Anaesthesia 2020, 75 (Suppl. 1), e165–e173 doi:10.1111/anae.14920

Review Article

Peri-operative cardiac biomarker screening: a narrative review

S. M. Ruzycki,[1] **M. Prystajecky,**[2] **M. R. Driedger**[3] and **R. Kachra**[4]

1 Clinical Lecturer, Department of Medicine, Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, AB, Canada
2 Assistant Professor, Department of Medicine, University of Saskatchewan, Saskatoon, SK, Canada
3 Clinical Fellow, Division of Hepatobiliary and Pancreatic Surgery, Mayo Clinic, Rochester, MN, USA
4 Clinical Associate Professor, Division of General Internal Medicine, Department of Medicine, University of Calgary, AB, Canada,

Summary

Peri-operative risk estimation has traditionally focused on assessing the likelihood of postoperative morbidity and mortality using pre-operative functional assessment. Although this strategy is currently recommended by most major society guidelines, contemporary evidence suggests that cardiac biomarker measurement has important advantages over pre-operative functional assessment. These advantages include superior predictive discrimination and inclusion of the postoperative course in risk estimation. In this review, we provide an overview of the evidence supporting the peri-operative utilisation, compare risk estimation methods and discuss which patients may benefit most from cardiac biomarker screening. We also discuss protocols for biomarker screening and management of patients with abnormal results.

Correspondence to: S. M. Ruzycki
Email: shannon.ruzycki@ucalgary.ca
Accepted: 29 September 2019
Keywords: peri-operative cardiac biomarkers; peri-operative risk estimation; troponin
Twitter: @ShannonRuzycki; @RahimKachra

Introduction

It is estimated that over 300 million operations are performed every year worldwide [1, 2]. The 30-day mortality rate for the average patient undergoing non-cardiac surgery is between 1% and 2% [3–5]. Recent estimates suggest that 1 in every 13 deaths worldwide occurs within the first 30 days after surgery, making this the third most common cause of death in the world [2]. An additional 5% of patients will have a postoperative myocardial infarction (MI) and up to 1% will suffer a stroke in the first 30 days after surgery [4, 5]. Although cardiovascular complications are a leading cause of postoperative morbidity and mortality, up to 50% of deaths in the 30 days after surgery are from other causes [5, 6]. The aim of peri-operative medicine is to decrease peri-operative morbidity and mortality by identifying patients at increased risk of postoperative complications, advising patients and surgical teams of these risks, and implementing risk reduction strategies [7, 8].

To this end, peri-operative physicians have used multiple methods to screen and manage high-risk patients awaiting surgery [8]. Risk stratification has traditionally involved using risk scores such as the revised cardiac risk index (RCRI), risk calculators such as the National Surgical Quality Improvement Program (NSQIP) surgical risk calculator, functional assessment and cardiac stress testing in higher risk patients (Table 1) [8–14]. These strategies have important limitations, including cost, availability of test equipment and personnel and a lack of consistent evidence demonstrating improved outcomes [15–20]. Importantly, these strategies focus on the pre-operative phase and do not address postoperative identification or management of complications [7, 14]. This is especially relevant for urgent

Table 1 Comparison of national society guideline recommendations for peri-operative cardiac risk estimation.

	Year	Pre-operative testing	Cardiac testing	Postoperative management
American College of Cardiology and American Heart Association [9]	2014	Subjective functional assessment Clinical risk scores Recommend against using cardiac biomarkers	For select patients with an exercise capacity < 4 METSa	Recommend against postoperative troponin surveillance
European Society of Cardiology and European Society of Anaesthesiology [28]	2014	Subjective functional assessment Clinical risk scores Natriuretic peptide testing in patients with a predicted risk of > 5% ECG in high-risk patients	For select patients with an exercise capacity < 4 METSa Echocardiogram for patients undergoing high-risk surgeryb	Consider postoperative troponin surveillance in high-risk patients
Canadian Cardiovascular Society	2016	Natriuretic peptide testing in high-risk patients	For patients with acute coronary syndrome	Postoperative troponins in patients with abnormal natriuretic peptide or in patients without natriuretic peptide testing who meet high-risk criteria
NICE guidelines[53]c	2018	Consider ECG in ASA 3 or 4 patients for all surgeries and in all patients undergoing major surgery	Consider echocardiography for patients with heart murmur or signs and symptoms of heart failure.	No recommendations

METS, metabolic equivalents of a task; ECG, electrocardiogram; NICE, National Institute for Health and Care Excellence.
[a]4 METS refers to walking at moderate speed, ballroom dancing, golfing with a cart, playing a musical instrument [9].
[b]High-risk surgery includes aortic and major vascular surgery, lower limb revascularisation or amputation, liver resection, bile duct or duodeno-pancreatic surgery, oesophagectomy, repair of perforated bowel, adrenal resection, cystectomy, pneumonectomy or liver or pulmonary transplant surgery.
[c]Used to inform recommendations made by the Association of Anaesthetists guidelines for pre-operative assessment and patient preparation [30].

and emergency surgery where current strategies do not address identifying and managing high-risk patients after their procedures [7].

Improved methods for identifying high-risk patients both before and after surgery are needed. Cardiac biomarkers are a promising way forward in peri-operative assessment. Both pre-operative natriuretic peptides, including B-type natriuretic peptide (BNP) and N-terminal pro-BNP, and postoperative troponins predict 30-day mortality [4, 5, 21–24]. Cardiac biomarkers are not only less expensive and resource intensive than cardiac imaging but they have also been shown to better predict both cardiac and non-cardiac morbidity and mortality compared with exercise tolerance assessment [16]. Furthermore, evidence is accumulating that therapies, such aspirin, statins and direct oral anticoagulants, may improve outcomes in patients with abnormal cardiac biomarkers, providing evidence linking peri-operative assessment to therapies that reduce postoperative mortality [22, 25].

Due to these advantages, the Canadian Cardiovascular Society and European Cardiology Society recommend using cardiac biomarkers for peri-operative cardiac risk assessment [26]. Despite this, widespread implementation of peri-operative cardiac biomarker screening has been met with challenges [27]. These include limited availability of same-day natriuretic peptide testing, difficulties coordinating pre-operative outpatient natriuretic peptide testing with inpatient postoperative troponin management, lack of dissemination of knowledge among surgeons, anaesthetists and general practitioners and a lack of consensus from physicians about the utility of screening and management of patients with abnormal results.

In this review, we provide an overview of peri-operative cardiac biomarker surveillance. We will review the evidence supporting pre-operative natriuretic peptide testing and postoperative troponin surveillance as methods of peri-operative risk stratification, propose pathways for patient selection and discuss management of patients with abnormal testing.

Limitations of conventional strategies

Most peri-operative guidelines focus on pre-operative identification of patients at high risk of morbidity and mortality [9, 14, 28]. These recommendations concentrate almost exclusively on identifying patients with unrecognised cardiac disease through history and physical

examination. American, Australian, British and European guidelines for peri-operative risk stratification recommend estimating patients' risk of peri-operative cardiovascular complications through the application of a clinical risk index and subjective estimation of functional capacity (Table 1) [9, 10, 14, 29, 30]; patients who can complete less than four metabolic equivalents of exercise may be referred for additional cardiac testing, including stress testing or angiography [8, 9, 14, 28, 29].

However, available cardiovascular risk indices have important limitations. The most commonly recommended risk prediction tool in peri-operative medicine is the RCRI because it is simple to apply, based on readily available clinical parameters and has been externally validated in multiple surgical populations [9, 14, 26]. The RCRI is scored out of six, with one point assigned for each of: history of diabetes mellitus requiring insulin; chronic kidney disease; history of transient ischaemic attack or stroke; history of clinical congestive heart failure; history of MI; and high-risk surgery [31]. However, the RCRI provides only moderate discrimination for cardiovascular complications, with a C-statistic of 0.77 [32]. The NSQIP surgical risk calculator and MI and cardiac arrest calculator can also be used for cardiovascular risk estimation but have important limitations. Both scores were derived from a prospective cohort study that did not routinely measure troponin levels postoperatively and therefore likely underestimate cardiac risk. This is supported by a recent study that demonstrated that the NSQIP surgical risk calculator provided only fair discrimination (C-statistic 0.70) for postoperative MI and myocardial injury after non-cardiac surgery (MINS) [32].

Despite being endorsed by several major cardiovascular societies, subjective functional capacity is an unreliable predictor of postoperative cardiovascular complications. A single-centre prospective cohort study found that poor self-reported functional capacity was associated with a significantly increased risk of peri-operative myocardial ischaemia but not major cardiac complications. More recently, a large multicentre, prospective cohort study found that functional capacity by history taking was only 19.2% sensitive for identifying patients who could complete fewer than four metabolic equivalents when using cardiopulmonary exercise testing (CPET) as the gold standard [16]. In this study, neither subjectively assessed functional capacity nor CPET results correlated with 30-day MI or death [16]. Furthermore, studies evaluating pre-operative management strategies in patients with decreased functional capacity, including pre-operative exercise testing, have produced conflicting results [33, 34].

Accurate identification of patients with low functional capacity is thought to be important because most peri-operative guidelines recommend cardiac stress testing in high-risk patients with reduced exercise capacity. Cardiac stress testing, including physical or pharmacological methods, has been shown to reduce postoperative mortality in large observational studies comparing high-risk patients who underwent testing to those who did not [35]. However, this reduction in mortality was not driven by higher rates of cardiac revascularisation but was thought to be due to increased postoperative monitoring in high-risk patients [35]. Pharmacological stress testing is unlikely to be a cost-effective screening strategy; the number needed to treat to prevent one postoperative death using pharmacological stress testing was shown to be greater than 200 [35].

Pre-operative cardiac stress testing might also not be helpful in defining or mitigating pre-operative risk and may be harmful in certain patient groups. A large meta-analysis demonstrated that one-third of the deaths and MIs occurred in patients who had a normal pre-operative cardiac stress test, suggesting low sensitivity [36]. Additional data suggest that pre-operative stress testing is associated with increased mortality in low-risk patients (hazard ratio 1.35; 95%CI 1.05–1.74) [35]. This is especially worrisome as observational data suggest that nearly three-quarters of pre-operative stress tests are ordered in low-risk patients [37]. The reasons for the increase in mortality in low-risk patients is hypothesised to be due to unnecessary surgical delays to complete pre-operative cardiac testing that leads to deterioration of the surgical condition.

It is important to recognise that coronary artery revascularisation with percutaneous coronary intervention has not been shown to improve mortality outside of ST segment elevation MI or sudden cardiac death [38]. Even in patients with angina, percutaneous coronary intervention and cardiac stenting do not improve exercise capacity or symptoms of angina [39]. For these reasons, angiography and revascularisation are not recommended by major society guidelines outside of acute coronary syndrome or MI, even in the pre-operative period in patients with abnormal cardiac stress test results [9, 10, 26]. Medical management is the preferred management of patients with symptomatic or asymptomatic coronary artery disease.

While pre-operative echocardiography should be completed in all patients who are suspected to have obstructive cardiac disease, including pulmonary hypertension, aortic stenosis, hypertrophic cardiomyopathy and mitral stenosis [26], routine pre-operative echocardiography does not improve outcomes in surgical

patients [40]. Patients who have abnormal pre-operative echocardiography have nearly nine times greater risk of postoperative death compared with patients with normal results (RR 8.7; 95%CI 2.6–26.6, $p < 0.005$) [40]. However, when used to predict if a patient is at increased risk of postoperative death or MI, pre-operative echocardiogram demonstrates poor predictive accuracy (area under the curve 0.61; 95%CI 0.59–0.64) and does not provide incremental prediction when combined with the RCRI [40].

Pre-operative natriuretic peptide testing

In contrast to the above methods, natriuretic peptide measurement does improve pre-operative risk prediction. Applying the results of natriuretic peptide testing to patients undergoing cardiac surgery has been shown to improve risk estimation. After classifying patients as high- or low-risk based on RCRI and surgery type, the addition of natriuretic peptide testing correctly reclassified 16% of patients to a different risk category, demonstrating that natriuretic peptide testing adds value to current methods [23, 24]. Observational studies have demonstrated that abnormal pre-operative natriuretic peptide values can reasonably predict postoperative mortality [23]. A large meta-analysis of observational data demonstrated that elevated natriuretic peptide is associated with an OR of 19.3 (95%CI 8.5–43.7) for postoperative adverse cardiac complications [23]. Additional analyses demonstrate that 21.8% of patients with abnormal pre-operative natriuretic peptide values either died or had a MI within 30 days of surgery compared with less than 5% of patients with a normal measurement [21, 26]. Natriuretic peptide testing also outperforms functional assessment and echocardiography in predicting postoperative morbidity and mortality [16, 40].

The major cardiovascular societies have provided conflicting recommendations regarding which patients should undergo pre-operative natriuretic peptide screening. The Canadian Cardiovascular Society strongly recommends testing pre-operative natriuretic peptide levels in patients whose risk of postoperative complications is greater than 5%. This includes patients who are ≥ 65 years of age, have known cardiovascular disease or have a RCRI score of one or greater. The European Society of Cardiology also recommended using natriuretic peptide for pre-operative cardiac risk assessment in high-risk patients; however, this is categorised as a weak recommendation. In contrast, the American Heart Association does not make a recommendation regarding pre-operative natriuretic peptide testing, citing the methodological limitations of the available studies and the uncertain impact of pre-operative natriuretic peptide testing on patient outcomes.

We believe that pre-operative natriuretic peptide testing is beneficial in patients undergoing non-cardiac surgery. The incremental prediction provided by natriuretic peptide levels supports informed decision making for patients and clinicians. Pre-operative natriuretic peptide testing also facilitates selection of patients for increased postoperative surveillance, which has the potential improve patient outcomes through early detection of complications and initiation of therapies. Although this benefit is yet to be proven, definitive data linking other risk stratification modalities (e.g. clinical risk indices, stress testing and echocardiography) with patient outcomes are similarly lacking. We generally test pre-operative natriuretic peptide levels in patients who are at a greater than 5% risk of postoperative cardiovascular complications as per the Canadian Cardiovascular Society guidelines but acknowledge that this risk threshold is arbitrary. Centres considering implementing pre-operative natriuretic peptide testing should take into consideration natriuretic peptide test availability, turnaround time and funding availability when making this decision. An important limitation of pre-operative natriuretic peptide testing is the lack of validated risk prediction indices that incorporate both established clinical risk factors and biomarker data. Until such risk indices are available, we quote the risk of cardiovascular complications associated with a normal (5%) and elevated (22%) natriuretic peptide level when consulting patients pre-operatively.

Clinicians should ensure that patients with elevated natriuretic peptide results do not have signs of decompensated heart failure, such as peripheral oedema, pulmonary oedema or signs of low cardiac output. Patients in decompensated heart failure have increased postoperative mortality, and when possible should be stabilised before surgery. Patients with abnormal natriuretic peptide results who are not in decompensated heart failure do not require additional testing or delay of surgery [26]; however, these patients have increased risk of morbidity and mortality [24]. Peri-operative physicians can use the results to inform pre-operative risk counselling and informed consent [26]. In addition, patients with elevated pre-operative natriuretic peptide testing should undergo postoperative troponin surveillance for postoperative risk stratification [26].

Postoperative troponin surveillance

Cardiac biomarkers have been used to screen postoperative patients for cardiac complications for

almost 25 years [41, 42]. Universal measurement of cardiac biomarkers in high-risk postoperative patients consistently identifies a group of asymptomatic patients with MI who were otherwise unrecognised [3–6]. Contemporary studies using modern troponin assays estimate that between 50% and 80% of postoperative MIs are asymptomatic [3, 6, 22, 25, 43, 44]. Importantly, patients who have a recognised postoperative MI have a 30-day mortality as high as 20% [6, 22]. Without postoperative monitoring, asymptomatic patients with MI receive no intervention and are expected to have even higher mortality [7, 22].

In addition to identifying asymptomatic MI, comprehensive postoperative troponin measurement can be used to risk-stratify postoperative patients. Isolated postoperative troponin elevations are strongly correlated with 30-day mortality after surgery, even in the absence of MI (Table 2) [4–6, 24, 44]. Nearly one in five postoperative patients has elevated postoperative troponin measurements and the majority will not have ECG changes or other ischaemic features [3–6, 22, 42, 44]. These myocardial injuries arise due to complex interplays between patient-specific factors, such as diabetes or previous coronary artery disease, anaesthetic factors, such as intra-operative hypotension or tachycardia, and surgical factors, such as bleeding [44, 45]. This is in keeping with angiography data demonstrating that the pathophysiology of postoperative MI is more likely to be due to supply–demand mismatch (type-2 MI) rather than acute thrombus formation (type-1 MI), which is more common in non-operative settings [45].

Table 2 The association between 30-day mortality rate and increasing high-sensitivity troponins [4–6, 22].

Postoperative clinical presentation	Proportion of patients affected	30-day all-cause mortality
All patients	100%	1.9%
No troponin elevation	80–85%	0.8%
Any troponin elevation	15–20%	7.3%
MINS	11%	
High-sensitivity troponin T		
20–65 ng.l^{-1}	18.6%	3.0%
66–1000 ng.l^{-1}	5.1%	9.1%
> 1000 ng.l^{-1}	0.2%	30.0%
Troponin I		
0.02 ng.ml^{-1}	3.3%	4.0%
0.03–0.29 ng.ml^{-1}	7.4%	9.3%
≥ 0.30 ng.ml^{-1}	1.1%	16.9%
Postoperative myocardial infarction	3.9%	
STEMI	0.5%	11–22%
NSTEMI	4.5%	11–22%
Systemic illness	Variable	33%

MINS, myocardial injury after non-cardiac surgery; ECG, electrocardiogram; NSTEMI, non-ST segment myocardial infarction; STEMI, ST segment elevation myocardial infarction.

Selecting patients for postoperative troponin surveillance

The major cardiovascular societies generally recommend postoperative surveillance in patients at increased risk of postoperative cardiac complications. In keeping with recommendations from the Canadian Cardiovascular Society, we suggest measuring a troponin immediately postoperatively and once daily until postoperative day 3 in patients with elevated pre-operative natriuretic peptide testing or patients with greater than 5% risk of postoperative mortality. Similarly, both the American Heart Association and European Society of Cardiology also recommend performing postoperative troponin surveillance in patients at high risk of cardiac complications. These are graded as weak recommendations due to the non-specific nature of postoperative troponin elevations and the paucity of evidence linking pre-operative troponin surveillance with improved patient outcomes. We believe that postoperative troponin surveillance is warranted given the asymptomatic nature of postoperative myocardial injury and recent data demonstrating that medical therapy improves outcomes in these patients. We acknowledge that postoperative troponin surveillance may be costly given the high incidence of postoperative myocardial injury and the downstream costs associated with evaluating MINS, which includes patient follow-up, echocardiography and cardiac stress testing in select patients. The threshold for ordering postoperative troponins must therefore be individualised to specific institutions and take into consideration clinical volume, staffing levels and funding availability.

Management of patients with postoperative troponin elevation

Elevated troponins are a non-specific marker of risk and have a broad differential diagnosis (Table 3) [45, 46]. Once a postoperative troponin elevation is recognised, patients should be urgently assessed to determine if they meet criteria for MI; this requires ECG and clinical assessment for ischaemic symptoms (Table 3; Fig. 1) [46, 47]. Importantly, the absence of typical ischaemic chest pain is

Table 3 Diagnosis of common cardiovascular and non-cardiovascular medical complications after surgery [26, 46].

Postoperative outcome	Definition	Diagnostic criteria			
		Troponin	ECG	Symptoms	Comments
MINS	Postoperative troponin elevation not caused by systemic illness	≥ 99th percentile for upper limit of normal	No criteria		Exclude systemic illness
Acute coronary syndromes	Group of conditions caused by decreased coronary artery perfusion				
Unstable angina		Normal	No criteria	Ischaemic chest pain[a]	Exclude non-cardiac chest pain
NSTEMI		≥ 99th percentile for upper limit of normal and rise on serial measurements[b]	Ischaemic ECG findings without ST segment elevation	Ischaemic chest pain[a]	Required: troponin elevation plus one of: symptoms; ECG changes; or imaging abnormalities
STEMI		≥ 99th percentile for upper limit of normal	New ST-T segment elevations or development of pathologic Q waves	Ischaemic chest pain[a]	Required: troponin elevation plus one of: symptoms; ECG changes; or imaging abnormalities
Systemic illness	Non-cardiac disease which may or may not cause reduced coronary perfusion.				Sepsis, pneumonia and pulmonary embolism are the most common medical complications of surgery

MINS, myocardial injury after non-cardiac surgery; ECG, electrocardiogram; NSTEMI, non-ST segment myocardial infarction; STEMI, ST segment elevation myocardial infarction.
[a]Ischaemic chest pain is a pressure-type retrosternal sensation that occurs either at rest or with minimal exertion that lasts greater than 10 min. However, this presentation may vary depending on patient sex, age and comorbidities including diabetes. Alternate presentations include nausea, sweating, fatigue and exertional dyspnoea [46].
[b]Serial change refers to an increase of > 20% of the initial value or an absolute increase of > 7 $ng.l^{-1}$ for high-sensitivity cardiac troponin T assays [46].

not reassuring as the majority of patients with postoperative MI are thought to be asymptomatic [4–6, 22, 44, 48]. Patients may have ischaemic cardiac symptoms that are masked by pain, nausea, medications and delirium [22]. Non-ischaemic causes of myocardial injury should be ruled out by history and physical exam, including congestive heart failure, tachyarrhythmia or pulmonary embolism [46]. Patients who have a suspected cardiac aetiology for their troponin elevation should be considered for referral to a cardiologist.

Half of the postoperative mortality in patients with elevated troponin is due to non-cardiovascular causes, of which sepsis and pneumonia are most common [4, 6]. All patients with elevated troponins require a comprehensive assessment for postoperative complications, including: pulmonary embolism; MI; sepsis; bleeding; hypotension; and hypoxaemia. Importantly, patients who have elevated postoperative troponins from a non-cardiac cause have higher 30-day mortality than patients with elevated troponins from cardiac ischaemia [4, 5] (Table 2).

Patients with elevated postoperative troponins for which there is no alternate explanation fulfil the diagnostic criteria for MINS (Table 3; Fig. 1). Diagnosis of MINS requires an elevated postoperative troponin (typically greater than the 99th percentile) and exclusion of non-ischaemic aetiologies, such as sepsis, pulmonary embolism, tachycardia or chronic troponin elevation. Myocardial injury after non-cardiac surgery includes patients who meet diagnostic criteria for acute MI and patients who are asymptomatic with normal ECGs. However, management of patients who have MINS and postoperative MI are different, and are discussed separately in this review (Fig. 1) [7].

There is growing evidence that supports treating patients with MINS. Observational data suggest that patients with MINS may benefit from aspirin and statins [22]. Patients with MINS who have cardiac medication intensification (e.g. the addition or increase in dose of aspirin, a statin, a beta-blocker or an angiotensin converting enzyme inhibitor or angiotensin receptor blocker) have

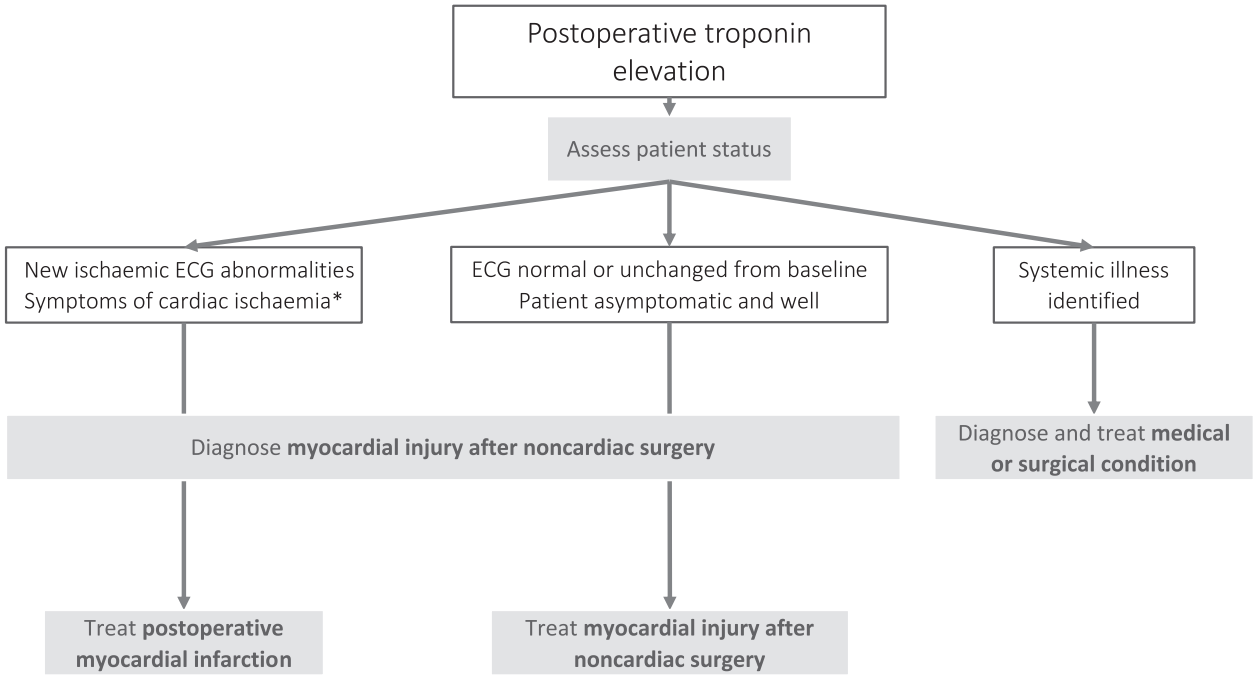

Figure 1 Management of patients with postoperative troponin elevation.

improved 1-year survival [49]. An international, multicentre, randomised, placebo-controlled trial demonstrated that dabigatran reduced vascular morbidity in patients with MINS, although interpretation of this evidence is limited due to high dropout rates [25]. Patients with MINS who do not have MI or systemic illness requiring hospitalisation do not require extended monitoring and can be discharged when otherwise appropriate [26].

Limitations of cardiac biomarker testing

Although peri-operative cardiac biomarker testing has many advantages, there are important limitations. First, selecting patients who may benefit from pre-operative natriuretic peptide measurement and postoperative troponin surveillance is challenging [27]. In some settings, pre-operative assessments incorrectly estimate risk in up to 75% of patients [37]. Second, natriuretic peptide testing is not available in all centres [27]. The role of pre-operative troponin measurement and management of patients with chronically elevated troponins is not known. Importantly, treatment of patients with MINS has not been definitively demonstrated to reduce mortality and improve outcomes in high-quality, prospective data [25]. With the exception of dabigatran, all evidence for the treatment of patients with MINS has been based on observational data [22, 49].

Furthermore, studies examining the cost effectiveness of peri-operative cardiac biomarker screening are limited by the lack of data demonstrating improved clinical outcomes as a result of surveillance programmes [50, 51]. With this in mind, cost–benefit analyses from Canada and South Africa suggest that cardiac biomarker surveillance is likely cost effective [44, 50]. This is important because, depending on the setting, between 40% and 60% of surgical patients may meet criteria for peri-operative cardiac biomarker screening and patients who undergo peri-operative cardiac biomarker screening have increased rates of subsequent healthcare utilisation [6, 52].

Conclusions

The introduction of cardiac biomarkers for peri-operative risk assessments represents a paradigm shift in peri-operative medicine. Pre-operative natriuretic peptide levels provide incremental risk prediction over clinical risk indices and are less costly than cardiac stress testing. Postoperative troponin surveillance identifies patients with asymptomatic myocardial injury and facilitates postoperative cardiac risk stratification, which in turn enables risk reduction strategies to be implemented. We anticipate that ongoing research on risk stratifying and treating patients with MINS will further improve outcomes for patients undergoing non-cardiac surgery.

Acknowledgements

We thank R. Alemao for her contributions to the preparation of the manuscript. No external funding or competing interests declared.

References

1. Weiser TG, Haynes AB, Molina G, et al. Size and distribution of the global volume of surgery in 2012. *Bulletin of the World Health Organization* 2016; **94**: 201–9F.
2. Nepogodiev D, Martin J, Biccard B, Makupe A, Bhangu A. Global burden of postoperative death. *Lancet* 2019; **393**: 401.
3. The Vision Pilot Study Investigators. An international prospective cohort study evaluating major vascular complications among patients undergoing noncardiac surgery: the VISION Pilot Study. *Open Medicine* 2011; **5**: e193–200.
4. Devereaux P, Chan M, Alonso-Coello P, et al. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *Journal of the American Medical Association* 2012; **307**: 2295–304.
5. Writing Committee for the VISION Study Investigators. Association of postoperative high-sensitivity troponin levels with myocardial injury and 30-day mortality among patients undergoing noncardiac surgery. *Journal of the American Medical Association* 2017; **317**: 1642–51.
6. Puelacher C, Lurati Buse G, Seeberger D, et al. Perioperative myocardial injury after noncardiac surgery: incidence, mortality, and characterization. *Circulation* 2018; **137**: 1221–32.
7. Biccard BM, Devereaux PJ, Rodseth RN. Cardiac biomarkers in the prediction of risk in the non-cardiac surgery setting. *Anaesthesia* 2014; **69**: 484–93.
8. Lee LKK, Tsai PNW, Ip KY, Irwin MG. Pre-operative cardiac optimisation: a directed review. *Anaesthesia* 2019; **74**(Suppl. 1): 67–79.
9. 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.
10. Kristensen SD, Knuuti J. New ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management. *European Heart Journal* 2014; **35**: 2344–5.
11. Liu Y, Cohen ME, Hall BL, Ko CY, Bilimoria KY. Evaluation and enhancement of calibration in the American College of Surgeons NSQIP surgical risk calculator. *Journal of the American College of Surgeons* 2016; **223**: 231–9.
12. Cohn SL, Fernandez R. Comparison of 4 cardiac risk calculators in predicting postoperative cardiac complications after noncardiac operations. *American Journal of Cardiology* 2018; **121**: 125–30.
13. 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.
14. Scott IA, Shohag HA, Kam PC, Jelinek MV, Khadem GM. Preoperative cardiac evaluation and management of patients undergoing elective non-cardiac surgery. *Medical Journal of Australia* 2013; **199**: 667–73.
15. Wijeysundera DN, Austin PC, Beattie WS, Hux JE, Laupacis A. Outcomes and processes of care related to preoperative medical consultation. *Archives of Internal Medicine* 2010; **170**: 1365–74.
16. Wijeysundera DN, Pearse RM, Shulman MA, et al. Assessment of functional capacity before major non-cardiac surgery: an international, prospective cohort study. *Lancet* 2018; **391**: 2631–40.
17. Lee TC. Is there value in a preoperative medical consultation? *Archives of Internal Medicine* 2011; **171**: 365–9.
18. Vazirani S, Lankarani-Fard A, Liang LJ, Stelzner M, Asch SM. Perioperative processes and outcomes after implementation of a hospitalist-run preoperative clinic. *Journal of Hospital Medicine* 2012; **7**: 697–701.
19. Auerbach AD, Rasic MA, Sehgal N, Ide B, Stone B, Maselli J. Opportunity missed: medical consultation, resource use, and quality of care of patients undergoing major surgery. *Archives of Internal Medicine* 2007; **167**: 2338–44.
20. Katz RI, Cimino L, Vitkun SA. Preoperative medical consultations: impact on perioperative management and surgical outcome. *Canadian Journal of Anesthesia* 2005; **52**: 697–702.
21. Rodseth R, Padayachee L, Biccard BJA. 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.
22. 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. *Annals of Internal Medicine* 2011; **154**: 523–8.
23. 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. *Journal of the American College of Cardiology* 2009; **54**: 1599–606.
24. 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. *Journal of the American College of Cardiology* 2014; **63**: 170–80.
25. Devereaux PJ, Duceppe E, Guyatt G, et al. Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomised, placebo-controlled trial. *Lancet* 2018; **391**: 2325–34.
26. Duceppe E, Parlow J, MacDonald P, et al. Canadian Cardiovascular Society guidelines on perioperative cardiac risk assessment and management for patients who undergo noncardiac surgery. *Canadian Journal of Cardiology* 2017; **33**: 17–32.
27. Ruzycki SM, Prystajecky M. Point-counterpoint: perioperative cardiac biomarkers. *Canadian Journal of General Internal Medicine* 2019; in press.
28. 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). *European Journal of Anaesthesiology* 2014; **31**: 517–73.
29. Levett DZH, Jack S, Swart M, et al. Perioperative cardiopulmonary exercise testing (CPET): consensus clinical guidelines on indications, organization, conduct, and physiological interpretation. *British Journal of Anaesthesia* 2018; **120**: 484–500.
30. Association of Anaesthetists. AAGBI Safety Guideline: Pre-operative Assessment and Patient Preparation: The Role of the Anaesthetist. 2010. https://anaesthetists.org/Home/Resources-publications/Guidelines/Pre-operative-assessment-and-pa

tient-preparation-the-role-of-the-anaesthetist-2 (accessed 30/9/2019).
31. 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.
32. Fronczek J, Polok K, Devereaux PJ, et al. External validation of the revised cardiac risk index and national surgical quality improvement program myocardial infarction and cardiac arrest calculator in noncardiac vascular surgery. *British Journal of Anaesthesia* 2019; **123**: 421–9.
33. Cabilan CJ, Hines S, Munday J. The impact of prehabilitation on postoperative functional status, healthcare utilization, pain, and quality of life: a systematic review. *Orthopedic Nursing* 2016; **35**: 224–37.
34. Tew GA, Ayyash R, Durrand J, Danjoux GR. Clinical guideline and recommendations on pre-operative exercise training in patients awaiting major non-cardiac surgery. *Anaesthesia* 2018; **73**: 750–68.
35. Wijeysundera DN, Beattie WS, Austin PC, Hux JE, Laupacis A. Non-invasive cardiac stress testing before elective major non-cardiac surgery: population based cohort study. *British Medical Journal* 2010; **340**: b5526.
36. Beattie WS, Abdelnaem E, Wijeysundera DN, Buckley DN. A meta-analytic comparison of preoperative stress echocardiography and nuclear scintigraphy imaging. *Anesthesia and Analgesia* 2006; **102**: 8–16.
37. Peterson B, Ghahramani M, Emerich M, Foy AJ. Frequency of appropriate and low-risk noncardiac preoperative stress testing across medical specialties. *American Journal of Cardiology* 2018; **122**: 744–8.
38. Wong EY, Lawrence HP, Wong DT. The effects of prophylactic coronary revascularization or medical management on patient outcomes after noncardiac surgery: a meta-analysis. *Canadian Journal of Anesthesia* 2007; **54**: 705–17.
39. Gelman A, Carlin JB, Nallamothu BK. Objective Randomised Blinded Investigation with Optimal Medical Therapy of Angioplasty in Stable Angina (ORBITA) and coronary stents: a case study in the analysis and reporting of clinical trials. *American Heart Journal* 2019; **214**: 54–9.
40. 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 Circulation Journal* 2011; **41**: 505–11.
41. Neill F, Sear JW, French G, et al. Increases in serum concentrations of cardiac proteins and the prediction of early postoperative cardiovascular complications in noncardiac surgery patients. *Anaesthesia* 2001; **55**: 641–7.
42. Lee TH, Thomas EJ, Ludwig LE, et al. Troponin T as a marker for myocardial ischemia in patients undergoing major noncardiac surgery. *American Journal of Cardiology* 1996; **77**: 1031–6.
43. Böttiger BW, Motsch J, Teschendorf P, et al. Postoperative 12-lead ECG predicts peri-operative myocardial ischemia associated with myocardial cell damage. *Anaesthesia* 2004; **59**: 1083–90.
44. 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.
45. Sheth T, Natarajan M, Hsieh V, et al. Incidence of thrombosis in perioperative and non-operative myocardial infarction. *British Journal of Anaesthesia* 2018; **120**: 725–33.
46. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology* 2014; **64**: e139–228.
47. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction. *Journal of the American College of Cardiology* 2018; **72**: 2231–64.
48. Devereaux P, Sessler DI. Cardiac complications in patients undergoing major noncardiac surgery. *New England Journal of Medicine* 2015; **373**: 2258–69.
49. 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. *Anesthesia and Analgesia* 2014; **119**: 1053–63.
50. Buse GL, Manns B, Lamy A, et al. Troponin T monitoring to detect myocardial injury after noncardiac surgery: a cost–consequence analysis. *Canadian Journal of Surgery* 2018; **61**: 185–94.
51. 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. *South African Medical Journal* 2014; **104**: 619–23.
52. Ruzycki SM, Kachra R, Li P, Walsh J, Minty E, Zarnke KB. Characterization of current CCS perioperative guideline uptake in a single pre-admission clinic. In: Abstracts from the Rocky Mountain ACP/AMA Internal Medicine Conference: Alberta, Canada. 2017. https://cjgim.ca/index.php/csim/article/view/274/816 (accessed 18/10/2019).
53. NICE. Routine preoperative tests for elective surgery. NG45. 2016. London: NICE. https://www.nice.org.uk/guidance/ng45 (accessed 30/9/2019).

