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ACEF (AGE, CREATININE, EJECTION FRACTION) SCORES AS A PREDICTOR OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION IN ADAM MALIK GENERAL HOSPITAL

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Abstract

Introduction: Several clinical scores are available for risk stratification of patients with STEMI, such as TIMI Risk score and GRACE score, but all are complex to use. The ACEF score, a simple score that considers age, creatinine, and ejection fraction, was originally been developed for risk stratification of patients undergoing elective cardiac surgery and validated in patients undergoing PCI. This study aimed to assess the predictive value of the ACEF score for in-hospital MACE in patients with STEMI.

Method: This cohort ambispective study included 112 consecutive patients with STEMI from January 2020 until December 2020 admitted to Adam Malik General Hospital. The ACEF score was calculated when admission for each patient using the equation of age/ejection fraction +1 if creatinine level is >2 mg/dl. Then, subjects were observed in-hospital major cardiovascular events (MACE), which are mortality, acute heart failure, cardiogenic shock, and malignant arrhythmias. Statistical analysis was performed using mean difference and receiver operating curve (ROC).

Result: Among 112 patients, MACE were observed in 40 patient (35,7%) with the most common MACE was acute heart failure (19,6%). Bivariate analysis showed a significant relationship between ACEF score and in-hospital MACE ($p < 0,001$) with OR value of 4.96 (95% CI 4.68 – 30.7). The ACEF score AUC prediction value was 0,850 (95% CI: 0.775-0.925) with sensitivity 80% and specificity 78%.

Conclusion: The ACEF score is a simple and useful risk stratification to predict in-hospital MACE in a patient with STEMI.

Introduction

Cardiovascular disease still ranks first as the highest cause of death in the world, with an estimated 17.9 million people dying each year, and 75% of all cases occur in developing countries, especially in the lower middle class.¹

One of the cardiovascular emergency problems is acute coronary syndrome (ACS), which can occur due to sudden obstruction due to atherosclerosis of the coronary arteries. Acute coronary syndrome (ACS) can cause an irreversible heart muscle necrosis condition, leading to immediate or later death.²

ACS is categorized into three different conditions based on electrocardiography (ECG) examination and cardiac biomarkers, namely myocardial infarction ST-segment elevation (STEMI), acute myocardial infarction non-ST elevation segment (NSTEMI), and unstable angina pectoris (UA). ST-segment elevation myocardial infarction (STEMI) is a complex clinical scenario that requires immediate diagnosis, rapid therapeutic management, and early risk stratification. Studies show deaths after IMA-EST remain significant, reported at 6-14% in hospitals and 12% at 6 months.³

The death in STEMI patients after further investigation was caused by a major cardiovascular event (MACE). Major Cardiovascular Events (MACE) refers to a combination of various adverse effects associated with the cardiovascular system instability that can lead to unfavorable outcomes for SKA patients.⁴

There is a simple system for assessing cardiovascular risk, namely ACEF (Age, Creatinine, Ejection Fraction) scores. This score was first created by Ranucci, et al. in 2009 to assess the risk of death in elective heart surgery and then updated to the ACEF II risk score in 2018.⁷



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Although originally designed for heart surgery patients, several later studies have validated the prognostic strength of ACEF scores in ACS patients treated with Primary PCI. Significantly higher ACEF scores are associated with an increased risk of adverse events after coronary revascularization.⁸ Another advantage in using ACEF scores is that the ACEF score is very simple, practical, and easy to calculate when compared to other risks stratification models such as TIMI, CRUSADE, and GRACE scores.⁸

In this study, the authors will examine the ability of ACEF scores as a predictor in predicting MACE during treatment, so it is expected to be a consideration in determining prognosis in patients with STEMI.

Method

Study Population

The study included all patients with a diagnosis of STEMI who were admitted to the H. Adam Malik Medan Hospital starts from January 2020 until December 2020 according to inclusion and exclusion criteria. Subjects who experienced complications of PCI intervention (MI type 4), patients with CKD, patients with COVID-19, patients with incomplete examination data will not be included in the study.

ACEF Score Evaluation

This study was an analytical retrospective study that uses data from medical records. Researchers examined medical records to look at patient data profiles, anamnesis, physical examination, electrocardiography (ECG), blood laboratory results, echocardiography, coronary angiography, and major cardiovascular events (MACE). The MACE in this study is one of the following four events; death, acute heart failure, cardiogenic shock, and malignant arrhythmias. ACEF scores and GRACE (Global Registry of Acute Coronary Events) scores will be calculated from the patients with or without MACE. ACEF scores was calculated by the following methods: age (years) / left ventricular ejection fraction (%) + 1 (if serum creatinine > 2 mg / dl).

Statistical Analysis

Statistical analysis of this study will be conducted using the SPSS software program. The data will be presented in numerical and categorical form. Bivariate tests on numerical and categorical variables were performed with an independent t-test on normal-distributing data or a Mann-Whitney test when the data were not normally distributed. Bivariate analysis tests between categorical data were conducted with chi-square tests or Fisher exact tests. Predictive ability of ACEF scores and GRACE scores were analyzed with receiver operating characteristic curve (ROC) analysis to get the under the curve (AUC) area of both scoring systems. Sensitivity, specificity, and AUC scores from both scoring systems will be compared. The Hosmer-Lemeshow test was also conducted to assess the fit-to-model aspects of both scoring systems.

Results

The total number of subjects in the study was 112. There were 40 samples (35.7%) who had MACE and 72 samples (64.3%) who did not have MACE during treatment. The average age of the subjects was 56.38 years. There were 89 (79.5%) male and 23 (20.5%) female subjects. There were 50 subjects (44.6%) who had hypertension, 55 subjects (49.1%) had diabetes mellitus, 48 subjects (42.8%) had dyslipidemia, and 87 subjects (77.7%) had a history of smoking.

There were 70 samples (62.5%) with an anteriorly located infarct and 42 people with an inferior located infarct (37.5%). The mean left ventricular ejection fraction was 46.5%. The angiographic result showed that there were 51(45.5%) subjects who had 1VD, 31 subjects (27.7%) had 2VD, and 30 (26.8%) subjects had 3VD. The median GRACE score was 121 with a range (77-179) and the median ACEF score was 1.17 with range (0.68 – 3.59).

Table 1. Distribution of demographic and clinical characteristics of research subjects

| Characteristics | N=112 |
|--------------------------------------|--------------|
| Demographics and risk factors | |
| Age | 56.38±9.22 |
| Gender (n %) | |
| Man | 89 (79.5%) |
| Woman | 23 (20.5%) |
| Body Mass Index | 24.87 ± 3.35 |



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| | |
|---------------------------------|--------------------|
| Hypertension (n %) | 50 (44.6%) |
| Diabetes Mellitus (n %) | 55 (49.1%) |
| Dyslipidemia (n%) | 48 (42.8%) |
| Smoke | 87 (77.7%) |
| Clinical Characteristics | |
| Pulse Frequency | 83.22 ± 18.79 |
| Systolic Blood Pressure | 120 (80 – 220) |
| Diastolic Blood Pressure | 80 (50 – 120) |
| Infarct location (n %) | |
| Anterior | 70 (62.5%) |
| Inferior | 42 (37.5%) |
| Killip Class (n %) | |
| Killip I | 79 (70.5%) |
| Killip II | 23 (20.5%) |
| Killip III | 7 (6.3%) |
| Killip IV | 3 (2.7%) |
| Median GRACE score (Min-max) | 121 (77 – 179) |
| Median ACEF score (Min-Max) | 1.17 (0.68 – 3.59) |
| Average LVEF (SB) | 46.5±12.13 |
| <i>Vessel Disease</i> (n %) | |
| 1VD | 51 (45.5%) |
| 2VD | 31 (27.7%) |
| 3VD | 30 (26.8%) |
| <i>Culprit Lesion</i> | |
| LAD | 66 (58.9%) |
| LCX | 11 (9.8%) |
| RCA | 35 (31.3%) |

Data are presented as mean±SD if normally distributed, and presented in median (minimum-maximum) if not normally distributed

From the revascularization strategy aspect, 87.5% of subjects underwent PCI while 12.5% were conservative subjects or recommended for CABG. Of the types of MACE that occur, acute heart failure was the most common, occurred in 22 people (19.6%). The cardiogenic shock occurred in 14 people (12.5%), malignant arrhythmias in 6 people (5.4%), and cardiovascular death occurred in 12 people (10.7%).

Table 2. Distribution of revascularization strategy and MACE among research subjects

| Revascularization Strategy and KKvM | N=112 |
|--|------------|
| The onset of chest pain (n%) | |
| < 12 hours | 40 (35.7%) |
| > 12 hours | 72 (64.3%) |
| Action | |
| PCI | 98 (87.5%) |
| Non-PCI | 14 (12.5%) |
| KKvM, (n%) | |
| Yes | 40 (35.7%) |
| No | 72 (64.3%) |
| Type of KKvM (n %) | |
| Death | 12 (10.7%) |
| Acute Heart Failure | 22 (19.6%) |
| Cardiogenic Shock | 14 (12.5%) |
| Malignant Arrhythmia | 6 (5.4%) |

Wykrzykowska et al in 2011 first validated ACEF scores to assess MACE in ACS populations undergoing PCI in the LEADER Trial by dividing the risk stratification into 3 levels namely low-risk ACEF score (≤ 1.0225), medium risk ACEF score (1.0225 - 1,277), and high-risk ACEF score ($> 1,277$).⁸ This study also used the same category



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to determine ACEF score risk classification. There were significant differences in patient characteristics, characteristics of laboratory results, ejection of left ventricular fraction, and GRACE scores in subjects with medium-risk ACEF scores and high-risk ACEF scores.

Table 3 Baseline characteristics based on ACEF scores

| Category | high risk ACEF (n=50) | ACEF low-medium risk (n=62) | P-value |
|--------------------------|--------------------------|--------------------------------|--------------------|
| Age | 60.32±8.58 | 53.21±8.52 | 0.001a |
| Gender | | | |
| Man | 38 | 51 | 0.562c |
| Woman | 12 | 11 | |
| BMI | 23.70 ± 3.20 | 25.81 ± 3.20 | 0.001a |
| Pulse Frequency | 85.52 ± 22.10 | 81.37±15.56 | 0.265a |
| Systolic Blood Pressure | 110 (80 -180) | 130 (90 – 220) | 0.017b |
| Diastolic Blood Pressure | 70 (50 – 100) | 80 (50 – 120) | 0.036b |
| Hypertension | | | |
| Yes | 33 | 27 | 0.650c |
| No | 27 | 35 | |
| Diabetes mellitus | | | |
| Yes | 27 | 28 | 0.447c |
| No | 23 | 34 | |
| Dyslipidemia | | | |
| Yes | 19 | 29 | 0.443c |
| No | 31 | 33 | |
| Smoke | | | |
| Yes | 40 | 47 | 0.653c |
| No | 10 | 15 | |
| Infarction Location | | | |
| Anterior | 32 | 38 | 0.845c |
| Inferior | 18 | 24 | |
| The onset of chest pain | | | |
| < 12 hours | 20 | 20 | 0.432c |
| > 12 hours | 30 | 42 | |
| Killip class | | | |
| I | 34 | 45 | 0.379c |
| II | 12 | 11 | |
| III | 4 | 3 | |
| IV | 0 | 3 | |
| Vessel Disease | | | |
| 1VD | 27 | 24 | 0.104c |
| 2VD | 9 | 22 | |
| 3VD | 14 | 16 | |
| Culprit Lesion | | | |
| LAD | 32 | 34 | 0.410c |
| LCX | 3 | 8 | |
| RCA | 15 | 20 | |
| Action | | | |
| PCI | 45 | 53 | 0.472c |
| Non PCI | 5 | 9 | |
| GRACE score | 136.28 ± 23.48 | 110.74 ± 18.51 | < 0.001a |
| LVEF | 38.28 ± 10.25 | 53.13±9.13 | 0.001a |
| Hemoglobin | 12.06±2.44 | 13.64 ± 2.20 | 0.001a |
| Leukocytes | 11714.28 ± 4053.87 | 12046.73 ± 4848.46 | 0.699a |
| Platelets | 267640.00 ± 90615.97 | 281758.06 ± 65433.90 | 0.341a |



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| | | | |
|----------------------------|---------------------|---------------------|---------------|
| Creatinine | 1.74±1.13 | 1.02±0.29 | 0.001a |
| Blood Sugar Level | 139 (83 – 547) | 128.5 (75 – 389) | 0.208b |
| Glomerular Filtration Rate | 188.66 ± 111.26 | 80.60±19.87 | 0.001a |
| CKMB | 119 (6 – 744) | 103 (23 – 684) | 1,000b |
| Troponin I | 6.28 (0.03 – 32.00) | 3.11 (0.02 – 32.00) | 0.084b |
| HbA1C | 6.65 (4.9 - 14.4) | 6.2 (4.8 – 12.9) | 0.263b |
| HDL | 36.42 ± 13.03 | 39.24 ± 11.42 | 0.225a |
| LDL | 117.50 ± 37.92 | 131.97 ± 44.90 | 0.072a |

Data are presented as mean±SD if normally distributed, and presented in median (minimum-maximum) if not normally distributed

a: T test; b: Mann whitney; c: chi square

There were 32 subjects (64%) who experienced MACE during treatment and belongs to the high-risk ACEF score group, while 8 subjects (12.9%) experienced MACE during treatment belong to the low- to medium-risk ACEF score group. A total of 18 subjects (4.3%) were in the high-risk score group and 54 people (64.83%) were in the low to medium risk score group of ACEF score, and they did not experience MACE during treatment. There was a significant association between MACE during the treatment period to ACEF score value (p-value < 0.001) with an odds ratio of 4.96.

Table 4 Overview of ACEF scores on subjects experiencing MACE

| ACEF Score | MACE | | Total | P-value | OR | CI 95% |
|-----------------|------------|------------|------------|---------|------|-------------|
| | Yes | No | | | | |
| High risk | 32 (64%) | 18 (36%) | 50 (100%) | <0.001 | 4.96 | 4.68 – 30.7 |
| Low-medium risk | 8 (12.9%) | 54 (87.1%) | 62 (100%) | | | |
| Amount | 40 (37.7%) | 72 (64.3%) | 112 (100%) | | | |

The description of the different types of MACE that occurred based on the ACEF score stratification is presented fully in Table 5.

Table 5 Overview of ACEF scores on the MACE Subset

| | high risk ACEF (n:50) | ACEF low-medium risk (n:62) | P Value | OR | 95% CI |
|----------------------|-----------------------|-----------------------------|---------|-------|-----------|
| KKvM | 32 (64%) | 8 (12.9%) | <0.001 | 4.96 | 4.68-30.7 |
| Mortality | 11 (22%) | 1 (1.6%) | 0.002 | 13.64 | 1.82-102 |
| Acute Heart Failure | 17 (34%) | 5 (8.1%) | 0.001 | 4.21 | 1.67-10.6 |
| Cardiogenic Shock | 12 (24%) | 2 (3.2%) | 0.003 | 7.44 | 1.74-31.7 |
| Malignant arrhythmia | 5 (10%) | 1 (1.6%) | 0.870 | 6.20 | 0.75-51.3 |

The AUC of ACEF score was 0,850 with 95% CI 0.775-0.925 (p<0.001), with a sensitivity of 80% and specificity of 78%. The AUC of GRACE score was 0,872 with 95% CI 0,809 – 0,935 (p<0.001). This result showed that both ACEF and GRACE scores are very reliable in predicting MACE events in STEMI patients. The Hosmer-Lemeshow test showed R²= 0,42 with p = 0,290 for ACEF Score and R²= 0,46 with p = 0,329 for GRACE score. This showed that both of the predictive models have good accuracy and are very useable in real-life clinical practice.

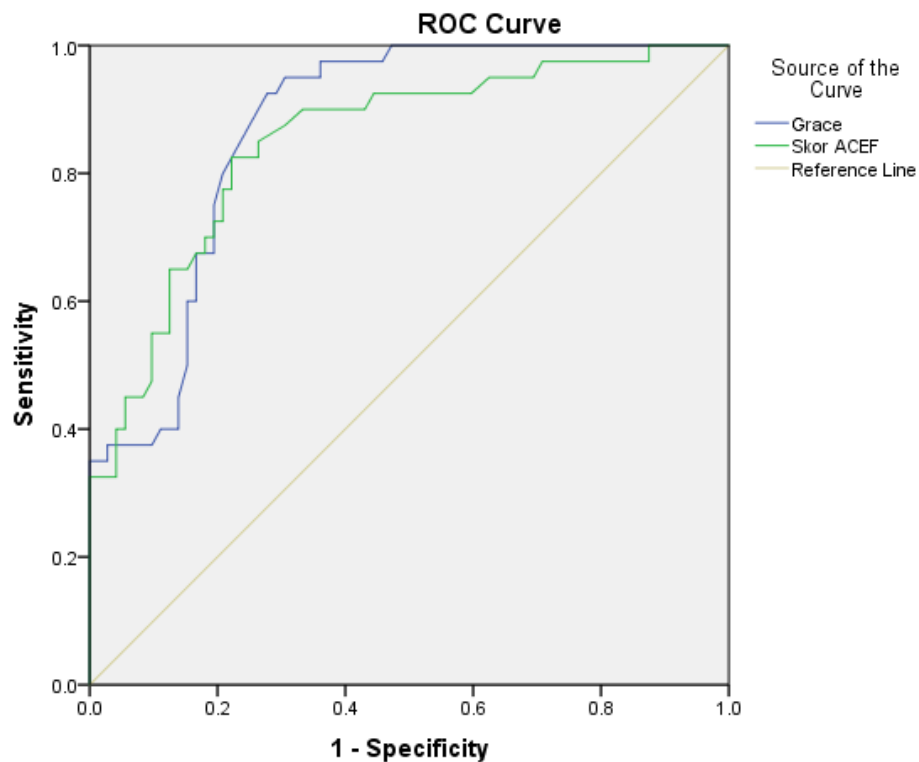


Figure 1 ROC curve comparison AUC score ACEF score and GRACE score

This study also conducted the Spearman correlation test to find out the correlation between ACEF score and GRACE score. The results showed that there was a meaningful positive correlation between the ACEF score and the GRACE score where the correlation strength value was statistically moderate ($r = 0.550$; $p < 0.001$). The correlation between these two variables is also displayed in the form of scatter plots as in Figure 2.

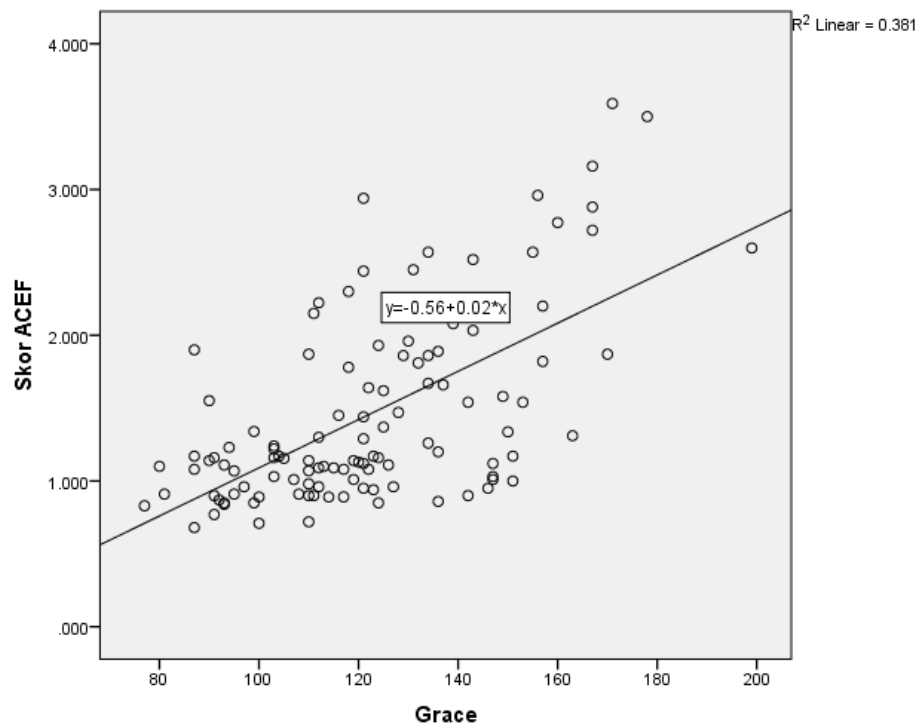


Figure 2. Graph Scatter Plot between ACEF score and GRACE score

Discussion

In this study, significant differences were found in terms of hemoglobin, creatinine levels, and glomerular filtration rate in the high-risk ACEF score group compared to low-to-medium risk. There was also a difference in GRACE scores and left ventricular ejection fractions between the two groups. Previous research has shown significantly lower average mean age in the low-medium-risk ACEF score group compared to high risk in the STEMI population where there was also a significant difference between LVEF and LFG in both groups.⁹

This study showed that the median ACEF score was 1,117 and the median GRACE score was 121, which is lower than another study that showed the median ACEF score was 1.20 and the median GRACE score was 140.¹⁰ This happened because the average age in this study was lower than in previous studies which could affect ACEF score and GRACE score, and the average LVEF in this study is better compared to previous studies.

The description of MACE that occurred based on differences in risk classification of ACEF scores in this study is quite in line with research by Wang, et al¹¹, who also studied ACEF scores in the STEMI population. In that study, the highest percentage of MACE occurred the high-risk ACEF score group (34.7%), followed by medium and low-risk groups (15.5%, 9.8% respectively, with p-value < 0.001).

In this study, acute heart failure was the most common MACE recorded (22 events or 19.6% of the total sample). This is in accordance with the publication by Kaul, et al.¹² where acute heart failure during treatment was the most common complication of the group of patients with a diagnosis of STEMI which was 13.6% compared to other ACS subtypes.

In this study, ACEF scores were seen to have an association with MACE, death, cardiogenic shock, and acute heart failure and this was slightly different compared to some previous studies, which showed that ACEF scores had a significant association with MACE incidence especially in the form of new-onset/acute heart failure, deaths, and strokes¹³

The result of the study also showed that ACEF scores are associated with MACE in the form of death, non-fatal MI, and cerebrovascular events. The previous research showed that ACEF scores are very good for predicting



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MACE in both the short and long term. This can be explained by the fact that each variable of ACEF scores in the form of age, LVEF, and creatinine are a strong predictor of the occurrence of MACE.¹⁰

The study showed an AUC result for ACEF score was 0.850 (95% CI = 0.627 - 0.775-0.925) (> 0.8) which means this score has a strong predictive ability for MACE events in STEMI patients. The study also compared the ability of the ACEF score with the gold standard GRACE score which is very popular to be used in predicting AMCE. GRACE score also has a good AUC score of 0.872 with a confidence interval of 0.809 – 0.935 (CI 95%, p<0.001). The advantage of the ACEF score is mainly related to its simplicity in its calculations compared to other more complex scores.

Spearman correlation test was also conducted to find out the correlation between ACEF score and GRACE score. It showed that there was a meaningful positive correlation between the ACEF score and the GRACE score where the correlation strength value was statistically moderate. This is in line with previous research. There was a positive correlation between the ACEF score and GRACE score, which means that the increase in the ACEF score will cause also an increase in the GRACE score.

Conclusion

ACEF scores may be used as predictors of major cardiovascular events during treatment in STEMI patients. There was a significant association between ACEF and MACE events especially in the form of death, acute heart failure, cardiogenic shock during treatment in STEMI patients. ACEF score has a positive correlation value with GRACE score and has discriminatory performance and calibration that is not much different from GRACE score so that it can be used as an alternative prediction model for simpler calculations.

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