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Journal

JACC Cardiovascular Imaging, 8(4)

ISSN

1936-878X

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Publication Date

2015-04-01

DOI

10.1016/j.jcmg.2014.11.015

Peer reviewed

A Clinical Model to Identify Patients With High-Risk Coronary Artery Disease

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ABSTRACT

OBJECTIVES This study sought to develop a clinical model that identifies patients with and without high-risk coronary artery disease (CAD).

BACKGROUND Although current clinical models help to estimate a patient's pre-test probability of obstructive CAD, they do not accurately identify those patients with and without high-risk coronary anatomy.

METHODS Retrospective analysis of a prospectively collected multinational coronary computed tomographic angiography (CTA) cohort was conducted. High-risk anatomy was defined as left main diameter stenosis $\geq 50\%$, 3-vessel disease with diameter stenosis $\geq 70\%$, or 2-vessel disease involving the proximal left anterior descending artery. Using a cohort of 27,125, patients with a history of CAD, cardiac transplantation, and congenital heart disease were excluded. The model was derived from 24,251 consecutive patients in the derivation cohort and an additional 7,333 nonoverlapping patients in the validation cohort.

RESULTS The risk score consisted of 9 variables: age, sex, diabetes, hypertension, current smoking, hyperlipidemia, family history of CAD, history of peripheral vascular disease, and chest pain symptoms. Patients were divided into 3 risk categories: low (≤ 7 points), intermediate (8 to 17 points) and high (≥ 18 points). The model was statistically robust with area under the curve of 0.76 (95% confidence interval [CI]: 0.75 to 0.78) in the derivation cohort and 0.71 (95% CI: 0.69 to 0.74) in the validation cohort. Patients who scored ≤ 7 points had a low negative likelihood ratio (< 0.1), whereas patients who scored ≥ 18 points had a high specificity of 99.3% and a positive likelihood ratio (8.48). In the validation group, the prevalence of high-risk CAD was 1% in patients with ≤ 7 points and 16.7% in those with ≥ 18 points.

CONCLUSIONS We propose a scoring system, based on clinical variables, that can be used to identify patients at high and low pre-test probability of having high-risk CAD. Identification of these populations may detect those who may benefit from a trial of medical therapy and those who may benefit most from an invasive strategy. (J Am Coll Cardiol Img 2015;■:■-■) © 2015 by the American College of Cardiology Foundation.

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**ABBREVIATIONS
AND ACRONYMS****CAD** = coronary artery disease**CTA** = computed tomographic angiography**HRA** = high-risk anatomy**ICA** = invasive coronary angiography**ROC** = receiver operating characteristic

The diagnosis and subsequent stratification of patients with suspected coronary artery disease (CAD) are important to management. Traditionally, patients with CAD are categorized according to the presence and absence of high-risk coronary anatomy because those patients with high-risk CAD often derive the greatest mortality benefit with revascularization (1-3). Conversely, a trial of optimal medical therapy may be appropriate for those patients with non-high-risk CAD (4).

The current standard for the anatomic diagnosis of CAD is invasive coronary angiography (ICA); however, ICA is expensive and has associated procedural hazards (5). Therefore, it would be desirable to identify patients at greatest probability of high-risk CAD who require further investigations and those patients with low probability of high-risk CAD in whom a trial of optimal medical therapy may be appropriate. Current clinical models estimate a patient's pre-test probability for obstructive CAD, but they do not accurately predict the presence or absence of high-risk CAD (left main coronary artery diameter stenosis $\geq 50\%$, 3-vessel disease [diameter stenosis $\geq 70\%$] or 2-vessel disease involving the proximal left anterior descending artery). Previous models have defined significant CAD as ≥ 1 vessel with a $\geq 50\%$ or $\geq 75\%$ lesion (6-8). To our knowledge, no studies have examined models to ascertain likelihood of 'high-risk coronary anatomy'. This is most relevant given recent evidence that optimal medical therapy is a reasonable treatment option in patients with CAD.

Using a large, prospective international registry of patients referred to coronary computed tomographic angiography (CTA) for suspected CAD, this study sought to develop a clinical model to identify the presence and absence of high-risk CAD.

METHODS

PATIENTS AND EXCLUSION CRITERIA. Patients referred to coronary CTA for suspected CAD were included in the study. Patients with documented CAD or a history of myocardial infarction, coronary revascularization, cardiac transplantation, and congenital heart disease were excluded from analysis. Between 2005 and 2009, 27,125 consecutive adult patients ≥ 18 years old who were undergoing ≥ 64 -detector row coronary CTA were prospectively enrolled into the CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter) registry and were used for the derivation cohort (9). Using the same inclusion and exclusion criteria, an additional nonoverlapping cohort (comprising the CONFIRM validation cohort and the University of Ottawa Heart Institute Cardiac CT Registry) of 7,333 patients was used as a validation cohort.

Each center obtained approval from the Institutional Review Board, and all patients provided informed consent for study participation.

CLINICAL DEFINITIONS. At the time of coronary CTA, medical history and available laboratory results were recorded for all patients (6,10). A detailed description of the methods has been previously published (9). Symptoms were analyzed according to the criteria for angina pectoris, in which patients with typical angina exhibited all 3 characteristics (chest pain, onset with exertion, improvement with rest) and atypical angina with any 1 or 2 characteristics (6).

Hypertension was defined as a known history of systolic blood pressure >140 mm Hg or treatment with antihypertensive medications. Diabetes mellitus was defined as a previous diagnosis of diabetes or use of oral hypoglycemic drugs or insulin. Dyslipidemia was defined as a known history of dyslipidemia or

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Manuscript received September 18, 2014; accepted November 10, 2014.

treatment with lipid-lowering agents. Family history of premature CAD was defined as a first-degree relative with myocardial infarction (<55 years for men, <65 years for women). The CONFIRM registry used standardized definitions of cardiovascular risk factors for data collection to minimize differences among centers (9,10). Sites with at least 80% overlap with predefined data dictionary were enrolled into the CONFIRM registry, and they had uniform collection of major categories of patient information including demographics and cardiovascular risk factors (9).

To compare our model with existing models, the pre-test probability of obstructive CAD ($\geq 50\%$ diameter stenosis) was calculated for each patient according to age, sex, and type of chest pain by using the updated Diamond-Forrester model (11).

CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY.

Coronary CTA image acquisition and interpretation, as previously described, were performed according to clinical routine at each participating center using single- or dual-source 64-slice CT scanners (9). Coronary artery diameter stenosis was graded using a 4-point score (normal or mild, <50%; moderate, 50% to 69%; or severe, $\geq 70\%$) (12). Patients were further categorized according to the presence and absence of high-risk CAD, defined as left main coronary artery stenosis ($\geq 50\%$), 3-vessel disease ($\geq 70\%$), or 2-vessel disease ($\geq 70\%$) involving the proximal left anterior descending artery (13,14). Previous study has shown that coronary CTA is a highly specific and sensitive method for detecting high-risk anatomy compared with ICA (sensitivity, 100%; specificity, 95%) (15).

STATISTICAL ANALYSIS. Statistical analysis was performed using SAS 9.2 software (version 9.2, SAS Institute Inc., Cary, North Carolina). Statistical significance was defined as $p < 0.05$. Continuous variables were presented as means and standard deviations, and categorical variables were presented as frequencies with percentages. To compare patients' characteristics, Student *t* test was used for continuous variables and chi-square test was used for categorical variables.

All clinical variables potentially associated with high-risk coronary anatomy were evaluated. Medications and diagnostic tests were excluded to obtain a model based entirely on clinical history. Variables for which more than 10% of data was missing were not included in the analysis (cerebrovascular disease). Using these criteria, the variables of age, sex, symptoms, diabetes, current smoking, family history of cardiovascular disease, hypertension, body mass

index, hyperlipidemia and history of peripheral vascular disease were identified for univariable analysis. Variables statistically significant in the univariable analysis (defined as $p < 0.1$ to include more variables) were included in a multivariable logistic regression model. Interaction between sex and other variables in the multivariable model was examined to explore for differences between male and female patients. From this model, a scoring system was developed by assigning points for each variable using the method demonstrated by the Framingham Risk Score (16). The classification performance of this score was evaluated using sensitivity, specificity, positive or negative predictive values, and likelihood ratios with 95% confidence interval (CI) by applying this score in the derivation cohort. The receiver operating characteristic (ROC) curves for the score were generated. The area under the ROC curve with 95% CI was calculated to evaluate the discrimination ability of the score over the updated Diamond-Forrester model in predicting high-risk CAD by using method proposed by DeLong et al. (17). To assess the applicability of the score to a population with a higher clinical risk, the model was also applied to a subgroup of symptomatic patients (with either chest pain or dyspnea) in the derivation cohort. The calibration of the score was assessed using the Hosmer-Lemeshow statistic, where $p < 0.05$ indicates an inadequate fit. The prediction accuracy and classification performance of the score were also validated using an external validation cohort.

RESULTS

A total of 35,711 consecutive patients (derivation cohort, 27,125 patients; and validation cohort, 8,586 patients) from 12 sites in 6 countries across North America, Europe, and Asia were screened. Excluding patients with a history of coronary revascularization, cardiac transplantation, myocardial infarction, or congenital heart disease (2,874 patients), the derivation cohort comprised 24,251 patients, with 3.6% (877) patients with high-risk CAD. Of these, 14,142 patients were symptomatic with either chest pain or shortness of breath. Results of the derivation cohort were validated in an external validation set consisting of 7,333 patients, after excluding 1,253 patients for missing data (Table 1); 4.8% (349) of patients in the validation cohort had high-risk CAD.

DERIVATION COHORT. Using univariable analysis, age, sex, hyperlipidemia, hypertension, diabetes, current smoking, family history, history of peripheral vascular disease and chest pain symptoms were associated with high-risk CAD and used in a

TABLE 1 Clinical Characteristics of Derivation and Validation Cohorts

	Derivation Cohort		Validation Cohort	
	High-Risk CAD N = 877	Non-High-Risk CAD N = 23,374	High-Risk CAD N = 349	Non-High-Risk CAD N = 6984
Mean age	66.0 ± 10.5	57.2 ± 12.6	63.8 ± 10.3	57.3 ± 11.7
Mean BMI	27.6 ± 5.0	27.5 ± 5.3	27.6 ± 4.9	28.8 ± 7.0
Male	616 (70.2%)	12,537 (53.6%)	242 (69.3%)	3,671 (52.6%)
Hypertension	546 (62.3%)	11,563 (49.5%)	241 (69.1%)	3,799 (54.4%)
Diabetes	227 (25.9%)	3,340 (14.3%)	136 (39.0%)	1,393 (20.0%)
Hyperlipidemia	578 (65.9%)	12,753 (54.6%)	199 (57.0%)	3,591 (51.4%)
Current smoking	201 (22.9%)	4,101 (17.6%)	86 (24.6%)	1,313 (18.8%)
PVD history	37 (4.2%)	373 (1.6%)	14 (4.0%)	217 (3.1%)
Symptoms				
Asymptomatic	217 (24.7%)	7,536 (32.2%)	103 (29.5%)	2,316 (33.2%)
Atypical	447 (50.4%)	12,423 (53.1%)	155 (44.4%)	3,509 (50.2%)
Typical	213 (24.3%)	3,415 (14.6%)	91 (26.1%)	1,159 (16.6%)
Family history of CAD	420 (47.9%)	8,448 (36.1%)	98 (28.1%)	2,752 (39.4%)
Ethnicity				
Caucasian	315 (35.9%)	7,154 (30.6%)	N/A	N/A
African	19 (2.17%)	885 (3.79%)		
Latin America	39 (4.4%)	317 (1.62%)		
East Asian	62 (7.07%)	4,244 (18.2%)		
South Asian	2 (0.23%)	62 (0.27%)		
Middle Eastern	12 (1.37%)	148 (0.63%)		
Other/mixed	0	92 (0.39%)		
Unknown	428 (48.8%)	10,472 (44.8%)		

Values are mean ± SD or n (%).
BMI = body mass index; CAD = coronary artery disease; N/A = not available; PVD = peripheral vascular disease.

multivariable logistic analysis to generate the final model (Table 2). Interaction between sex and other variables was examined and was found to be insignificant. Points for each variable were assigned based on its regression coefficient to generate a scoring system (Table 3). Using the score from -1 to 25, the predictive probability of high-risk CAD ranged from 0.1% (95% CI: 0.1 to 0.1) to 51.1% (95% CI: 45.6 to 56.6). The diagnostic value for each threshold of high-risk CAD score was calculated (Table 4). Based on positive and negative likelihood ratios, 3 categories

TABLE 2 Multivariable Model for High-Risk CAD

	Beta	Standard Error	Odds Ratio	Lower CI	Upper CI	p Value
Age	0.067	0.003	1.069	1.063	1.076	<0.001
Male	1.008	0.078	2.739	2.350	3.192	<0.001
Diabetes	0.528	0.083	1.695	1.440	1.995	<0.001
Hyperlipidemia	0.221	0.076	1.248	1.076	1.447	0.003
Hypertension	0.133	0.076	1.143	0.985	1.325	0.077
Current smoking	0.516	0.087	1.675	1.414	1.985	<0.001
Symptoms	0.211	0.033	1.235	1.158	1.317	<0.001
Family history	0.600	0.072	1.822	1.584	2.096	<0.001
PVD	0.633	0.185	1.883	1.310	2.708	<0.001

CAD = coronary artery disease; CI = confidence interval; PVD = peripheral vascular disease.

TABLE 3 Scoring Method*

	Points
Age, yrs	
<30	-1
30-39	0
40-49	2
50-59	4
60-69	6
70-79	8
≥80	10
Male	3
Symptoms	
Asymptomatic	0
Nonanginal/atypical chest pain	1
Typical angina	2
Family history of CAD	
History of PVD	
Diabetes	2 (each)
Current smoking	
Hyperlipidemia	
Hypertension	1 (each)

*Clinical probability: low risk, ≤7 points; intermediate risk, 8-17 points; high risk, ≥18 points.

were derived: low (≤7 points), intermediate (8 to 17 points), and high (≥18 points), and the prevalence of CAD was calculated for each probability group (Table 5). Patients who scored ≤7 points had a high negative predictive value (99.7%) and a very low negative likelihood ratio for high-risk CAD (<0.1) (Table 4). Conversely, patients who scored ≥18 points had a high specificity of 99.3% for high-risk CAD with a high positive likelihood ratio of 8.48 (Table 4). The Hosmer-Lemeshow statistic suggests that fit of model was adequate for the derivation cohort (p > 0.05).

Using the derivation cohort, the proposed model for predicting presence of high-risk CAD had an area under ROC curve of 0.76 (95% CI: 0.75 to 0.78) and was significantly better than the updated Diamond-Forrester model (0.64 [95% CI: 0.62 to 0.67], p < 0.001) (Figure 1). The model was applied in a subgroup of 14,142 symptomatic patients, and the area under the ROC curve was similar with 0.78 (95% CI: 0.76 to 0.79). Calibration of the score was acceptable at low and intermediate score values, but it decreased at higher score values because of the small number of cases (Figure 2).

VALIDATION COHORT. In an external validation set of nonoverlapping patients comprising the CONFIRM validation cohort and the University of Ottawa Heart Institute Cardiac CT Registry, the model was robust with an area under the curve of 0.71 (95% CI: 0.69 to 0.74) (Figure 3). The accuracy of the score and the

TABLE 4 Operating Characteristics for Each Threshold of High-Risk CAD Score in Derivation Cohort

Score	Sensitivity 95% CI	Specificity 95% CI	PPV 95% CI	NPV 95% CI	PLR 95% CI	NLR 95% CI
-1	1.000	0.000	0.036 (0.034-0.039)	—	1.000	—
0	1.000	0.000	0.036 (0.034-0.039)	—	1.000	—
1	0.999 (0.997-1.000)	0.003 (0.002-0.004)	0.036 (0.034-0.039)	0.985 (0.957-1.000)	1.002 (0.999-1.004)	0.398 (0.055-2.862)
2	0.999 (0.997-1.000)	0.009 (0.008-0.010)	0.036 (0.034-0.039)	0.995 (0.986-1.000)	1.008 (1.005-1.010)	0.131 (0.018-0.936)
3	0.999 (0.997-1.000)	0.018 (0.017-0.020)	0.036 (0.034-0.039)	0.998 (0.993-1.000)	1.018 (1.015-1.021)	0.062 (0.009-0.439)
4	0.999 (0.997-1.000)	0.042 (0.039-0.044)	0.038 (0.035-0.040)	0.999 (0.997-1.000)	1.042 (1.039-1.046)	0.027 (0.004-0.194)
5	0.999 (0.997-1.000)	0.070 (0.067-0.073)	0.039 (0.036-0.041)	0.999 (0.998-1.000)	1.074 (1.070-1.079)	0.016 (0.002-0.116)
6	0.992 (0.986-0.998)	0.122 (0.118-0.126)	0.041 (0.038-0.043)	0.998 (0.996-0.999)	1.130 (1.121-1.138)	0.066 (0.031-0.137)
7	0.984 (0.976-0.992)	0.193 (0.188-0.198)	0.044 (0.041-0.047)	0.997 (0.995-0.999)	1.219 (1.206-1.232)	0.083 (0.049-0.139)
8	0.964 (0.951-0.976)	0.283 (0.277-0.289)	0.048 (0.045-0.051)	0.995 (0.994-0.997)	1.344 (1.324-1.365)	0.129 (0.092-0.181)
9	0.927 (0.910-0.944)	0.391 (0.385-0.397)	0.054 (0.050-0.058)	0.993 (0.991-0.995)	1.522 (1.490-1.555)	0.187 (0.147-0.236)
10	0.877 (0.855-0.899)	0.505 (0.498-0.511)	0.062 (0.058-0.067)	0.991 (0.989-0.993)	1.771 (1.722-1.821)	0.244 (0.204-0.291)
11	0.774 (0.747-0.802)	0.623 (0.617-0.629)	0.072 (0.066-0.077)	0.987 (0.985-0.988)	2.054 (1.975-2.137)	0.362 (0.320-0.410)
12	0.650 (0.618-0.682)	0.728 (0.723-0.734)	0.082 (0.076-0.089)	0.982 (0.980-0.984)	2.391 (2.268-2.521)	0.481 (0.439-0.526)
13	0.513 (0.480-0.546)	0.818 (0.813-0.823)	0.095 (0.087-0.104)	0.978 (0.976-0.980)	2.812 (2.622-3.016)	0.596 (0.556-0.638)
14	0.396 (0.363-0.428)	0.889 (0.885-0.893)	0.118 (0.106-0.129)	0.975 (0.973-0.977)	3.554 (3.250-3.887)	0.680 (0.645-0.718)
15	0.257 (0.228-0.286)	0.937 (0.934-0.940)	0.132 (0.116-0.149)	0.971 (0.969-0.973)	4.068 (3.597-4.601)	0.794 (0.76-0.825)
16	0.166 (0.142-0.191)	0.967 (0.965-0.969)	0.160 (0.136-0.184)	0.969 (0.966-0.971)	5.067 (4.302-5.967)	0.862 (0.837-0.888)
17	0.105 (0.085-0.125)	0.985 (0.984-0.987)	0.209 (0.171-0.247)	0.967 (0.965-0.969)	7.026 (5.641-8.751)	0.909 (0.888-0.930)
18	0.056 (0.041-0.071)	0.993 (0.992-0.994)	0.241 (0.183-0.300)	0.966 (0.963-0.968)	8.480 (6.193-11.612)	0.950 (0.935-0.966)
19	0.027 (0.017-0.038)	0.998 (0.997-0.998)	0.316 (0.211-0.420)	0.965 (0.962-0.967)	12.301 (7.620-19.859)	0.975 (0.964-0.986)
20	0.010 (0.004-0.017)	0.999 (0.999-1.000)	0.300 (0.136-0.464)	0.964 (0.962-0.967)	11.422 (5.247-24.867)	0.991 (0.984-0.997)
21	0.007 (0.001-0.012)	1.000	0.462 (0.191-0.733)	0.964 (0.962-0.966)	22.845 (7.694-67.834)	0.994 (0.988-0.999)
22	0.000	1.000	0.000	0.964 (0.962-0.966)	—	1.000

CAD = coronary artery disease; CI = confidence interval; NLR = negative likelihood ratio; NPV = negative predictive value; PLR = positive likelihood ratio; PPV = positive predictive value.

proportion of patients classified into each probability category were similar to those of the derivation group (Table 5). The calibration of the score was also similar in both derivation and validation groups (Figure 2).

DISCUSSION

This study derived a scoring system to predict high-risk CAD in patients with suspected CAD, and it includes variables that can be easily obtained from a patient's history. These variables are similar to other clinical models used to predict obstructive CAD (e.g., Morise, Duke, and Diamond-Forrester scores), but our current variables were developed in a diverse population from multiple centers, thereby validating the model's applicability (6-8). This model appears to be most useful in identifying those patients with the greatest likelihood of having "high-risk coronary anatomy," thereby identifying a group that could benefit most from ICA with or without fractional flow reserve measurements. All other symptomatic patients could potentially be diagnosed and stratified using available noninvasive modalities such as coronary CTA, perfusion imaging, or stress echocardiography.

PROBABILITY OF HIGH-RISK CORONARY ARTERY DISEASE.

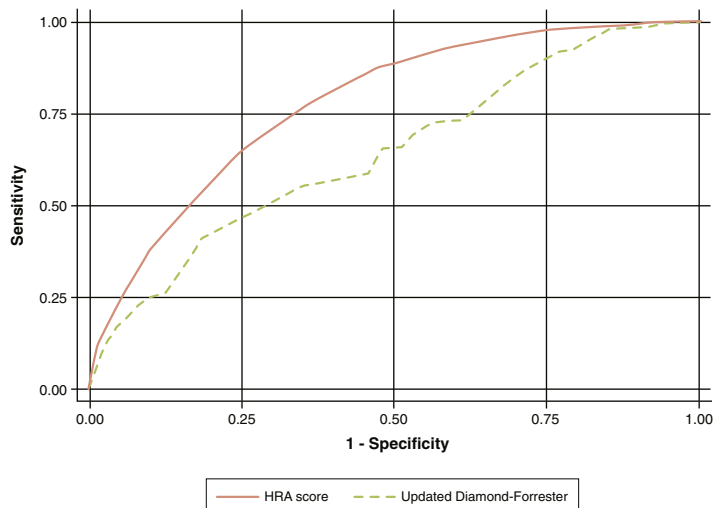
High-risk CAD is associated with more frequent adverse events, and these patients typically derive the greatest benefit from revascularization (18-23). Clinical trials have shown that, compared with medical therapy, coronary artery bypass graft significantly improves survival of patients with high-risk CAD (1,2,24). Therefore, patients with a high probability of high-risk CAD should be considered for definitive anatomic imaging (e.g., invasive angiography) and possible revascularization. Conversely,

TABLE 5 Proportion of Patients Classified by High-Risk CAD Score in Each Clinical Probability Category and Predictive Accuracy of the Score

Clinical Probability	Derivation Cohort		Validation Cohort	
	Patients	Patients With Confirmed HRA	Patients	Patients With Confirmed HRA
Low (≤ 7)	6,651 (27.4)	32 (0.5)	1,738 (23.7)	17 (1.0)
Intermediate (8-17)	17,397 (71.7)	796 (4.6)	5,547 (75.6)	324 (5.8)
High (≥ 18)	203 (0.8)	49 (24.1)	48 (0.7)	8 (16.7)
All	24,251	877 (3.6)	7,333	349 (4.8)

Values are n (%).
CAD = coronary artery disease; HRA = high-risk anatomy.

FIGURE 1 ROC Curves Comparing Model's Ability to Predict High-Risk CAD With Updated Diamond-Forrester Model in Derivation Cohort



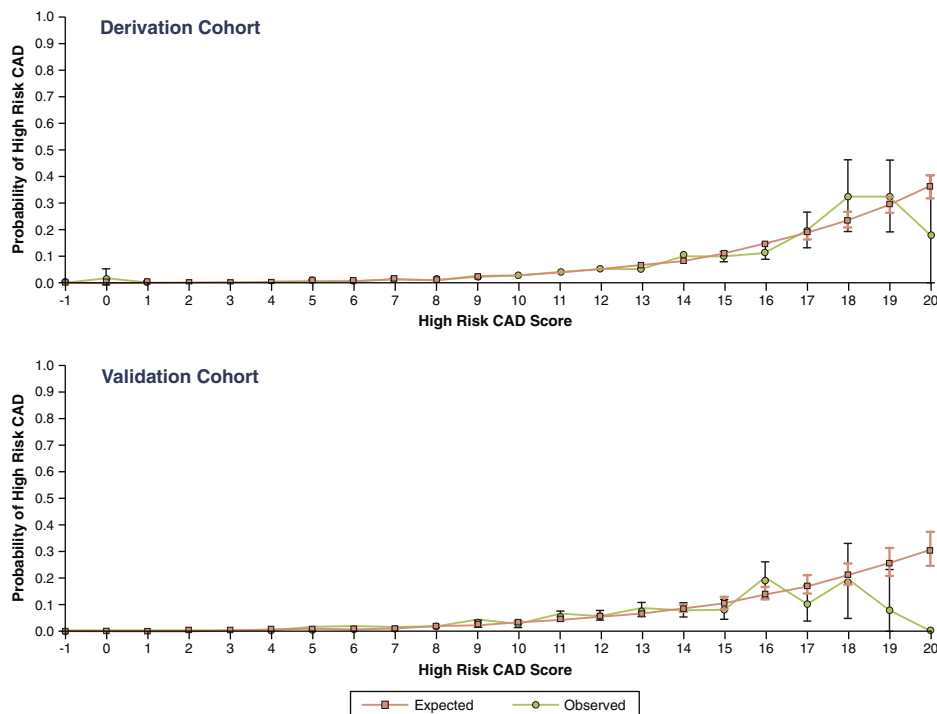
Our model had an area under the receiver operating characteristic (ROC) curve of 0.76, which was significantly better than the modified Diamond-Forrester model in predicting high-risk coronary artery disease (CAD). HRA = high risk anatomy.

patients with a low probability of high-risk CAD may be initially treated with optimal medical therapy (4). The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial compared outcomes of non-high-risk CAD patients treated with medical therapy or with percutaneous coronary intervention coupled with medical therapy and concluded that revascularization did not significantly reduce mortality or other adverse cardiovascular events in these patients (4). Patients with an intermediate probability of high-risk CAD should be further investigated and stratified noninvasively.

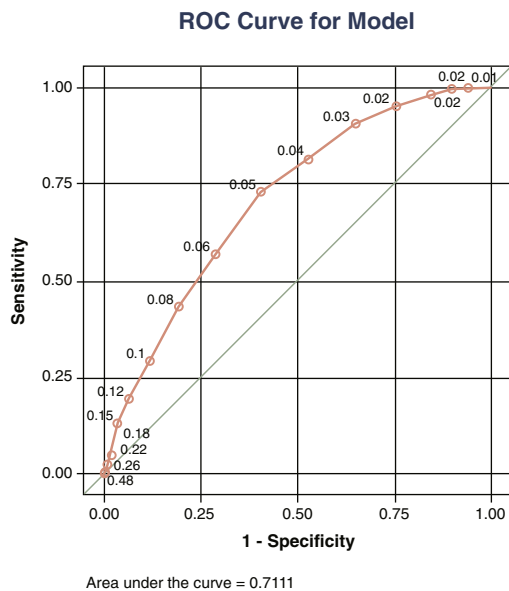
Our model contains 9 variables derived from 877 events, is sufficiently robust, and was validated in an independent cohort with similar results (25). The performance of our scoring system is compared with the updated Diamond-Forrester model in predicting CAD, and our model performs significantly better, with nonoverlapping CI.

This study population consists of patients with stable CAD who were referred for coronary CTA, a highly specific and sensitive method for detecting coronary artery stenosis (15). In fact, a meta-analysis suggests that coronary CTA should be used to rule

FIGURE 2 Observed Versus Expected Probability of High-Risk CAD Score in Derivation and Validation Cohorts



Observed and expected probabilities of high-risk coronary artery disease (CAD) were similar for low and intermediate scores and decreased at higher scores, likely from the small number of cases. Our model was able to predict high-risk CAD with similar accuracy in both derivation and validation groups.

FIGURE 3 ROC Curves of High-Risk CAD Score in Validation Cohort

The area under receiver operating characteristic (ROC) curve in the external validation group was robust at 0.71 (95% confidence interval: 0.69 to 0.74), confirming applicability of the model. CAD = coronary artery disease.

out obstructive CAD in patients with intermediate probability, to avoid inappropriate ICA testing (26). Given the size and diverse patient population in the study, these results should be applicable to stable symptomatic outpatients with suspected CAD. A high score (≥ 18) is specific (99.3%) for high-risk CAD and could sway a physician to proceed directly to ICA.

STUDY LIMITATIONS. Although, the current gold standard for diagnosing obstructive CAD is ICA, this study uses coronary CTA to define high-risk CAD. Thus, these results will be subject to the diagnostic inaccuracies of coronary CTA. An earlier study compared the performance of noninvasive coronary CTA with ICA in detecting high-risk CAD and reported that coronary CTA was both highly sensitive and highly specific (sensitivity, 100%; specificity, 95%), and it had a very high positive likelihood ratio (18.0) and a reasonable positive predictive value of 76.9% (15).

Referral bias may be a factor; differences in clinical practice across the 12 sites can influence the selection of patients referred for coronary CTA. The CONFIRM registry sets standardized definitions for

cardiovascular risk factors across centers, and it enlists only centers where coronary CTA is incorporated into daily practice, with uniform collection of major categories including demographics, earlier CAD, and revascularization history (9). This standardization helps to reduce inconsistencies among protocols and guidelines across sites.

We also recognize that patients with severe symptoms and other high-risk factors are more likely to be referred directly to ICA. Therefore, our study population may be more reflective of patients with stable CAD in which ICA may not be immediately indicated.

Blood results and medications were not included into the risk model. The intention was to create a simple and easily applied model that was built entirely on clinical factors that could be used at every clinical encounter. In addition, medications were excluded from analysis. Because the duration of medication therapy was not captured, some medications may have been recently initiated in response to the suspicion of CAD and may introduce bias into the model.

CONCLUSIONS

We propose a scoring system based on clinical variables that can be used to identify patients at high and low risk of having high-risk CAD. Identification of these populations may detect those who may benefit from a trial of medical therapy and those who may benefit most from an invasive strategy. This score likely applies to those patients with a stable low to intermediate risk for CAD.

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PERSPECTIVES

CLINICAL COMPETENCIES: A scoring system using clinical variables may be used to identify patients at high and low pre-test probability of having high-risk CAD. This scoring system may detect those who benefit from a trial of medical therapy and those who may benefit most from an invasive strategy.

TRANSLATIONAL OUTLOOK: Additional studies are needed to validate this scoring system further in the stable outpatient population referred for noninvasive testing.

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KEY WORDS computed tomographic coronary angiography, high-risk coronary artery disease, risk factors