

Comparison of Coronary Artery Disease Consortium 1 and 2 Scores and Duke Clinical Score to Predict Obstructive Coronary Disease by Invasive Coronary Angiography

João Almeida, MD; Paulo Fonseca, MD; Tiago Dias, MD; Ricardo Ladeiras-Lopes, MD; Nuno Bettencourt, MD, PhD; José Ribeiro, MD; Vasco Gama, MD
Department of Cardiology, Gaia/Espinho Hospital Center, Vila Nova de Gaia, Portugal

ABSTRACT

Background: The first step in evaluating a patient with suspected stable coronary artery disease (CAD) is the determination of the pretest probability. The European Society of Cardiology guidelines recommend the use of the CAD Consortium 1 score (CAD₁), which contrary to CAD Consortium 2 (CAD₂) score and Duke Clinical Score (DCS), does not include modifiable cardiovascular risk factors.

Hypothesis: Using scores that include modifiable risk factors (DCS and CAD₂) enhances prediction of CAD.

Methods: We retrospectively included all patients referred to invasive coronary angiography for suspected CAD from January/2008–December/2012 (N = 2234). Pretest probability was calculated using 3 models (CAD₁, DCS, and CAD₂), and they were compared using the net reclassification improvement.

Results: Mean patient age was 63.7 years, 67.5% were male, and the majority (66.9%) had typical angina. Coronary artery disease was diagnosed in 58.5%, and the area under the curve was 0.685 for DCS, 0.664 for CAD₁, and 0.683 for CAD₂, with a statistically significant difference between CAD₁ and the others ($P < 0.001$). The net reclassification improvement was 20% for DCS, related to adequate reclassification of 32% of patients with CAD to a higher risk category, and 5% for CAD₂, at the cost of adequate reclassification of 34% of patients without CAD to a lower risk category.

Conclusions: Prediction of CAD using scores that include modifiable cardiovascular risk factors seems to improve accuracy. Our results suggest that, in high-prevalence populations, DCS may better identify patients at higher risk and CAD₂ those at lower risk for CAD.

Introduction

The initial evaluation of a patient with suspected stable obstructive coronary artery disease (CAD) includes the clinical assessment of the pretest probability (PTP).¹ This step is of major importance because it influences further diagnostic management.² Although invasive coronary angiography (ICA) remains the gold standard for diagnosis of CAD, Patel et al reported a diagnostic yield of only 41%, concluding that better stratification tools were needed.³ The Diamond-Forrester score (DF) was introduced in 1979 and it includes age, sex, and type of chest pain for the calculation of PTP.⁴ This method overestimates the probability of CAD, especially in low-risk populations⁵ and in women.⁶ Recently, it was updated using contemporary cohorts and extended to include patients age >70 years.⁷ This model was designated CAD Consortium 1 (CAD₁) and recommended by the most recent European Society of Cardiology (ESC) guidelines.² The American Heart Association/American College of Cardiology (AHA/ACC) guidelines recommend

the use of DF or the Duke Clinical Score (DCS).¹ The DCS was first described in 1983, based on a large cohort of patients referred to ICA, and it includes modifiable cardiovascular risk factors.^{8,9} Although DCS seems to improve prediction of CAD in patients referred to coronary computed tomographic angiography (CCTA) as compared with DF,¹⁰ it still appears to overestimate PTP.^{11,12} Recently, CAD Consortium 2 (CAD₂), which also includes modifiable cardiovascular risk factors, was created and demonstrated accuracy for the prediction of CAD in low-risk populations.¹¹ The accuracy of this method in patients referred to ICA is not known. We aimed to assess whether the use of scores that include modifiable risk factors (DCS and CAD₂) enhances the prediction of CAD in a contemporary population referred to ICA.

Methods

Study Design

This retrospective, single-center study included consecutively all patients with chest pain and suspected CAD referred to ICA between January 2008 and December 2012 in a country in southwestern Europe. Data were collected

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from patient medical records. Patients with a history of CAD, acute coronary syndrome, or coronary revascularization were excluded.

Definitions

Angina pectoris was classified as typical angina if the following criteria were present: substernal chest pain, provoked by exertion or emotional stress, and relieved by rest and/or nitroglycerin. Atypical angina was defined by 2 of those criteria, and nonanginal chest pain if only 1 or none of those characteristics were present. The presence of the following cardiovascular risk factors was collected: hypertension (blood pressure >140/90 mm Hg or antihypertensive medication), diabetes mellitus (DM; fasting plasma glucose >126 mg/dL, postprandial plasma glucose >200 mg/dL, glycated hemoglobin >6.5%, or anti-diabetic agents), dyslipidemia (total cholesterol >220 mg/dL, low-density lipoprotein cholesterol >140 mg/dL, fasting triglycerides >150 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, or lipid-lowering agents), and smoking (patients who had smoked during the past 1 year). The presence of obstructive CAD was defined as a stenosis of >50% in at ≥ 1 major epicardial vessel.

Pretest Probability Calculation

Pretest probability of CAD was calculated using 3 scores: CAD1, based on age, sex, and type of chest pain⁷; DCS, based on sex, age, smoking, DM, history of myocardial infarction, type of chest pain, dyslipidemia, and electrocardiogram changes (ST-segment and Q-wave changes)⁸; and the CAD2 clinical model, which used age, sex, type of chest pain, DM, hypertension, dyslipidemia, and smoking. For DCS calculation, we assumed normal resting electrocardiogram because that information was unavailable and patients with evidence of previous CAD were excluded. The population was classified according to the risk of having obstructive CAD: low (<15%), intermediate (15%–85%), and high (>85%), in line with the ESC guidelines.

Statistical Analysis

Continuous variables are presented as mean \pm SD and categorical variables are presented as absolute numbers and percentages. Continuous data were compared using Student *t* tests or Mann-Whitney *U* tests, as appropriate, and categorical variables were compared using the χ^2 test or Fisher exact test, as appropriate. Area under the receiver operating characteristic curve (ROC) was used to compare the scores' performances for the diagnosis of CAD. Reclassification tables were constructed to evaluate how many patients changed risk category after using a score with modifiable cardiovascular risk factors (CAD1 vs CAD2 and DCS). To assess the appropriateness of the risk category change, the net reclassification improvement (NRI) was calculated.^{13,14} A 2-tailed test with $P < 0.05$ was considered statistically significant. Data analysis was performed using SPSS version 22 (SPSS Inc., Chicago, IL) and Stata/IC version 13.1 (StataCorp LP, College Station, TX).

Results

Patient Characteristics

The study population included 2234 patients (male, 67.5%; mean age, 63.7 ± 9.7 years). Most were referred with typical angina (66.9%). The overall prevalence of obstructive CAD was 58.5% ($n = 1308$). Men presented CAD in 67.4% of cases and women in 40.1% of cases. As expected, patients with CAD were older (64.4% vs 62.6% ; $P < 0.001$), mostly male (77.8% vs 53% ; $P < 0.001$), and with higher frequency of smoking (15% vs 9.4% ; $P < 0.001$), dyslipidemia (74% vs 63.9% ; $P = 0.017$), and DM (34.3% vs 23.9% ; $P < 0.001$). There were no statistical differences in the prevalence of arterial hypertension (75.1% vs 72.4% ; $P = 0.163$) and family history of premature coronary disease (11.8% vs 9.8% ; $P = 0.165$). Baseline characteristics are detailed in Table 1.

Pretest Probability Estimation and Risk Classification

The expected prevalence of CAD was underestimated by CAD2 (41.5%) and overestimated by CAD1 (63.5%) and DCS (71.1%), as seen in Table 1. All scores showed significantly superior PTP in patients with CAD. In those patients (Figure 1, left side), DCS classified correctly more than half of patients as high risk, whereas only 2% were incorrectly classified as low risk. On the contrary, in patients without CAD (Figure 1, right side), CAD2 classified correctly almost one-third of patients as low risk and only 0.5% as high risk.

Predictive Performance of the Risk Scores

For the prediction of obstructive CAD, the DCS score had superior area under the curve (AUC: 0.685, 95% confidence interval [CI]: 0.663–0.708, $P < 0.001$), followed by CAD2 (AUC: 0.683, 95% CI: 0.661–0.706, $P < 0.001$) and at last CAD1 (AUC: 0.664, 95% CI: 0.641–0.687, $P < 0.001$), as shown in Figure 2. Compared with CAD1, the DCS and CAD2 areas under the curve were significantly different ($P < 0.001$) and there was no statistically significant difference between CAD2 and DCS ($P = 0.52$).

Reclassification of Risk

Given the small and non-statistically significant difference between the performances of CAD2 and DCS evaluated by the area under the ROC curve, we decided to construct reclassification tables to assess the improvement in reclassification of the risk category of each score compared with CAD1.

Using DCS (Table 2), 434 patients with CAD were reclassified from an intermediate risk with CAD1 to a higher risk category, and 20 were reclassified to a lower risk category, resulting in 32% (414/1308) of patients being correctly reclassified. However, in patients without CAD, DCS inadequately reclassified 165 patients from intermediate risk with CAD1 to high-risk category, whereas only 57 were correctly stratified to low-risk category, resulting in 12% (108/926) of patients incorrectly classified. The total net reclassification improvement of DCS was 20% (continuous NRI: 0.18, $P < 0.001$). The CAD2 model showed better risk reclassification in patients without CAD (Table 3), correctly reclassifying 314 of 926 patients to a lower risk category (34%). On the other hand, in patients

Table 1. Baseline Characteristics and Pretest Probability of CAD

Characteristic	All Patients, N = 2234	With CAD, n = 1308	Without CAD, n = 926	P Value
Age, y	63.7 ± 9.7	64.4 ± 9.5	62.6 ± 9.9	<0.001
Male sex	1508 (67.5)	1017 (77.8)	491 (53)	<0.001
Arterial hypertension	1652 (73.9)	982 (75.1)	670 (72.4)	0.163
Smoking	283 (12.7)	196 (15)	87 (9.4)	<0.001
Dyslipidemia	1610 (72.1)	968 (74)	642 (63.9)	0.017
DM	669 (29.9)	448 (34.3)	221 (23.9)	<0.001
Family history (premature CHD)	245 (11)	154 (11.8)	91 (9.8)	0.165
Typical angina	1495 (66.9)	954 (72.9)	541 (58.4)	<0.001
Atypical angina	306 (13.7)	152 (11.6)	154 (16.6)	<0.001
Nonanginal chest pain	433 (19.4)	202 (15.4)	231 (24.9)	<0.001
CAD1, %	63.5 ± 21.8	68.7 ± 19.3	56.1 ± 22.9	<0.001
DCS, %	71.1 ± 26.6	78.4 ± 22	60.9 ± 29	<0.001
CAD2, %	41.5 ± 23.2	47.6 ± 21.9	32.9 ± 22.3	<0.001

Abbreviations: CAD, coronary artery disease; CAD1, Coronary Artery Disease Consortium 1 score; CAD2, Coronary Artery Disease Consortium 2 score; CHD, coronary heart disease; DCS, Duke Clinical Score; DM, diabetes mellitus; SD, standard deviation. Data are presented as n (%) or mean ± SD.

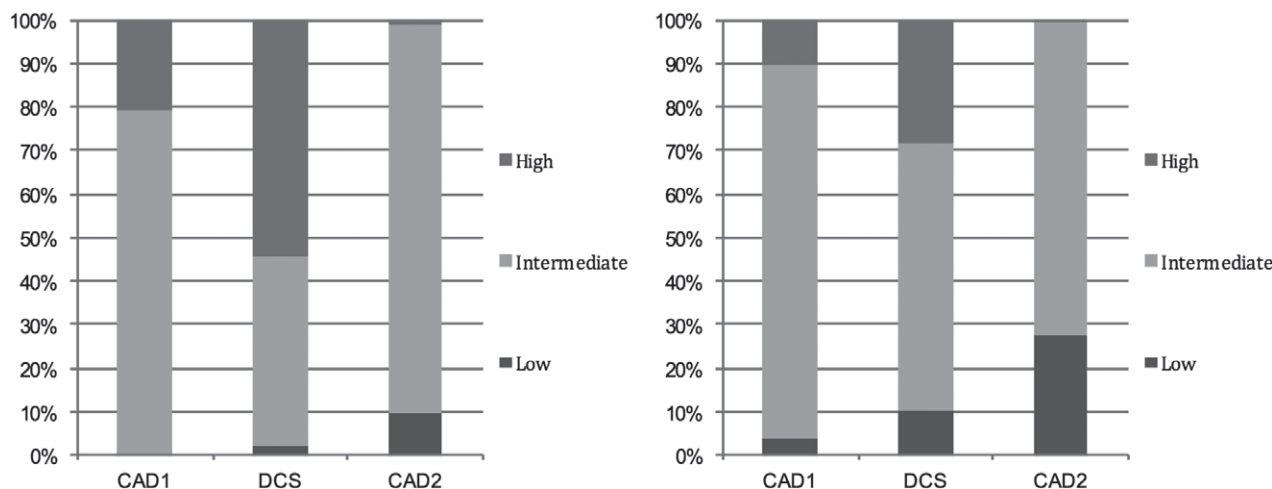


Figure 1. Risk classification in patients with CAD (left) and without CAD (right). Abbreviations: CAD, coronary artery disease; CAD1, Coronary Artery Disease Consortium 1 score; CAD2, Coronary Artery Disease Consortium 2 score; DCS, Duke clinical score.

with CAD, 379 of 1308 patients were incorrectly reclassified to lower risk categories (29%). Total NRI was 5% (continuous NRI: 0.23, $P < 0.001$).

Discussion

Performance and Comparison of Pretest Probability Scores

Overall, the discriminatory power of the 3 scores was modest for the prediction of angiographically significant CAD in our cohort of patients (all with AUC <0.7). In this specific population of patients referred to ICA, DCS and CAD1 scores overestimated the prevalence of obstructive CAD. This was previously demonstrated for DCS score in patients referred

to CCTA.^{12,15} It may be related to a contemporary lower prevalence of CAD as compared with the historic cohorts that served as the base for the development of that model.⁸ Even though CAD1 is an updated version of the original DF method, which was shown to overestimate the probability of CAD in patients referred to ICA^{3,7,16} or noninvasive tests,^{5,10,17,18} it still overestimated the prevalence of CAD in our population. Recently, the same was shown by Zorlak et al in patients referred to ICA or noninvasive testing.¹⁹ As expected, CAD2 underestimated the actual prevalence of CAD, because this model was created for the estimation of the PTP of CAD in low-prevalence populations.

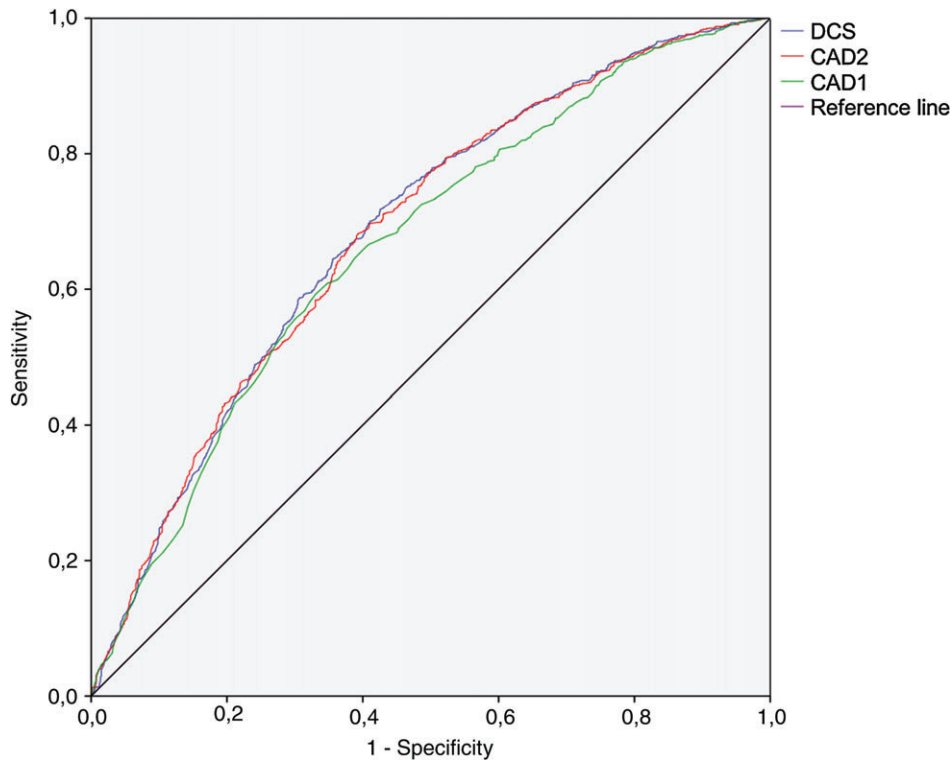


Figure 2. ROC analysis of CAD1, DCS, and CAD2 for the prediction of CAD. Abbreviations: CAD, coronary artery disease; CAD1, Coronary Artery Disease Consortium 1 score; CAD2, Coronary Artery Disease Consortium 2 score; DCS, Duke clinical score; PTP, pretest probability; ROC, receiver operating characteristic.

Table 2. Reclassification Tables of DCS in Patients with CAD and Without CAD

	DCS			Total
	Low	Intermediate	High	
With CAD				
CAD1				
Low	6	0	0	6
Intermediate	20 ^a	572	434 ^b	1026
High	0	0	276	276
Total	26	572	710	1308
Without CAD				
CAD1				
Low	35	0	0	35
Intermediate	57 ^a	572	165 ^b	794
High	0	0	97	97
Total	92	572	262	926

Abbreviations: CAD, coronary artery disease; CAD1, Coronary Artery Disease Consortium 1 score; DCS, Duke Clinical Score.

^aInadequate reclassification. ^bCorrect reclassification.

Table 3. Reclassification Tables of CAD2 in Patients With CAD and Without CAD

	CAD2			Total
	Low	Intermediate	High	
With CAD				
CAD1				
Low	6	0	0	6
Intermediate	121 ^a	905	0	1026
High	0	258 ^a	18	276
Total	127	1163	18	1308
Without CAD				
CAD1				
Low	35	0	0	35
Intermediate	222 ^b	572	0	794
High	0	92 ^b	5	97
Total	257	664	5	926

Abbreviations: CAD, coronary artery disease; CAD1, Coronary Artery Disease Consortium 1 score; CAD2, Coronary Artery Disease Consortium 2 score; DCS, Duke Clinical Score.

^aInadequate reclassification. ^bCorrect reclassification.

Modifiable cardiovascular risk factors such as smoking, DM, and dyslipidemia seem to have a predictive effect inferior to sex, age, and chest pain.⁷ Nevertheless, the use of models that include those risk factors appears to increase performance in the prediction of CAD, as demonstrated by the superior AUC of CAD2 and DCS compared with CAD1.

Clinical Implications

According to the most recent ESC guidelines for the diagnosis of CAD, in patients with high risk (PTP >85%) or low risk (PTP <15%), no further diagnostic tests are needed, because in the first case the clinical diagnosis of CAD can be made, whereas in the second, other causes of chest pain should be investigated.² Despite a small but statistically significant difference in AUC of DCS and CAD2 compared with CAD1, the evaluation of the NRI showed that both improved the predictability of CAD in our cohort of patients. The reclassification improvement was 20% for DCS and 5% for CAD2; therefore, the stratification of risk categories was significantly enhanced by the application of models that included modifiable cardiovascular risk factors. As mentioned earlier, because each risk category has a distinct clinical meaning, the improvement in correct classification has a direct impact on clinical decisions. The reclassification of risk using DCS showed improved discrimination of the high-risk category in patients with CAD. Therefore, that model performed better for the identification of patients in whom it was safe to assume obstructive CAD, requiring optimal medical treatment and risk stratification of events. On the other side, CAD2 more accurately classified patients without CAD as low risk, predicting those who would not benefit from further diagnostic testing. Although DCS had superior NRI over CAD2, these results have to be interpreted in the context of high prevalence of CAD (almost 60%). Indeed, DCS was developed on the basis of patients referred to ICA, and CAD2 mostly with low-prevalence populations. Possibly, CAD2 would perform even better in more heterogeneous populations, including patients referred to ICA and CCTA, a hypothesis that needs to be tested in future studies.

Study Limitations

The studied patients represent a highly selected population, because only patients from a single institution who underwent ICA were retrospectively included. Therefore, the PTP is inherently higher. Although DCS was validated for the prediction of ≥ 1 stenosis >75%, in this study it was tested for the prediction of a different cutoff (>50%), and CAD2, as previously stated, was validated for low-risk populations. Also, no information regarding previous noninvasive testing or follow-up was obtained.

Conclusion

The estimation of likelihood pretest of CAD using scores that include modifiable cardiovascular risk factors (CAD2 and DCS) seems to improve the accuracy of CAD prediction. Our results suggest that, in high-risk populations, DCS may better select patients at higher risk and CAD2 may better predict those at lower risk for CAD. Developing better

models, probably with the inclusion of those risk factors, will enhance the pretest likelihood prediction and improve clinical decisions, because it will help the clinician to decide whether further diagnostic testing is needed.

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