original article

The relationship between degree of coronary artery stenosis detected by coronary computed tomography angiography and ACEF risk score in patients with chronic coronary syndrome

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BACKGROUND: The ACEF risk score (age, creatinine, and ejection fraction) has been associated with satisfactory predictive values not only for short-term and long-term mortality but also for major adverse cardiovascular events.

OBJECTIVES: Investigate the relationship between ACEF risk score and degree of coronary artery stenosis.

DESIGN: Retrospective, observational study.

SETTING: Tertiary percutaneous coronary intervention center.

PATIENTS AND METHODS: In patients with coronary coronary artery stenosis <70% were compared with patients with stenosis ≥70%. All were diagnosed with chronic coronary syndrome (CCS) and had undergone coronary computed tomography angiography (CTA). Receiver operating characteristic analysis was performed for the cut-off value of the ACEF risk score. Univariable and multivariable regression analyses were performed for significant parameters related to degree of coronary artery stenosis in coronary CTA.

MAIN OUTCOME MEASURES: Relationship between ACEF risk score and degree of coronary artery stenosis in coronary CTA.

SAMPLE SIZE: 148 patients.

RESULTS: In the multivariable regression analysis; left ventricular ejection fraction (OR: 0.94; 95%CI: 0.89-0.99, *P*=.015) and ACEF risk score (OR: 5.63; 95% CI: 1.62- 19.57, *P*=.007) were independent predictors for degree of coronary artery stenosis. The ACEF risk score was statistically significantly higher in with patients with stenosis ≥70% (1.43 [0.59]) than in patients with stenosis <70% (0.98 [0.35]), *P*<.001). An ACEF risk score value >1.04 was a predictor of the presence of severe coronary artery stenosis detected by coronary CTA in patients with CCS, with 66% sensitivity and 69% specificity.

CONCLUSIONS: A high ACEF risk score (age, creatinine, ejection fraction) in patients with CCS is associated with the presence of severe coronary artery stenosis detected by coronary CTA, and was useful as an assessment tool for coronary angiography in patients with CCS.

LIMITATIONS: Since we do not have long-term follow-up results, we do not know the prognostic value of the ACEF risk score in the long-term follow-up of patients with CCS.

CONFLICT OF INTEREST: None.

Atherosclerotic cardiovascular disease is the leading cause of death worldwide, but advancements in percutaneous coronary intervention (PCI) and pharmacological treatments have led to a decrease in early and late death rates in coronary artery disease (CAD).[1,2] While invasive coronary angiography is the standard method for detecting CAD, coronary computed tomography angiography (CTA) is increasingly being used as a diagnostic tool to determine the severity of coronary artery occlusion without intervention and to visualize plaque in the coronary arteries. The European Society of Cardiology's 2019 chronic coronary syndrome (CCS) guidelines recommend using CTA rather than invasive methods for diagnosis in patients with a low clinical probability of CAD.[3] Additionally, there has been a growing emphasis on the importance of proper risk stratification to reduce mortality.

The ACEF risk score is a simple scoring system calculated from basic data such as age, creatinine, and left ventricular ejection fraction (LVEF). The score produces satisfactory predictive values that predict major adverse cardiovascular events (MACE).[4] In patients who underwent PCI, higher rates of stent thrombosis and myocardial infarction (MI) were observed in patients with high ACEF risk scores.[5] The ACEF risk score also predicted MACE more effectively over the long-term than other risk scores (GRACE, SYNTAX) in patients with non-ST-elevation myocardial infarction (NSTEMI) who underwent various treatment strategies.[6] The investigators concluded that the ACEF risk score is a quick and simple tool for classifying NSTEMI patients.

Mortality in patients with ST elevation myocardial infarction (STEMI) is affected by many factors, including age, delay in treatment, history of MI, diabetes mellitus (DM), renal failure, number of diseased coronary arteries, and LVEF.[1] Three of the factors constitute the ACEF risk score (age, creatinine and LVEF). However, the ACEF risk score has not been widely studied in patients with CCS. Patients at high risk for CAD may benefit from early invasive treatment, reduced use of contrast material, and close monitoring and follow-up.[7] Therefore, in this study, we aimed to investigate the relationship between the ACEF risk score and the degree of coronary artery stenosis in patients with CCS who underwent coronary CTA.

PATIENTS AND METHODS

The study was conducted on patients diagnosed with CCS who had undergone coronary CTA from August 2020 to July 2022. Patients with severe liver failure, active cancer, acute kidney failure, inability to undergo optimal echocardiographic examination, current dialysis, and those who did not give informed consent were excluded from the study. To measure the degree of atherosclerotic stenosis, the percentage of lumen narrowing was calculated using the equation (reference artery internal diameter - narrowed lumen internal diameter) ×100/reference artery internal diameter. Patients were divided into two groups based on the degree of luminal stenosis: one group had stenosis ≥70% (severe stenosis) in any coronary artery in the CTA and the other patients had stenosis <70%. Hypertension was defined as blood pressure above 140/90 mmHg on repeated measurements or use of anti-hypertensive medication.[8] DM was defined as patients with fasting glucose ≥126 mg/dL, HbA1c ≥6.5 or under diabetes treatment.[9] Hyperlipidemia was defined as total cholesterol >200 mg/dL, LDL cholesterol >130 mg/dL, triglyceride >150 mg/dL, or use of statin therapy.[10] Chronic renal failure was defined as a glomerular filtration rate below 60 mL/min.[11] To examine the correlation between the ACEF risk score and the severity of coronary artery narrowing in coronary computed tomography angiography (CTA), the ACEF risk score was calculated using the following previously established formula: ACEF=(age/LVEF)+1 (if creatinine >2.0 mg/dL).[4-7]

The analysis was performed using IBM SPSS version 25.0. The normality of numerical variables was assessed using the Kolmogorov-Smirnov test. Numerical variables were presented as mean (standard deviation). For numerical variables that were normally distributed, an independent samples t-test was used, and for those that were not normally distributed, a Mann-Whitney U test was used. Categorical variables were presented as numbers and percentages. The comparison of categorical variables was done using the Pearson chi-square and Fisher exact tests. The ability of the ACEF risk score to predict stenosis severity was evaluated using univariable and multivariable analyses, with odds ratios (OR) and 95% confidence intervals (CI) recorded. Variables with a *P* value of less than .05 were used for the selection of variables in the multivariable logistic regression. Receiver operating characteristic (ROC) analysis was also performed to determine the cut-off value for the ACEF risk score. A *P* value of less than .05 was considered statistically significant.

RESULTS

The mean (SD) age of 148 patients included in the study was higher in patients with coronary artery stenosis ≥ 70% (**Table 1**). There were slightly more male than female patients overall, the body mass index was similar in both groups, while hypertension was somewhat more common in patients with coronary artery stenosis ≥70%. There were 33 (22.3%) active smokers in the study population but the differences between groups were not statistically significant. Statistically significant differences were found only for age, hypertension , history of CAD, and PAD. The most common comorbidities were hypertension in 66 patients (44.6%) and hyperlipidemia in 48 patients (32.4%). In biochemical parameters, HbA1c was lower in patients with coronary artery stenosis <70% (5.69 [1.04] vs 6.24 [1.16], respectively, *P*=.003) (**Table 2**). On echocardiography, the mean LVEF value of the patients was 53.9%. LVEF was lower in patients with coronary artery stenosis ≥70% (49.74 [10.86] % vs 57.12 [7.56]%, respectively; *P*<.001). There was no difference in medication use except for the dihydropyridine calcium channel blocker (**Table 3**).

The median value of the ACEF risk score was 1.00 (0.84-1.40). The ACEF risk score was statistically significantly lower in patients with <70% compared to ≥70% (0.92 [0.73-1.08] vs 1.18 [0.98-1.69], respectively; *P*<.001).

In the univariable regression analysis of the factors affecting the degree of coronary artery stenosis in coronary CT angiography, age, hypertension, CAD, PAD, HbA1c, LVEF and ACEF risk score were statistically significant. In the multivariable regression analysis; LVEF (OR: 0.94; 95% CI: 0.89-0.99, *P*=.015) and ACEF risk score (OR: 5.63; 95% CI: 1.62- 19.57, *P*=.007) were independent predictors of the degree of luminal stenosis (**Table 4**). The ACEF risk score value> 1.04 was a predictor of the presence of severe coronary artery stenosis detected by coronary CTA in patients with CCS, with 66% sensitivity and 69% specificity (ROC AUC: 0.765, 95% CI: 0.690-0.840, *P*<.001) (**Figure 1**).

DISCUSSION

In this study we investigated the relationship between the ACEF risk score and the presence of severe coro-

Table 1. Demographic and clinical features of the study participants (n=148).

	Coronary lesion <70% (n=83)	Coronary lesion >70% (n=65)	Total (n=148)	*P* value
Age (years)	52.9 (12.7)	57.3 (10.3)	54.80 (11.9)	**.024**
Body mass index (kg/m^2)	26.3 (3.8)	25.9 (4.1)	26.14 (3.9)	.533
Male sex	41 (49.4)	37 (56.9)	78 (52.7)	.363
Systolic blood pressure (mmHg)	135.2 (15.7)	139.6 (20.3)	137.1 (18.0)	.135
Diastolic blood pressure (mmHg)	76.6 (13.3)	80.4 (13.1)	78.3 (13.3)	.081
Heart rate (min)	75.2 (13.0)	74.3 (10.2)	74.8 (11.8)	.630
Smoking	16 (19.3)	17 (26.2)	33 (22.3)	.319
Alcohol use	3 (3.6)	1 (1.5)	4 (2.7)	.440
Hypertension	31 (37.3)	35 (53.8)	66 (44.6)	**.045**
Coronary artery disease	20 (24.1)	27 (41.5)	47 (31.8)	**.024**
Diabetes mellitus	19 (22.9)	16 (24.6)	35 (23.6)	.807
Hyperlipidemia	23 (27.7)	25 (38.5)	48 (32.4)	.166
Chronic obstructive pulmonary disease	5 (6.0)	5 (7.7)	10 (6.8)	.688
Asthma	6 (7.2)	2 (3.1)	8 (5.4)	.268
Chronic kidney disease	5 (6.0)	8 (12.3)	13 (8.8)	.180
Peripheral artery disease	3 (3.6)	9 (13.8)	12 (8.1)	**.024**
Pacemaker / Implantable cardioverter defibrillator/ Cardiac resynchronization therapy	2 (2.4)	2 (3.1)	4 (2.7)	0.804

Data are n (%) for categorical variables and mean (standard deviation) for continuous variables.

nary artery stenosis detected in coronary CTA patients. ACEF risk score is a simple and readily calculable index in patients with CCS. As a result of this study, it was determined that high ACEF risk score was associated with severe coronary artery stenosis detected by coronary CTA in patients with CCS. In CCS patients, a low ACEF risk score can be used to assess whether coronary CTA/coronary angiography, which can reduce exposure to radiation and opaque material, can be used to determine the degrees of stenosis.

Since the introduction of coronary CTA in 2008, the image quality of CTs has improved and the radiation dose has been significantly reduced. Over the 10-year period, the proportion of patients referred for invasive coronary angiography after coronary CTA slightly decreased, while the proportion of patients undergoing revascularization increased.[12] As CT scanners developed, coronary CTA became a rapid, low-radiation test with a high negative predictive value.[13,14] The application of coronary CTA as the primary modality to diagnose CCS appears to improve patient selection for invasive coronary angiography. Thus, fewer patients in whom there is a suspicion of CCS are referred directly for invasive coronary angiography. The SCOTHEART and PROMISE studies have shown that the use of coronary CTA as a first-line test is associated with more appropriate administration of invasive coronary angiography and a higher revascularization rate.[15,16] According to the subgroup analysis of the PROMISE study, which was conducted to determine whether the non-invasive fractional flow reserve obtained from computed tomography (FFRCT) predicts coronary revascularization

Table 2. Laboratory and echocardiographic findings (n=148).

	Coronary lesion <70% (n=83)	Coronary lesion ≥70% (n=65)	Total (n=148)	*P* value
Urea (mg/dL)	21.7 (16.0)	24.9 (16.3)	23.1 (16.1)	.228
Creatinine (mg/dL)	1.0 (0.4)	1.1 (0.6)	1.0 (0.5)	.104
Total cholesterol (mg/dL)	196.4 (44.6)	189.6 (45.0)	193.3 (44.7)	.387
Triglyceride (mg/dL)	192.3 (106.8)	166.6 (57.6)	180.4 (88.2)	.091
High density lipoprotein (mg/dL)	44.7 (9.7)	41.6 (10.2)	43.3 (10.0)	.079
Low density lipoprotein (mg/dL)	108.8 (34.8)	108.7 (37.7)	108.8 (36.0)	.982
White blood count (per mm^3)	9.5 (2.5)	8.7 (2.1)	9.2 (2.4)	**.039**
Hemoglobin (g/dL)	13.3 (1.7)	13.1 (1.9)	13.2 (1.8)	.608
Platelet	261.3 (59.1)	274.3 (89.6)	267.0 (74.0)	.291
Fasting glucose (mg/dL)	111.7 (42.8)	113.4 (27.0)	112.4 (36.6)	.777
Thyroid stimulating hormone (mU/L)	1.4 (0.8)	1.6 (1.3)	1.5 (1.1)	.248
Thyroxine (ug/dL)	8.6 (5.4)	7.3 (6.7)	8.0 (6.0)	.216
Calcium (mg/dL)	9.0 (0.4)	8.9 (0.6)	9.0 (0.5)	.383
Sodium	138.6 (2.6)	137.7 (3.7)	138.2 (3.2)	.074
Potassium	4.2 (0.4)	4.4 (0.5)	4.3 (0.5)	.085
Hemoglobin A1c	5.35 (5.10-5.98)	6.00 (5.70-6.31)	5.70 (5.20- 6.30)	**.003**
Age, creatinine, ejection fraction	0.92 (0.73-1.08)	1.18 (0.98-1.69)	1.00 (0.84-1.40)	**<.001**
Left ventricular ejection fraction (%)	60.0 (55.0-60.0)	50.0 (40.0-60.0)	58.5 (50.0-60.0)	**<.001**

Data are n (%) for categorical variables and mean (standard deviation) for continuous variables.

and its results, an FFRCT of ≤0.80 was a better predictor of revascularization or major adverse cardiac events than severe stenosis in CTA. FFRCT may improve the effectiveness of referring patients to ICA from CTA alone.[17] Both the PROMISE and SCOT-HEART studies found that more than half of future MACE occurred in non-obstructive CAD, which may have been negative on initial functional testing.[15-18] Therefore, in our study, we wanted to investigate whether ACEF risk scoring is a useful parameter in order to refer fewer patients to coronary CTA and thus avoid unnecessary invasive coronary angiography. Although the results of the study are promising, it is clear that there is a need for larger-scale studies on this subject.

Identifying patients at high risk for CAD and applying appropriate examination and treatment according to the risk classification have improved clinical outcomes.[3,19,20] Various risk classification methods have been developed to evaluate these patients, with simpler, less time-consuming and easily evaluable risk scores. One of these scores is the ACEF risk score (age, creatinine, ejection fraction) consists of three indepen-

Table 3. Treatment of participants (n=148).

	Coronary lesion <70% (n=83)	Coronary lesion ≥70% (n=65)	Total (n=148)	*P* value
Betablockers	21 (25.3)	25 (38.5)	46 (31.1)	.086
Angiotensin converting enzyme inhibitors	19 (22.9)	20 (30.7)	39 (26.4)	.280
Statins	20 (24.1)	20 (30.8)	40 (27.0)	.364
Antiplatelet	26 (31.3)	30 (46.2)	56 (37.8)	.065
Anticoagulant	7 (8.4)	1 (1.5)	8 (5.4)	.066
Angiotensin receptor blockers	9 (10.8)	9 (13.8)	18 (12.2)	.579
Dihydropyridine calcium channel blockers	10 (12.0)	16 (24.6)	26 (17.6)	**.046**
Non-Dihydropyridineropırıdıne calcium channel blockers	9 (10.8)	3 (4.6)	12 (8.1)	.168
Oral antidiabetic	14 (12.0)	12 (18.5)	26 (17.6)	.800
Insulin	7 (8.4)	4 (6.1)	11 (7.4)	.600
Statin	20 (24.1)	20 (30.8)	40 (27.0)	.364

Data are n (%).

Table 4. Multivariate logistic regression analysis with degree of luminal stenosis as dependent variable (<70% or ≥70%).

Variables	Univariate OR (95% CI)	*P* value	Multivariate OR (95% CI)	*P* value
Age	1.03 (1.00-1.06)	.027	0.99 (0.95-1.03)	.472
Hypertension	0.51 (0.26-0.99)	.046	0.75 (0.34-1.65)	.476
Coronary artery disease	0.45 (0.22-0.90)	.025	1.84 (0.66-5.11)	.245
Peripheral artery disease	0.23 (0.06-0.90)	.035	0.23 (0.05-1.09)	.064
Hemoglobin A1c	1.61 (1.15-2.26)	.006	1.38 (0.93-2.06)	.113
Left ventricle ejection fraction	0.92 (0.88-0.96)	<.001	0.94 (0.89-0.99)	.015
ACEF risk score	8.81 (3.38-22.95)	<.001	5.63 (1.62-19.57)	.007

Model fit statistics: Omnibus test of model coefficients (*P*=.023), deviance=197.830, Cox & Snell R Square=.034, Nagelkerke R Square=.046 ACEF: age, creatinine, ejection fraction

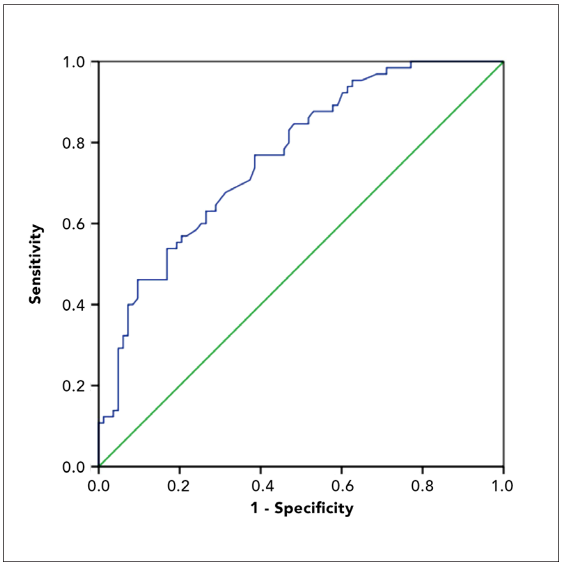

Figure 1. ROC analysis of the sensitivity and specificity of ACEF risk score (age, creatinine, ejection fraction) to degree of coronary artery stenosis in coronary CT angiography.

dent factors that are extremely easy to calculate. The ACEF risk score is a simple, useful and easily applicable score.[19] In a study including 658 NSTE-ACS patients, the ACEF score was significantly higher in the group with high mortality than in the group with low mortality (2.1 [0.53] vs. 1.34 [0.56], respectively, *P*=.001). In addition, there was a positive correlation between ACEF score and GRACE risk score (*P*<.001).[19] In a study of 1146 patients with STEMI who underwent primary PCI, the 1-year incidence of major adverse cardiac and cerebrovascular events increased with increasing age, creatinine and LVEF score tertiles (*P*<.001). A higher ACEF score was significantly associated with increased endpoint risk (OR=3.75, 95% CI; 2.44-5.77, *P*<.001).[21] Therefore, we investigated the ACEF risk score, which was previously evaluated with positive results in CCS patients with STEMI and NSTEMI patients.

As in previous studies, the rate of patients with pre-existing CAD was higher in the high ACEF risk score group.[5,19] In addition, hypertension and PAH rates were also high in the group with high ACEF risk score in our study. According to the results of our study, the ACEF risk score is a useful scoring method for identifying patients at high risk of CAD, referral of patients for early invasive coronary angiography, and in identifying and monitoring patients who require close follow-up for CAD in clinical practice.

A limitation of the study was that the ACEF risk score of the patients was calculated when the patients were admitted to the hospital with CCS and had already undergone coronary CTA. Long-term follow-up results of patients with CCS are needed to determine the prognostic value of the ACEF risk score, but these data are not available to us. Although the number of patients included in the study was small, the statistical correlation between ACEF risk score and degree of coronary artery stenosis in coronary CTA supports the conclusion that high ACEF risk score is associated with severe coronary artery stenosis detected by coronary CTA in CCS patients. The ACEF risk score may be useful to exclude the presence of severe coronary artery stenosis in this patient population. In addition, the ACEF risk score was a useful parameter as an assessment tool for coronary angiography in patients with CCS.

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