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ORIGINAL ARTICLE

ESC pre-test probability estimates for obstructive coronary artery disease: can they be used in Brazil?

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Abstract

Aims Cardiovascular disease, primarily coronary artery disease (CAD), is the leading cause of mortality worldwide. Accurate diagnosis of CAD often requires pre-test probability (PTP) estimation, traditionally performed using scoring systems like the Diamond-Forrester (DF) and European Society of Cardiology (ESC) models. However, the applicability of such models in specific populations may vary. This study compares the performance of DF and PTP scores in the Brazilian context, using coronary computed tomography angiography (CCTA) as a reference standard.

Methods and results PTP for obstructive CAD was calculated using DF and ESC scores in 409 symptomatic patients without known CAD who underwent CCTA between 2019 and 2022. Predicted PTP was compared with actual CAD prevalence. DF overestimated CAD prevalence across age and symptom categories, while ESC showed better alignment with actual prevalence.

Conclusion Our study confirms that the ESC PTP model is more appropriate than the DF model for determining PTP in the Brazilian population.

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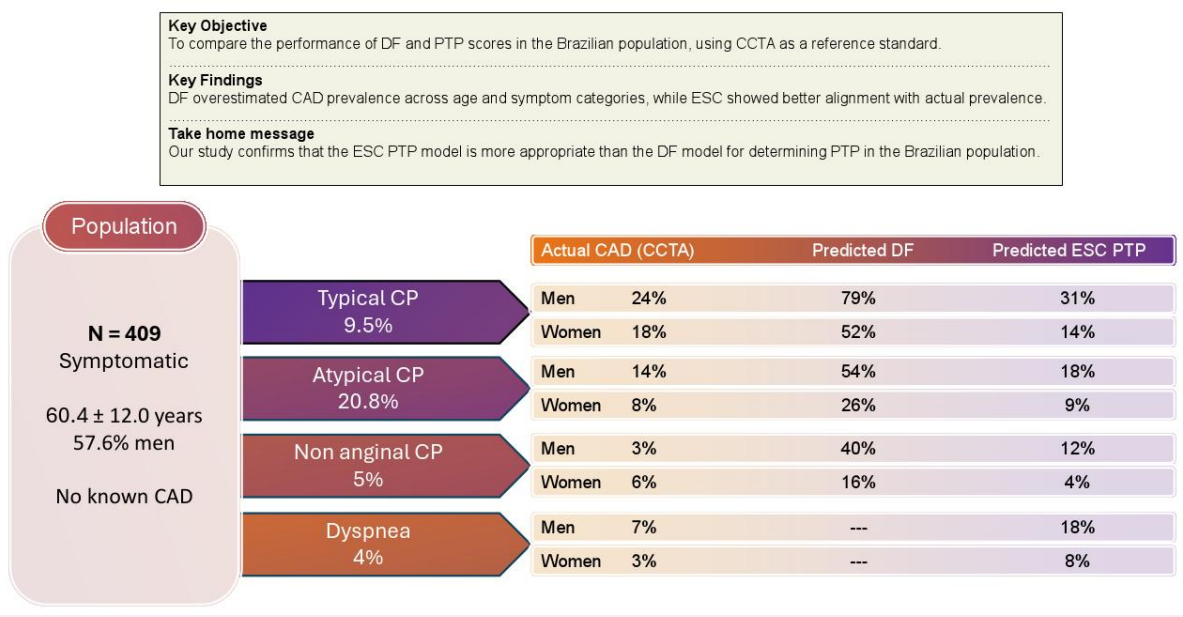
Graphical Abstract



Keywords coronary atherosclerotic disease • CCTA • PTP

Introduction

Cardiovascular disease is the leading cause of death worldwide primarily driven by coronary artery disease (CAD), and accounts for approximately 9 million deaths annually.[1–3] The diagnosis of CAD can be challenging, and in addition to a detailed medical history and clinical examination, complementary tests are often necessary. Typically, following medical evaluation, an individual's obstructive CAD pre-test probability (PTP) is calculated using one of the available risk prediction scores, and a personalized investigation strategy is formulated.[2,4–9] In Brazil, it is estimated that more than 4 million people have CAD, and this condition has been the leading cause of death in both men and women in the last decade.[10] As a developing nation with its own socioeconomic, genetic, and lifestyle factors, scores that have been developed in other nations may not apply to the Brazilian population. Diamond-Forrester (DF) score originally published in 1979[5] and updated in 2011[5] is one of the most commonly used. Although it has limitations and omits other known risk factors for CAD in its analysis (like diabetes, dyslipidemia, smoking, family history, obesity) the Diamond-Forrester model holds significant clinical utility, and its use is still recommended by many major international guidelines including that of Brazil.[4,11–14]

Previous publications have shown DF score overestimates the likelihood of obstructive in some populations[15–17] In 2019, the European Society of Cardiology (ESC) updated its PTP score and proposed a new PTP model to assist in the clinical management of patients undergoing investigation for CAD.[18]

Coronary computed tomography angiography (CCTA) has been endorsed by current guidelines as an initial diagnostic tool for the diagnosis of CAD.[14,19–21]

CCTA holds high diagnostic value for the detection of obstructive CAD (sensitivity 97.5%, specificity 91%, positive predictive value 93%) and, due to its high negative predictive value (96.5%),[22] has become the method of choice for excluding CAD.

Using CCTA as the reference standard, we sought to understand the performance of the DF and ESC PTP scores in the Brazilian population.

Methods

Population

Consecutive patients ≥18 years of age who underwent a clinically indicated CCTA, were enrolled into our institutional cardiac CTA registry between January 2019 and December 2022. At the time of CCTA, a medical history and indications for CCTA were recorded for all patients. Asymptomatic patients and those with known CAD were excluded. Individual PTP for obstructive CAD was calculated using Diamond-Forrester model[5] and the ESC 2019 updated score[18] (*Figure 1*). The study was approved by the research ethics board and all patients provided consent for the cardiac CT registry.

CT coronary angiography

Cardiac CTA was acquired using Aquilion One 320 (Canon Medical Systems, USA) following current guidelines.[23] Prior to image acquisition, propranolol, ivabradine, or metoprolol (oral and/or intravenous) was administered targeting a heart rate of ≤65 beats per minute and isosorbide dinitrate (5 mg) was administered sublingually.

A non-contrast, prospective, electrocardiogram-synchronized computed tomography (CT) scan (tube voltage of 120 kVp) was acquired. Images were reconstructed with a slice thickness of 3 mm for the evaluation of the Agatston calcium score.[24]

CCTA image acquisition was performed using a biphasic intravenous contrast administration protocol (100% contrast [50–60 cc], and saline [40–50 cc]). Prospective ECG-triggered data sets were acquired with

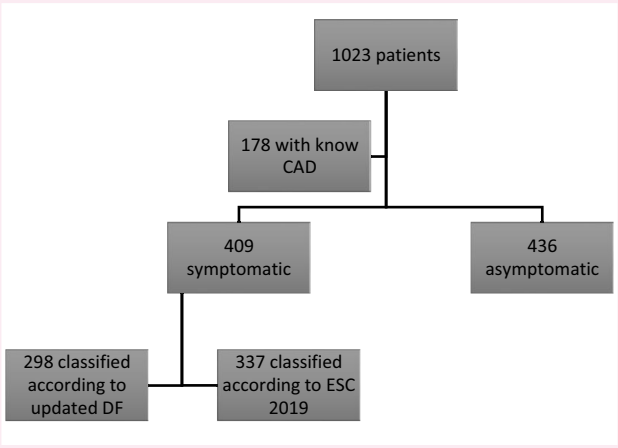


Figure 1 Study population.

320 × 0.5 mm slice collimation and a gantry rotation of 275 ms (mA = 400–800, kVp = 100–120).

CTA image analysis

ECG-gated CT images were post-processed using the Intellispace Portal Workstation (Philips, Veenpluis, Netherlands) and a blinded research interpretation was used for analysis. Patients were categorized according to CAD-RADS (Coronary Artery Disease Reporting and Data System),[25] and obstructive CAD was defined if diameter stenosis ≥50%.

Statistical analysis

Statistical analyses were performed using SAS (version 9.4, SAS, SAS Institute Inc., Cary, North Carolina, 2013) and statistical significance was defined as $P < 0.05$. Continuous variables were presented as means and standard deviations. Categorical variables were presented as frequencies with percentages.

PTP for each patient was calculated using the DF and ESC scores and compared with the actual prevalence of obstructive CAD in our population. To compare the DF and ESC groups with the results of CCTA, we employed a negative binomial regression model with a logarithmic link function.[26] This choice was made considering that these outcomes are discrete quantitative variables rather than continuous. Additionally, Tukey's *post hoc* test was utilized for multiple comparisons. Normalcy rate—frequency of normal studies in a population with a low PTP for CAD[27]—was calculated.

All graphs presented were created using the IBM SPSS statistics (version 29.0, IBM Corp., Armonk, New York, 2020).

Results

A total of 845 patients (mean age = 60.4 ± 12.0 years, and 57.6% men) without known CAD were identified. Of these, 451 (53.4%) patients were asymptomatic and were excluded from analysis. Eighty (9.5%) patients had typical CP and 177 (20.8%) had atypical chest pain. Hypertension was present in 480 (56.8%) patients and 391 (46.6%) had dyslipidemia. Approximately one-third of the patients were smokers or ex-smokers and one-quarter had family history of early CAD (*Table 1*).

281 (33%) patients had normal CCTA studies (CAC = 0 and no coronary atherosclerotic plaque), while two-thirds of patients (564) had an abnormal CCTA exam. Calcium score > 0 was present in 516 (61%) patients and obstructive CAD (≥50% stenosis) was diagnosed in 164 (19%).

Of the 31 patients with a mean PTP of 3%, only 1 patient had obstructive CAD. The normalcy rate in our population with low PTP was calculated in 96.8%.

Table 1 Patient characteristics

Demographics	Number (%)/(SD) all = 845
Age	60 (12)
Male gender	487 (57.6%)
Body mass index (kg/m^2)	28 (4.6)
Cardiac risk factors	
hypertension	480 (56.8%)
Dyslipidemia	391 (46.3%)
Diabetes	221 (26.2%)
Smoker | Ex-smoker	265 (32%)
Family history of CAD	212 (25.1%)
Symptom	
Asymptomatic	451 (53.4%)
Atypical chest pain	177 (20.8%)
Typical angina	80 (9.5%)
Non-angina chest pain	43 (5%)
Dyspnoea	37 (4%)
Others	69 (8.2%)
Medications	
Statin	377 (44.6%)
Aspirin	124 (14.7%)
Beta-blocker	199 (23.5%)
Ace-inhibitor	94 (11.1%)

ACE, Angiotensin converting enzyme; CAC, coronary artery calcium score; CAD, Coronary artery disease; CCTA, Coronary computed tomography angiography; SD, standard deviation.

Among symptomatic patients, a total of 300 patients could be classified using the updated DF classification and 334 in the ESC 2019 score. A larger proportion of individuals could have their PTP assessed using the ESC classification as it includes symptoms of dyspnoea. Applying the modified DF classification, 21 (7%) were classified as low PTP, 219 (73%) as intermediate PTP, and 60 (20%) as high PTP. Applying the ESC classification, 32 (9%) were classified as low PTP, 133 (40%) as intermediate PTP, and 169 (51%) as high PTP.

The prevalence of obstructive CAD in the population distributed by age and symptoms is summarized in *Table 2*. The DF model overestimated the prevalence of obstructive CAD in all age and symptoms categories (*Table 3*). The ESC PTP score performed better than DF for estimating obstructive CAD (*Table 4*).

Discussion

We assessed the performance of the updated DF and the ESC 2019 PTP scores in the Brazilian population.

Patients were classified into low, intermediate, and high PTP categories following the guidelines of two widely used clinical scores: modified DF and the ESC 2019 classification. Most patients, when classified by modified DF, were in the intermediate PTP category. However, when classified by ESC, most were in the high PTP category. A higher prevalence of obstructive CAD was observed in groups with higher clinical risk.

When evaluated by symptom and sex, it was observed that the DF score overestimated the prevalence of obstructive CAD in all groups. When compared with ESC, the prevalence of obstructive CAD in our population was lower in men with any type of symptom (typical chest pain, atypical chest pain, non-anginal chest pain, and dyspnoea)

Table 2 **Prevalence of obstructive CAD in our population distributed by sex and symptoms**

	Typical chest pain						Atypical CP						Non-angina						Dyspnoea					
	Men			Women			Men			Women			Men			Women			Men			Women		
	Total	Stenosis ≥50%	Prev	Total	Stenosis ≥50%	Prev	Total	Stenosis ≥50%	Prev	Total	Stenosis ≥50%	Prev	Total	Stenosis ≥50%	Prev	Total	Stenosis ≥50%	Prev	Total	Stenosis ≥50%	Prev	Total	Stenosis ≥50%	Prev
n patients	46	11	24%	34	7	18%	79	10	14%	98	5	8%	20	1	3%	23	3	6%	17	2	7%	17	1	3%

n, number of patients; Prev, prevalence.

Table 3 **Prevalence of obstructive CAD in our population compared with DF and ESC**

	Typical chest pain						Atypical CP						Non-angina						Dyspnoea			
	Men			Woman			Men			Woman			Men			Woman			Men		Woman	
	Brazil	ESC	DF	Brazil	ESC	DF	Brazil	ESC	DF	Brazil	ESC	DF	Brazil	ESC	DF	Brazil	ESC	DF	Brazil	ESC	Brazil	ESC
Average prevalence of obstructive CAD	24%	31%	79%	18%	14%	52%	14%	18%	54%	8%	9%	26%	3%	12%	40%	6%	4%	16%	7%	18%	3%	8%

CAD, Coronary artery disease; DF, Diamond-Forrester updated score; ESC, European society of cardiology 2019 score.
$P < 0.05$ for all variables, except for dyspnoea in women.

Table 4 Comparison of mean prevalence of obstructive CAD according to Diamond-Forrester (a) and ESC 2019 (b) PTP categories

Table 4a

	n	Observed stenosis ≥50%	DF
Low PTP	21	1 (5%)	10%
Intermediate PTP	219	36 (17%)	39%
High PTP	60	22 (37%)	78%

DF, Diamond-Forrester updated score; PTP, pre-test probability.

Table 4b

	n	Observed stenosis ≥50%	ESC
Low PTP	32	1 (3%)	3%
Intermediate PTP	133	17 (13%)	10%
High PTP	169	47 (28%)	28%

ESC, European society of cardiology 2019 score; PTP, pre-test probability.

and in women with atypical chest pain and non-anginal chest pain. In women with typical chest pain, we observed a higher prevalence of obstructive CAD than expected by the ESC PTP score, and there was no difference in women with dyspnoea.

The prevalence of obstructive CAD diagnosed by CCTA in our population, when compared with that expected by the modified DF PTP, tended to be lower in all three groups. In the low PTP group (prevalence estimated by DF 2011 between 5% and 14% [mean 10%]), we had 5%, in the intermediate group (17–65% [mean 39%] by DF 2011) we had 17%, and in the high PTP group (≥68% [mean 78%]), we found a prevalence of 37%.[5]

These findings suggest that when the modified DF is applied to the Brazilian population, there was tendency to overestimate the prevalence of obstructive CAD and that CCTA played an important role in reclassifying these patients.

When we used the ESC PTP classification, we noticed that the actual prevalence of obstructive CAD in our population was within the estimated range: in the low ESC probability group, the expected prevalence of obstructive CAD ranges from 1% to 5% (mean 3%), while we found 3% in our population. In the intermediate group, ESC estimates from 6% to 14% (mean 10%), and we found 13%, while in the high PTP group we found 28%, while ESC estimates from 17% to 52% (mean 28%).[18] These findings suggest that the ESC score, which also considers the symptom of dyspnoea, in addition to globally estimating a lower prevalence of CAD, might be more suitable for the Brazilian population.

Our study demonstrates the gap between traditional PTP scores and the actual prevalence of coronary atherosclerosis in a specific symptomatic population, consistent with previously published studies.[15–17] This overestimation can lead to a significant number of unnecessary and potentially invasive exams, increasing costs and risks for patients.

The importance of validating clinical scores in specific populations is crucial to ensure an accurate assessment of PTP of CAD. Studies show that the application of unvalidated clinical scores in different populations can lead to inaccurate results and overestimation of risks. Adapting and validating clinical scores in specific populations can improve the accuracy of diagnosis and reduce the need for additional exams.

CCTA, as a non-invasive method, emerges as a valuable tool in evaluating CAD in specific populations. In addition to providing detailed images of the coronary arteries, CCTA allows direct assessment of the presence and severity of atherosclerotic disease, helping to confirm or rule out the presence of obstructive CAD with high accuracy. Therefore, CCTA can play a key role in validating and refining clinical scores in specific populations, avoiding unnecessary invasive exams and providing a more effective and safer diagnostic strategy.

Limitations

This was a single-centre study and therefore patient's baseline characteristics, indications for CCTA and prevalence of disease may differ from other practices and institutions in Brazil. Referral bias may also exist in this private clinic resulting in a lower proportion of patients with high-risk category. Despite these limitations, our findings are consistent with previous studies and are aligned with the most contemporary guidelines and PTP estimates.[28]

We do not have follow-up data and cannot calculate specificity of CCTA in our population. Given the potential issues of referral and verification bias, studies have demonstrated that once a test has been adopted into clinical practice, specificity decreases. In our population, we do not have follow-up data. However, the normalcy rate[27] has been used as a surrogate marker for specificity and our normalcy rate was 96.8%.

It was observed that the ESC guidelines might overestimate the prevalence of CAD in patients with dyspnoea. Although the numbers are too small to make definitive conclusions, it raises the possibility of cultural subjective differences in dyspnoea. The recognition and interpretation of dyspnoea symptoms may be influenced by cultural backgrounds, individual experiences, and subjective perceptions, potentially leading to variations in symptom reporting.

Conclusion

Our study confirms that the ESC PTP model is more appropriate than the DF model for determining PTP in the Brazilian population.

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Data availability

The data underlying this article will be shared on request to the corresponding author.

Lead author biography

Dr Fernanda Erthal is a cardiologist and specialist in cardiac imaging at CDPI/DASA in Rio de Janeiro, Brazil. She received her medical degree from Universidade Federal Fluminense and, after completing her residencies in internal medicine and cardiology, she undertook a clinical and research fellowship at the University of Ottawa Heart Institute in Canada. Dr Erthal holds a master's degree in cardiovascular science and currently serves as the head of the Cardiovascular CT and MRI Department at DASA, Rio de Janeiro.

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