

**Clinical and Prognostic Utility of Visually Estimated Coronary Artery Calcium in Patients
undergoing Myocardial Perfusion Positron Emission Tomography Imaging**

Supplementary Material

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Supplementary Methods

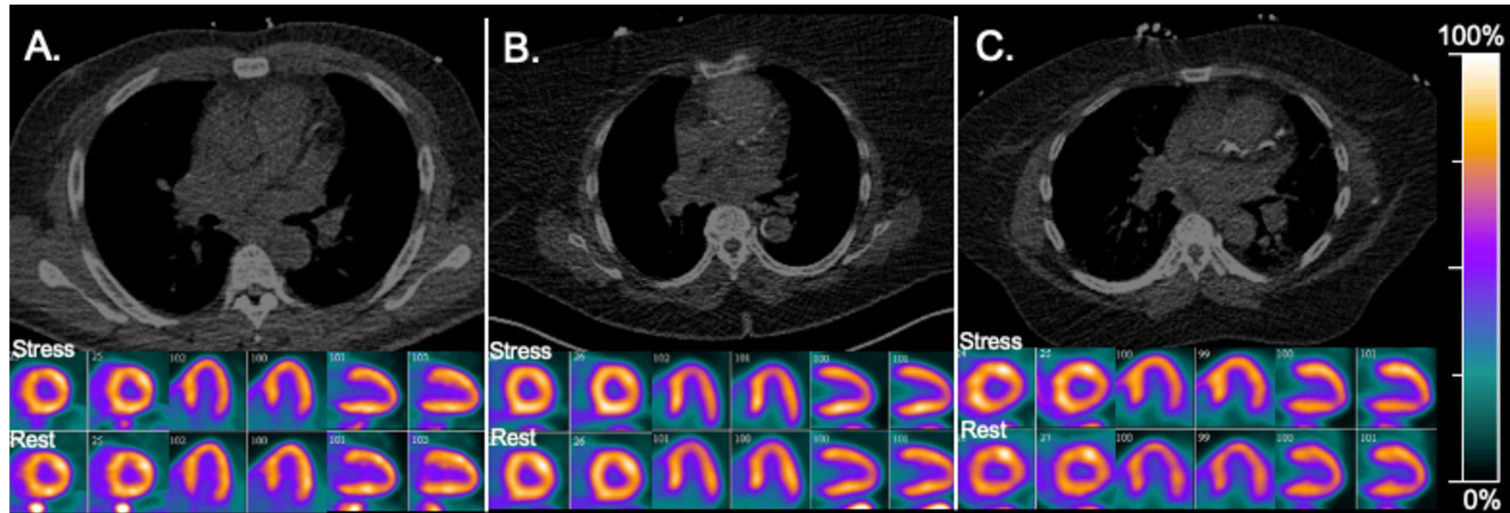
Data collection

Demographics, vital signs, comorbidities, medications, and imaging parameters available at the time of presentation were collected from the electronic health record. The primary outcome of this study was a composite of acute coronary syndrome, stroke, and all-cause mortality. Outcomes were identified by descriptions in physician visit notes or discharge summaries after PET scan, as previously reported.⁽¹⁾ Outcomes were assessed by reviewers blinded to PET and CT imaging findings.

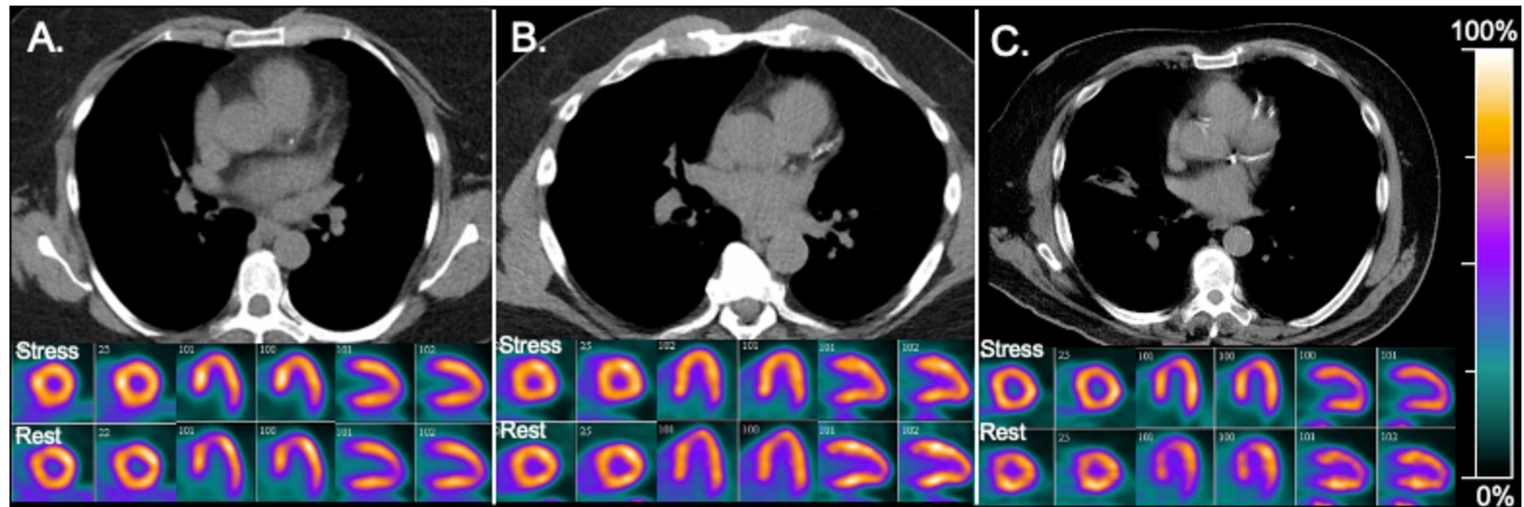
Validation of VECAC assessment

During the training period, one investigator reviewed 334 dedicated, clinically performed CAC scans to learn VECAC categorization, using the measured AU CAC score to provide post-hoc feedback to the correct classification. Subsequently, VECAC was validated in two cohorts, including 1) 115 patients with dedicated CAC scans and ungated chest CT performed within 30 days and 2) 104 patients with dedicated CAC scans and hybrid PET/CT performed within 1 year. Kappa statistics and percentage agreement between these methods were robust (**Supplementary Table 1**) and comparable to visual estimations reported previously in other clinical settings.^(2,3)

SUPPLEMENTARY FIGURE 1. Representative images of VECAC categories ≤ 10 (A), 11-400 (B) and >400 (C) from AC-CT images in patients with normal myocardial perfusion PET images.



SUPPLEMENTARY FIGURE 2. Representative images of VECAC categories ≤ 10 (A), 11-400 (B) and >400 (C) from diagnostic chest CT images in patients with normal myocardial perfusion PET images.



SUPPLEMENTARY TABLE 1. Assessment of Visual Estimations of Coronary Artery Calcium Compared to Dedicated Coronary Artery Calcium Scan

Comparison	N	Median Days between scans	Agreement	Kappa
Gated Coronary CT VECAC vs. CAC*	334	N/A	92.51%	0.86 [S.E. 0.042]
Diagnostic Chest CT VECAC vs. CAC	115	9.6 [0.7 – 19]	95.65%	0.92 [S.E. 0.073]
AC-CT VECAC vs. CAC	104	85 [29 – 205]	90.38%	0.84 [S.E. 0.072]

*VECAC estimated on the same scan that clinical CAC scoring was performed

AC, attenuation correction; CAC, coronary artery calcium; CT, computed tomography; SE, standard error; VECAC, visually estimated coronary artery calcium.

SUPPLEMENTARY TABLE 2. Adjusted Hazard Ratios for the Composite Outcome by Visually Estimated Coronary Artery Calcium with Multiple Imputation for Missing Covariates

Outcomes, n (%)	VECAC ≤ 10	VECAC 11-400	VECAC >400
Composite endpoint			
• Multivariable adjusted model 1 HR (95% CI)	Ref	2.25 (1.25, 4.07)	2.78 (2.25, 3.42)
• Multivariable adjusted model 2 HR (95% CI)	Ref	2.09 (1.61, 2.71)	2.56 (2.08, 3.15)

HR, hazard ratio; CI, confidence interval; VECAC, visually estimated coronary artery calcium

Model 1 covariates include age, sex, race, high density cholesterol, total cholesterol, systolic blood pressure, history of diabetes mellitus, current smoking, and use of blood pressure medication.

Model 2 covariates additionally include myocardial perfusion imaging (normal/abnormal) and coronary flow reserve.

SUPPLEMENTARY TABLE 3. Sequential Impact of Clinical and Imaging Parameters on Area Under the Curve for the Composite Endpoint

Outcomes, n (%)	Area under the Curve (95%CI)	P-value*
Composite endpoint		
• Clinical risk factors	0.67 (0.62, 0.73)	NA
• Clinical risk factors + MPI + CFR	0.71 (0.66, 0.77)	0.02
• Clinical risk factors + MPI + CFR + VECAC	0.75 (0.70, 0.80)	0.01

*Compared to previous model

CI, confidence interval; MPI, myocardial perfusion imaging; CFR, coronary flow reserve; VECAC, visually estimated coronary artery calcium

Clinical risk factors include age, sex, race, history of hyperlipidemia, systolic blood pressure, heart rate, history of diabetes mellitus, current smoking, and use of blood pressure medication.

MPI reflects fixed or reversible defects.

SUPPLEMENTARY TABLE 4. Crude and Adjusted Hazard Ratios for the Composite Outcome for the Combined Sub-Groups between Visually Estimated Coronary Artery Calcium and Coronary Flow Reserve

Sub-groups	N	Crude Analysis	*Adjusted Analysis
VECAC \leq 10 & CFR \geq 1.5	413	Reference	Reference
VECAC \leq 10 & CFR < 1.5	77	HR 1.45 [95% CI: 0.77, 2.75]; p=0.25	HR 1.26 [95% CI: 0.66, 2.40]; p=0.69
VECAC > 10 & CFR \geq 1.5	77	HR 3.02 [95% CI: 1.86, 4.89]; p<0.001	HR 2.05 [95% CI: 1.22, 3.44]; p<0.001
VECAC > 10 & CFR < 1.5	41	HR 5.61 [95% CI: 3.31, 9.52]; p<0.0001	HR 2.91 [95% CI: 1.57, 5.38]; p<0.0001

VECAC, visually estimated coronary artery calcium; CFR, coronary flow reserve; HR, hazard ratio; CI, confidence interval;

*Model adjusted for clinical risk factors, myocardial perfusion imaging status, and left ventricular ejection fraction.

Clinical risk factors include age, sex, race, history of hyperlipidemia, systolic blood pressure, heart rate, history of diabetes mellitus, current smoking, and use of blood pressure medication.

Supplementary References

1. Guerraty MA, Rao HS, Anjan VY, et al. The role of resting myocardial blood flow and myocardial blood flow reserve as a predictor of major adverse cardiovascular outcomes. *PLoS One*. 2020;15:e0228931.
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3. Einstein AJ, Johnson LL, Bokhari S, et al. 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.