BJA

British Journal of Anaesthesia, 130 (1): 21–28 (2023)

doi: 10.1016/j.bja.2022.08.041
Advance Access Publication Date: 1 December 2022
Review Article

CARDIOVASCULAR

Perioperative troponin surveillance in major noncardiac surgery: a narrative review

Michelle S. Chew[1,*], Bernd Saugel[2,3] and Giovanna Lurati-Buse[4]

[1]Departments of Anaesthesia and Intensive Care, Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden, [2]Department of Anesthesiology, Center of Anesthesiology and Intensive Care Medicine, University Medical Center Hamburg–Eppendorf, Hamburg, Germany, [3]Outcomes Research Consortium, Cleveland, OH, USA and [4]Department of Anaesthesiology, University Hospital Düsseldorf, Düsseldorf, Germany

*Corresponding author. E-mail: Michelle.chew@liu.se

Summary

Myocardial injury is now an acknowledged complication in patients undergoing noncardiac surgery. Heterogeneity in the definitions of myocardial injury contributes to difficulty in evaluating the value of cardiac troponins (cTns) measurement in perioperative care. Pre-, post-, and peri-operatively increased cTns are encompassed by the umbrella term 'myocardial injury' and are likely to reflect different pathophysiological mechanisms. Increased cTns are independently associated with cardiovascular and non-cardiovascular complications, poor short-term and long-term cardiovascular outcomes, and increased mortality. Preoperative measurement of cTns aids preoperative risk stratification beyond the Revised Cardiac Risk Index. Systematic measurement detects acute perioperative increases and allows early identification of acute myocardial injury. Common definitions and standards for reporting are a prerequisite for designing impactful future trials and perioperative management strategies.

Keywords: biomarker; cardiac troponins; MINS; myocardial injury; noncardiac surgery; perioperative outcome

Editor's key points

- Myocardial injury is common after noncardiac surgery and is associated with poorer short-term and longer-term outcomes.
- The causes remain unclear, in part because common, standardized definitions are lacking.
- Surveillance monitoring of cardiac troponin remains controversial.

Myocardial injury in now an acknowledged complication in patients undergoing noncardiac surgery. High-sensitivity cardiac troponins (hs-cTns) are sensitive, quantitative markers of cardiomyocyte injury, and increased levels of these biomarkers are required for a diagnosis of myocardial injury. Myocardial injury occurs commonly in high-risk surgical populations.[1–6] A recent meta-analysis estimated the pooled incidence of myocardial injury across 139 studies with systematic biomarker screening at 19.6% (confidence interval [CI], 17.8–21.4%).[7]

The vast majority of patients with myocardial injury in the perioperative period do not fulfil the universal definition of myocardial infarction or experience ischaemic symptoms. Although perioperative timeframes vary across studies (from 30 days before to 30 days after surgery), large observational studies have established that myocardial injury, regardless of whether it is detected preoperatively, postoperatively, or as a perioperative change, is independently associated with early or delayed mortality[1–4,6–10] and adverse cardiovascular outcomes.[3–5,7–10] The risk of mortality appears to be greatest among those with perioperative cTn increases, with greater increases indicating greater risk.[2,4,6] Myocardial injury occurring during the perioperative period is a heterogeneous

Received: 18 January 2022; **Accepted:** 31 August 2022

syndrome that reflects different pathophysiologies, including ischaemic and non-ischaemic, cardiac, and extracardiac causes, and which carry different prognoses.[6,9] Furthermore, inflammation may play a role in the pathogenesis of cardiomyocyte injury.[11,12]

Both cardiac and noncardiac complications occur among patients with myocardial injury.[9,13–16] Moreover, mortality and disability-free survival after sustaining myocardial injury are related to whether the injury is associated with these complications. For example, a study with systematic screening of cTns showed a two-to three-fold increased hazard for 30-day mortality among patients with perioperative myocardial injury (PMI) who develop acute myocardial infarction (AMI). For patients with PMI and extracardiac complications or acute heart failure, the hazard was increased six-to 10-fold.[9] This is supported by a sub-analysis of the Evaluation of Nitrous Oxide in the Gas Mixture for Anaesthesia (ENIGMA) trial showing that the occurrence of cardiac and noncardiac complications within the setting of postoperative myocardial injury was associated with short- and long-term mortality and disability-free survival.[16] Finally, among patients undergoing vascular surgery a two-fold increase in long-term mortality (median follow-up, 26.9 months) was found among patients with increased preoperative cTns and AMI.[6]

Challenges with variable definitions: myocardial injury, acute myocardial injury, myocardial injury after noncardiac surgery, or perioperative myocardial injury?

Definitions, terminology, and diagnostic criteria of myocardial injury that occur during the perioperative period are highly heterogeneous. In 2021, the Standardized Endpoints in Perioperative Medicine (StEP) initiative[17] adopted myocardial injury and myocardial infarction as defined by the 4th Universal Definition of Myocardial Infarction (4th UDMI)[18] as two of nine consensus cardiovascular outcomes. Both AMI and acute myocardial injury require the demonstration of an increase or decrease in cTns. Myocardial injury is defined any evidence of elevated cTn values above the 99th percentile upper reference limit, whereas *acute* myocardial injury requires the demonstration of an increase, decrease, or both of cTn values. AMI distinguishes itself from acute myocardial injury by requiring the presence of new ischaemic ECG changes, clinical symptoms, or imaging evidence of loss of viable myocardium or regional wall motion abnormalities. AMI may further be classified as Type I (related to acute atherosclerotic plaque disruption) and Type II (oxygen supply–demand imbalance, i.e. non-atherothrombotic mechanisms). Importantly, Type II AMI and acute myocardial injury can be difficult to differentiate.[18]

Within perioperative medicine, other terms and definitions of myocardial injury have been used. The Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION) study defined myocardial injury after noncardiac surgery (MINS) as a postoperative hs-cTn T concentration (hs-cTnT) of 20 to <65 ng L^{-1} with an absolute change of ≥5 ng L^{-1} or any postoperative absolute hs-cTnT value ≥65 ng L^{-1} attributable to presumed ischaemic causes.[2] This approach requires systematically adjudicating whether hs-cTnT changes are caused by ischaemia or other causes (defined in the VISION study as atrial fibrillation, cardioversion, sepsis, pulmonary embolism, chronic elevation, or other causes). As postoperative ECGs were not universally available in the VISION study, both

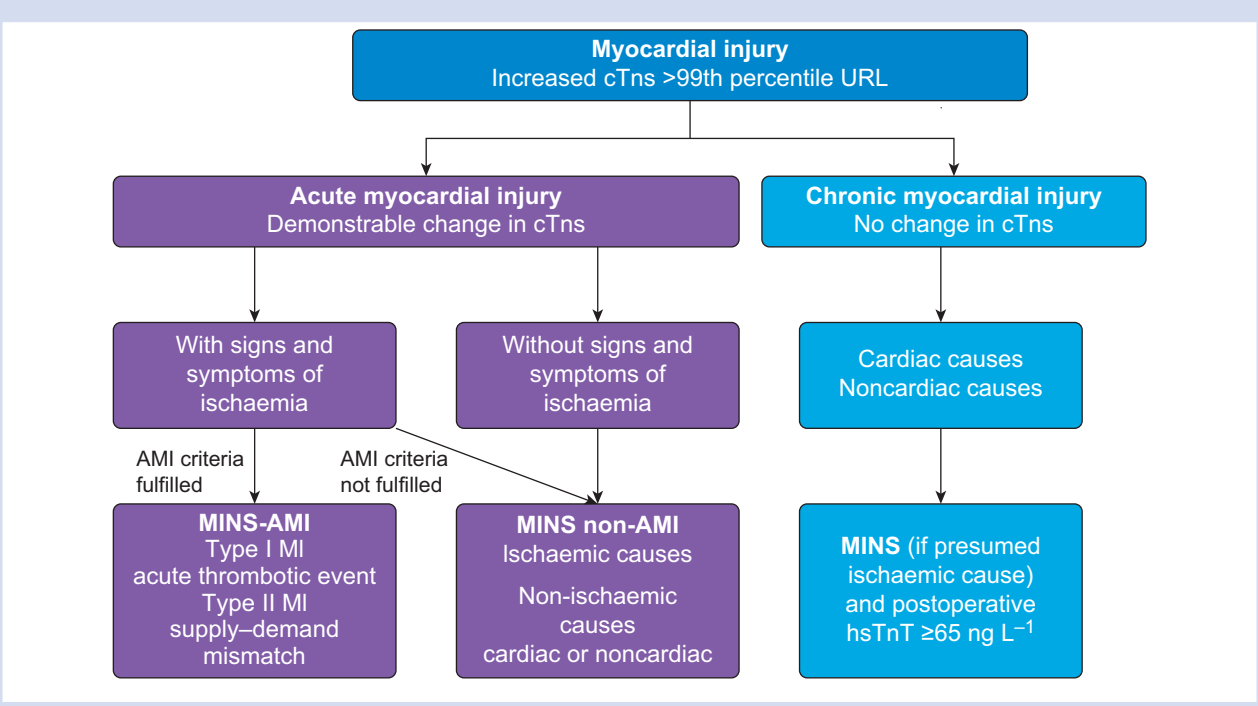

Fig 1. Classification of myocardial injury occurring during the perioperative period. UR, upper reference limit in a normal, healthy population; AMI, acute myocardial infarction; cTn, cardiac troponin; MINS, myocardial injury after noncardiac surgery; URL, upper reference limit.

under- and overdiagnosis of MINS may have occurred. Moreover, clinical conditions precluding the diagnosis of MINS such as atrial fibrillation or sepsis may be accompanied by supply–demand ischaemia, making the adjudication process challenging and potentially lowering the accuracy of this definition. Despite clearly defined criteria in the VISION studies, heterogeneous definitions of MINS have been used in perioperative literature, as demonstrated by a recent meta-analysis.[7] MINS may thus be seen as a subset of acute myocardial injury occurring in the perioperative period when there is a presumed ischaemic cause and that does not necessarily require comparison with a preoperative value (Fig 1). For the identification of acute myocardial injury in line with the 4th UDMI, recent publications suggest comparing postoperative high sensitivity cTns with a preoperative value.[3–5] Acute PMI, defined as any change in hs-cTnT >14 ng L^{-1} compared with preoperative values, captures acute perioperative changes and encompasses ischaemic and non-ischaemic cardiac causes and noncardiac aetiology.[3,4] However, many patients may not have an opportunity to have preoperative measurements (e.g. in emergent surgery), and some patients may already suffer from acute myocardial injury before surgery, making it difficult to distinguish between acute injury, acute on chronic injury, and chronic injury. To further complicate matters, the type of assay appears to be of importance as the incidence of PMI is lower when using hs-cTnI instead of hs-cTnT.[19] Heterogeneity in the definition of myocardial injury that occurs during perioperative period was recently highlighted by the StEP-COMPAC: cardiovascular outcomes initiative.[17] In this consensus statement, 'myocardial injury' – rather than 'MINS' – received a higher rating for validity, clarity, and feasibility. In extension to this, the 4th UDMI recommends a baseline preoperative value to determine whether the increase is acute or more chronic, in order to properly interpret the aetiology of elevated postoperative values. However, any dynamic change (e.g. between two postoperative measurements) is consistent with acute injury. Table 1 summarises currently used definitions for myocardial injury, comparing them with AMI. The existence of multiple thresholds for cTns and ambiguity regarding definitions of myocardial injury and type of assay have led to considerable difficulty in evaluating the value of hs-cTns surveillance in perioperative care.

Measurement of both pre- and postoperative hs-cTnT differentiates between acute and chronic myocardial injury, consistent with the recommendation of the Joint European Society of Cardiology/American College of Cardiology/American Heart Association/World Heart Federation Task Force for the Universal Definition of Myocardial Infarction.[18] Two recent prospective studies demonstrated that an additional increase above preoperatively increased hs-cTnT will identify acute perioperative events that increases the risk of complications

Table 1 Currently used definitions of myocardial injury and myocardial infarction and underlying pathophysiological mechanisms. Basel-PMI, Basel Perioperative Myocardial Injury Study; cTn, cardiac troponin; hs-cTnT, high-sensitivity cardiac troponin T; MINS, myocardial injury after noncardiac surgery; SD, standard deviation; URL, upper reference limit; VISION, Vascular Events in Noncardiac Surgery Patients Cohort Evaluation Study.

	Myocardial injury[18]	**Acute myocardial injury**[18]	**Myocardial injury after noncardiac surgery (MINS, VISION definition)**[2]	**Perioperative myocardial injury (Basel-PMI definition)**[34]	**Acute myocardial infarction**[18]
Criteria for definition	cTn >99th percentile URL for each specific assay	cTn change equal than or greater than 3 SD around measurement of individual assay In patients with initial values > 99th percentile URL, serial changes >20%	Postoperative hs-cTnT concentration 20 to <65 ng L^{-1} with an absolute change of ≥5 ng L^{-1} *or* any postoperative absolute value ≥65 ng L^{-1}	Absolute increase in hs-cTnT >14 ng L^{-1} above preoperative values within 3–7 days of surgery	Increase and decrease in cTn values with at least one value >URL *and* Signs, symptoms, or both of myocardial ischaemia. Type I myocardial infarction: Identification of a coronary thrombus required. Type II myocardial infarction: evidence of myocardial oxygen supply–demand imbalance unrelated to acute coronary atherothrombosis.
Pathophysiology	Causes may be ischaemic or non-ischaemic. May be acute or chronic. Type II myocardial infarction and non-ischaemic myocardial injury may coexist.	Acute, causes may be ischaemic or non-ischaemic. May be difficult to distinguish from Type II myocardial infarction.	Presumed ischaemic causes (i.e. excludes non-ischaemic aetiology such as sepsis, pulmonary embolus, atrial fibrillation, cardioversion, chronic elevation)	Causes may be ischaemic or non-ischaemic, cardiac, or extracardiac (e.g. sepsis and pulmonary embolus)	Cause must be ischaemic and attributable to atherothrombosis (Type I) or oxygen supply–demand imbalance (Type II).

even further.[3,4] Puelacher and colleagues[4] demonstrated a stepwise relationship with short- and long-term mortalities for a spectrum of hs-cTnT ranging from no increase to preoperative increases only to pre- and postoperative increases.[4] Similarly, Chew and colleagues[3] demonstrated that perioperative changes in hsTnT (maximal postoperative minus preoperative) provided better prognostic value for 30-day major adverse cardiovascular and cerebrovascular events (MACCE) and mortality, than only preoperative or postoperative changes alone, independently of the Revised Cardiac Risk Index (RCRI).[3] Thus, both preoperatively (likely chronic) and perioperatively (acute) increased cTns are encompassed by the umbrella term 'myocardial injury', that may be used for preoperative risk stratification and early detection respectively, and are likely to reflect different pathophysiological mechanisms.

Pathophysiology of myocardial injury in perioperative care

According to the 4th UDMI, acute myocardial injury may be attributable to ischaemic (plaque rupture or supply–demand imbalance or MINS) or non-ischaemic causes.[18] Non-ischaemic causes may be further classified into cardiac and systemic causes (Fig 1). MINS necessarily involves ruling out other causes of increased cTns including atrial fibrillation, sepsis, and pulmonary embolus. Acute myocardial injury and Type II AMI may be difficult to distinguish clinically without systematic surveillance of clinical and ECG changes. Thus, the pathophysiology of PMI is heterogeneous and covers both acute and chronic causes, and ischaemic and non-ischaemic aetiology.

Chronic myocardial injury includes cardiac (e.g. arrythmias, heart failure, cardiomyopathies) and noncardiac causes (e.g. critical illness, chronic kidney disease). Acute PMI encompasses both ischaemic and non-ischaemic causes. Non-ischaemic causes include noncardiac (e.g. sepsis, pulmonary embolus, acute kidney injury) and cardiac causes (arrythmias, heart failure). Ischaemic causes include MINS (see text for definition), Type I myocardial infarction (acute thrombotic event), Type II myocardial infarction (O_2 supply–demand mismatch). Although a diagnosis of MINS may be made regardless of whether signs or symptoms of ischaemia are present, a diagnosis of AMI requires the presence of signs or symptoms of ischaemia.

An understanding of pathophysiological mechanisms underlying myocardial injury is a prerequisite for designing future trials and treatment pathways for myocardial injury in perioperative patients. Although baseline cardiovascular risk is a significant risk factor for myocardial injury, coronary thrombosis appears not to be the dominating pathophysiological mechanism. Among patients suffering from a perioperative myocardial infarction, thrombosis detected by optical coherence tomography was less common despite similar plaque pathology compared with patients with non-perioperative myocardial infarction.[20] In the Coronary CTA VISION study, overt and covert coronary artery disease were detected in a large proportion of patients undergoing coronary CT angiography before noncardiac surgery. However, perioperative myocardial infarction occurred in patients with and without preoperative obstructive coronary artery disease.[21] These findings suggest that coronary artery disease alone does not explain the pathophysiological mechanism for patients with poor cardiovascular outcomes after noncardiac surgery. Similarly, among patients undergoing vascular surgery the risk of long-term mortality was independent of the mechanism of myocardial injury (baseline cTn elevation *vs* Type 1 MI *vs* Type II MI) despite a demonstrable relationship between the degree of cTn increase and mortality.[6]

Perioperative cTns are also increased in patients with non-cardiovascular complications suggesting multimodal mechanisms.[13,14] A recent study showed that the aetiology of PMI varied considerably and included extra-cardiac causes such as sepsis among patients with increased cardiovascular risk. Type 1 myocardial infarction occurred in a minority. This study also demonstrated that mortality associated with tachyarrhythmias, heart failure, and extracardiac PMI was higher than for Type 1 myocardial infarction, indicating the need to address causes other than coronary artery disease and ischaemia.[9] Finally, the contribution of inflammation to myocardial injury has been demonstrated in critically ill patients, but is still unknown within the context of perioperative care.[11,12]

Implementation of cardiac troponin surveillance in perioperative care

Current data indicate that cTn measurement adds value to the RCRI for preoperative risk stratification and postoperative

Table 2 Summary of recommendations from the European Society of Anaesthesiology and Intensive Care (ESAIC),[23,24] ESAIC and European Society of Cardiology (ESC),[24] Canadian Cardiovascular Society Guidelines (CCSG),[25] and the American Heart Association (AHA).[26] BNP, B-type natriuretic peptide; CAD, coronary artery disease; NT-proBNP, N-terminal B-type natriuretic peptide; RCRI, Revised Cardiac Risk Index; VD, vascular disease.

ESAIC/ESC[23,24]	CCSG[25]	AHA[26]
Assessment of cardiac troponins in high-risk patients, both before and 48–72 h after major surgery, may be considered. Suggest using preoperative hsTnT measurement to aid risk assessment in patients at risk of coronary artery disease and in patients undergoing major surgery.	If a patient's age ≥65 yr, RCRI ≥1, or age 45–64 yr with significant cardiovascular disease order NT-proBNP/BNP AND Positive NT-proBNP ≥300 mg L^{-1} or BNP ≥92 mg L^{-1} OR NT-proBNP or BNP not available THEN Measure troponin daily × 48–72 h Obtain ECG in PACU (no routine hsTnT monitoring if NT-proBNP <300 mg L^{-1}).	High-risk individuals (i.e. >65 yr or >45 yr old with established CAD or peripheral atheroscrlerotic VD) having noncardiac surgery should have serial cTn measurements during the first 48–72 h postoperatively while hospitalised. MINS diagnostic criteria should be used to standardise assessment and reporting of ischaemic events in clinical practice and future clinical trials.

measurement allows early and systematic detection of myocardial injury.[2–5,8,10,13–16,22] Although preoperative hs-cTnT screening is yet not established and is currently only recommended by one society guideline (Table 2), available studies show that it is independently prognostic of short- and long-term poor outcomes.[2–10,13–16] Preoperatively increased cTns appear to confer additional value when added to the RCRI for the prediction of major cardiovascular complications[3–5,22,27] although biomarker-enhanced risk prediction tools still require large-scale validation.

A cTn-surveillance system is useful for three reasons. Firstly, better preoperative risk stratification provides the opportunity to give patients more accurate information to facilitate decisions about surgery. For example, among patients aged ≥65 or 45–64 yr with cardiovascular risk factors, increased preoperative cTns may be used as a trigger for cardiac consultation, optimisation of cardiovascular medications, and further investigation before major noncardiac surgery. It may also provide an argument for increased perioperative monitoring (e.g. advanced perioperative haemodynamic monitoring) and increased postoperative vigilance (e.g. extended PACU stay or elective admission to the ICU). Secondly, postoperative cTn surveillance detects asymptomatic cTn increases. Early detection should prompt the clinician to look for causes of elevated cTns. These may range from noncardiac causes to non-ischaemic and ischaemic cardiac causes, and may aid postoperative real-time stratification of the level of care (e.g. ICU admission).[13] Thirdly, cTn surveillance identifies risk groups for further treatment. Even if there is no established treatment yet for MINS, clinical pathways exist for AMI, pulmonary embolism, sepsis, and arrythmias that may be heralded by increased cTns.

Varying recommendations in current perioperative management guidelines for hs-cTn surveillance (Table 2) are likely a reflection of a lack of consensus definitions, and a lack of evidence-based and clinically accepted management plans. To date, only one trial has investigated specific treatment for patients suffering from myocardial injury. Among patients suffering from MINS, dabigatran 110 mg twice daily lowered the risk of a composite of vascular mortality, non-fatal myocardial infarction, non-haemorrhagic stroke, peripheral arterial thrombosis, amputation, and symptomatic venous thromboembolism, with no significant increase in major bleeding.[28] Yet, the incidences of myocardial infarction or a cardiac revascularisation procedure were similar in treatment and control groups, and dabigatran was discontinued permanently in nearly half of patients thus precluding an assessment of the long-term bleeding risk. Notably, as MINS was the prerequisite for randomisation, non-ischaemic causes of acute cTn increase were excluded from this study. Other limitations including the use of placebo for the control arm of the study may raise questions about clinical applicability.

Preoperative and intraoperative studies addressing the prevention of myocardial injury are emerging. Recent studies targeting higher intraoperative blood pressures (≥60 *vs* ≥75 mm Hg) or aggressive perioperative warming to 37°C did not result in a reduction in myocardial injury or other adverse cardiovascular events.[29,30] Although myocardial injury was not specifically studied, results from the PeriOperative ISchemic Evaluation-1 (POISE-1) study showed that perioperative beta-blocker therapy reduced the incidence of cardiovascular death, non-fatal MI, and non-fatal cardiac arrest, but increased overall mortality, strokes, clinically important hypotension, and bradycardia.[31] The POISE-2 studies showed that perioperative aspirin and clonidine did not decrease the incidence of death or myocardial infarction but increased in the incidence of major bleeding, hypotension, and bradycardia.[32,33] In POISE-3, tranexamic acid given before and after surgery decreased the incidence of major bleeding but could not establish non-inferiority for MINS.[34] Although these studies collectively add knowledge regarding how adverse cardiovascular outcomes may/may not be mitigated in the perioperative setting, the general lack of effect may reflect of the heterogeneous aetiology of myocardial injury and poses challenges for clinical implementation of cTn screening. Blood pressure management strategies are also the subject of ongoing studies Perioperative Personalized Blood Pressure Managementt (IMPROVE-MULTI [NCT05416944], Tight Perioperative Blood Pressure Management to Reduce Serious Cardiovascular, Renal, and Cognitive Complications GUARDIAN [NCT04884802]) and the POISE-3 trial, that is pending publication (NCT03505723). Finally, in a systematic review no conclusions could be made for aspirin, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, perioperative beta-blockers, statins, and type of anaesthesia (propofol or sevoflurane) for the prevention of myocardial injury.[7]

Current data suggest that a two-step approach for cTn surveillance may be helpful. The first step involves the measurement of preoperative hs-cTnT in addition to the RCRI for preoperative risk stratification. This would likely be of greatest benefit for patients at elevated cardiovascular risk, that is those aged ≥65 or 45–64 yr with cardiovascular risk factors (e.g. history of coronary artery disease or peripheral vascular disease, diabetes mellitus, stroke, heart failure, chronic kidney disease) undergoing major noncardiac surgery. The purpose of this first step would be the identification of patients at high risk of acute PMI, major adverse cardiovascular events, and death. Although the RCRI is the most widely accepted tool for preoperative cardiovascular risk assessment, it performs only moderately well across noncardiac surgical populations and lacks sensitivity among patients in the lowest risk groups.[15] The addition of biomarkers such as N-terminal B-type natriuretic peptide (NT-proBNP) and cTns to the RCRI seems to improve preoperative risk stratification.[27,35] However, head-to-head comparisons between cTns and NT-proBNP as part of a preoperative risk stratification strategy are still lacking, as are large-scale validation studies.

Some clinicians argue that implementing cTn surveillance preoperatively is futile and costly in the absence of evidence-based guidelines for management.[36] Yet, a Canadian study showed that implementation of a risk-management system that includes cTn surveillance is not only feasible, but is not associated with increased costs.[37] In a cost-consequence analysis from the VISION group, it was shown that the incremental cost of detecting MINS was moderate.[38] It is worth noting that clinically accepted risk stratification tools, such as the RCRI, are also not coupled to specific perioperative management strategies. The lack of evidence-based management strategies based on biomarker surveillance should therefore not preclude its measurement.

Previous studies have demonstrated the importance of preoperative anaemia,[39,40] perioperative tachycardia,[41] perioperative hypotension,[42] hypertension,[41] and renal dysfunction[43] for poor perioperative outcomes. In the absence of evidence, it seems prudent to manage patients with increased preoperative hs-cTnT as high-risk patients, taking into account the added effects of multiple risk factors. This may include preoperative optimisation of cardiovascular medications including cardiac

workup and consultation as needed, correction of preoperative anaemia, extended perioperative haemodynamic monitoring, meticulous attention to intraoperative homeostasis including avoidance of intraoperative hypotension, hypertension, and tachycardia, and increased postoperative monitoring. In addition to guiding preventive measures, this first step also serves as a basis for informing patients of their perioperative risks. This raises several implications for patient information. Firstly, informed consent is enhanced by more accurate estimation of the risk of complications. Patients are likely to be unaware of the occurrence of complications that are seemingly unrelated to their surgery. Secondly, the appreciation of an increased risk of complications may facilitate management decisions, including preoperative optimisation and extended monitoring that should be explained to the patient who may otherwise be unprepared for these procedures. Thirdly, it would be prudent to explain to patients the need for increased tests that may be conducted in the perioperative period, despite being asymptomatic.

The second step involves postoperative measurement of hs-cTnT on days 1 and 2 after surgery. The purpose of this step is to identify patients with acute myocardial events at an early stage, in a population that is largely asymptomatic. Patients with acute changes in perioperative cTns should be followed closely and AMI Types I and II should be ruled out. This is because a disproportional number of patients with myocardial injury will suffer from a myocardial infarction, which is in turn associated with at least two-fold increased risk of mortality.[9,16] Other potential causes of myocardial injury such as heart failure, arrythmias, anaemia, hypotension, sepsis, and pulmonary embolus should be identified and treated. Intensification of cardiovascular medications such as aspirin and statins when PMI or infarction is detected[44,45] may be useful and is currently recommended by the Canadian Cardiovascular Society Guidelines[25] albeit based only on observational data.

The decision to implement perioperative troponin screening very much depends on the underlying prevalence of patients at risk of myocardial injury, available interventions, national and local practices, the availability of resources including adequate follow-up strategies, and a risk–benefit assessment. Published data show that different thresholds for hs-cTnT appear to be associated with increased cardiovascular complications, death, or both. Choosing a lower biomarker threshold would increase test sensitivity at the expense of a higher false positive rate, hence decreasing its net benefit.[3] Conversely, choosing high biomarker thresholds may miss clinically important disease. Clinicians and patients must therefore weigh the risks and benefits of increased detection of disease against increased probability of false positives, and the distress and unnecessary investigations that this may entail. Differences between contemporary and high-sensitivity assays, and between different high sensitivity cTn assays further add to these challenges.[19,46] In the only available cost-consequence analysis for troponin surveillance, it was found that postoperative cTn monitoring would benefit those at higher risk for myocardial injury; however, this study only investigated patients with MINS.[38]

Ongoing research and future directions

Myocardial injury has now been identified as a clinically important perioperative complication. A key challenge of future research will be to elucidate the pathophysiology and causative mechanisms of PMI. This may include translational approaches to better understand genomic or transcriptomic profiles in patients developing myocardial injury. Clinical studies should explore the contributions of baseline patient and perioperative procedural factors to myocardial injury and whether these may be causally linked. In the near future, we can expect the results of large, randomised controlled trials that will allow robust conclusions about causal relationships between intraoperative blood pressure and postoperative myocardial injury (e.g. GUARDIAN [NCT04884802], POISE-3 [NCT03505723], and IMPROVE-multi [NCT05416944]).

Future research must also focus on establishing approaches for routine perioperative troponin testing and management of test-positive patients. Appropriately powered randomised trials are necessary to evaluate the effectiveness of preoperative, intraoperative and postoperative strategies (e.g. haemodynamic management, pharmacological interventions) for reducing the incidence of acute myocardial injury. Finally, interventional studies to improve perioperative outcomes among patients with established myocardial injury are also a research priority.

Conclusions

Heterogeneous definitions of myocardial injury occurring during the perioperative period contribute to a lack of standardisation for reporting and difficulties for comparisons across studies. Global consensus definitions as reported in the 4th UDMI and endorsed by the StEP COMPAC initiative should be adopted. Nevertheless, myocardial injury occurring in the perioperative period is independently associated with adverse short- and long-term outcomes, regardless of the definitions used. Current data support the measurement of perioperative cTns to aid preoperative risk stratification beyond the Revised Cardiac Risk Index, and for the early detection of acute myocardial injury. Future initiatives should use common definitions and standards for reporting as a prerequisite for designing future trials and perioperative management strategies.

Authors' contributions

All authors take responsibility for the intellectual content of this manuscript and all authors contributed to its writing.

Declarations of interest

MSC has received speaker's fees and honoraria from B Braun AB and Edwards Lifesciences outside the submitted work and holds editorial roles with the *European Journal of Anaesthesiology*.

BS is a consultant for and has received honoraria for giving lectures from Edwards Lifesciences Inc. (Irvine, CA, USA). BS is a consultant for and has received institutional restricted research grants and honoraria for giving lectures from Pulsion Medical Systems SE (Feldkirchen, Germany). BS has received institutional restricted research grants and honoraria for giving lectures from CNSystems Medizintechnik GmbH (Graz, Austria). BS is a consultant for and has received honoraria for giving lectures from Philips Medizin Systeme Böblingen GmbH (Böblingen, Germany). BS is a consultant for and has received institutional restricted research grants and honoraria for giving lectures from GE Healthcare (Chicago, IL, USA). BS is a consultant for and has received honoraria for giving lectures from Vygon (Aachen, Germany). BS is a consultant for and has received honoraria for giving lectures from Baxter (Deerfield,

IL, USA). BS is a consultant for and has received institutional restricted research grants from Retia Medical LLC (Valhalla, NY, USA). BS has received institutional restricted research grants from Osypka Medical (Berlin, Germany). BS was a consultant for and has received institutional restricted research grants from Tensys Medical Inc. (San Diego, CA, USA). GL-B reports grants from the European Society of Anesthesiology and Intensive Care, the Swiss Society of Anesthesiology and Resuscitation, the German Society of Anesthesiology and Intensive Care outside the submitted work and participated to an advisory board on perioperative myocardial injury hosted by Roche Diagnostics (no honoraria).

Funding

Swedish Research Council (2019-02833) and Linköping University-Region Östergötland, ALF (grants 687681 and 792291), Sweden.

References

1. Botto F, Alonso-Coello P, Chan MTV, 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
2. Devereaux P, Biccard BM, Sigamani A, et al. Association of postoperative high-sensitivity troponin levels with myocardial injury and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2017; **317**: 1642–51
3. Chew MS, Puelacher C, Patel A, et al. Identification of myocardial injury using perioperative troponin surveillance in major noncardiac surgery and net benefit over the Revised Cardiac Risk Index. *Br J Anaesth* 2022; **128**: 26–36
4. Puelacher C, Lurati Buse G, Seeberger D, et al. Perioperative myocardial injury after noncardiac surgery: incidence, mortality, and characterization. *Circulation* 2018; **137**: 1221–32
5. Gillmann H-J, Meinders A, Grohennig A, et al. Perioperative levels and changes of high-sensitivity troponin T are associated with cardiovascular events in vascular surgery patients. *Crit Care Med* 2014; **42**: 1498–506
6. Reed GW, Horr S, Young L, et al. Associations between cardiac troponin, mechanism of myocardial injury, and long-term mortality after noncardiac vascular surgery. *J Am Heart Assoc* 2017; **6**, e005672
7. Smilowitz NR, Redel-Traub G, Hausvater A, et al. Myocardial injury after noncardiac surgery: a systematic review and meta-analysis. *Cardiol Rev* 2019; **27**: 267–73
8. Humble CAS, Huang SH, Jammer I, Bjork J, Chew MS. Prognostic performance of preoperative cardiac troponin and perioperative changes in cardiac troponin for the prediction of major adverse cardiac events and mortality in noncardiac surgery: a systematic review and meta-analysis. PLoS ONE 14: e0215094.
9. Puelacher C, Gualandro DM, Lurati Buse G, et al. Etiology of peri-operative myocardial infarction/injury after noncardiac surgery and associated outcome. *J Am Coll Cardiol* 2020; **76**: 1910–2
10. Hietala P, Strandberg M, Kiviniemi T, Strandberg N, Airaksinen KE. Usefulness of troponin T to predict short-term and long-term mortality in patients after hip fracture. *Am J Cardiol* 2014; **114**: 193–7
11. Wu AHB. Release of cardiac troponin from healthy and damaged myocardium. *Front Lab Med* 2017; **1**: 144–50
12. Ostermann M, Ayis S, Tuddenham E, et al. Cardiac troponin release is associated with biomarkers of inflammation and ventricular dilatation during critical illness. *Shock* 2017; **47**: 702–8
13. Ackland GL, Abbott TEF, Jones TF, et al. Early elevation in plasma high-sensitivity troponin T and morbidity after elective noncardiac surgery: prospective multicentre observational cohort study. *Br J Anaesth* 2020; **124**: 535e543
14. Noordzij PG, von Geffen O, Dijkstra IM, et al. High-sensitive cardiac troponin T measurements in prediction of non-cardiac complications after major abdominal surgery. *Br J Anaesth* 2015; **114**: 909–18
15. Roshanov PS, Sessler DI, Chow CK, et al. Predicting myocardial injury and other cardiac complications after elective noncardiac surgery with the Revised Cardiac Risk Index: the VISION study. *Can J Cardiol* 2021; **37**: 1215–24
16. Beattie WS, Wijeysundera DN, Chan MTV, et al. Implication of major adverse postoperative events and myocardial injury on disability and survival: a planned subanalysis of the ENIGMA-II trial. *Anesth Analg* 2018; **127**: 1118–26
17. Beattie WS, Lalu M, Bocock M, et al. On behalf of the StEP COMPAC Group. Systematic review and consensus definitions for the Standardized Endpoints in Perioperative Medicine (StEP) initiative: cardiovascular outcomes. *Br J Anaesth* 2021; **126**: 56e66
18. Thygessen K, Alpert AS, Jaffe AS, et al. On behalf of the Joint European society of Cardiology (ESC)/American College of Cardiology (ACC)/American heart association (AHA)/World heart federation (WHF) Task Force for the universal definition of myocardial infarction. Fourth universal definition of myocardial infarction (2018). expert consensus document. *Eur Heart J* 2019; **40**: 237–69
19. Gualandro DM, Puelacher C, Lurati Buse G, et al. Comparison of high-sensitivity cardiac troponin I and T for the prediction of cardiac complications after non-cardiac surgery. *Am Heart J* 2018; **203**: 67–73
20. Sheth T, Natarajan MK, Hsieh V, et al. Incidence of thrombosis in perioperative and non-operative myocardial infarction. *Br J Anaesth* 2018; **120**: 725–33
21. Sheth T, Chan M, Butler C, et al. For the coronary computed tomographic angiography and vascular events in noncardiac surgery patients cohort evaluation study investigators. Prognostic capabilities of coronary computed tomographic angiography before non-cardiac surgery: prospective cohort study. *BMJ* 2015; **350**: h1907
22. Weber M, Luchner A, Seeberger, et al. Incremental value of high-sensitive troponin T in addition to the revised cardiac index for peri-operative risk stratification in non-cardiac surgery. *Eur Heart J* 2013; **34**: 853–62
23. De Hert S, Staender S, Fritsch G, et al. Pre-operative evaluation of adults undergoing elective surgery. Updated guideline from the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2018; **35**: 407–65
24. 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). 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management. *Eur J Anaesthesiol* 2014; **31**: 517–73

25. Duceppe E, Parlow J, MacDonald P, et al. Canadian Cardiovascular Society guidelines on perioperative cardiac risk assessment and management for patients who undergo noncardiac surgery. *Can J Cardiol* 2017; **33**: 17e32
26. Ruetzler K, Smilowitz NR, Berger JS, et al. Diagnosis and management of patients with myocardial injury after noncardiac surgery. A scientific statement from the American Heart Association. *Circulation* 2021; **144**: e287–305
27. Vernooij LM, van Klei WA, Moons KGM, Takada T, van Waes J, Damen JAAG. The comparative and added prognostic value of biomarkers to the Revised Cardiac Risk Index for preoperative prediction of major adverse cardiac events and all-cause mortality in patients who undergo noncardiac surgery. *Cochrane Database Syst Rev* 2021; **12**: CD013139
28. Devereaux PJ, Duceppe E, Guyatt G, et al. For the MANAGE investigators. Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomised, placebo-controlled trial. *Lancet* 2019; **10137**: 2325–34
29. Wanner PM, Wulff DU, Djurdjevic M, Korte W, Schneider TW, Filipovic M. Targeting higher intraoperative blood pressures does not reduce adverse cardiovascular events following noncardiac surgery. *J Am Coll Cardiol* 2021; **78**: 1753–64
30. Sessler DI, Pei L, Cui S, et al. Aggressive intraoperative warming versus routine thermal management during non-cardiac surgery (PROTECT): a multicentre, parallel group, superiority trial. *Lancet* 2022; **399**: 1799–808
31. POISE Study Group. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomized controlled trial. *Lancet* 2008; **371**: 1839–47
32. Devereaux PJ, Mrkobrada M, Sessler DI, et al. For the POISE-2 Investigators. Aspirin in patients undergoing noncardiac surgery. *New Engl J Med* 2014; **370**: 1494–503
33. Devereaux PJ, Sessler DI, Leslie K, et al. For the POISE-2 Investigators. Clonidine in patients undergoing noncardiac surgery. *New Engl J Med* 2014; **370**: 1504–13
34. Devereaux PJ, Marucci M, Painter TW, et al. For the POISE-3 Investigators. Tranexemic acid in patients undergoing noncardiac surgery. *New Engl J Med* 2022; **386**: 1986–97
35. Duceppe E, Patel A, Chan MTV, et al. Preoperative N-terminal pro-B-type natriuretic peptide and cardiovascular events after noncardiac surgery: a cohort study. *Ann Intern Med* 2020; **172**: 96–104
36. Buse GL, Matot I. Pro-Con debate: cardiac troponin measurement as part of routine follow-up of myocardial damage following noncardiac surgery. *Anesth Analg* 2022; **134**: 257–65
37. McIsaac DI, Montroy J, Gagne S, et al. Implementation of the Canadian Cardiovascular Society guidelines for perioperative risk assessment and management: an interrupted time series study. *Can J Anaesth* 2021; **68**: 1135–45
38. Lurati Buse G, Manns B, Lamy A, et al. Troponin T monitoring to detect myocardial injury after noncardiac surgery: a cost–consequence analysis. *Can J Surg* 2018; **61**: 185–94
39. Fowler AJ, Ahmad T, Phull MK, Allard S, Gillies MA, Pearse RM. Meta-analysis of the association between preoperative anaemia and mortality after surgery. *Br J Surg* 2015; **102**: 1314–24
40. Musallam KM, Tamim HM, Richards T, et al. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. *Lancet* 2011; **378**: 1396–407
41. Abbott TEF, Pearse RM, Andrew Archbold R, et al. A prospective international multicentre cohort study of intraoperative heart rate and systolic blood pressure and myocardial injury after noncardiac surgery: results of the VISION study. *Anesth Analg* 2018; **126**: 1936–45
42. Sessler DI, Khanna AK. Perioperative myocardial injury and the contribution of hypotension. *Int Care Med* 2018; **44**: 811–22
43. Prowle JR, Kam EPY, Ahmad T, Smith NCE, Protopapa K, Pearse RM. Preoperative renal dysfunction and mortality after non-cardiac surgery. *Br J Surg* 2016; **103**: 1316–25
44. 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
45. Devereaux PJ, Xavier D, Pogue J, et al. For the POISE investigators. Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. *Ann Intern Med* 2011; **154**: 523–8
46. Brown JC, Samaha E, Rao S, et al. High-sensitivity cardiac troponin T improves the diagnosis of perioperative MI. *Anesth Analg* 2017; **125**: 1455–62

Handling editor: Gareth Ackland