Circulation

ORIGINAL RESEARCH ARTICLE

# Existing Nongated CT Coronary Calcium Predicts Operative Risk in Patients Undergoing Noncardiac Surgeries (ENCORES)

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**BACKGROUND:** Preoperative cardiovascular risk stratification before noncardiac surgery is a common clinical challenge. Coronary artery calcium scores from ECG-gated chest computed tomography (CT) imaging are associated with perioperative events. At the time of preoperative evaluation, many patients will not have had ECG-gated CT imaging, but will have had nongated chest CT studies performed for a variety of noncardiac indications. We evaluated relationships between coronary calcium severity estimated from previous nongated chest CT imaging and perioperative major clinical events (MCE) after noncardiac surgery.

**METHODS:** We retrospectively identified consecutive adults age ≥45 years who underwent in-hospital, major noncardiac surgery from 2016 to 2020 at a large academic health system composed of 4 acute care centers. All patients had nongated (contrast or noncontrast) chest CT imaging performed within 1 year before surgery. Coronary calcium in each vessel was retrospectively graded from absent to severe using a 0 to 3 scale (absent, mild, moderate, severe) by physicians blinded to clinical data. The estimated coronary calcium burden (ECCB) was computed as the sum of scores for each coronary artery (0 to 9 scale). A Revised Cardiac Risk Index was calculated for each patient. Perioperative MCE was defined as all-cause death or myocardial infarction within 30 days of surgery.

**RESULTS:** A total of 2554 patients (median age, 68 years; 49.7% women; median Revised Cardiac Risk Index, 1) were included. The median time interval from nongated chest CT imaging to noncardiac surgery was 15 days (interquartile range, 3–106 days). The median ECCB was 1 (interquartile range, 0–3). Perioperative MCE occurred in 136 (5.2%) patients. Higher ECCB values were associated with stepwise increases in perioperative MCE (0: 2.9%, 1–2: 3.7%, 3–5: 8.0%; 6–9: 12.6%, $P<0.001$). Addition of ECCB to a model with the Revised Cardiac Risk Index improved the C-statistic for MCE (from 0.675 to 0.712, $P=0.018$), with a net reclassification improvement of 0.428 (95% CI, 0.254–0.601, $P<0.0001$). An ECCB ≥3 was associated with 2-fold higher adjusted odds of MCE versus an ECCB <3 (adjusted odds ratio, 2.11 [95% CI, 1.42–3.12]).

**CONCLUSIONS:** Prevalence and severity of coronary calcium obtained from existing nongated chest CT imaging improve preoperative clinical risk stratification before noncardiac surgery.

**Key Words:** cardiovascular risk ■ computed tomography ■ coronary calcium ■ mortality, myocardial infarction, nongated ■ perioperative ■ risk index, surgical outcomes



Major adverse cardiovascular events account for significant perioperative morbidity and mortality, occurring in 1 of every 33 hospitalizations for major noncardiac surgery.[1] Preoperative cardiovascular risk stratification before noncardiac surgery is a common clinical challenge, and risk discrimination remains

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## Clinical Perspective

### What Is New?

- A simple semiquantitative scoring of coronary artery calcium, the estimated coronary calcium burden, can be derived from nongated computed tomography chest imaging with good interreader reliability.
- Higher estimated coronary calcium burden values from nongated computed tomography studies were associated with stepwise increases in perioperative death or myocardial infarction after noncardiac surgery.
- Addition of estimated coronary calcium burden to a model with the Revised Cardiac Risk Index improved the C-statistic for perioperative major clinical events.

### What Are the Clinical Implications?

- The estimated coronary calcium burden is a pragmatic approach to enhance perioperative risk stratification for patients who have had nongated computed tomography chest imaging performed within 1 year before noncardiac surgery.
- The estimated coronary calcium burden can improve preoperative risk assessments without the need for additional imaging or added cost to the health care system.

### Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **CAC** | coronary artery calcium |
| **CT** | computed tomography |
| **ECCB** | estimated coronary calcium burden |
| ***ICD*** | *International Classification of Diseases* |
| **MCE** | major clinical event |
| **MI** | myocardial infarction |
| **NT-proBNP** | N-terminal pro-B-type natriuretic peptide |
| **RCRI** | Revised Cardiac Risk Index |

suboptimal, particularly for patients with poor or unknown functional status.[2,3] Thus, novel approaches to perioperative risk prediction are needed.

Coronary artery calcium (CAC) imaged by ECG-gated, noncontrast, chest computed tomography (CT) is an independent predictor of overall long-term cardiovascular events in multiple large cohort studies.[4–7] CAC scores measured from ECG-gated CT scans before noncardiac surgery have also been shown to independently predict perioperative cardiovascular events.[8–11] However, the effect of this observation has been limited, because at the time of preoperative evaluation, results of a CT coronary angiography or ECG-gated CAC score are not commonly available.

Conveniently, many surgical candidates will have had non–ECG-gated chest CT imaging already performed for a variety of nongated indications, within the previous 12 months. Repurposing these nongated chest CT studies might provide a cost-effective and efficient approach to risk discrimination during preoperative assessment. To our knowledge, no previous studies have examined the utility of coronary calcium measurements from nongated CT chest imaging to improve perioperative risk stratification. Therefore, we investigated associations between coronary calcium estimates from existing nongated chest CT imaging and the incidence of perioperative major clinical events (MCE) in a large cohort of patients undergoing major, noncardiac surgery.

## METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Study Cohort

In the ENCORES study (Existing Nongated CT Coronary Calcium Predicts Operative Risk in Patients Undergoing Noncardiac Surgeries), we retrospectively identified adults ages ≥45 years undergoing in-hospital, nongated, intermediate-to-high-risk surgery between January 1, 2016, and September 15, 2020, at New York University Langone Health, a large, urban, academic health system composed of 4 acute care centers in the New York metropolitan area. Individuals undergoing outpatient surgeries without a planned overnight hospital stay were not included. Patients with a nongated chest CT (including contrast or noncontrast studies) performed within 1 year before the index noncardiac surgery were eligible for inclusion. Patients were excluded if they had documentation of previous percutaneous coronary intervention or coronary artery bypass grafting. Patients were further excluded at the time of CT review if they had imaging evidence of percutaneous coronary intervention or coronary artery bypass grafting (not reported on history), previous prosthetic valve replacement or left ventricular assist device, missing CT studies, or CT studies with uninterpretable image quality for the purpose of coronary calcium determination, or if they underwent low-risk surgeries (endoscopic, cosmetic, or ophthalmologic procedures). For patients with 2 or more surgeries during the study period, only the most recent surgery was included in the final analysis. This study was approved by the New York University School of Medicine Institutional Review Board.

### Data Collection

Clinical data, including demographics, relevant clinical comorbidities, and type of noncardiac surgery, were obtained from the electronic health record (Epic Systems, Verona, WI), which is an integrated electronic health record including all inpatient and outpatient visits across the health system. We queried all data in the electronic health record, including data entered during previous inpatient or outpatient visits in encounter diagnoses, problem lists, or medical histories, as previously described.[12] Patients were determined to have established cardiovascular disease if they had a diagnosis of ischemic heart disease, peripheral artery disease, or cerebrovascular disease. The Revised Cardiac Risk Index (RCRI) was determined for each surgical candidate on the basis of a history of ischemic heart disease, heart failure, transient ischemic attack, or stroke, diabetes with preoperative insulin use, preoperative creatinine >2.0, and high-risk surgery, defined as intraperitoneal, intrathoracic, or suprainguinal vascular surgery.[13]

## CT Interpretation

CT studies were retrospectively reviewed for each patient undergoing surgery. If >1 CT chest imaging study was performed within the year before surgery, the most recent study was selected for review. All CT chest protocols that did not use ECG gating were acceptable, including noncontrast CT and contrast-enhanced CT imaging of the chest.

The extent and severity of coronary artery calcium was estimated from nongated CT chest images. In each study, if both contrast and noncontrast enhanced images were available, the noncontrast images were preferentially reviewed because intravascular contrast may obscure adjacent coronary calcium in some cases. Window widths and levels were optimized for calcium viewing. When available, 2.0-mm slice thickness reconstructions were used; if unavailable, reconstructions closest to 2.0 mm were used, with priority given to thinner reconstructions.

Each of the 3 major epicardial coronary vessels and their associated branches was assessed (ie, left main/left anterior descending artery, left circumflex artery, and right coronary artery), with the left main and left anterior descending coronary artery combined as a single vessel due to the difficulty of visually separating these 2 vessels on nongated studies. The calcium severity in each vessel was scored on the basis of the approximate length of calcium visualized, as previously described.[14] These predetermined scoring criteria were as follows: absent (0% calcified), mild (1%–24% of the total artery length calcified), moderate (25%–49% of the total artery length calcified), or severe (≥50% of the total artery length calcified). Calcium in a branch vessel was added to the total length of calcium of the parent vessel (eg, the length of calcium in a diagonal branch was added to the length of calcium in the left anterior descending). Grades of calcium were subsequently assigned a corresponding numerical score on an ordinal scale as 0 (absent), 1 (mild), 2 (moderate), or 3 (severe).

An estimated coronary calcium burden (ECCB) was recorded for each patient as the sum of these scores (range: 0–9). Clinically relevant ECCB thresholds (ECCB 0: no calcium, 1–2: includes only mild or moderate coronary calcification, 3–5: may include severe disease in 1 vessel, and 6–9: may include severe disease in at least 2 vessels) were selected for subgroup analyses.

To ensure a pragmatic approach, 4 physicians (D.Y.C., D.H., S.D.M., N.D.) without previous formal training in CT interpretation reviewed chest CT imaging to estimate coronary calcium severity. Each physician completed a brief training (approximately 90 minutes in total) that included a video tutorial, written instructions, and case review. All readers were blinded to patient information and surgical outcomes at the time of CT interpretation. To evaluate the interreader reliability of coronary calcium assessment from CT imaging, a sample of 100 randomly selected studies (50 contrast studies and 50 noncontrast studies) was independently interpreted by 2 nonradiologist physician readers, each blinded to the CAC estimation by the other.

## Clinical Outcomes

The primary outcome was perioperative MCE, defined as in-hospital myocardial infarction (MI) during the index surgical admission or all-cause death within the first 30 postoperative days. Postoperative diagnoses were identified by relevant *International Classification of Diseases, Ninth Revision* (*ICD-9*) and *Tenth Revision* (*ICD-10*) diagnosis codes. MI was adjudicated according to the Fourth Universal Definition of Myocardial Infarction and required the presence of a cardiac troponin measurement exceeding the 99th percentile of the upper reference limit, with documented ischemic symptoms, ECG changes, or new ventricular wall motion abnormalities.[15] MI adjudication was performed blinded to the results of the CT-derived ECCB.

## Statistical Analyses

Categorical variables are reported as frequencies and percentages and were compared by chi-square tests. Continuous variables are shown using mean (SD) and median (interquartile range) and were compared using *t* tests or the nonparametric Mann-Whitney test for nonnormally distributed data. The area under the receiver operating characteristic curve (C-statistic) was calculated on the basis of the Harrell method for models with and without the ECCB, and model performance was compared using the Delong test.[16] The discriminative value of the ECCB was further characterized by the continuous net reclassification improvement and the integrated discrimination index, with *P* values calculated using the Hosmer-Lemeshow goodness-of-fit test. Model discrimination was also assessed by the likelihood ratio test. Interreader reliability was assessed by percent agreement, Cohen kappa coefficient, and the intraclass correlation coefficient. Multivariable logistic-regression models were generated to estimate associations between coronary calcium and perioperative outcomes, adjusted for age, sex, and RCRI. Sensitivity analyses were performed in patients without known atherosclerotic disease. Statistical analyses were performed using SPSS 27 (IBM SPSS Statistics, Armonk, NY) and R (Vienna, Austria). Statistical tests are 2-sided, and *P* values <0.05 were considered to be statistically significant.

# RESULTS

## Study Population

We identified 24 939 in-hospital, intermediate-to-high risk, nongated surgeries, performed on adults age ≥45 years. In 4190 (16.8%) of these surgical cases, patients had a nongated chest CT performed within 1 year before the index surgery. A total of 2554 patients (52.0%) met full eligibility criteria and were included in the final analyses (Figure 1).

Baseline characteristics of patients included in the study analyses are described in Table 1. The median age was 68 years, 49.7% were women, and 60.1% were of White race. The median RCRI score was 1. The most common surgical subtypes were general (29.4%), orthopedic (16.8%), neurosurgical (13.9%), thoracic (13.4%), and vascular (12.4%) surgery. High-risk surgeries, defined as intraperitoneal, intrathoracic, or suprainguinal vascular surgeries, were

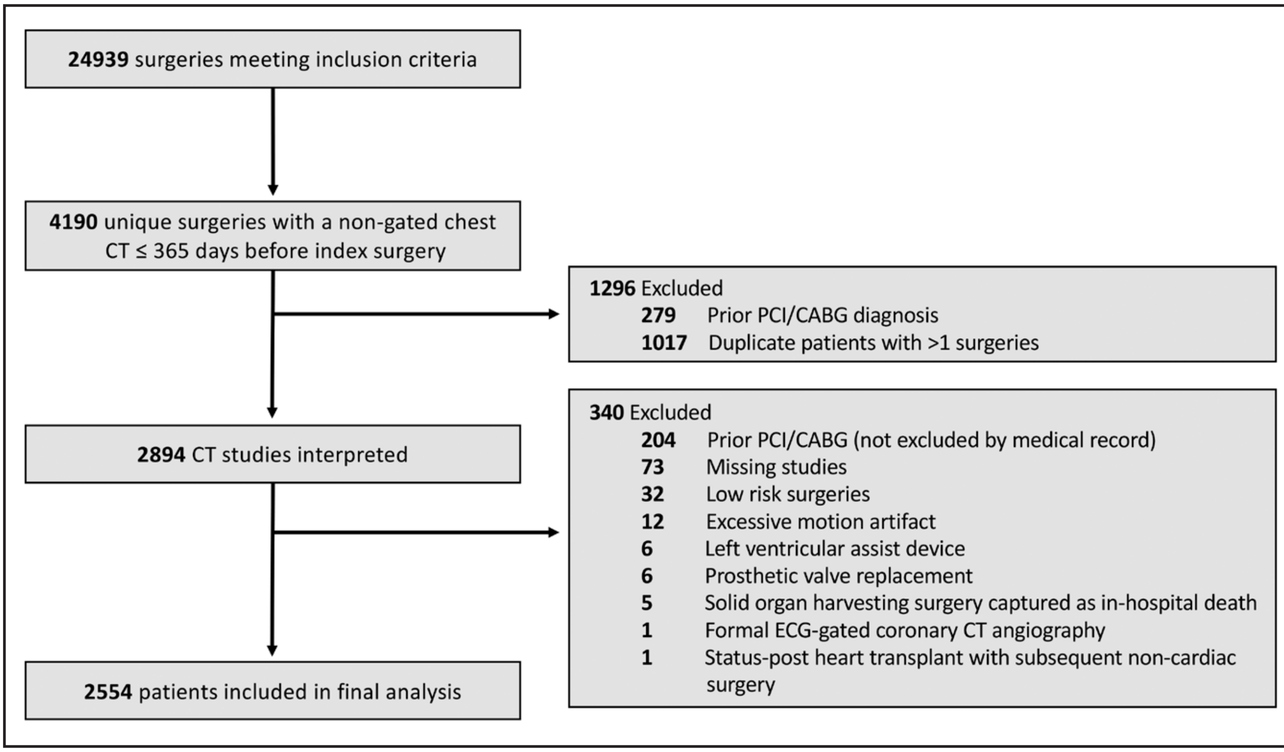


**Figure 1. Patient selection flow diagram.**
CABG indicates coronary artery bypass grafting; CT, computed tomography; and PCI, percutaneous coronary intervention.



performed in 23.0% of cases. General anesthesia was used in 82.3% of surgical procedures, with monitored anesthesia care or regional block used in the remaining cases.

## CT Interpretation

The median time interval from nongated chest CT imaging to noncardiac surgery was 15 days (interquartile range, 3–106 days). CT imaging included 1070 (41.9%) noncontrast and 1484 (58.1%) contrast-enhanced scans (Table 2). Overall, 60.3% of patients had at least mild coronary artery calcification in 1 or more coronary vessels (Figure 2A), and 22.8% had at least mild calcium involving all 3 coronary arteries (Table 2). The most commonly calcified coronary vessel was the left anterior descending (in 58.8% of cases), followed by the right coronary artery (32.7%) and left circumflex artery (31.6%). The median ECCB, the sum of semiquantitative estimates of calcium severity, was 1 (interquartile range, 0–3). The frequency distribution of ECCB is shown in Figure 2B.

Interreader reliability for CT interpretation of the ECCB was excellent overall, with an intraclass correlation coefficient of 96% (95% CI, 0.94–0.98), and in subgroups by contrast enhancement and when stratified by coronary artery (Table 3).

## Perioperative Outcomes

The incidence of perioperative death or MI was 5.2%; 56 (2.2%) patients had a perioperative MI, and 86 (3.4%) died in-hospital or within 30 days of surgery. Baseline characteristics of patients with and without perioperative MCE are shown in Table S1. Patients with any CAC had a higher risk of perioperative MCE versus those without any detectable CAC (6.8% versus 2.9%, $P<0.001$) (Figure 3A). Higher MCE was observed with increasing number of vessels with any calcium (no calcium: 2.9%, 1 vessel: 4.2%, 2 vessels: 4.8%, 3 vessels: 10.6%, $P<0.001$), and the number of vessels with moderate-to-severe calcium (no moderate-to-severe calcium: 3.6%, 1 vessel: 7.2%, 2 vessels: 9.8%, 3 vessel: 13.5%, $P<0.001$), as shown in Figure 3B and 3C.

The ECCB was associated with perioperative outcomes. The incidence of perioperative MCE increased in a stepwise fashion by ECCB (ECCB of 0: 2.9%, ECCB range 1–2: 3.7%, ECCB range 3–5: 8.0%, and ECCB range 6–9: 12.6%, $P<0.001$) (Figure 3D). As a continuous function, the ECCB was associated with a C-statistic of 0.657 (95% CI ,0.608–0.706) for MCE. Addition of ECCB to a model with the RCRI improved the C-statistic for MCE from 0.675 to 0.712 ($P=0.018$), with a net reclassification improvement of 0.428 (95% CI, 0.254–0.601, $P<0.0001$) an integrated discrimination index of 0.010 (95% CI, 0.004–0.017, $P=0.0067$), and a likelihood ratio test $P<0.001$. When the ECCB was added to a model including age, sex, and RCRI, there was a trend toward an improvement in the C-statistic from 0.704 to 0.718 ($P=0.135$), with a net reclassification improvement of 0.312 (95% CI, 0.138–0.485, $P=0.0043$) an integrated discrimination index of 0.006 (95% CI,

**Table 1. Patient Demographics, Medical History, and Surgical Characteristics**

| Patient characteristics (n=2554) | CT (n=2554) |
|---|---|
| Age in years, median [IQR] | 68 [59–77] |
| Female sex, n (%) | 1270 (49.7%) |
| Race and ethnicity, n (%) | |
| White | 1536 (60.1%) |
| Black | 274 (10.7%) |
| Asian | 243 (9.5%) |
| Other race and ethnicity | 435 (17.0%) |
| Native American | 8 (0.3%) |
| Unknown/declined to answer | 58 (2.3%) |
| Body mass index in kg/m², median [IQR]* | 25.6 [22.1–30.2] |
| Left ventricular ejection fraction, median [IQR]† | 65 [57–67] |
| Baseline comorbidities, n (%) | |
| Hypertension | 1192 (46.7%) |
| Atherosclerotic cardiovascular disease ‡ | 714 (28.0%) |
| Ischemic heart disease | 317 (12.4%) |
| Peripheral artery disease | 222 (8.7%) |
| Cerebrovascular disease | 349 (13.7%) |
| Heart failure | 369 (14.4%) |
| Chronic kidney disease with preoperative creatinine >2.0 | 324 (12.7%) |
| Diabetes with preoperative insulin use | 550 (21.5%) |
| Chronic obstructive pulmonary disease | 250 (9.8%) |
| Previous deep venous thrombosis/pulmonary embolism | 39 (1.5%) |
| Medications on admission, n (%) | |
| ACE/ARB§ | 380 (14.9%) |
| β-Blocker | 533 (20.9%) |
| Statin | 691 (27.1%) |
| Aspirin | 361 (14.1%) |
| P2Y12 inhibitor‖ | 73 (2.9%) |
| Direct oral anticoagulant | 90 (3.5%) |
| Warfarin | 17 (0.7%) |
| Preoperative laboratory results, median [IQR] | |
| Hemoglobin (g/dL) | 11.9 [10–13.5] |
| Creatinine (mg/dL) | 0.94 [0.74–1.31] |
| Revised Cardiac Risk Index, median [IQR] | 1 [0–2] |
| Revised Cardiac Risk Index, n (%) | |
| 0 | 1094 (42.8%) |
| 1 | 793 (31.0%) |
| 2 | 416 (16.3%) |
| 3+ | 251 (9.8%) |
| Surgical characteristics | |
| Types of surgeries, n (%) | |
| General surgery | 750 (29.4%) |
| Orthopedic surgery | 428 (16.8%) |
| Neurosurgery | 356 (13.9%) |
| Thoracic surgery | 343 (13.4%) |
| Vascular surgery | 317 (12.4%) |
| Urological surgery | 166 (6.5%) |
| Otolaryngology | 86 (3.4%) |
| Plastic surgery | 60 (2.3%) |
| Gynecologic surgery | 48 (1.9%) |
| Other | 0 (0%) |
| Surgery risk, n (%) | |
| High risk | 588 (23.0%) |
| Intermediate risk | 1966 (77.0%) |
| Anesthesia type, n (%) | |
| General | 2102 (82.3%) |
| Monitored care | 329 (12.9%) |
| Regional block | 123 (4.8%) |

CT indicates computed tomography; and IQR, interquartile range.
*Body mass index available for 2520 of 2554 patients (98.7%).
†Left ventricular ejection fraction data were available for 1467 of 2554 patients (57.4%).
‡Defined as established coronary artery disease, myocardial infarction, peripheral artery disease, or cerebrovascular disease before noncardiac surgery.
§ACE/ARB = angiotensin-converting enzyme inhibitors/angiotensin receptor blockers.
‖P2Y12 inhibitor = clopidogrel, ticagrelor, or prasugrel.

0.0012–0.0104, $P$=0.013), and a likelihood ratio test $P$=0.0012. In analyses adjusted for age, sex, and RCRI, each increase in ECCB was significantly associated with perioperative MCE (adjusted odds ratio, 1.12 [95% CI, 1.05–1.21], $P$<0.001). When ECCB was evaluated as a categorical variable, ECCB 3 to 5 (adjusted odds ratio, 1.82 [95% CI, 1.06–3.12]) and 6 to 9 (adjusted odds ratio, 2.58 [95% CI, 1.43–4.66]) were associated with higher adjusted odds of MCE compared with patients without any evidence of coronary calcium (ECCB 0) (Figure 3D). An ECCB ≥3 was associated with a higher adjusted odds of MCE versus an ECCB <3 (adjusted odds ratio, 2.11 [95% CI, 1.42–3.12]).

Although the ECCB positively correlated with the RCRI (Spearman coefficient [$\rho$]: 0.283, $P$<0.001), at each RCRI stratification, a wide range of ECCB values were observed (Figure S1A). Among patients with an RCRI of 0, for example, 49.5% had detectable coronary calcium (ECCB ≥1), while 19.5% of patients with RCRI ≥3 had no coronary calcium (ECCB 0). As expected, the incidence of MCE was highest among patients with elevated RCRI. Within each RCRI stratum, the incidence of MCE was numerically lower among patients without detectable coronary calcium (ECCB of 0) versus those with ECCB >0 (Figure 4A). Patients with an ECCB of 0 to 2, indicative of only mild calcium, had a significantly lower risk of MCE across multiple RCRI subgroups compared with patients with higher ECCB ≥3 (Figure 4B). The relationship between RCRI, ECCB

**Table 2. Computed Tomography Imaging Characteristics and Estimated Coronary Calcium Burden**

| Imaging characteristics | |
|---|---|
| Time from CT to surgery in days, median [IQR] | 15 [3–106] |
| CT characteristics, n (%) | |
| Noncontrast studies reviewed | 1070 (41.9%) |
| Contrast enhanced studies reviewed | 1484 (58.1%) |
| Average CT slice (mm) | 1.9 ± 0.7 |
| Coronary calcium by vessel | |
| Left anterior descending, n (%) | |
| None | 1051 (41.2%) |
| Mild (0%–24% length) | 798 (31.2%) |
| Moderate (25%–49% length) | 345 (13.5%) |
| Severe (50%–100% length) | 360 (14.1%) |
| Right coronary artery, n (%) | |
| None | 1719 (67.3%) |
| Mild (0%–24% length) | 521 (20.4%) |
| Moderate (25%–49% length) | 127 (5.0%) |
| Severe (50%–100% length) | 187 (7.3%) |
| Left circumflex artery, n (%) | |
| None | 1746 (68.4%) |
| Mild (0%–24% length) | 548 (21.4%) |
| Moderate (25%–49% length) | 132 (5.2%) |
| Severe (50%–100% length) | 128 (5.0%) |
| Extent and severity of coronary calcium | |
| Extent of any coronary calcium, n (%) | |
| 0-vessel | 1013 (39.7%) |
| 1-vessel | 519 (20.3%) |
| 2-vessel | 439 (17.2%) |
| 3-vessel | 583 (22.8%) |
| Extent of moderate-to-severe coronary calcium, n (%) | |
| 0-vessel | 1794 (70.2%) |
| 1-vessel | 404 (15.8%) |
| 2-vessel | 193 (7.6%) |
| 3-vessel | 163 (6.4%) |

CT indicates computed tomography; and IQR, interquartile range.

thresholds, and the incidence of perioperative MCE is shown in Figure S1B.

We observed associations between the ECCB and perioperative MCE in subgroups of younger (age <65 years) and older (age ≥65 years) adults, with and without established atherosclerotic cardiovascular disease, and in patients with low RCRI <2 or elevated RCRI ≥2 (Figure S2A). In a sensitivity analysis excluding patients with established cardiovascular disease, the incidence of perioperative MCE increased in a stepwise fashion by ECCB (Figure S2B). Findings were also similar in an analysis of the overall cohort including statin use as a covariate in the multivariable model (Figure S3A and S3B).

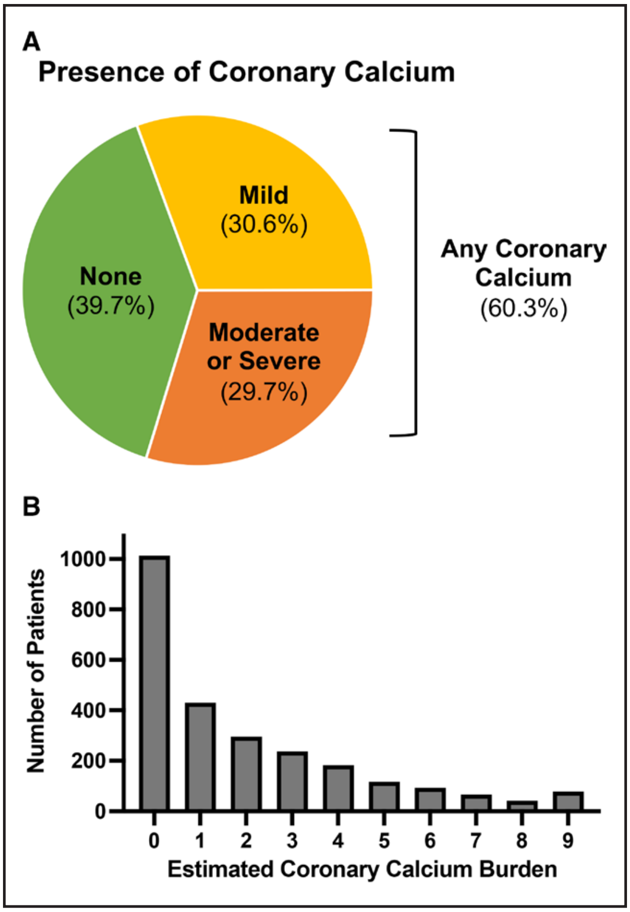


**Figure 2. Distribution of coronary calcium severity and estimated coronary calcium burden.**
Pie chart demonstrating the prevalence of coronary calcium by severity (**A**) and a frequency distribution of the estimated coronary calcium burden (ECCB) (**B**) are shown. ECCB was calculated for each patient as the sum of ordinal qualitative estimates of coronary calcium (from absent [0] to severe [3]) for all 3 coronary arteries.

When stratified by age and RCRI (Figures S4 and S5), younger adults (age <65 years) with an RCRI of 0 and an ECCB of 0 exhibited a low risk of MCE (0.6%, Figure S4A). Among younger adults with a mild ECCB of 0 to 2, MCE occurred in <6%, irrespective of RCRI score. In contrast, young adults with an ECCB ≥3 and an RCRI >2 had a substantially elevated incidence of MCE (Figure S5A). Older adults (≥65 years) with ECCB ≥3 also had a higher incidence of MCE compared to those with milder coronary calcium (ECCB 0–2), but this was only observed among patients with lower RCRI ≤1 (Figure S5B).

Estimation of coronary calcium from both noncontrast and contrast-enhanced CT studies correlated with perioperative MCE (Figure S2A), with durable associations between the number of calcified coronary vessels (Figure S6A and S6B) and the ECCB (Figure S7A and S7B) and clinical outcomes. However, for contrast-enhanced studies, risk discrimination was poorer in patients with a lower extent and severity of coronary calcium.

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**Table 3. Interreader Reliability Among Computed Tomography Readers**

| Interreader reliability | ECCB: ICC (95% CI) | Any CAC: kappa (95% CI) | Moderate-to-severe CAC: kappa (95% CI) |
|---|---|---|---|
| Per-patient analysis (n) | | | |
| All CT studies (100) | 0.96 (0.94–0.98) | 0.82 (0.70–0.94) | 0.85 (0.73–0.96) |
| Contrast-enhanced CT (50) | 0.95 (0.91–0.97) | 0.74 (0.56–0.93) | 0.89 (0.74–1.00) |
| Noncontrast CT (50) | 0.97 (0.95–0.98) | 0.90 (0.77–1.00) | 0.80 (0.64–0.97) |
| Stratified by coronary artery (n) | | | |
| Left anterior descending (100) | 0.93 (0.90–0.96) | 0.91 (0.83–1.00) | 0.82 (0.70–0.94) |
| Left circumflex (100) | 0.91 (0.87–0.94) | 0.76 (0.62–0.89) | 0.76 (0.55–0.96) |
| Right coronary (100) | 0.94 (0.91–0.96) | 0.73 (0.60–0.86) | 0.83 (0.68–0.99) |

A sample of 100 CT studies (including 50 contrast-enhanced and 50 noncontrast) were independently interpreted by 2 readers. Interreader reliability for CT interpretation of the estimated coronary calcium burden was excellent overall, with an intraclass correlation coefficient (ICC) of 0.96 (95% CI, 0.94–0.98). CAC indicates coronary artery calcium; CT, computed tomography; and ECCB, estimated coronary calcium burden.

## DISCUSSION

In a large cohort of patients undergoing major noncardiac surgery, we identified that coronary calcium derived from nongated chest CT studies, performed in the year before surgery, demonstrated a positive correlation with perioperative outcomes. Stepwise increases in MCE were observed with increasing ECCB. When combined in a model with the RCRI, the ECCB significantly improved risk prediction. Among patients with an RCRI of 0 and absent or mild coronary calcium, the risk of MCE was low, a finding that was most striking in older adults age ≥65 years. To our knowledge, this is the first study to use preexisting, preoperative nongated chest CT imaging to evaluate perioperative risks of noncardiac surgery.

Previous studies demonstrate that CAC from ECG-gated CT imaging before noncardiac surgery is associated with perioperative cardiovascular events.[8–11] In a single-center study of 239 patients undergoing preoperative ECG-gated chest CT imaging, patients with CAC scores ≥113 were 4-fold more likely to experience 30-day postoperative cardiovascular events than patients with lower scores.[8] Previous studies also report strong agreement between CAC scores derived from non–ECG-gated versus ECG-gated CT imaging,[17] with extensive data reported from low-dose CT imaging from COPD databases and lung cancer screening trials.[18–22] In a cohort of patients undergoing lung cancer screening, the incidental finding of coronary calcification on nongated CT imaging conferred higher risk for long-term cardiac events.[17] Sheth et al reported that preoperative ECG-gated coronary CT angiography provided independent and additive prognostic information to the RCRI, although in that study, CT imaging was more likely to lead to inappropriate overestimation of risk.[23] In contrast with previous studies that prospectively evaluated ECG-gated CAC scoring or coronary CT angiography, the present analyses demonstrate the value of leveraging existing non–ECG-gated CT studies, performed for indications other than cardiovascular risk stratification, with no added cost to the health care system. We demonstrate the feasibility and outstanding reproducibility of pragmatic estimates of coronary calcium from existing non–ECG-gated imaging and additional associations with short-term surgical outcomes.

The ordinal scale for the ECCB in the present analyses was developed on the basis of previous reports in which increasing ordinal CAC scores from low-dose chest CT imaging correlated with cardiovascular death.[14,24,25] Although we estimated the degree of severity of calcium in each vessel on the basis of the length of calcium visualized as previously described,[14] the current scoring differs from the previous literature by lowering the threshold of severity across all levels: for mild calcium, the threshold was lowered from less than one-third of vessel length to less than one-fourth of vessel length; for moderate calcium from between one-third and two-thirds of vessel length to between one-fourth and one-half of vessel length, and for severe calcium from two-thirds to one-half of vessel length. These lower thresholds were chosen to enhance the sensitivity of the scoring system.

There are several important clinical implications of this study. First and foremost, coronary calcium estimated from existing CT scans, performed for noncoronary indications in the year preceding surgery, may serve as a simple, pragmatic, and cost-effective adjunct to traditional preoperative risk scores. Coronary calcium may be particularly helpful for guiding risk assessment in patients in whom coronary artery calcium is absent or minimal, with corresponding low rates of expected MCE. Conversely, a high burden of coronary calcium may signal higher adverse perioperative outcomes, even in patients with a low RCRI. For example, in the present cohort, the incidence of perioperative MCE occurred in 1 in every 22 hospitalizations among patients with an RCRI of 0 and higher ECCB ≥3, versus only 1 in every 71 hospitalizations for those with an RCRI of 0 and lower ECCB <3.

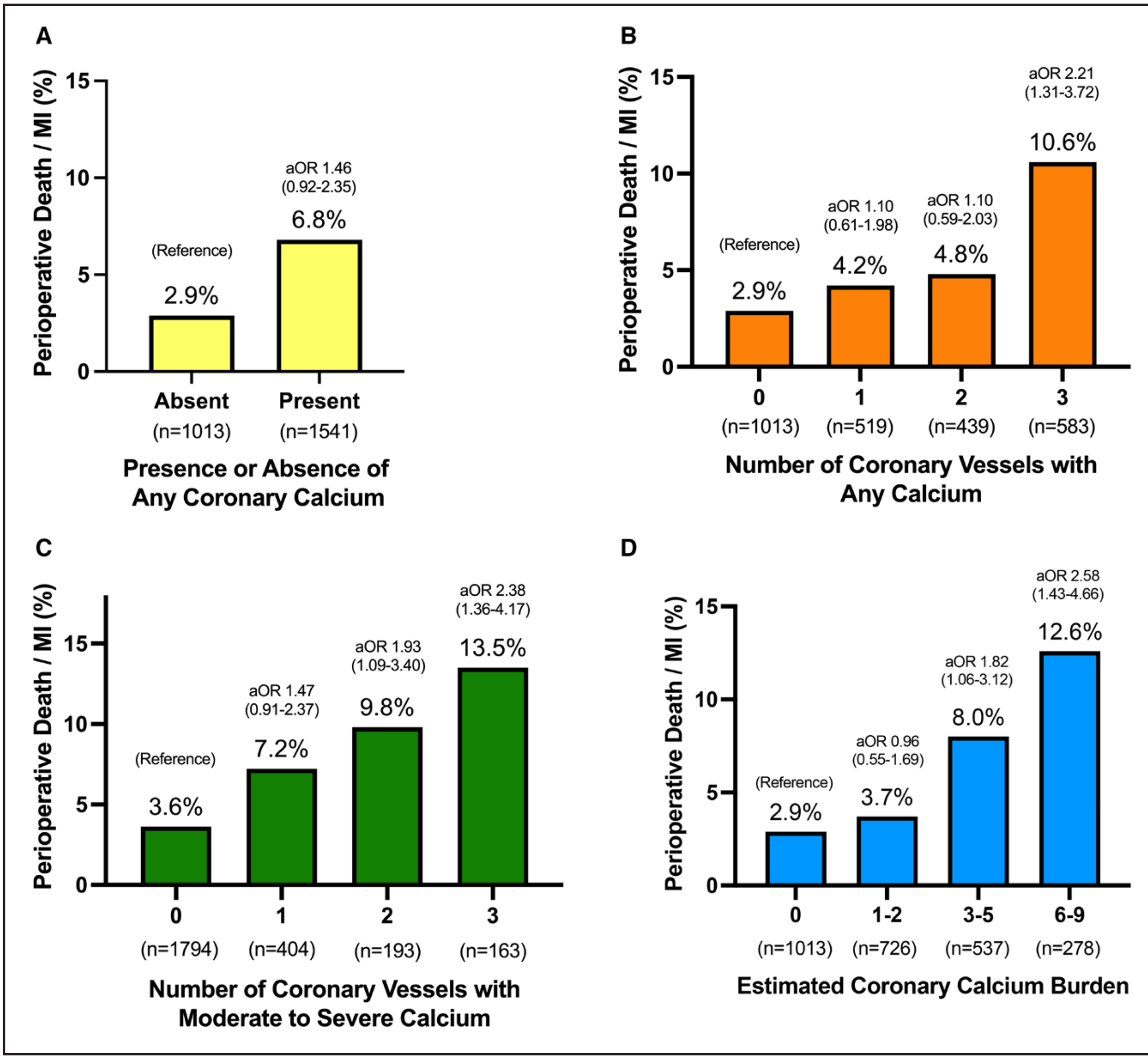


**Figure 3. Incidence of perioperative MCE stratified by prevalence and severity of coronary artery calcium.**
The incidence of perioperative major clinical events (MCE) increased with any coronary calcium ($P<0.001$; **A**), and in a stepwise pattern for increasing number of coronary vessels with any calcium ($P<0.001$; **B**), number of coronary vessels with moderate-to-severe calcium ($P<0.001$; **C**), and according to the estimated coronary calcium burden ($P<0.001$; **D**). Odds ratios for MCE adjusted for age, sex, and Revised Cardiac Risk Index score are shown. aOR indicates adjusted odds ratio; and MI, myocardial infarction.

Associations between ECCB and MCE were consistent across age and RCRI subgroups. We observed a trend toward substantial excess risk associated with coronary calcium among younger patients <65 years old who had a high RCRI ≥3. Furthermore, although the RCRI generally selects for high-risk patients in whom additional cardiac testing may be recommended before surgery, a low ECCB in this setting may identify a subset at substantially lower risk of perioperative MCE and in whom additional testing may not be warranted.

Second, coronary artery calcifications were present in 60% of adults age ≥45 years undergoing noncardiac surgery in this study. Despite the high prevalence, coronary calcification is frequently underreported. Previous studies identified that 31% to 56% of radiology reports failed to report coronary calcium from nongated chest CT studies when it was present.[26,27] Our findings support the emphasis in guidelines to report coronary calcium on nongated chest CT studies.[25] Deep learning models have been used to automate calcium scoring on nongated CT imaging, which may lead to more widespread incorporation of calcium scores in chest CT reporting.[28] The NOTIFY-1 study (Incidental Coronary Artery Calcium: Opportunistic Screening of Previous Nongated Chest Computed Tomography Scans to Improve Statin Rates) demonstrated that automated CAC detection using a

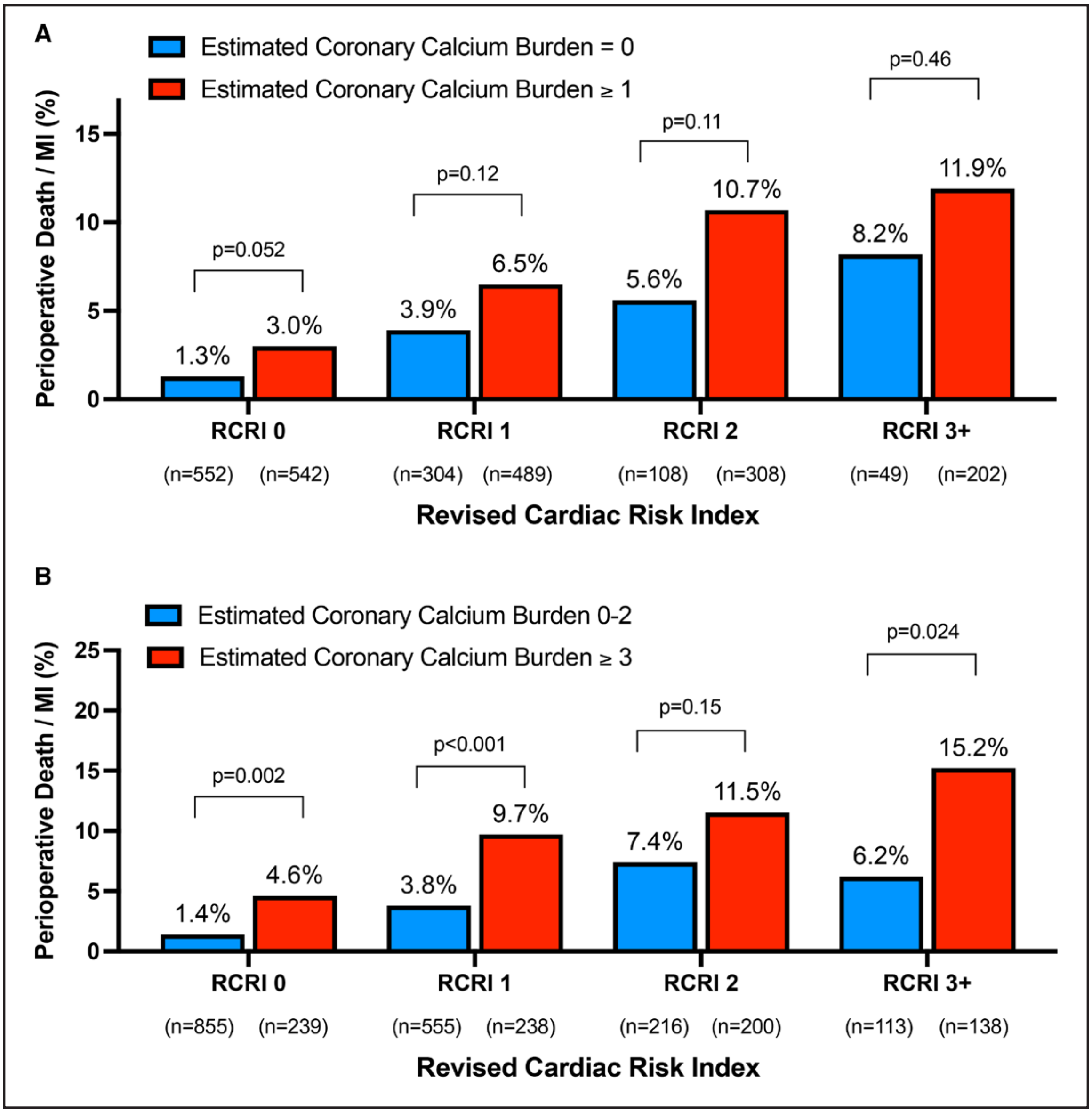


**Figure 4. Incidence of perioperative MCE stratified by ECCB and RCRI.**
Perioperative major clinical events (MCE) in patients with an estimated coronary calcium burden (ECCB) of 0 vs ≥1 (**A**) or an ECCB of 0 to 2 vs ≥3 (**B**), stratified by the Revised Cardiac Risk Index (RCRI), are shown.

deep learning algorithm from non–ECG-gated CT imaging led to significant increases in statin prescriptions.[29] In the future, the application of similar machine learning approaches to automatically quantify coronary calcium from pre-existing chest imaging may also be used to inform perioperative risk prediction.

Third, although mild calcium detected by noncontrast imaging was associated with increases in perioperative MCE, contrast-enhanced imaging was less reliable to detect lower levels of coronary calcium and its association with outcomes. This is an expected finding that is consistent with previous studies that report contrast-enhanced CT imaging may miss subtle coronary calcium.[30] Contrast in the coronary arteries and adjacent structures can potentially camouflage small foci of calcium, particularly for patients with lower calcium scores.[30] Therefore, when preoperative noncontrast and contrast CT scans are both available, noncontrast studies should be preferentially reviewed. Even so, contrast-enhanced images with a higher ECCB were still associated with perioperative MCE.

Last, we demonstrated that novice CT readers with limited training can reliably estimate coronary calcium from non–ECG-gated CT imaging that confers important prognostic associations in the perioperative period. This demonstrates the potential for broad applicability of this approach to risk stratification among clinicians without extensive training in CT imaging.

## Study Limitations

This study has some notable limitations. First, this was a retrospective cohort study, and events were identified and adjudicated through review of the electronic medical record. Second, systematic troponin surveillance was not performed, and because symptoms associated with ischemia may be masked by anesthesia and analgesia in the perioperative period, the incidence of MI may be underestimated. Similarly, perioperative biomarkers for risk stratification were not routinely measured, and the performance of the ECCB in addition to clinical risk scores and high-sensitivity troponin or NT-proBNP (N-terminal pro-B-type natriuretic peptide) before surgery could not be evaluated and requires further study. Third, this was a highly selected population of patients with clinically indicated chest CT imaging in the year before surgery, and the findings of this pragmatic study may not be applicable to other patient populations. Still, these analyses demonstrate the value of leveraging existing CT to glean important prognostic data without the costs of additional testing dedicated for cardiovascular risk stratification. Fourth, coronary calcium is not a perfect surrogate for coronary risk, and the absence of calcium cannot exclude noncalcified atherosclerotic plaques, particularly in younger individuals. Fifth, we included contrast-enhanced CT imaging in our analyses, which may limit the accurate detection of small foci of coronary calcium, especially when located near contrast-enhanced structures (eg, coronary arteries themselves or other cardiac chambers). However, inclusion of contrast studies made this study pragmatic and broadly applicable to a larger number of patients, because many patients will have only contrast-enhanced CT imaging for review at the time of preoperative risk assessment. Sixth, the RCRI was initially validated to predict a composite of cardiac complications, including MI, pulmonary edema, ventricular fibrillation or primary cardiac arrest, and complete heart block; all-cause mortality was not included as an end point in RCRI derivation. Accordingly, the performance of the RCRI in predicting our clinically relevant definition of MCE (perioperative MI or death) in the current analysis may be suboptimal. Still, this distinction reinforces the notion that the ECCB and RCRI are complementary perioperative risk indicators that may be used to better predict MCE. Last, we used a semiquantitative visual scoring system to estimate coronary calcification.[31] Although this may be less reliable than formal Agatston scoring for coronary calcium, it provides a practical approach to enhance risk assessment that can be quickly performed by the clinician at the time of preoperative evaluation. In addition, visual scoring of coronary calcium has been shown to have good agreement with formal CAC scoring, even when interpreting from low-dose nongated CT scans.[19,21]

## Conclusions

Prevalence and severity of coronary calcium from preexisting, preoperative, nongated chest CT imaging were associated with stepwise increases in perioperative MCE after major, noncardiac surgery. Because many patients have had recent nongated CT chest imaging before the time of preoperative risk assessment, this measure of coronary calcium may enhance clinical risk stratification before noncardiac surgery.

## ARTICLE INFORMATION

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### Supplemental Material

Table S1
Figure S1–S7

## REFERENCES


1. Smilowitz NR, Gupta N, Ramakrishna H, Guo Y, Berger JS, Bangalore S. Perioperative major adverse cardiovascular and cerebrovascular events associated with noncardiac surgery. *JAMA Cardiol*. 2017;2:181–187. doi: 10.1001/jamacardio.2016.4792
2. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, Davila-Roman VG, Gerhard-Herman MD, Holly TA, Kane GC, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation*. 2014;130:e278–e333. doi: 10.1161/CIR.0000000000000106
3. Smilowitz NR, Berger JS. Perioperative cardiovascular risk assessment and management for noncardiac surgery: a review. *JAMA*. 2020;324:279–290. doi: 10.1001/jama.2020.7840
4. Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, Liu K, Shea S, Szklo M, Bluemke DA, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med*. 2008;358:1336–1345. doi: 10.1056/NEJMoa072100
5. McClelland RL, Jorgensen NW, Budoff M, Blaha MJ, Post WS, Kronmal RA, Bild DE, Shea S, Liu K, Watson KE, et al. 10-Year coronary heart disease risk prediction using coronary artery calcium and traditional risk factors. *J Am Coll Cardiol*. 2015;66:1643–1653. doi: 10.1016/j.jacc.2015.08.035
6. Budoff MJ, Shaw LJ, Liu ST, Weinstein SR, Mosler TP, Tseng PH, Flores FR, Callister TQ, Raggi P, Berman DS. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. *J Am Coll Cardiol*. 2007;49:1860–1870. doi: 10.1016/j.jacc.2006.10.079
7. Budoff MJ, Young R, Burke G, Jeffrey Carr J, Detrano RC, Folsom AR, Kronmal R, Lima JAC, Liu KJ, McClelland RL, et al. Ten-year association of coronary artery calcium with atherosclerotic cardiovascular disease (AS-

CVD) events: the multi-ethnic study of atherosclerosis (MESA). *Eur Heart J*. 2018;39:2401–2408. doi: 10.1093/eurheartj/ehy217
8. Ahn JH, Park JR, Min JH, Sohn JT, Hwang SJ, Park Y, Koh JS, Jeong YH, Kwak CH, Hwang JY. Risk stratification using computed tomography coronary angiography in patients undergoing intermediate-risk noncardiac surgery. *J Am Coll Cardiol*. 2013;61:661–668. doi: 10.1016/j.jacc.2012.09.060
9. Ghadri JR, Fiechter M, Veraguth K, Gebhard C, Pazhenkottil AP, Fuchs TA, Templin C, Gaemperli O, Kaufmann PA. Coronary calcium score as an adjunct to nuclear myocardial perfusion imaging for risk stratification before noncardiac surgery. *J Nucl Med*. 2012;53:1081–1086. doi: 10.2967/jnumed.111.100206
10. Koshy AN, Ha FJ, Gow PJ, Han HC, Amirul-Islam FM, Lim HS, Teh AW, Farouque O. Computed tomographic coronary angiography in risk stratification prior to non-cardiac surgery: a systematic review and meta-analysis. *Heart*. 2019;105:1335–1342. doi: 10.1136/heartjnl-2018-314649
11. Mahla E, Vicenzi MN, Schrottner B, Maier R, Tiesenhausen K, Watzinger N, Rienmuller R, Moser RL, Metzler H. Coronary artery plaque burden and perioperative cardiac risk. *Anesthesiology*. 2001;95:1133–1140. doi: 10.1097/00000542-200111000-00017
12. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, Tobin KA, Cerfolio RJ, Francois F, Horwitz LI. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ*. 2020;369:m1966. doi: 10.1136/bmj.m1966
13. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KK, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100:1043–1049. doi: 10.1161/01.cir.100.10.1043
14. Shemesh J, Henschke CI, Shaham D, Yip R, Farooqi AO, Cham MD, McCauley DI, Chen M, Smith JP, Libby DM, et al. Ordinal scoring of coronary artery calcifications on low-dose CT scans of the chest is predictive of death from cardiovascular disease. *Radiology*. 2010;257:541–548. doi: 10.1148/radiol.10100383
15. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD; Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth Universal Definition of Myocardial Infarction (2018). *Circulation*. 2018;138:e618-e651. doi: 10.1161/CIR.0000000000000617
16. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics*. 1988;44:837–845.
17. Xie X, Zhao Y, de Bock GH, de Jong PA, Mali WP, Oudkerk M, Vliegenthart R. Validation and prognosis of coronary artery calcium scoring in nontriggered thoracic computed tomography: systematic review and meta-analysis. *Circ Cardiovasc Imaging*. 2013;6:514–521. doi: 10.1161/CIRCIMAGING.113.000092
18. Budoff MJ, Nasir K, Kinney GL, Hokanson JE, Barr RG, Steiner R, Nath H, Lopez-Garcia C, Black-Shinn J, Casaburi R. Coronary artery and thoracic calcium on noncontrast thoracic CT scans: comparison of ungated and gated examinations in patients from the COPD Gene cohort. *J Cardiovasc Comput Tomogr*. 2011;5:113–118. doi: 10.1016/j.jcct.2010.11.002
19. Einstein AJ, Johnson LL, Bokhari S, Son J, Thompson RC, Bateman TM, Hayes SW, Berman DS. Agreement of visual estimation of coronary artery calcium from low-dose CT attenuation correction scans in hybrid PET/CT and SPECT/CT with standard Agatston score. *J Am Coll Cardiol*. 2010;56:1914–1921. doi: 10.1016/j.jacc.2010.05.057
20. Kim SM, Chung MJ, Lee KS, Choe YH, Yi CA, Choe BK. Coronary calcium screening using low-dose lung cancer screening: effectiveness of MDCT with retrospective reconstruction. *AJR Am J Roentgenol*. 2008;190:917–922. doi: 10.2214/AJR.07.2979
21. Kirsch J, Buitrago I, Mohammed TL, Gao T, Asher CR, Novaro GM. Detection of coronary calcium during standard chest computed tomography correlates with multi-detector computed tomography coronary artery calcium score. *Int J Cardiovasc Imaging*. 2012;28:1249–1256. doi: 10.1007/s10554-011-9928-9
22. Wu MT, Yang P, Huang YL, Chen JS, Chuo CC, Yeh C, Chang RS. Coronary arterial calcification on low-dose ungated MDCT for lung cancer screening: concordance study with dedicated cardiac CT. *AJR Am J Roentgenol*. 2008;190:923–928. doi: 10.2214/AJR.07.2974
23. Sheth T, Chan M, Butler C, Chow B, Tandon V, Nagele P, Mitha A, Mrkobrada M, Szczeklik W, Faridah Y, et al; Coronary Computed Tomographic Angiography and Vascular Events in Noncardiac Surgery Patients Cohort Evaluation Study Investigators. Prognostic capabilities of coronary computed tomographic angiography before non-cardiac surgery. *BMJ*. 2015;350:h1907. doi: 10.1136/bmj.h1907
24. Chiles C, Duan F, Gladish GW, Ravenel JG, Baginski SG, Snyder BS, DeMello S, Desjardins SS, Munden RF; NLST Study Team. Association of Coronary Artery Calcification and Mortality in the National Lung Screening Trial: a comparison of three scoring methods. *Radiology*. 2015;276:82–90. doi: 10.1148/radiol.15142062
25. Hecht HS, Cronin P, Blaha MJ, Budoff MJ, Kazerooni EA, Narula J, Yankelevitz D, Abbara S. 2016 SCCT/STR guidelines for coronary artery calcium scoring of noncontrast noncardiac chest CT scans. *J Cardiovasc Comput Tomogr*. 2017;11:74–84. doi: 10.1016/j.jcct.2016.11.003
26. Balakrishnan R, Nguyen B, Raad R, Donnino R, Naidich DP, Jacobs JE, Reynolds HR. Coronary artery calcification is common on nongated chest computed tomography imaging. *Clin Cardiol*. 2017;40:498–502. doi: 10.1002/clc.22685
27. Williams KA Sr, Kim JT, Holohan KM. Frequency of unrecognized, unreported, or underreported coronary artery and cardiovascular calcification on noncardiac chest CT. *J Cardiovasc Comput Tomogr*. 2013;7:167–172. doi: 10.1016/j.jcct.2013.05.003
28. Eng D, Chute C, Khandwala N, Rajpurkar P, Long J, Shleifer S, Khalaf MH, Sandhu AT, Rodriguez F, Maron DJ, et al. Automated coronary calcium scoring using deep learning with multicenter external validation. *NPJ Digit Med*. 2021;4:88. doi: 10.1038/s41746-021-00460-1
29. Sandhu AT, Rodriguez F, Ngo S, Patel BN, Mastrodicasa D, Eng D, Khandwala N, Balla S, Sousa D, Maron DJ. Incidental coronary artery calcium: opportunistic screening of previous nongated chest computed tomography scans to improve statin rates (NOTIFY-1 Project). *Circulation*. 2023;147:703–714. doi: 10.1161/CIRCULATIONAHA.122.062746
30. Fresno CU, Tijmes FS, Thavendiranathan P, Akhtari S, Karur GR, Torres FS, Halankar J, Nguyen ET, Hanneman K. Visual ordinal scoring of coronary artery calcium on contrast-enhanced and noncontrast chest CT. *AJR Am J Roentgenol*. 2022;219:569–578. doi: 10.2214/AJR.22.27664
31. Hecht H, Blaha MJ, Berman DS, Nasir K, Budoff M, Leipsic J, Blankstein R, Narula J, Rumberger J, Shaw LJ. Clinical indications for coronary artery calcium scoring in asymptomatic patients: expert consensus statement from the Society of Cardiovascular Computed Tomography. *J Cardiovasc Comput Tomogr*. 2017;11:157–168. doi: 10.1016/j.jcct.2017.02.010