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ORIGINAL PAPER

THE ASSESSMENT OF THE 2019 ESC PRE-TEST PROBABILITY FOR PREDICTING OBSTRUCTIVE CORONARY ARTERY DISEASE IN STABLE ANGINA

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Abstract

Introduction. The 2019 European Society of Cardiology (ESC) pre-test probability (PTP) model is widely used for predicting obstructive coronary artery disease (CAD) in patients with stable angina, though its accuracy in various populations is uncertain.
The objective of the study was to evaluate the diagnostic accuracy of the 2019 ESC PTP model in predicting obstructive CAD in stable angina patients and to assess the added value of incorporating traditional cardiovascular risk factors.
Material and methods. A cross-sectional study included 366 stable angina patients who underwent coronary computed tomography angiography. Obstructive CAD was defined as ≥50% stenosis. The 2019 ESC PTP model was applied, and a revised model including additional risk factors (hypertension, diabetes, smoking, family history of premature CAD, and LDL-C/HDL-C ratio) was developed. Discrimination and calibration were evaluated using c-statistic and Hosmer-Lemeshow test.

Résumé

Évaluation du modèle de probabilité pré-test ESC 2019 pour prédire la maladie coronarienne obstructive dans l'angine stable

Introduction. Le modèle de probabilité pré-test (PTP) de l'ESC 2019 est largement utilisé pour prédire la maladie coronarienne obstructive (CAD) chez les patients souffrant d'angine stable, bien que son exactitude dans diverses populations reste incertaine.
L'objectif de l'étude a été d'évaluer la précision diagnostique du modèle PTP ESC 2019 dans la prédiction de la CAD obstructive chez les patients ayant une angine stable et évaluer la valeur ajoutée de l'incorporation de facteurs de risque cardiovasculaires traditionnels.
Matériel et méthodes. Une étude transversale a inclus 366 patients ayant une angine stable qui ont subi une angiographie par tomodensitométrie coronarienne. La CAD obstructive était définie par une sténose ≥50%. Le modèle PTP ESC 2019 a été appliqué, et un modèle révisé incluant des facteurs de risque

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Results. The actual prevalence of obstructive CAD was 73.8%, higher than the predicted values from the 2019 ESC PTP model across all risk categories (low 11.1%, intermediate 55.2%, high 82.8%). The 2019 ESC PTP model had modest discriminatory power (c-statistic =0.701, 95% confidence interval [CI]: 0.640–0.761), but incorporating traditional cardiovascular risk factors improved both discrimination (c-statistic = 0.785, 95% CI: 0.735–0.835) and calibration (Hosmer-Lemeshow test: p = 0.219). The optimism-corrected c-statistic from internal validation was 0.769, and the corrected calibration slope was 0.8891.

Conclusions. The 2019 ESC PTP model underestimates the prevalence of obstructive CAD in stable angina patients. Incorporating additional cardiovascular risk factors significantly improves the model's predictive accuracy. External validation is needed to confirm the effectiveness of this updated nomogram in broader clinical practice.

Keywords: cardiovascular risk factors, coronary computed tomography angiography, LDL-C/HDL-C ratio, obstructive coronary artery disease, pre-test probability.

List of abbreviations:
AUC – area under the curve
BMI – body mass index
CAD – coronary artery disease
CCS – Canadian Cardiovascular Society
CCTA – coronary computed tomography angiography
CI – confidence interval
ESC – European Society of Cardiology
FH-PCAD – family history of premature coronary artery disease
HDL-C – high-density lipoprotein cholesterol
ICA – invasive coronary angiography
IQR – interquartile range
LDL-C – low-density lipoprotein cholesterol
M – mean
Me – median
NPV – negative predictive value
OR – odds ratio
PPV – positive predictive value
PTP – pre-test probability
SD – standard deviation

Résultats. La prévalence réelle de la CAD obstructive était de 73,8%, supérieure aux valeurs prédites par le modèle PTP ESC 2019 dans toutes les catégories de risque (faible 11,1%, intermédiaire 55,2%, élevé 82,8%). Le modèle PTP ESC 2019 avait un pouvoir discriminant modeste (c-statistique = 0,701, intervalle de confiance [IC] à 95% 0,640–0,761), mais l'incorporation de facteurs de risque cardiovasculaires traditionnels a amélioré à la fois la discrimination (c-statistique = 0,785, IC à 95% 0,735–0,835) et la calibration (test de Hosmer-Lemeshow, p = 0,219). La c-statistique corrigée pour l'optimisme de la validation interne était de 0,769, et la pente de calibration corrigée était de 0,8891.

Conclusions. Le modèle PTP ESC 2019 sous-estime la prévalence de la CAD obstructive chez les patients ayant une angine stable. L'incorporation de facteurs de risque cardiovasculaires supplémentaires améliore considérablement la précision prédictive du modèle. Une validation externe est nécessaire pour confirmer l'efficacité de ce nomogramme mis à jour dans la pratique clinique plus large.

Mots-clés: facteurs de risque cardiovasculaires, angiographie par tomodensitométrie coronaire, ratio LDL-C/HDL-C, maladie coronarienne obstructive, probabilité pré-test.

Introduction

Coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide[1]. In 2020, CAD accounted for 382,820 deaths in the United States alone[2]. The pathophysiology of CAD is closely linked to the development of atherosclerotic plaques within the epicardial arteries, either obstructive or non-obstructive[3]. An accurate diagnosis of CAD is essential for guiding appropriate management strategies. In clinical practice, CAD can be diagnosed using both invasive procedures, such as invasive coronary angiography (ICA), and non-invasive methods, including coronary computed

tomography angiography (CCTA), which has a high negative predictive value for excluding obstructive CAD[4].

An accurate assessment of the pre-test probability (PTP) of obstructive CAD is a crucial step in determining the most appropriate diagnostic approach. This is emphasized in the 2019 European Society of Cardiology (ESC) Guidelines for the diagnosis and management of chronic coronary syndromes[3]. These guidelines recommend using an updated PTP model based on patients' characteristics such as age, gender, and symptom presentation, improving upon the 2013 guidelines[5] that employed the modified Diamond-Forrester model[6]. Since the 2013 guidelines were introduced, studies have shown a lower prevalence of obstructive CAD among patients suspected of having CAD[7,8], necessitating an update to the PTP model.

The 2019 ESC Guidelines present a revised PTP table that categorizes patients into three risk groups: those with PTP > 15%, for whom non-invasive testing is highly recommended; those with PTP between 5% and 15%, for whom further testing should be considered based on additional clinical factors; and those with PTP ≤ 5%, where the likelihood of disease is low, and testing may be performed only under compelling circumstances[3]. Importantly, this revision also includes patients presenting with dyspnea as the main symptom, broadening the model's applicability. However, it is essential to recognize that the effectiveness of the 2019 ESC PTP model may significantly differ across geographic regions and varying socio-demographic characteristics of patients.

The objective of the study was to assess the diagnostic accuracy of the 2019 ESC PTP model in Vietnamese patients with stable angina suspected of obstructive CAD, who were referred for CCTA. Additionally, this study aimed to explore the added diagnostic value of incorporating traditional cardiovascular risk factors into the PTP model.

Material and methods

Study population

This was a cross-sectional study that included patients aged ≥18 years who were diagnosed with stable angina and suspected obstructive CAD referred for CCTA between January 2023 and December 2023, at the Tam Duc Cardiology Hospital (Ho Chi Minh city, Vietnam). We excluded patients diagnosed with acute coronary syndrome at admission, those with previous myocardial infarction or revascularization, with acute conditions (such as fever, infection, or decompensated heart failure), and those with missing CCTA or chest pain symptom data. The diagnosis of stable angina was based on current clinical guidelines[3], which define typical angina as the presence of all three following characteristics: 1) a sensation of retrosternal chest discomfort with characteristic quality and duration, 2) triggered by physical exertion or emotional stress, and 3) relieved by rest or sublingual nitroglycerin in minutes. Atypical angina is defined as having two of these characteristics, while non-anginal chest pain has only one or none of these features. The study followed the principles outlined in the Declaration of Helsinki. The ethics approval was obtained from the local ethics committee of the Tam Duc Cardiology Hospital and Ethics Committee in Biomedical Research of Pham Ngoc Thach University of Medicine before the commencement of data collection (approval number 959/TĐHYKPNT-HĐĐĐ, dated December 19, 2023). All patients provided informed consent to participate in the study.

Data collection

The variables of interest included clinical characteristics, cardiovascular risk factors, including hypertension, diabetes mellitus, dyslipidemia, smoking, family history of premature CAD (FH-PCAD), comorbidities, lipid profile and data on the presence of CAD were recorded. Lipid profiles were obtained within 24 hours of admission. Hypertension was defined as previous history of hypertension, or if the patient was on antihypertensive medication[9]. Diabetes mellitus was diagnosed when fasting blood glucose was ≥ 126 mg/dL, or HbA1c was ≥ 6.5%, or if the patient was on antidiabetic medications[10]. Smoking was defined as current smoking or having quit smoking within the past 5 years[11]. Dyslipidemia was defined as total cholesterol ≥ 5.2 mmol/L, or triglycerides ≥ 2.3 mmol/L, or low-density lipoprotein cholesterol (LDL-C) ≥ 3.2 mmol/L, or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L, or if the patient was on lipid-lowering therapy[12,13]. FH-PCAD was defined as if this was known in a first- degree male relative of age <55 years or a first- degree female relative of age <65 years[14].

All patients were assigned a PTP using chest pain type, age, gender and dyspnoea according to the 2019 ESC PTP model[3]. The patients were then categorized as low (<5%), intermediate (5–15%), or high PTP (>15%).

CCTA Acquisition and Interpretation

CCTA was performed using a Brilliance TM 64-slice multidetector CT scanner (Philips Medical Systems) in accordance with the Society of Cardiovascular Computed Tomography guidelines[15] within 24 hours of hospital admission. The imaging

data were stored on the Carestream PACS system and processed using the PACS Vue Motion software. The following techniques were employed for image analysis: multiplanar reconstruction, maximum intensity projection, and volume rendering technique. Coronary lesion assessment on CCTA was performed by two experienced radiologists, accredited at the expert level in radiology. Obstructive CAD was defined as coronary artery stenosis of ≥ 50% of the luminal diameter[16].

Statistical Analysis

Data were analyzed using IBM SPSS Statistics 25.0 (SPSS Inc., Chicago, IL, USA) and R software (version 3.6.3). Categorical variables were presented as counts (n) and percentages (%). Normally distributed continuous variables were expressed as mean (M) and standard deviation (SD), while non-normally distributed variables were presented as median (Me) and interquartile range (IQR). The Kolmogorov-Smirnov test was used to assess normality, with $p > 0.05$ indicating a normal distribution. Categorical variables were compared using the Chi-square or Fisher-exact test, and normally distributed continuous variables were analyzed using Student's t-test. For non-normal distributions, the Mann-Whitney U test or Kruskal-Wallis test was applied. The discrimination and calibration of the 2019 ESC PTP model were assessed using the area under the receiver operating characteristic curve (AUC) accompanied by 95% confidence interval (CI) and Hosmer–Lemeshow goodness-of-fit chi-square statistic[17]. Based on the 2019 ESC PTP model, we used logistic regression to develop clinical models with obstructive CAD as outcome, which in addition included traditional cardiovascular risk factors and clinical characteristics. The discriminatory power of the clinical models was assessed by AUC and compared with 2019 ESC PTP model using the method of DeLong[18]. A nomogram was constructed to assess the risk of obstructive CAD ("rms" package in R). Performance of nomogram was assessed by AUC and internally validated by bootstrap method[19]. In this method, replication on 1000 bootstrapped samples drawn with replacement was performed to form optimism corrected c-statistic from ROC curves. For assessing nomogram calibration, Hosmer-Lemeshow goodness of fit test was used[17] with constructing a calibration plot ("rms" package in R). Significance was used when two-sided p-values <0.05 for all analysis.

Results

Baseline characteristics of the study population

During the study period, we included 366 patients (62.6% men, mean age 64.8±9.1 years) referred to CCTA, of whom 270 patients (73.8%) had obstructive CAD. The baseline patient characteristics are shown in Table 1.

Compared to non-obstructive CAD, obstructive CAD was more frequently observed in men, had more cardiovascular risk factors (smoking, hypertension, FH-PCAD), higher prevalence of typical, atypical angina, higher rate of angina severity classified as grade II-III according to the Canadian Cardiovascular Society (CCS) classification system and lower rate of dyspnoea. Body mass index (BMI) and other comorbidities were similar between groups. The patients with obstructive CAD had higher levels of total cholesterol, triglycerides, LDL-C/HDL-C ratio, and lower level of HDL-C.

The median of 2019 ESC PTP was 24.5±12.8%, 71.3% (n=261) patients had PTP >15%. Patients with obstructive CAD had higher PTP values (26.9±12.7% vs. 17.8±10.3%, p<0.001) and a greater proportion with PTP >15% (80% vs. 46.9%).

The coronary severity stratified by PTP categories is showed in Table 2. There was an increase in severe CAD (stenosis ≥70%) across PTP categories.

The actual prevalence of obstructive CAD according to PTP categories was 11.1% (1/9) in the low PTP group, 55.2% (53/96) in the intermediate group, and 82.8% (216/261) in the high PTP group. These observed prevalences exceeded the expected values from the 2019 ESC guidelines, which predicted 1-5% (mean 3%) for the low PTP group, 6-14% (mean 10%) for the intermediate group, and 17-52% (mean 28%) for the high PTP group (Figure 1).

In ROC curve analysis, the AUC of 2019 ESC PTP for predicting the risk of obstructive CAD were 0.701, 95% CI: 0.640-0.761, p<0.001, sensitivity 80%, specificity 53.1%, positive predictive value (PPV) 82.8%, negative predictive value (NPV) 48.6%. The calibration analysis demonstrated a poor fit of 2019 ESC PTP model (Hosmer-Lemeshow test: Chi-square 27.468, p<0.001).

Incorporating conventional cardiovascular risk factors into PTP model (Model 2), including smoking, hypertension, diabetes mellitus, FH-PCAD, dyslipidemia improved the calibration (Hosmer-Lemeshow test: Chi-square 10.433, p=0.236) and discrimination ability (AUC=0.767, 95% CI: 0.716-0.817, p<0.001) of the PTP model in predicting the risk of obstructive CAD (Table 3). The De Long method showed that there was no significant difference in AUC between the models (p=0.103).

The local logistic regression model (Model 3) was developed from model 2, which included LDL-C/HDL-C ratio instead of dyslipidemia (Table 3). For model 3, obstructive CAD was found to be significantly associated with smoking (odds ratio [OR], 2.705; 95% CI, 1.387-5.274), FH-PCAD (OR, 5,5; 95% CI 1,227-24,659), and LDL-C/HDL-C ratio (OR, 1,708; 95% CI, 1.221-2.388).

Table 1. Baseline patient characteristics, with and without obstructive coronary artery disease (CAD)

Variables	*All patients (n=366)*	*Non-obstructive CAD (n =96)*	*Obstructive CAD (n =270)*	*P*
Age, M ± SD, years	64.8± 9.1	64.9 ± 11.9	64.7 ± 7.9	0.898
Age ≥60 years, n (%)	270 (73.8)	67 (69.8)	203 (75.2)	0.344
Sex, male, n (%)	229 (62.6)	40 (41.7)	189 (70)	<0.001
BMI, M ± SD, kg/m^2	24.0 ± 3.0	24.4± 2.7	23.8 ±3.0	0.100
Smoking, n (%)	132 (36.1)	15 (15.6)	117 (43.3)	<0.001
Hypertension, n (%)	304 (83.1)	73 (76)	231 (85.6)	0.039
Diabetes, n (%)	139 (38)	28 (29.2)	111 (41.1)	0.05
Dyslipidemia, n (%)	326 (89.1)	87 (90.6)	239 (85.5)	0.704
FH-PCAD, n (%)	34 (9.3)	2 (2.1)	32 (11.9)	0.003
Atrial fibrillation, n (%)	17 (4.6)	6 (6.3)	11 (4.1)	0.401
PAD, n (%)	21 (5.7)	3 (3.1)	18 (6.7)	0.306
COPD, n (%)	5 (1.4)	1 (1.0)	4 (4.1)	1.0
Symptom characteristics:				
Typical chest pain, n (%)	129 (35.2)	13 (13.5)	116 (43)	<0.001
Atypical chest pain, n (%)	133 (36.3)	23 (24)	110 (40.7)	0.003
Non-specific chest pain, n (%)	34 (9.3)	23 (24.0)	11 (4.1)	<0.001
Dyspnoea, n (%)	148 (40.4)	48 (50)	100 (37)	0.03
CCS classification, n (%):				
I	238 (65)	83 (86.5)	155 (57.4)	<0.001
II	61 (16.7)	6 (6.3)	55 (20.4)	
III	63 (17.2)	7 (7.3)	56 (20.7)	
IV	4 (1.1)	0 (0)	4 (1.5)	
Lipid profile:				
Total cholesterol, Me (IQR), mmol/L	4.24 (3.64; 5.45)	4.08 (3.60; 4.71)	4.34 (3.65; 5.71)	0.025
HDL-C, Me (IQR), mmol/L	1.25 (1.06; 1.48)	1.39 (1.17; 1.65)	1.19 (1.03; 1.42)	<0.001
LDL-C, Me (IQR), mmol/L	2.40 (1.80; 3.30)	2.40 (1.82; 2.90)	2.45 (1.80; 3.50)	0.555
Triglyceride, Me (IQR), mmol/L	1.86 (1.33; 2.62)	1.79 (1.14; 2.33)	1.94 (1.35; 2.81)	0.031
LDL-C/HDL-C	1.98 (1.41; 2.72)	1.63 (1.35; 2.22)	2.14 (1.48; 2.93)	<0.001
Pre-test probability model:				
2019 ESC PTP model, M ± SD, %	24.5 ± 12.8	17.8± 10.3	26.9 ±12.7	<0.001
PTP <5%, n (%)	9 (2.5)	8 (8.3)	1 (0.4)	<0.001
PTP 5-15%, n (%)	96 (26.2)	43 (44.8)	53 (19.6)	
PTP >15%, n (%)	261 (71.3)	45 (46.9)	216 (80)	

Abbreviations: BMI: body mass index; CAD: coronary artery disease; CCS: Canadian Cardiovascular Society; COPD: chronic obstructive pulmonary disease; FH-PCAD: family history of premature coronary artery disease; HDL-C: high-density lipoprotein cholesterol; IQR: interquartile range; LDL-C: low-density lipoprotein cholesterol; M: mean; Me: median; PAD: peripheral arterial disease; PTP: pre-test probability; SD: standard deviation.

Table 2. Coronary severity on computed tomography coronary angiography stratified by 2019 ESC pre-test probability

Variables	*PTP <5% (n=9)*	*PTP 5-15% (n=96)*	*PTP >15% (n=261)*	*P*
Mild (<50%), n (%)	8 (88.9)	43 (44.8)	45(17.2)	<0.001
Moderate (50-70%), n (%)	1 (11.1)	13 (13.5)	35 (13.4)	
Severe CAD (≥70%), n (%)	0 (0)	40 (41.7)	181 (69.4)	

Abbreviations: CAD: coronary artery disease, PTP: pre-test probability.

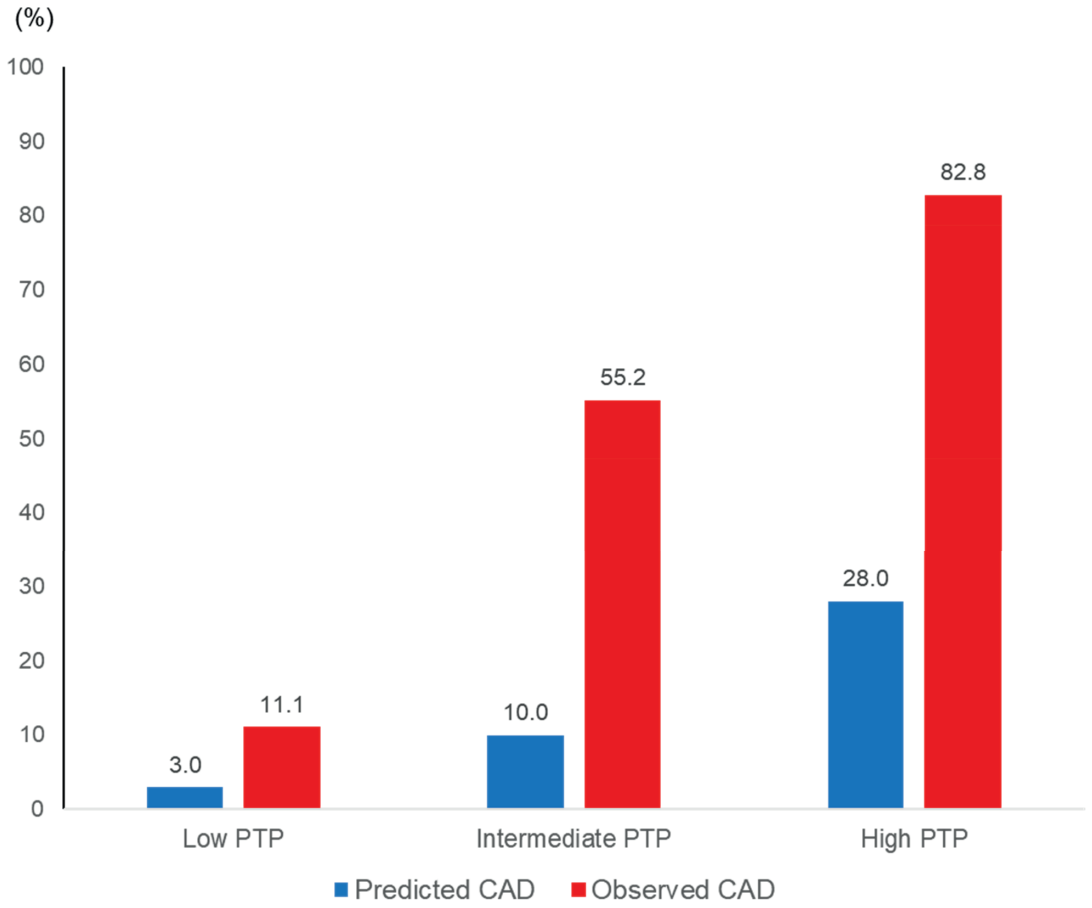


Figure 1. Distribution of patients into the 2019 ESC pre-test probability categories
Abbreviations: *CAD: coronary artery disease, PTP: pre-test probability.*

Table 3. Clinical models for prediction of obstructive coronary artery disease (CAD)

Variables	*Model 2*			*Model 3*		
	Coef.	*OR (95% CI)*	*P*	*Coef.*	*OR (95% CI)*	*P*
Intercept	–1.339	–	–	–2.176	–	–
2019 ESC PTP	0.056	1.057 (1.031-1.084)	<0.001	0.053	1.055 (1.029-1.082)	<0.001
Smoking	1.018	2.766 (1.433-5.342)	0.002	0.995	2.705 (1.387-5.274)	0.004
Hypertension	0.595	1.814 (0.912-3.607)	0.09	0.514	1.671 (0.842-3.314)	0.142
Diabetes mellitus	0.570	1.768 (1.001-3.123)	0.05	0.527	1.701 (0.963-3.003)	0.067
FH-PCAD	1.836	6.271 (1.420-27.700)	0.015	1.245	5.500 (1.227-24.659)	0.026
Dyslipidemia	–0.638	1.892 (0.767-4.670)	0.528	–	–	–
LDL-C/HDL-C	–	–	–	0.534	1.708 (1.221-2.388)	0.002
AUC of model	–	0.767 (0.716-0.817)	<0.001	–	0.785 (0.735-0.835)	<0.001
Hosmer-Lemeshow test	–	$\chi2$ = 10.433	0.236	–	$\chi2$ =10.703	0.219

Abbreviations: AUC: area under the curve; Coef., beta- coefficient; ESC: European society of cardiology; FH-PCAD: family history of premature coronary artery disease; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; OR: odds ratio; PTP: pre-test probability.

Model 3 showed improved discrimination compared to its PTP counterpart (AUC, 0.785 vs. 0.701; p = 0.035) (Figure 2).

Using the estimated variables of the Model 3, a clinical nomogram was established for predicting the risk of obstructive CAD (AUC, 0.785; 95% CI, 0.735-0.835, sensitivity: 63.7%, specificity: 83.3%, PPV: 91.5%, NPV: 44.9%) (Figure 3).

Bootstrap method (1000 times) revealed that the model 3 demonstrated a good discriminative power

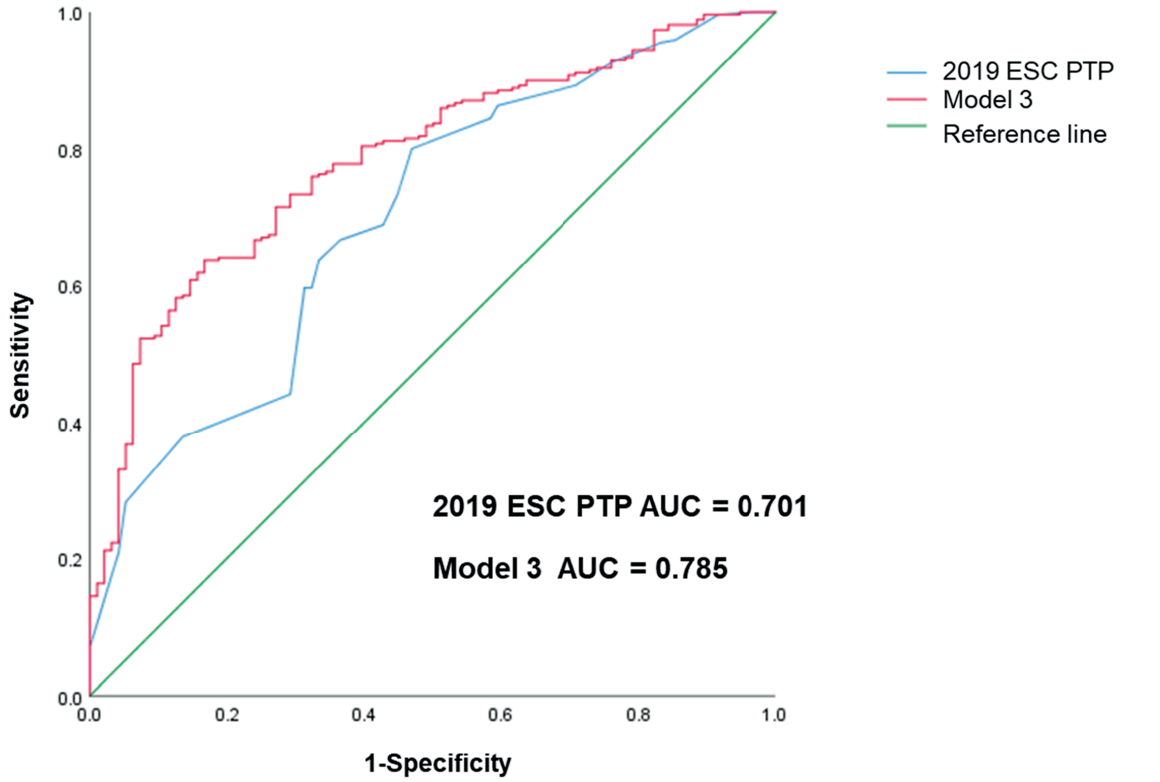


Figure 2. Comparison of ROC curves demonstrating discrimination of the model 3 (red), and the 2019 ESC pre-test probability model (blue) in predicting obstructive coronary artery disease
Abbreviations. *AUC: the area under the curve; ESC: European Society of Cardiology; PTP: pretest probability.*

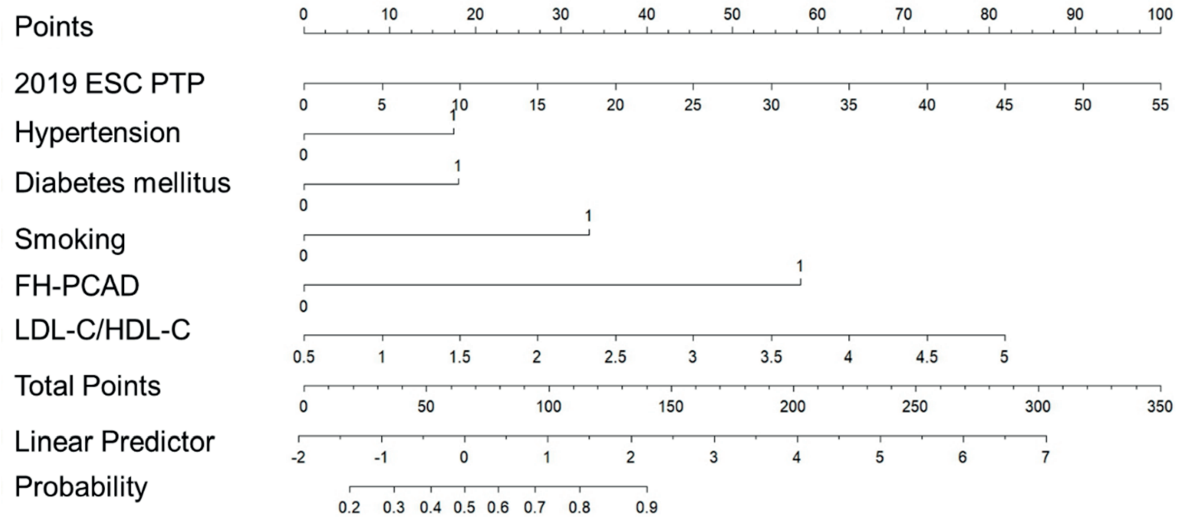


Figure 3. Clinical nomogram based on Model 3 for prediction of obstructive coronary artery disease.
Abbreviations: *AUC: the area under the curve; ESC: European Society of Cardiology; FH-PCAD: family history of premature coronary artery disease; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; PTP: pretest probability.*

(optimism corrected c-statistic = 0.769). In addition, calibration plots demonstrated an outstanding correlation between the probabilities predicted by the nomogram and actual probabilities (corrected slope = 0.8891, intercept = 0.0802) (Figure 4).

Discussion

In this study, we assessed the performance of the 2019 ESC PTP model for predicting obstructive CAD in a high-risk Vietnamese population with stable

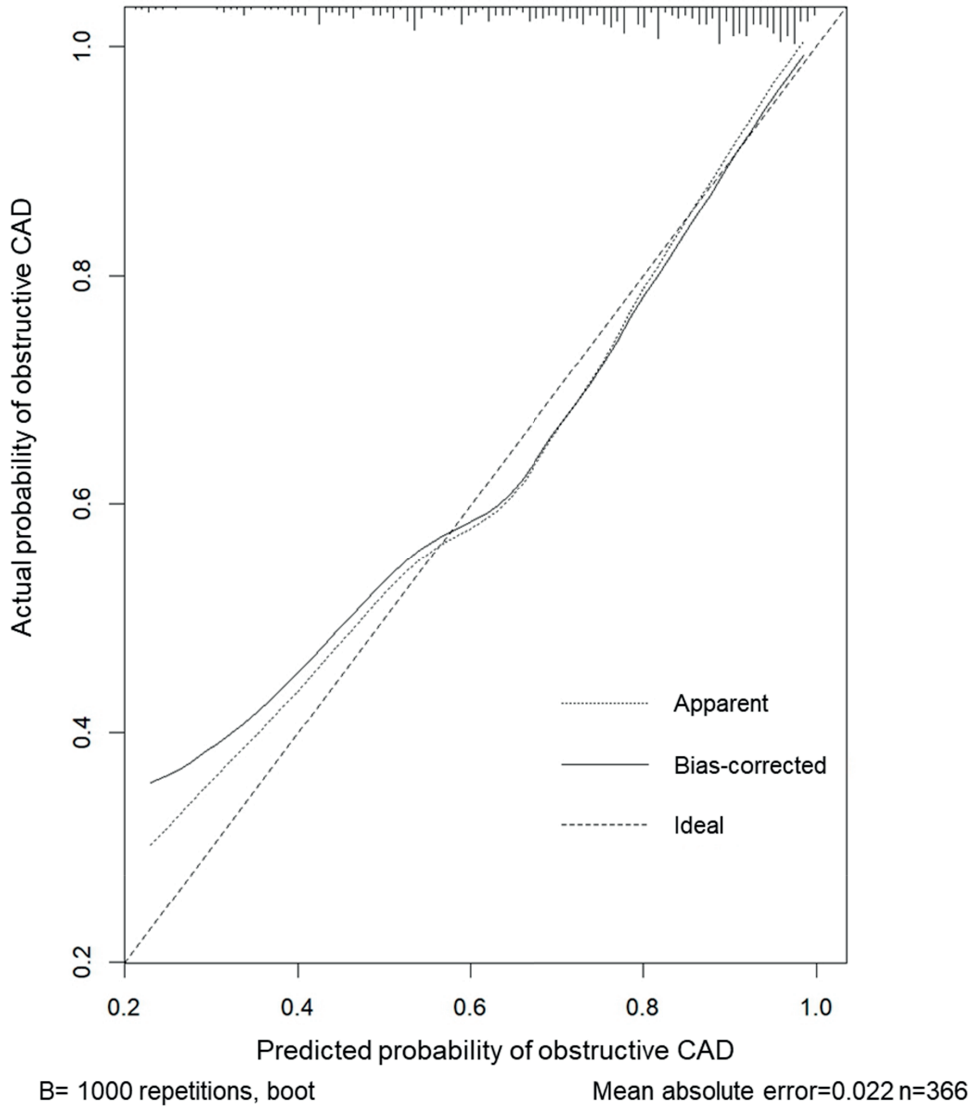


Figure 4. Calibration plot for internal validation of the nomogram with a 1000 bootstrap samples (calibration slope = 0.8891)
Abbreviation: *CAD: coronary artery disease.*

angina. Our results demonstrated that the 2019 ESC PTP model had modest discriminative power and tended to underestimate the actual prevalence of obstructive CAD compared to what was observed on CCTA. Additionally, incorporating cardiovascular risk factors such as hypertension, diabetes mellitus, smoking, family history of premature CAD, and LDL-C/HDL-C ratio significantly improved the model's discriminatory ability and calibration after internal validation.

The prevalence of obstructive CAD diagnosed by CCTA in our study population was 71.3%, significantly higher than that predicted by the 2019 ESC PTP model in all three PTP categories. For example, in the PROMISE study (*Prospective Multicenter Imaging Study for Evaluation of Chest Pain*) conducted in North America on 4415 symptomatic outpatients without prior CAD or unstable presentation, the prevalence of obstructive CAD (defined as ≥50% stenosis on CCTA) was only 13.9%[20]. Notably, 97% of the patients in the PROMISE study were classified as intermediate-risk by the 2019 ESC PTP model, while the low- and high-risk categories accounted for only 3.6% and 0.6% of the study population, respectively.

Similarly, in a sub-study by Bing et al.[21], which included 3755 patients aged 18–75 years with stable chest pain from the SCOT-HEART (*Scottish Computed Tomography of the Heart*) trial[22], the overall prevalence of obstructive CAD was 22% among the 1,613 patients who underwent CCTA. The observed prevalence of obstructive CAD in the low, intermediate, and high-risk groups was 13.2% (41/311), 29.2% (166/569), and 57.6% (423/733), respectively, all of which were substantially lower than the prevalence we observed in our cohort.

Another study by Lopes et al. involving 320 consecutive patients undergoing CCTA for suspected CAD reported a prevalence of 16.3% (n=52), with 1.9%, 86.5%, and 11.6% of patients in the low, intermediate, and high-risk groups, respectively[23]. In contrast, a study conducted by Erthal et al. in Brazil assessed the performance of the 2019 ESC PTP model in 409 symptomatic patients without known CAD, and found that the model performed reasonably well, with a prevalence of obstructive CAD of 3% in the low-risk group, 13% in the intermediate group, and 28% in the high-risk group[24]. These results indicate that the model may be more suitable for populations with lower baseline cardiovascular risk, such as the Brazilian cohort.

Our findings suggest that the 2019 ESC PTP model tends to underestimate the prevalence of obstructive CAD in high-risk populations. This is consistent with the study by Vranic et al. which included 1294 symptomatic patients referred for ICA[25]. In their study, the prevalence of obstructive CAD (defined as ≥50% stenosis) was 41.2%, with the ESC model underestimating CAD prevalence at all PTP levels (calibration intercept 1.15, slope 0.96). The modest discriminatory power of the model in Vranic's study (AUC 0.711, 95% CI 0.685–0.735) closely mirrors the results of our study. When comparing our cohort with that of Vranic et al, both populations shared similar cardiovascular risk profiles, with high rates of hypertension (83.1% vs. 92.3%), dyslipidemia (89.1% vs. 70.7%), and diabetes mellitus (38% vs. 31.9%). Additionally, our study cohort was slightly older, with 73.8% of patients being older than 60 years, compared to 70.4% in Vranic's cohort.

Our findings indicate that the 2019 ESC PTP model is not well calibrated for high-risk populations such as ours, which could lead to underdiagnosis of CAD in these patients. Importantly, incorporating additional cardiovascular risk factors, as recommended by other validated models such as the CAD Consortium 2 and CONFIRM scores[26,27], significantly improved the discriminatory performance of the 2019 ESC PTP model. This is consistent with the findings of Bjerking et al, who evaluated the performance of both the ESC 2019 PTP model and a clinical model incorporating risk factors such as diabetes mellitus, family history of CAD, and dyslipidemia in a large cohort of 42328 patients without previous CAD[28]. They found that while the ESC PTP model overestimated the prevalence of CAD (calibration slope 1.13 vs. 0.70), both models performed well in terms of discrimination (AUC = 0.76 for both). However, it is important to note that Bjerking's study was conducted in a low-risk cohort, while our population had a much higher prevalence of risk factors, including hypertension (83.1% vs. 46.7%), dyslipidemia (89.1% vs. 35.4%), and diabetes (38% vs. 8.8%).

These findings underscore the need for external validation of the ESC 2019 PTP model with additional clinical risk factors in high-risk populations, particularly in regions with a high incidence of CAD. In our study, we demonstrated that the LDL-C/HDL-C ratio is a useful predictor of obstructive CAD, consistent with the results of recent studies and meta-analyses[29,30]. For instance, Sun et al. reported that a higher LDL-C/HDL-C ratio was significantly associated with obstructive CAD (defined as ≥50% stenosis) in a cohort of 1,351 patients undergoing ICA[30]. This association remained significant even after adjusting for traditional cardiovascular risk factors in multivariate analysis.

Our updated nomogram, which integrates key cardiovascular risk factors such as hypertension, smoking, diabetes mellitus, FH-PCAD, and LDL-C/HDL-C ratio, demonstrated significant improvements in both discriminatory ability and calibration compared to the original 2019 ESC PTP model. As highlighted by the 2019 ESC guidelines, proper calibration of PTP models is crucial, especially when applied to high-risk populations. Without such adjustments, these models may lead to the underdiagnosis of obstructive CAD, potentially delaying necessary diagnostic and therapeutic interventions. If externally validated, our nomogram could serve as a valuable tool in clinical practice for better identifying high-risk patients and improving CAD diagnosis across diverse populations.

This study has several limitations. First, it was conducted in a single large medical center, which may limit the generalizability of the findings to other populations or settings. Second, the relatively small sample size (366 patients) reduces the statistical power of the analysis, and the lack of external validation restricts the broader applicability of our model. Future studies should include larger, multicenter cohorts to confirm these findings. Third, the study focused exclusively on patients referred for CCTA, introducing potential selection bias and limiting generalization to other patient groups or diagnostic methods. Furthermore, the absence of a control group makes it difficult to directly compare outcomes across different populations.

Conclusions

The 2019 ESC PTP model underestimates the prevalence of obstructive CAD in Vietnamese patients with stable angina referred for CCTA. Adding cardiovascular risk factors, such as hypertension, diabetes, smoking, family history of premature CAD, and LDL-C/HDL-C ratio significantly improved model discrimination and calibration. Future studies,

including external validation in diverse populations, are necessary to confirm the utility of this updated model in clinical practice.

Author Contributions:

Conceptualization, T.H.H. and M.Q.D.; methodology, T.H.H., T.L.K.; software, T.L.K., P.D.D., Q.C.T.; validation, T.H.H. and D.V.B.D.; formal analysis, T.H.H., M.Q.D., Q.C.T., T.L.P.N., D.V.B.D.; investigation, M.Q.D., P.D.D., Q.C.T.; resources, T.H.H., T.L.K., T.L.P.N., D.V.B.D.; data curation, T.H.H., M.Q.D., P.D.D., D.V.B.D., Q.C.T.; writing–original draft preparation, T.H.H., T.L.P.N, D.V.B.D.; writing–review and editing, T.H.H., T.L.K., T.L.P.N., D.V.B.D., P.D.D.; visualization, T.H.H. and M.Q.D.; supervision, T.H.H., D.V.B.D.; project administration, T.H.H., M.Q.D., T.L.K., D.V.B.D. All the authors have read and agreed with the final version of the article.

Compliance with Ethics Requirements:

"The authors declare no conflict of interest regarding this article"

"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study"

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