Postoperative Myocardial Infarction after Non-Cardiac Surgery

Subjects: Cardiac & Cardiovascular Systems
Contributor: Carlo Rostagno, Anna Craighero

In patients undergoing major non-cardiac surgery, perioperative myocardial infarction (PMI) is a threatened complication. Every year, not less than 300 million non-cardiac surgery interventions are performed in the world. Perioperative mortality after non-cardiac surgery is estimated at 2% in patients over 45 years of age. Cardiovascular events account for half of these deaths, and most are due to perioperative myocardial infarction (MINS). The diagnosis of postoperative myocardial infarction, before the introduction of cardiac biomarkers, was based on symptoms and electrocardiographic changes and its incidence was largely underestimated. The incidence of MINS when a 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 a definite diagnosis of myocardial infarction, are associated with an increase in 30-day and 1-year mortality.

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

1. Introduction

In patients undergoing major non-cardiac surgery, perioperative myocardial infarction (PMI) is a threatened complication. Before the introduction of biomarkers of ischemic damage and of troponin, postoperative myocardial infarction was diagnosed based on symptoms and electrocardiographic changes, and its incidence was largely underestimated. Analgesia often masks pain. Moreover, postoperative ECG monitoring is uncommonly utilized; therefore, transient ischemic changes may remain undetected, contributing significantly to a missed diagnosis. Myocardial damage that occurs after non-cardiac surgery is defined by the acronym MINS (Myocardial Injury after Non-cardiac Surgery). Myocardial injury, according to the IV universal definition of myocardial infarction, 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 chest pain or other symptoms due to myocardial ischemia, new electrocardiographic ischemic abnormalities, development of pathological Q waves, evidence, with a diagnostic imaging technique, of a new loss of viable myocardium or new abnormalities of regional wall motion compatible with ischemic etiology, and, finally, evidence of a coronary thrombus by angiography or autopsy.

In a small proportion of patients (<15 to 20 percent), perioperative myocardial injury has nonischemic causes (e.g., sepsis, tachyarrhythmias, heart failure).

Even with a clearer definition of the diagnosis of MINS and postoperative myocardial infarction, the relative difference in 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 the ECG is repeated at fixed intervals after surgery. Moreover, the involvement of cardiologists in postoperative care is uncommon, leading to a lower sensitivity for acute cardiac complications. The clinical relevance of diagnosis of perioperative myocardial injury/infarction is sustained by survival data that report a significant increase in both early and 1-year mortality associated with increasing postoperative troponin levels. Moreover, the hospitalization rate for cardiovascular causes is significantly higher in comparison to patients without postoperative myocardial injury. Preoperative evaluation is often not fully exhaustive in risk stratification before surgery. In the perioperative period, routine evaluation of cardiac biomarkers is still largely underused, and the diagnosis underestimated. Finally, no clear indications have been provided about postoperative clinical evaluation, the need for coronary angiography (or ischemia imaging test), and, eventually, the treatment to limit late mortality.

2. Epidemiology

Every year in the world, about 300 million people undergo non-cardiac surgical procedures. Perioperative mortality is close to 2% in patients aged more than 45 years [2]. Cardiovascular events account for 50% of postoperative deaths [3]. About 170,000 cardiac complications related to non-cardiac surgery are reported in the US each year, with a 5% mortality [4]. Guidelines recommend performing a careful assessment of cardiovascular risk in patients undergoing non-cardiac surgery when high-risk procedures are scheduled, and postoperative troponin and NT pro-BNP monitoring [5].

In a large cohort study of patients aged >45 years, 8% had a cardiac event after non-cardiac surgery. More than 50%, however, 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 was particularly high within the first 7 postoperative days. This has a relevant clinical implication in considering therapeutic/preventive interventions aimed at preventing cardiac events.

In the first VISION study, 15,065 non-cardiac surgery patients aged >45 years had a measurement of troponin T in the first 3 postoperative days [6]. The incidence of MINS was 8%. Ischemic electrocardiographic findings (mainly T-wave inversion and ST depression) were found in less than 40% and only 41.8% would have fulfilled the universal definition of myocardial infarction. Vascular surgery (24.0%) was more frequently associated with myocardial injury. Myocardial injury was significantly associated with 30-day mortality (HR 2.2, 95% CI 1.9–2.6) and was one of the main causes of death. The use of a standard cTnT assay may have underestimated the true prevalence.

In the POISE study, in which a standard troponin assay (or alternatively CK-MB) was used for diagnosis, the incidence of postoperative MI was 5 percent at 30 days (4.2 and 5.7 in the beta blocker and placebo groups) [7]. Most (74%) occurred within 48 h of surgery. Also, in this study, symptoms occurred only in 35%. To be remarked upon, the finding of 30-day mortality was not different between asymptomatic MIs and symptomatic MIs (adjusted odds ratio 4; 95% CI 2.65–6.06 vs. 4.76; 95% CI 2.68–8.43, respectively). The non-uniform cut-off troponin in different centers, however, limits results interpretation.

A postoperative peak cTroponin I level ≥0.5 µg/L was found in 129/1030 elderly patients who underwent hip fracture surgery. In-hospital and 1-year mortality was significantly higher in patients with high troponin levels (12.5% vs. 3.5%, p = 0.0012 and, respectively, 44% vs. 16.1% at 12 months, p = 0.001 [8]. Coronary angiography was performed within 1 week of hip surgery in 18 patients. Multivessel coronary artery disease was found in all patients. One patient died after angiography. At multivariate logistic analysis, coronary revascularization (OR = 0.15, 95% CI = 0.03 to 0.78, p = 0.024) was an independent factor associated with improved survival while age and creatinine clearance were independent predictive factors of 1-year mortality.

The BASEL-PMI study, a prospective single-center cohort study, evaluated high-risk patients defined as patients aged between 65 and 85 years or between 45 and 65 years and a history of cardiovascular disease (stroke, coronary artery disease, peripheral artery disease) undergoing non-cardiac surgery [9]. A total of 2265 patients, 43% of whom were female, underwent various non-cardiac surgeries (emergency, orthopedic, urological, thoracic, vascular, visceral) and were followed for one year. End points of the study were heart failure, clinically relevant arrhythmias, sudden cardiac death, pulmonary embolism, cardiovascular hemorrhage, and PMI (defined as the absolute hs-cTnT increase of 14 ng/mL above the preoperative concentration or between two postoperative determinations). To distinguish a PMI from a pre-existing hs-cTnT elevation, a preoperative measurement of hs-cTnT was used as a baseline. Two postoperative measures were obtained at the first and second 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%), and the incidence of PMI alone was 14.8%.

Hs-cTnT was measured during the first three postoperative days in the second VI-SION cohort including 21,842 patients ≥45 years [10]. The diagnosis of MINS required an 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. The perioperative myocardial injury was detected in 20%. Perioperative myocardial infarction was detected only in 846 patients (3.9 percent). A total of 93% of MINS and 68% of myocardial infarctions did not experience an ischemic symptom.

In high-risk populations, e.g., patients undergoing revascularization for critical limb ischemia, 25,5% had a myocardial injury (defined as hsTnT levels above the 99th URL of 14 ng/L and relative increase by ≥30% from the baseline level) [11]. One-year mortality was 14.2% and MACE incidence was 20.5%. Myocardial injury was an independent predictor of 1-year mortality and the risk of MACE increased from 3- to 5-folds in relation to hs-TnT levels. Again, in most patients with myocardial injury (85.2%), ischemic clinical symptoms or electrocardiography changes were not found.

Resuming the data from previously reported studies, the incidence of PMI varies from 3.5% to more than 20%. The demographic and therefore clinical characteristics of the population considered the relative risk related to each different site and type of intervention, the design of the study, the definition used for the diagnosis of myocardial infarction, and, finally, the troponin assay used to account for this large difference reported [12][13]. The introduction of the high-sensitivity troponin assay in fact led to a significant increase in MINS detection, from 8 to 19%, when standard cTnI-cTnT levels were assayed to the actual 20–30%. As will be discussed later, the clinical relevance of the introduction of the hs troponin assay in this setting should still be fully clarified.

3. Risk Factors

Accurate assessment of cardiac risk is critical before elective surgery to identify patients at high risk of PMI.

The main risk factors are divided into the following:

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. A known coronary artery disease is associated with a higher risk of postoperative myocardial injury and related mortality. The CARP trial [13] included patients with CAD with an indication of vascular surgery. MI was more frequent in patients aged >70 years, needing AAA surgery, symptomatic for angina, or with ECG ST-T abnormalities. In a subproject of the VISION study, 955 patients awaiting non-cardiac surgery underwent a preoperative coronary CT scan. Ninety-six percent of the 71 patients who developed PMI following surgery had extensive coronary artery disease on the coronary CT. Other factors related to an increased incidence of complications are emergency/urgent surgery and the 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: Hemodynamic abnormalities in the operating room are associated with a higher risk of postoperative MI. The duration of intraoperative hypotension (mean arterial pressure < 55 mmHg) is an independent risk factor for PMI. Bradycardia, heart rate < 55/min, as well prolonged tachycardia, and heart rate > 110 are associated with a higher risk of MIMS [14][15]. Other factors include open surgery and the need for transfusions.

Postoperative risk factors: Postoperative bleeding, sepsis, hypoxia, sustained tachycardia, hypotension, and severe anemia are all factors associated with the risk of MINS. For every 1 g/dL Hb decrease after surgery, the risk of PMI increases by 1.46-fold [15].

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 the RCRI (Revised Cardiac Risk Index), a risk calculator for people over 45 years of age [16]. 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 mg/dL [17]. For each risk factor, 1 point is assigned. Patients with 0, 1, 2, and, finally, 3 or more factors are assigned to classes I, II, III, and IV, respectively. Cardiac complications increase from lower to higher classes [18].

The role of echocardiography, stress imaging for coronary artery disease, and, finally, coronary CT or coronary angiography is still a matter of debate. In patients who need emergent/urgent surgery, a bedside echocardiography may add significant elements to the history and ECG for risk stratification, particularly in elderly patients, in whom functional capacity and symptoms may not be valuable due to limited physical activity, or with left-sided murmurs. Left ventricle wall motion abnormalities, left and right ventricular function, hemodynamic-relevant valve disease, pulmonary artery pressure estimates, and, finally, evaluation of overall volume status may give prognostic information, guide volume replacement, and suggest the need for hemodynamic monitoring to limit postoperative complications. Echocardiography does not take more than a few minutes and skilled cardiologists or anesthesiologists should be included in the group for preoperative evaluation. ESC 2022 guidelines [5] suggest echocardiography in class 1 B for patients with poor functional capacity and/or high NT-pro-BNP BNP, or if murmurs are detected before high-risk NCS while TTE should be considered in patients with suspected new CVD or unexplained signs or symptoms before high-risk NCS (IIa, B recommendation). In patients who need elective surgery, a comprehensive evaluation should be considered for the identification of CAD and its severity. Symptomatic patients should be assessed and treated according to guidelines and surgery delayed.

In asymptomatic patients, stress imaging is recommended before high-risk elective NCS in subjects with poor functional capacity and a high likelihood of CAD or high clinical risk (evidence Ia). Stress imaging should be considered before high-risk NCS in asymptomatic patients with poor functional capacity, and previous PCI or CABG (Evidence IIb). Further management requires the multidisciplinary assessment and evaluation of the risk–benefit ratio between CAD management and scheduled surgery.

4. Pathogenesis

PMI after non-cardiac surgery has different underlying pathogenetic mechanisms. According to the fourth universal definition of infarction, most MINS may be classified as type 2 myocardial infarctions.

Type 1 myocardial infarction is due to acute plaque rupture, ulceration leading to occlusive coronary thrombosis, and severe acute myocardial ischemia. It is usually associated with ST elevation at ECG. In the postoperative period, this condition is infrequent (not more than 5–10%). The postoperative inflammatory state may have a pivotal role in the pathogenesis of type 1 MI. Inflammation acts as a trigger, exacerbating ischemic heart damage, embolic vessel obstruction, and thrombosis. The OPTIMUS study [19] included 30 patients with perioperative MI and 30 patients with non-perioperative MI who were studied with CT. Thrombosis was found in the culprit vessel in only 4 out of 30 patients (13%) with perioperative MI, in comparison to 20 out of 30 (66.7%) who had had spontaneous MI. Nevertheless, patients with MINS frequently had coronary artery disease and fibroatheroma was demonstrated in 18 patients (60%) with perioperative MI.

Type 2 postoperative myocardial infarction is the consequence of a mismatch between myocardial oxygen demand and supply in the absence of coronary thrombosis. This occurs more frequently in patients with known or occult coronary artery disease in whom acute stressors may result in myocardial ischemia and injury reflected by troponin release. In the postoperative setting, patients rarely suffer from chest pain, while dyspnea or unappropriated tachycardia may raise clinical suspicion, and the ECG gives information in less than 50% of patients; therefore, diagnosis often depends on a troponin assay. Surgical stress, bleeding, hypotension related to hypovolemia or altered vasoreactivity, the activation of hemostasis, and a marked inflammatory response (CRP, TNFα, 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. After The presence of tachycardia also increases the oxygen demand, limits the perfusion time during diastole, and contributes to myocardial damage [15].

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 are more frequently associated with vascular surgery.

References

1. Thygesen, K.; Alpert, J.S.; Jaffe, A.S.; Chaitman, B.R.; Bax, J.J.; Morrow, D.A.; White, H.D. Fourth universal definition of myocardial infarction. Eur. Heart J. 2018, 40, 237–269.
2. Smilowitz, N.R.; Gupta, N.; Ramakrishna, H.; Guo, Y.; Berger, J.S.; Bangalore, S. Perioperative Major Adverse Cardiovascular and Cerebrovascular Events Associated with Noncardiac Surgery. JAMA 2017, 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, 9, 910879.
4. Ruetzler, K.; Smilowitz, N.R.; Berger, J.S.; Devereaux, P.J.; Maron, B.A.; Newby, L.K.; de Jesus Perez, V.; Sessler, D.I.; Wijeysundera, D.N. Diagnosis and Management of Patients with Myocardial Injury after Noncardiac Surgery: A Scientific Statement from the American Heart Association. Circulation 2021, 144, e287–e305.
5. Halvorsen, S.; Mehilli, J.; Cassese, S.; Hall, T.S.; Abdelhamid, M.; Barbato, E.; De Hert, S.; de Laval, I.; Geisler, T.; Hinterbuchner, L.; et al. ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. Eur. Heart J. 2022, 43, 3826–3924.
6. Botto, F.; Alonso-Coello, P.; Chan, M.T.V.; Villar, J.C.; Xavier, D.; Srinathan, S.; Guyatt, G.; Cruz, P.; Graham, M.; Wang, C.Y.; et al. Myocardial injury after noncardiac surgery: A large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. Anesthesiology 2014, 120, 564–578.

7. Devereaux, P.J.; Biccard, B.M.; Sigamani, A.; Xavier, D.; Chan, M.T.; Srinathan, S.K.; Walsh, M.; Abraham, V.; Pearse, R.; Wang, C.Y.; et al. Association of Postoperative High-Sensitivity Troponin Levels with Myocardial Injury and 30-Day Mortality among Patients Undergoing Noncardiac Surgery. JAMA 2017, 317, 1642–1651.
8. Devereaux, P.J.; Xavier, D.; Pogue, J.; Guyatt, G.; Sigamani, A.; Garutti, I.; Leslie, K.; Rao-Melacini, P.; Chrolavicius, S.; Yang, H.; et al. Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: A cohort study. Ann. Intern. Med. 2011, 154, 523–528.
9. Rostagno, C.; Cartei, 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, 9, 4043.
10. Sazgary, L.; Puelacher, C.; Lurati Buse, G.; Glarner, N.; Lampart, A.; Bolliger, D.; Steiner, L.; Gürke, L.; Wolff, T.; Mujagic, E.; et al. Incidence of major adverse cardiac events following non-cardiac surgery. Eur. Heart J. Acute Cardiovasc. Care 2021, 10, 550–558.
11. Szczeklik, W.; Krzanowski, M.; Maga, P.; Partyka, Ł.; Kościelniak, J.; Kaczmarczyk, P.; Maga, M.; Pieczka, P.; Suska, A.; Wachsmann, A.; et al. Myocardial injury after endovascular revascularization in critical limb ischemia predicts 1-year mortality: A prospective observational cohort study. Clin. Res. Cardiol. 2018, 107, 319–328.
12. Ravanavena, A.; Ravindra, C.; Igweonu-Nwakile, E.O.; Ali, S.; Paul, S.; Yakkali, S.; Teresa Selvin, S.; Thomas, S.; Bikeyeva, V.; Abdullah, A.; et al. Absolute Versus Relative Changes in Cardiac Troponins in the Diagnosis of Myocardial Infarction: A Systematic Review and Meta-Analysis. Cureus 2022, 14, e27414.
13. McFalls, E.O.; Ward, H.B.; Moritz, T.E.; Apple, F.S.; Goldman, S.; Pierpont, G.; Larsen, G.C.; Hattler, B.; Shunk, K.; Littooy, F.; 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, 394–401.
14. Hietala, P.; Strandberg, M.; Strandberg, N.; Gullichsen, E.; Airaksinen, K.E. Perioperative myocardial infarctions are common and often unrecognized in patients undergoing hip fracture surgery. J. Trauma Acute Care Surg. 2013, 74, 1087–1091.
15. 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, 39, 145–151.
16. Duceppe, E.; Parlow, J.; MacDonald, P.; Lyons, K.; McMullen, M.; Srinathan, S.; Graham, M.; Tandon, V.; Styles, K.; Bessissow, A.; et al. Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery. Can. J. Cardiol. 2017, 33, 17–32.
17. 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, 49, 448–454.
18. Hulme, R.A.; Forssten, M.P.; Pourlotfi, A.; Cao, Y.; Bass, G.A.; 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, 111, 14574969211037588.
19. Sheth, T.; Natarajan, M.K.; Hsieh, V.; Valettas, N.; Rokoss, M.; Mehta, S.; Jolly, S.; Tandon, V.; Bezerra, H.; Devereaux, P.J.; et al. Incidence of thrombosis in perioperative and non-operative myocardial infarction. Br. J. Anaesth. 2018, 120, 725–733.
