EDITORIAL

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Postoperative troponin surveillance: A diagnostic dilemma

A MAJOR GOAL of perioperative medicine is to prevent, detect, and treat postoperative complications—in particular, cardiovascular complications. In the Perioperative Ischemic Evaluation (POISE) study,[1] the 30-day mortality rate was four times higher in patients who had a perioperative myocardial infarction (MI) than in those who did not.[1] Yet fewer than half of patients who have a postoperative MI have ischemic symptoms, suggesting that routine monitoring of cardiac biomarkers could detect these events and allow early intervention.

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From 10% to 20% of patients have troponin elevations after noncardiac surgery.[2] But until recently, many of these elevations were thought to be of minor importance and were ignored unless the patient met diagnostic criteria for MI. A new entity called MINS (myocardial injury after noncardiac surgery)[3] was defined as a troponin level exceeding the upper limit of normal with or without ischemic symptoms or electrocardiographic changes and excluding noncardiac causes such as stroke, sepsis, and pulmonary embolism. Because elevations of troponin at any level have been associated with increased 30-day mortality rates, the question of the value of routine screening of asymptomatic postoperative patients for troponin elevation has been raised.

In this issue of *Cleveland Clinic Journal of Medicine*, Horr et al[4] review the controversy of postoperative screening using troponin measurement and propose an algorithm for management.

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QUESTIONS TO CONSIDER

Before recommending screening asymptomatic patients for troponin elevation, we need to consider a number of questions:

- Which patients should be screened?
- How should troponin elevations be treated?
- Would casting a wider net improve outcomes?
- What are the possible harms of troponin screening?

The bottom line is, will postoperative troponin screening change management and result in improved outcomes?

Postoperative troponin elevations are linked to bad outcomes, but should we screen everyone?

WHICH PATIENTS SHOULD BE SCREENED?

Why routine screening may be indicated

Elevated or even just detectable troponin levels are associated with adverse outcomes. A systematic review and meta-analysis of 3,318 patients[2] demonstrated that high troponin levels after noncardiac surgery were independently associated with a risk of death three times higher than in patients with normal troponin levels.

In the Vascular Events in Noncardiac Surgery Patients Cohort Evaluation (VISION) study,[5] troponin T was measured in 15,133 patients after surgery. The overall mortality rate was 1.9%, and the higher the peak troponin T level the higher the risk of death.

In a single-center Canadian retrospective cohort analysis of 51,701 consecutive patients by Beattie et al,[6] the peak postoperative level of troponin I improved the ability of a multivariable model to predict the risk of death. As in the VISION study, the mortality rate rose with the troponin level.[6]

In a study by van Waes et al[7] in 2,232 consecutive noncardiac surgery patients over age 60 at intermediate to high risk, the all-cause mortality rate was 3%, and troponin I was elevated in 19% of patients. As in VISION and the Canadian retrospective study, the mortality rate increased with the troponin level.

Why routine screening may not help

In VISION,[5] the probability of detecting myocardial injury was three times higher if patients were screened for 3 days after surgery than if they were tested only if clinical signs or symptoms indicated it.

However, in deciding whether to screen troponin levels in postoperative patients, we must take into account the patient's clinical risk as well as the risk of the surgical procedure. Troponin elevation in low-risk patients is associated with a low mortality rate, and troponin elevations often are secondary to causes other than myocardial ischemia. In the study by van Waes et al,[7] the association was stronger with all-cause mortality than with myocardial infarction, and in VISION[5] there were more nonvascular deaths than vascular deaths, suggesting that troponin elevation is a nonspecific marker of adverse events.

Lacking evidence, we can only speculate whether troponin screening helps or harms

Beattie et al[6] found that the probability that a patient's postoperative troponin level would be elevated increased as the patient's clinical risk increased, but the yield was very low and the mortality rate was less than 1% in patients in risk classes 1 through 3 (of a possible 5 classes). In risk class 4, troponin I was elevated in 21.8%, and the mortality rate was 2.5%; in risk class 5 troponin I was elevated in 18.6%, and the mortality rate was 11.9%. Analyzing the data according to the type of surgery, mortality rates were highest in patients undergoing vascular surgery, neurosurgery, general surgery, and thoracic procedures, with all-cause mortality rates ranging from 2.6% to 5.2%.[6]

Screening should depend on risk

If postoperative troponin screening is to be recommended, it should not be routine for all patients but should be restricted to those with high clinical risk and those undergoing high-risk surgical procedures.

Rodseth and Devereaux[8] recommended routine postoperative troponin measurement not only after vascular surgery, but also after high-risk surgery (general, neurosurgery, emergency surgery), as well as in patients over age 65 and patients with established atherosclerotic disease or risk factors for it. However, I believe this latter group may not be at high enough risk to justify routine screening.

Beattie et al[6] advocated limiting postoperative troponin screening to patients with at least a moderate risk of MI and also suggested an international consensus conference to define criteria for postoperative MI, populations who should have routine postoperative screening, and consensus on treatment of patients with troponin elevations but not meeting the criteria for MI. Without this consensus on treatment, it is unclear if protocols for universal postoperative screening would improve outcomes.

For these reasons, the 2014 joint guidelines of the American College of Cardiology and American Heart Association[9] (ACC/AHA) stated that the benefit of postoperative screening of troponin levels in patients with a high perioperative risk of MI but no signs or symptoms of myocardial ischemia or MI is "uncertain in the absence of established risks and benefits of a defined management strategy." This recommendation was given a class IIb rating (may be considered) and level of evidence B (usefulness or efficacy less well established). On the other hand, the guidelines recommend measuring troponin levels if signs or symptoms suggest myocardial ischemia or MI (class I recommendation, level of evidence A) but state there is no benefit in routine screening of unselected patients without signs or symptoms of ischemia (class III recommendation, level of evidence B).

HOW SHOULD ELEVATIONS BE TREATED?

Because a troponin elevation in a patient without signs or symptoms of ischemia does not predict a specific type of death, physicians need to treat patients individually. Perioperative ischemia and inflammation could lead to injury of other organs, and death could result from multiorgan injury rather than from myocardial injury. Treating these troponin elevations in the same way we treat MI—ie, with antiplatelet therapy and anticoagulation—

may result in increased bleeding or unnecessary cardiac catheterization, and starting beta-blockers in the perioperative period may be harmful. Because it is unclear how to manage these patients, cardiac medications have not routinely been given in previous studies.

POISE provided some evidence that patients with postoperative MI who were given aspirin and a statin did better.[1] And the results of a smaller study[10] suggested that intensification of drug therapy (aspirin, statin, beta-blocker, angiotensin-converting enzyme inhibitor) in patients with postoperative troponin I elevations was associated with improved outcomes at 1 year. If the bleeding risk is low, I believe that there is potential benefit in prescribing aspirin and statins for these patients.

CASTING A WIDER NET

Further complicating matters in the near future is the issue of using fifth-generation high-sensitivity troponin T assays. The European Society of Cardiology guidelines[11] are somewhat more liberal than the ACC/AHA guidelines, stating that measuring high-sensitivity troponin after surgery "may be considered in high-risk patients to improve risk stratification." This is a class IIB recommendation, level of evidence B.

With fifth-generation high-sensitivity troponin assays, troponin may be elevated in as many as 20% of patients preoperatively and 40% postoperatively, significantly increasing the number of patients said to have a complication. Besides potentially subjecting these patients to unproven treatments, such results would give the false impression that hospitals and surgeons using the screening tools actually had higher complication rates than those that did not screen.

POSSIBLE HARMS OF SCREENING

Elevated postoperative troponin may identify patients at higher risk of any adverse event but not specifically of cardiac-specific events. In an editorial, Beckman[12] stated that routine measurement of troponin "is more likely to cause harm than to provide benefit and should not be used as a screening modality" because of the lack of a proven beneficial treatment strategy, because of the possible harm from applying the standard treatment for type 1 MI, and because it could divert attention from a true cause of an adverse event to a false one—ie, from a nonvascular condition to MI.[11]

There is clearly a need for clinical trials to determine which treatment, if any, can improve outcomes in these patients, and several trials have been started. But until we have evidence, we can only speculate as to whether screening postoperative patients for troponin elevation is beneficial or detrimental.

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Perioperative MI: Data, practice, and questions

Except in emergency or specific high-risk surgery, or for extremely fragile high-risk patients, we anticipate a successful outcome from noncardiac surgery. The skills and tools of our anesthesiology colleagues have advanced to the point that severe intraoperative and immediate postoperative complications are rare.

Preoperative risk assessment and perioperative medical management in large medical centers are now largely done by hospital-based physicians with interest and expertise in this subspecialty, and are integrated into the care of the surgical patient. This has likely contributed to improved patient outcomes. Yet postoperative cardiovascular events still cause significant morbidity (although they generally occur in less than 10% of patients).

The entity of perioperative myocardial infarction (MI) has an interesting history. We have recognized for several decades that its presentation is often different than the usually diagnosed MI: perioperative MI is often painless and may manifest as unexplained sinus tachycardia, subtle changes in mental status, or mild dyspnea. These symptoms, if they occurred while the patient was at home, would often be mild enough that the patient would not seek immediate medical attention. Autopsy studies suggested that many of these MIs result from a different pathophysiology than the garden variety MI; plaque rupture with or without secondary thrombosis may be less common than myocardial injury resulting from an imbalance between cardiac demand and blood flow. Studies initially suggested that postoperative MI occurred many days after the surgery. But as tests to diagnose myocyte injury became more sensitive (electrocardiography, creatine kinase, creatine kinase MB, and now troponin), it was recognized that cardiac injury actually occurred very soon after or even during surgery.

With the advent of highly sensitive and fairly specific troponin assays, it seems that perioperative cardiac injury is extremely common, perhaps occurring in up to 20% of patients (if we include patients at high risk based on traditional criteria). This has led to the newly described entity of "myocardial injury after noncardiac surgery" (MINS). MINS patients, diagnosed by troponin elevations, usually are asymptomatic, and many do not meet criteria for any type of MI. But strikingly, as discussed in this issue of the *Journal* by Horr et al (page 595), simply having a postoperative troponin elevation predicts an increased risk of clinical cardiovascular events and a decreased 30-day survival rate.

Adding postoperative troponin measurement to the usual preoperative screening protocol significantly increases our ability to predict delayed cardiovascular events and mortality. As pointed out by Cohn in his accompanying editorial (page 603), the benefit, if any, of screening low-risk patients remains to be defined. But an even more important issue, as commented upon in both papers, is what to do when an elevated troponin is detected in a postoperative patient who is otherwise doing perfectly well. Given our current knowledge of the pathophysiology of postoperative MI and the still overall low mortality, it seems unreasonable to immediately take all of these patients

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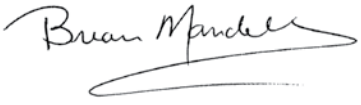
to the catheterization suite. Yet with current knowledge of the prognostic significance of troponin elevation, this can't be ignored. Should all patients receive immediate high-intensity statin therapy, antiplatelet therapy if safe in the specific perioperative setting, and postdischarge physiologic stress studies, or should we "just" take it as a potential high-impact teaching moment and advise patients of their increased cardiovascular risk and offer our usual heart-healthy admonitions?

The confirmed observation that postoperative troponin elevation predicts morbidity and mortality over the subsequent 30 days, and perhaps even longer, has triggered the start of several interventional trials. The results of these will, hopefully, help us to further improve perioperative outcomes.



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CME CREDIT ***EDUCATIONAL OBJECTIVE:*** Readers will interpret the evidence for and against measuring troponin levels in noncardiac postoperative patients

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Troponin elevation after noncardiac surgery: Significance and management

ABSTRACT

How to interpret and manage troponin elevations after noncardiac surgery is a common clinical question for cardiologists and internists. An estimated 5% to 25% of patients who undergo noncardiac surgery have an elevated postoperative troponin level. Patients with troponin elevation are at higher short-term and long-term risk of morbidity and mortality. Current guidelines provide few recommendations on how to manage these patients. The authors review the evidence and guidelines and propose treatment strategies.

KEY POINTS

Cardiovascular events are a major cause of morbidity and mortality in patients undergoing noncardiac surgery and occur frequently, especially in high-risk patients.

Myocardial injury or infarction after noncardiac surgery heightens the short- and long-term risk of mortality and major adverse cardiac events.

The dominant mechanism of myocardial injury after noncardiac surgery remains uncertain.

In the absence of therapies proven to affect the outcome, the benefit of screening to identify these patients remains uncertain.

Clinical trials are under way to help clinicians provide optimal care to this at-risk population.

*Dr. Menon has disclosed that he has received a research grant from Astra Zeneca to conduct the INTREPID study.

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More than 200 million patients undergo noncardiac surgery each year, and the volume is increasing.[1] Cardiovascular complications are a major cause of morbidity and mortality in the perioperative period.

See related editorial, page 603

Before the advent of modern cardiac biomarkers, an estimated 2% to 3% of all patients undergoing noncardiac surgery had a major adverse cardiac event.[2] However, more recent studies suggest that 5% to 25% of patients have troponin elevations after noncardiac surgery, depending on the patient population,[3–6] and many are asymptomatic, suggesting that many patients are sustaining undetected myocardial injury. Those who suffer a myocardial infarction or myocardial injury have elevated morbidity and mortality rates, not only perioperatively, but also at 30 days and even at up to 1 year.[3–5,7–11]

Yet there are almost no data on how best to manage these patients; the available guidelines, therefore, do not provide sufficient recommendations for clinical practice.

To address the lack of guidelines, we examine the incidence and proposed mechanisms of myocardial injury after noncardiac surgery, suggest an approach to identifying patients at risk, recommend treatment strategies, and consider future directions.

CARDIAC BIOMARKERS

When cardiac cellular injury from ischemia, direct trauma, or other cause disrupts the cell membrane, intracellular contents enter

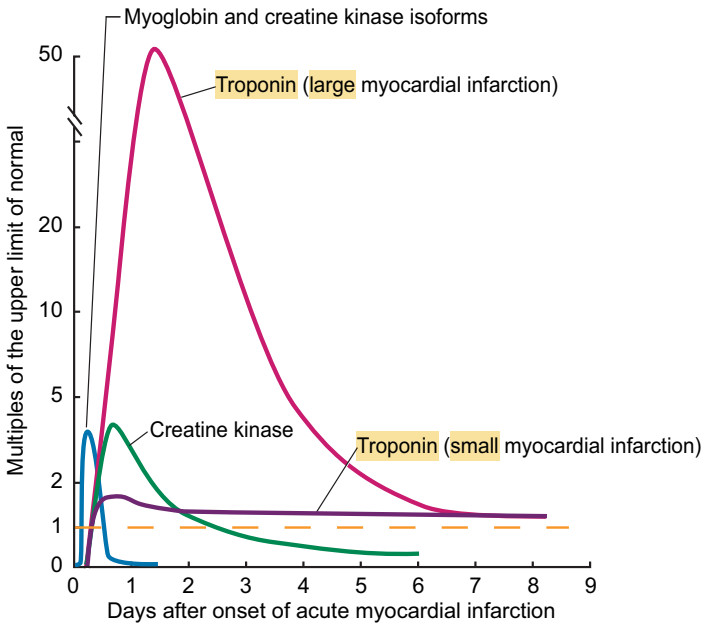

FIGURE 1. Time of release of selected cardiac biomarkers after myocardial infarction.

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Troponin assays are not standardized, so levels from different laboratories cannot be compared

the extracellular space, including the blood stream. If the myocyte damage is extensive enough, biochemical assays can detect these substances.

Troponin, creatine kinase, myoglobin, and lactate dehydrogenase are common biomarkers of necrosis that, when detected in the plasma, may indicate cardiac injury. Each can be detected at varying times after cardiac injury (**Figure 1**).[12]

Cardiac troponins I and T

Of the biomarkers, cardiac troponin I and cardiac troponin T are now the most widely used and are the most specific for myocyte injury.

Troponins are proteins that regulate the calcium-induced interaction between myosin and actin that results in muscle contraction. Troponin is a complex consisting of three subunits: troponin C, troponin I, and troponin T. The cardiac troponin I and T isoforms are distinct from those found in skeletal muscle, making them specific for myocyte injury, and they are currently the recommended markers for diagnosing acute myocardial infarction.[13]

The troponin immunoassays currently available are not standardized among laboratories and point-of-care methods, and thus, levels cannot be compared across testing centers.[14] Each assay has unique performance characteristics, but guidelines recommend using the 99th percentile value from a normal reference population for a given assay to define whether myocardial injury is present.[13]

Troponin elevation has prognostic value in patients presenting with acute coronary syndromes,[15–18] and the degree of elevation correlates with infarct size.[19–21]

Controversy exists as to whether troponin and other biomarkers are released only after myocardial necrosis or after reversible injury as well. Using newer, highly sensitive assays, troponin elevations have been detected after short periods of ischemia during stress testing[22,23] and in patients with stable angina,[24] suggesting that reversible cardiac stress and injury can lead to troponin release. This mechanism may play an important role during the myocardial injury that can occur in patients undergoing noncardiac surgery.

MYOCARDIAL INFARCTION VS MYOCARDIAL INJURY

In 2000, the Joint Task Force of the European Society of Cardiology, American College of Cardiology Foundation, American Heart Association, and World Heart Federation revised the criteria for the diagnosis of myocardial infarction created by the World Health Organization in 1979. The definition was revised again in 2007 and once more in 2012 to create the third universal definition of myocardial infarction.

Acute myocardial infarction

Acute myocardial infarction is defined as evidence of myocardial necrosis in a setting of myocardial ischemia, not related to causes such as trauma or pulmonary embolism, with a rise or a fall (or a rise *and* a fall) of cardiac biomarkers (at least one value being above the 99th percentile in the reference population) and any of the following:

- Symptoms of ischemia
- New ST-segment changes or new left bundle branch block
- Pathologic Q waves
- Imaging evidence of new loss of viable

myocardium or new regional wall-motion abnormality
- Intracoronary thrombus by angiography or autopsy.[13]

Myocardial injury after noncardiac surgery

Studies[10,11] have shown that many patients undergoing noncardiac surgery have evidence of cardiac biomarker release but do not meet the universal definition of myocardial infarction.

The Perioperative Ischemic Evaluation (POISE) trial[10] reported that 415 (5%) of its patients met the definition of myocardial infarction, of whom only about 35% had symptoms of ischemia. Another 697 patients (8.3%) had isolated elevations in biomarkers without meeting the definition of myocardial infarction.

The VISION study[11] (Vascular Events in Noncardiac Surgery Patients Cohort Evaluation) prospectively screened more than 15,000 patients in several countries for troponin elevation during the first 3 postoperative days and for ischemic symptoms and features. Of the patients screened, approximately 1,200 (8%) had troponin elevations, with fewer than half fulfilling the criteria for myocardial infarction.

In another study, van Waes et al[6] prospectively screened 2,232 patients ages 60 and older undergoing intermediate- to high-risk noncardiac surgery. Troponin levels were elevated in 19% of the patients, but only 10 of these patients met the universal definition of myocardial infarction.

In all of these studies, patients with isolated elevation in myocardial biomarkers had worse short-term and long-term outcomes than those without. These observations led to a proposed definition of "myocardial injury after noncardiac surgery" that is broader than that of myocardial infarction and requires only elevation of cardiac biomarkers judged to be due to myocardial ischemia (ie, not from another obvious cause such as pulmonary embolism or myocarditis).[3]

FIVE TYPES OF MYOCARDIAL INFARCTION

The Joint Task Force[13] categorizes myocardial infarction into five distinct types:
- Type 1—due to plaque rupture
- Type 2—due to imbalance between oxygen supply and demand
- Type 3—sudden cardiac death
- Type 4a—associated with percutaneous coronary intervention
- Type 4b—associated with stent thrombosis
- Type 5—associated with coronary artery bypass surgery.

Types 1 and 2 have both been implicated in perioperative myocardial infarction and injury. Patient characteristics and the physiologic response to surgical and anesthetic stressors likely contribute to the development of myocardial infarction and injury after noncardiac surgery.

Plaque rupture as a cause of postoperative myocardial infarction

The mechanism of type 1 myocardial infarction—plaque rupture or erosion leading to thrombosis and infarction—plays a significant role in most cases of acute coronary syndromes. Its role in perioperative and postoperative myocardial infarction or injury, however, is less clear.

In an autopsy study of 26 patients who died of myocardial infarction after noncardiac surgery, plaque rupture was evident in 12 (46%).[25] A prospective angiographic study of 120 patients with acute coronary syndromes after noncardiac surgery found that nearly 50% had evidence of plaque rupture.[26]

Is troponin released only after necrosis, or also after reversible injury?

Higher levels of catecholamines, cortisol,[27,28] platelet reactivity,[29] procoagulant factors,[30] and coronary artery shear stress[31] are all present in the postoperative period and may contribute to an increased propensity for plaque rupture or erosion. Whether plaque rupture is present in patients who have isolated troponin elevation but do not meet the criteria for myocardial infarction has not been investigated.

Oxygen supply-demand imbalance during and after surgery

Oxygen supply-demand imbalance (the mechanism in type 2 myocardial infarction) leading to myocyte stress, ischemia, and subsequent infarction is likely common in the perioperative and postoperative periods. As previously discussed, this imbalance may be present with or without symptoms.

Oxygen demand may increase in this period as a result of tachycardia[32] caused by bleeding, pain, and catecholamines or in-

creased wall stress from hypertension due to vasoconstriction or pain.[33] Oxygen supply can be decreased secondary to tachycardia, anemia,[34] hypotension, hypoxemia, hypercarbia, intravascular fluid shifts (bleeding or volume overload), or coronary vasoconstriction.[33,35]

These mechanisms of myocardial injury, infarction, or both can occur with or without underlying significant obstructive coronary artery disease. However, severe coronary artery disease is more common in those who have had a perioperative myocardial infarction.[36]

POSTOPERATIVE TROPONIN ELEVATION CARRIES A WORSE PROGNOSIS

Patients who suffer a myocardial infarction after noncardiac surgery have worse short- and long-term outcomes than their counterparts.[4,5,7,8,10,33] In the POISE trial,[10] the 30-day mortality rate was 11.6% in those who had had a perioperative myocardial infarction, compared with 2.2% in those who did not ($P < .001$). The patients who had had a myocardial infarction were also more likely to have nonfatal cardiac arrest, coronary revascularization, and congestive heart failure.

'Myocardial injury after noncardiac surgery' requires only troponin elevation for diagnosis

Myocardial injury not fulfilling the criteria for myocardial infarction after noncardiac surgery is also associated with worse short-term and long-term outcomes.[3,6,10,11,37,38] POISE patients with isolated elevations in cardiac biomarkers had a higher 30-day risk of coronary revascularization and nonfatal arrest.[10] In the VISION trial, an elevation in troponin was the strongest predictor of death within 30 days after noncardiac surgery. This analysis also showed that the higher the peak troponin value, the greater the risk of death and the shorter the median time until death.[11]

A meta-analysis of 14 studies in 3,139 patients found that elevated troponin after noncardiac surgery was an independent predictor of death within 1 year (odds ratio [OR] 6.7, 95% confidence interval [CI] 4.1–10.9) and beyond 1 year (OR 1.8, 95% CI 1.4–2.3).[37]

SHOULD SCREENING BE ROUTINE AFTER NONCARDIAC SURGERY?

Since patients suffering myocardial infarction or injury after noncardiac surgery have a worse prognosis, many experts advocate routinely screening all high-risk patients and those undergoing moderate- to high-risk surgery. Many tools exist to determine which patients undergoing noncardiac surgery are at high risk of cardiac complications.

The revised Goldman Cardiac Risk Index is commonly used and well validated. Variables in this index that predict major cardiac complications are:

- High-risk surgery (vascular surgery, orthopedic surgery, and intraperitoneal or intrathoracic surgery)
- History of ischemic heart disease
- History of congestive heart failure
- History of cerebrovascular disease
- Diabetes requiring insulin therapy
- Chronic kidney disease with a creatinine > 2.0 mg/dL.

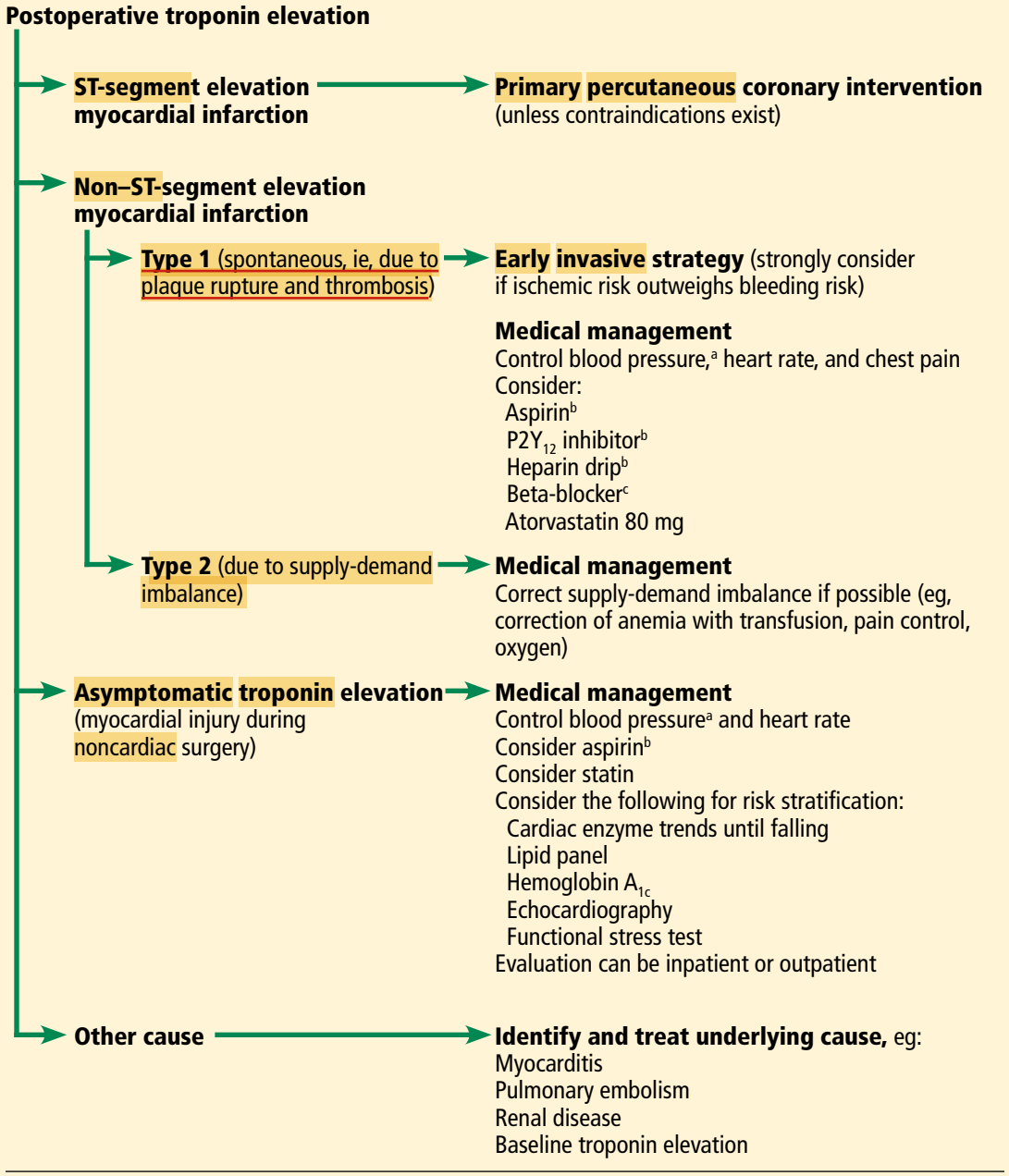
The more of these variables that are present, the higher the risk of perioperative cardiac events[2,4]:

- No risk factors: 0.4% risk (95% CI 0.1–0.8)
- One risk factor: 1.0% risk (95% CI 0.5–1.4)
- Two risk factors: 2.4% risk (95% CI 1.3–3.5)
- Three or more risk factors: 5.4% risk (95% CI 2.7–7.9).

Current guidelines from the American College of Cardiology and the American Heart Association give a class I recommendation (the highest) for measuring troponin levels after noncardiac surgery in patients who have symptoms or signs suggesting myocardial ischemia. They give a class IIb recommendation (usefulness is less well established) for screening those at high risk but without symptoms or signs of ischemia, despite the previously cited evidence that patients with troponin elevation are at increased risk. The IIb recommendation is due to a lack of validated treatment strategies to modify and attenuate the recognized risk with troponin elevation in this setting.[39]

LITTLE EVIDENCE TO GUIDE TREATMENT

In current practice, internists and cardiologists are often asked to consult on patients with troponin elevations noted after noncardiac surgery. Although published and ongoing studies examine strategies to prevent cardiovascular events *during* noncardiac surgery, we lack data on managing the cases of myocardial



[a]Goal blood pressure should be 110–140/70–90 mm Hg.
[b]Consider only if ischemic risk outweighs bleeding risk; decision should be made jointly with surgeon.
[c]Goal heart rate 50–70 beats per minute, if blood pressure is tolerated, and there is no concern for depressed left ventricular ejection fraction or cardiogenic shock.

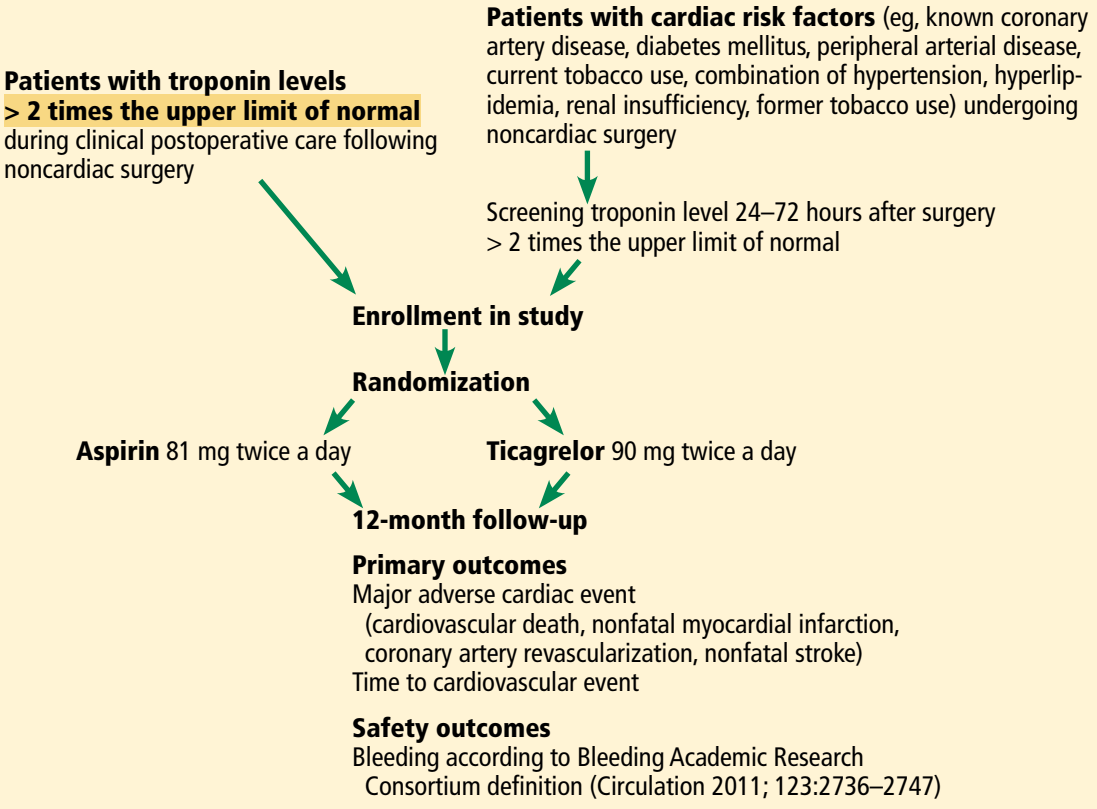
FIGURE 2. Proposed treatment algorithm for patients with postoperative troponin elevation after noncardiac surgery.

Ultimately, treatment decisions should be tailored to the individual patient

infarction and injury that actually occur *after* noncardiac surgery.

When managing a patient who has a troponin elevation after surgery, many clinical factors must be weighed, including hemodynamic and clinical stability and risk of bleeding. Confronted with ST-segment elevation myocardial infarction or high-risk non–ST-segment elevation myocardial infarction, most clinicians would favor an early invasive

INTREPID study design



INTREPID: Study of Ticagrelor Versus Aspirin Treatment in Patients With Myocardial Injury Post Major Non-Cardiac Surgery (ClinicalTrial.gov Identifier NCT02291419).

FIGURE 3

INTREPID will enroll about 1,000 patients with troponin levels > 2 times the upper limit of normal

reperfusion strategy in accordance with guidelines on managing acute coronary syndrome. Fibrinolytic drugs for ST-segment elevation myocardial infarction are likely to be contraindicated in the postoperative period because they pose an unacceptable risk of bleeding.

Guideline-directed medical therapies for those suffering perioperative myocardial infarction may lower the risk of future cardiovascular events, as suggested by a retrospective study of 66 patients diagnosed with perioperative myocardial infarction after vascular surgery.[40] Those in whom medical therapy for coronary artery disease was not intensified—defined as adding or increasing the dose of antiplatelet agent, statin, beta-blocker, or angiotensin-converting enzyme inhibitor—had higher rates of cardiovascular events at 12 months (hazard ratio [HR] 2.80, 95% CI 1.05–24.2).[40]

In those with asymptomatic myocardial infarction or isolated elevation in cardiac biomarkers, no treatment strategies have been assessed prospectively or in randomized trials. However, statins and aspirin have been suggested as providing some benefit. In a substudy of the POISE trial, the use of aspirin was associated with a 46% reduction in the 30-day mortality rate in those suffering a perioperative myocardial infarction, and statins were associated with a 76% reduction.[10] In a single-center retrospective analysis of 337 patients undergoing moderate- to high-risk vascular surgery, statin therapy was associated with a lower 1-year mortality rate (OR 0.63, 95% CI 0.40–0.98).[38]

We propose a treatment algorithm for patients identified as having cardiovascular events after noncardiac surgery (**Figure 2**), based on current evidence and guidelines. Ultimately, treatment decisions should be tailored to the individual patient. Discussion of the risks and benefits of therapeutic options should include the patient and surgeon.

Ongoing and future trials

Ongoing and future trials are aimed at addressing definitive treatment strategies in this patient population.

The MANAGE trial (Management of Myocardial Injury After Non-cardiac Surgery Trial) is randomizing patients suffering myocardial injury after noncardiac surgery to receive either dabigatran and omeprazole or placebo to assess the efficacy of these agents in preventing major adverse cardiac events and the safety of anticoagulation (ClinicalTrials.gov Identifier: NCT01661101).

The INTREPID trial (Study of Ticagrelor Versus Aspirin Treatment in Patients With Myocardial Injury Post Major Non-Cardiac Surgery) will assess the efficacy and safety of ticagrelor treatment compared with aspirin in a similar population (ClinicalTrial.gov Identifier: NCT02291419). The trial will enroll approximately 1,000 patients identified as having a postoperative troponin elevation more than two times the upper limit of normal of the assay during the index hospitalization (**Figure 3**). Enrollment was to have begun in mid-2015. ■

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