

SUPPLEMENTAL MATERIAL

Supplemental digital content 1, Appendix 1. Ischemic symptoms and electrocardiography findings

1. Ischemic symptoms included any of the following: chest discomfort, arm discomfort, neck discomfort, jaw discomfort, shortness of breath, or pulmonary edema. These ischemic symptoms had to have occurred within 24 hours of an elevated troponin measurement.

2. Ischemic electrocardiography findings included any of the following:

- i. development of pathologic Q waves in any two contiguous leads that were ≥ 30 milliseconds;
- ii. development of left bundle branch block (LBBB); or
- iii. development of ST segment elevation (≥ 2 mm in leads V_1 , V_2 , or V_3 OR ≥ 1 mm in the other leads), ST segment depression (≥ 1 mm), or symmetric inversion of T waves ≥ 1 mm in at least two contiguous leads.

ST segment elevation, ST segment depression, and LBBB had to have occurred within 3 days of an elevated troponin measurement, and symmetric T wave inversion had to have occurred within 5 days of an elevated troponin measurement. Adjudicators evaluated preoperative electrocardiograms to ensure the ischemic electrocardiographic findings developed during or after surgery.

Supplemental digital content 1, Appendix 2. Definitions related to cause of death

1. Vascular death was defined as any death with a vascular cause and included those deaths following a myocardial infarction, cardiac arrest, stroke, cardiac revascularization procedure (i.e., percutaneous coronary intervention [PCI] or coronary artery bypass graft [CABG] surgery), pulmonary embolus, hemorrhage, or deaths due to an unknown cause.
2. Non-vascular death was defined as any death due to a clearly documented non-vascular cause (e.g. trauma, infection, malignancy).

Supplemental digital content 1, Appendix 3. Perioperative outcome definitions

1. Mortality – All cause mortality.
2. Stroke – Stroke was defined as a new focal neurological deficit thought to be vascular in origin with signs and symptoms lasting more than 24 hours.
3. Leg or arm deep venous thrombosis – The diagnosis of deep venous thrombosis required any one of the following:
 - i. a persistent intraluminal filling defect on contrast venography;
 - ii. non-compressibility of one or more venous segments on B mode compression ultrasonography; or
 - iii. a clearly defined intraluminal filling defect on contrast enhanced computed tomography (CT).
4. Pulmonary embolus – The diagnosis of pulmonary embolus required any one of the following:
 - i. a high probability ventilation/perfusion lung scan;
 - ii. an intraluminal filling defect of segmental or larger artery on a helical CT scan;
 - iii. an intraluminal filling defect on pulmonary angiography; or
 - iv. a positive diagnostic test for deep venous thrombosis (e.g., positive compression ultrasound) and one of the following: non-diagnostic (i.e., low or intermediate probability) ventilation/perfusion lung scan, or a non-diagnostic (i.e., subsegmental defects or technically inadequate study) helical CT scan.
5. Infection – Infection was defined as a pathologic process caused by the invasion of normally sterile tissue or fluid or body cavity by pathogenic or potentially pathogenic organisms.
6. Pneumonia – The diagnosis of pneumonia required any one of the following:
 - i. rales or dullness to percussion on physical examinations of chest AND any of the following:
 - A. new onset of purulent sputum or change in character of sputum,

- B. isolation of organism from blood culture, or
 - C. isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy; OR
- ii. chest radiography showing new or progressive infiltrate, consolidation, cavitation, or pleural effusion AND any of the following:

- A. new onset of purulent sputum or change in character of sputum,
- B. isolation of organism from blood culture,
- C. isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy,
- D. isolation of virus or detection of viral antigen in respiratory secretions,
- E. diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen, or
- F. histopathologic evidence of pneumonia.

7. Sepsis – Sepsis is a clinical syndrome defined by the presence of both infection and a systemic inflammatory response. Systemic inflammatory response requires 2 or more of the following factors: core temperature $>38\text{ }^{\circ}\text{C}$ or $<36\text{ }^{\circ}\text{C}$; heart rate >90 beats per minute; respiratory rate >20 breaths per minute; white blood cell count $>12 \times 10^9/\text{L}$ or $<4 \times 10^9/\text{L}$.

Supplemental digital content 1, Appendix 4. Preoperative patient characteristics included in the Myocardial Injury after Noncardiac Surgery (MINS) diagnostic criteria models

1. Age – Patient age in years was recorded and subsequently evaluated as: i. 65-74 years of age versus 45-64 years of age; and ii. ≥ 75 years of age versus 45-64 years of age.

2. Recent high-risk coronary artery disease – A physician diagnosis ≤ 6 months prior to noncardiac surgery of: a myocardial infarction, acute coronary syndrome, Canadian Cardiovascular Society Class (CCSC) III angina, or CCSC IV angina

CCSC III angina - angina occurring with level walking of 1-2 blocks or climbing ≤ 1 flight of stairs at a normal pace

CCSC IV angina - inability to carry on any physical activity without the development of angina.

3. History of stroke – A physician diagnosis of a current or prior stroke, or CT or magnetic resonance evidence of a stroke.

4. History of peripheral vascular disease – A physician diagnosis of a current or prior history of: intermittent claudication, vascular surgery for atherosclerotic disease, an ankle/arm systolic blood pressure ratio ≤ 0.90 in either leg at rest, or angiographic or doppler study demonstrating $\geq 70\%$ stenosis in a noncardiac artery.

5. Chronic obstructive pulmonary disease (COPD) – A physician current or prior diagnosis of chronic bronchitis, emphysema, or COPD, or a patient provided a history of daily production of sputum for at least 3 months in 2 consecutive years.

6. Active cancer – A patient was designated as having active cancer if they fulfilled any of the following criteria: i. undergoing surgery for cancer; ii. known metastatic disease; or iii. patient had received active treatment for their cancer (e.g., chemotherapy, radiation, or surgery) within

the 6 months prior to their surgery, but this did not apply to patients with non-melanoma skin cancers or surgery for a biopsy.

7. Urgent/Emergency surgery – Surgery that occurred within 72 hours after a patient developed an acute surgical condition.

8. Major general surgery – A patient undergoing one or more of the following general surgeries: complex visceral resection, partial or total colectomy or stomach surgery, other intra-abdominal surgery, or major head and neck resection for non-thyroid tumor.

9. Major neurosurgery – A patient undergoing one or more of the following neurosurgeries: craniotomy or major spine surgery (i.e., surgery involving multiple levels of the spine).

Supplemental digital content 1, Appendix 5. Preoperative patient characteristics and types of surgery included in the Myocardial Injury after Noncardiac Surgery (MINS) prediction model

1. Age – Patient age in years was recorded and subsequently evaluated as: i. 65-74 years of age versus 45-64 years of age; and ii. ≥ 75 years of age versus 45-64 years of age.
2. Sex – Male or female.
3. Diabetes – Patient stated that they have a diagnosis of diabetes or a physician has previously recorded that the patient has diabetes. This included gestational diabetes at the time of noncardiac surgery, but not past gestational diabetes that had resolved.
4. Hypertension – A physician diagnosis of hypertension.
5. History of congestive heart failure – A physician diagnosis of a current or prior episode of congestive heart failure or prior radiographic evidence of vascular redistribution, interstitial pulmonary edema, or frank alveolar pulmonary edema.
6. History of coronary artery disease – A current or prior history of any one of the following: i. angina; ii. myocardial infarction or acute coronary syndrome; iii. a segmental cardiac wall motion abnormality on echocardiography or a segmental fixed defect on radionuclide imaging; iv. a positive radionuclide exercise, echocardiographic exercise, or pharmacological cardiovascular stress test demonstrating cardiac ischemia; v. coronary angiographic or CT coronary angiographic evidence of atherosclerotic stenosis $\geq 50\%$ of the diameter of any coronary artery; vi. electrocardiogram with pathological Q waves in two contiguous leads.
7. Recent high-risk coronary artery disease – A physician diagnosis ≤ 6 months prior to noncardiac surgery of: a myocardial infarction, acute coronary syndrome, CCSC III angina, or CCSC IV angina

CCSC III angina - angina occurring with level walking of 1-2 blocks or climbing ≤ 1 flight of stairs at a normal pace

CCSC IV angina - inability to carry on any physical activity without the development of angina.

8. History of cardiac arrest – A patient with a prior history of a cardiac arrest.

9. History of peripheral vascular disease – A physician diagnosis of a current or prior history of: intermittent claudication, vascular surgery for atherosclerotic disease, an ankle/arm systolic blood pressure ratio ≤ 0.90 in either leg at rest, or angiographic or doppler study demonstrating $\geq 70\%$ stenosis in a noncardiac artery.

10. History of stroke – A physician diagnosis of a current or prior stroke, or CT or magnetic resonance evidence of a stroke.

11. Chronic obstructive pulmonary disease (COPD) – A physician current or prior diagnosis of chronic bronchitis, emphysema, or COPD, or a patient provided a history of daily production of sputum for at least 3 months in 2 consecutive years.

12. Current atrial fibrillation – A patient with a current history of atrial fibrillation

13. Preoperative estimated glomerular filtration rate (eGFR) rate as categorical variables (i.e., eGFR < 30 ml/minute/1.73m² or receiving dialysis; eGFR of 30 to 44 ml/minute/1.73m²; eGFR of 45 to 59 ml/minute/1.73m²; and the reference group eGFR of ≥ 60 ml/minute/1.73m²).

14. Active cancer – A patient was designated as having active cancer if they fulfilled any of the following criteria: i. undergoing surgery for cancer; ii. known metastatic disease; or iii. patient had received active treatment for their cancer (e.g., chemotherapy, radiation, or surgery) within the 6 months prior to their surgery, but this did not apply to patients with non-melanoma skin cancers or surgery for a biopsy.

15. Urgent/Emergency surgery – Emergency surgery was surgery that occurred <24 hours after a patient developed an acute surgical condition, and urgent surgery was surgery that occurred 24-72 hours after a patient developed an acute surgical condition.

16. Major vascular surgery – A patient undergoing one or more of the following vascular surgeries: thoracic aorta reconstructive vascular surgery, aorto-iliac reconstructive vascular surgery, peripheral vascular reconstruction without aortic cross-clamping, extracranial cerebrovascular surgery, or endovascular abdominal aortic aneurysm repair.

17. Major general surgery – A patient undergoing one or more of the following general surgeries: complex visceral resection, partial or total colectomy or stomach surgery, other intra-abdominal surgery, or major head and neck resection for non-thyroid tumor.

18. Major thoracic surgery – A patient undergoing one or more of the following thoracic surgeries: pneumonectomy, lobectomy, wedge resection of lung, resection of mediastinal tumor, or major chest wall resection.

19. Major urology or gynecology surgery – A patient undergoing one or more of the following major urology or gynecology surgeries: nephrectomy, ureterectomy, bladder resection, retroperitoneal tumor resection, exenteration, cytoreduction surgery, hysterectomy, radical prostatectomy, or transurethral prostatectomy.

20. Major orthopedic surgery – A patient undergoing one or more of the following orthopedic surgeries: major hip or pelvis surgery, internal fixation of femur, knee arthroplasty, above knee amputations, or lower leg amputation (amputation below knee but above foot).

21. Major neurosurgery – A patient undergoing one or more of the following neurosurgeries: craniotomy or major spine surgery (i.e., surgery involving multiple levels of the spine).

22. Low-risk surgeries – A patient undergoing one or more of the following surgeries:
parathyroid, thyroid, breast, hernia, local anorectal procedure, oophorectomy, salpingectomy,
endometrial ablation, peripheral nerve surgery, ophthalmology, ears/nose/throat surgery,
vertebral disc surgery, hand surgery, cosmetic surgery, arterio-venous access surgery for dialysis,
or any other surgery not mentioned above.

Supplemental digital content 1, Appendix 6. Perioperative cardiovascular outcome definitions

1. Congestive heart failure – The definition of congestive heart failure required at least one of the following clinical signs (i.e. elevated jugular venous pressure, respiratory rales/crackles, crepitations, or presence of S3) and at least one of the following radiographic findings (i.e., vascular redistribution, interstitial pulmonary edema, or frank alveolar pulmonary edema).
2. Nonfatal cardiac arrest – Nonfatal cardiac arrest was defined as successful resuscitation from either documented or presumed ventricular fibrillation, sustained ventricular tachycardia, asystole, or pulseless electrical activity requiring cardiopulmonary resuscitation, pharmacological therapy, or cardiac defibrillation.
3. Stroke – Stroke was defined as a new focal neurological deficit thought to be vascular in origin with signs and symptoms lasting more than 24 hours.
4. Mortality – All cause mortality.