

Saadet Demirtas Inci¹, Mustafa Agah Tekindal²¹ Health Sciences University Yildirim Beyazit Diskapi Education and Research Hospital, Cardiology Department, Ankara, Turkey² Izmir Katip Celebi University Faculty of Medicine Biostatistics, Izmir, Turkey

THE NEW CLASSIFICATION METHOD IN ACEF SCORE IS MORE USEFUL IN PATIENTS WITH ACUTE CORONARY SYNDROME WITHOUT ST SEGMENT ELEVATION

<i>Goal</i>	In this study, it was investigated whether the age, creatinine, and ejection fraction (ACEF) score [age (years)/ejection fraction (%) + 1 (if creatinine >2 mg/dL)] could predict in-hospital mortality in patients with non-ST-elevation acute coronary syndrome (NSTEMI-ACS) and its relationship with the Global Record of Acute Coronary Events (GRACE) risk score were investigated.
<i>Material and methods</i>	The study enrolled 658 NSTEMI-ACS patients from January 2016 to August 2020. The patients were divided into two groups according to the ACEF score with an optimum cut-off value of 1.283 who were divided into two groups according to the ACEF score: low ACEF (≤ 1.283 , n:382) and high ACEF (> 1.283 , n: 276). The primary outcome of the study was in-hospital all-cause mortality. The primary outcome of the study was in-hospital all-cause mortality. Statistically accuracy was defined with area under the curve by receiver-operating characteristic curve analysis.
<i>Results</i>	In total, 13 (4.71%) patients had in-hospital mortality. The ACEF score was significantly higher in the group with higher mortality than in the group with low mortality (2.1 ± 0.53 vs. 1.34 ± 0.56 $p=0.001$). The ACEF score was positively correlated with GRACE risk score ($r=0.188$ $p<0.0001$). In ROC curve analysis, the AUC of the ACEF score for predicting in-hospital mortality was 0.849 (95% CI, 0.820 to 0.876; $p<0.0001$); sensitivity, 92.3%; specificity, 59.2%, and the optimum cut-off value was > 1.283 .
<i>Conclusion</i>	The ACEF score presented excellent discrimination in predicting in-hospital mortality. We obtained an easier and more useful result by dividing the ACEF score into two groups instead of three in NSTEMI-ACS patients. As a simple, useful, and easily applicable risk stratification in the evaluation of an emergency event such as the ACEF score, it can significantly contribute to the identification of patients at high risk.
<i>Keywords</i>	Age; ejection fraction; creatinine
<i>For citation</i>	Saadet Demirtas Inci, Mustafa Agah Tekindal. The new classification method in ACEF score is more useful in patients with acute coronary syndrome without ST segment elevation. Kardiologiia. 2021;61(2):83–90. [Russian: Саадет Демирташ Инджи, Мустафа Ага Текиндаль. Новый метод классификации пациентов с острым коронарным синдромом без подъема сегмента ST – шкала ACEF является хорошим прогностическим инструментом для предсказания госпитальной летальности. Кардиология. 2021;61(2):83–90]
<i>Corresponding author</i>	Saadet Demirtas Inci. E-mail: saadet_demirtas@yahoo.com

Introduction

Non-ST segment elevation acute coronary syndrome (NSTEMI-ACS) remains an important cause of mortality among ischemic heart diseases [1]. Patients with NSTEMI-ACS represent a heterogeneous subgroup consisting of non-ST segment elevation myocardial infarction (NSTEMI) and unstable angina pectoris (USAP) in acute coronary syndrome (ACS) [2, 3]. NSTEMI-ACS is the most common and increasingly common cause of coronary events in patients with previous heart disease [3]. In NSTEMI-ACS patients, it is important to undertake a risk assessment in patients when deciding on different therapeutic strategies that can significantly affect short-term and long-term outcomes such as conservative or invasive therapy. Determining the appropriate treatment according to the risk classification in these patients has the potential to improve clinical results [4, 5]. In order to evaluate these patients over

time, various risk classification systems with simpler, less time-consuming and easily evaluable risk scores have been developed. One of these scores is the age, creatinine, and left ventricular ejection fraction (LVEF) (ACEF) score, which is a simple and extremely easy to calculate a cardiovascular risk score, consists of three independent factors such as age, creatinine, and LVEF. The ACEF score was first used by Ranucci et al, in patients undergoing elective coronary artery bypass surgery (CABG), it has been reported to show similar or better predictive value for mortality compared to more complex risk scores [6]. The ACEF score was stated to be the predictor of mortality in patients undergoing percutaneous coronary intervention (PCI) [7]. Similarly, different studies have been reported to provide a good prognostic contribution to the identification of high-risk patients undergoing PCI due to serious coronary lesions such as bifurcation lesions and chronic total occlusion [8, 9].

Data on the predictive value of the ACEF score in patients presenting with NSTEMI-ACS are scarce.

We aimed to investigate the association between ACEF score and the Global Record of Acute Coronary Events (GRACE) risk score and in-hospital mortality in patients with NSTEMI-ACS.

Material and Methods

Data of 658 NSTEMI-ACS patients over 18 years of age who were identified as 74 USAP and 584 NSTEMI-myocardial infarction (MI) hospitalized in a coronary care unit (CICU) between January 2016 and August 2020 were retrospectively recorded by the physician in the CICU. In total, the age range of patients was 28–91 years, an average of 61.7 ± 12.8 years, and 69.1% of men ($n=455$). A total of 361 patients (55.4%) were hypertensive, 240 patients (36.8%) were diabetic, 269 patients (41.2%) were smoking, 240 patients (36.4%) were LVEF <50% and 302 patients (46.4%) had CAD before.

The diagnosis of NSTEMI was defined as patients with typical angina and increased cardiac biomarker level (troponin-I >0.06 ng/mL) without ST-segment elevation criteria on electrocardiography (ECG). The USAP diagnosis was defined as patients with normal cardiac biomarker level (troponin-I <0.06 ng/mL), without ST-segment elevation criteria on ECG, and with typical angina [10]. When the patients were admitted to the CICU, they were immediately monitored, ECG was taken and blood samples were taken for biochemical analysis. The treatments of the patients were organized according to the guidelines of the European Society of Cardiology (ESC) and antiaggregant was started. Angiotensin converting enzyme inhibitors, beta blockers and statins were started within the first 24 hours after hospital admission without contraindications. All patients underwent coronary angiography and were referred to PCI or CABG as indicated. Later, transthoracic echocardiographic examination was performed before coronary angiography in all patients using Philips Epic 5 (Philips Healthcare, Andover, Massachusetts) device with a 1–5 MHz converter. Standard 2-dimensional and Doppler echocardiographic measurements were made to the patients included in the study according to the American Echocardiography Association/European Echocardiography Association guidelines [11]. LVEF was calculated using the modified Simpson's method and LVEF was considered <50% decreased and LVEF $\geq 50\%$ was considered normal.

Exclusion criteria from the study; 1) acute ST-segment elevation myocardial infarction, 2) patients without serum creatinine value or LVEF records. 42 patients whose ACEF score could not be calculated due to lack knowledge of LVEF and creatinine were excluded from the study.

The medical records of the patients were examined retrospectively. Data of demographic and clinical features,

such as age, gender, history of hypertension (HT), diabetes mellitus (DM), smoking, family coronary artery disease (CAD) history, hyperlipidemia, previous CAD, vital signs, laboratory results (glucose, creatinine, troponin I, etc.) and echocardiographic results were collected by the CICU doctor and recorded on standard patient data collection pages.

Besides, DM was defined as a previous history of DM, or a fasting blood glucose level ≥ 126 mg/dL, or above 200 mg/dL at any measurement, or use of oral hypoglycemic agents and/or insulin, or $HbA_{1c} > 6.5\%$ [12]. Existing or former smokers were recorded as 'smokers'. HT was defined as having blood pressure $\geq 140/90$ mmHg and/or antihypertensive drug use.

For the GRACE risk score, patients' age, heart rate, systolic blood pressure (SBP), creatinine value, Killip degree, pre-hospital cardiac arrest, ST-segment deviation on ECG, and increase in troponin I were recorded and GRACE risk scores were calculated [13].

The ACEF score calculated without treatment (PCI or drug treatment) of patients yet. The ACEF score was calculated as follows: formula age (years)/LVEF (%) +1 score for serum creatinine >2 mg/dL [6]. The patients were divided into two groups according to the ACEF score with an optimum cut-off value of 1.283; low ACEF (≤ 1.283 , $n=382$), and high ACEF (> 1.283 , $n=276$). During their hospital stay, all clinical data of the patients were examined and analyzed, and death due to all causes before discharge was accepted as in-hospital mortality. The primary outcome of the study was in-hospital all-cause mortality.

The study protocol was prepared after the local ethical committee approval. The study was designed and conducted under the principles of the Helsinki Declaration.

Statistical analysis

The required sample size power analysis results, including at least 647 individuals were determined. In this case, 82.96% of the power test is expected to be obtained. SPSS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) statistical package program was used to evaluate the data. Variables were determined as mean $\pm$ standard deviation and percentage and frequency values. Variables were evaluated after controlling the preconditions for normality and homogeneity of variances (Shapiro Wilk and Levene Test). While analyzing the data, Independent 2 group t test (Student's t test) was used for the comparison of two groups, and Mann Whitney-U test was used if the prerequisites were not met. The relationship between two continuous variables was evaluated with the Pearson correlation coefficient and the Spearman correlation coefficient if the parametric test did not meet the prerequisites. Multivariate logistic regression analysis was used to see the effect of other variables when the ACEF score value is categorically

Table 1. Demographic and Biochemical Characteristics of Patients according to ACEF Score

Variables	ACEF score		P
	≤1.283	>1.283	
	n=382	n=276	
Age (years)	55.66±10.74	70.15±10.59	0.001^ε
LVEF (%)	56.98±6.33	43.11±9.84	0.001^ε
Creatinine (mg/dL)	1±0.2	1.67±1.53	0.001^Δ
Glucose (mg/dL)	135.8±65.91	162.94±89.31	0.001^ε
Body mass index(kg/m ²)	28.25±4.65	28.05±4.89	0.670 ^ε
Heart rate (pulse/min)	77.41±16.5	81.23±18.03	0.010^ε
SBP (mmHg)	136.41±27.65	135.58±30	0.720 ^ε
DBP (mmHg)	78.85±16.08	77.37±17.11	0.260 ^ε
ALT (mg/dL)	28.07±24.63	31.75±34.78	0.140 ^Δ
Hb (g/dL)	14.35±1.88	13.07±2.28	0.001^ε
Platelet (10 ⁹ /L)	251.58±73.27	239.95±70.37	0.040^ε
Total cholesterol (mg/dL)	185.48±46.88	175.13±45.95	0.060 ^ε
Leukocyte (10 ⁹ /L)	9.66±3.03	10.36±3.68	0.010^ε
Hs-CRP (mg/L)	31.17±50.76	33.16±54.66	0.770 ^Δ
Log-NT-pro-BNP (pg/mL)	3.01±0.65	3.08±0.62	0.550 ^Δ
Troponin I (ng/mL)	337.37±1842.75	1065.06±3618.78	0,001^Δ
GRACE risk score	116.35±31.37	124,52±29,17	0,003^ε

LVEF: left ventricular ejection fraction, SBP: systolic blood pressure, DBP: diastolic blood pressure, ALT: Alanine aminotransferase, Hb: hemoglobin, BNP: B-type natriuretic peptide, ^ε(Student's-t test), ^Δ(Mann–Whitney – U Test), The significance of the differences between the p-value groups and statistically significant values are highlighted in bold.

Table 2. Basic clinical features and ACEF score

			ACEF score		Total	p
			≤1.283	>1.283		
Gender	Male	n	275 ^a	180 ^a	455	0.063
		%	60.40%	39.60%	100.00%	
	Female	n	107 ^a	96 ^a	203	
		%	52.70%	47.30%	100.00%	
HT, n (%)	Yes	n	184 ^a	177 ^b	361	0.001
		%	51.00%	49.00%	100.00%	
	No	n	194 ^a	96 ^b	290	
		%	66.90%	33.10%	100.00%	
DM, n (%)	No	n	259 ^a	152 ^b	411	0.001
		%	63.00%	37.00%	100.00%	
	Yes	n	119 ^a	121 ^b	240	
		%	49.60%	50.40%	100.00%	
Current smoker, n (%)	Yes	n	193 ^a	76 ^b	269	0.001
		%	71.70%	28.30%	100.00%	
	No	n	185 ^a	198 ^b	383	
		%	48.30%	51.70%	100.00%	
Previous CAD, n (%)	No	n	229 ^a	119 ^b	348	0.001
		%	65.80%	34.20%	100.00%	
	Yes	n	149 ^a	153 ^b	302	
		%	49.30%	50.70%	100.00%	

HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease, ^a and ^b indicate groups that are different, the significance of the differences between the p-value groups and statistically significant values are highlighted in bold.

Figure 1. Correlation between continious variables

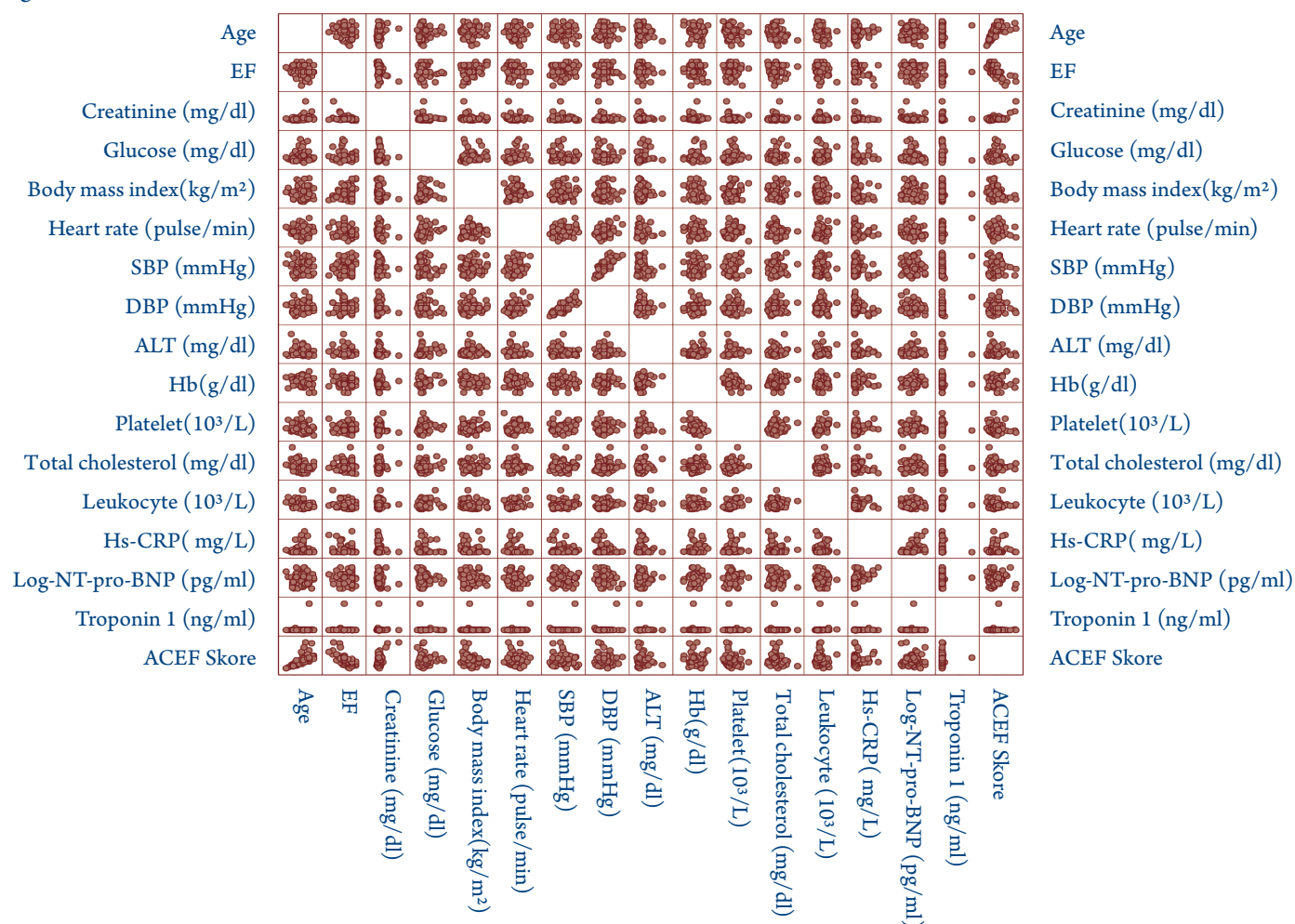
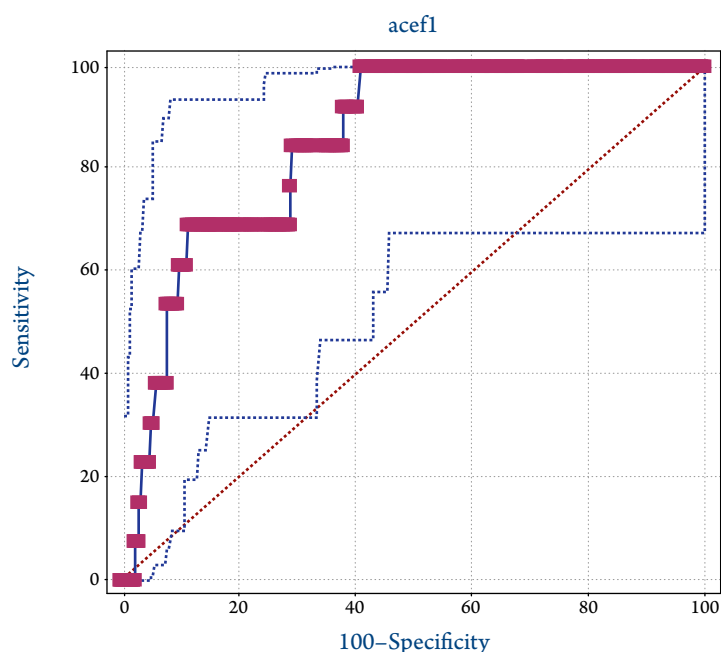


Figure 2. Receiver operating characteristic (ROC) curve of ACEF score in predicting in-hospital in the overall population



Area under the ROC curve (AUC)	0,849
Standard Error ^a	0,0400
95% Confidence interval ^b	0,820 to 0,876
z statistic	8,728
Significance level P (Area=0.5)	<0,0001

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	95% CI	-LR	95% CI	+PV	95% CI	-PV	95% CI
>1,283	92,31	64,0–99,8	59,22	55,3–63,0	2,26	1,9–2,7	0,13	0,02–0,9	4,4	2,3–7,5	99,7	98,6–100,0

dependent variable. The adjusted odd ratios (OR) and 95% confidence intervals (CI) are presented. Cut-off values in the responses of the variables were evaluated by the receiver operating characteristic curve (ROC) analysis Youden index method. Area under curve (AUC) value, Sensitivity, Selectivity LR +, LR- values were calculated. For the significance level of the tests, $p < 0.05$ and $p < 0.01$ values were accepted.

Results

The distribution of demographic findings and biochemicals according to ACEF risk groups is shown in Table 1. In addition to age, kidney function, and LVEF, which are components of the ACEF score, in the higher ACEF score group were found higher glucose, lower hemoglobin value, lower platelet value, higher leukocyte value, higher troponin I value and higher GRACE risk score (Table 1). Patients in the higher ACEF score group had a higher prevalence of cardiovascular comorbidity, as did previous CAD and DM (Table 2).

When the patients were compared in two groups as those with and without mortality; the ACEF score was significantly higher in the group with mortality than the group without mortality (2.1 ± 0.53 vs. 1.34 ± 0.56 , $p = 0.001$) (Table 3). The group with mortality had higher age, higher GRACE risk score, low LVEF value, low hemoglobin value, high glucose value, and high leukocyte count compared to the group without mortality (Table 3–4).

In the correlation analysis, the ACEF score was positively correlated with age ($r = 0.64$, $p < 0.0001$), creatinine ($r = 0.47$, $p < 0.0001$), GRACE risk score ($r = 0.188$, $p < 0.0001$), glucose ($r = 0.17$, $p < 0.0001$), heart rate ($r = 0.19$, $p = 0.006$), leukocyte ($r = 0.1$, $p = 0.01$), troponin I value ($r = 0.176$, $p < 0.0001$) while the ACEF score was negatively correlated with LVEF ($r = -0.7$, $p < 0.0001$), hemoglobin ($r = -0.355$, $p < 0.0001$), platelet ($r = -0.11$, $p = 0.004$) and total cholesterol ($r = -0.11$, $p = 0.04$) respectively (Figure 1).

NSTE-ACS patients with high ACEF score are highly selective group with in-hospital mortality of 4.71% (Table 4). In ROC curve analysis, ACEF score presented excellent discrimination in predicting in-hospital mortality: The AUC of ACEF score for predicting in-hospital mortality was 0.849 (95% CI, 0.820 to 0.876; $p < 0.0001$); sensitivity 92.3%; specificity 59.2%, and the optimum cut-off value was > 1.283 (Figure 2).

Predictive predictors for values below and above 1.283 (cut off value) of the ACEF risk score were determined in logistic regression analysis. In the regression analysis, age, creatinine and LVEF which are components of the ACEF score are not included. Decreased hemoglobin (OR=0.7, $p = 0.003$), decreased platelet count (OR=0.99, $p = 0.02$), increased leukocyte count (OR=1.1, $p = 0.01$), increased troponin I (OR=1.0001, $p = 0.03$), GRACE risk score (OR=1.09, $p = 0.003$) and smoking (OR=0.4, $p = 0.01$) are independent determinants of the high ACEF score in the multivariate regression (Table 5).

Table 3. Demographic and Biochemical Characteristics of Patients with and without In-Hospital Mortality

	Mortality (-) n=645	Mortality (+) n=13	p, value
Age (years)	61.49±12.81	74.31±7.47	0.001
LVEF (%)	51.37±10.37	40.92±12.84	0.001
Creatinine (mg/dL)	1.27±1.05	1.6±1.06	0.260
Glucose (mg/dL)	145.09±75.34	247.85±119.09	0.010
Body mass index (kg/m ²)	28.16±4.76	28.82±4.35	0.660
Heart rate (pulse/min)	78.78±16.89	90.38±28.64	0.170
SBP (mmHg)	136.03±28.63	137.62±29.47	0.840
DBP (mmHg)	78.18±16.42	80.62±21.78	0.600
ALT (mg/dL)	29.4±29.19	41.36±35.64	0.180
Hb (g/dL)	13.84±2.14	12.63±2.26	0.040
Platelet (10 ⁹ /L)	247.39±72.62	213.54±39.73	0.090
Total cholesterol (mg/dL)	181.63±46.98	166.75±12.58	0.530
Leukocyte (10 ⁹ /L)	9.84±3.16	15.17±6.54	0.010
Hs-CRP (mg/L)	32.44±52.79	12.4±16.44	0.400
Log-NT-pro-BNP (pg/mL)	3.06±0.63	2.61±0.57	0.120
Troponin I (ng/mL)	629.4±2761.4	1273.2±2249.1	0.400
GRACE risk score	118.37 ±29.63	137.61±36.93	0.003
ACEF score	1.34±0.56	2.1±0.53	0.001

LVEF: left ventricular ejection fraction, SBP: systolic blood pressure, DBP: diastolic blood pressure, ALT: Alanine aminotransferase, Hb: hemoglobin, the significance of the differences between the p-value groups and statistically significant values are highlighted in bold.

Table 4. Basic clinical features and in-hospital mortality

			Mortality		Total	p
			No	Yes		
Gender, n (%)	Male	n	446 ^a	9 ^a	455	0.99
		%	98.00%	2.00%	100.00%	
	Female	n	199 ^a	4 ^a	203	
		%	98.00%	2.00%	100.00%	
HT	Yes	n	355 ^a	6 ^a	361	0.49
		%	98.30%	1.70%	100.00%	
	No	n	283 ^a	7 ^a	290	
		%	97.60%	2.40%	100.00%	
DM	No	n	403 ^a	8 ^a	411	0.904
		%	98.10%	1.90%	100.00%	
	Yes	n	235 ^a	5 ^a	240	
		%	97.90%	2.10%	100.00%	
Current smoker, n (%)	Yes	n	264 ^a	5 ^a	269	0.83
		%	98.10%	1.90%	100.00%	
	No	n	375 ^a	8 ^a	383	
		%	97.90%	2.10%	100.00%	
Previous CAD	No	n	341 ^a	7 ^a	348	0.98
		%	98.00%	2.00%	100.00%	
	Yes	n	296 ^a	6 ^a	302	
		%	98.00%	2.00%	100.00%	
ACEF score	≤1.283	n	381 ^a	1 ^b	382	0.001
		%	100.00%	0.00%	100.00%	
	>1.283	n	264 ^a	12 ^b	276	
		%	95.28%	4.71%	100.00%	

HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease, ^a and ^b indicate groups that are different, the significance of the differences between the p-value groups and statistically significant values are highlighted in bold.

Table 5. Independent determinants of high ACEF (> 1.283) score in multivariate regression analysis

	B	S. E.	Wald	df	p	OR	Lower	Upper
							95% C. I. for OR	
Heart rate	0.009	0.007	1.438	1	0.231	1.009	0.995	1.023
Hemoglobin	−0.284	0.076	13.976	1	0.001	0.752	0.648	0.873
Platelet	−0.005	0.002	4.553	1	0.033	0.995	0.991	1.000
Total cholesterol	0.001	0.003	0.190	1	0.663	1.001	0.995	1.008
Leukocyte	0.104	0.045	5.317	1	0.021	1.109	1.016	1.212
Troponin	0.000	0.000	4.849	1	0.028	1.000	1.000	1.001
GRACE	0.009	0.003	8.863	1	0.003	1.090	1.003	1.915
Gender (male)	−0.644	0.345	3.485	1	0.062	0.525	0.267	1.033
Hypertension	−0.642	0.307	4.383	1	0.036	0.526	0.289	0.960
Diabetes mellitus	0.176	0.289	0.373	1	0.542	1.193	0.677	2.102
Smoker	0.984	0.306	10.348	1	0.001	2.676	1.469	4.874
Previous CAD	0.247	0.286	0.748	1	0.387	1.280	0.731	2.242
Constant	2.189	1.423	2.367	1	0.124	8.924		

OR: Odds ratio, CI: confidence interval, CAD: coronary artery disease, the significance of the differences between the p-value groups and statistically significant values are highlighted in bold.

Discussion

In this study, we analyzed the association between ACEF score and GRACE risk score and in-hospital mortality in patients with NSTEMI-ACS. We found that the ACEF score has a good predictive ability for in-hospital mortality. The ACEF score was positively correlated with GRACE risk score.

According to the ACEF score, two different risk groups can be defined. The ACEF score can provide a very simple and easy-to-calculate tool to classify the daily clinical practice risk of NSTEMI-ACS patients.

There are pathophysiological differences between NSTEMI-ACS and ST-segment elevation myocardial infarction. In

NSTE-ACS, it usually involves situations in which coronary blood flow is reduced, such as incomplete (partial) or temporary total coronary occlusion, rather than complete coronary artery occlusion. This difference is important when determining the treatment of patients with NSTEMI-ACS [14, 15]. In NSTEMI-ACS, treatment plan is made according to the patient's risk. Although mortality rates have decreased significantly compared to the pre-PCI period, a significant number of patients with NSTEMI-ACS still suffer from death. Therefore, there is an urgent need to identify patients at high risk of mortality. Moreover, we can say that a risk assessment is the most important step to organize the treatment of each patient with NSTEMI-ACS (early invasive or conservative) after hospitalization and to determine the short and long term prognosis. Because the success of the treatment of patients who apply with NSTEMI-ACS is often directly related to the risk of the patients [16]. Since risk stratification in NSTEMI-ACS patients is a very important step in directing treatment, different risk assessment strategies have been developed over time. The 2018 ESC myocardial revascularization guidelines highlight the role of the NSTEMI-ACS risk classification in the decision-making process (especially invasive strategy) for the treatment of patients [17]. It is recommended to calculate the GRACE risk score in nowadays international guidelines for risk stratification in patients with NSTEMI-ACS [15]. In addition, it has been reported that the GRACE risk score has a superior discriminating performance compared to other ACS risk scores [18]. Our study is the study to examine the relationship between GRACE risk score and ACEF score in patients with NSTEMI-ACS. A positive correlation was found between the GRACE risk score and ACEF score ($p < 0.001$). Included the ACEF score in the ESC myocardial revascularization guidelines (Class IIB) in 2010 [19] and the 2018 update was similarly done [17]. In previous studies, in-hospital mortality rate of NSTEMI-ACS was found to be approximately 4.9–5.2% [20]. In our study, in-hospital mortality was 4.71%, and this is very similar to in-hospital mortality data of the GRACE risk score and data from previous studies [2, 21]. Data on the predictive value of the ACEF score in patients presenting with NSTEMI-ACS are scarce. In an Acute Catheterization and Emergency Response Triage Strategy (ACUTE) study conducted in patients with NSTEMI-ACS, we retrospectively compared the existing 6 risk scores and analyzed the ACEF score as a subgroup, but as a result of the study, a very good distinction was not determined for the ACEF score [21]. In previous studies evaluating ACEF scores in various patient groups, ACEF was generally divided into three groups as low, medium and high. Unlike previous studies, it is a simpler classification to divide patients into two groups based on the cut-off value of 1.23 instead of three groups based on ACEF value and it may be more advantageous for this [21–23]. We also found that NSTEMI-ACS patients had

very good predictive accuracy in ACEF score for in-hospital mortality (AUC 0.849). Therefore, our classification method could be a practical and simple solution for grouping these patients. In our study, it was determined that ACEF scores of patients before taking coronary angiography or PCI had strong accuracy in predicting in-hospital mortality (AUC 0.849). Determination of the ACEF score before coronary angiography or PCI may have eliminated possible effects on creatinine value and LVEF.

Similar to the data in previous studies, the proportion of patients with DM and previously CAD was higher in the high ACEF score group [7]. Also, in our study, a high ACEF score group was found to be associated with worse clinical markers, such as higher troponin value, lower hemoglobin value, higher leukocyte, lower platelet, etc. Therefore, the ACEF score accurately reflects the comorbidities that can be encountered in patients with NSTEMI-ACS by correctly including three variables.

Our study has some limitations. This study is a single-center retrospective study and may be small in number and needs further validation with multicenter and larger cohort studies. Multivariate analysis was done to adjust possible risk factors, but confounding factors may affect clinical outcomes. The ACEF score was calculated only when patients were hospitalized. Because we do not have long-term follow-up results, so we do not know the prognostic value of this score in the long-term follow-up.

Conclusions

The ACEF score could be considered as a simple, easy to calculate, highly useful risk classification tool for the initial assessment of patients with NSTEMI-ACS. Also, this score includes 3 independent variables such as age, creatine, and LVEF, and they are constantly variable. Besides, the ACEF score may provide a more objective assessment compared to other more complex risk scores, since it does not contain any categorical variable such as Killip classification or any variables that may include inter-observer variability in comments such as coronary angiography [13, 24, 25]. We found that the ACEF score correlates with the GRACE risk score and the ACEF score has a very strong ability to assess in-hospital mortality. We think that the ACEF score may be more useful in identifying high-risk patients very quickly and in referring patients to urgent or early invasive treatment, or in the detection and follow-up of patients who need close monitoring, especially in clinical practice, compared to other complex risk scores.

Funding

No funding was received for our study. Authors declared no financial support.

No conflict of interest is reported.

The article was received on 11/10/2020

REFERENCES

- Giugliano RP, Braunwald E. The Year in Non-ST-Segment Elevation Acute Coronary Syndrome. *Journal of the American College of Cardiology*. 2012;60(21):2127–39. DOI: 10.1016/j.jacc.2012.08.972
- Granger CB. Predictors of Hospital Mortality in the Global Registry of Acute Coronary Events. *Archives of Internal Medicine*. 2003;163(19):2345–53. DOI: 10.1001/archinte.163.19.2345
- Chiara AD, Fresco C, Savonitto S, Greco C, Lucci D, Gonzini L et al. Epidemiology of non-ST elevation acute coronary syndromes in the Italian cardiology network: the BLITZ-2 study. *European Heart Journal*. 2006;27(4):393–405. DOI: 10.1093/eurheartj/ehi557
- Roffi M, Patrono C, Collet J-P, Mueller C, Valgimigli M, Andreotti F et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *European Heart Journal*. 2016;37(3):267–315. DOI: 10.1093/eurheartj/ehv320
- Jneid H, Anderson JL, Wright RS, Adams CD, Bridges CR, Casey DE et al. 2012 ACCF/AHA Focused Update of the Guideline for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 Guideline and Replacing the 2011 Focused Update): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2012;126(7):875–910. DOI: 10.1161/CIR.0b013e318256f1e0
- Ranucci M, Castelvichio S, Conte M, Megliola G, Speziale G, Fiore F et al. The easier, the better: Age, creatinine, ejection fraction score for operative mortality risk stratification in a series of 29,659 patients undergoing elective cardiac surgery. *The Journal of Thoracic and Cardiovascular Surgery*. 2011;142(3):581–6. DOI: 10.1016/j.jtcvs.2010.11.064
- Wykrzykowska JJ, Garg S, Onuma Y, de Vries T, Goedhart D, Morel M-A et al. Value of Age, Creatinine, and Ejection Fraction (ACEF Score) in Assessing Risk in Patients Undergoing Percutaneous Coronary Interventions in the 'All-Comers' LEADERS Trial. *Circulation: Cardiovascular Interventions*. 2011;4(1):47–56. DOI: 10.1161/CIRCINTERVENTIONS.110.958389
- Biondi-Zoccai G, Romagnoli E, Castagno D, Sheiban I, De Servi S, Tamburino C et al. Simplifying clinical risk prediction for percutaneous coronary intervention of bifurcation lesions: the case for the ACEF (age, creatinine, ejection fraction) score. *EuroIntervention*. 2012;8(3):359–67. DOI: 10.4244/EIJV8I3A55
- Di Serafino L, Borgia F, Maeremans J, Pyxaras SA, De Bruyne B, Wijns W et al. The Age, Creatinine, and Ejection Fraction Score to Risk Stratify Patients Who Underwent Percutaneous Coronary Intervention of Coronary Chronic Total Occlusion. *The American Journal of Cardiology*. 2014;114(8):1158–64. DOI: 10.1016/j.amjcard.2014.07.034
- Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD et al. Third Universal Definition of Myocardial Infarction. *Global Heart*. 2012;7(4):275–95. DOI: 10.1016/j.jheart.2012.08.001
- Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal – Cardiovascular Imaging*. 2015;16(3):233–71. DOI: 10.1093/ehjci/jev014
- Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N et al. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: The Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). *European Heart Journal*. 2013;34(39):3035–87. DOI: 10.1093/eurheartj/ehi108
- Fox KAA, Dabbous OH, Goldberg RJ, Pieper KS, Eagle KA, Van de Werf F et al. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). *BMJ*. 2006;333(7578):1091. DOI: 10.1136/bmj.38985.646481.55
- DeWood MA, Stifter WF, Simpson CS, Spores J, Eugster GS, Judge TP et al. Coronary Arteriographic Findings Soon after Non-Q-Wave Myocardial Infarction. *New England Journal of Medicine*. 1986;315(7):417–23. DOI: 10.1056/NEJM198608143150703
- Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE et al. 2011 ACCF/AHA Focused Update Incorporated Into the ACC/AHA 2007 Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011;123(18):e426–579. DOI: 10.1161/CIR.0b013e318212bb8b
- Morrow D. Cardiac-Specific Troponins Beyond Ischemic Heart Disease. P. 149-170 [DOI: 10.1007/978-1-59259-385-9_9]. In: *Cardiac Markers* [ISBN: 978-1-59259-385-9] Wu AHB, editor -Totowa, NJ: Humana Press;2003.
- Neumann F-J, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *European Heart Journal*. 2019;40(2):87–165. DOI: 10.1093/eurheartj/ehy394
- Yan AT, Yan RT, Tan M, Casanova A, Labinaz M, Sridhar K et al. Risk scores for risk stratification in acute coronary syndromes: useful but simpler is not necessarily better. *European Heart Journal*. 2007;28(9):1072–8. DOI: 10.1093/eurheartj/ehm004
- Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliquet T et al. Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *European Heart Journal*. 2010;31(20):2501–55. DOI: 10.1093/eurheartj/ehq277
- Peterson ED, Roe MT, Mulgund J, DeLong ER, Lytle BL, Brindis RG et al. Association Between Hospital Process Performance and Outcomes Among Patients with Acute Coronary Syndromes. *JAMA*. 2006;295(16):1912–20. DOI: 10.1001/jama.295.16.1912
- Palmerini T, Caixeta A, Genereux P, Cristea E, Lansky A, Mehran R et al. Comparison of clinical and angiographic prognostic risk scores in patients with acute coronary syndromes: Analysis from the Acute Catheterization and Urgent Intervention Triage Strategy (ACUTY) trial. *American Heart Journal*. 2012;163(3):383–391.e5. DOI: 10.1016/j.ahj.2011.11.010
- Gao S, Liu Q, Ding X, Chen H, Zhao X, Li H. Predictive value of the combination of age, creatinine, and ejection fraction score and diabetes in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: Coronary Artery Disease. 2020;31(2):109–17. DOI: 10.1097/MCA.0000000000000791
- Stähli BE, Wischnowsky MB, Jakob P, Klingenberg R, Obeid S, Heg D et al. Predictive value of the age, creatinine, and ejection fraction (ACEF) score in patients with acute coronary syndromes. *International Journal of Cardiology*. 2018; 270:7–13. DOI: 10.1016/j.ijcard.2018.05.134
- Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA et al. TIMI risk score for ST-elevation myocardial infarction: A convenient, bedside, clinical score for risk assessment at presentation: An intravenous nPA for treatment of infarcting myocardium early II trial substudy. *Circulation*. 2000;102(17):2031–7. PMID: 11044416
- Garg S, Girasis C, Sarno G, Goedhart D, Morel M-A, Garcia-Garcia HM et al. The SYNTAX score revisited: A reassessment of the SYNTAX score reproducibility. *Catheterization and Cardiovascular Interventions*. 2010;75(6):946–52. DOI: 10.1002/ccd.22372