

Comparison of Framingham risk score and pooled cohort equations for the prediction of coronary atherosclerosis in patients who meet the target LDL-C level of Korean dyslipidemia guideline

Su Bin Kim, MD^a , Hae Won Jung, MD^b

Abstract

This study aims to compare the predicting performance of coronary atherosclerosis between Framingham Risk Score (FRS) and Pooled Cohort Equations (PCE) in moderate to high-risk patients who meet the target low-density lipoprotein cholesterol (LDL-C) level of Korean dyslipidemia guidelines. Among 1207 patients aged 40 to 65 who underwent coronary computed tomography angiography at outpatient for chest discomfort, we included 414 moderate-risk patients (non-diabetes) and 86 high-risk patients (diabetes). They were divided into 3 groups according to FRS and PCE, then compared with coronary artery calcification score (CACS) and plaque burden degree strata. We presented receiver operating characteristic curves for the presence of coronary artery calcification (CAC) and any plaque. In moderate-risk patients, the distribution of CACS and plaque burden degree according to FRS and PCE risk strata showed significant differences between groups and a consistent trend ($P < .001$). Both FRS and PCE showed good discrimination for the presence of CAC [area under the curve (AUC); 0.711 vs 0.75, $P = .02$] and any plaque (AUC; 0.72 vs 0.756, $P = .025$). However, in high-risk patients, there was no significant differences or consistent trend between groups and the AUC values of FRS and PCE were (0.537 vs 0.571, $P = .809$) for CAC and (0.478 vs 0.65 $P = .273$) for any plaque showing poor discrimination. In predicting coronary atherosclerosis in moderate to high-risk patients who meet the target LDL-C level of Korean dyslipidemia guidelines, both FRS and PCE can be used in moderate-risk patients but not in high-risk patients.

Abbreviations: ASCVD = atherosclerotic cardiovascular disease, AUC = area under the curve, CACS = coronary artery calcification score, CAC = coronary artery calcification, CAD = coronary artery disease, CCTA = coronary computed tomography angiography, CVD = cardiovascular disease, FRS = Framingham risk score, HDL = high-density lipoprotein, LDL-C = Low-density lipoprotein cholesterol, PCE = pooled cohort equations.

Keywords: coronary artery disease, diabetes mellitus, LDL cholesterol

1. Introduction

Low-density lipoprotein cholesterol (LDL-C) is the most critical factor in the occurrence of atherosclerotic cardiovascular disease (ASCVD) and is the main target for preventing it.^[1] Although ASCVD risk stratification is recommended worldwide, it is generally believed that the incidence of cardiovascular disease (CVD) differs from region and time changing due to the different distribution of CVD risk factors. According to the 2021 Canadian cardiovascular society guideline, it is recommended to perform cardiovascular risk assessment using the Framingham risk score (FRS), which is a multivariable statistical model that considers age, sex, current smoking status, blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, and history of diabetes.^[2] Moreover, the 2018 AHA Cholesterol Clinical

Practice Guidelines recommend using the US-derived pooled cohort equations (PCE) to estimate the 10-years risk for hard ASCVD events.^[3] These 2 methods are widely used all over the world. Both guidelines recommend risk stratification for patients between the ages of 40 and 75 for guiding therapy, including the use of statins to reduce major cardiovascular events.

However, in the case of FRS, some study results showed that it overestimates coronary risk in Korean.^[4] Also, in the case of PCE, because PCE targets white and black men and women in the US, the performance of the PCE in diverse racial/ethnic groups from outside the United States is highly variable, as would be expected given the heterogeneous nature of the populations, differences in the prevalence of risk factors, and differences in underlying hazards for ASCVD.^[5] Therefore, the Korean Society of lipids and atherosclerosis does not

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

^a Division of Cardiology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, ^b Department of Cardiology, Daegu Catholic University Medical Center, Daegu, Korea.

* Correspondence: Hae Won Jung, Department of Cardiology, Daegu Catholic University Medical Center, 33 Duryugongwonro 17-Gil, Nam-gu, Daegu 42472, Republic of Korea (e-mail: fdssgj@naver.com).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Kim SB, Jung HW. Comparison of Framingham risk score and pooled cohort equations for the prediction of coronary atherosclerosis in patients who meet the target LDL-C level of Korean dyslipidemia guideline. *Medicine* 2022;101:47(e31816).

Received: 9 August 2022 / Received in final form: 24 October 2022 / Accepted: 25 October 2022

<http://dx.doi.org/10.1097/MD.00000000000031816>

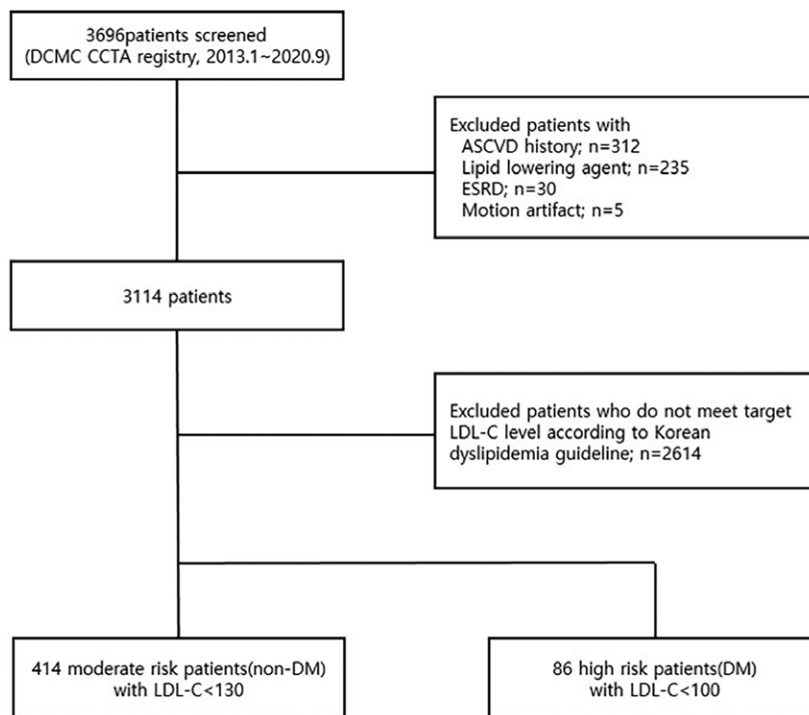


Figure 1. Enrollment flow chart for analysis. ASCVD = atherosclerotic cardiovascular disease, CCTA = coronary computed tomographic angiography, DCMC = Daegu catholic medical center, DM = diabetes mellitus, ESRD = end-stage renal disease, LDL-C = low-density lipoprotein cholesterol.

Table 1
Baseline characteristics divided by risk stratification.

	Moderate risk group	High risk group	P Value
Total patients, n	414	86	
Male	249 (60.1)	66 (76.7)	.005
Age, yr	55.64 ± 6.49	56.76 ± 6.39	.146
Hypertension	142 (34.3)	51 (59.3)	<.001
Hypertension medication	123 (29.7)	45 (52.3)	<.001
Diabetic medication	0 (0)	60 (69.8)	<.001
Smoking status			.015
Current smoker	32 (7.7)	15 (17.4)	
Ex-smoker	100 (24.9)	16 (18.6)	
Non-smoker	282 (67.4)	55 (64.0)	
BMI, kg/m ²	24.31 ± 3.50	24.43 ± 3.68	.773
FBG, mg/dL	102.31 ± 22.15	152.93 ± 56.83	<.001
SBP, mm Hg	125.27 ± 16.92	127.22 ± 18.74	.34
DBP, mm Hg	74.98 ± 11.37	76.26 ± 12.97	.357
TC, mg/dL	155.10 ± 26.79	134.50 ± 22.07	<.001
TG, mg/dL	115.96 ± 81.67	136.01 ± 110.97	.053
LDL-C, mg/dL	94.75 ± 22.72	77.89 ± 15.26	<.001
HDL-C, mg/dL	48.22 ± 15.06	40.82 ± 14.04	<.001
ApoA1, mg/dL	131.53 (30.36)	117.86 ± 27.62	<.001
ApoB, mg/dL	84.95 ± 18.35	77.12 ± 14.33	<.001
Lp(a), mg/dL	20.34 ± 23.37	20.52 ± 28.05	.948
Hb, mg/dL	13.63 ± 1.73	12.83 ± 2.13	.001
Creatine, mg/dL	0.79 ± 0.20	1.13 ± 1.05	.003
EF, %	57.29 ± 11.81	55.43 ± 11.20	.187
FRS	11.93 ± 8.09	21.46 ± 8.61	<.001
PCE	5.26 ± 4.16	12.35 ± 8.74	<.001
CAC score	136.61 ± 424.15	603.62 ± 1115.24	<.001
CAC > 0	190(54.1)	67(77.9)	<.001
Any plaque	241(58.2)	75(87.2)	<.001
Obstructive CAD	108 (26.1)	38 (44.2)	.001
Revascularization	46(11.1)	24(27.9)	<.001

Values are given as mean ± standard deviation or n (%).

Apo A1 = apolipoprotein A1, Apo B = apolipoprotein, BMI = body mass index, CAC = coronary artery calcification, DBP = diastolic blood pressure, EF = Ejection fraction, FBG = fasting blood glucose, FRS = Framingham Risk Score, Hb = hemoglobin, HDL = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, LP(a) = lipoprotein (a), CAD = coronary artery disease, PCE = Pooled Cohort Equations, SBP = systolic blood pressure, TC = total cholesterol, TG = triglyceride.

recommend these tools as guidelines for the treatment of dyslipidemia.

The Korean Society of Lipid and Atherosclerosis divided the risk group for ASCVD into 4 groups (very high-risk group, high-risk group, moderate-risk group, and low-risk group). Those with a history of CVD [coronary artery disease (CAD), peripheral artery disease, ischemic stroke, transient ischemic attack] were defined as very high-risk group, those with carotid disease, abdominal aortic aneurysm, or diabetes as high-risk group, those with 2 or more major risk factors as moderate-risk group, and those with less than 2 as low-risk group. Major risk factors were defined as age (male ≥ 45 years, female ≥ 55 years), family history of premature CAD hypertension, smoking, and hypo-HDL-C. Each group set LDL-C level as a treatment target, and made a guideline on whether to use statin and treatment direction according to LDL-C level (LDL-C target – very high risk < 70 mg/dL, high risk < 100 mg/dL, moderate risk < 130 mg/dL, low risk < 160 mg/dL).¹⁶ However, even in patients whose LDL-C values satisfy the LDL-C target, ASCVD occurs. Therefore, the purpose of this study is to evaluate the predictive performance of FRS and PCE for coronary atherosclerosis in moderate and high-risk patients who meet the target LDL-C level of the Korean dyslipidemia guidelines.

2. Methods

2.1. Study population and data collection

The study population was patients aged 40 to 65 who underwent coronary computed tomography angiography (CCTA)

at outpatient for chest discomfort. From January 2013 to September 2020, a total of 3696 patients visited the outpatient with chest pain, then CCTA and laboratory tests including LDL-C, HDL-C, triglyceride, apolipoprotein A1, apolipoprotein B, and lipoprotein (a) were performed. We excluded 312 patients with ASCVD history (very high risk and high-risk group except for diabetes), 235 patients already taking lipid-lowering agent, 30 patients with end-stage renal disease, and 5 patients with difficulty in CCTA image evaluation with motion artifact. Then 2614 patients who did not meet the target LDL-C level according to Korean dyslipidemia guideline were also excluded. Finally, we included 414 moderate-risk patients (non-diabetes) with LDL-C less than 130 mg/dL and 86 high-risk patients (diabetes) with LDL-C less than 100 mg/dL. The inclusion and exclusion criteria are shown in a flow diagram (Fig. 1). The patients' baseline characteristics and laboratory and radiographic test results were collected retrospectively. The institutional review board of Daegu catholic university medical center approved the study and waived the requirement for patient informed consent because of the study's retrospective nature.

2.2. Framingham risk score and pooled cohort equation

FRS and PCE were used to evaluate 10-years ASCVD risk. They were calculated using various variables (age, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure (including treated or untreated status), history of diabetes mellitus, and current smoking status).^{17,81} For each patient, the

Table 2
Distribution of CAC score and plaque degree according to FRS and PCE strata in moderate group (non-diabetes).

	FRS strata in moderate risk group (non-diabetes)			P Value*	P value for trend†
	Low (~10%)	Intermediate (10~20%)	High (20%~)		
n	211	131	72		
CAC score strata				<.001	<.001
CAC = 0	144 (68.2)	56 (42.7)	24 (33.3)		
CAC 1–99	42 (19.9)	38 (29.0)	18 (25.0)		
CAC 100–399	17 (8.1)	20 (15.3)	15 (20.8)		
CAC ≥ 400	8 (3.8)	17 (13.0)	15 (20.8)		
CAC > 0	67 (31.8)	75 (57.3)	48 (66.7)	<.001	<.001
CAC ≥ 100	25 (11.8)	37 (28.2)	30 (41.7)	<.001	<.001
CAC ≥ 400	8 (3.8)	17 (13.0)	15 (20.8)	<.001	<.001
Plaque degree strata				<.001	<.001
No plaque	119 (56.4)	43 (32.8)	11 (15.3)		
Plaque stenosis < 50%	60 (28.4)	46 (35.1)	27 (37.5)		
Plaque stenosis $\geq 50\%$	32 (15.2)	42 (32.1)	34 (47.2)		
Any plaque	92 (43.6)	88 (67.2)	61 (84.7)	<.001	<.001
	PCE strata in moderate risk group (non-diabetes)			P Value*	P Value for trend†
	Low (~5%)	Borderline or Intermediate (5~20%)	High (20%~)		
n	236	176	2		
CAC score strata				<.001	<.001
CAC = 0	163 (69.1)	60 (34.1)	1 (50.0)		
CAC 1–99	48 (20.3)	50 (28.4)	0 (0.0)		
CAC 100–399	19 (8.1)	33 (18.8)	0 (0.0)		
CAC ≥ 400	6 (2.5)	33 (18.8)	1 (50.0)		
CAC > 0	73 (30.9)	116 (65.9)	1 (50.0)	<.001	<.001
CAC ≥ 100	25 (10.6)	66 (37.5)	1 (50.0)	<.001	<.001
CAC ≥ 400	6 (2.5)	33 (18.8)	1 (50.0)	<.001	<.001
Plaque degree strata				<.001	<.001
No plaque	133 (56.4)	40 (22.7)	0 (0.0)		
Plaque stenosis < 50%	65 (27.5)	67 (38.1)	1 (50.0)		
Plaque stenosis $\geq 50\%$	38 (16.1)	69 (39.2)	1 (50.0)		
Any plaque	103 (43.6)	136 (77.3)	2 (100.0)	<.001	<.001

CAC = coronary artery calcification, FRS = Framingham Risk Score, PCE = Pooled Cohort Equations.

*Chi-square test or Fisher exact test.

†Linear association test.

10-years risk for ASCVD was categorized as low-risk (<5%), borderline or intermediate risk (5% to <20%) and high risk (≥20%) according to 2018 AHA dyslipidemia guideline using PCE and low risk (<10%), intermediate risk (10% to <20%), and high risk (>20%) according to 2021 CCS dyslipidemia guideline using FRS.^[2,3] The predictive performance of these 2 tools was indirectly analyzed through the presence or absence of coronary artery calcification (CAC) and plaque.

2.3. Acquisition and analysis of CCTA images

CT scans were performed with a 256-slice CT (Definition Flash; Siemens Healthineers AG) or a 512-slice CT (Revolution CT; GE Healthcare). All patients with an initial heart rate ≥ 60 beats/min were given an oral beta-blocker (propranolol 20 mg) to achieve a target heart rate of 50 to 60 beats/minute. Sublingual nitroglycerin was administered immediately before scanning. An iodine contrast agent (60–70 mL) was administered into the antecubital vein within 10 seconds, followed by 25 mL of saline solution injected at 5.0 mL/second. The CT-reconstructed imaging data were transferred to a GE Centricity system (GE Healthcare Bio-Sciences Corp) for postprocessing and subsequent image analysis. A radiologist read each scan independently at a central reading center. Plaque incidence and its severity were investigated. Plaques were defined as structures ≥ 1 mm² within and/or adjacent to the vessel lumen and were clearly distinguishable from the lumen and the surrounding pericardial tissue. Coronary atherosclerosis is defined as the presence of any

CAC or plaque.^[9] Stenosis of 50% or more in coronary artery was defined as obstructive CAD.^[10] The coronary artery calcium score (CACS) was acquired with the Agatston method using a commercially available reconstruction program for 3-dimensional reconstruction and measurement (Aquarius iNtuition TM Ver.4.4.12 TeraRecon).^[11] The CACS was classified according to the cutoff values (0, 1–100, 101–400, >400) mainly used in the clinic.^[12] After CCTA evaluation, medical treatment or revascularization (percutaneous coronary intervention or coronary artery bypass grafting) was performed according to the physician’s judgment, and the rate of revascularization was also investigated.

2.4. Statistics

Continuous values are reported as mean ± standard deviations and as frequencies (percentages) for categorical values. *T*-test or Wilcoxon rank-sum test for continuous values was used to compare the group and chi-square test or Fisher exact test for categorical values. Baseline characters were compared by dividing them into high-risk group (diabetes) and moderate risk group (non-diabetes). Distribution of CACS and plaque degree with various FRS, PCE strata were compared by using the chi-square test or Fisher exact test, and the trend test was also done by linear association test. In addition, the weight kappa coefficient was used to analyze the agreement between FRS and PCE. To compare the predicting performance of FRS and PCE according to CAC and plaque observed in CCTA, receiver operating

Table 3

Distribution of CAC score and plaque degree according to FRS and PCE strata in high-risk group (diabetes).

	FRS strata in high-risk group (diabetes)			P Value*	P value for trend†
	Low (~10%)	Intermediate (10–20%)	High (20%~)		
n	11	25	50		
CAC score strata				.785	.496
CAC = 0	3 (27.3)	4 (16.0)	12 (24.0)		
CAC 1–99	3 (27.3)	7 (28.0)	9 (18.0)		
CAC 100–399	2 (18.2)	7 (28.0)	9 (18.0)		
CAC ≥ 400	3 (27.3)	7 (28.0)	20 (40.0)		
CAC > 0	8 (72.7)	21 (84.0)	38 (76.0)	.665	.889
CAC ≥ 100	5 (45.5)	14 (56.0)	29 (58.0)	.75	.497
CAC ≥ 400	3 (27.3)	7 (28.0)	20 (40.0)	.502	.282
Plaque degree strata				.519	.409
No plaque	2 (18.2)	2 (8.0)	7 (14.0)		
Plaque stenosis < 50%	5 (45.5)	14 (56.0)	18 (36.0)		
Plaque stenosis ≥ 50%	4 (36.4)	9 (36.0)	25 (50.0)		
Any plaque	9 (81.8)	23 (92.0)	43 (86.0)	.724	.996

	PCE strata in high-risk group (diabetes)			P value*	P Value for trend†
	Low (~5%)	Borderline or intermediate (5–20%)	High (20%~)		
n	15	57	14		
CAC score strata				.738	.064
CAC = 0	5 (33.3)	12 (21.1)	2 (14.3)		
CAC 1–99	4 (26.7)	13 (22.8)	2 (14.3)		
CAC 100–399	3 (20.0)	12 (21.1)	3 (21.4)		
CAC ≥ 400	3 (20.0)	20 (35.1)	7 (50.0)		
CAC > 0	10 (66.7)	45 (78.9)	12 (85.7)	.504	.216
CAC ≥ 100	6 (40.0)	32 (56.1)	10 (71.4)	.234	.09
CAC ≥ 400	3 (20.0)	20 (35.1)	7 (50.0)	.238	.092
Plaque degree strata				.411	.246
No plaque	3 (20.0)	8 (14.0)	0 (0.0)		
Plaque stenosis < 50%	7 (46.7)	22 (38.6)	8 (57.1)		
Plaque stenosis ≥ 50%	5 (33.3)	27 (47.4)	6 (42.9)		
Any plaque	12 (80.0)	49 (86.0)	14 (100.0)	.282	.112

CAC = coronary artery calcification, FRS = Framingham Risk Score, PCE = Pooled Cohort Equations.

*Chi-square test or Fisher exact test.

†Linear association test.

characteristic curves were presented for each, and area under the curve (AUC) was measured.

3. Results

3.1. Base characteristics

The mean age, LDL-C and CACS of the patients were 55.83 ± 6.48 , 91.85 ± 22.53 mg/dL and 216.936 ± 626 , respectively. When comparing the moderate (non-diabetic) group and the high-risk group (diabetic), the high-risk group had a higher incidence of male, hypertension, antihypertensive drugs, antidiabetic drugs, current smoking, and higher FRS, PCE, and CAC scores. The LDL-C level was significantly lower in high-risk group. The presence of CAC and any plaque, which were used as indicators to predict future ASCVD were observed at a significantly higher rate in the high-risk group (Table 1).

3.2. Distribution of CACS and plaque burden degree in various FRS and PCE strata

The distribution of CACS and plaque burden degree according to FRS and PCE strata in the moderate risk group (non-diabetes) showed significant differences (all $P < .001$) and a consistent trend (All trend test $P < .001$) among groups (Table 2). However, there was no significant difference and consistent trend in high-risk group (diabetes) (Table 3).

3.3. Comparison of FRS and PCE in moderate risk group and high-risk group

FRS and PCE strata showed consistency in moderate and high-risk group (weight kappa = $0.424 [0.363-0.486]$; $0.313 [0.185-0.442]$, $P < .001$). Although there was a good consistency, most patients judged as high risk by FRS were not judged as high risk by PCE. In non-diabetes patients, 72 patients (17.3%) were judged as high risk by FRS, but only 2 patients (0.4%) were judged as high risk by PCE. Similar results were observed in diabetes patients, with 50 (58.1%) high risk patients in FRS, but only 14 (16.2%) high risk patients in PCE (Fig. 2).

3.4. Predicting the performance of FRS and PCE in coronary atherosclerosis

Both FRS and PCE showed good discrimination for the presence of CAC and any plaque in moderate risk group (non-diabetes) and PCE showed better predictability for coronary atherosclerosis than FRS (AUC for CAC; FRS vs PCE: 0.711 vs 0.75 , $P = .02$, AUC for any plaque; FRS vs PCE: 0.72 vs 0.756 , $P = .025$). However, in high-risk group (diabetic), AUC values of FRS and PCE were (0.537 vs 0.571 , $P = .809$) for CAC and (0.478 vs 0.65 , $P = .273$) for any plaque. Both scores showed poor discrimination (Fig. 3).

4. Discussion

Most guidelines recommend that LDL-C is the main target for preventing ASCVD, and according to Korean dyslipidemia guideline, statin use was unnecessary for patients in this study. However, in this study, 29% of patients had obstructive CAD, and 14% ultimately needed revascularization despite the low LDL-C levels. In addition, the incidence of obstructive CAD and revascularization was significantly higher in high-risk group than moderate risk group. However, LDL-C values were significantly lower than those of moderate risk group. This means that although LDL-C is the main target of ASCVD, LDL-C levels do not account for all ASCVD occurrences. A Korean cohort study that analyzed the population attributable risk to CVD

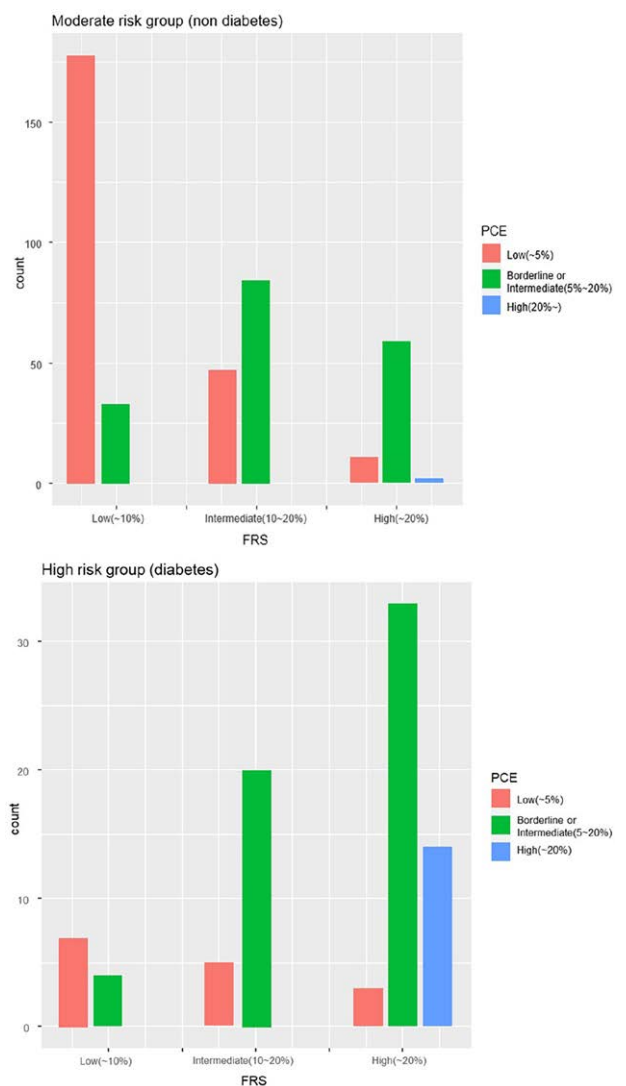


Figure 2. Framingham Risk Score and Pooled Cohort Equations strata in moderate (non-diabetes) and high-risk group (diabetes). FRS = Framingham Risk Score, PCE = Pooled Cohort Equations.

found that the contribution is the highest for hypertension, followed by smoking, dyslipidemia, and diabetes in men. In Korean women, the factor with the highest contribution to CVD risk was hypertension, followed by dyslipidemia, diabetes, and smoking.^[6] Therefore, managing the other modifiable risk factors in addition to LDL-C is recommended for CVD prevention.

FRS and PCE are widely used tools worldwide, and risk stratification is possible easily. In the moderate risk group of this study, both FRS and PCE strata for CACS and plaque degree distribution showed significant differences between groups and both AUC values for CAC and any plaque were more than 0.7, indicating good discrimination. Also, of the 2 methods, PCE was better in predicting coronary atherosclerosis than FRS. Although these 2 methods showed moderate agreement with each other, considering that there were significantly more patients judged as high risk by FRS than by PCE, it can be considered that FRS overestimates CV risk compared to PCE in Korean patients. In fact, although FRS has been continuously updated until recently,^[13] overestimation after applying the FRS to ethnic populations has been problematic in Western countries.^[14] To overcome the limitations of FRS, the pooled cohort equation (PCE) has been introduced by the American College of Cardiology/American Heart Association.^[7] There are few studies comparing FRS and PCE in Koreans. In a study, the AUC value of the PCE

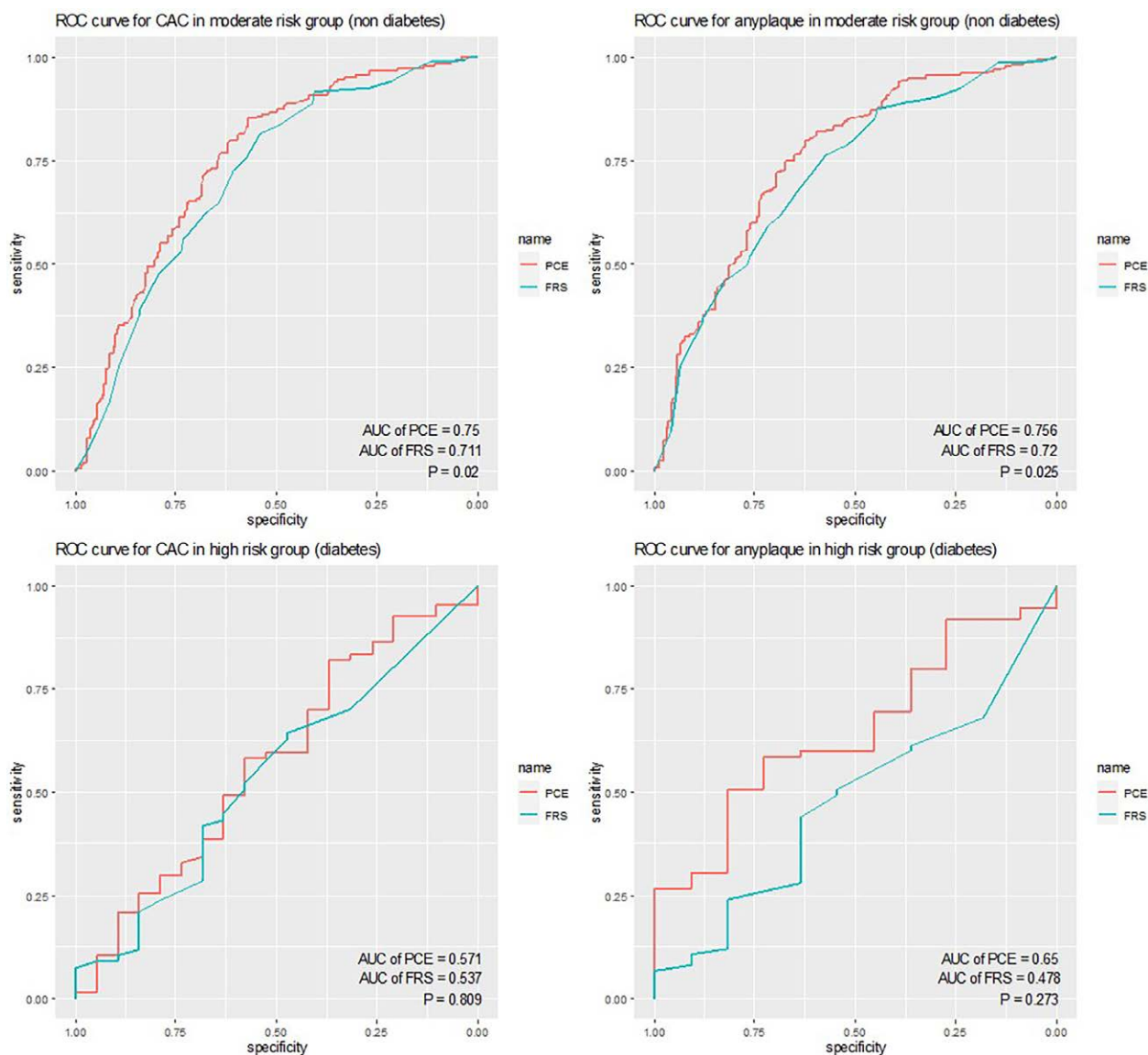


Figure 3. Receiver operating characteristic curve for coronary artery calcification and any plaque in moderate (non-diabetes) and high-risk group (diabetes). AUC = area under the curve, CAC = coronary artery calcification, FRS = Framingham Risk Score, PCE = Pooled Cohort Equations, ROC = receiver operating characteristic.

score for CAC progression was observed to be slightly higher than that of FRS (AUC 0.67 vs 0.66).^[15] Then in another study with Asians, there was a result that PCE brought an improvement of 3.1% Net reclassification Index (NRI) compared to FRS for ASCVD.^[16] However, neither study showed a significant difference. In addition, the previous study demonstrated PCE also overestimates or underestimates ASCVD when targeting Koreans.^[17] Therefore, ASCVD risk prediction models are being developed for Korean.^[18]

Unlike the moderate risk group, in the high-risk group with diabetes, the FRS and PCE strata did not show significant differences in the CACS and plaque degree distribution, and the predictive performance of coronary atherosclerosis was also poor. When calculating FRS and PCE scores, there is only a binary option regarding history of diabetes and current smoking status, which are subjects of FRS and PCE scores. They are not categorized in detail, such as according to diabetes morbidity period, current diabetes control status, smoking period, etc. Diabetes is a significant risk factor for CAD, and controlling it is just as important as lowering LDL to prevent CAD. In a study, it was reported that controlled diabetes showed no significant difference from normal individuals for risk of any plaque and

obstructive CAD. Still, the risk significantly increased in uncontrolled diabetes patients.^[19] However, PCE and FRS do not contain detailed information about diabetes, and we thought this may have influenced the prediction performance of FRS, PCE for coronary atherosclerosis in the high-risk group. Although this study did not investigate the degree of diabetes control and disease duration in detail, when performing risk stratification in diabetic patients, it would be helpful to increase the predictive performance by applying exact values such as hemoglobin A1c rather than a binary option.

As mentioned above, tools such as FRS and PCE were developed based on Western populations, and there are some prediction models for Korean.^[4,18] However, the current Korean dyslipidemia guidelines do not recommend the use of risk assessment tools. According to the results of our study, we found that FRS or PCE can be usefully used to discriminate patients with residual ASCVD risk in moderate-risk group who meet the target LDL-C level of Korean dyslipidemia guideline, and the need for statin use is not recommended. Therefore, we hope the research can predict future ASCVD risk by fusion of Korean dyslipidemia guideline with FRS or PCE. It will take a long time to develop and general use of the risk stratification

model for Koreans. In contrast, FRS and PCE are easily and quickly available online. Therefore, using FRS or PCE should be considered in ASCVD risk stratification and treatment direction in Korean.

There are several limitations to this study. First, Although FRS and PCE tools were made to directly screen 10-years risk of clinical ASCVD in asymptomatic patients, we attempted to predict coronary atherosclerosis on CCTA through the presence of CAC and any plaque in symptomatic patients using FRS and PCE. However, considering that the CAC score is used as an independent marker for predicting ASCVD,^[20] and the atherosclerotic plaque burden is the main driver of ASCVD risk in CAD patients,^[21] these 2 values are acceptable as predictive indicators for ASCVD. Therefore, this study showed that 2 representative tools could be helpful for predicting future ASCVD even in symptomatic moderate risk patients with low LDL-C as well as asymptomatic patients and PCE was superior to ASCVD prediction in these patient groups than FRS. Second, this study was for patients who came to the hospital with chest pain. In addition, most of the patients visited had more than 1 major risk factor, so low risk group patients were not included. As a result, there must have been a selection bias. Third, the total number of patients was small, among them, the number of the high-risk group patients was particularly small. Therefore, it is difficult to apply the results of this study to all diabetic patients in general. However, considering that most diabetic patients have dyslipidemia, the number of diabetic patients with LDL-C below 100mg/dL without lipid-lowering drugs in this study was inevitably small. We hope that future studies will be conducted with a large number of diabetic patients with low LDL-C.

5. Conclusion

In predicting coronary atherosclerosis in moderate to high-risk patients who meet the target LDL-C level of Korean dyslipidemia guidelines, both FRS and PCE can be used in moderate-risk patients but not in high-risk patients. PCE showed better predictability for coronary atherosclerosis than FRS.

Author contributions

Conceptualization: Su Bin Kim, Hae Won Jung.

Formal analysis: Su Bin Kim, Hae Won Jung.

Writing – original draft: Su Bin Kim, Hae Won Jung.

Writing – review & editing: Hae Won Jung.

References

- [1] National Cholesterol Education Program Expert Panel on Detection Evaluation, Treatment of High Blood Cholesterol in Adults. Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. *Circulation*. 2002;106:3143–421.
- [2] Pearson GJ, Thanassoulis G, Anderson TJ, et al. 2021 Canadian cardiovascular society guidelines for the management of dyslipidemia for the prevention of cardiovascular disease in adults. *Can J Cardiol*. 2021;37:1129–50.
- [3] Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. *Circulation*. 2019;139:e1082–143.
- [4] Jee SH, Jang Y, Oh DJ, et al. A coronary heart disease prediction model: the Korean heart study. *BMJ Open*. 2014;4:e005025.
- [5] Lloyd-Jones DM, Braun LT, Ndumele CE, et al. Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease: a special report from the American heart association and American college of cardiology. *J Am Coll Cardiol*. 2019;73:3153–67.
- [6] Rhee EJ, Kim HC, Kim JH, et al. 2018 Guidelines for the management of dyslipidemia. *Korean J Intern Med*. 2019;34:723–71.
- [7] Goff DC, Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American college of cardiology/American heart association task force on practice guidelines. *Circulation*. 2014;129:S49–73.
- [8] Expert Panel on Detection Evaluation, Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *JAMA*. 2001;285:2486–97.
- [9] Won KB, Park GM, Yang YJ, et al. Independent role of low-density lipoprotein cholesterol in subclinical coronary atherosclerosis in the absence of traditional cardiovascular risk factors. *Eur Heart J Cardiovasc Imaging* 2019;20:866–72.
- [10] Andersson HB, Pedersen F, Engström T, et al. Long-term survival and causes of death in patients with ST-elevation acute coronary syndrome without obstructive coronary artery disease. *Eur Heart J*. 2018;39:102–10.
- [11] Agatston AS, Janowitz WR, Hildner FJ, et al. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol*. 1990;15:827–32.
- [12] Budoff MJ, Nasir K, McClelland RL, et al. Coronary calcium predicts events better with absolute calcium scores than age-sex-race/ethnicity percentiles: MESA (multi-ethnic study of atherosclerosis). *J Am Coll Cardiol*. 2009;53:345–52.
- [13] D’Agostino RBS, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham heart study. *Circulation*. 2008;117:743–53.
- [14] Brindle P, Emberson J, Lampe F, et al. Predictive accuracy of the Framingham coronary risk score in British men: prospective cohort study. *BMJ*. 2003;327:1267.
- [15] Cho YK, Jung CH, Kang YM, et al. 2013 ACC/AHA Cholesterol guideline versus 2004 NCEP ATP III guideline in the prediction of coronary artery calcification progression in a Korean population. *J Am Heart Assoc*. 2016;5.
- [16] Chia YC, Lim HM, Ching SM. Validation of the pooled cohort risk score in an Asian population – a retrospective cohort study. *BMC Cardiovasc Disord*. 2014;14:163.
- [17] Jung KJ, Jang Y, Oh DJ, et al. The ACC/AHA 2013 pooled cohort equations compared to a Korean risk prediction model for atherosclerotic cardiovascular disease. *Atherosclerosis*. 2015;242:367–75.
- [18] Choi SH, Lee SM, Kim SH, et al. Prediction of 8-year risk of cardiovascular diseases in Korean adult population. *Sci Rep*. 2021;11:14339.
- [19] Park GM, Lee CH, Lee SW, et al. Impact of diabetes control on subclinical atherosclerosis: analysis from coronary computed tomographic angiography registry. *Diabetes Metab J*. 2020;44:470–9.
- [20] Neves PO, Andrade J, Moncao H. Coronary artery calcium score: current status. *Radiol Bras*. 2017;50:182–9.
- [21] Dzaye O, Razavi AC, Blaha MJ, et al. Evaluation of coronary stenosis versus plaque burden for atherosclerotic cardiovascular disease risk assessment and management. *Curr Opin Cardiol*. 2021;36:769–75.