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## THE ACCURACY OF THE ACEF SCORE IN PREDICTING IN-HOSPITAL MORTALITY RATE AMONG HEART FAILURE PATIENTS WITH LEFT VENTRICULAR EJECTION FRACTION LESS THAN 50%

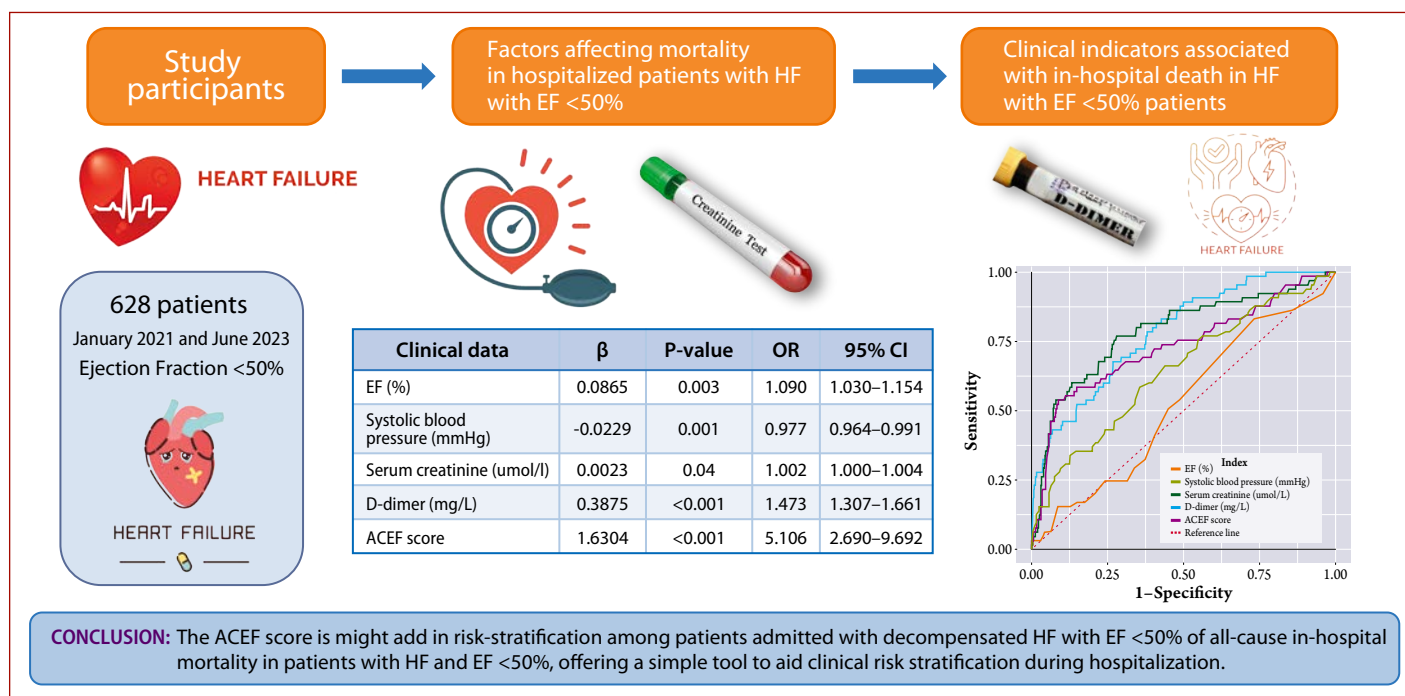
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| <i>Background</i>           | The age, creatinine, and left ventricular ejection fraction (ACEF) score is recognized as an effective predictor of poor in-hospital outcome across various clinical settings. However, its predictive utility for hospitalized heart failure (HF) patients with ejection fraction (EF) <50%, i.e., HF with non-preserved EF, has not been validated. This is despite the critical need for simple risk stratification tools for this high-risk subgroup. Thus, this study aimed to evaluate the ability of the ACEF score to predict all-cause in-hospital mortality in patients hospitalized with HF and EF <50%.                                                                                                 |
| <i>Material and methods</i> | This retrospective analysis included 628 HF patients with EF <50% who were admitted to the Cardiovascular Medicine and Intensive Care Medicine Department of the People's Hospital of Chongqing Liang Jiang New Area between January 2021 and June 2023. The ACEF score was calculated using the formula: ACEF = age (yrs)/EF (%) + 1 point if serum creatinine $\geq 176.8 \mu\text{mol/l}$ (2.0 mg/dl). Multivariate logistic regression and receiver operating characteristic (ROC) curve analysis were employed to assess the association between the ACEF score and all-cause in-hospital mortality after adjusting for significant covariates identified through univariate screening and stepwise selection. |
| <i>Results</i>              | Of the 628 included patients, 65 (10.35%) died during hospitalization. The ACEF score was 1.75 (1.53–2.04) in the non-death group and 2.55 (1.7–2.85) in the death group ( $p < 0.001$ ). Multivariate logistic regression confirmed that the ACEF score was a significant predictor of in-hospital mortality (adjusted odds ratio = 5.106, 95% confidence interval: 2.690–9.692, $p < 0.001$ ). ROC analysis showed that an ACEF score $> 2.46$ predicted mortality risk with an area under the curve of 0.732 (95% CI: 0.696–0.766, $p < 0.001$ ), yielding a sensitivity of 53.85% and specificity of 91.12%.                                                                                                    |
| <i>Conclusion</i>           | The ACEF score demonstrated high predictive utility for all-cause in-hospital mortality in HF patients and EF <50%. Specificity was 91.12% and sensitivity was 53.85% at the optimal threshold of 2.46. The ACEF score should be valuable for risk-stratification of hospitalized HF patients with EF <50%.                                                                                                                                                                                                                                                                                                                                                                                                         |
| <i>Keywords</i>             | ACEF score; heart failure with ejection fraction <50%; in-hospital mortality; predictive value                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <i>For citations</i>        | Xiaohong Liu, Huanyun Liu. The Accuracy of the ACEF Score in Predicting In-Hospital Mortality Rate Among Heart Failure Patients With Left Ventricular Ejection Fraction Less Than 50%. <i>Kardiologiia</i> . 2026;66(4):73–79. [Russian: Сяохун Лю, Хуаньюн Лю. Точность шкалы ACEF в прогнозировании внутрибольничной смертности среди пациентов с сердечной недостаточностью и фракцией выброса левого желудочка менее 50%. <i>Кардиология</i> . 2026;66(4):73–79].                                                                                                                                                                                                                                               |
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### Introduction

Heart failure (HF) continues to represent a considerable public health challenge. The Global Burden of Disease (GBD) study indicates that over 55 million people worldwide suffered from heart failure (HF) in 2021, with China accounting for nearly one-third of the global increase in HF patients over the past three decades [1, 2]. This epidemic imposes substantial mortality risk, particularly among patients with reduced left ventricular function, and it increasingly burdens health care resources [3]. Accurate risk stratification during hospitalization is essential for optimizing resource allocation, such as admission to intensive care units and intensity of monitoring, and for guiding other clinical decisions. Yet simple, validated prognostic tools for evaluation of HF patients with EF <50% remain limited [4].

Current HF guidelines emphasize evidence-based risk prediction, but they predominantly employ complex models like the MAGGIC-HF score, which incorporates 13 variables [5]. While comprehensive, such tools face significant implementation barriers in urgent clinical settings due to their complexity. The age, creatinine, ejection fraction (ACEF) score represents a more parsimonious metric that includes only three parameters (age, creatinine, and EF). ACEF offers substantial logistical advantages, yet it lacks guideline endorsement for HF risk assessment [6]. This omission may stem from insufficient validation of ACEF in contemporary HF cohorts, particularly for those patients with impaired systolic function (EF <50%). Since these patients exhibit higher acute mortality than those with preserved-EF, risk stratification is particularly crucial in this high-risk subgroup [7].

**Central Illustration.** The efficacy of the ACEF score in forecasting in-hospital mortality rates among heart failure patients with ejection fraction less than 50% ejection fraction



The ACEF score's prognostic utility is well-established in cardiac surgery and percutaneous coronary intervention [8, 9], and recent studies support its role in myocarditis and endocarditis [10–12]. ACEF score's physiological basis encompasses age-related vulnerability, renal dysfunction, and cardiac impairment, which aligns with key mortality drivers in acute HF [13]. However, its applicability for clinical risk assessment in hospitalized HF patients with EF <50% remains unverified. This study, therefore, evaluated the ACEF score's ability to predict in-hospital mortality in high-risk, hospitalized HF patients with EF <50%. It aimed to address a critical scientific gap in rapid risk stratification tools and assist clinicians in making informed decisions regarding patient monitoring and resource allocation.

## Material and methods

### Study participants

This was a retrospective analysis of HF patients admitted to the Cardiovascular Medicine and Intensive Care Medicine Department at the People's Hospital of Chongqing Liang Jiang New Area between January 2021 and June 2023. During this period, 672 patients had HF with EF <50%. After excluding 44 patients with incomplete records, 628 patients comprised the final cohort for analysis. Most of these patients had required urgent admission for treatment of acute, decompensated HF. The recorded comprehensive clinical characteristics including demographics, comorbidities, vital signs, and laboratory markers were documented. The investigation followed the ethical standards of the Declaration of Helsinki and included rigorous patient confidentiality protocols.

### Data collection and definitions

For patients admitted during 2022 and 2023, the diagnosis of HF was performed in line with the 2022 guidelines established by the American Heart Association (AHA), the American College of Cardiology (ACC), and the Heart Failure Society of America (HFSA) [14]. For patients admitted prior to 2022 (January 2021–December 2021), diagnostic assessments followed the contemporary 2016 European Society of Cardiology Guidelines for acute/chronic HF diagnosis [15] and the 2017 ACC/AHA/HFSA Focused Update [16]. This maintained core diagnostic consistency with the 2022 guidelines.

These guidelines included:

- 1) presence of HF symptoms/signs;
- 2) objective evidence of cardiac structural/functional abnormalities (LVEF<50%);
- 3) elevated natriuretic peptides (BNP>100 pg/ml) [14–16].

This multi-guideline approach ensured standardized diagnostic rigor throughout the study period.

The data collected included in-hospital mortality, demographic details, and various clinical characteristics. These characteristics comprised patient age, gender, and vital signs, e.g., pulse rate and systolic and diastolic blood pressure. Also included were medical history, smoking history, and the presence of hypertension, diabetes, stroke, coronary artery disease, and any previous percutaneous coronary intervention (PCI). The recorded laboratory measurements included serum albumin, creatinine, uric acid, B-type brain natriuretic peptide (BNP), hemoglobin (Hb), D-dimer, fibrinogen,

and total lymphocyte count; additionally, the EF values were computed.

The ACEF score was determined by first applying the following calculation as originally described by Ranucci et al. [17]: the patient's age (expressed in yrs) was divided by the EF (expressed as a percentage, e.g., 40%, input as 40). This formula:  $ACEF = \text{age}/EF$ , forms the core of the scoring system. Additionally, one point was added if the serum creatinine concentration equaled or exceeded  $176.8 \mu\text{mol/l}$  ( $2.0 \text{ mg/dl}$ ). This is the threshold established in the original derivation study [17]. This standardized score integrates age, cardiac function, and renal status into a single prognostic metric.

**Grouping Strategy:** The patients were classified into non-death and death groups based on whether they experienced all-cause mortality during hospitalization.

### Statistical power calculation

To ensure the robustness of the findings, a post-hoc power analysis was performed using PASS 2021 software (NCSS, LLC). Based on the observed in-hospital mortality rate of 10.35% (65 events among 628 patients, see Results) and the ACEF score's odds ratio of 5.106 (derived from the multivariate logistic regression analysis), the statistical power for a significance difference with of  $\alpha = 0.05$  was calculated. This analysis indicated a power of 99.6%, substantially exceeding the conventional threshold of 80%. This confirmed that the sample size was more than adequate to detect significant associations between the ACEF score and in-hospital mortality.

### Statistical analyses

All analyses were performed with SAS 9.4 (SAS Institute Inc., Cary, NC, USA), and a p-value less than 0.05 was considered significant. Normality was checked with the Shapiro-Wilk test. Data following a normal distribution are presented as mean  $\pm$  standard deviation (SD). For non-normally distributed data, medians and interquartile ranges are reported. Group comparisons were performed using the Mann-Whitney U test. The large-sample approximation of the Mann-Whitney U test (Z-test) may be denoted by the symbol Z. Qualitative data are described as frequencies and percentages, with differences between groups assessed with the  $\chi^2$  test. Logistic regression was used to identify mortality predictors. Variables for multivariate logistic regression were selected through a two-step process: first, all parameters showing significant association with mortality in the univariate analyses were included as candidate predictors; second, backward stepwise selection with Akaike Information Criterion optimization was applied to identify the final set of independent variables [18]. The accuracy of the ACEF score for predicting in-hospital all-cause mortality was eval-

uated with a receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) was employed to evaluate the overall classification performance of the clinical indicator.

DeLong's test was used to evaluate the differences in the area under the receiver operating characteristic curve (AUC) between each indicator and the reference value of 0.5. This assessment enables the estimation of each indicator's predictive value. A p-value  $< 0.05$  indicates that the indicator's predictive performance is significantly better than random guessing. The cut-off value was determined by maximizing the Youden index (Youden = sensitivity + specificity - 1), representing the optimal balance between predictive accuracy and clinical utility. The positive predictive value (PPV), negative predictive value (NPV), and their calculation methods for the relevant indicators are described below.

### Definitions and calculations of positive and negative predictive values

Positive Predictive Value (PPV) is defined as the proportion of individuals with a positive test result who actually have the condition. PPV is calculated as True Positives divided by (True Positives + False Positives). Negative Predictive Value (NPV) is defined as the proportion of individuals with a negative test result who are truly disease-free. NPV is calculated as True Negatives divided by (True Negatives + False Negatives).

Sensitivity is computed as True Positives divided by (True Positives + False Negatives) and expressed as a percentage. Specificity is computed as True Negatives divided by (True Negatives + False Positives) and expressed as a percentage. These metrics reflect the ability to identify patients with the condition and to exclude those without the condition, respectively.

## Results

### Comparison of the basic clinical data and the ACEF score between the in-hospital death and non-death groups of patients with HF and EF $< 50\%$ (Table 1)

Of the 65 patients who did not survive, their age, heart rate, serum creatinine, serum uric acid, BNP, D-dimer, and ACEF scores were significantly higher than those who survived. In contrast, systolic and diastolic blood pressure, serum albumin concentrations, hemoglobin, total lymphocyte count, and smoking history were lower in the non-survivor group ( $p < 0.05$ ). These findings indicate that non-surviving patients were typically older with compromised cardiac and renal function, potentially increasing their susceptibility to thromboembolic events. The 46% greater ACEF score in the death group clearly demonstrates the value of the ACEF score as a predictive indicator of an unfavorable outcome for HF patients with EF  $< 50\%$ .

**Table 1.** Clinical data and the ACEF score of HF patients with EF <50%

| Variable                                   | Non-death group (n=563) | Death group (n=65) | Z/ $\chi^2$ | p-value |
|--------------------------------------------|-------------------------|--------------------|-------------|---------|
| Age (yrs)                                  | 72 (64–81)              | 77 (69–83)         | 2.596       | 0.009   |
| EF (%)                                     | 44 (37–47)              | 42 (39–46)         | –0.646      | 0.519   |
| Heart rate (beats per min)                 | 89 (75–105)             | 97 (82–115)        | 2.604       | 0.009   |
| Systolic blood pressure (mmHg)             | 130 (116–146)           | 120 (99–133)       | –3.866      | <0.001  |
| Diastolic blood pressure (mmHg)            | 80 (70–92)              | 71 (58–84)         | –4.440      | <0.001  |
| Serum albumin (g/l)                        | 38.9 (35.7–41.8)        | 34.7 (29.9–37.4)   | –6.101      | <0.001  |
| Serum creatinine ( $\mu$ mol/l)            | 85.6 (67–120)           | 182 (113–303)      | 7.525       | <0.001  |
| Serum uric acid ( $\mu$ mol/l)             | 420 (337–529)           | 477 (356–646)      | 2.481       | 0.013   |
| BNP (pg/ml)                                | 1083 (568–2240)         | 1592 (713–4400)    | 2.918       | 0.004   |
| Hb (g/l)                                   | 126 (110–140)           | 118 (101–132)      | –2.531      | 0.011   |
| Total lymphocyte count ( $\times 10^9$ /l) | 1.12 (0.76–1.56)        | 0.72 (0.47–1.27)   | –4.329      | <0.001  |
| D-dimer (mg/l)                             | 0.43 (0.2–0.99)         | 1.54 (0.64–6.35)   | 7.511       | <0.001  |
| Fibrinogen (g/l)                           | 3.25 (2.66–4.13)        | 3.51 (2.44–5.4)    | 0.869       | 0.385   |
| ACEF score                                 | 1.75 (1.53–2.04)        | 2.55 (1.7–2.85)    | 6.139       | <0.001  |
| <b>Sex</b>                                 |                         |                    | 0.052       | 0.819   |
| Female                                     | 217 (38.54)             | 26 (40)            |             |         |
| Male                                       | 346 (61.46)             | 39 (60)            |             |         |
| <b>History of Smoking</b>                  |                         |                    | 4.442       | 0.035   |
| No                                         | 331 (58.79)             | 47 (72.31)         |             |         |
| Yes                                        | 232 (41.21)             | 18 (27.69)         |             |         |
| <b>History of Hypertension</b>             |                         |                    | 0.119       | 0.730   |
| No                                         | 230 (40.85)             | 28 (43.08)         |             |         |
| Yes                                        | 333 (59.15)             | 37 (56.92)         |             |         |
| <b>History of Diabetes</b>                 |                         |                    | 2.539       | 0.111   |
| No                                         | 416 (73.89)             | 42 (64.62)         |             |         |
| Yes                                        | 147 (26.11)             | 23 (35.38)         |             |         |
| <b>History of Stroke</b>                   |                         |                    | 0.711       | 0.399   |
| No                                         | 489 (86.86)             | 54 (83.08)         |             |         |
| Yes                                        | 74 (13.14)              | 11 (16.92)         |             |         |
| <b>History of Coronary Heart Disease</b>   |                         |                    | 1.402       | 0.236   |
| No                                         | 379 (67.32)             | 39 (60)            |             |         |
| Yes                                        | 184 (32.68)             | 26 (40)            |             |         |
| <b>History of PCI</b>                      |                         |                    | 0.578       | 0.447   |
| No                                         | 483 (85.79)             | 58 (89.23)         |             |         |
| Yes                                        | 80 (14.21)              | 7 (10.77)          |             |         |

Data are median and (interquartile range) or frequency and (percentage).

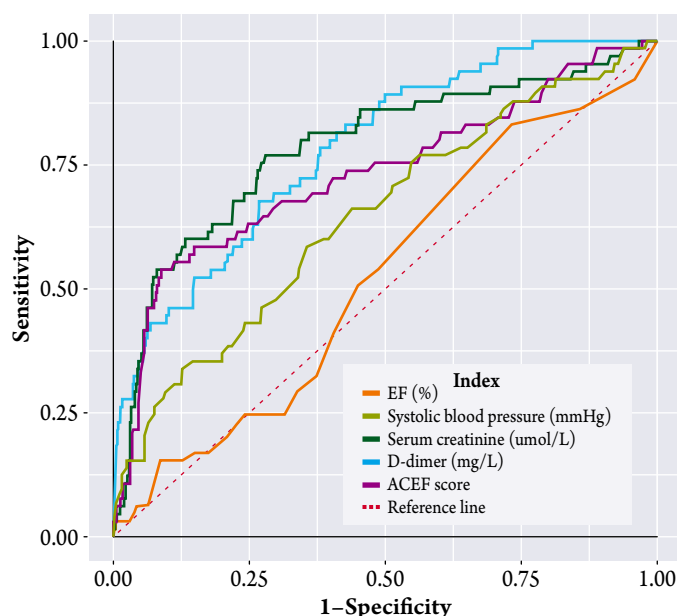
Z, The Mann-Whitney U test's large-sample approximation (Z-test)./ $\chi^2$ , Chi-square test

**Table 2.** Multivariate logistic regression analysis of the factors influencing any cause, in-hospital mortality of patients with HF and EF <50%

| Variable                        | $\beta$ | p-value | OR    | 95% CI      |
|---------------------------------|---------|---------|-------|-------------|
| EF (%)                          | 0.0865  | 0.003   | 1.090 | 1.030–1.154 |
| Systolic blood pressure (mmHg)  | –0.0229 | 0.001   | 0.977 | 0.964–0.991 |
| Serum creatinine ( $\mu$ mol/l) | 0.0023  | 0.04    | 1.002 | 1.000–1.004 |
| D-dimer (mg/l)                  | 0.3875  | <0.001  | 1.473 | 1.307–1.661 |
| ACEF score                      | 1.6304  | –       | 5.106 | 2.690–9.692 |

EF, left ventricular ejection fraction; ACEF score, age, creatinine, ejection fraction score;  $\beta$ , beta coefficient; OR, odds ratio; CI, confidence interval.

**Figure 1.** ROC curve of the predictive values of the clinical indicators for in-hospital mortality in the patients with HF and EF <50%



Factors affecting mortality and the ACEF score in hospitalized patients with HF and EF <50% (Table 2)

Multivariate logistic regression analysis was employed, using the previously mentioned clinical markers as independent variables. The findings indicated that EF, systolic blood pressure, serum creatinine, and D-dimer significantly influenced any cause mortality ( $p < 0.05$ ). These effects were reflected in the ACEF score ( $p < 0.001$ ).

Predictors of in-hospital death in HF patients with EF <50% (Table 3, Figure 1).

Predictive performance of ejection fraction (EF), systolic blood pressure (SBP), serum creatinine, D-dimer, and the ACEF score for in-hospital mortality among patients with left ventricular ejection fraction below 50% was assessed using receiver operating characteristic (ROC) curves. The ROC curves visually depict each indicator's discriminative capacity (Figure 1). Table 3 presents the area under the curve (AUC), 95% confidence intervals (CIs), p-val-

**Table 3.** The predictive value of various clinical indicators for in-hospital mortality in the patients with HF and EF <50%

| Variable                  | AUC   | 95% CI      | p-value | Cut-off | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---------------------------|-------|-------------|---------|---------|-----------------|-----------------|---------|---------|
| EF (%)                    | 0.524 | 0.484–0.564 | 0.510   | ≤46     | 83.08           | 27.00           | –       | –       |
| SBP (mmHg)                | 0.646 | 0.607–0.684 | <0.001  | ≤123    | 58.46           | 64.48           | –       | –       |
| Serum creatinine (μmol/l) | 0.785 | 0.751–0.816 | <0.001  | >111    | 76.92           | 72.11           | –       | –       |
| D-dimer (mg/l)            | 0.784 | 0.750–0.816 | <0.001  | >0.905  | 67.69           | 73.18           | –       | –       |
| ACEF score                | 0.732 | 0.696–0.766 | <0.001  | >2.46   | 53.85           | 91.12           | 41.2    | 94.5    |

AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value; EF, left ventricular ejection fraction; SBP, systolic blood pressure; ACEF score, age, creatinine, and left ventricular ejection fraction score.

ues, and the sensitivity and specificity at the optimal cut-off. Overall, serum creatinine (AUC=0.785, 95% CI: 0.751–0.816,  $p<0.001$ ) and D-dimer (AUC=0.784, 95% CI: 0.750–0.816,  $p<0.001$ ) demonstrated comparable and optimal discriminative performance, with both AUCs significantly above 0.75. The ACEF score also showed favorable predictive value (AUC=0.732, 95% CI: 0.696–0.766,  $p<0.001$ ), with an optimal cut-off of 2.46 yielding a sensitivity of 53.85%, specificity of 91.12%, PPV of 41.2%, and NPV of 94.5%. The AUC for SBP was 0.646 (95% CI: 0.607–0.684,  $p<0.001$ ), indicating moderate predictive capability, while EF had an AUC of 0.524 (95% CI: 0.484–0.564,  $p=0.510$ ), suggesting limited discriminatory capacity. Figure 1 demonstrates that the ROC curves for serum creatinine and D-dimer lie close to the upper-left corner, consistent with their higher AUCs. Regarding optimal cut-offs (Table 3), serum creatinine (>111 μmol/L) and D-dimer (>0.905 mg/L) achieved specificity >72% with high sensitivities (76.92% and 67.69%, respectively). Notably, at a cut-off of >2.46, the ACEF score yielded a sensitivity of 53.85% and specificity of 91.12%, highlighting its clinical utility in ruling out low-risk patients. Detailed indicator data are provided in Table 3.

## Discussion

The primary strength and novelty of this study lie in its demonstration that the ACEF score – a simple metric integrating age, creatinine, and ejection fraction – effectively predicts in-hospital mortality, specifically in HF patients with EF <50%, a population in which its utility had not been comprehensively established. Among 628 analyzed patients with 10.35% mortality, multivariate regression confirmed the value of the ACEF score as a significant, independent predictor of mortality, with an AUC of 0.732 and high specificity (91.12%) at the threshold of 2.46. However, the sensitivity was only 53.85%, indicating that nearly half of the deceased patients were not identified by this score, and the wide confidence interval for the odds ratio reflects uncertainty in the magnitude of risk. In general, deceased patients were older, and they had impaired cardiac and/or renal function along with elevated thromboembolic risk markers. These findings aligned well with the score's physiological rationale.

Consistent with previous studies of HF patients, EF was closely associated with patient outcome [19–21]. The current research demonstrated that, while EF is highly sensitive in forecasting in-hospital mortality for HF patients with EF <50%, its specificity remains limited [22]. In our results, the use of the ACEF score, which includes age, serum creatinine, and EF, considerably improved specificity. This indicates that using the ACEF scoring model, could be a practical and efficient method for managing HF patients with EF <50%, and who are at a higher risk of in-hospital mortality. An optimal ACEF score threshold of 2.46 was established, with a significant predictive value ( $p<0.001$ ). These findings indicated that ACEF scores might help to improve patient outcomes due to its potential for early identification of high-risk individuals.

The current study demonstrated that increased D-dimer can serve as an effective predictor of the risk of death during hospitalization of patients with HF and EF <50%. This is consistent with the findings of Huang et al. [13]. They found that elevated D-dimer was independently predictive of one-year overall mortality in HF patients, especially in those with HF and preserved EF (HFpEF). It should be noted, however, that our study did not include patients with HFpEF.

It has been reported that the ACEF scoring system has great potential as an effective tool for evaluating the risk levels among patients with coronary heart disease following PCI [9, 23, 24]. Gao et al. [25] recently analyzed data from 1,179 patients and found that elevated ACEF scores were associated with adverse clinical outcomes. During a median follow-up period of 41.7 months, patients with non-obstructive myocardial infarction (MINOCA) who were in the highest ACEF score tertile exhibited a significantly higher incidence of major adverse cardiovascular events (MACE) (6.3%, 12.5% and 23.8% respectively;  $p<0.001$ ). Additionally, Tsai and colleagues found that in post-extracorporeal membrane oxygenation (ECMO) patients, the ACEF score was an important and reliable tool for predicting mortality [26]. Lower scores indicated higher survival rates for post-ECMO patients. Similarly, Wei et al. [12] found that the in-hospital mortality rate of infective endocarditis patients increased with increasing ACEF scores, indicating that

the ACEF score can be useful for predicting mortality in patients with infective endocarditis. Moreover, Liu et al. [10] illustrated the prognostic value of the ACEF score in predicting in-hospital mortality in patients with acute fulminant myocarditis. The current study was a logical extension of prior research.

The present study does have some limitations. The analysis focused only on evaluating the ACEF score's predictive capability for all-cause mortality risk among hospitalized patients with HF and EF <50%. The sample size was small, so the results might not represent the broader population. This might limit the reliability and applicability of the conclusions. However, studies with larger sample size are expected to confirm the current findings. It is important for future studies to directly compare the ACEF with the MAGGIC-HF score and other prognostic tools to further demonstrate the ACEF score's efficiency, relative effectiveness, and dis-

criminative power. Finally, different hospital care, e.g., ICU utilization, and treatment protocols might produce different results regarding the value of the ACEF score predicting all-cause mortality risk among hospitalized patients with HF and EF <50% patients.

## Conclusion

The ACEF score demonstrated high predictive utility for all-cause, in-hospital mortality in heart failure patients and EF <50%. Specificity was 91.12% and sensitivity was 53.85% at the optimal threshold of 2.46. The ACEF score may assist clinicians in stratifying mortality risk during hospitalization of seriously ill HF patients.

*No conflicts of interest are reported.*

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