Published in final edited form as:

Int J Cardiol. 2019 March 15; 279: 1–5. doi:10.1016/j.ijcard.2018.12.032.

Medical Therapy for Atherosclerotic Cardiovascular Disease in Patients with Myocardial Injury after Non-cardiac Surgery

Jin F. Chen, MD^{a,*}, Nathaniel R. Smilowitz, MD^{b,*}, Jung T. Kim, MD^c, Germaine Cuff, PhD^c, Alina Boltunova, MD^d, Jason Toffey, MD^e, Jeffrey S. Berger, MD, MS^b, Andrew Rosenberg, MD^c, and Samir Kendale, MD^c

^aDepartment of Anesthesiology, Columbia University Medical Center, New York, NY

^bDepartment of Medicine, Division of Cardiology, New York University Langone Medical Center, New York, NY

^cDepartment of Anesthesiology, Perioperative Care, and Pain Medicine, New York University Langone Medical Center, New York, NY

^dDepartment of Anesthesiology, Weill Cornell Medical Center, New York, NY

^eDepartment of Anesthesiology, Georgetown University Medical Center, Washington D.C.

Abstract

Background: Myocardial injury after non-cardiac surgery (MINS) is a common postoperative cardiovascular complication and is associated with short and long-term mortality. The objective of the study was to describe the contemporary management of patients with and without MINS after total joint and spine orthopedic surgery at a large tertiary care hospital.

Methods: Adults admitted for total joint and major spine surgery from January 2013 through December 2015 with 1 cardiac troponin (cTn) measurement during their hospitalization were identified. MINS was defined by a peak cTn above the 99th percentile of the upper reference limit. Demographics, medical comorbidities, and admission and discharge medications were reviewed for all patients.

Results: A total of 2,561 patients underwent 2,798 orthopedic surgeries, and 236 cases of MINS were identified. Patients with MINS were older (71.9 ± 10.9 vs. 67.0 ± 10.0 , $p < 0.001$) and more likely to have cardiovascular risk factors, including hypertension, chronic kidney disease, prior stroke, coronary artery disease, prior MI, and a history of heart failure. Among patients with MINS, only 112 (47.5%) were discharged on a combination of aspirin and statin. Patients with

Corresponding Author: Nathaniel Smilowitz MD, FACC, FSCAI, Leon H. Charney Division of Cardiology, New York University School of Medicine, 530 First Avenue, HCC-14, New York, NY 10016, Nathaniel.Smilowitz@nyumc.org, Ph. 212-263-4992, Fax 212-263-8354.

*Drs. Chen and Smilowitz contributed equally to this study.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflicts of Interest

The authors report no relationships that could be construed as a conflict of interest.

MINS were more likely to be prescribed a statin (154 [65.3%] vs. 1463 [57.1%], $p=0.018$), beta-blocker (147 [62.3%] vs. 1194 [46.6%], $p<0.001$), and oral anticoagulation (65 [27.5%] vs. 436 [17.0%], $p<0.001$) than patients without MINS.

Conclusions: The proportion of patients with MINS who were prescribed medical therapy for atherosclerotic cardiovascular disease was low. Additional efforts to determine optimal management of MINS are warranted.

Keywords

Acute Coronary Syndrome; Biomarkers; Coronary Artery Disease; Ischemic Heart Disease; Myocardial Infarction; Myocardial Injury; Myocardial Injury after Noncardiac Surgery; Medical Therapy; Surgery; Troponin; Perioperative

Introduction

More than 1.5 million total joint and/or spine surgeries are performed in the United States each year.¹ Cardiovascular complications of non-cardiac surgery are a major source of morbidity and mortality. Myocardial injury after non-cardiac surgery (MINS) is a common post-operative cardiovascular complication that is detected in 8–22% of patients and is associated with short and long-term mortality.^{2–7} Perioperative acute myocardial infarction (MI), a subgroup of MINS with clinical evidence of ischemia that meets the universal definition of MI,⁸ only occurs 5% of elevated-risk patients undergoing non-cardiac surgery.^{9–11} Since the latest American clinical practice guidelines recommend against the routine measurement of troponin in the post-operative period following non-cardiac surgery, MINS may be underdiagnosed.¹²

Despite the incidence of MINS, contemporary perioperative and cardiovascular disease guidelines do not provide specific treatment recommendations for surgical patients with these syndromes.^{12–14} Guideline-directed medical therapy (GDMT) for atherosclerotic cardiovascular disease (ASCVD) in patients with MINS may provide benefit but requires further investigation.^{15, 16} Consequently, there may be significant variability in the post-operative medical management of MINS. Given the uncertainty of diagnostic and therapeutic strategies in these high-risk patients, the objective of the study was to describe the contemporary post-operative management of MINS in patients undergoing total joint and spine orthopedic surgery at a large urban health system in the United States.

Methods

Study Population

We performed a retrospective cohort study of consecutive adults age ≥45 undergoing total joint and major spine surgery at NYU Langone Health Tisch Hospital and NYU Langone Orthopedic Hospital, 2 high-volume tertiary-care facilities within the same urban health system, between January 1, 2013 and December 31, 2015. This time period was selected based on data availability from the electronic health record. Patients were identified using International Classification of Disease, Ninth Revision (ICD-9) and Tenth Revision (ICD-10) procedure codes for spine and total joint replacement surgeries. Patients were

eligible for study inclusion if 1 cardiac troponin measurement (cTnI) was performed in the post-operative period during the surgical hospitalization. All troponin measurements were performed at the discretion of the treating clinicians. For patients who underwent multiple surgeries during a single hospital admission, only the first surgery was included in the final analysis. Among patients with multiple orthopedic surgery admissions, each surgical admission was included separately in the final analysis. All surgical patients were managed as per usual care practices at our institution, with management decisions made at the discretion of the treating clinicians.

Patient demographics and comorbidities were obtained from hospital administrative databases and retrospective review of the medical record. Cardiovascular comorbidities were defined by ICD-9 and ICD-10 diagnosis codes. American Society of Anesthesiologists (ASA) physical status classifications were prospectively determined prior to surgery by the treating anesthesiologists and recorded in the electronic medical record for all patients. MINS was defined as 1 cardiac troponin-I (cTnI) in the postoperative period with a peak level above the 99th percentile of the upper reference limit (URL) determined in a healthy population. Plasma cTnI was measured using the VITROS cTnI ES assay (Ortho Clinical Diagnostics, Rochester, NY; 99th percentile URL >0.04 ng/mL), or the ST AIA-PACK 2nd generation cTnI assay (Tosoh Bioscience, Tokyo, Japan; 99th percentile URL >0.06 ng/mL). Perioperative acute MI was defined by the presence of 1 cardiac troponin-I (cTnI) with a peak level >99% of the laboratory upper reference limit and an ICD-9 diagnosis code for acute MI. Cardiovascular medications prescribed at hospital admission (pre-operative) and at discharge (postoperative) were reviewed for all patients.

Statistical Analysis—Clinical characteristics and treatments of patients with and without MINS were compared. Continuous variables were compared with the independent samples t test for normally distributed variables and the Mann Whitney U test for non-normally distributed variables. Categorical variables are reported as percentages and compared by Chi-square and Fisher exact tests. Multivariable logistic regression models were generated to estimate odds ratios (OR) for the diagnosis of MINS. Logistic regression models were also generated to estimate the odds of cardiovascular medication prescribing at hospital discharge. Models were adjusted for demographics, baseline medical comorbidities, including hypertension, hyperlipidemia, diabetes, renal disease, coronary artery disease, prior myocardial infarction, prior percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), peripheral artery disease, prior stroke, heart failure, chronic obstructive pulmonary disease (COPD), malignancy, and when applicable, pre-operative cardiovascular medications. A subgroup analysis comparing characteristics and treatment of patients with MINS with and without AMI was also performed. Statistical analyses were performed using SPSS 25 (IBM SPSS Statistics, Armonk, NY). Two-sided p-values <0.05 were considered to be statistically significant. The study was approved by the New York University School of Medicine Institutional Review Board with a waiver of informed consent.

Results

Clinical Characteristics

A total of 2,561 patients underwent 2,798 orthopedic surgeries, with 2,185 joint replacements (78.1%) and 613 spine surgeries (22.0%). Demographics and preoperative cardiovascular risk factors and procedural characteristics are displayed in Table 1. The mean age was 67.4 ± 10.2 years and 53.0% of patients were female. The majority of participants were classified as either ASA class 2 (39.2%) or ASA class 3 (54.1%) prior to surgery.

Overall, MINS was detected in the post-operative period of 236 (8.4%) orthopedic surgeries. Patients with MINS were older, had lower BMI, and a higher frequency of cardiovascular risk factors, including hypertension, chronic kidney disease, prior stroke, coronary artery disease, prior MI, and a history of heart failure (Table 1). There were no significant differences in the frequency of MINS among patients who underwent spine surgery compared to those who underwent total joint replacement. In multivariable analyses, age (adjusted OR [aOR] 1.04 95% CI 1.02 – 1.05), heart failure (aOR 2.82 95% CI 1.9 – 4.19), renal disease (aOR 2.14 95% CI 1.36 – 3.35), coronary artery disease (aOR 1.74 95% CI 1.23 – 2.48), and prior MI (aOR 2.39 95% CI 1.32 – 4.33) were independently associated with the development of MINS (Table 2). Among patients with MINS, the median peak post-operative troponin was 0.22 ng/mL (IQR 0.09–0.60 ng/mL) and in 42 cases (17.8%) the peak troponin was greater than 1.0 ng/mL. The median peak troponin was 0.27 ng/mL (IQR 0.10 – 0.79 ng/mL) when MINS was detected by the ST AIA-PACK 2nd generation cTnI assay (n=176) and was 0.12 ng/mL (IQR 0.05 – 0.45 ng/mL) when MINS was detected by the VITROS cTnI ES assay (n=60).

Preoperative Medical Therapy

Guideline directed medical therapy for ASCVD prescribed preoperatively and at discharge are shown in Table 3. At hospital admission prior to surgery, patients were prescribed aspirin in 43.1% of cases, a P2Y12 inhibitor in 9.2%, warfarin in 6.1%, a statin in 56.3%, a beta-blocker in 44.1%, and an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) in 46.6% of cases. Patients who developed MINS were more likely to have received a beta-blocker prior to surgery than patients who did not develop MINS (53.8% vs. 43.2%, $p=0.002$), but beta-blocker use was not a significant predictor of MINS after multivariable adjustment. No other differences in pre-operative medical therapy between patients with and without MINS were observed.

Post-operative Medical Therapy

Overall, a total of 2,558 patients (99.9%) survived to hospital discharge. At the time of hospital discharge after surgery, aspirin was prescribed in 61.9% of cases, a P2Y12 inhibitor in 9.3% of cases, warfarin in 12% of cases, a statin in 57.8% of cases, a beta-blocker in 47.9% of cases, and an ACE inhibitor or ARB in 45.9% of cases overall (Table 3). Among patients with MINS, 64.0% received aspirin at discharge, 11.9% received a P2Y12 inhibitor, 20.3% received warfarin, 65.3% received a statin, and 62.3% received a beta-blocker (Table 3). Only 47.5% were discharged on a combination of aspirin and statin. In univariate analyses, patients with MINS were more likely to be prescribed a statin (65.3% vs. 57.1%,

$p=0.018$), a beta-blocker (62.3% vs. 46.6%, $p<0.001$), and oral anticoagulation (27.5% vs. 17.0%, $p<0.001$) at discharge than patients without MINS. There were no differences in the prescribing frequency of other medication classes (Table 3).

Associations between MINS and Changes in Medical Therapy

Overall, aspirin was added at discharge in 37.1% of cases when it had not been prescribed pre-operatively, P2Y12 inhibitor was added in 1.9% of cases, a statin was added in 4.4% of cases, and a beta-blocker was added in 8.6% of cases. Patients with MINS were more likely to be prescribed 1 new cardiovascular medication at hospital discharge in comparison to patients without MINS. Specifically, MINS patients were more likely to be discharged with a new prescription for oral anticoagulation (22.5% vs. 9.9%, $p<0.001$), a statin (23.3% vs. 2.3%, $p<0.001$), a beta-blocker (22.9% vs. 7.5%, $p<0.001$), and the combination of aspirin and statin (26.3% vs. 14.7%, $p<0.001$) compared with patients without MINS (Table 4).

Discussion

In this retrospective cohort study, MINS was identified after 8.4% of major non-cardiac joint and spine surgeries. Patients with MINS were older and had a greater burden of cardiovascular risk factors than patients without MINS. Detection of MINS was associated with greater intensification of medical therapy at hospital discharge in comparison to patients without MINS. Even so, few patients with MINS were discharged on GDMT for ASCVD.

Perioperative cardiovascular events are an important cause of mortality and morbidity in non-cardiac surgery.^{9, 11, 17} Myocardial injury after non-cardiac surgery, the most common cardiovascular complication, remains a challenging clinical problem. In the large Vascular Events In Non-cardiac Surgery Patients Cohort Evaluation (VISION) study of patients 45 years of age undergoing non-cardiac surgery, low-level elevations in troponin and high-sensitivity troponin were significant predictors of 30-day mortality.^{2,5} Other studies of MINS have also reported associations between MINS and short and long-term outcomes.^{4,18,19}

Mechanisms of MINS remain unknown, contributing to provider uncertainty and the variability in post-operative medical management of this condition. Conventional GDMT for ASCVD, such as antiplatelet therapy, carry risks of postoperative bleeding.²⁰ However, in a recent retrospective observational study of high-risk patients undergoing major orthopedic surgery, the use of antiplatelet therapy throughout the perioperative period appeared to be safe.²¹ Lipid-lowering therapy with statins reduces the risk of cardiovascular events in non-surgical populations for primary and secondary prevention,^{22, 23} but declines in perioperative cardiovascular events due to statin use remain somewhat speculative.^{23–27} In large observational studies, preoperative statin use was associated with significantly reduced risk of MINS, cardiovascular complications, and all-cause mortality.^{23, 27} However, a recent Cochrane review of randomized controlled trials of statins in non-cardiac surgery identified insufficient evidence to conclude that statins reduce perioperative cardiovascular events.²⁸ Thus, current ESC/ESA and ACC/AHA clinical practice guidelines recommend the continuation of statins in the perioperative period, and consider the initiation of statins

reasonable in patients undergoing vascular surgery or with clinical risk factors and undergoing elevated-risk procedures.^{12, 29} GDMT for ASCVD is likely beneficial in patients with MINS, and recent clinical trials have tested novel approaches to management of this high-risk condition. In the MANAGE trial, patients age 45 years with MINS who were randomly assigned to receive low dose dabigatran 110mg twice daily within 35 days of surgery had a significantly lower incidence of the composite endpoint of all-cause mortality, arterial and venous events at 2 years compared with patients who received placebo.³⁰ Based on these findings, MINS patients appear to derive benefit from intensification of antithrombotic therapy, and it is plausible that they may benefit from other cardiovascular medical therapy for secondary prevention of MI as well.

There are several limitations of the present study. First, patients without postoperative troponin measurements were not included in this analysis, and troponin measurements were performed at the discretion of the treating providers. As such, troponin measurements were limited to patients with the greatest cardiovascular risk factors and a higher pretest probability of perioperative myocardial injury. In prior studies of patients undergoing orthopedic surgery, patients with any clinically indicated troponin measurement, including those with a result within the normal reference range, had less favorable long-term outcomes in comparison to patients for whom troponin was not measured.⁴ Despite this selection bias, the study population represents a real-world cohort of orthopedic surgery patients with clinically indicated post-operative troponin measurements. Second, initiation, continuation, and discontinuation of medical therapy were performed at the discretion of the clinical providers. Standardized clinical risk assessments were not employed. The clinical rationale for the choice of therapy was not available from available documentation. Third, this study was conducted at a single high-volume tertiary care center, which may affect the generalizability of the study findings to smaller centers. Still, this represents the largest cohort of patients undergoing major orthopedic surgery with perioperative troponin measurements and data on changes in medical therapy for ASCVD before and after surgery.

In conclusion, in a large retrospective cohort study of patients undergoing major non-cardiac orthopedic surgery, 8.4% of patients developed MINS. Patients with MINS were more likely to have intensification of medical therapy for ASCVD in comparison to patients without MINS. However, the proportion of MINS patients prescribed GDMT for ASCVD remained low. Additional efforts to determine optimal management of MINS are warranted.

Funding Acknowledgements:

Support was provided from institutional sources and the Foundation for Anesthesia Education and Research (FAER) Medical Student Anesthesia Research Fellowship Program. Nathaniel R. Smilowitz was supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under award 5T32HL098129-09.

Abbreviations:

ACC	American College of Cardiology
AHA	American Heart Association
ASA	American Society of Anesthesiologists

ACE	Angiotensin Converting Enzyme Inhibitor
ARB	Angiotensin Receptor Blocker
ASCVD	Atherosclerotic Cardiovascular Disease
BMI	Body Mass Index
cTnI	Cardiac Troponin Measurement
COPD	Chronic Obstructive Pulmonary Disease
CABG	Coronary Artery Bypass Grafting
ESA	European Society of Anaesthesiology
ESC	European Society of Cardiology
GDMT	Guideline-directed medical therapy
ICD	International Classification of Disease
MI	Myocardial Infarction
MINS	Myocardial Injury after Non-cardiac Surgery
PCI	Percutaneous coronary intervention
VISION	Vascular Events In Non-cardiac Surgery Patients Cohort Evaluation

References:

1. Weiss AJ and Elixhauser A. Trends in Operating Room Procedures in U.S. Hospitals, 2001–2011: Statistical Brief #171 Healthcare Cost and Utilization Project (HCUP) Statistical Briefs Rockville (MD); 2006.
2. Vascular Events In Noncardiac Surgery Patients Cohort Evaluation Study I, Devereaux PJ, Chan MT, Alonso-Coello P, Walsh M, Berwanger O, Villar JC, Wang CY, Garutti RI, Jacka MJ, Sigamani A, Srinathan S, Bickard BM, Chow CK, Abraham V, Tiboni M, Pettit S, Szczeklik W, Lurati Buse G, Botto F, Guyatt G, Heels-Ansdell D, Sessler DI, Thorlund K, Garg AX, Mrkobrada M, Thomas S, Rodseth RN, Pearce RM, Thabane L, McQueen MJ, VanHelder T, Bhandari M, Bosch J, Kurz A, Polanczyk C, Malaga G, Nagele P, Le Manach Y, Leuwer M and Yusuf S. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA*. 2012;307:2295–304. [PubMed: 22706835]
3. Botto F, Alonso-Coello P, Chan MT, Villar JC, Xavier D, Srinathan S, Guyatt G, Cruz P, Graham M, Wang CY, Berwanger O, Pearce RM, Bickard BM, Abraham V, Malaga G, Hillis GS, Rodseth RN, Cook D, Polanczyk CA, Szczeklik W, Sessler DI, Sheth T, Ackland GL, Leuwer M, Garg AX, Lemanach Y, Pettit S, Heels-Ansdell D, Lurati Buse G, Walsh M, Sapsford R, Schunemann HJ, Kurz A, Thomas S, Mrkobrada M, Thabane L, Gerstein H, Paniagua P, Nagele P, Raina P, Yusuf S, Devereaux PJ, Devereaux PJ, Sessler DI, Walsh M, Guyatt G, McQueen MJ, Bhandari M, Cook D, Bosch J, Buckley N, Yusuf S, Chow CK, Hillis GS, Halliwell R, Li S, Lee VW, Mooney J, Polanczyk CA, Furtado MV, Berwanger O, Suzumura E, Santucci E, Leite K, Santo JA, Jardim CA, Cavalcanti AB, Guimaraes HP, Jacka MJ, Graham M, McAlister F, McMurtry S, Townsend D, Pannu N, Bagshaw S, Bessissow A, Bhandari M, Duceppe E, Eikelboom J, Ganame J, Hankinson J, Hill S, Jolly S, Lamy A, Ling E, Magloire P, Pare G, Reddy D, Szalay D, Tittley J, Weitz J, Whitlock R, Darvish-Kazim S, Debeer J, Kavsak P, Kearon C, Mizera R, O'Donnell M, McQueen M, Pinthus J, Ribas S, Simunovic M, Tandon V, Vanhelder T, Winemaker M, Gerstein H, McDonald

- S, O'Bryne P, Patel A, Paul J, Punthakee Z, Raymer K, Salehian O, Spencer F, Walter S, Worster A, Adili A, Clase C, Cook D, Crowther M, Douketis J, Gangji A, Jackson P, Lim W, Lovrics P, Mazzadi S, Orovan W, Rudkowski J, Soth M, Tiboni M, Acedillo R, Garg A, Hildebrand A, Lam N, Macneil D, Mrkobrada M, Roshanov PS, Srinathan SK, Ramsey C, John PS, Thorlacius L, Siddiqui FS, Grocott HP, McKay A, Lee TW, Amadeo R, Funk D, McDonald H, Zacharias J, Villar JC, Cortes OL, Chaparro MS, Vasquez S, Castaneda A, Ferreira S, Coriat P, Monneret D, Goarin JP, Esteve CI, Royer C, Daas G, Chan MT, Choi GY, Gin T, Lit LC, Xavier D, Sigamani A, Faruqui A, Dhanpal R, Almeida S, Cherian J, Furrugh S, Abraham V, Afzal L, George P, Mala S, Schunemann H, Muti P, Vizza E, Wang CY, Ong GS, Mansor M, Tan AS, Vasanthan V, Hashim NH, Undok AW, Ki U, Lai HY, Ahmad WA, Razack AH, Malaga G, Valderrama-Victoria V, Loza-Herrera JD, De Los Angeles Lazo M, Rotta-Rotta A, Szczeklik W, Sokolowska B, Musial J, Gorka J, Iwaszczuk P, Kozka M, Chwala M, Raczek M, Mrowiecki T, Kaczmarek B, Biccadd B, Cassimjee H, Gopalan D, Kisten T, Mugabi A, Naidoo P, Naidoo R, Rodseth R, Skinner D, Torborg A, Paniagua P, Urrutia G, Maestre ML, Santalo M, Gonzalez R, Font A, Martinez C, Pelaez X, De Antonio M, Villamor JM, Garcia JA, Ferre MJ, Popova E, Alonso-Coello P, Garutti I, Cruz P, Fernandez C, Palencia M, Diaz S, Del Castillo T, Varela A, de Miguel A, Munoz M, Pineiro P, Cusati G, Del Barrio M, Membrillo MJ, Orozco D, Reyes F, Sapsford RJ, Barth J, Scott J, Hall A, Howell S, Lobley M, Woods J, Howard S, Fletcher J, Dewhirst N, Williams C, Rushton A, Welters I, Leuwer M, Pearse R, Ackland G, Khan A, Niebrzegowska E, Benton S, Wragg A, Archbold A, Smith A, McAlees E, Ramballi C, Macdonald N, Januszewska M, Stephens R, Reyes A, Paredes LG, Sultan P, Cain D, Whittle J, Del Arroyo AG, Sessler DI, Kurz A, Sun Z, Finnegan PS, Egan C, Honar H, Shahinyan A, Panjasawatwong K, Fu AY, Wang S, Reineks E, Nagele P, Blood J, Kalin M, Gibson D, Wildes T, Vascular events In noncardiac Surgery patIents cOhort evaluationN Writing Group oboTVeInSpceI, Appendix 1. The Vascular events In noncardiac Surgery patIents cOhort evaluatio NSIWG, Appendix 2. The Vascular events In noncardiac Surgery patIents cOhort evaluatio NOC and Vascular events In noncardiac Surgery patIents cOhort evaluatio NVSI. Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. *Anesthesiology*. 2014;120:564–78. [PubMed: 24534856]
4. Oberweis BS, Smilowitz NR, Nukala S, Rosenberg A, Xu J, Stuchin S, Iorio R, Errico T, Radford MJ and Berger JS. Relation of perioperative elevation of troponin to long-term mortality after orthopedic surgery. *Am J Cardiol*. 2015;115:1643–8. [PubMed: 25890628]
 5. Writing Committee for the VSI, Devereaux PJ, Biccadd BM, Sigamani A, Xavier D, Chan MTV, Srinathan SK, Walsh M, Abraham V, Pearse R, Wang CY, Sessler DI, Kurz A, Szczeklik W, Berwanger O, Villar JC, Malaga G, Garg AX, Chow CK, Ackland G, Patel A, Borges FK, Belley-Cote EP, Duceppe E, Spence J, Tandon V, Williams C, Sapsford RJ, Polanczyk CA, Tiboni M, Alonso-Coello P, Faruqui A, Heels-Ansdell D, Lamy A, Whitlock R, LeManach Y, Roshanov PS, McGillion M, Kavsak P, McQueen MJ, Thabane L, Rodseth RN, Buse GAL, Bhandari M, Garutti I, Jacka MJ, Schunemann HJ, Cortes OL, Coriat P, Dvirnik N, Botto F, Pettit S, Jaffe AS and Guyatt GH. Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery. *JAMA*. 2017;317:1642–1651. [PubMed: 28444280]
 6. van Waes JA, Nathoe HM, de Graaff JC, Kemperman H, de Borst GJ, Peelen LM, van Klei WA and Cardiac Health After Surgery I. Myocardial injury after noncardiac surgery and its association with short-term mortality. *Circulation*. 2013;127:2264–71. [PubMed: 23667270]
 7. Maile MD, Jewell ES and Engoren MC. Timing of Preoperative Troponin Elevations and Postoperative Mortality After Noncardiac Surgery. *Anesthesia and analgesia*. 2016;123:135–40. [PubMed: 27314692]
 8. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD and Executive Group on behalf of the Joint European Society of Cardiology/American College of Cardiology/American Heart Association/World Heart Federation Task Force for the Universal Definition of Myocardial I. Fourth Universal Definition of Myocardial Infarction (2018). *J Am Coll Cardiol*. 2018.
 9. Smilowitz NR, Gupta N, Ramakrishna H, Guo Y, Berger JS and Bangalore S. Perioperative Major Adverse Cardiovascular and Cerebrovascular Events Associated With Noncardiac Surgery. *JAMA Cardiol*. 2017;2:181–187. [PubMed: 28030663]

10. Smilowitz NR, Gupta N, Guo Y, Berger JS and Bangalore S. Perioperative acute myocardial infarction associated with non-cardiac surgery. *Eur Heart J*. 2017 (E-pub ahead of print July 1st, 2017).
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 and Investigators P. Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. *Ann Intern Med*. 2011;154:523–8. [PubMed: 21502650]
12. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, Davila-Roman VG, Gerhard-Herman MD, Holly TA, Kane GC, Marine JE, Nelson MT, Spencer CC, Thompson A, Ting HH, Uretsky BF and Wijeyesundera DN. 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137. [PubMed: 25091544]
13. Smith SC, Jr., Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, Gibbons RJ, Grundy SM, Hiratzka LF, Jones DW, Lloyd-Jones DM, Minissian M, Mosca L, Peterson ED, Sacco RL, Spertus J, Stein JH and Taubert KA. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation endorsed by the World Heart Federation and the Preventive Cardiovascular Nurses Association. *J Am Coll Cardiol*. 2011;58:2432–46. [PubMed: 22055990]
14. Wright RS, Anderson JL, Adams CD, Bridges CR, Casey DE, Jr., Ettinger SM, Fesmire FM, Ganiats TG, Jneid H, Lincoff AM, Peterson ED, Philippides GJ, Theroux P, Wenger NK, Zidar JP, Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE, Jr., Chavey WE, 2nd, Fesmire FM, Hochman JS, Levin TN, Lincoff AM, Peterson ED, Theroux P, Wenger NK and Wright RS. 2011 ACCF/AHA focused update of the Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction (updating the 2007 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2011;57:1920–59. [PubMed: 21450428]
15. Kilic A, Sultan IS, Arnaoutakis GJ, Black JH, 3rd and Reifsnnyder T. Significant Differences between Vascular and Nonvascular Surgeons in the Perioperative Management of Antiplatelet Therapies in Patients with Coronary Stents. *Annals of vascular surgery*. 2015;29:526–533 e2. [PubMed: 25476748]
16. Focquier A, Rodseth R, Aissaoui M, Ibanes C, Goarin JP, Landais P, Coriat P and Le Manach Y. The long-term impact of early cardiovascular therapy intensification for postoperative troponin elevation after major vascular surgery. *Anesthesia and analgesia*. 2014;119:1053–63. [PubMed: 24937347]
17. Landesberg G, Beattie WS, Mosseri M, Jaffe AS and Alpert JS. Perioperative myocardial infarction. *Circulation*. 2009;119:2936–44. [PubMed: 19506125]
18. Reed GW, Horr S, Young L, Clevenger J, Malik U, Ellis SG, Lincoff AM, Nissen SE and Menon V. Associations Between Cardiac Troponin, Mechanism of Myocardial Injury, and Long-Term Mortality After Noncardiac Vascular Surgery. *Journal of the American Heart Association*. 2017;6.
19. van Waes JA, Grobbee RB, Nathoe HM, Kemperman H, de Borst GJ, Peelen LM, van Klei WA and Cardiac Health After Surgery I. One-Year Mortality, Causes of Death, and Cardiac Interventions in Patients with Postoperative Myocardial Injury. *Anesthesia and analgesia*. 2016;123:29–37. [PubMed: 27111647]
20. Devereaux PJ, Mrkobrada M, Sessler DI, Leslie K, Alonso-Coello P, Kurz A, Villar JC, Sigamani A, Bickard BM, Meyhoff CS, Parlow JL, Guyatt G, Robinson A, Garg AX, Rodseth RN, Botto F, Lurati Buse G, Xavier D, Chan MT, Tiboni M, Cook D, Kumar PA, Forget P, Malaga G, Fleischmann E, Amir M, Eikelboom J, Mizera R, Torres D, Wang CY, VanHelder T, Paniagua P, Berwanger O, Srinathan S, Graham M, Pasin L, Le Manach Y, Gao P, Pogue J, Whitlock R, Lamy A, Kearon C, Baigent C, Chow C, Pettit S, Chrolavicius S, Yusuf S and Investigators P-. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med*. 2014;370:1494–503. [PubMed: 24679062]

21. Smilowitz NR, Oberweis BS, Nukala S, Rosenberg A, Stuchin S, Iorio R, Errico T, Radford MJ and Berger JS. Perioperative antiplatelet therapy and cardiovascular outcomes in patients undergoing joint and spine surgery. *Journal of clinical anesthesia*. 2016;35:163–169. [PubMed: 27871515]
22. Mills EJ, Rachlis B, Wu P, Devereaux PJ, Arora P and Perri D. Primary prevention of cardiovascular mortality and events with statin treatments: a network meta-analysis involving more than 65,000 patients. *J Am Coll Cardiol*. 2008;52:1769–81. [PubMed: 19022156]
23. Lindenauer PK, Pekow P, Wang K, Gutierrez B and Benjamin EM. Lipid-lowering therapy and in-hospital mortality following major noncardiac surgery. *JAMA*. 2004;291:2092–9. [PubMed: 15126437]
24. Durazzo AE, Machado FS, Ikeoka DT, De Bernoche C, Monachini MC, Puech-Leao P and Caramelli B. Reduction in cardiovascular events after vascular surgery with atorvastatin: a randomized trial. *J Vasc Surg*. 2004;39:967–75; discussion 975–6. [PubMed: 15111846]
25. Xia J, Qu Y, Yin C and Xu D. Preoperative rosuvastatin protects patients with coronary artery disease undergoing noncardiac surgery. *Cardiology*. 2015;131:30–7. [PubMed: 25832289]
26. Suckow BD, Kraiss LW, Schanzer A, Stone DH, Kalish J, DeMartino RR, Cronenwett JL, Goodney PP and Vascular Study Group of New E. Statin therapy after infrainguinal bypass surgery for critical limb ischemia is associated with improved 5-year survival. *J Vasc Surg*. 2015;61:126–33. [PubMed: 25037607]
27. Berwanger O, Le Manach Y, Suzumura EA, Biccard B, Srinathan SK, Szczeklik W, Santo JA, Santucci E, Cavalcanti AB, Archbold RA, Devereaux PJ and Investigators V. Association between pre-operative statin use and major cardiovascular complications among patients undergoing non-cardiac surgery: the VISION study. *Eur Heart J*. 2016;37:177–85. [PubMed: 26330424]
28. Sanders RD, Nicholson A, Lewis SR, Smith AF and Alderson P. Perioperative statin therapy for improving outcomes during and after noncardiac vascular surgery. *Cochrane Database Syst Rev*. 2013:CD009971.
29. Kristensen SD, Knuuti J, Saraste A, Anker S, Botker HE, De Hert S, Ford I, Gonzalez Juanatey JR, Gorenek B, Heyndrickx GR, Hoeft A, Huber K, Iung B, Kjeldsen KP, Longrois D, Luescher TF, Pierard L, Pocock S, Price S, Roffi M, Sirnes PA, Uva MS, Voudris V, Funck-Brentano C and Authors/Task Force M. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *European journal of anaesthesiology*. 2014;31:517–73. [PubMed: 25127426]
30. 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, Hoeft A, Yusuf S and Investigators M. Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomised, placebo-controlled trial. *Lancet*. 2018;391:2325–2334. [PubMed: 29900874]

Highlights

Myocardial injury after non-cardiac surgery (MINS) is a common complication.

Patients with MINS are older and more likely to have cardiovascular risk factors.

Among patients with MINS, only 47.5% were discharged on aspirin and a statin.

Few patients with MINS are prescribed medical therapy for cardiovascular disease

Table 1:

Baseline characteristics

Variable	Total cohort (n=2798)	No MINS (n=2562)	MINS (n=236)	p-value
Age, mean (SD) (year)	67.4 ± 10.2	67.0 ± 10.0	71.9 ± 10.9	<0.001
Female Sex	1482 (53.0)	1352 (52.8)	130 (55.1)	0.54
Race				0.004
White	1940 (69.3)	1754 (68.5)	186 (78.8)	-
African American	390 (13.9)	369 (14.4)	21 (8.9)	-
Other	468 (16.7)	439 (17.1)	29 (12.3)	-
Ethnicity				0.09
Hispanic	205 (7.9)	195 (7.6)	10 (3.7)	-
Non-Hispanic	2463 (88.0)	2245 (87.0)	218 (93.1)	-
Unknown	130 (4.0)	122 (4.8)	8 (3.2)	-
Body Mass Index, median (IQR) (kg/m ²)	30.0 (26.4–34.5)	30.1 (26.5–34.6)	28.6 (25.2–32.9)	0.001
Hypertension	1635 (58.4)	1485 (58.0)	150 (63.6)	0.10
Hyperlipidemia	1064 (38.0)	976 (38.1)	88 (37.3)	0.81
Diabetes Mellitus	626 (22.4)	564 (26.3)	62 (26.3)	0.13
Chronic Kidney Disease	169 (6.0)	135 (5.3)	34 (14.4)	<0.001
Coronary Artery Disease	941 (33.6)	833 (32.5)	108 (45.8)	<0.001
Prior PCI	389 (13.9)	360 (14.1)	29 (12.3)	0.52
Prior CABG	59 (2.1)	50 (2.0)	9 (3.8)	0.10
Prior Myocardial Infarction	81 (2.9)	62 (2.4)	19 (8.1)	<0.001
Prior Stroke	127 (4.5)	106 (4.1)	21 (8.9)	0.001
Heart Failure	188 (6.7)	141 (5.5)	47 (19.9)	<0.001
Cancer	265 (9.5)	244 (9.5)	21 (8.9)	0.84
COPD	187 (6.7)	171 (6.7)	16 (6.8)	1.00
Peripheral Artery Disease	115 (4.1)	103 (4.0)	12 (5.1)	0.54

COPD: chronic obstructive pulmonary disease; SD: standard deviation.

Table 2:

Multivariable predictors of myocardial injury after non-cardiac surgery.

Variable	Adjusted OR (95% CI)
Age	1.04 (1.02 – 1.05)
Female Sex	1.17 (0.88 – 1.57)
Race	
White	<i>Reference</i>
Black	0.57 (0.35 – 0.93)
Other/Unknown	0.65 (0.43 – 1)
Hypertension	1.07 (0.78 – 1.46)
Hyperlipidemia	0.72 (0.52 – 0.99)
Diabetes Mellitus	1.19 (0.85 – 1.66)
Chronic Kidney Disease	2.14 (1.36 – 3.35)
Prior Myocardial Infarction	2.39 (1.32 – 4.33)
Coronary artery disease	1.74 (1.23 – 2.48)
Prior PCI	0.5 (0.31 – 0.81)
Prior CABG	0.93 (0.42 – 2.07)
Prior Stroke	1.24 (0.49 – 3.16)
Heart failure	2.82 (1.9 – 4.19)
Cancer	0.73 (0.45 – 1.18)
COPD	0.74 (0.42 – 1.3)
Peripheral Artery Disease	0.72 (0.37 – 1.4)

CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; OR: odds ratio; PAD: peripheral artery disease; PCI: percutaneous coronary intervention.

Table 3:

Preoperative and postoperative medical therapy in patients with and without MINS

	Total Cohort		No MINS		MINS		P1	P2	P3	P4
	(n = 2798)		(n = 2562)		(n = 236)					
	Pre-Operative	Discharge	Pre-Operative	Discharge	Pre-Operative	Discharge				
Medication										
Aspirin	1206 (43.1)	1733 (61.9)	1104 (43.1)	1582 (61.7)	102 (43.2)	151 (64.0)	0.9 9	0.5 4	<0.0 01	<0.0 01
P2Y ₁₂ Inhibitor	257 (9.2)	260 (9.3)	234 (9.1)	232 (9.1)	23 (9.7)	28 (11.9)	0.8 5	0.1 9	1.0	0.55
Oral Anticoagulation	231 (8.3)	501 (17.9)	213 (8.3)	436 (17.0)	18 (7.6)	65 (27.5)	0.8 1	<0.00 1	<0.0 01	<0.0 01
Statin	1575 (56.3)	1617 (57.8)	1442 (56.3)	1463 (57.1)	133 (56.4)	154 (65.3)	0.9 9	0.0 18	0.57	0.06
Beta Blockers	1234 (44.1)	1341 (47.9)	1107 (43.2)	1194 (46.6)	127 (53.8)	147 (62.3)	0.0 02	<0.00 1	0.01 6	0.08
ACEi/A RBs	1304 (46.6)	1283 (45.9)	1202 (46.9)	1179 (46.0)	102 (43.2)	104 (44.1)	0.3 1	0.6 1	0.54	0.92
Combinations										
No Aspirin or Statin	908 (32.5)	598 (21.4)	831 (32.4)	555 (21.7)	77 (32.6)	43 (18.2)	0.9 9	0.2 5	<0.0 01	<0.0 01
Aspirin only	315 (11.3)	583 (20.8)	289 (11.3)	544 (21.2)	26 (11.0)	39 (16.5)	0.9 9	0.1 1	<0.0 01	0.11
Statin only	684 (24.4)	467 (16.7)	627 (24.5)	425 (16.6)	57 (24.2)	42 (17.8)	0.9 8	0.7 0	<0.0 01	0.11
Aspirin + Statin	891 (31.8)	1150 (41.1)	815 (31.8)	1038 (40.5)	76 (32.2)	112 (47.5)	0.9 6	0.0 45	<0.0 01	<0.0 01
DAPT	206 (7.4)	229 (8.2)	187 (7.3)	204 (8.0)	19 (8.1)	25 (10.6)	0.7 7	0.2 0	0.40	0.43
DAPT + Statin	181 (6.5)	208 (7.4)	167 (6.5)	186 (7.3)	14 (5.9)	22 (9.3)	0.8 3	0.3 1	0.32	0.23

P1: Comparison of pre-operative medical therapy in patients with MINS versus without MINS

P2: Comparison of post-operative (discharge) medical therapy in patients with MINS versus without MINS

P3: Comparison of pre-operative versus post-operative (discharge) medical therapy in patients without MINS

P4: Comparison of pre-operative versus post-operative (discharge) medical therapy in patients with MINS

ACEi: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; DAPT: dual anti-platelet therapy (aspirin + P2Y₁₂ inhibitor).

Table 4:

Proportion of patients with and without MINS receiving guideline directed medical therapy for atherosclerotic disease at discharge among those not previously prescribed therapy.

	All Patients	No MINS	MINS	p-value
Change in Medical Therapy				
Aspirin added (%)	37.1	36.6	43.3	0.15
P2Y12 Inhibitor added (%)	1.9	1.8	3.3	0.21
Oral Anticoagulation added (%)	11.0	9.9	22.5	<0.001
Statin added (%)	4.4	2.3	23.3	<0.001
Beta-Blocker added (%)	8.6	7.5	22.9	<0.001
Change in Medication Combinations				
Aspirin + Statin added (%)	15.7	14.7	26.3	<0.001
DAPT only added (%)	2.2	2.1	3.2	0.38
DAPT + Statin added (%)	2.2	2.0	4.1	0.08

ACEi: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; DAPT: dual anti-platelet therapy (aspirin + P2Y12 inhibitor).