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The Coronary Artery Disease–Reporting and Data System (CAD-RADS)

Prognostic and Clinical Implications Associated With Standardized Coronary Computed Tomography Angiography Reporting

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ABSTRACT

OBJECTIVES This study sought to assess clinical outcomes associated with the novel Coronary Artery Disease–Reporting and Data System (CAD-RADS) scores used to standardize coronary computed tomography angiography (CTA) reporting and their potential utility in guiding post-coronary CTA care.

BACKGROUND Clinical decision support is a major focus of health care policies aimed at improving guideline-directed care. Recently, CAD-RADS was developed to standardize coronary CTA reporting and includes clinical recommendations to facilitate patient management after coronary CTA.

METHODS In the multinational CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) registry, 5,039 patients without known coronary artery disease (CAD) underwent coronary CTA and were stratified by CAD-RADS scores, which rank CAD stenosis severity as 0 (0%), 1 (1% to 24%), 2 (25% to 49%), 3 (50% to 69%), 4A (70% to 99% in 1 to 2 vessels), 4B (70% to 99% in 3 vessels or ≥50% left main), or 5 (100%). Kaplan-Meier and multivariable Cox models were used to estimate all-cause mortality or myocardial infarction (MI). Receiver-operating characteristic (ROC) curves were used to compare CAD-RADS to the Duke CAD Index and traditional CAD classification. Referrals to invasive coronary angiography (ICA) after coronary CTA were also assessed.

RESULTS Cumulative 5-year event-free survival ranged from 95.2% to 69.3% for CAD-RADS 0 to 5 ($p < 0.0001$). Higher scores were associated with elevations in event risk (hazard ratio: 2.46 to 6.09; $p < 0.0001$). The ROC curve for prediction of death or MI was 0.7052 for CAD-RADS, which was noninferior to the Duke Index (0.7073; $p = 0.893$) and traditional CAD classification (0.7095; $p = 0.783$). ICA rates were 13% for CAD-RADS 0 to 2, 66% for CAD-RADS 3, and 84% for CAD-RADS ≥4A. For CAD-RADS 3, 58% of all catheterizations occurred within the first 30 days of follow-up. In a patient subset with available medication data, 57% of CAD-RADS 3 patients who received 30-day ICA were either asymptomatic or not receiving antianginal therapy at baseline, whereas only 32% had angina and were receiving medical therapy.

CONCLUSIONS CAD-RADS effectively identified patients at risk for adverse events. Frequent ICA use was observed among patients without severe CAD, many of whom were asymptomatic or not taking antianginal drugs. Incorporating CAD-RADS into coronary CTA reports may provide a novel opportunity to promote evidence-based care post-coronary CTA.
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Nearly 15 million patients undergo diagnostic testing for suspected coronary artery disease (CAD) annually in the United States (1,2). Within this population, numerous investigations have reported that post-test management, including referral to invasive coronary angiography (ICA) and implementation of medical therapy, is markedly variable and often suboptimal (2–6). From the National Cardiovascular Data Registry, previous reports have found that less than one-half of patients undergoing ICA had obstructive CAD, even in the setting of a positive stress test (5,6). Additionally, underuse of medical therapy is frequently documented in symptomatic CAD patients (7–10). To this end, clinical decision support is increasingly the focus of efforts to improve point-of-care decision-making and adherence to guideline-directed care. Although recent initiatives have targeted the appropriate referral of patients for diagnostic testing (11), efforts to standardize and improve post-test care are still warranted.

SEE PAGE 90

Recently, a multisociety-sponsored statement from the Society of Cardiovascular Computed Tomography (SCCT), American College of Cardiology, American College of Radiology, and the North American Society of Cardiovascular Imaging entitled the "Coronary Artery Disease–Reporting and Data System (CAD-RADS)" was published, aiming to standardize classification of CAD severity while incorporating clinical management recommendations after coronary computed tomography angiography (CTA) (12,13). Although standardized reporting of image interpretation is an integral component of CAD imaging (14), post-test recommendations have not been routinely included as part of a clinical report. Thus, the goals of CAD-RADS are both to provide consistent communication of coronary CTA findings and to guide optimal post-coronary CTA clinical management decisions, such as risk factor modification, implementation of medical therapy, and/or additional testing with ICA. By linking noninvasive findings with appropriate follow-up care, CAD-RADS has the potential to promote guideline-supported clinical management and reduce unnecessary downstream testing (15).

The aims of this analysis were: 1) to assess long-term prognosis associated with CAD-RADS scores in a real-world registry compared to other CAD classification schemes; and 2) to assess real-world utilization of ICA after coronary CTA in order to infer the potential utility of CAD-RADS in guiding post-coronary CTA care. The implications of our analysis may serve as the basis for future quality

ABBREVIATIONS AND ACRONYMS

AUC = appropriate use criteria

CAD = coronary artery disease

CAD-RADS = Coronary Artery Disease-Reporting and Data System

CTA = computed tomography angiography

DM = diabetes mellitus

HLD = hyperlipidemia

HTN = hypertension

ICA = invasive coronary angiography

MI = myocardial infarction

ROC = receiver-operating characteristic

SCCT = Society of Cardiovascular Computer Tomography

SIHD = stable ischemic heart disease

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TABLE 1 CAD-RADS Classification System*

	Maximal Coronary Stenosis	Interpretation	Further Cardiac Testing	Management
CAD-RADS 0	0%	Absence of CAD	None	Reassurance; consider nonatherosclerotic causes of chest pain
CAD-RADS 1	1%–24% (or plaque without stenosis)	Minimal nonobstructive CAD	None	Consider nonatherosclerotic causes of chest pain; consider preventive therapy and risk factor modification
CAD-RADS 2	25%–49%	Mild nonobstructive CAD	None	Consider nonatherosclerotic causes of chest pain; consider preventive therapy and risk factor modification, particularly for patients with nonobstructive plaque in multiple segments
CAD-RADS 3	50%–69%	Moderate stenosis	Consider functional assessment	Consider symptom-guided anti-ischemic and preventive pharmacotherapy as well as risk factor modification per guideline-directed care†; other treatments should be considered per guideline-directed care†
CAD-RADS 4A	70%–99% in 1 or 2 vessels	Severe stenosis	Consider ICA or functional assessment	Consider symptom-guided anti-ischemic and preventive pharmacotherapy as well as risk factor modification per guideline-directed care†; other treatments (including options for revascularization) should be considered per guideline-directed care†
CAD-RADS 4B	70%–99% in 3 vessels, or left main ≥50%	Severe stenosis	ICA recommended	Consider symptom-guided anti-ischemic and preventive pharmacotherapy as well as risk factor modification per guideline-directed care†; other treatments (including options for revascularization) should be considered per guideline-directed care†
CAD-RADS 5	100%	Total coronary occlusion	Consider ICA and/or viability assessment	Consider symptom-guided anti-ischemic and preventive pharmacotherapy as well as risk factor modification per guideline-directed care†; other treatments (including options for revascularization) should be considered per guideline-directed care†

*Extrapolated with permission from Cury et al. (13) and †Fihn et al. (15).
CAD = coronary artery disease; CAD-RADS = Coronary Artery Disease–Reporting and Data System; ICA = invasive coronary angiography.

initiatives aimed at improving the noninvasive diagnostic evaluation of CAD.

METHODS

STUDY COHORT. Eligible patients were enrolled in the long-term CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) registry of stable outpatients who were referred for elective coronary CTA to evaluate clinically suspected CAD. Previous reports have fully described the methods of this registry and are presented here with limited detail (16,17). Patients were enrolled from 17 participating sites across 9 countries between 2002 and 2009 and followed prospectively for a mean 5.1 ± 1.8 years. Institutional review board approval and oversight were obtained at all sites. Patient identifiers were not entered into the CONFIRM database.

Patients included in our analysis reflect the enrollment criteria of the CONFIRM registry (16,17): 1) adults age ≥18 years; 2) referral for coronary CTA to evaluate CAD using a ≥64-detector row scanner; 3) data collection of CAD risk factors and coronary CTA data; and 4) standardized reporting of segmental coronary stenosis, per SCCT guidelines (18,19). A total of 5,039 patients without known CAD or previous coronary revascularization were included in our analysis.

CORONARY CTA PROTOCOL AND CAD-RADS DEFINITIONS. Each participating site performed coronary CTA following standardized protocols defined by SCCT guidelines (18,19). The SCCT coronary model was used for segmental analysis of the coronary arterial tree for vessels >1.5 mm in diameter (17). The percent luminal stenosis in each segment was categorized as 0%, 1% to 24%, 25% to 49%, 50% to 69%, 70% to 99%, or 100% as measured by visual assessment.

Standardized CAD-RADS categories were based on the highest grade coronary stenosis detected in any vessel and defined as follows: CAD-RADS 0 (0% stenosis and no plaque), CAD-RADS 1 (1% to 24% stenosis or plaque with positive remodeling but no stenosis), CAD-RADS 2 (25% to 49% mild stenosis), CAD-RADS 3 (50% to 69% moderate stenosis), CAD-RADS 4A (70% to 99% severe stenosis in 1 or 2 vessels), CAD-RADS 4B (70% to 99% severe stenosis in 3 vessels or left main ≥50%), and CAD-RADS 5 (any 100% stenosis or total occlusion). CAD-RADS recommendations for post-coronary CTA patient management are also detailed (**Table 1**). Briefly, among patients with CAD-RADS 0 to 2, additional diagnostic testing is not recommended. In patients with CAD-RADS 3, implementation and maximization of medical therapy are recommended along with additional functional assessment. In contrast, further invasive testing is recommended for CAD-RADS 4A to 5 along with preventive therapies and risk factor modification.

Although CAD-RADS includes modifiers for grafts (G) and stents (S), we chose to restrict our analysis to patients without known CAD or previous revascularization; thus, these modifiers were not incorporated in our analysis. Moreover, detailed plaque analysis was not available in the CONFIRM registry to fully assess the CAD-RADS vulnerable plaque modifier (V) based on atherosclerotic plaque morphology.

CLINICAL DESCRIPTIVE DATA. All enrolled patients underwent evaluation by a physician or nurse before coronary CTA. Each CONFIRM site collected self-reported baseline clinical data, including age, gender, hypertension (HTN), diabetes mellitus (DM), hyperlipidemia (HLD), smoking, family history of premature CAD (first-degree male relative age <55 years or first-degree female relative age <65 years), chest pain characteristics (no chest pain, noncardiac, atypical angina, typical angina), history of previous stress testing, and left ventricular ejection fraction. The appropriateness of the index coronary CTA for assessment of stable ischemic heart disease (SIHD) was also estimated using the Framingham risk score (in asymptomatic patients) and the Diamond-Forrester pretest probability (in symptomatic patients) as defined by the multimodality appropriate use criteria (AUC) for evaluation of SIHD (11). Although CAD-RADS also provided recommendations for pharmacotherapy and functional assessment, data on medication use and stress testing were not prospectively collected in the CONFIRM registry and thus were not included in our analysis.

OUTCOME DATA COLLECTION. Our primary outcome was a composite of all-cause mortality or nonfatal myocardial infarction (MI) through 5 years of follow-up. For cause of death in the United States, the National Death Index was queried. For death outside of the United States, events were determined through direct interview with the patient's family or physician, telephone call, or review of medical records. MI events were confirmed through hospital documentation of biomarker elevation and electrocardiographic changes consistent with the universal definition of MI (20). Referrals for ICA post-coronary CTA were also confirmed through chart review or telephone interview. Additional ascertainment and adjudication methods have been previously described (17).

STATISTICAL METHODS. Baseline characteristics were compared across CAD-RADS categories using the chi-square test for categorical variables and analysis of variance for continuous variables. We estimated cumulative event-free survival using the Kaplan-Meier method. Death and MI were included only if events occurred >24 h after the index coronary CTA.

Univariable and multivariable Cox proportional hazards survival models reporting hazard ratio with 95% confidence interval were calculated. After meeting the proportional hazards assumption by graphical assessment, the following covariables were included in multivariable Cox models, which were defined a priori based on clinical judgment and previous CONFIRM analyses: age, sex, HTN, DM, HLD, smoking, and presenting chest pain symptoms.

The prognostic performance of CAD-RADS was also compared to the Duke CAD Prognostic Index, which has been described previously (21), and to the traditional method of characterizing CAD extent/severity (e.g., no CAD, nonobstructive CAD or <50% stenosis, 1-vessel obstructive CAD, 2-vessel obstructive CAD, or 3-vessel obstructive/left main CAD). Model discrimination and calibration were assessed using receiver-operating characteristic (ROC) curves and the Hosmer-Lemeshow goodness-of-fit test.

Next, we examined real-world ICA utilization patterns after coronary CTA. Specifically, we assessed rates of invasive angiography across CAD-RADS scores within 30 days after coronary CTA, 90 days after coronary CTA, and throughout 5 years of follow-up. Furthermore, in a subset of patients with available baseline medication data, we assessed the distribution of presenting symptoms and medication use among patients with intermediate stenosis (CAD-RADS 3) who underwent ICA. Because medication use was not prospectively followed, only patients who underwent ICA within 30 days were examined in this exploratory analysis. A 2-tailed value of $p < 0.05$ was considered statistically significant for all analyses, which were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

BASELINE CLINICAL CHARACTERISTICS OF THE STUDY COHORT. Of the 5,039 patients in the overall cohort, 33% were classified as CAD-RADS 0, 12% as CAD-RADS 1, 12% as CAD-RADS 2, 15% as CAD-RADS 3, 20% as CAD-RADS 4A, 4% as CAD-RADS 4B, and 4% as CAD-RADS 5 (**Table 2**). Patient age, comorbidities (HTN, HLD, DM), and the Framingham risk score were significantly different across CAD-RADS scores ($p < 0.0001$ for all comparisons). Only a history of previous stress testing and baseline left ventricular ejection fraction were not significantly different across CAD-RADS scores ($p = 0.0996$ and $p = 0.1335$, respectively).

ESTIMATING ALL-CAUSE DEATH OR MI BASED ON CAD-RADS SCORES. A total of 314 deaths and 457 non-fatal MIs occurred in the overall cohort.

TABLE 2 Baseline Characteristics of Study Cohort by CAD-RADS

	CAD-RADS 0 (n = 1,688)	CAD-RADS 1 (n = 603)	CAD-RADS 2 (n = 619)	CAD-RADS 3 (n = 732)	CAD-RADS 4A (n = 989)	CAD-RADS 4B (n = 198)	CAD-RADS 5 (n = 210)	p Value*
Age, yrs	54 ± 13	60 ± 11	63 ± 10	64 ± 10	63 ± 10	66 ± 10	65 ± 9	<0.0001
Male	874 (52)	389 (65)	402 (65)	526 (72)	717 (73)	143 (72)	161 (77)	<0.0001
Hypertension	722 (43)	308 (51)	342 (55)	436 (60)	631 (64)	140 (73)	141 (68)	<0.0001
Hyperlipidemia	690 (41)	332 (55)	372 (60)	473 (65)	600 (61)	120 (63)	126 (61)	<0.0001
Diabetes	204 (12)	85 (14)	93 (15)	142 (19)	252 (26)	56 (29)	65 (31)	<0.0001
Current smoking	289 (17)	104 (17)	113 (18)	169 (23)	248 (25)	50 (26)	75 (36)	<0.0001
Family history of early CAD	500 (30)	155 (26)	153 (25)	223 (31)	298 (31)	57 (30)	67 (33)	0.0451
Chest pain typicality								<0.0001
Typical angina	170 (11)	26 (6)	44 (8)	97 (14)	256 (29)	56 (31)	35 (21)	
Atypical angina	563 (37)	147 (33)	153 (29)	237 (35)	258 (29)	52 (29)	41 (25)	
Noncardiac	155 (10)	50 (11)	49 (9)	76 (11)	112 (13)	14 (8)	30 (18)	
No chest pain	642 (42)	218 (49)	276 (53)	261 (39)	265 (30)	58 (32)	57 (35)	
Past stress test	602 (53)	142 (62)	158 (52)	231 (52)	367 (50)	76 (48)	86 (53)	0.0996
LVEF <50%	59 (4)	25 (4)	20 (3)	21 (3)	41 (4)	7 (4)	15 (7)	0.1335
Framingham Risk Score								<0.0001
≥20%	160 (9)	106 (18)	143 (23)	242 (33)	381 (39)	90 (45)	116 (55)	
10%–19%	446 (26)	225 (37)	222 (36)	285 (39)	342 (35)	57 (29)	52 (25)	
<10%	1082 (64)	272 (45)	254 (41)	205 (28)	266 (27)	51 (26)	42 (20)	
Rarely appropriate use of Coronary CTA	710 (42)	202 (34)	231 (37)	194 (27)	178 (18)	30 (15)	28 (13)	<0.0001

Values are mean ± SD or n (%). *Comparison across CAD-RADS groups using chi-square test for categorical variables and analysis of variance for continuous variables.
CTA = computed tomography angiography; LVEF = left ventricular ejection fraction; other abbreviations as in Table 1.

Cumulative event-free survival at 5 years ranged from 95.2% for CAD-RADS 0 to 69.3% for CAD-RADS 5 ($p < 0.0001$ across all strata) (Figure 1). In a multivariable Cox model, CAD-RADS scores were strongly associated with an elevated risk for death or MI, with hazard ratios ranging from 2.46 for CAD-RADS 1 to 6.09 for CAD-RADS 5, using CAD-RADS 0 as the reference group ($p < 0.0001$ for all comparisons) (Table 3).

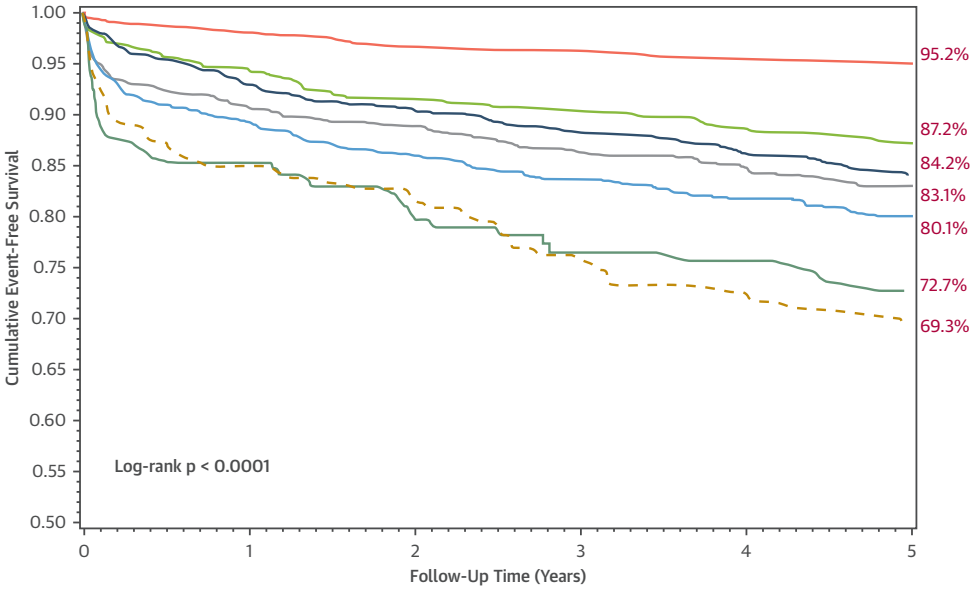
The prognostic performance of CAD-RADS compared to the Duke CAD Prognostic Index and the traditional method of characterizing CAD extent/severity are shown in Figure 2. The area under the ROC curve for prediction of death or MI was 0.7052 for CAD-RADS, which was similar compared to the Duke CAD Index (0.7073; $p = 0.893$) and traditional CAD classification (0.7095; $p = 0.783$) (Figure 3).

ICA USE AFTER CORONARY CTA BY CAD-RADS SCORES. Real-world ICA utilization patterns at 30 days, 90 days, and throughout 5-year follow-up across CAD-RADS scores are shown in Figure 4. Among patients with nonobstructive CAD (CAD-RADS 0 to 2), ICA use was infrequent within the first 30 days (6%), at 90 days (7%), and at any time point throughout follow-up (13%). Conversely, among patients with severe obstructive CAD (CAD-RADS ≥4A), the majority underwent ICA during follow-up (84%). Most of these referrals for ICA occurred soon after coronary CTA: 61% of these catheterizations occurred within 30 days and 83% by 90 days. Notably, patients with intermediate coronary CTA stenosis (CAD-RADS 3) were also frequently sent for ICA (66%), with more than one-half (58%) of these catheterizations occurring in the first 30 days of follow-up.

Next, in a subset of patients with available baseline medication data (n = 2,757) (Online Table 1) and a similar pattern of ICA utilization (Online Figure 1), we examined the distribution of presenting symptoms and baseline medication use in patients who underwent 30-day ICA. Specifically among CAD-RADS 3 patients, the majority (57%) of these early, 30-day catheterizations occurred in those who were either asymptomatic or not receiving any antianginal therapy at baseline (Figure 5). In contrast, only 32% of these early, 30-day catheterizations occurred in CAD-RADS 3 patients who had angina (typical or atypical) and were taking at least 1 antianginal drug at baseline.

Overall, 38% (n = 536) of referrals for ICA within 90 days occurred in patients without severe obstructive CAD (CAD-RADS <4A). Of these early ICAs performed, 29% (n = 158) were in patients who underwent the index coronary CTA with a "rarely appropriate" indication.

FIGURE 1 **Cumulative Event-Free Survival Through 5 Years of Follow-Up by CAD-RADS Scores**



Number at Risk

CAD-RADS 0	1679	1646	1614	1602	1589	1581
CAD-RADS 1	592	559	537	529	516	505
CAD-RADS 2	616	571	534	516	500	483
CAD-RADS 3	712	636	576	521	487	461
CAD-RADS 4A	963	838	672	562	502	465
CAD-RADS 4B	190	161	120	87	80	74
CAD-RADS 5	206	168	135	107	91	82

Cumulative event-free survival from death or myocardial infarction and the number at risk through follow-up displayed across Coronary Artery Disease–Data And Reporting System (CAD-RADS) scores.

DISCUSSION

Our study was the first to examine long-term prognosis associated with the novel CAD-RADS scores, which were strongly predictive of death or MI among patients in a real-world registry and were noninferior to other coronary CTA prognostic scores. Our findings suggest for the first time that standardized post-coronary CTA recommendations with CAD-RADS may have the potential to facilitate guideline-directed care at the point of testing, as we identified high rates of early invasive testing in stable patients with intermediate coronary stenosis (CAD-RADS 3), many of whom were either asymptomatic or not receiving guideline-directed medical therapy at baseline. With the growing utilization of coronary CTA (22–24), integration of CAD-RADS-guided recommendations into clinical practice may provide a novel opportunity to reduce over-referral for downstream ICA and promote more appropriate follow-up care among patients undergoing a diagnostic evaluation for CAD.

RATIONALE FOR STANDARDIZED REPORTING IN IMAGING. Standardized reporting is an important quality element of care within cardiovascular imaging (14). In 2006, proceedings from an American College of Cardiology Think Tank on Quality in Cardiovascular Imaging put forth the concept that only if the "right" procedure were performed and reported correctly could optimal post-imaging outcomes then be attained (14). Currently, all cardiac imaging modalities have documents for standardized reporting, which include integral components for image interpretation (e.g., resting heart rate, obstructive stenosis, radiation dose) (25–28). Recently, pre-test clinical indications for testing have been aggregated into

TABLE 3 Risk of Death or Myocardial Infarction by CAD-RADS

	Composite Outcome				All-Cause Mortality			
	Univariable HR (95% CI)	p Value	Multivariable* HR (95% CI)	p Value	Univariable HR (95% CI)	p Value	Multivariable* HR (95% CI)	p Value
CAD-RADS 0	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
CAD-RADS 1	2.45 (1.82–3.29)	<0.0001	2.46 (1.82–3.31)	<0.0001	2.04 (1.37–3.02)	<0.0001	1.81 (1.21–2.69)	0.0036
CAD-RADS 2	3.28 (2.48–4.34)	<0.0001	3.19 (2.40–4.24)	<0.0001	2.82 (1.95–4.06)	<0.0001	2.22 (1.52–3.23)	<0.0001
CAD-RADS 3	3.67 (2.81–4.80)	<0.0001	3.42 (2.59–4.51)	<0.0001	2.27 (1.55–3.33)	<0.0001	1.67 (1.12–2.49)	0.0107
CAD-RADS 4A	4.23 (3.30–5.43)	<0.0001	3.73 (2.87–4.86)	<0.0001	2.18 (1.51–3.14)	<0.0001	1.55 (1.05–2.28)	0.0264
CAD-RADS 4B	6.31 (4.46–8.93)	<0.0001	5.39 (3.76–7.73)	<0.0001	4.31 (2.59–7.17)	<0.0001	2.78 (1.64–4.71)	0.0001
CAD-RADS 5	7.11 (5.14–9.83)	<0.0001	6.09 (4.34–8.54)	<0.0001	4.71 (2.97–7.48)	<0.0001	3.09 (1.87–4.92)	<0.0001

TABLE 3 Continued

	Nonfatal MI			
	Univariable HR (95% CI)	p Value	Multivariable* HR (95% CI)	p Value
CAD-RADS 0	1.00	Reference	1.00	Reference
CAD-RADS 1	2.98 (1.89–4.71)	<0.0001	3.25 (2.15–4.91)	<0.0001
CAD-RADS 2	3.93 (2.55–6.05)	<0.0001	3.75 (2.50–5.64)	<0.0001
CAD-RADS 3	5.78 (3.89–8.58)	<0.0001	6.03 (4.18–8.70)	<0.0001
CAD-RADS 4A	7.19 (4.96–10.45)	<0.0001	6.87 (4.85–9.75)	<0.0001
CAD-RADS 4B	9.15 (5.58–15.01)	<0.0001	9.24 (5.87–14.55)	<0.0001
CAD-RADS 5	9.97 (6.23–15.94)	<0.0001	9.07 (5.79–14.20)	<0.0001

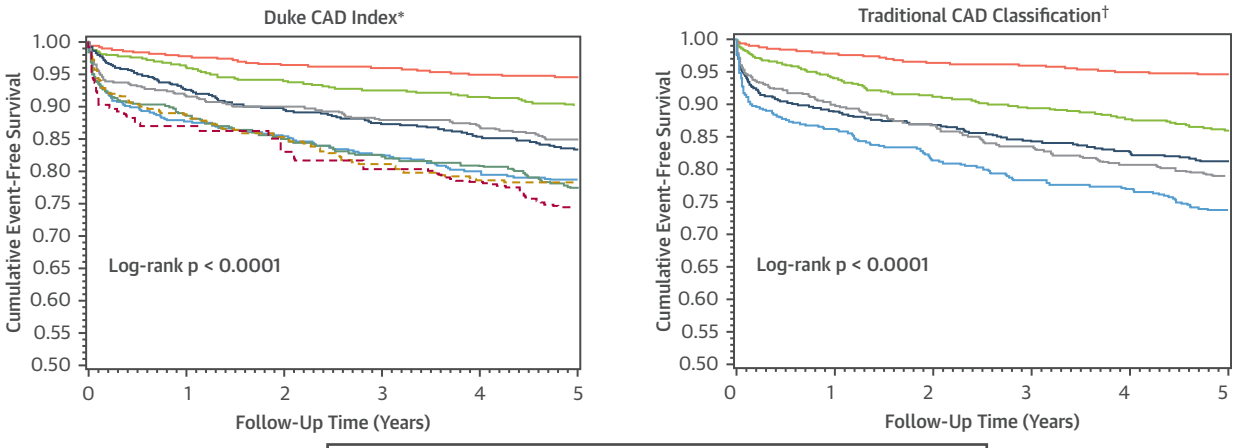
*Multivariable models were adjusted for patient age, sex, hypertension, diabetes, hyperlipidemia, smoking, and chest pain characteristics.
CAD-RADS = Coronary Artery Disease–Reporting and Data System; CI = confidence interval; HR = hazard ratio; MI = myocardial infarction.

multimodality AUC (i.e., appropriate, maybe appropriate, or rarely appropriate indications) (11). Goals of the AUC are to identify optimal candidates for an imaging procedure, to reduce unnecessary testing, and to improve efficiency in patient diagnosis (11). CAD-RADS can now extend these goals to provide guidance on clinical decision-making after noninvasive imaging and may provide an important bridge between test abnormalities and optimal patient care.

LINKING NONINVASIVE IMAGING WITH PATIENT OUTCOMES AND GUIDELINE-DIRECTED CARE. From the CONFIRM registry, CAD-RADS scores were strongly associated with death or MI, ranging from a 2- to 6-fold increase in risk with progressively higher scores compared to a normal coronary CTA. We further found that CAD-RADS provided similar discrimination for future events compared to the Duke CAD Prognostic Index and the traditional CAD reporting method. Although accurate identification of patient risk remains vital for therapeutic decision-making, an imaging procedure in and of itself does not directly improve clinical outcomes. A critical link must be established between an abnormal imaging finding and post-test management with risk-reducing therapies to ultimately impact patient outcomes. However, clinical practice guidelines have frequently lacked specific details for appropriate care based on noninvasive imaging results, and, as a result, evidence-based recommendations are often not implemented by referring physicians, despite abnormal anatomic or functional testing (15,29,30). From the Study of Myocardial Perfusion and Coronary Anatomy Imaging Roles in CAD (SPARC) registry, only 62% of patients with severe abnormalities detected on coronary CTA had a guideline-supported ICA within 90 days (31), similar to the rates of early ICA we observed among CAD-RADS 4B and 5 patients. Thus, the current status quo in coronary CTA reporting has not uniformly or consistently translated to guideline-directed patient management, as considerable heterogeneity exists in the interpretation of "obstructive" CAD and post-coronary CTA patient care, particularly with the use of invasive angiography. CAD-RADS not only has the capability of providing accurate prognostic information that can be easily conveyed to physicians using standardized and clinically intuitive coronary CTA definitions, but it could also, for the first time, serve as a clinical decision support tool by including actionable, guideline-directed recommendations for each score within the coronary CTA report.

Our study specifically highlights the frequent and early use of ICA in lower-risk patients. Almost 40% of patients who were referred for ICA within 30 days did not have severe obstructive CAD based on

FIGURE 2 Event-Free Survival by Other CAD Classification Indices



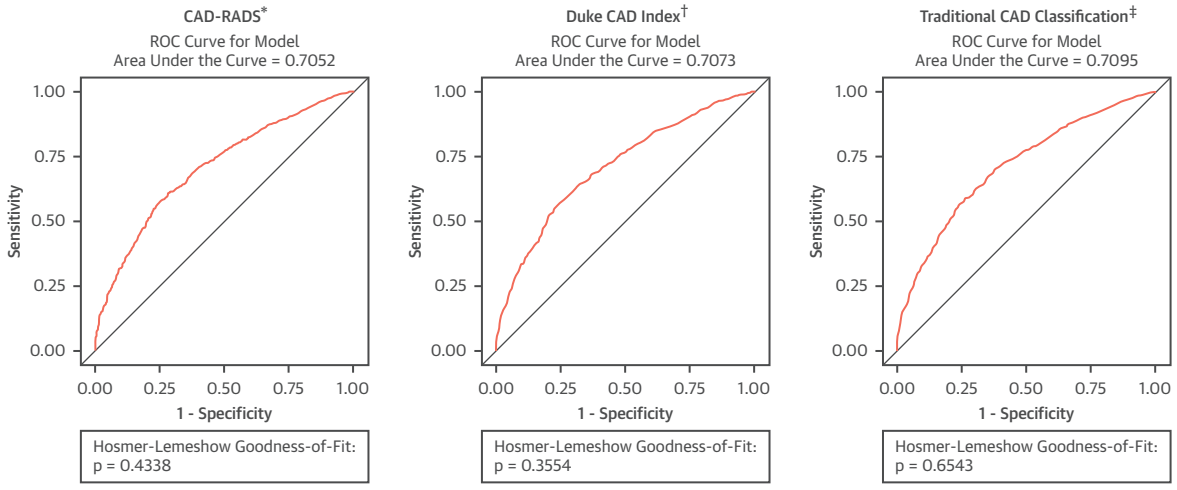
5-Year Event-Free Survival Rates			
Duke CAD Index		**Traditional CAD Classification**	
Duke CAD 0	94.50%	No CAD	94.50%
Duke CAD 1	90.20%	Nonobstructive CAD	95.90%
Duke CAD 2	83.30%	1-Vessel Obstructive CAD	81.10%
Duke CAD 3	84.90%	2-Vessel Obstructive CAD	78.90%
Duke CAD 4	78.60%	3-Vessel/LM Obstructive CAD	73.80%
Duke CAD 5	77.40%		
Duke CAD 6	78.20%		
Duke CAD 7	74.40%		

Cumulative 5-year event-free survival from death or myocardial infarction displayed across the Duke CAD Index and traditional CAD classification. *The Duke CAD Index is defined as follows: 0 = 0% stenosis in all vessels; 1 = 1% to 24% stenoses or at most 1 with 25% to 49% stenosis; 2 = ≥2 stenoses 25% to 49%; 3 = 1 vessel with 50% to 69% stenosis; 4 = 2 stenoses 50% to 69% or 1 vessel with ≥70% stenosis; 5 = 3 stenoses 50% to 69% or 2 vessels with ≥70% stenosis or proximal left anterior descending stenosis ≥70%; 6 = 3 vessels ≥70% stenoses or 2 vessels with ≥70% stenosis with proximal left anterior descending; 7 = left main stenosis ≥50%. †Traditional CAD classification is defined as follows: no CAD, nonobstructive (<50% stenosis) CAD, 1-vessel obstructive (≥50% stenosis) CAD, 2-vessel obstructive CAD, or 3-vessel/obstructive LM CAD. CAD = coronary artery disease; LM = left main.

coronary CTA. Notably, nearly 30% of these patients underwent the index coronary CTA under rarely appropriate indications (because of low pre-test probability or global CAD risk), which illustrates how a nonguideline-supported study may be further compounded by additional unnecessary downstream testing. In the United Kingdom's National Institute of Health and Care Excellence stable chest pain pathway guidance document, coronary CTA has been recommended as a frontline procedure, with recent evidence showing significant cost savings and a nearly 50% reduction in the need for follow-up testing (32). Based on the CONFIRM registry findings, it remains plausible that follow-up or layered testing could also be substantially reduced after implementation of CAD-RADS into coronary CTA reporting.

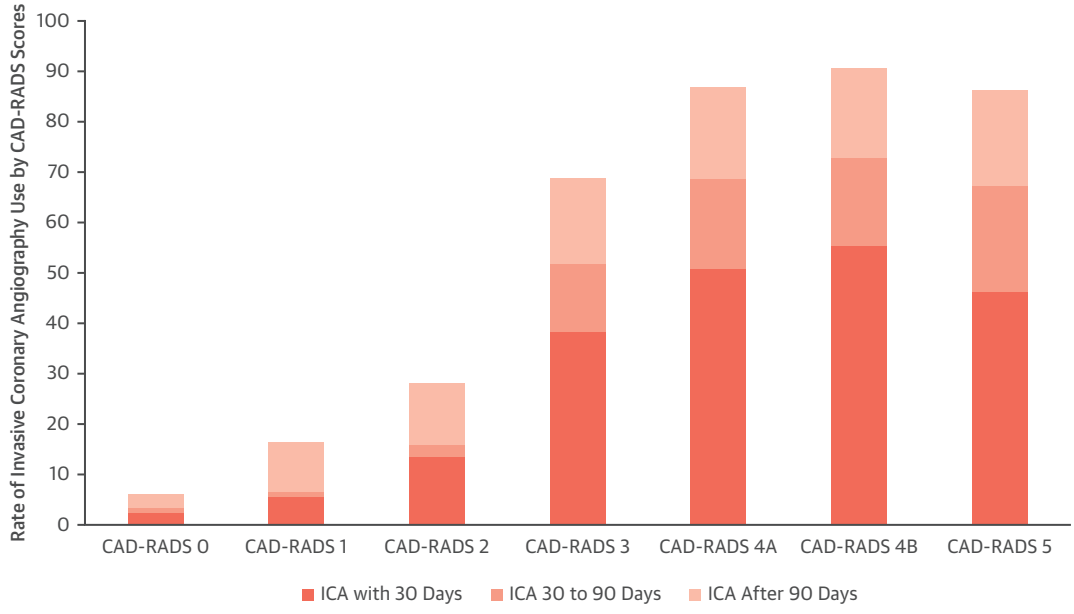
In particular, CAD-RADS may be a valuable aid in guiding post-coronary CTA care of patients with intermediate CAD stenosis (CAD-RADS 3). More than one-half of all catheterizations in CAD-RADS 3 patients occurred within the first 30 days of follow-up, and the majority of these 30-day ICAs occurred in patients who were either asymptomatic or not receiving any antianginal therapy at baseline. These results suggest that many patients who could potentially be managed conservatively by SIHD guidelines are undergoing invasive angiography soon after coronary CTA and likely before adequate trials of medical therapy. Although we were unable to prospectively assess changes in medical therapy after coronary CTA, several recent trials have found that only ~10% of patients had a modification or intensification of anti-ischemic therapy after abnormal stress testing (4,31). Other studies have also reported that less than one-half (44%) of patients with SIHD were receiving optimal medical therapy before catheterization (33). As such, we propose that CAD-RADS may provide a unique opportunity to directly link coronary CTA findings with current SIHD recommended care, including more appropriate selection of patients for additional testing and optimization of medical therapy, especially for the large proportion of stable patients

FIGURE 3 ROC Curves for Prediction of All-Cause Mortality or Myocardial Infarction



Receiver-operating characteristic (ROC) curves, area under the ROC curve, and Hosmer-Lemeshow goodness-of-fit tests for each model to predict the composite outcome of death or nonfatal myocardial infarction. *CAD-RADS = model contains CAD-RADS plus age, sex, hypertension, hyperlipidemia, diabetes, smoking history, and chest pain characteristics. †Duke CAD Index = model contains the Duke CAD Index, as defined previously, plus age, sex, hypertension, hyperlipidemia, diabetes, smoking history, and chest pain characteristics. ‡Traditional CAD classification = model contains the traditional CAD classification, as defined previously, plus age, sex, hypertension, hyperlipidemia, diabetes, smoking history, and chest pain characteristics. Abbreviations as in Figures 1 and 2.

FIGURE 4 Use of ICA After Coronary CTA by CAD-RADS Scores



Rates of ICA use at 30 days, 90 days, and throughout 5-year follow-up after coronary CTA shown across CAD-RADS scores. CAD-RADS = Coronary Artery Disease-Data and Reporting System; CTA = computed tomography angiography; ICA = invasive coronary angiography.

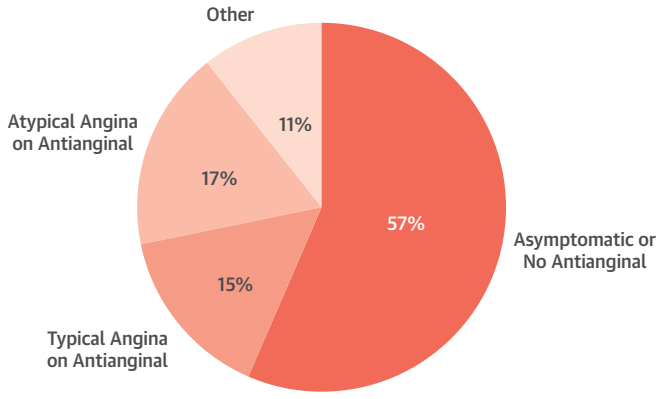
without severe CAD. Whether the prospective use of CAD-RADS would impact medical therapy and downstream ICA use requires additional investigation.

STUDY LIMITATIONS. Our study did not include CAD-RADS modifiers to describe patients with vulnerable plaque features (modifier V), stents (modifier S), or grafts (modifier G), as we restricted our analysis to stable patients without previously known CAD. Both external and prospective validation of our results remain to be performed, including additional studies among patients with known CAD, those with previous revascularization, and patients presenting for acute evaluation in the emergency department. In addition, CAD-RADS does not take into account lesion location, such as differentially weighing coronary stenosis in the left anterior descending artery or proximal versus distal vessel disease, which may have provided further prognostic information; the performance of CAD-RADS should be compared to other coronary CTA-derived CAD scores beyond the Duke CAD Index in additional validation studies. A chronic total occlusion (e.g., CAD-RADS 5) may also have varying clinical significance based on lesion acuity, length, collateralization, or the severity and extent of co-occurring CAD; additional revisions to the CAD-RADS classification scheme could be considered in the future. Finally, the CONFIRM registry had limited data on medication usage or additional functional testing after coronary CTA, which may have affected the observed ICA and revascularization rates across CAD-RADS scores or downstream patient outcomes. However, the aim of our analysis was to identify "real-world" patterns of post-coronary CTA care and not to validate current CAD-RADS recommendations. The impact of medication optimization, functional assessment, and other recommendations by CAD-RADS scores should be examined in future studies.

CONCLUSIONS

CAD-RADS provided important prognostic information for patients undergoing noninvasive evaluation of CAD in a real-world registry. Our study also identified the potential for improved point-of-testing management decisions with CAD-RADS recommendations, particularly among patients with less severe CAD. The integration of CAD-RADS into daily coronary CTA laboratory reporting may provide a means to promote appropriate, guideline-driven follow-up care, thereby augmenting the quality of coronary CTA-directed evaluation of SIHD.

FIGURE 5 Distribution of Baseline Symptoms and Medical Therapy Among CAD-RADS 3 Patients Undergoing 30-Day ICA



Distribution of presenting symptoms and baseline medications for CAD-RADS 3 patients who underwent 30-day ICA. Categories include patients who were asymptomatic or not taking any antianginal drug (including beta-blocker, calcium-channel blocker, or nitrate); patients with typical angina taking at least 1 antianginal drug; patients with atypical angina taking at least 1 antianginal drug; or other (any noncardiac chest pain or asymptomatic on antianginal therapy). Abbreviations as in Figures 1 and 4.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Standardized coronary CTA-derived definitions for CAD severity using CAD-RADS were strongly associated with risk for death or MI. High referral rates for early ICA were also identified among patients without severe CAD. As such, CAD-RADS–directed recommendations for post–coronary CTA management may provide a novel opportunity to improve evidence-based care after a noninvasive imaging study.

TRANSLATIONAL OUTLOOK: Standardized coronary CTA reporting with CAD-RADS not only allows for accurate communication of patient prognosis but may also be an important mechanism to link coronary CTA findings with appropriate follow-up care.

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KEY WORDS appropriate use, clinical decision support, coronary computed tomography angiography, prognosis

APPENDIX For a supplemental table and figure, please see the online version of this paper.