

Clinical Research

Association Between Electrocardiographic Changes and Myocardial Injury or Death After Cardiac Surgery

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ABSTRACT

Background: The relationship between myocardial injury after cardiac surgery (MICS), ischemia on electrocardiogram (ECG), and mortality is uncertain. In this study we aimed to determine whether potential ischemic ECG changes after cardiac surgery are associated with 30-day mortality.

Methods: In a cohort of adults who underwent cardiac surgery, experts interpreted ECGs preoperatively; on postoperative days 0, 1, 2, and 3; and on the last day before discharge (59,539 total ECGs reviewed) for new potential ischemic ECG changes.

Results: Among 12,594 patients, 9097 (72.2%) had potential ischemic ECG changes; 259 (2.1%) died within 30 days after surgery. Among patients with troponin elevation meeting MICS criteria, in models adjusting for EuroSCORE II, the hazard ratio (HR) for 30-day mortality was 0.57 (95% confidence interval [CI] 0.35–0.94, $P = 0.03$) for new Q waves, 2.17 (95% CI 1.14–4.13, $P = 0.02$) for ST depression ≥ 2 mm, and 0.58 (95% CI 0.39–0.87, $P = 0.007$) for T-wave inversion 1–1.9 mm. ST elevation was not significantly associated with 30-day mortality. The only ECG change for which coronary artery bypass grafting (CABG) was an effect modifier was new left bundle branch block (LBBB), with an HR of 2.78 (95% CI 1.69–4.60, $P = 0.0001$) with CABG and an HR of 1.10 (95% CI 0.54–2.21, $P = 0.27$) without CABG (P value for interaction = 0.03).

Conclusions: After cardiac surgery, potential ischemic ECG changes are common and have divergent associations with mortality. ST depression was associated with a higher risk of death, whereas new Q waves and T-wave inversions were associated with a lower risk of death. A new LBBB was associated with a higher risk of death only among patients who underwent CABG. Potential ischemic ECG changes are common after cardiac surgery and lack specificity for the diagnosis of myocardial infarction.

RÉSUMÉ

Contexte: La relation entre la lésion myocardique après chirurgie cardiaque (MICS), l'ischémie à l'électrocardiogramme (ECG) et la mortalité demeure incertaine. Nous avons cherché à déterminer si la présence de changements potentiellement ischémiques à l'ECG après une chirurgie cardiaque était associée à la mortalité à 30 jours.

Méthodologie: Dans une cohorte d'adultes ayant subi une chirurgie cardiaque, des experts ont interprété les ECG préopératoires, ceux des jours postopératoires 0-1-2-3, ainsi que le dernier ECG avant le congé (total = 59 539), afin d'identifier de nouveaux changements potentiellement ischémiques.

Résultats: Parmi 12 594 patients, 9 097 (72,2 %) présentaient des changements potentiellement ischémiques à l'ECG; 259 (2,1 %) sont décédés dans les 30 jours suivant la chirurgie. Chez les patients présentant une élévation de troponine répondant aux critères de MICS, dans des modèles ajustés pour l'EuroSCORE II, le rapport de risque (HR) pour la mortalité à 30 jours était de 0,57 (IC95 % 0,35–0,94; $p=0,03$) pour l'apparition de nouvelles ondes Q; de 2,17 (IC95 % 1,14–4,13; $p=0,02$) pour une dépression du segment ST ≥ 2 mm; et de 0,58 (IC95 % 0,39–0,87; $p=0,007$) pour une inversion de l'onde T de 1–1,9 mm. L'élévation du segment ST n'était pas significativement associée à la mortalité à 30 jours. La seule modification ECG pour laquelle le pontage aortocoronarien (PAC) modifiait l'effet était le nouveau bloc de branche gauche (BBG) : HR 2,78 (IC95 % 1,69–4,60; $p=0,0001$) avec PAC et HR 1,10 (IC95 % 0,54–2,21; $p=0,27$) sans PAC (interaction $p=0,03$).

Conclusions: Après une chirurgie cardiaque, les changements potentiellement ischémiques à l'ECG sont fréquents et présentent des associations divergentes avec la mortalité. La dépression du segment ST était associée à un risque accru de décès, tandis que l'apparition de nouvelles ondes Q et les inversions de l'onde T étaient associées à un risque moindre. Un nouveau BBG était associé à un risque plus élevé de décès uniquement chez les patients ayant subi un PAC. Les changements potentiellement ischémiques à l'ECG sont fréquents après une chirurgie cardiaque et manquent de spécificité pour le diagnostic d'infarctus du myocarde.

Approximately 2% of adults undergoing cardiac surgery die within 30 days, and myocardial ischemia is thought to be a common cause.^{1,2} Many cardiac surgery studies addressing perioperative cardiac complications have focused on myocardial infarction (MI).^{3–5} Several consensus statements have developed diagnostic criteria for MI ≤ 48 hours after coronary artery bypass (CABG) surgery.^{6–8} These diagnostic criteria require an elevated troponin and an additional criterion, such as a new ischemic electrocardiography (ECG) change (eg, pathologic Q waves and left bundle branch block [LBBB]; see [Supplemental Table S1](#)). Studies demonstrated that many patients sustain myocardial injury in the perioperative period, which does not satisfy the currently proposed

diagnostic criteria for MI.⁹ These events nevertheless presage a poor prognosis. Patient important outcomes need to be prognostically relevant and diagnostic criteria need to reflect this requirement.¹⁰

As part of the Vascular events In Surgery patients cOhort evaluationN (VISION) Cardiac Surgery Study, we previously reported that high-sensitivity troponin I (hsTnI) thresholds were associated with an increased risk of 30-day mortality after cardiac surgery, which we termed myocardial injury after cardiac surgery (MICS).¹ These analyses did not establish whether the poor prognosis associated with MICS was a reflection of the poor prognosis associated with MI (ie, the patients who had troponin elevations above our established thresholds associated with an increased risk of death also had a new ischemic ECG change, thus fulfilling the definition of MI). As part of the VISION Cardiac Surgery Study, we undertook a large ECG substudy to determine whether: 1) new Q waves or other new potential ischemic ECG findings after cardiac surgery were independently associated with mortality; and 2) whether postoperative hsTnI elevations require ischemic ECG changes to be associated with 30-day mortality (ie, if the diagnostic criteria for MICS require the presence of ischemic ECG changes).

Keywords: cardiac surgery; electrocardiogram; myocardial infarction; myocardial injury

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See page 2609 for disclosure information.

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Methods

Study organization and funding

The VISION Cardiac Surgery Study was a prospective cohort study of patients undergoing cardiac surgery. The coordinating centre, the Population Health Research Institute, managed the database, validated the data, and performed the analyses. The investigators obtained ethics approval from all participating centres before starting enrolment. Some centres used deferred or waived consent models to facilitate the recruitment of patients undergoing urgent or emergent surgery. The investigators acquired funding from 23 sources, mostly as peer-reviewed grants. These funders had no role in the design, conduct, or analyses of the study.

Patients

Study personnel enrolled a representative sample of patients undergoing cardiac surgery from 24 hospitals in 12 countries. We described the cohort study procedures and reported the study protocol in a previous article.¹

In brief, patients who were ≥ 18 years old and underwent cardiac surgery were eligible. We excluded patients who underwent isolated pericardial window, pericardiectomy, permanent pacemaker, or defibrillator implantation. Patients could only be enrolled once in the study. The analyses for this substudy included patients enrolled in the VISION Cardiac Surgery Study, who had at least 1 hsTnI measurement during the first 3 days after surgery and 1 ECG after surgery. We excluded patients who: 1) had a preoperative MI on the same day or the day before their cardiac surgery; 2) had a preoperative hsTnI ≥ 300 ng/L within 12 hours before surgery; 3) underwent salvage cardiac surgery (ie, cardiopulmonary resuscitation on the way to the operating room or just before anaesthesia induction), cardiac transplant, isolated aorta surgery, or isolated insertion of a ventricular assist device; 4) had no vital status data after enrollment; or 5) had ventricular pacing on all postoperative ECGs.

Procedures

After obtaining written informed consent from eligible patients or their family members, research personnel interviewed and examined patients and reviewed their charts to obtain information on patients' characteristics that are potential predictors of mortality. Research personnel followed patients throughout their hospital stay and contacted patients by phone at 30 days after surgery.

Patients had blood samples taken to measure hsTnI using the ARCHITECT STAT (Abbott Laboratories, N Chicago, IL) assay within 4 hours before surgery. Postoperative hsTnI measurements were done 3–12 hours after surgery and on postoperative days 1, 2, and 3. ECGs obtained in routine care were obtained both preoperatively (closest to the time of surgery) and postoperatively to the time of hospital discharge. Patients, clinical care teams, and research teams were blinded to the hsTnI results.

The primary outcome was all-cause mortality during the 30 days after surgery.

ECG adjudication

An event adjudication committee was responsible for the blinded evaluation of ECGs for all patients in the VISION Cardiac Surgery Study. The committee members were chosen based on clinical expertise and all adjudicators had passed a preadjudication calibration exercise to ensure a uniform standard of ECG evaluation. The adjudicators evaluated clinically obtained ECGs at the following time-points for each patient: preoperatively; on postoperative days 0, 1, 2, 3; and at final ECG before hospital discharge. Specifically, experts reported data on standardized forms regarding the presence of new Q waves, contiguous ST-segment changes (elevation and/or depression categorized as 1–1.9 mm or ≥ 2 mm), T-wave inversions (categorized as 1–1.9 mm or ≥ 2 mm), LBBB, and ventricular pacing. We used the criteria outlined in the Fourth Universal Definition of Myocardial Infarction Consensus Document.⁷ The experts also commented on whether they thought ST elevation was related to pericarditis. In the analyses, we excluded pericarditis-related ST elevations. Adjudicators were provided with the preoperative ECG as a comparison whenever available and interpreted a patient's ECGs sequentially.

Statistical analysis

We described the cohort, assessed incidence of ECG changes, and compared patients with and without ECG changes using descriptive statistics. Proportions across the groups were compared using the Fisher exact test and continuous variables were compared using the Student *t* test or Mann-Whitney *U* test as appropriate. Among patients with a troponin at or above our established thresholds for MICS on day 1¹ (Table 1), we undertook separate Cox proportional hazards models where the dependent variable was death within 30 days after surgery. Independent variables included the **European System for Cardiac Operative Risk Evaluation II** (EuroSCORE II) score and each of the ECG changes separately. For ST elevation, we only included the ST elevations that were not thought to be related to pericarditis. We then assessed whether surgery, including any CABG, was an effect modifier in these models by adding this variable as an interaction term in the models. If patients did not complete the 30-day follow-up, we censored them at the time of their last assessment. For all regression analyses, we report hazard ratios (HRs) and 95% confidence intervals (CIs) and *P* values.

We assessed results for consistency using models with the same dependent and independent variables but including all substudy participants, irrespective of whether they had a troponin at or above our established thresholds for MICS.¹ We also undertook a model where the dependent variable was death within 30 days after surgery, and we simultaneously included all ECG changes as independent variables as well as a troponin at or above our established thresholds for MICS.

To determine whether the diagnostic criteria for MICS would require an elevated troponin plus a potential ischemic ECG change, we undertook a model limited to patients without any potential ischemic ECG changes to determine whether patients with postoperative hsTnI values at or above our established thresholds were independently associated with

Table 1. High-sensitivity troponin I thresholds

	Isolated CABG or aortic valve replacement or repair	Other cardiac surgery
High-sensitivity troponin I thresholds within 1 day after surgery associated with a HR of > 1.00 for death within 30 days of surgery	5670 ng/L (95% CI 1045-8260), 218-fold the upper reference limit	12,981 ng/L (95% CI 2673-16,591), 499-fold the upper reference limit

CABG, coronary artery bypass grafting; CI, confidence interval; HR, hazard ratio.

an increased risk of 30-day mortality. This model also included EuroSCORE II as an independent variable.

In secondary analyses, we used unadjusted and EuroSCORE II—adjusted Cox proportional hazards models to assess the association between MICS and postoperative outcomes (nonfatal cardiac arrest, new heart failure, death, stroke, redo surgery, percutaneous coronary intervention, new clinically important atrial fibrillation, and length of stay) at 30 days.

In EuroSCORE II—adjusted Cox proportional hazards models, we also explored whether the territory (eg, anterior, inferior) of potential ischemic ECG changes was associated with 30-day mortality. In similar models, we evaluated whether simultaneous ST elevation and reciprocal ST depression were associated with 30-day mortality independently of EuroSCORE II.

For all models, we assessed collinearity using the variance inflation factor, which measures the extent to which the variance of the model coefficients is inflated (because of the correlation of the variable with other predictor variables) if that variable is included in the model. We considered variables with a variance inflation factor > 10 to be collinear and, if this occurred, we planned to exclude 1 of the variables from the analysis. We performed all analyses using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Study population

At 24 sites in 12 countries, we enrolled 15,984 adults who underwent cardiac surgery in the VISION Cardiac Surgery Study between May 2013 and April 2019 ([Supplemental Fig. S1](#)). One study site did not contribute ECG data and was not included in this substudy. A total of 12,594 patients from 23 sites in 12 countries met the eligibility criteria for this substudy. The mean age of the cohort was 64.4 years, 9022 (71.6%) were male, 7902 (62.7%) underwent CABG with or without other procedures, and 4692 (37.3%) underwent other procedures without CABG. Of the patients in this substudy, 5924 (47.0%) had a troponin equal to or exceeding our established thresholds for MICS. Follow-up at 30 days was complete for 99.3%; death occurred in 259 patients (2.1%) at 30 days.

Potential ischemic ECG changes and mortality

The study-blind experts interpreted 59,539 ECGs; a preoperative ECG was available for 12,183 participants (96.7%). Based on all postoperative ECGs, 9097 (72.2%) patients had a potential ischemic ECG change (ST elevation, ST depression, T-wave inversion, Q waves, or new LBBB). The median peak postoperative troponin among patients with any

potential ischemic ECG change was 4223 (interquartile range [IQR] 1969-9613) ng/L and 3763 (IQR 1773-8196) ng/L in patients without any potential ischemic ECG change. [Table 2](#) reports the baseline and surgical characteristics of patients who did and did not have potential ischemic ECG changes.

New potential ischemic ECG changes after cardiac surgery occurred in 5689 of 7902 (72.0%) patients who underwent CABG and in 3408 of 4692 (72.6%) patients who underwent cardiac surgery without CABG. Overall, ST elevation (excluding ST elevation thought to be related to pericarditis, which occurred in 1315 patients [10.4%]) occurred in 4174 (33.1%) patients, ST depression in 3049 (24.2%), T-wave inversion in 5642 (44.8%), Q waves in 1844 (14.6%), and new LBBB in 872 (6.9%). [Table 3](#) presents the frequency of ECG changes after cardiac surgery in patients who did and did not undergo CABG and in patients with a troponin below and at or above the established threshold for MICS on day 1.

Associations between postoperative ECG changes and outcomes

[Table 4](#) presents HRs for 30-day mortality associated with the various potential ischemic ECG changes among patients with hsTnI elevation above the established thresholds for MICS, in separate models adjusting for EuroSCORE II. ST elevation 1-1.9 mm (HR 0.95, 95% CI 0.67-1.33) and ≥ 2 mm (HR 0.94, 95% CI 0.51-1.74) were not significantly associated with 30-day mortality. ST depression 1-1.9 mm demonstrated an HR of 1.25 (95% CI 0.91-1.71, $P = 0.17$) and ST depression ≥ 2 mm was associated with a significantly increased risk (HR of 2.17, 95% CI 1.14-4.13, $P = 0.02$) of 30-day mortality. T-wave inversion 1-1.9 mm was associated with a significantly reduced risk with an HR of 0.58 (95% CI 0.39-0.87, $P = 0.007$) for 30-day mortality, whereas T-wave inversion ≥ 2 mm had an HR of 0.72 (95% CI 0.50-1.03, $P = 0.07$). New Q waves were associated with a decreased risk of 30-day mortality (HR, 0.57, 95% CI 0.35-0.94, $P = 0.03$). The only ECG change for which CABG was an effect modifier was new LBBB with an HR of 2.78 (95% CI 1.69-4.60, $P = 0.0001$) with CABG and an HR of 1.10 (95% CI 0.54-2.21, $P = 0.27$) without CABG (P for interaction = 0.03) for 30-day mortality.

In models including all patients (ie, patients who did and did not have hsTnI elevation), associations were consistent in direction and magnitude of association ([Supplemental Table S2](#)). In a model adjusting simultaneously for all potential ischemic ECG changes and for EuroSCORE II, an hsTnI at or above our established thresholds remained strongly associated with 30-day mortality (HR 2.64, 95% CI 2.00-3.47, $P < 0.0001$) ([Supplemental Table S3](#)).

Table 2. Baseline and surgical characteristics of patients who did and did not have any new potential ischemic ECG change

	ECG change, N = 9097	No ECG change, N = 3497	P value
Age, years, mean (SD)	64.0 (11.8)	65.3 (11.2)	< 0.0001
Male sex (%)	6553 (72.0%)	2469 (70.6%)	0.11
Clinical history (%)			
Myocardial infarction	2823 (31.0%)	1023 (29.3%)	0.05
Myocardial infarction within 90 days of surgery	1479 (16.3%)	537 (15.4%)	0.21
CCS class 4 angina	836 (9.2%)	254 (7.3%)	0.0006
Stroke	517 (5.7%)	173 (4.9%)	0.10
Peripheral arterial disease	601 (6.6%)	256 (7.3%)	0.15
Hypertension	6157 (67.7%)	2428 (69.4%)	0.06
Heart failure	1565 (17.2%)	609 (17.4%)	0.79
NYHA class			
I	99 (1.1%)	34 (1.0%)	0.57
II	632 (6.9%)	239 (6.8%)	0.82
III	593 (6.5%)	246 (7.0%)	0.30
IV	236 (2.6%)	90 (2.6%)	0.95
Previous cardiac surgery	333 (3.7%)	156 (4.5%)	0.04
Chronic obstructive pulmonary disease	762 (8.4%)	330 (9.4%)	0.06
Tobacco use	4929 (54.2%)	1919 (54.9%)	0.50
Diabetes	2735 (30.1%)	1114 (31.9%)	0.05
Diabetes, receiving insulin	1144 (12.6%)	474 (13.6%)	0.14
EuroSCORE II, % (SD)	2.4 (3.6)	2.6 (4.1)	0.03
Poor mobility (%)	340 (3.7%)	183 (5.2%)	0.0002
Type of surgery			
Any CABG	5689 (62.5%)	2213 (63.3%)	0.44
Isolated CABG	4345 (47.8%)	1733 (49.6%)	0.07
CABG + MV replacement/repair	198 (2.2%)	94 (2.7%)	0.09
CABG + AV replacement/repair	716 (7.9%)	245 (7.0%)	0.10
Aortic valve replacement/repair without CABG	1935 (21.3%)	678 (19.4%)	0.02
Mitral valve replacement/repair without CABG	1497 (16.5%)	586 (16.8%)	0.68
Tricuspid valve replacement/repair without CABG	495 (5.4%)	218 (6.2%)	0.08
Preoperative eGFR			
≥ 60 mL/min per 1.73 m ²	7135 (78.4%)	2751 (78.7%)	0.77
45-59 mL/min per 1.73 m ²	1186 (13.0%)	438 (12.5%)	0.42
30-44 mL/min per 1.73 m ²	435 (4.8%)	185 (5.3%)	0.24
< 30 mL/min per 1.73 m ² or on dialysis	293 (3.2%)	110 (3.1%)	0.82
Urgent/emergent surgery (%)	2121 (23.3%)	809 (23.1%)	0.83
On-pump procedure (%)	8342 (91.7%)	3242 (92.7%)	0.10
Mean cardiopulmonary bypass time, min (SD)	110 (49%)	108 (50%)	0.06
Mean cross-clamp time, min (SD)	81 (39%)	80 (38%)	0.13

AV, aortic valve; CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; MV, mitral valve; NYHA, New York Heart Association;

SD, standard deviation.

Exploratory analyses for reciprocal changes and territories

We assessed the risk of 30-day mortality in patients with a hsTnI at or above our established thresholds with simultaneous ST elevation and reciprocal ST depression, adjusting for EuroSCORE II (HR 1.59, 95% CI 1.08-2.35, $P = 0.02$). When looking at ST elevation 1-1.9 mm with reciprocal ST depression, the HR was 1.57 (95% CI 1.02-2.40, $P = 0.04$) and, when looking at ST elevation ≥ 2 mm, HR was 1.53 (95% CI 0.68-3.45, $P = 0.31$).

We also explored whether the territory (eg, anterior, inferior) of potential ischemic ECG changes influenced prognosis in models where mortality at 30 days was the dependent variable and adjusting for EuroSCORE II. For septal changes, the HR was 0.99 (95% CI 0.75-1.31, $P = 0.95$); for anterior, HR was 1.03 (95% CI 0.79-1.34, $P = 0.84$); for lateral changes, HR was 1.12 (95% CI 0.88-1.44, $P = 0.35$); and, for inferior, HR was 1.11 (95% CI 0.85-1.45, $P = 0.43$).

Diagnostic criteria for MICS

The model restricted to patients without potential ischemic ECG changes demonstrated that an hsTnI measurement at or above our established thresholds was associated with an increased risk of 30-day mortality (HR 3.51, 95% CI 2.16-5.73, $P < 0.0001$). On the basis of this analysis, our diagnostic criteria for MICS were as follows: 1) an acute elevated postoperative troponin measurement in an adult ≥ 18 years of age with clear evidence of a dynamic troponin elevation, in patients who did not have an MI on the day of or the day before their cardiac surgery, and they had a preoperative hsTnI that was < 300 ng/L; 2) the event occurred within the first 3 days after cardiac surgery; and 3) the outcome did not require a potential ischemic ECG finding.

Associations between MICS and outcomes

Table 5 presents the associations between MICS and other outcomes at 30 days. In both unadjusted and analyses adjusted for EuroSCORE II, MICS was associated with a

Table 3. Frequencies of new potential ischemic ECG changes, incidences of mortality at 30 days

	ST elevation*	ST depression	TWI	Q waves	LBBB	Any potential ischemic ECG change
All patients, N = 12,594	4174 (33.1%)	3049 (24.2%)	5642 (44.8%)	1844 (14.6%)	872 (6.9%)	9097 (72.2%)
Patients who had CABG, N = 7902	2938 (37.2%)	1653 (20.9%)	3447 (43.6%)	1189 (15.0%)	342 (4.3%)	5688 (72.0%)
Patients who had cardiac surgery without CABG, N = 4692	1236 (26.3%)	1396 (29.8%)	2195 (46.8%)	655 (14.0%)	530 (11.3%)	3408 (72.6%)
Patients with postoperative troponin measurement at or above threshold, N = 5924	1976 (33.4%)	1714 (28.9%)	2786 (47.0%)	914 (15.4%)	499 (8.4%)	4392 (74.1%)
Patients with postoperative troponin measurement below threshold, N = 6670	2198 (33.0%)	1335 (20.0%)	2856 (42.8%)	930 (13.9%)	373 (5.6%)	4705 (70.5%)
Death at 30 days, N = 12,594	74 (1.8%)	89 (2.9%)	96 (1.7%)	26 (1.4%)	33 (3.8%)	175 (1.9%)

Data expressed as number (%).

CABG, coronary artery bypass graft surgery; ECG, electrocardiogram; LBBB, left bundle branch block; TWI, T-wave inversion.

* Excluding ST elevation thought to be related to pericarditis.

significantly higher hazard of nonfatal cardiac arrest, new heart failure, death, stroke, redo cardiac surgery, percutaneous coronary intervention, and new clinically significant atrial fibrillation within 30 days of surgery. Length of stay in hospital and in the intensive care unit was longer in patients with MICS.

Discussion

Key findings

In this large, prospective, international cohort study that included a representative sample of eligible patients undergoing cardiac surgery from participating centres, we examined the association between potential ischemic ECG changes and mortality at 30 days. ECG changes were common, even among patients who did not undergo CABG and had a low likelihood of a coronary perfusion issue. New Q waves, the one ECG finding that is part of the Fourth Universal Definition of MI,⁷ was independently associated with a lower risk of mortality at 30 days. T-wave inversions were also independently associated with a lower risk of 30-day mortality. Although ST elevations were not independently associated with mortality at 30 days, ST depressions ≥ 2 mm were independently associated with an increased risk of 30-day mortality. The only ECG change for which CABG surgery was an effect modifier was new LBBB; it was not associated with 30-day mortality in patients who had cardiac surgery but did not undergo CABG, yet it was associated with an almost 3-fold increase in 30-day mortality in patients who underwent CABG. A troponin level at or above our previously established thresholds was strongly associated with 30-day mortality independent of ECG changes and EuroSCORE II. We used this analysis to refine diagnostic criteria for MICS, which was associated with a higher risk of other important cardiovascular outcomes within 30 days of surgery.

Findings in context

Our analysis focused on patients without potential ischemic ECG changes, and adjusted for EuroSCORE II, demonstrated that an elevated hsTnI above our established thresholds was associated with 30-day mortality (HR 3.52, 95% CI 2.16-5.73, $P < 0.0001$). We also demonstrated that the poor prognosis associated with MICS was not restricted

to patients who fulfilled the definition of MI (ie, troponin elevation with ECG changes) and confirms the prognostic relevance of biomarker-based diagnostic criteria for MICS. The poor prognosis of patients with MICS highlights the need for further research to establish optimal evaluation and management of these patients.¹¹

Our findings also have relevance for the diagnosis of MI after cardiac surgery. Establishing diagnostic criteria for MI after cardiac surgery is challenging. First, surgical trauma to the myocardium, cardiac arrest, air emboli to the coronary arteries, and cardioplegia may all cause biomarker release, which is likely commensurate with the myocardial mass and complexity of the procedure. Second, the majority of perioperative myocardial injuries occur during the first few days after surgery,² a period during which most patients receive analgesics (eg, opioids) that can blunt the perception of cardiac ischemic pain. In addition, a small but high-risk group of surgery patients will remain intubated and sedated during the highest risk period, limiting their ability to communicate symptoms. Moreover, surgical patients experiencing possible symptoms (eg, shortness of breath, nausea) or signs (eg, hypotension, tachycardia) of myocardial injury have a host of other common potential explanations (eg, atelectasis, pneumonia, hypovolemia, bleeding, incisional pain, medication side effect), and physicians may therefore not consider myocardial injury. As such, clinicians have to rely on objective measures, with biomarkers and ECG changes being the ones historically used in consensus definitions of MI after cardiac surgery (Supplemental Table S1).^{6-8,12} Alternative approaches to the classification of MI have been proposed to improve the specificity of the diagnosis of MI after cardiac surgery where imaging evidence is required that myocardial injury has resulted in new ventricular impairment or was a consequence of early graft failure.¹¹

We and others have previously established that the hsTnI elevations associated with an increased risk of death at 30 days after cardiac surgery are markedly higher than those proposed to define MI in the Fourth Universal Definition and other consensus statements.^{1,13} In the VISION Cardiac Surgery Study cohort, we established that, in patients who underwent CABG or isolated aortic valve replacement/repair, an hsTnI level of 218-fold the upper reference limit, measured within 1 day after surgery, was associated with an HR of > 1.00 for death within 30 days. The level was 499-fold the upper reference limit for patients who underwent other cardiac

Table 4. Association between new potential ischemic ECG changes and 30-day mortality among patients who met an elevated troponin threshold, adjusted for EuroSCORE II in individual models

ST elevation model			ST depression model			TWI model		
EuroSCORE II		HR 1.06, 95% CI 1.05-1.07, $P < 0.0001$	EuroSCORE II		HR 1.06, 95% CI 1.05-1.07, $P < 0.0001$	EuroSCORE II		HR 1.06, 95% CI 1.05-1.07, $P < 0.0001$
No ST elevation	131 / 3948, 3.3%, 95% CI 2.8-3.9	Reference	No ST depression	121 / 4210, 2.9%, 95% CI 2.4-3.4	Reference	No TWI	118 / 3138, 3.8%, 95% CI 3.1-4.4	Reference
ST elevation 1-1.9 mm	46 / 1597, 2.9%, 95% CI 2.1-3.7	HR 0.95, 95% CI 0.67-1.33, $P = 0.76$	ST depression 1-1.9 mm	57 / 1544, 3.7%, 95% CI 2.8-4.6	HR 1.25 95% CI 0.91-1.71, $P = 0.17$	TWI 1-1.9 mm	31 / 1347, 2.3%, 95% CI 1.5-3.1	HR 0.58, 95% CI 0.39-0.87, $P = 0.007$
ST elevation ≥ 2 mm	11 / 379, 2.9%, 95% CI 1.0-4.3	HR 0.94, 95% CI 0.51-1.74, $P = 0.85$	ST depression ≥ 2 mm	10 / 170, 5.9%, 95% CI 2.3-9.4	HR 2.17, 95% CI 1.14-4.13, $P = 0.02$	TWI ≥ 2 mm	39 / 1439, 2.7%, 95% CI 1.9-3.5	HR 0.72, 95% CI 0.50-1.03, $P = 0.07$
Q-wave model			LBBB model					
EuroSCORE II			Patients who had CABG			P for interaction 0.03		
			EuroSCORE II			HR 1.06, 95% CI 1.05-1.07, $P < 0.0001$		
No Q wave	171 / 5010, 3.4%, 95% CI 2.9-3.9	Reference	No LBBB	98 / 3147, 3.1%, 95% CI 2.5-3.7	Reference			
Q wave	17 / 914, 1.9%, 95% CI 1.0-2.7	HR 0.57, 95% CI 0.35-0.94, $P = 0.03$	LBBB	21 / 342, 6.1%, 95% CI 3.6-8.7	HR 2.93, 95% CI 1.85-4.64, $P < 0.0001$			
			Patients who had cardiac surgery without CABG					
			EuroSCORE II in patients who did not have CABG			HR 1.06, 95% CI 1.05-1.08, $P < 0.0001$		
			No LBBB	58 / 1905, 3.0%, 95% CI 2.3-3.8	Reference			
			LBBB	12 / 530, 2.3%, 95% CI 1.0-3.5	HR 1.16, 95% CI 0.63-2.13, $P = 0.63$			

Data expressed as number of deaths / total number, percent of sample, 95% confidence interval.

CABG, coronary artery bypass graft; ECG, electrocardiogram; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; HR, hazard ratio; LBBB, left bundle branch block; TWI, T-wave inversion.

Table 5. Outcomes at 30 days of follow-up among patients with and without MICS

Outcome	Patients without MICS N = 6670	Patients with MICS, N = 5924	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Nonfatal cardiac arrest	48 (0.7%)	134 (2.3%)	3.18 (2.29-4.42)	2.96 (2.13-4.12)
New heart failure	83 (1.2%)	230 (3.9%)	3.18 (2.48-4.09)	2.96 (2.30-3.80)
Mortality	71 (1.1%)	188 (3.2%)	3.01 (2.29-3.96)	2.76 (2.10-3.63)
New clinically important atrial fibrillation	1657 (24.8%)	1791 (30.2%)	1.25 (1.17-1.33)	1.24 (1.16-1.33)
Stroke	76 (1.1%)	168 (2.8%)	2.52 (1.92-3.30)	2.40 (1.83-3.15)
Redo cardiac surgery	34 (0.5%)	64 (1.1%)	2.13 (1.41-3.23)	2.04 (1.35-3.10)
Percutaneous coronary intervention	34 (0.5%)	53 (0.9%)	1.77 (1.15-2.72)	1.80 (1.17-2.78)
Length of ICU stay, days*				
Median (IQR)	2 (1-3)	2 (1-4)		
Mean (SD)-RR	2 (3)	4 (6)	1.53 (1.48-1.58)	1.42 (1.37-1.46)
Length of postoperative hospital stay, days*				
Median (IQR)	6 (5-8)	7 (5-11)		
Mean (SD)-RR	8 (7)	10 (12)	1.32 (1.29-1.36)	1.26 (1.23-1.29)

Data expressed as number (%) unless noted otherwise.

CI, confidence interval; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; HR, hazard ratio; ICU, intensive care unit; IQR, interquartile range; MICS, myocardial injury after cardiac surgery; RR, relative risk.

* Present mean difference (95% CI) rather than HR (95% CI).

surgery (Table 1). The associations between potential ischemic ECG changes and 30-day mortality after cardiac surgery presented here further challenge the way clinicians and researchers have traditionally diagnosed MI after cardiac surgery. Previously used diagnostic criteria such as new Q waves did not have the expected relationship with mortality. Valid diagnostic criteria for MI should carry a worse prognosis; therefore, our results suggest that diagnostic criteria for MI after cardiac surgery pertaining to potential ischemic ECG changes need to be reconsidered.

Before our study, limited data suggested that development of new Q waves on ECG was associated with a worse prognosis. In a report from the Coronary Artery Surgery Study (CASS), the 62 patients with Q-wave MI had a higher in-hospital mortality (9.7%) than the 1278 patients without Q-wave MI (1.0%).¹⁴ Ramsay et al. studied a cohort of 800 patients followed for 30 days after elective CABG and postoperatively reviewed ECGs in a blinded core laboratory.¹⁵ Q-wave MI was associated with an odds ratio (OR) of 3.48 (95% CI 1.37-8.86), but this association lost statistical significance when adjusting for age, diabetes, previous CABG, peak CK-MB ≥ 100 ng/mL, cardiopulmonary bypass, and cross-clamp times. In a recent retrospective cohort study of 2829 consecutive patients undergoing CABG at 2 centres in Austria, 262 (9.9%) patients had new Q waves, poor R-wave progression, ST elevation, and depression within the first 48 hours after surgery.¹⁶ The authors found that ST elevation was an independent predictor of death at 30 days (OR 6.28, 95% 2.33-16.95) as were new Q waves or lack of R-wave progression (OR 12.42, 95% CI 4.86-31.70). However, the study had several limitations that decreased the credibility of the findings, such as its retrospective design, an unclear ECG adjudication process and completeness of ECG data, and a risk of overfitted models with only 51 deaths at 30 days.

In the Emory Angioplasty versus Surgery Trial, 20 of 194 patients had new Q waves after CABG.¹⁷ Of the 13 patients with new inferior Q waves, 10 of 11 had postoperative cardiac catheterization showing normal left ventricular ejection fraction without regional wall motion abnormalities on left ventriculogram as well as patent grafts. Of the 7 patients with new Q waves in other territories, 5 of 6 had normal left

ventricular ejection fraction, 3 of 6 had no regional wall motion abnormalities, and 3 of 6 had patent grafts. In another study of 206 consecutive patients undergoing cardiac surgery, 15 patients developed new Q waves, but this was not associated with worse postoperative outcomes.¹⁸ These data already challenged the relevance of new Q waves as a diagnostic criterion for MI after CABG. The VISION Cardiac Surgery Study with 1844 patients with new Q waves after cardiac surgery provides the largest most representative data set addressing this issue. Contrary to what may be expected, the study has established that new Q waves: are associated with a reduced risk of 30-day mortality, are equally common among patients who underwent CABG (15%) and patients with cardiac surgery without CABG (14%), and do not contribute to diagnostic criteria for MI after cardiac surgery.

In our cohort, potential ischemic ECG changes were present in 72.2% of patients at some point after surgery and individual changes were present in up to 44.8% of the patients (T-wave inversions). With such high incidences, even in patients who underwent cardiac surgery without CABG, these changes almost certainly lack specificity for the diagnosis of MI after cardiac surgery. It is also unlikely that ischemia was the underlying cause for many of these changes; ST-segment and T-wave changes may result from myocardial and pericardial manipulation, pericardial inflammation, and difficulty with lead placement due to surgical incision. The only changes associated with worse outcomes were ST depression ≥ 2 mm and new LBBB (for patients who underwent CABG only). ST elevation 1-1.9 mm with reciprocal ST depression may be relevant but requires further study. Therefore, these are the ECG changes that should be considered in future definitions of MI after cardiac surgery. Future studies should explore the mechanisms underlying ECG changes in the post-cardiac surgery setting.

Strengths and limitations

This study represents the largest and most rigorous effort to assess the incidence of potential ischemic ECG changes postoperatively in a representative sample of patients undergoing cardiac surgery. All ECGs available at prespecified

time-points were reviewed by experts and calibrated through a qualifying exercise, and adjudicators were blinded to troponin levels and other clinical information. Our study also has limitations. We did not mandate or systematically collect measures of cardiac function, which may be related to biomarker release and ECG changes. Our results do not imply that all ST elevations are without prognostic relevance. When caring for a patient with marked ST elevation early after cardiac surgery, transthoracic or transoesophageal echocardiography to assess for regional wall motion abnormalities may guide clinicians regarding the need to invasively assess for surgery-related issues with the native coronary arteries and coronary bypasses.

Conclusions

ECG changes were common after cardiac surgery, even among patients who did not undergo CABG and had a low likelihood of MI, suggesting these changes lack specificity for diagnostic criteria for MI. ST depression ≥ 2 mm was associated with a higher risk of death at 30 days, whereas new Q waves and T-wave inversions were associated with a lower risk of death. New LBBB was associated with a higher risk of death only in patients who underwent CABG. Consensus statements and guidelines focused on the diagnostic criteria for MI after cardiac surgery need to reconsider which new ECGs changes should be included. The increased risk of death associated with MICS was not restricted to patients who fulfilled an ECG-based definition of MI, reinforcing the prognostic relevance of our biomarker-based diagnostic criteria for MICS. Research is needed to establish the optimal evaluation and management of these patients.

Data Availability

The data collected for this study will not be made available.

Ethics Statement

The investigators obtained ethics approval from all participating centres before starting enrolment.

Patient Consent

Most patients enrolled in the study provided written informed consent. Ten centres used a deferred consent process for patients unable to provide consent (eg, patients who were mechanically ventilated) and with no designated decision-maker available, allowing collection of high-sensitivity cardiac troponin I measurements while awaiting consent. One centre's institutional review board waived the need to obtain written informed consent.

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Disclosures

Refer to [Supplemental Appendix S3](#).

Editorial Disclaimer

Given their role as Associate Editor, Stephen Fremes had no involvement in the peer review of this article and has no access to information regarding its peer review.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at <https://doi.org/10.1016/j.cjca.2025.09.035>