

Review

Not peer-reviewed version

Postoperative Myocardial Infarction After Non-cardiac Surgery. An Update.

[Carlo Rostagno](#)^{*} and Anna Craighero

Posted Date: 24 January 2024

doi: 10.20944/preprints202401.1777.v1

Keywords: non-cardiac surgery, myocardial infarction/injury, troponin



Preprints.org is a free multidiscipline platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This is an open access article distributed under the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Review

Postoperative Myocardial Infarction after Non-Cardiac Surgery. An Update

Carlo Rostagno * and Anna Craighero

Dipartimento medicina sperimentale e clinica, Università di Fire 1; annacraighero25@gmail.com

* Correspondence: carlo.rostagno@unfi.it

Abstract. Approximately 300 million non-cardiac surgeries are performed each year. Perioperative mortality after non-cardiac surgery is estimated at 2% in patients over 45 years of age. Half of these deaths are attributable to cardiovascular complications, and most to perioperative myocardial infarction (MINS). Before introduction of cardiac biomarkers, the diagnosis of postoperative myocardial infarction was based on symptoms and electrocardiographic changes and its incidence was largely underestimated. The incidence of MINS when standard troponin assay is used ranges between 8 and 19% but increases to 20-30% with high sensitivity troponin assays. Higher troponin values suggesting myocardial injury, both with or without definite diagnosis of myocardial infarction, are associated with increased 30 day and 1-year mortality. Diagnostic and therapeutic strategies are reported.

Keywords: non-cardiac surgery; myocardial infarction/injury; troponin

1. Introduction

Perioperative myocardial infarction (PMI) is a threatened complication after major non-cardiac surgery. Before the introduction of biomarkers of ischemic damage, and in particular of troponin, the diagnosis of postoperative myocardial infarction was based on symptoms and electrocardiographic changes and its incidence was largely underestimated. Analgesia other than uncommon postoperative ECG monitoring contribute significantly to missed diagnosis. When myocardial damage occurs in the presence of non-cardiac surgery, it is referred to by the acronym MINS (Myocardial Injury after Non-cardiac Surgery). According to the IV universal definition of myocardial infarction myocardial injury is defined by at least one troponin value above the 99th percentile of the upper reference values [1]. It is considered acute when associated with an increase/decrease in troponin values.

The diagnosis of postoperative myocardial infarction requires additional factors such as: Symptoms of ischemia, new electrocardiographic changes indicative of ischemia, development of pathological Q waves, evidence, with diagnostic imaging technique, of new loss of viable myocardium or new abnormalities of regional wall motion compatible with ischemic etiology, and finally identification of a coronary thrombus by angiography or autopsy.

A small proportion of patients (<15 to 20 percent) with perioperative myocardial injury have nonischemic causes of myocardial injury (eg, sepsis, tachyarrhythmias, heart failure).

Even with a more clear definition the diagnosis of MINS and postoperative myocardial infarction the relative difference of incidence between the two conditions may be conditioned by analgesic drugs that may mask symptoms, the absence of ECG monitoring and/or the missing, despite troponin changes, of ischemic abnormalities when ECG are repeated at fixed intervals after surgery. Moreover cardiologists are usually not directly involved in post-operative care leading to a lower sensitivity for acute cardiac complications.

2. Epidemiology

Approximately 300 million non-cardiac surgeries are performed each year. Perioperative mortality after non-cardiac surgery is estimated at 2% in patients over 45 years of age [2]. Half of

these deaths are attributable to cardiovascular complications [3]. In the U.S. every year about 170,000 cardiac complications related to non-cardiac surgery are reported, and cardiac death occur in 5% of patients [4]. 2022 European Society of Cardiology/European Society of Anaesthesiology (ESC/ESA) Guidelines recommended to perform a careful assessment of cardiovascular risk also in patients undergoing non-cardiac surgery [5].

The incidence of PMI varies from 3.5% to 19% depending on the characteristics of the population considered, the type of intervention performed, the design of the study, the criteria used for the diagnosis of myocardial infarction, and finally the type of troponin assay used [6,7]. The incidence of MINS when standard troponin assay is used ranges between 8 and 19% but increases to 20-30% with high sensitivity troponin assays. Results from a cohort of 15,065 patients over 45 years of age undergoing non-cardiac surgery showed that 1200 patients (8%) developed a cardiac event of which 52% did not meet the universal definition of MI [2]. Most of these events affect patients already suffering from coronary artery disease. The risk of MACE is particularly high within the first 7 postoperative days. This has a relevant clinical implication in considering therapeutic/preventive interventions aimed at reducing the rate of major cardiac events. In the first VISION study troponin T was measured during the first 3 postoperative in 15,065 patients aged 45 yr or older who underwent in-patient non-cardiac surgery [8]. The incidence of MINS was 8%. 34.9% of patients with MINS had an ischemic electrocardiographic finding, of which T-wave inversion and ST depression were the most common. Among patients with MINS, 41.8% had an ischemic feature and would have fulfilled the universal definition of myocardial infarction. The prevalence was more common in vascular surgery (633 patients, 24.0%) and less common in urologic or gynecologic surgery (503 patients, 10.4%). More relevant, the occurrence of myocardial injury after non-cardiac surgery was significantly associated to 30-day mortality (314 deaths; adjusted HR 2.2, 95% CI 1.9–2.6) and was one of the main causes of death. cTnT levels were measured 6–12 h after the surgery and on day 1, 2 and 3 after surgery using a not hs method, thus possibly underestimating the prevalence of myocardial injury. In the BASEL-PMI study, a prospective single-center cohort study, were included high-risk patients undergoing non-cardiac surgery. A high-risk patient was defined as a patient between 65 and 85 years of age or between 45 and 65 years of age and history of cardiovascular disease: stroke, coronary artery disease (CAD), peripheral artery disease (PAD) [9]. 2265 patients, 43% of whom were female underwent various non-cardiac surgeries (emergency, orthopedic, urological, thoracic, vascular, visceral) and were followed for one year with the aim of evaluating the onset of heart failure, dynamically relevant arrhythmias, sudden cardiac death, pulmonary embolism, cardiovascular hemorrhage and PMI. PMI was defined as the absolute increase in hs-cTnT ≥ 14 ng/mL above the preoperative concentration or between two postoperative determinations. To distinguish a PMI from a pre-existing hs-cTnT elevation secondary to chronic or other acute cardiac disorders, routine screening consisted of a preoperative measurement of hs-cTnT, used as a baseline, and two postoperative measures in 1st and 2nd day after surgery. The 365-day follow-up, completed in 99.5% of patients, showed an incidence of major cardiovascular events in 466 patients (20.6%), the incidence for PMI alone was 14.8%.

In the second VISION cohort of 21,842 patients ≥ 45 years old, hs-cTnT was measured during the first three postoperative days [10]. Diagnosis of MINS was made with elevated postoperative hs-cTnT 20 to <65 ng/L with an absolute change of at least 5 ng/L between measurements or a single hs-cTnT level ≥ 65 ng/L. Perioperative myocardial injury was detected in 20%. Perioperative myocardial infarction was detected only in 846 patients (3.9 percent). 93% of MINS and 68% of myocardial infarction did not experience an ischemic symptom. Diagnosis would have likely gone undetected without perioperative troponin screening.

The incidence of MI in POISE was 5 percent at 30 days (4.2 and 5.7 in the beta blocker and placebo groups, respectively) although due to non-uniform cut-off troponin in different centers true incidence may be higher [11]. Most (74%) occurred within 48 hours of surgery. 65 percent of the patients who had a perioperative MI did not experience ischemic symptoms. Perioperative, asymptomatic MIs were associated with a similar increased risk of 30-day mortality (adjusted odds ratio 4; 95% CI 2.65-6.06) as with symptomatic MIs (adjusted odds ratio, 4.76; 95% CI 2.68-8.43).

In high risk population , e.g. patients undergoing revascularization for critical limb ischemia, myocardial injury with the hsTnT threshold of 14 ng/L and relative increase by $\geq 30\%$ from the baseline level occurred in 61 patients (25.5%) [12]. At 1 year, there were 34 deaths (14.2%), and 48 MACE (20.5%). Myocardial injury was independently associated with 1-year mortality. Myocardial injury was also independently associated with a three to five fold increase of 1-year MACE depending on hs-TnT levels . 85.2% patients who had myocardial injury did not have ischemic clinical symptoms or electrocardiography changes.

In elderly patients underwent hip fracture surgery cTroponin I levels $\geq 0.5 \mu\text{g/l}$ were found in 129/1030(12.5%) in hospital and 1 year mortality were significantly higher than in controls (12.5% vs 3.5%, $p = .0012$ and respectively 44% vs 16.1% at 12 months, $p = 0.001$) [13]. 18 patients underwent coronary angiography within 1 week from hip surgery. All had multivessel coronary artery disease. One patient died after angiography. At multivariate logistic analysis age (OR 1.09, 95% CI=1.01 to 1.19, $p = .044$) and creatinine values (OR=7.55, 95% CI=1.26 to 45.3, $p = .02$) were independent predictive factors of 1 year mortality whereas coronary revascularization (OR=0.15, 95% CI=0.03 to 0.78, $p = .024$) was an independent factor associated with improved survival.

3. Risk factors

Accurate assessment of cardiac risk is a critical part that precedes elective surgery and high risk patients for PMI can be identified before surgery.

The main risk factors that underlie that affect the balance between myocardial oxygen demand and supply after surgery are divided into:

Preoperative risk factors: Age (≥ 75 years) and comorbidities are the main risk factors in patients undergoing non-cardiac surgery. Although perioperative mortality from MI is higher in older people, age is not an independent predictor of perioperative cardiovascular risk. Main comorbidities include CAD, heart failure, hypertension, stroke, kidney failure and diabetes. In the context of multimorbidity, the presence of coronary artery disease is associated with an increase in post operative myocardial injury and related mortality. The CARP trial [14] evaluated patients with CAD undergoing vascular surgery. The risk of MI was higher in patients aged > 70 years , undergoing AAA surgery, and with angina or ST-T abnormalities. The relation of postoperative MI and the presence of previous obstructive coronary artery disease was also demonstrated by the VISION study, which included 955 patients awaiting non-cardiac surgery who underwent a preoperative coronary CT scan. Of the 71 patients who developed PMI following surgery, 96% had extensive coronary artery disease on coronary CT. Other factors related to an increased incidence of complications are an emergency/urgency surgery, patient's nutritional and functional status. A compromised functional status correlates with a worse postoperative outcome: ADL and IADL are considered independent risk factors.

Intraoperative risk factors: An independent risk factor for PMI is the duration of intraoperative hypotension (mean arterial pressure ≤ 55 mmHg). Other factors include open surgery, an intraoperative heart rate of >110 or <55 beats per minute, and the need for transfusions.

Postoperative risk factors: The main risk factors are postoperative bleeding, sepsis, hypoxia, sustained tachycardia, hypotension, and severe anemia. For every 1g/dL Hb decrease after surgery the risk of PMI increases by 1.46-fold [14].

Physicians have different tools to assess cardiac risk before surgery, however, validated risk models have been created. The 2016 guidelines of the Canadian Cardiovascular Society recommend risk stratification using RCRI (revised cardiac risk index), a risk calculator in people over 45 years of age [15]. Only six variables are required for the risk to be quantified: a high-risk type of surgery including intrathoracic surgery, intraperitoneal surgery, and supra femoral vascular procedures, the presence of ischemic heart disease, the presence of congestive heart failure, cerebrovascular disorders, diabetes requiring insulin, and preoperative serum creatinine $> 2 \text{ mg/dL}$ [16]. One point is assigned for each risk factor, and patients with 0,1,2, or more factors are assigned to classes I, II, III, IV, respectively. Rates of cardiac complications vary from lower to higher class [17].

Table 1. MACE according to revised cardiac risk index.

Risk Class	30-day risk of death,MI or cardiac arrest
0	0.6%
1	0.9%
2	6.6%
3 or more	11%

4. Pathogenesis

PMI after non-cardiac surgery is a heterogeneous syndrome with different underlying etiologies. Most of myocardial injury/infarction, according to the fourth universal definition of infarction, may be considered type 2 myocardial infarctions. Infrequent is type 1 myocardial infarctions (not more than 5-10%) . The postoperative inflammatory state seems to play an important role in the pathogenesis of type 1 MI. Inflammation acts as a trigger, exacerbating ischemic heart damage, embolic vessel obstruction, and thrombosis. In the OPTIMUS study [18] 30 patients with perioperative MI and 30 patients with non-perioperative MI were studied with CT. At culprit lesion, thrombosis was found in 4 out of 30 patients (13%) who had perioperative MI, in 20 out of 30 (66.7%) who had had non-operative MI. Although thrombosis is less common, fibroatheroma has been demonstrated in 18 patients (60%) with perioperative MI and in 20 patients (66.7%) with non-perioperative MI. Therefore thrombotic mechanism is rare as a cause of postoperative myocardial injury/infarction

Type 2 postoperative myocardial infarction is the consequence of a mismatch between myocardial oxygen demand and supply often in the setting of chronic coronary disease. Factors such as surgical stress, bleeding, hypotension related to hypovolemia or altered vasoreactivity, the activation of hemostasis, a marked inflammatory response (CRP, TNF α , IL-1 and IL-6) can lead to reduced oxygen supply to the myocardium. The same systemic inflammation, resulting from surgical trauma, increases the myocardial oxygen demand. The presence of tachycardia, defined as a heart rate of ≥ 100 beats per minute, also increases oxygen demand, limits perfusion time during diastole, and contributes to myocardial damage [19].

Table 2. Symptoms and ECG changes in post-operative myocardial infarction/injury.

	PMI 397	Cardiac PMI 342	Non Cardiac PMI 55
Chest pain	24 – 6%	19- 6%	5 -9%
Dyspnea	46 -12%	39 -11%	7-13%
Any possible ischemia related symptom	72-18%	59-17%	13-24%
ECG changes	60- 24%	54- 25%	6-23%

Modified from [20].

The occurrence of tachyarrhythmias, acute heart failure (AHF) and extracardiac situations such as severe sepsis and pulmonary embolism are not uncommon causes of hs TnT increase after surgery .

The two types of PMI have different incidences depending on the type of surgery: type 2 perioperative infarctions often follow general, orthopedic, and thoracic surgery while type 1 infarctions more frequently are associated with vascular surgery.

5. Clinical manifestations

At variance with spontaneous myocardial infarction, classic symptoms of myocardial ischemia are infrequent in patients with MI after non cardiac surgery . Chest pain is often masked by the administration of analgesic drugs for postoperative pain management, or by anesthesia itself or

postoperative sedation. Dyspnea may be frequently overlooked as symptom of ischemia. More than 65% of patients with PMI are asymptomatic, ECG monitoring is rarely applied and this accounts for the low detection rate before biomarkers' introduction. Due to variable ECG monitoring, ECG signs of myocardial ischemia are often missed. For example, in the international POISE-1 trial among 415 patients who had a perioperative myocardial infarction, approximately 65 percent of patients did not experience ischemic symptoms or signs [20]. Only 2% of patients had ST elevation at ECG.

6. Screening

The use of troponin I or T and, more recently, of high-sensitivity troponin I and T (hs-cTnI, hs-cTnT) allowed to diagnose post-operative myocardial damage/infarction, otherwise frequently missed (21,22). Potentially confounding factors may be the type of method used for troponin assay, the presence of preoperative values already outside the reference range (above the 99th Upper Reference Limit), the presence of chronic release-reduced cessation conditions (heart failure, renal failure).

The introduction of the hs-cTn assay increased the sensitivity of the method but has significantly reduced the specificity, often creating interpretative difficulties that are not easy to solve. The increase in preoperative values must be contextualized in the clinical situation: in the patient who requires emergency time-dependent surgery, the underlying clinical problem may have triggered hemodynamic, inflammatory and metabolic alterations capable of causing myocardial damage prior to and independent of the intervention. The possible interpretation in elective surgery is quite different.

Recently, the European Society of Cardiology issued a Class IB recommendation for active surveillance for PMI. Screening for myocardial infarction after non-cardiac surgery with measurement of troponin blood levels and ECG perioperatively in high-risk patients according to the Revised Cardiac Risk Index (5). Similar recommendations were made by the American Heart Association (23).

Few studies compared different troponin assay methods. In a prospective study recently concluded and under evaluation, our group compared cTnI with hs-cTnT assays in patients undergoing hip fracture surgery. A significant lower number of patients did not show increase above 99th percentile of URL when were assayed hs-cTnT values (7.6 %) in comparison to cTnI (71%). In hospital and 1 year mortality of patients with peak troponin level < 99th of URL was respectively 0 and 2 % for hs-cTnT and 4.1 and 23% for cTnI. For values >99th percentile of URL an incremental risk of both in hospital and 1 year mortality was observed with both methods, as well as an increase in hospitalization for cardiac causes. Pelouchier et al compared hs-cTnI and hs-cTnT, The incidence of overall PMI was 9% lower versus using hs-cTnT (overall PMI 15%) (24). Non-biological equivalence of the approved URL of each assay may have contributed the lower incidence observed with hs-cTnI, but a different release pattern after perioperative triggers might contribute as well.

Independently from the assay used it is extremely useful to have a preoperative troponin value, to distinguish acute from chronic increases. The preoperative measurement of troponin has been sometimes questioned since patients with high values (perhaps even chronic) may see their surgery unnecessarily delayed. When a post-operative cTn concentration is elevated but a recent prior cTn measurement (pre- or post-operative) is not available, a second cTn measurement should be obtained to determine whether a rising or falling pattern indicative of acute myocardial injury is present [25].

The European Society of Cardiology guidelines recommend the measurement of blood levels of hs-cTn before, 24 and 48 hours after surgery in intermediate- and high-risk patients.

When elevated troponin values are detected, it is necessary to remember before making a diagnosis of MINS that: the diagnosis cannot be based only on post-operative values, since a "chronic" increase in blood troponin has been reported. In the VISION study among patients with high postoperative hs-cTn levels, 13.8% had preoperative values greater than or similar to the post-operative peak. Elevated blood levels of troponin may be due to non-ischemic causes, which should be excluded.

According to the ESC 2022 guidelines in intermediate or high-risk patients, with known cardiovascular disease, cardiovascular risk factors, or typical ischemic symptoms, preoperative BNP or NT-proBNP dosing should be considered (5).

Preoperative 12-lead ECG is recommended in all intermediate- and high-risk patients with symptoms of ischemic heart disease, cardiovascular disease, and cardiovascular risk factors. Preoperative ECG, hs-cTnT/I, or BNP are not recommended in low-risk patients undergoing non-cardiac surgery without perioperative troponin screening, >90 percent of patients with MINS and >65 percent of patients with perioperative myocardial infarction would escape detection. Patients with MINS should be evaluated for cardiovascular risk factors, treated for any contributing conditions (eg, anemia), considered for medical therapy, and appropriately evaluated for obstructive CAD (eg, stress echocardiography, stress radionuclide myocardial perfusion, coronary computed tomographic angiography).

7. Diagnosis

In patients who present with typical signs or symptoms of myocardial infarction after surgery, the evaluation of these findings is like to that of patients who present with typical signs or symptoms of myocardial infarction in other settings. Differential diagnosis should be considered for patients with nonspecific signs and troponin increase, in particular pulmonary embolism. In patients who underwent postoperative screening and have an elevated troponin level, ECG and troponin assay should be repeated and compared with previous examination and any preoperative data available. Since the ECG has low sensitivity, cardiac troponin measurement is critical to detect PMI. The diagnosis is made when there is an absolute increase in blood concentrations of cardiac troponins, cTn and high-sensitivity cT (hs-cTnT and hs-cTnI), above the 99th^o percentile associated with typical symptoms of myocardial ischemia and pathognomonic changes in instrumental examinations (26). Among patients with elevated troponin levels, only a small number have electrocardiographic abnormalities. In the VISION study, in which a non-high-sensitivity troponin was dosed, approximately 35% of patients had altered electrocardiographic findings, of which inverted T (23%) and ST depression (16%) were the most frequent (8). It is likely that a high proportion of patients with MINS have electrocardiographic abnormalities at some point in the post-operative course. But these changes are rarely appreciated for the following reasons: several patients do not perceive typical symptoms that require an ECG during the ischemic period; most ECGs are performed after detecting the presence of an elevated troponin level, which is usually observed about 24 hours after surgery; the increase in troponin levels usually occurs after the ischemic event has already begun.

Therefore, the differential diagnosis between PMI and MINS may be often missed.

In patients in whom the diagnosis remains uncertain after evaluation of symptoms, ECGs, and repeat troponin assays, additional noninvasive studies (eg, echocardiography, radionuclide myocardial perfusion imaging, cardiovascular magnetic resonance imaging) may be required to confirm or exclude the presence of myocardial infarction. The approach to additional testing in patients who recently underwent surgery should be like to that in patients in the general population, however availability of examination may be limited, and patient's condition as well may delay the study.

In patients diagnosed with myocardial injury after noncardiac surgery who recover from surgery, it is reasonable to obtain stress or anatomic imaging to assess for obstructive CAD unless another clear explanation for an elevated troponin level is present. However, the small number of prospective studies that describe the yield of such testing does not allow to draw conclusions .

8. Treatment

Preoperative treatment with antiplatelets, statins, beta blockers and ACEi in high-risk patients is associated with a decreased risk of PMI and overall better outcome. According to updated ESC guidelines (, patients with indications for statins should start taking statins perioperatively, and it is recommended to continue taking statins and beta blockers perioperatively if they were previously taken. A monitoring analysis of perioperative troponin after non-cardiac surgery showed that the 30-

day cardiovascular mortality rate and myocardial infarction are reduced by 25% after initiation of treatment with acetylsalicylic acid and statins in high-risk patients.

In patients without heart failure, discontinuation of RAAS (renin angiotensin system) inhibitors on the day of surgery should be considered to prevent perioperative hypotension, while those with stable heart failure could continue to take RAAS inhibitors.

In the small cohort of patients with perioperative STEMI the approach to management is similar to that in other patients with STEMI, provided that the risk of bleeding with antiplatelet agents and anticoagulation may be acceptable. In patients with high bleeding risk the use of angiography and percutaneous coronary intervention (PCI) must be individualized.

Apart from ST elevated myocardial infarction, the high 1-year mortality associated not only with PMI but also with MINS raises several question about postoperative management. In patients with myocardial injury has been suggested to reevaluate the patient two weeks after discharge to manage cardiovascular risk factors, monitor therapy ed eventually determine the need for imaging to detect obstructive CAD. Anatomic imaging of the coronary arteries (CT) to assess for CAD should be obtained in patients with MINS and without significant cognitive or functional impairment. The advantage of such strategy is not supported by randomized studies. As well available data are still insufficient to support the usefulness of coronary angiography. A study including 34,650 patients with perioperative MI showed that coronary angiography was associated with lower in-hospital mortality compared to medical treatments (8.9 vs. 18.1%) (27). The presence of major bleeding due to double antiplatelet therapy is associated with a worse outcome after non-cardiac surgery.

In a study by Parashar et al. (28) from 2003 to 2012 a total of 1093 patients underwent diagnostic coronary angiography : 281 underwent PCI. Mortality rate after perioperative myocardial infarction remained high even after PCI: one-year mortality was 15% in the overall population. In the PCI subpopulation, mortality was 11.3% with more than 1/4 patients and 1/10 patients not surviving beyond 30 days after STEMI and NSTEMI, respectively. Risk analysis showed that increasing age, bleeding after PCI, renal failure, and vascular surgery are all significant predictors of long-term mortality after PCI. In a small group of patients with postoperative MI after hip surgery we found a significant decrease in mortality after revascularization in comparison to age and sex matched patients who did not underwent angiography (29) . Similar results were reported in other study (30). In clinical practice however the postoperative evaluation of patients with MINS is still largely overlooked.

About medical treatment , in patients without significant risk of bleeding, the use of dabigatran for two years after MINS may be considered, based on the MANAGE study in which 110mg twice daily of dabigatran were administered (31) . The use of dabigatran in patients who developed MINS, (started on average 7 days after surgery) has been shown to be effective in reducing the risk of major cardiovascular events by 30% (Hazard Ratio = 0.7; 95% confidence interval: 0.55 – 0.93), and without increasing the risk of postoperative bleeding. In an observational sub-study of POISE-1, aspirin and statin use were each associated with a reduction in the risk for 30-day mortality among patients who had suffered a perioperative myocardial infarction (adjusted OR for aspirin 0.54, 95% CI 0.29-0.99 and adjusted OR for statins 0.26, 95% CI 0.13-0.54) [32].

8. Prognosis

The presence of MINS is associated with a worse prognosis in the short, medium, and long term. MINS that do not meet the universal diagnosis of perioperative myocardial infarction are independently associated with mortality after 30 days. Long-term mortality is increased in patients with elevated troponin blood levels, regardless of whether there is a diagnosis of PMI or MINS. An incremental risk is associated with higher peak troponin values (). A prospective study showed that 30-day mortality was 8.9% in patients with MINS and 1.5% in comparison to controls (). In addition, there was no difference in 30-day mortality between those who had true MI and those who did not meet the criteria and were diagnosed with MINS. Long-term mortality (at one year) was also higher in patients with MINS (22.5%) than in those without (9.3%).

Perioperative MI is associated with an increased risk of death at 30 days. Although all etiologies of PMI are associated with an increased risk of death within 1 year, the mortality rate differs substantially between causes. A large prospective international multicenter study showed that mortality and development of MACE within one year increased in patients with PMI due to heart failure and tachy- arrhythmia. Similar risks are present in patients with type 1 MI. Patients who develop PMI due to a mismatch between oxygen supply and demand have lower mortality.

Nonfatal perioperative MI is a major risk factor for acute coronary syndrome, nonfatal cardiac arrest, heart failure, stroke, 30-day rehospitalization, or progressive angina requiring revascularization after surgery. Patients with PMI have an increased risk of readmission to hospital within 90 days compared to patients without PMI. No major differences are observed between the various underlying causes except that they are more likely to be readmitted to type 1 SMEs than other etiologies.

A large U.S. study identified 8085 patients who were diagnosed with perioperative MI. These patients, compared to those without MI, have a 13% higher absolute mortality and a longer hospital stay of six days. Among surviving patients, the rehospitalization rate was higher in patients with MI (19.1%) than in those without MI (6.5%). The main causes of rehospitalization at 30 days were infectious complications (30%), cardiovascular complications (25.3%) and hemorrhagic complications (10.4%) among patients with MI; infectious (30.6%), gastrointestinal (12.0%) and cardiovascular (8.2%) complications among patients without MI.

Regarding in-hospital mortality depending on the type of surgery in patients with perioperative MI, a study conducted by Smilowitz et al. (2) showed that the surgeries most at risk are: thoracic surgery (28.4%), general surgery (15.3%) and neurosurgery (12.5%).

Table 3. Mortality and 30-day rehpspitalization in function of type of surgery.

Type of surgery	Death (%)	30-day rehpspitalization (%)
Thoracic	28	12
General	20	15
Vascular	15	16
Orthopedic	11	17
Skin/breast	7	21
Genitourinary	7	20
Otolaryngology	5	18
Neurosurgery	13	8

In the VISION study (8), 30-day mortality was 1.2% (266 patients). In this study, an increase in high-sensitivity troponin values >5 ng/L between two different measurements without ischemic symptoms was associated with an increase in 30-day mortality. In addition, an increase in maximum values had prognostic relevance: patients with hs-cTn 20-65 ng/L had a 30-day mortality of 3%, with hs-cTn 65-1000 ng/L of 9.1%, with hs-cTn >1000ng/L of 29.6%.

Author Contributions: “Conceptualization, C.R.; writing—original draft preparation, C.R., A.C. ; writing—review and editing, C.R.; All authors have read and agreed to the published version of the manuscript.”

Funding: None.

Conflicts of Interest: None to be declared.

References

1. Thygesen, K. Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD ;Fourth universal definition of myocardial infarction. *Eur Heart J* **2018**, *40*, 237–269

2. Smilowitz, N. R. , Gupta N, Ramakrishna H, Guo Y, Berger JS, Bangalore S. Perioperative Major Adverse Cardiovascular and Cerebrovascular Events Associated With Noncardiac Surgery. *JAMA* **2017**, *Cardiol* *2*, 181-187

3. Gao L, Chen L, He J, Wang B, Liu C, Wang R, Fan L, Cheng R. Perioperative Myocardial Injury/Infarction After Non-cardiac Surgery in Elderly Patients. *Front Cardiovasc Med*. **2022** May 19;9:910879. doi: 10.3389/fcvm.2022.910879.
4. Ruetzler K, Smilowitz NR, Berger JS, Devereaux PJ, Maron BA, Newby LK, de Jesus Perez V, Sessler DI, Wijeyesundera DN. Diagnosis and Management of Patients With Myocardial Injury After Noncardiac Surgery: A Scientific Statement From the American Heart Association. *Circulation*. **2021** Nov 9;144(19):e287-e305. doi: 10.1161/CIR.0000000000001024.
5. Halvorsen S, Mehilli J, Cassese S, Hall TS, Abdelhamid M, Barbato E, De Hert S, de Laval I, Geisler T, Hinterbuchner L, Ibanez B, Lenarczyk R, Mansmann UR, McGreavy P, Mueller C, Muneretto C, Niessner A, Potpara TS, Ristić A, Sade LE, Schirmer H, Schüpke S, Sillesen H, Skulstad H, Torracca L, Tutarel O, Van Der Meer P, Wojakowski W, Zacharowski K; ESC Scientific Document Group. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. *Eur Heart J*. **2022** Oct 14;43 (39):3826-3924. doi: 10.1093/eurheartj/ehac270.
6. Ravanavena A, Ravindra C, Igweonu-Nwakile EO, Ali S, Paul S, Yakkali S, Teresa Selvin S, Thomas S, Bikeyeva V, Abdullah A, Radivojevic A, Abu Jad AA, Balani P. Absolute Versus Relative Changes in Cardiac Troponins in the Diagnosis of Myocardial Infarction: A Systematic Review and Meta-Analysis. *Cureus*. **2022** Jul 28;14(7):e27414. doi: 10.7759/cureus.27414.
7. Puelacher C, Lurati Buse G, Seeberger D, et al. Perioperative Myocardial Injury After Noncardiac Surgery: Incidence, Mortality, and Characterization. *Circulation* **2018**; 137:1221.
8. Botto F, Alonso-Coello P, Chan MT, et al Vascular events In noncardiac Surgery patlents cOhort evaluationN (VISION) Writing Group, on behalf of The Vascular events In noncardiac Surgery patlents cOhort evaluationN (VISION) Investigators; Appendix 1. The Vascular events In noncardiac Surgery patlents cOhort evaluationN (VISION) Study Investigators Writing Group; Appendix 2. The Vascular events In noncardiac Surgery patlents cOhort evaluationN Operations Committee; Vascular events In noncardiac Surgery patlents cOhort evaluationN VISION Study Investigators. Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. *Anesthesiology*. 2014 Mar;120(3):564-78. doi: 10.1097/ALN.0000000000000113
9. Sazgary L, Puelacher C, Lurati Buse G, et al. Incidence of major adverse cardiac events following non-cardiac surgery. *Eur Heart J Acute Cardiovasc Care* **2021**, 10, 550–558 (2021)
10. Devereaux PJ, Biccadd BM, et al. Writing Committee for the VISION Study Investigators, Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery. *JAMA* **2017**; 317:1642
11. Devereaux PJ, Xavier D, Pogue J, Guyatt G, Sigamani A, Garutti I, Leslie K, Rao-Melacini P, Chrolavicius S, Yang H, Macdonald C, Avezum A, Lanthier L, Hu W, Yusuf S; POISE (PeriOperative ISchemic Evaluation) Investigators. Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. *Ann Intern Med*. **2011** Apr 19;154(8):523-8. doi: 10.7326/0003-4819-154-8-201104190-00003.
12. Szczeklik W, Krzanowski M, Maga P, Partyka Ł, Kościelniak J, Kaczmarczyk P, Maga M, Pieczka P, Suska A, Wachsmann A, Górka J, Biccadd B, Devereaux PJ. Myocardial injury after endovascular revascularization in critical limb ischemia predicts 1-year mortality: a prospective observational cohort study. *Clin Res Cardiol*. **2018** Apr;107(4):319-328. doi: 10.1007/s00392-017-1185-z. Epub 2017 Nov 24.
13. Rostagno C, Carlei A, Rubbieri G, Ceccofiglio A, Magni A, Forni S, Civinini R, Boccaccini A. Perioperative Myocardial Infarction/Myocardial Injury Is Associated with High Hospital Mortality in Elderly Patients Undergoing Hip Fracture Surgery. *J Clin Med*. **2020** Dec 14;9(12):4043. doi: 10.3390/jcm9124043.
14. McFalls EO, Ward HB, Moritz TE, et al. Predictors and outcomes of a perioperative myocardial infarction following elective vascular surgery in patients with documented coronary artery disease: results of the CARP trial. *Eur Heart J* **2008**; 29:394.
15. Ducepe 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**; 33:17.
16. Yao Y, Dharmalingam A, Tang C, Bell H, Dj McKeown A, McGee M, Davies A, Tay T, Collins N. Cardiac risk assessment with the Revised Cardiac Risk Index index before elective non-cardiac surgery: A retrospective audit from an Australian tertiary hospital. *Anaesth Intensive Care*. **2021** Nov;49(6):448-454. doi: 10.1177/0310057X211024661.
17. Hulme RA, Forssten MP, Pourlofti A, Cao Y, Bass GA, Matthiessen P, Mohseni S. The Association Between Revised Cardiac Risk Index and Postoperative Mortality Following Elective Colon Cancer Surgery: A Retrospective Nationwide Cohort Study. *Scand J Surg*. **2022** Jan-Mar;111(1):14574969211037588. doi: 10.1177/14574969211037588.
18. Sheth T, Natarajan MK, Hsieh V, et al. Incidence of thrombosis in perioperative and non-operative myocardial infarction. *Br J Anaesth* **2018**; 120:725.

19. Shcherbakov A, Bisharat N. Associations between different measures of intra-operative tachycardia during noncardiac surgery and adverse postoperative outcomes: A retrospective cohort analysis. *Eur J Anaesthesiol.* **2022** Feb 1;39(2):145-151. doi: 10.1097/EJA.0000000000001618.
20. POISE Study Group, Devereaux PJ, Yang H, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet* **2008**; 371:1839.
21. Sandoval, Y. Apple FS, Mahler SA, Body R, Collinson PO, Jaffe AS. High-Sensitivity Cardiac Troponin and the 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guidelines for the Evaluation and Diagnosis of Acute Chest Pain. *Circulation* **2022**; 146 569–581
22. Mullins K.E. , Christenson R.H. Optimal Detection of Acute Myocardial Injury and Infarction with Cardiac Troponin: Beyond the 99th Percentile, into the High-Sensitivity Era. *Current Cardiology Reports* **2020** vol. 22 Preprint at <https://doi.org/10.1007/s11886-020-01350-w>
23. Fleisher LA, Fleischmann KE, Auerbach AD, et al.. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* **2014**,130:2215–24.
24. Puelacher C., Mueller C. . Perioperative myocardial injury after noncardiac surgery incidence, mortality, and characterization. *Circulation* **2018**, 137, 1221–1232 (2018).
25. Chiang, C.-H. Chiang CH, Pickering JW, et al. Performance of the European Society of Cardiology 0/1-Hour, 0/2-Hour, and 0/3-Hour Algorithms for Rapid Triage of Acute Myocardial Infarction. *Ann Intern Med* **2022** 175, 101–113
26. Duceppe, E. Borges FK, Tiboni M, et al. High-Sensitivity Cardiac Troponin I Thresholds to Identify Myocardial Injury After Noncardiac Surgery: A Cohort Study. *Canadian Journal of Cardiology* **2023**, 39, 311–318
27. Smilowitz, N. R., Gupta, N., Guo, Y., Berger, J. S. & Bangalore, S. Perioperative acute myocardial infarction associated with non-cardiac surgery. *Eur Heart J* **2017**, 38, 2409–2417
28. Parashar A, Agarwal S, Krishnaswamy A, Sud K, Poddar KL, Bassi M, Ellis S, Tuzcu EM, Menon V, Kapadia SR. Percutaneous Intervention for Myocardial Infarction After Noncardiac Surgery: Patient Characteristics and Outcomes. *J Am Coll Cardiol.* **2016** Jul 26;68(4):329-38. doi: 10.1016/j.jacc.2016.03.602.
29. Rostagno, C. Peris A, Polidori GL, et al. Perioperative myocardial infarction in elderly patients with hip fracture. Is there a role for early coronary angiography? *Int J Cardiol* **2019**, 284, 1–5
30. Ujueta F, Berger JS, Smilowitz N. Coronary Angiography in Patients With Perioperative Myocardial Injury After Non-Cardiac Surgery. *J Invasive Cardiol.* **2018** Sep;30(9):E90-E92
31. Devereaux PJ, Duceppe E, Guyatt G, Tandon V, Rodseth R, Biccard BM, Xavier D, Szczeklik W, Meyhoff CS, Vincent J, Franzosi MG, Srinathan SK, Erb J, Magloire P, Neary J, Rao M, Rahate PV, Chaudhry NK, Mayosi B, de Nadal M, Iglesias PP, Berwanger O, Villar JC, Botto F, Eikelboom JW, Sessler DI, Kearon C, Pettit S, Sharma M, Connolly SJ, Bangdiwala SI, Rao-Melacini P, Hoefft A, Yusuf S; MANAGE Investigators. Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomised, placebo-controlled trial. *Lancet.* **2018** Jun 9;391(10137):2325-2334. doi: 10.1016/S0140-6736(18)30832-8.
32. Devereaux, P. J. Goldman L, Cook DJ, Gilbert K, Leslie K, Guyatt GH.. Perioperative cardiac events in patients undergoing noncardiac surgery: a review of the magnitude of the problem, the pathophysiology of the events and methods to estimate and communicate risk. *Can Med Assoc J* **2005**, 173, 627–634
33. Smilowitz, N. R., Beckman, J. A., Sherman, S. E. , Berger, J. S. Hospital Readmission After Perioperative Acute Myocardial Infarction Associated With Noncardiac Surgery. *Circulation* **2018**, 137, 2332–2339 (2018).

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.