysundera HC, Yun L, et al. Risk of elective major noncardiac surgery after coronary stent insertion: a population-based study. Circulation 2012;126:1355-62.

74. Thomsen T, Villebro N, Moller AM. Interventions for preoperative smoking cessation. Cochrane Database Syst Rev 2014:CD002294.

75. Devereaux PJ, Chan MT, Alonso-Coello P, et al. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. JAMA 2012;307:2295-304.

76. Beattie WS, Karkouti K, Tait G, et al. Use of clinically based troponin underestimates the cardiac injury in non-cardiac surgery: a single-centre cohort study in 51,701 consecutive patients. Can J Anaesth 2012;59: 1013-22.

77. Torborg A, Ryan L, Kantor G, Biccard BM. The pharmacoeconomics of routine postoperative troponin surveillance to prevent and treat myocardial infarction after non-cardiac surgery. S Afr Med J 2014;104: 619-23.

78. Mangano DT, Browner WS, Hollenberg M, et al. Association of peri-operative myocardial ischemia with cardiac morbidity and mortality in men undergoing noncardiac surgery. The Study of Perioperative Ischemia Research Group. N Engl J Med 1990;323:1781-8.

79. Landesberg G, Luria MH, Cotev S, et al. Importance of long-duration postoperative ST-segment depression in cardiac morbidity after vascular surgery. Lancet 1993;341:715-9.

80. Rinfret S, Goldman L, Polanczyk CA, Cook EF, Lee TH. Value of immediate postoperative electrocardiogram to update risk stratification after major noncardiac surgery. Am J Cardiol 2004;94:1017-22.

81. Bottiger BW, Motsch J, Teschendorf P, et al. Postoperative 12-lead ECG predicts peri-operative myocardial ischaemia associated with myocardial cell damage. Anaesthesia 2004;59:1083-90.

82. Landesberg G, Mosseri M, Zahger D, et al. Myocardial infarction after vascular surgery: the role of prolonged stress-induced, ST depression-type ischemia. J Am Coll Cardiol 2001;37:1839-45.

83. Raby KE, Barry J, Creager MA, et al. Detection and significance of intraoperative and postoperative myocardial ischemia in peripheral vascular surgery. JAMA 1992;268:222-7.

84. Landesberg G, Shatz V, Akopnik I, et al. Association of cardiac troponin, CK-MB, and postoperative myocardial ischemia with long-term survival after major vascular surgery. J Am Coll Cardiol 2003;42:1547-54.

85. Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. N Engl J Med 2003;348:5-14.

86. Shah MR, Hasselblad V, Stevenson LW, et al. Impact of the pulmonary artery catheter in critically ill patients: meta-analysis of randomized clinical trials. JAMA 2005;294:1664-70.

87. Grigoryan KV, Javedan H, Rudolph JL. Orthogeriatric care models and outcomes in hip fracture patients: a systematic review and meta-analysis. J Orthop Trauma 2014;28:e49-55.

88. Foucrier A, Rodseth R, Aissaoui M, et al. The long-term impact of early cardiovascular therapy intensification for postoperative troponin elevation after major vascular surgery. Anesth Analg 2014;119:1053-63.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at http://dx.doi.org/10.1016/j.cjca.2016.09.008.

Appendix 1. Members of guidelines' panels

Primary Panel Members
Co-chairs: Drs P.J. Devereaux, Joel Parlow
Members: Drs Amal Bessissow, Gregory Bryson, Emmanuelle Duceppe, Michelle Graham, Kristin Lyons, Paul MacDonald, Michael McMullen Daniel I. Sessler, Sadeesh Srinathan, Kim Styles, Vikas Tandon
Secondary Panel Members
Drs Rebecca Auer, Mohit Bhandari, Davy Cheng, Peter Choi, Benjamin Chow, Gilles Dagenais, Josée Fafard, Gordon Guyatt, John Harlock, David Hornstein, Michael Jacka, Andrea Kurz, Luc Lanthier, Yannick LeManach, Finlay McAlister, Edward McFalls, Michael McGillion, Marko Mrkobrada, Ameen Patel, Tej Sheth, Maria Tiboni, Duminda Wijeysundera