Expert consensus on peri-operative myocardial injury screening in noncardiac surgery

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REVIEW ARTICLE

Expert consensus on peri-operative myocardial injury screening in noncardiac surgery

A literature review

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Peri-operative myocardial injury, detected by dynamic and elevated cardiac troponin (cTn) concentrations, is a common complication of noncardiac surgery that is strongly associated with 30-day mortality. Although active screening for peri-operative myocardial injury has been suggested in recent guidelines, clinical implementation remains tentative due to a lack of examples on how to tackle such an interdisciplinary project at a local level. Moreover, consensus on which assay and cTn cut-off values should be used has not yet been reached, and guidance on whom to screen is lacking. In this article, we aim to summarise local examples of successfully implemented cTn screening practices and review the current literature in order to provide information and suggestions for patient selection, organisation of a screening programme, caveats and a potential management pathway.

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Introduction

Every year, over 300 million surgical procedures are performed worldwide, with numbers steadily increasing. Recent evidence suggests that postoperative death accounts for 7.7% of global mortality and is the third leading cause of mortality worldwide.[1] In patients undergoing major noncardiac surgery, peri-operative mortality remains high during the first 30 days postsurgery.[2–4]

Myocardial infarction following noncardiac surgery has been shown to be associated with poor long-term outcomes.[5,6] According to the Universal Definition of Myocardial Infarction, acute myocardial infarction is diagnosed when acute myocardial injury, defined as dynamic and elevated cardiac troponin (cTn) with at least 1 value above the 99th percentile, is accompanied by clinical evidence of myocardial ischaemia (Table 1).[7]

Due to the high reliance of the Universal Definition on symptoms for the detection of myocardial infarction, something that might not be so apparent in the peri-operative setting due to sedation and analgesia, further studies were needed to systematically screen for peri-operative myocardial injury using cTn, the cornerstone of the Universal Definition.[8,9] These showed that peri-operative myocardial injury, detected by elevated and dynamic changes in cTn with or without additional

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Table 1 Glossary including definitions of myocardial infarction and myocardial injury

Term	Definition	References
Myocardial infarction	Myocardial injury with clinical symptoms/evidence of acute myocardial ischaemia[a] Type 1 myocardial infarction Detection of a change in cTn values (≥1 value above the 99th percentile) and at least one of the following criteria; • Symptoms of ischaemia • New ST-segment changes or new left bundle branch block • Pathological Q waves • Imaging evidence of new loss of viable myocardium or new regional wall-motion abnormality • Intracoronary thrombus by angiography or autopsy Type 2 myocardial infarction Detection of a change in cTn values (≥1 value above the 99th percentile) and evidence of an imbalance between myocardial oxygen supply and demand, unrelated to acute coronary atherothrombosis, requiring at least one of the following criteria; • Symptoms of ischaemia • New ischaemic ECG changes • Pathological Q waves • Imaging evidence of new loss of viable myocardium or new regional wall-motion abnormality	Thygesen *et al.* [7]
Myocardial injury after noncardiac surgery (MINS)	Elevated postoperative cTn (myocardial injury) with or without ischaemic signs and symptoms, probably resulting from myocardial ischaemia (that may or may not result in necrosis) during or within 30 days after noncardiac surgery. This was defined clinically after exclusion of sepsis, pulmonary embolism or arrhythmia	VISION studies[8,10]
Peri-operative myocardial infarction/injury (PMI)	Elevated and dynamic peri-operative cTn with or without ischaemic signs and symptoms Can be categorised as cardiac PMI (probably caused by myocardial ischaemia, tachyarrhythmia or decompensated heart failure) and extra-cardiac PMI (probably caused by noncardiac conditions such as sepsis, pulmonary embolism, stroke)	Puelacher *et al.* [9]
Myocardial ischaemia	Lack of blood flow and oxygen to the tissues of the heart, caused by obstruction of the blood vessels and often resulting in myocardial infarction or necrosis	Crossman [49]

cTn, cardiac troponin; MI, myocardial infarction; PMI, peri-operative myocardial infarction/injury. [a]Other types of myocardial infarction observed are less relevant for the peri-operative context, hence are not mentioned here.

ischaemic symptoms or signs (Table 1), is a complication of noncardiac surgery that is strongly associated with 30-day mortality and is more common than previously known.[7,9–12] Following active screening, peri-operative myocardial injury has been shown to occur in approximately 16 to 20%[9,10] of high-risk patients undergoing noncardiac surgery, with reports ranging from 6 to 73%, depending on the diagnostic assay, the definition used and the cohort studied.[3,7–10,12–19] Two large studies (VISION and BASEL-PMI) compared the mortality of peri-operative myocardial injury that fulfilled the additional criteria for acute myocardial infarction (symptoms or signs of ischaemia) with those who did not, and no difference in mortality was observed.[9,10] Approaches to active screening for myocardial injury in high-risk patients have been proposed in recent guidelines with varying levels of recommendation (1B,[20] 'strong',[21] 'recommended',[7] and 2B[22,23]) and varying definitions of 'high-risk'.[7,20–23] As events detected with systematic screening using cTn include myocardial infarctions as well as myocardial injury, in this article, we chose to use 'peri-operative myocardial injury' as an umbrella term.

Although peri-operative myocardial injury is accepted as a peri-operative complication and its association with outcome was documented in recent studies using technically different definitions (Table 2), no consensus definition exists to date. The definition based on the largest body of evidence is that of myocardial injury after noncardiac surgery (MINS), proposed and refined by the VISION studies.[8,10] MINS is defined as elevated postoperative cTn (myocardial injury) due to ischaemia, with or without additional symptoms or ECG changes, that occurs during or within 30 days after noncardiac surgery (Table 1).[8] MINS criteria were derived using postoperative high-sensitivity cTnT (hs-cTnT) from a large observational study of adults aged at least 45 years undergoing in-hospital noncardiac surgery, and was defined as a concentration of at least 20 ng l^{-1} combined with an absolute change of at least 5 ng l^{-1}, or an absolute postoperative hs-cTnT of at least 65 ng l^{-1} (Table 2). Importantly, secondary causes of cTn elevation, including nonischaemic cardiac causes (tachyarrhythmia, direct myocardial trauma, pericarditis), and extra-cardiac causes (sepsis, pulmonary embolism and severe renal failure) were excluded during adjudication, with 11.0% of all detected peri-operative myocardial injuries adjudicated as originating from nonischaemic causes (Table 2).

The BASEL-PMI study prospectively defined peri-operative myocardial injury as an absolute increase in hs-cTnT of at least 14 ng l^{-1}, irrespective of maximum postoperative values, in patients considered to be at high risk [aged ≥65 years, or aged ≥45 years with history of coronary artery disease (CAD), peripheral artery disease or stroke] and without excluding secondary causes of cTn elevation (Table 2).[9]

Although these large cohort studies provide guidance for cut-off values using hs-cTnT assays, there are a number of other studies that offer insights into cut-offs using different (conventional) cTn assays. One example is a study that obtained cTnI measurements during the first

Table 2 Summary of studies of myocardial injury associated with noncardiac surgery

Study/ Studies	Patient population[a]	Patients (*n*)	Definition of myocardial injury	Incidence of event (%)	Cut-off	Timing of cTn measurements	Key data
hs-cTnT assay (Roche Diagnostics)							
VISION 2017[10]	Aged ≥45 years staying at least one night in-hospital after surgery	21 842	MINS	17.9	Absolute postoperative hs-cTnT of >20 ng l^{-1} combined with an absolute change of ≥5 ng l^{-1}, excluding extra-cardiac events	Pre-operative: 1 to 28 days before surgery (available in 40.4% of patients) Postoperative: 6 to 12 h postop and on days 1 to 3	Crude 30-day mortality: 4.1% (HR = 3.10; 95% CI: 2.39 to 4.02)
BASEL-PMI study 2018[9] (see also Liem *et al.* [17] and Mol *et al.* [18])	High-risk patients (aged ≥65 years of age, OR ≥45 years with history of CAD, peripheral artery disease or stroke)	2018	Peri-operative myocardial injury (PMI) Cardiac PMI Extra-cardiac PMI	15.6 13.4 2.2	Absolute increase of ≥14 ng l^{-1} hs-cTnT above pre-operative value within 7 days postsurgery	Pre-operative: Within 30 days before surgery Postoperative: Days 1 and 2	Crude 30-day mortality: 9.8% (HR = 2.73; 95% CI: 1.54 to 4.84) Crude 1-year mortality: 22.5% (HR = 1.58; 95% CI 1.16 to 2.15)
Gillmann *et al.* 2014[50]	Aged ≥18 years undergoing elective open aortic, peripheral vascular or carotid surgery	455	MACE	9.0	Absolute change of ≥6 ng l^{-1} hs-cTnT	Pre-operative: N/A Postoperative: 24 h postop	Increased risk of MACE independently associated with history of renal failure (OR = 3.4; 95% CI 1.4 to 8.1; *P* = 0.006) and heart failure (OR = 2.8; 95% CI 1.3 to 5.7; *P* = 0.006)
Fourth-generation Elecsys cTnT assay (Roche Diagnostics)							
VISION 2014[8] (see also VISION 2012[3])	Aged ≥45 years staying at least one night in-hospital after surgery	15 065	MINS	8.0	Peak conventional cTnT ≥0.04 μg l^{-1} postoperatively with an ischaemic feature	Pre-operative: N/A Postoperative: 6 to 12 h postop and on days 1 to 3	MINS was an independent predictor of 30-day mortality (HR = 3.87; 95% CI 2.96 to 5.08)
Dimension RxL cTnI assay (Siemens Healthcare)							
Nagele P *et al.* 2011[19]	Patients undergoing head and neck cancer surgery	378	Peri-operative myocardial injury	15.1	Peak conventional cTnI ≥0.07 μg l^{-1} postoperatively	Pre-operative: N/A Postoperative: Immediately after surgery, 8 h and 16 h after surgery	8-fold increase in mortality 60 days postop (OR = 8.01; 95% CI 2.03 to 31.56)
AccuTnI assay (Beckman Coulter)							
van Waes *et al.* [12]	Intermediate- to high-risk patients aged ≥60 years	1627	Postoperative myocardial injury	19.4	Peak conventional cTnI >0.06 μg l^{-1} postoperatively	Pre-operative: N/A Postoperative: Days 1 to 3	Crude 30-day mortality: 8.6%; 95% CI 6.0 to 12.2%
Architect$_{STAT}$ TnI assay (Abbott Diagnostics)							
Chong *et al.* [15]	Aged ≥60 years	102	Postoperative myocardial injury	52.9	Peak conventional cTnI >0.03 μg l^{-1} postoperatively	Pre-operative: Before surgery (unspecified) Postoperative: Days 1 to 3	Crude 1-year mortality: 37.0%
Architect$_{STAT}$ hs-TnI assay (Abbott Diagnostics)							
Gillies *et al.* [16]	Aged ≥65 years or aged 50 to 64 years with one or more of the following: nonelective surgery, acute or chronic renal impairment, diabetes mellitus or presence of a risk factor for cardiac or respiratory disease.	288	Peri-operative myocardial injury	Intervention group: 46.0 Usual care: 48.0	Peak hs-cTnI ≥26 ng l^{-1} postoperatively	Pre-operative: Induction of anaesthesia Postoperative: 24 and 72 h after surgery	Peak postoperative cTnI concentrations similar between intervention (haemodynamic therapy) and usual care groups
VISION (biobank cohort) Duceppe *et al.* [51]	Aged ≥45 years staying at least one night in-hospital after surgery	3953	MINS	6.1	Peak hs-cTnI ≥60 ng l^{-1} postoperatively	Pre-operative: N/A Postoperative: 6 to 12 h postop and on days 1 to 3	Overall incidence of MACE at 30 days was 1.7% (66/3947) Postoperative hs-cTnI ≥60 ng l^{-1} without clinical features of myocardial ischaemia was associated with six-fold increase in risk of subsequent major cardiac events at 30 days (adjusted HR 5.90; 95% CI 2.67 to 11.72)

Presented cut-offs were not validated in large external cohorts. CAD, coronary artery disease; CI, confidence interval; cTnI/cTnT, cardiac troponin I/T; EF, ejection fraction; HR, hazard ratio; hs, high-sensitivity; MACE, major adverse cardiac event; MINS, myocardial injury after noncardiac surgery; N/A, not applicable; PMI, peri-operative myocardial injury. [a]All patients were undergoing noncardiac surgery.

three days after surgery using a conventional assay[12] with the cut-off more than 0.06 $\mu g\,l^{-1}$ to define myocardial injury. Further examples can be found in Table 2.

Given that peri-operative myocardial injury is largely asymptomatic in more than 80% of patients but associated with high mortality rates,[9,10] developing effective screening and appropriate management strategies to improve peri-operative outcomes is paramount. However, there is currently little guidance on how and whom to screen.

The aim of this position paper was to summarise local practices of screening for peri-operative myocardial injury after noncardiac surgery to aid physicians and institutions in implementing guideline-recommended screening. To this end, we reviewed the existing literature and present our consensus on the application of peri-operative cTn screening in everyday clinical practice, with some insights into local approaches. Furthermore, potential knowledge gaps are identified. As publications especially relating to the management of peri-operative myocardial injury are scarce, consensus was reached by discussion in the writing group originating from an advisory board meeting organised by Roche Diagnostics. No formal consensus process, such as the Delphi process, was used. Note also that a consensus definition of peri-operative myocardial injury is currently lacking and was not the objective of this article.

Identifying patients for screening

In patients undergoing noncardiac surgery, cTn should only be measured when there is an elevated risk of developing peri-operative myocardial injury. The identification of 'high-risk' patients has varied over time and is different in current guidelines.[7,20–23] For example, the Canadian Cardiovascular Society (CCS) Perioperative Guidelines defines high risk as an expected baseline risk of 5% for myocardial infarction or vascular death.[21] The CCS strongly recommend cTn screening in patients undergoing noncardiac surgery requiring at least an overnight hospital stay and who meet any of the following criteria: aged at least 45 years with known significant cardiovascular disease, such as CAD, cerebral vascular disease, peripheral arterial disease or congestive heart failure OR a Revised Cardiac Risk Index (RCRI) score at least 1 OR aged 18 to 64 years with significant cardiovascular disease and scheduled for urgent or semi-urgent surgery (e.g. hip fracture surgery) OR aged at least 65 years.[8,24]

We believe that these criteria seem appropriate. Screening that included lower risk patients, for example, all patients more than 45 years irrespective of cardiovascular risk, was shown to have a worse cost vs. consequence effect.[25] More strict criteria, for example a metabolic equivalent capacity of 4 or less or with a RCRI value more than 1 for vascular surgery and more than 2 for nonvascular surgery,[22] have been proposed, but no data exist to date concerning the impact of such an approach. Capturing only the highest risk may miss important events in patients shown to have high rates of peri-operative myocardial injury.[9,10]

It is important that patients undergoing emergency or urgent surgery should be considered when developing a screening programme for peri-operative myocardial injury.[9,10,17,18,26] An observational study also recently derived cut-offs of NT-proBNP that might be used to identify patients at an increased risk of peri-operative myocardial injury, with external validation pending.[27]

Implementing a peri-operative myocardial injury screening programme

Peri-operative cardiac troponin

cTn in the peri-operative setting has been extensively studied over the last 20 years. Consistent with findings from other clinical settings, elevated postoperative cTn has been found to be associated with increased mortality after noncardiac surgery.[3,4,8–10] According to recent guidelines, hs-cTn is the recommended biomarker for peri-operative screening for myocardial injury.[7,20] Emphasis on differentiating acute peri-operative myocardial injury from pre-existing chronic myocardial injury is needed during peri-operative screening. With an increasing number of the elderly and patients with comorbidities undergoing noncardiac surgery, chronically elevated pre-operative hs-cTn levels are increasingly common. In recent studies, pre-operative hs-cTn levels above the 99th percentile were detected in 12 to 52% of all patients.[9,10,28–30] Thus, a pre-operative baseline hs-cTn value can help differentiate acute from chronic myocardial injury in the postoperative period and permits earlier event detection using delta change. In patients in whom a pre-operative hs-cTn value is not available, obtaining serial hs-cTn measurements after surgery may allow the detection of dynamic postoperative hs-cTn changes consistent with peri-operative myocardial injury. Although there is a growing body of evidence suggesting that pre-operative hs-cTn measurements may become helpful in risk prediction and the decision of whom to screen,[28,31–34] the primary purpose of pre-operative measurement is as a baseline measurement for peri-operative myocardial injury screening. In patients cleared by previous pre-operative evaluation, we advocate that surgery should not be delayed solely based on elevated pre-operative hs-cTn, as no interventions based on pre-operative cTn values have been shown to improve peri-operative outcomes.

It is important to note that conventional cTn assays exhibit poor sensitivity and considerable analytical variability in the low concentration range that may be too great to provide reliable information in the peri-operative setting, and the guidelines express a clear preference for sensitive or hs-cTn assays.[7,20] Conventional assays may fail to detect smaller increases above the 99th percentile upper reference limit (URL) and dynamic changes, particularly at low cTn concentrations, leading to lower rates of peri-operative myocardial injury diagnosis.[7] In our

Table 3 Summary of local practices for peri-operative cTn screening

Centre	Status	Patient group screened	Surgical departments	cTn-measurements	Process and teams involved	IT support
Switzerland						
University Hospital Basel	Established 2014 (active)	≥1 overnight stay in-hospital after noncardiac surgery Aged ≥65 years OR ≥45 years with pre-existing CAD, PAD or stroke	Orthopaedic/trauma/spinal Thoracic Urology Vascular Visceral	Hs-cTnT Pre-operative (baseline) Postoperative Days 1 and 2	Screening initiated by: Pre-operative: Anaesthesiology during pre-operative visit Postoperative: Anaesthesiology during postoperative visit Management: Automated review of postoperative values and automated request for structured cardiology visit Follow-up: By cardiology	Patient identification, automated comparison of cTn values and E-Mail to cardiology
Cantonal Hospital Aarau	2016 to 2018	≥1 overnight stay in-hospital after noncardiac surgery Aged ≥65 years OR ≥45 years with pre-existing CAD, PAD or stroke	Orthopaedic/trauma/spinal Thoracic Urology Vascular Visceral	cTnI conventional Pre-operative (baseline) Postoperative: Days 1 and 2	Screening initiated: Pre-operative: Anaesthesiology during preoperative visit Postoperative: Anaesthesiology during postoperative visit Management: Review of postoperative values and request for structured cardiology visit by dedicated team Follow-up: By cardiology	Patient identification
Spain						
Hospital Santa Creu i Sant Pau	Established 2016 (active)	≥1 overnight stay in-hospital after noncardiac surgery Aged ≥65 years OR <65 years with pre-existing CAD, PAD, stroke or renal insufficiency (eGFR $<60\,ml\,min^{-1}\,m^{-2}$)	Emergency Gynaecology Orthopaedic/trauma/spinal Otorhinolaryngology Plastic Thoracic Vascular Visceral	Hs-cTnT Pre-operative (baseline) Postoperative Days 2 and 3	Screening initiated by: Pre-operative: Surgery and/or anaesthesiology during pre-operative visit Postoperative: Anaesthesiology directly postoperative in postanaesthesia care unit Management: Surgery review postoperative values and in case of elevation request structured cardiology visit Follow-up: By cardiology	None
Canada						
Centre Hospitalier de l'Universite de Montreal, Quebec,	Established 2018 (active)	≥1 overnight stay in-hospital after noncardiac surgery Aged ≥65 years OR ≥45 years with pre-existing CAD, PAD, stroke, RCRI score ≥1,or pre-operative NT-proBNP $\geq 300\,ng\,l^{-1}$	Digestive Gynaecology Hepatobiliary Neurosurgery Oncology Orthopaedic/spinal Otorhinolaryngology Plastic Thoracic Urology Vascular	Hs-cTnT Postoperative Days 1 and 2	Screening initiated by: Pre-operative: Internal medicine during pre-operative visit Postoperative: Pre-operative standard set OR standardised order sets in high-risk surgical specialties (digestive, hepatobiliary and vascular surgery) Management: If postoperative hs-cTnT elevation, ECG ordered and medical consultation requested Follow-up: By internal medicine or cardiology	None

CAD, coronary artery disease; cTnI/cTnT, cardiac troponin I/T; eGFR, estimated glomerular filtration rate; hs, high sensitivity; NT-proBNP, N-terminal pro B-type natriuretic peptide; PAD, peripheral arterial disease; RCRI, Revised Cardiac Risk Index.

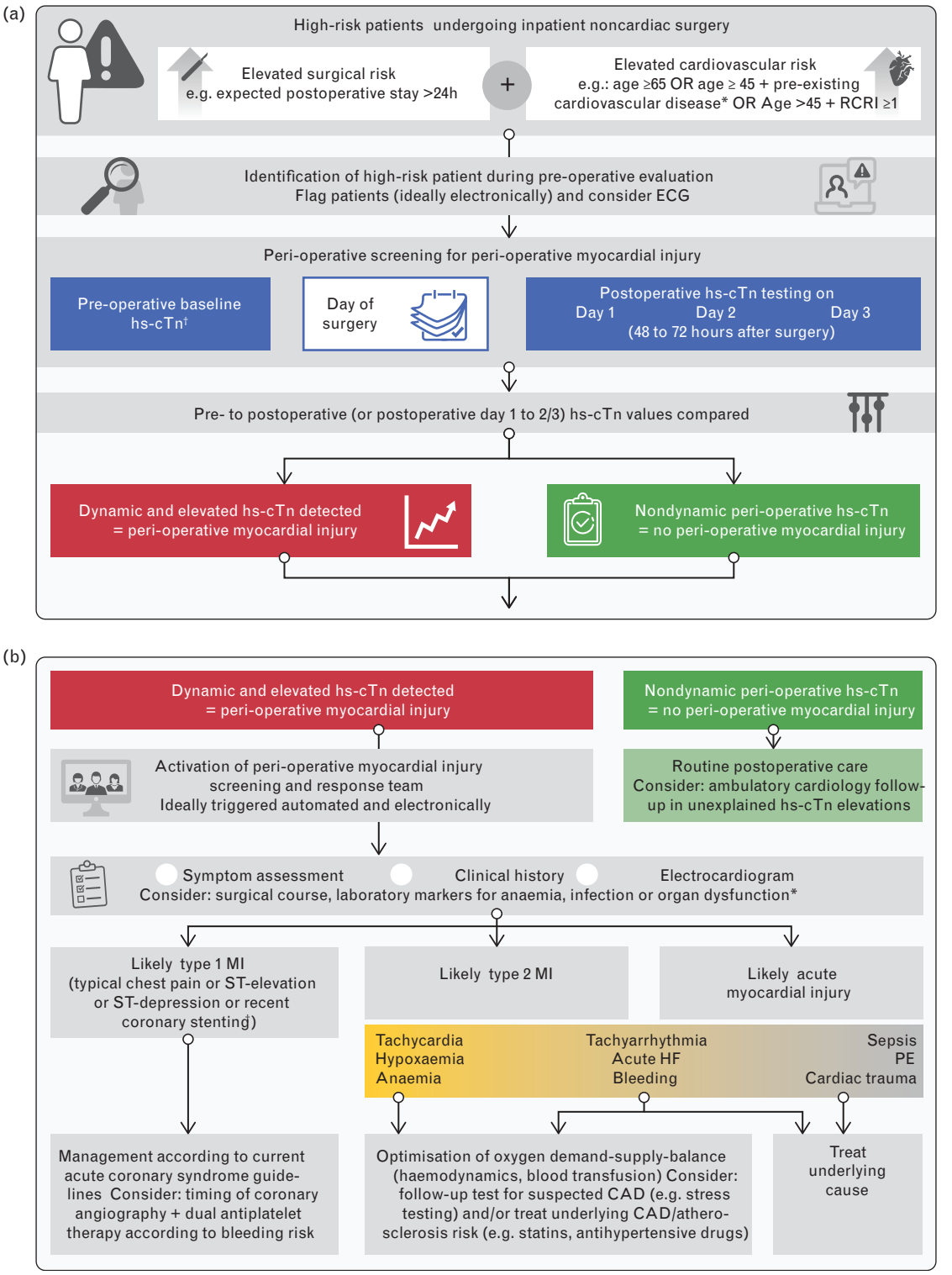
opinion, hs-cTn assays should be favoured. Of note, hs-cTn assays suitable for point-of-care settings are being developed and may be implemented in clinical practice in the near future.[35] Attention should be paid to differences in cTn assays, as there is no standardisation between assay manufacturers regarding percentiles. Moreover, there is variation in the assay precision at the URL.[36] When implementing screening, noncardiac surgery setting-specific cut-off values should be employed (Table 2), either prospectively tested or those derived from prognostic analysis.[9,10,12]

Screening programme

In the local screening algorithms discussed here, patients are identified during pre-operative assessment and selected for peri-operative myocardial injury screening (Table 3). Figure 1a depicts an option for a peri-operative myocardial injury screening and care programme that can be applied to patients undergoing elective and nonelective noncardiac surgery. In this programme, patients at a high risk of cardiac events are screened using a hs-cTn assay, beginning with a pre-operative hs-cTn measurement. If a pre-operative measurement is missed, for example following urgent surgery, hs-cTn can be requested from stored pre-operative blood samples. Postoperative hs-cTn measurements are taken on postoperative days 1,2, and potentially 3, perhaps in the morning, usually together with other routine postoperative samples. This is because most peri-operative myocardial injury events were found to occur within the first 48 to 72 h after surgery.[9,10]

The successful implementation of a screening programme will depend on the involvement of an interdisciplinary team including multiple peri-operative specialties that

Fig. 1 Example of a potential peri-operative cTn screening and care programme



(a) Known significant cardiovascular disease, such as coronary artery disease, cerebral vascular disease, peripheral arterial disease, congestive heart failure. [a]Pre-operative cTn may provide information for risk stratification, but it is mainly necessary as a baseline value for peri-operative myocardial injury screening. cTn, cardiac troponin; hs, high-sensitivity; RCRI, Revised Cardiac Risk Index. (b) For example, measuring haemoglobin, leucocyte count, electrolytes and BNP/NT-proBNP. [a]Antiplatelet discontinuation as a result of recent stent therapy. CAD, coronary artery disease; cTn, cardiac troponin; MI, myocardial injury; MINS, myocardial injury after noncardiac surgery; PCI, percutaneous coronary intervention; PE, pulmonary embolism; PMI, peri-operative myocardial injury.

might include anaesthesiology, surgery, intensive care, cardiology, internal medicine and laboratory medicine, professional groups and, crucially, hospital management. Anaesthesiology or internal medicine are the most likely disciplines to identify patients and initiate screening during pre-operative visits, while cardiology or internal medicine will probably be in charge of managing the patient. Involvement of these disciplines together with the surgical departments already on the concept phase before start of any screening is essential. An ideal scenario would be to automate the comparison of pre and postoperative cTn values, enabling timely notification, evaluation and management decisions.

Interpretation of peri-operative screening and derived measures

The first step after detection of peri-operative myocardial injury is a thorough patient evaluation, including a review of the patient's medical history and observation chart, a detailed physical examination and a 12-lead ECG from the time of detection. Elevation in hs-cTn in the peri-operative period can indicate type 1 myocardial infarction, type 2 myocardial infarction or acute myocardial injury (Fig. 1b). The initial step in the evaluation of patients with peri-operative myocardial injury should be to consider type 1 myocardial infarction. The presence of typical symptoms, ST-segment elevation or depression on the ECG, or antiplatelet discontinuation following recent percutaneous coronary intervention[37,38] are considered indicative, but the probability of type 1 myocardial infarction is also higher in those with known CAD or established cardiovascular risk factors. Although type 1 myocardial infarction appears to be an uncommon cause of peri-operative myocardial injury,[39–41] swift recognition and management according to acute coronary syndrome guidelines is paramount.[42]

A more common cause of peri-operative myocardial injury is type 2 myocardial infarction, wherein ischaemia is believed to be a consequence of myocardial oxygen supply-demand imbalance (tachycardia, hypotension, bleeding or tachyarrhythmia).[43] A recent prospective study found evidence of coronary thrombosis in only one in eight patients undergoing coronary angiography with peri-operative myocardial injury,[44] an observation corroborated by retrospective studies reporting that the majority of patients with peri-operative myocardial infarction had no evidence of plaque rupture, thrombosis or the need for revascularisation.[39–41] When myocardial ischaemia secondary to oxygen supply-demand imbalance is suspected, potential triggers should be managed and noninvasive imaging modalities such as stress testing or transthoracic echocardiography should be considered.[7]

In the evaluation of peri-operative myocardial injury, a high degree of suspicion is required for cardiac or extracardiac causes of acute myocardial injury such as acute heart failure, cardiac trauma, severe sepsis or pulmonary embolism, as these were shown to be associated with high mortality,[9,45] and strategies aimed at treating myocardial ischaemia are unlikely to be helpful in this setting.

An example of a management pathway after peri-operative myocardial injury screening is illustrated in Fig. 1b. This programme is based on the clinical experience of a small number of centres, with many questions concerning optimal work-up remaining. Importantly, treatment decisions will be influenced by the cause of peri-operative myocardial injury; in particular, guideline-recommended treatments from the nonoperative setting should be considered for patients with peri-operative myocardial injury that is suspected or known to be caused by type 1 myocardial infarction, tachyarrhythmia, acute heart failure, sepsis or pulmonary embolism.[45]

To date, there is no compelling evidence that justifies the recommendation of any specific treatment or follow-up testing option, and further clinical studies are needed to evaluate management strategies for patients with peri-operative myocardial injury. Potential management approaches have been suggested for MINS, most notably in the MANAGE trial. MANAGE was an international, randomised controlled trial of patients aged at least 45 years that compared dabigatran with placebo, initiated within 35 days of being diagnosed with MINS following noncardiac surgery.[46] Dabigatran reduced major vascular complication, a composite of vascular mortality and nonfatal myocardial infarction, nonhaemorrhagic stroke, peripheral arterial thrombosis, amputation and symptomatic venous thromboembolism, without increasing major bleeding. When considering this medication, initiation of dabigatran should be deferred until bleeding risk is acceptable from a surgical perspective. In the MANAGE trial, patients received the first dose a median of 6 days after surgery.[46] The primary endpoint of this study was a composite of venous and arterial complications. It is important to note that treatment with dabigatran increased the risk of clinically nonsignificant lower gastrointestinal bleeding and minor bleeding.[46]

Further options suggested by analysis of observational data include statins, acetylsalicylic acid and optimisation of cardiovascular medication including beta-blockers and angiotensin-converting enzyme inhibitors.[47,48] Due to their nonrandomised nature, these findings should be interpreted with caution, and treatment risks and benefits should be weighed according to presumed cause, especially in the case of acetylsalicylic acid, due to risk of postoperative bleeding.

Due to scarcity of treatment recommendations, it is important that healthcare providers ensure management is tailored to the individual patient. Patients without peri-operative myocardial injury, but starkly elevated chronic hs-cTn elevation without any history of known cardiovascular or renal disease, might postoperatively be referred to ambulatory cardiology check-up.

Follow-up after screening

On the basis of our experience, one of the healthcare professionals involved in screening with expertise in peri-operative care and the correct infrastructure for the required tasks, should take responsibility for patient follow-up. Follow-up can include ambulatory cardiac structural or ischaemia testing, discussion of test results with the patient and recommendations to subsequent healthcare providers. Interdisciplinary collaboration and experience exchange between centres is also encouraged.

Knowledge gaps and future research

There are several important knowledge gaps in the field of peri-operative myocardial injury, and it is important to note that the examples described in this paper were derived exclusively from the authors' local practices. Efforts should be made to

(1) find a consensus on the diagnostic criteria for peri-operative myocardial injury definitions
(2) develop and validate predictive models for peri-operative myocardial injury to allow identification of patients at risk and/or those likely to benefit from early invasive coronary angiography
(3) establish optimum thresholds for the diagnosis of peri-operative myocardial injury
(4) characterise and differentiate between the potential aetiologies of peri-operative myocardial injury, for example type 1 vs. type 2 myocardial infarction vs. acute myocardial injury
(5) test preventive strategies for peri-operative myocardial injury in randomised controlled trials
(6) test management strategies for patients with peri-operative myocardial injury in randomised controlled trials
(7) encourage further collaboration between medical specialties and organisations internationally
(8) evaluate the impact of implementing screening and care programmes
(9) examine the cost-effectiveness and resource utilisation of screening

Conclusion

Peri-operative myocardial injury screening and care programmes may provide an opportunity to improve peri-operative care and outcomes after noncardiac surgery in high-risk patients. Screening is suggested by recent guidelines, but has not yet been translated into routine clinical practice. We report successful examples of local implementation of screening approaches, which could contribute to the development of standardised programmes for peri-operative cTn monitoring. By the identification of crucial knowledge gaps, we aim to encourage data generation to establish evidence-based peri-operative cardiovascular care after noncardiac surgery.

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