

## Original Article

## AGE, CREATININE, AND EJECTION FRACTION (ACEF) SCORE IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY ANGIOPLASTY AND ITS RELATION WITH MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)

Muhammad Hammad Akhtar, Ahmad Salman, Ephraim Sheraz, Muhammad Ammar Rashid, Muhammad Irfan Tahir Khan and Aamir Hussain

**Objective:** To find the frequency of patients undergoing PCI with low, mid and high values of ACEF Score and to compare the major adverse cardiovascular events (MACE) among patients with different values of ACEF score.

**Methods:** This cross sectional comparative study was conducted at Cardiology Department Punjab Institute of Cardiology Lahore, Punjab, Pakistan from 01/02/2016 to 30/07/2016. In this study the non-probability purposive sampling technique was used. The Sample size was 170 patients undergoing elective PCI.

**Results:** The mean age of patients was  $49.84 \pm 14.11$  years, male to female ratio was 1.6:1. Low ACEF patients were 25(16.7%), middle ACEF were 29(19.3%) and high ACEF group patients were 96(64%). In this study MACE occur more frequently in patient with high ACEF score as compared to patients with moderate and low ACEF score.

**Conclusions:** There is positive correlation between ACEF score and MACE in patients undergoing elective PCI.

**Keywords:** Coronary artery disease, ACEF score, percutaneous coronary angioplasty and major adverse cardiovascular events (MACE)

### Introduction

Coronary heart disease (CHD) is the leading cause of mortality and morbidity in both developed and developing countries.<sup>1</sup> Percutaneous coronary intervention (PCI) is now widely used to manage angina and for survival benefit in the patients with CHD.<sup>2</sup> Early risk assessment of patients is crucial in adopting additional preventive measures to decrease the occurrence of further adverse clinical events. Various risk stratification modalities are in use for prediction of death and adverse events in STEMI patients. With the widening of the clinical spectrum needing PCI, intervention in the elderly patients and the presence of complex clinical conditions in the patients undergoing PCI, risk stratification for assessment of major adverse cardiovascular events (MACE) especially mortality has become pivotal aspect in clinical management and decision. Many tools for risk assessment have been developed to risk stratify the patients undergoing cardiac surgery and PCI, especially when decision regarding surgery versus PCI is mandated in patient with extensive CAD and multiple co-morbid conditions. Some of these models, like syntax score, have excellent risk prediction value.<sup>3</sup> ACEF score is a simple model for risk assessment which includes the variables: Age (A), Creatinine value (C), and left ventricular ejection fraction (EF) but its predictive value is comparable to more complex models like Euro

score, Syntex score, and Parsonnet Score. The variables included in Acef score are the known risk factors for both PCI and CABG. Hence, even though this model was not well validated previously for risk assessment in the patients undergoing PCI, it was accepted to be used as a tool for prediction of risks involved in PCI.<sup>4</sup> According to Biondi et al, ACEF score is simple, easy and user friendly model that can identify the high risk patients undergoing coronary bifurcation stenting and predicts fatal/ non- fatal, early or late complications including mortality.<sup>5</sup> Prediction of personal and population based mass clinical outcomes following invasive interventions are of vital paramount in clinical cardiology. Previously some complex scores are being used for this purpose. Therefore rationale of this study is to apply a simple and readily applicable ACEF score for selecting best treatment strategy and to identify the high risk patient undergoing PCI.

### Methods

This Cross sectional Comparative Study was conducted in Cardiology Department, Punjab Institute of Cardiology Lahore, Punjab, Pakistan for a period of 6 months from 1/2/2016 to 30/7/2016. 170 patients of 25-75 years of age of both sexes undergoing elective PCI were selected by consecutive Non Probability sampling. Patients not willing to participate in this study, with previous history of PCI, myocardial infarction or CABG in last 4 weeks were

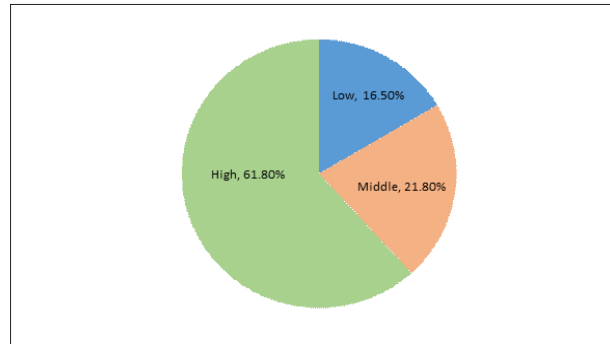
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- **ACEF score calculated as:** ACEF = age/left ventricle ejection fraction +1 (if serum creatinine is >2.0 mg/dl) (ACEF low <1.044, ACEF mid from 1.044 to 1.360, ACEF high >1.360)
- **Major Adverse Cardiovascular Events (MACE):** Any of the following events occurring during one month after PCI.
  - Death of the patient within one month of PCI.
  - **Myocardial infarction:** PCI related MI is defined by rise in troponin level (>5 × 99th percentile URL) in person with normal troponin level (≤99th percentile URL) or an increase in troponin level by >20% when the baseline level is raised and are static or decreasing. Along with, either (i) angina or (ii) new significant changes in ecg either ST segment >1mm elevation or depression in two or more contiguous leads or (iii) stenosis > 70 % or thrombus in coronary angiogram.
  - **Target Vessel Revascularization:** (TVR) any repeat percutaneous invasive procedure or CABG of the target artery.

Data was analyzed using SPSS version 19. Categorical data like gender and ACEF scores (low, mid and high) was expressed as frequency and percentages, continuous data like age of the patient, ACEF score as mean ± standard deviation (SD). Outcome variables like number of deaths, myocardial infarctions and target vessel revascularization was presented as frequency and percentages. The chi-square test was used to analyze the categorical data. P-value ≤0.05 was considered significant. Data will be stratified for age, gender, and creatinine level and ejection fraction to deal with effect modifiers. Post-stratification, chi-square test was applied. P-value ≤0.05 was considered significant.

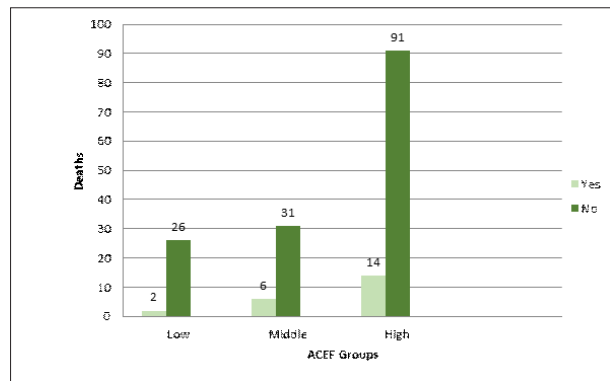
## Results

The age of patients ranged from 25-75 years with a mean of 49.98±14.35 Years. Total number of patients enrolled in the study was 170 with male to female ratio of 1.6:1. The study results showed that the mean creatinine of the patients was 1.85±0.66 with minimum and maximum values of 0.8 & 3.0 respectively. The mean EF of the patients was 43.17 ±10.52% with minimum and maximum values of 25% & 60% respectively. In this study, low ACEF was present in 28 (16.5%) cases, middle ACEF was present in 37 (21.8%) cases and high ACEF was present in 105 (61.8%) cases. **(Fig-1)**



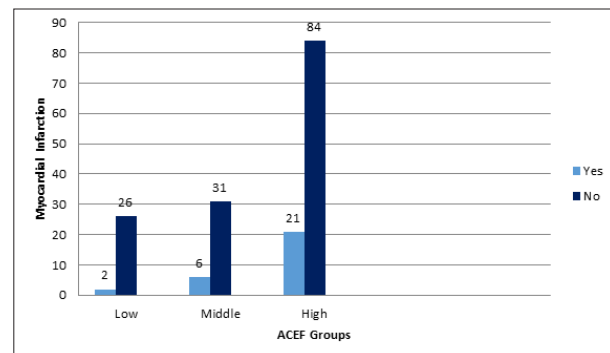
**Fig-1:** Frequency distribution of ACEF groups.

In 28 low ACEF patients, death occurred in 2 cases, out of 37 middle ACEF patients death occurred in 6 cases, similarly out of 105 high ACEF patients death occurred in 14 cases. This difference was statistically insignificant i.e. p-value = 0.548. **(Fig-2)**



**Fig-2:** Comparison of acef group with death of patients (p-value=0.548).

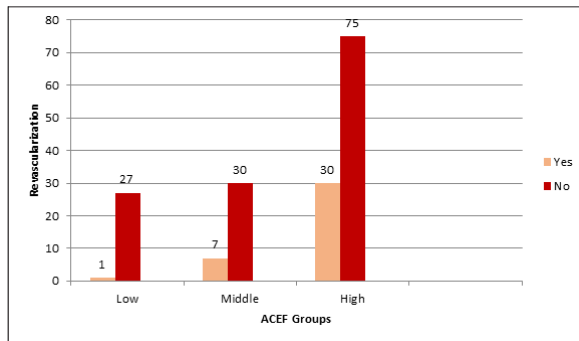
In 28 low ACEF patients, MI occurred in 2 cases, out of 37 middle ACEF patients death occurred in 6 cases, similarly out of 105 high ACEF patients death occurred in 21 cases. Statistically the insignificant difference was observed i.e. p-value=0.272. **(Fig-3)**



**Fig-3:** Comparison of ACEF group with MI (p-value=0.272)

In 28 low ACEF patients, revascularization occurred in 1 case, out of 37 middle ACEF patients

revascularization occurred in 7 cases, similarly out of 105 high ACEF patients revascularization occurred in 30 cases. Statistically the significant difference was observed i.e. p-value=0.016. **(Fig-4)**



**Fig-4:** Comparison of ACEF group with revascularization (p-value=0.016).

Data was stratified for age and it was noticed that in patients of age  $\leq 40$  years, with low ACEF patients, death occurred in 2 cases, in 1 cases of middle ACEF and in 5 cases of high ACEF score. Statistically the insignificant difference was observed i.e. p-value=0.231. In patients of age  $>40$  years, no death occurred in low ACEF score, in 5 cases of middle ACEF and in 9 cases of high ACEF score. Statistically the insignificant difference was observed i.e. p-value=0.506. Similarly, in patients of age  $\leq 40$  years, with low ACEF patients, MI occurred in 2 cases, no case of middle ACEF had MI but 2 cases had MI in high ACEF score. Statistically the insignificant difference was observed i.e. p-value=0.798. In patients of age  $>40$  years, no MI occurred in low ACEF score, in 6 cases of middle ACEF and in 19 cases of high ACEF score. Statistically insignificant difference was observed i.e. p-value=0.598. It was noticed that in patients of age  $\leq 40$  years, with low ACEF patients, revascularization occurred in 1 case, 3 cases of middle ACEF had revascularization and 7 cases had revascularization in high ACEF score. Statistically there was a significant difference i.e. p-value=0.001. In patients of age  $>40$  years, no revascularization occurred in low ACEF score, in 4 cases of middle ACEF and in 23 cases of high ACEF score. Statistically the insignificant difference was observed i.e. P-value=0.078. **(Table-1)** Data was stratified for creatinine and it was noticed that with creatinine  $\leq 1.5$ mg/dl, death occurred in 1 case with low ACEF, in 6 cases of middle ACEF and in 3 cases of high ACEF score. Statistically the insignificant difference was observed i.e. p-value=0.627. In creatinine

$>1.5$ mg/dl, 1 death occurred in low ACEF score, no death in middle ACEF but 11 deaths of high ACEF score patients. Statistically the insignificant difference was observed i.e. p-value=0.526. Similarly it was noticed that with creatinine  $\leq 1.5$ mg/dl, MI occurred in 2 cases with low ACEF, in 4 cases of middle ACEF and in 4 cases of high ACEF score. Statistically the insignificant difference was observed i.e. p-value=0.745. In creatinine  $>1.5$ mg/dl, no MI occurred in low ACEF score, 2 cases had MI in middle ACEF but 17 MIs of high ACEF score patients. Statistically the insignificant difference was observed i.e. p-value=0.107. It was noticed that with creatinine  $\leq 1.5$ mg/dl, revascularization occurred in 1 case with low ACEF, in 7 cases of middle ACEF and in 5 cases of high ACEF score. Statistically the insignificant difference was observed i.e. p-value=0.412. In creatinine  $>1.5$ mg/dl, no revascularization occurred in low ACEF score, no case had revascularization in middle ACEF but 25 cases had MI in high ACEF score. Statistically the significant difference was observed i.e. P-value=0.019. **(Table-2)** Data was stratified for EF and it was noticed that with EF  $\leq 40\%$ , death occurred in 1 case with low ACEF, in 5 cases of middle ACEF and in 8 cases of high ACEF score. Statistically the insignificant difference was observed i.e. p-value=0.228. In EF  $>40\%$ , 1 death occurred in low ACEF score, 1 death in middle ACEF but 6 deaths of high ACEF score patients. Statistically the insignificant difference was observed i.e. p-value=0.398. Similarly, with EF  $\leq 40\%$ , MI occurred in no case in low ACEF score, as well as no cases of middle ACEF but in 11 cases of high ACEF score. Statistically the insignificant difference was observed i.e. p-value=0.115. In EF  $>40\%$ , 2 cases had MI in low ACEF score, 6 cases had MI in middle ACEF and 10 cases had MI in high ACEF score patients. Statistically the insignificant difference was observed i.e. p-value=0.222. It was noticed that with EF  $\leq 40\%$ , revascularization occurred in no case in low ACEF score, but 5 cases of middle ACEF and 14 cases of high ACEF score had revascularization. Statistically the insignificant difference was observed i.e. p-value=0.483. In EF  $>40\%$ , 1 case had revascularization in low ACEF score, 2 cases had revascularization in middle ACEF and 16 cases had revascularization in high ACEF score patients. Statistically there was a significant difference i.e. p-value=0.007. **(Table-3)**

## Discussion

This cross sectional study was carried out at

**Table-1:** Comparison of ACEF group with death, MI and revascularization stratified by age.

Age	ACEF Group	Death			MI			Revascularization		
		Yes	No	P-value	Yes	No	P-value	Yes	No	P-value
=40 years	Low	2	26		2	26		1	27	
	Mid	1	3	0.231	0	4	0.798	3	1	0.001
	High	5	16		2	19		7	14	
> 40 years	Low	0	0		0	0		0	0	
	Mid	5	28	0.506	6	27	0.569	4	29	0.078
	High	9	75		19	65		23	61	

**Table-2:** Comparison of ACEF group with death, MI and revascularization stratified by creatinine.

Creatinine	ACEF Group	Death			MI			Revascularization		
		Yes	No	P-value	Yes	No	P-value	Yes	No	P-value
=1.5mg/dl	Low	1	12		2	11		1	12	
	Mid	6	25	0.627	4	27	0.745	7	24	0.412
	High	3	16		4	15		5	14	
> 1.5mg/dl	Low	1	14		0	15		0	15	
	Mid	0	6	0.526	2	14	0.107	0	6	0.019
	High	11	75		17	69		25	61	

**Table-2:** Comparison of ACEF group with death, MI and revascularization stratified by EF.

EF	ACEF Group	Death			MI			Revascularization		
		Yes	No	P-value	Yes	No	P-value	Yes	No	P-value
< 40%	Low	1	2		0	3		0	3	
	Mid	5	10	0.6=228	0	15	0.115	5	10	0.483
	High	8	46		4	43		14	40	
> 40%	Low	1	24		11	23		1	24	
	Mid	1	21	0.398	6	16	0.222	2	20	0.007
	High	6	45		10	41		16	35	

Cardiology department, Punjab Institute of Cardiology Lahore to find the frequency of patients in low, mid and high values of ACEF(Age, Creatinine and Ejection fraction) Score and to compare frequency of major adverse cardiovascular events (MACE) in low, mid and high values of ACEF (Age, Creatinine and Ejection fraction) score.

PCI is widely used effective and safe invasive procedure but major and minor complications do occur in both simple and complex bifurcation PCI. ACEF score is simple to use and user friendly while being equally effective tool for risk assessment in patient undergoing PCI.<sup>5</sup> In our study the low ACEF group patients were 25(16.7%), middle ACEF group patients were 29(19.3%) and the patients with high ACEF group were 96(64%). On one month follow up death occurred in 19(12.7%) patients, MI developed in 25(16.7%) and revascularization found in 36(24%) patients. MACE is more frequent in patient with higher ACEF score. A study by Jang Hoon Lee et al, stated that ACEF score was markedly higher among the patients who died following PCI and was a reliable predictor of one year mortality.<sup>6</sup> The ACEF score is highly predictive of one year mortality in patients

who survived for 1 months following primary PCI in acute MI. A multicentre, retrospective study enrolled 1,119 with low ACEF score, 1,190 with mid score and 1,153 in the highest score. There was the positive correlation between the higher ACEF score and the occurrence of 30 days MACE.<sup>5</sup> One study by Wykrzykowska JJ et al, resulted that ACEF(low)  $\leq 1.022$ ,  $1.022 < \text{ACEF}(\text{mid}) \leq 1.27$ , and ACEF(high)  $> 1.27$ .<sup>3</sup> On one year follow up, it was found that there was a significantly less no of patients with major adverse cardiac event free survival in the highest percentile of the ACEF score (ACEF(low)=92.%, ACEF(mid)=89.%, and ACEF(high)=86.%; P=0.021). Cardiac mortality was less common in ACEF (low) than in ACEF (mid) and ACEF (high) (0.70% vs 2.20% vs 4.50%; hazard ratio=2.220, P=0.0020) patients. Rates of MI were markedly higher in those with a high ACEF score (6.70% for ACEF(high) vs 5.20% for ACEF(mid) and 2.50% for ACEF (low); hazard ratio=1.60, P=0.0060. Target vessel revascularization was also more in the ACEF (high) group, but the difference over the three groups was not of statistical significance.

Increased ACEF score has been associated with

significantly different rates of 30-day mortality (0.1% in low ACEF score, 0.5% in mid and 3.0% in high ACEF score) with similar differences in myocardial infarction (0.3% vs. 0.7% and 1.8%) and major adverse cardiovascular events (MACE, 0.5% vs. 1.2% and 4.3% respectively). Overall 31.65% patients has been included in low ACEF score, 33.66% in mid and 32.66% in high ACEF score. One more study by Khan MR et al, described that the patients who stayed overnight had similar 30-day composite outcomes as their same-day discharge counterparts in the high ACEF score (odds ratio [OR], 1.213; 95% confidence interval [CI], 0.625-2.355; P=.57) and mid ACEF score (OR, 0.636; 95% CI, 0.356-1.134; P=.13) comparisons, but had worse outcomes in the low ACEF score comparison (OR, 1.867; 95% CI, 1.134-3.074; P=.01).<sup>8</sup>

One study showed that the age, ejection fraction and creatinine level indicate the best AUC value. Markedly high ACEF score (1.950±0.820 vs 1.28 ± 0.50) was found among non survivors. The ACEF score is the independent predictor of 1 year

mortality (adjusted hazard ratio, 2.260). A prediction tool with 12 risk factors was more accurate (AUC, 0.80), but not much difference with ACEF score (AUC, 0.790). For the ACEF low, ACEF mid, and ACEF\_high groups, the adjusted hazard ratios for one year mortality were 1 (reference), 3.110, and 10.380, respectively.<sup>9,10</sup> This study also verified that ACEF score can be used for risk stratification and prediction of clinical outcomes in the patients undergoing elective PCI.

## Conclusion

There is positive correlation between ACEF score and MACE in patients undergoing elective PCI. ACEF score is the simple and effective modality to assess the major risk involved in elective PCI.

*Department of Cardiology Labore.  
Punjab Institute of Cardiology  
[www.esculapio.pk](http://www.esculapio.pk)*

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