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ORIGINAL RESEARCH

# Age, Creatinine, and Ejection Fraction (ACEF) Score is Associated with the Presence of Depression and Anxiety Symptoms in PCI Patients

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**Background:** A significant proportion of patients after percutaneous coronary intervention (PCI) have or develop comorbid depression and/or anxiety symptoms, which are associated with adverse events. The age, creatinine, and ejection fraction (ACEF) score is a good predictor for the prognostic assessment of certain cardiac diseases. But it has never been used to predict post-PCI depression and anxiety symptoms.

**Aim:** To evaluate the possible association among ACEF score at admission, post-PCI anxiety, depression, comorbid anxiety and depression symptoms in hospital.

**Methods:** After exclusion, a total of 222 patients undergoing emergency or selective PCI were enrolled and completed Hospital Anxiety and Depression Scale (HADS) to measure anxiety and depression symptoms before discharging. Patients were divided into four groups according to HADS score (anxiety, depression, comorbid anxiety and depression, neither anxiety nor depression). Logistic regression, linear regression and smoothed curve fitting (based on the penalized spline method) were used to analyze the relationship between ACEF score and post-PCI anxiety, depression symptoms. Receiver operating characteristic (ROC) curve analysis were performed to assess the value of ACEF score for predicting post-PCI anxiety, depression, comorbid anxiety and depression symptoms and to determine its critical values.

**Results:** Of the sample, the number of patients who were diagnosed with post-PCI anxiety, depression and comorbid anxiety and depression symptoms were 16 (7.2%), 33 (14.9%) and 37 (16.7%), which increased with the ACEF score quartiles. In multivariate-adjusted logistic regression analysis, the odds ratios (ORs) of post-PCI anxiety, depression symptoms were 7.701 (1.613–36.766), 6.173 (1.608–28.028) for the lowest quartile of ACEF score compared with the highest quartile. Multivariate-adjusted linear regression and smoothed curve fitting analysis demonstrated that post-PCI anxiety and depression scores increased with higher ACEF scores, indicating a nonlinear positive correlation. The ROC curve showed that ACEF score was a good predictor for post-PCI anxiety, depression and comorbid anxiety and depression symptoms.

**Conclusion:** Higher ACEF score is positively correlated with the prevalences of anxiety and depression symptoms after PCI in hospital, suggesting that ACEF score can be a valid predictor of depression and anxiety symptoms.

**Keywords:** ACEF score, post-PCI, depression, anxiety

## Introduction

Percutaneous coronary intervention (PCI), which involves placing stents or balloons in the closed or obstructed coronary arteries, is a lifesaving treatment for patients with acute myocardial infarction. However, major adverse cardiovascular

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events, including mortality, myocardial reinfarction, and ischaemia-driven target vessel revascularization remain problems.[1]

Traditional factors such as diabetes mellitus, hypertension disease, hyperlipidemia and smoking partially contribute to poor prognosis. Furthermore, psychological factors such as depression and anxiety are well-established risk factors for the occurrence of adverse events.[2] In 2008, the American Heart Association issued an advisory to screen patients with coronary artery diseases for depression.[3] In particular, PCI patients who had undergone surgery were more likely to experience depression and anxiety symptoms. After PCI, approximately 23.5–66.5% of patients develop anxiety[4,5,] and 20–30% develop depression.[2,6] The presence of depression and anxiety symptoms was associated with 2.70-fold and 2.56-fold increases in the risk of adverse events, respectively.[6] Hence, it is critical to identify individuals at risk of depression and anxiety symptoms early and implement interventions in a timely manner. Currently, screening for post-PCI depression and anxiety symptoms mainly relies on various assessment scales, given the subjective nature of assessment scales, there was a need for more objective predictive indicators and models to be explored.

Ranucci et al were the first to develop the age, creatinine, and ejection fraction (ACEF) score, which is based on the law of parsimony, to assess mortality risk in elective cardiac operations.[7] Despite having only 3 variables, the ACEF score has comparable predictive power to complex scoring models.[8] The ACEF score has since been validated in a variety of other clinical practices and populations. Lee et al[9] reported that the ACEF was a good predictor of 1-year post-PCI mortality in patients with acute myocardial infarction. However, researches of the ACEF score have been restricted to the prognostic assessment of certain cardiac diseases. There have been no studies applying the ACEF score to the prediction of post-PCI depression and anxiety symptoms. Previous studies have shown that age and left ventricular ejection fraction were associated with post-PCI depressive and anxiety symptoms.[10,11] Accordingly, we proposed the hypothesis that ACEF score would have predictive value of post-PCI depression and anxiety symptoms.

# Materials and Methods

## Participants

In this cross-sectional study, we prospectively enrolled 265 consecutive patients between December 2023 and April 2024 at the Department of Cardiology, the Fifth Affiliated Hospital of Xinjiang Medical University. Patients aged 18 years or older who were diagnosed with acute coronary syndrome and underwent emergency or selective PCI were included. The exclusion criteria were as follows: (1) had a history of depression disorders, anxiety disorders or other mental illnesses, such as schizophrenia, obsessive-compulsive disorder, substance abuse or serious suicidal tendencies; (2) disagreed with the Hospital Anxiety and Depression Scale (HADS); (3) were unable to communicate in Mandarin; and (4) had incomplete demographic characteristics and clinical information. Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the Fifth Affiliated Hospital of Xinjiang Medical University ethics committee (XYDWFYLSk-2024-52).

## Measures

### Demographics

The following data were collected through the medical records, including age, sex, marital status, educational level, medical history, number of stents, culprit vessel, emergency or elective PCI, personal history of smoking, and post-operative medications used for at least 1 week continuously: aspirin, clopidogrel, ticagrelor, statins, $\beta$ receptor blockers, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and diuretics.

### Laboratory Analyses

Peripheral venous blood samples were collected before PCI. The concentrations of serum creatinine were measured and recorded. As for left ventricular ejection fraction, patients received a conventional 2-dimensional echocardiography examination before revascularization. Echocardiography was performed and measurements included at least 3 consecutive beats for patients with sinus rhythm. The modified biplane Simpson's rule was applied to calculate.

### Depression and Anxiety

After PCI, patients were asked to complete the HADS before they were discharged. As a self-report questionnaire, the HADS comprises two subscales (ie, the HADS-D and HADS-A), covering 14 items in total, and each subscale comprises seven multiple-choice items, with a score ranging from 0 to 21 for both subscales. A cut-off score of ≥8 points on each subscale is considered to indicate clinically relevant levels of depression and anxiety symptoms. The internal consistency of the HADS has been demonstrated previously, with a Cronbach's alpha of 0.83 for the anxiety subscale (HADS-A) and 0.82 for the depression subscale (HADS-D).[12]

### ACEF Score Calculation

The ACEF score was calculated: ACEF = age/left ventricle ejection fraction +1 (if creatinine was >2.0 mg/dL).[7]

### Covariables

In this study, we controlled for variables that, according to previous studies, might bias the results: age, sex, diabetes mellitus status, hypertension status and smoking status.

### Statistical Analysis

SPSS (V.26.0) and R software (V.4.4.2) were used for the statistical analysis of the collected data. All tests for statistical significance were two-sided, and $P< 0.05$ was considered to indicate statistical significance.

First, according to the normality of the distribution assessed by the *Shapiro–Wilk* test, continuous variables are described as the mean ± standard deviation (*SD*) or the median and interquartile range. Categorical variables are described as frequencies (percentages). One-way analysis of variance (ANOVA) or the *Kruskal–Wallis* was used to compare continuous variables and *Pearson's* chi-square test and *Fisher's* exact test was used to compare categorical variables among groups, Benjamini–Hochberg correction was used for multiple comparisons.

Second, multivariable logistic regression analyses were performed to assess the relationship between ACEF score categorized into quartile groups and presence of anxiety, depression symptoms. Meanwhile, linear trend tests across quartiles were examined using ordinal values in separate models. Linear regression analyses and smooth curves fitting (based on the penalized spline method) were utilized to examine the relationships of ACEF score with anxiety, depression symptoms. The models were adjusted for variables with $P< 0.05$ in the univariate analysis and conventional confounding factors.

Third, the discrimination of the ACEF score for post-PCI anxiety, depression, comorbid anxiety and depression symptoms was assessed by receiver operating characteristic (ROC) curves.

## Results

A total of 265 patients who underwent PCI were included in this study, and 43 of these patients were excluded, including 2 patients who could not communicate in Mandarin, 6 patients who refused to complete the HADS, 35 patients who were discharged from the hospital before the investigation. After exclusions, 222 patients were included in the final analysis (Figure 1). The sample included 183 (82.4%) males and 39 (17.6%) females, with an average age of 60.36±11.07 years. Overall, 123 (55.4%) underwent emergency PCI within 24 hours of symptom onset, while the remaining 99 (44.6%) patients received elective PCI. Only 3(1.4%) patients' creatinine >2.0 mg/dL, 16 (7.2%) patients were diagnosed with post-PCI anxiety symptoms, 33 (14.9%) patients were diagnosed with post-PCI depression symptoms and 37 (16.7%) patients were diagnosed with post-PCI comorbid anxiety and depression symptoms.

## Descriptive Analysis

Table 1 summarizes the demographic characteristics of participants in the four groups, all *P* value were adjusted by Benjamini–Hochberg correction. It showed statistical significance (all $P< 0.05$) among groups in oral aspirin, oral diuretics, LVEF and ACEF score. There were no statistically significant differences in the remaining variables.

In Table 2, the patients were divided into four subgroups according to the quartiles of ACEF score at admission: Quartile 1 (n = 56):0.515–0.923, Quartile 2 (n = 55): 0.923–1.116, Quartile 3 (n = 56): 1.116–1.259, Quartile 4 (n = 55): 1.259–3.160. After adjusted by *Benjamini–Hochberg* correction, age, sex, education levels, smoking, oral aspirin, oral

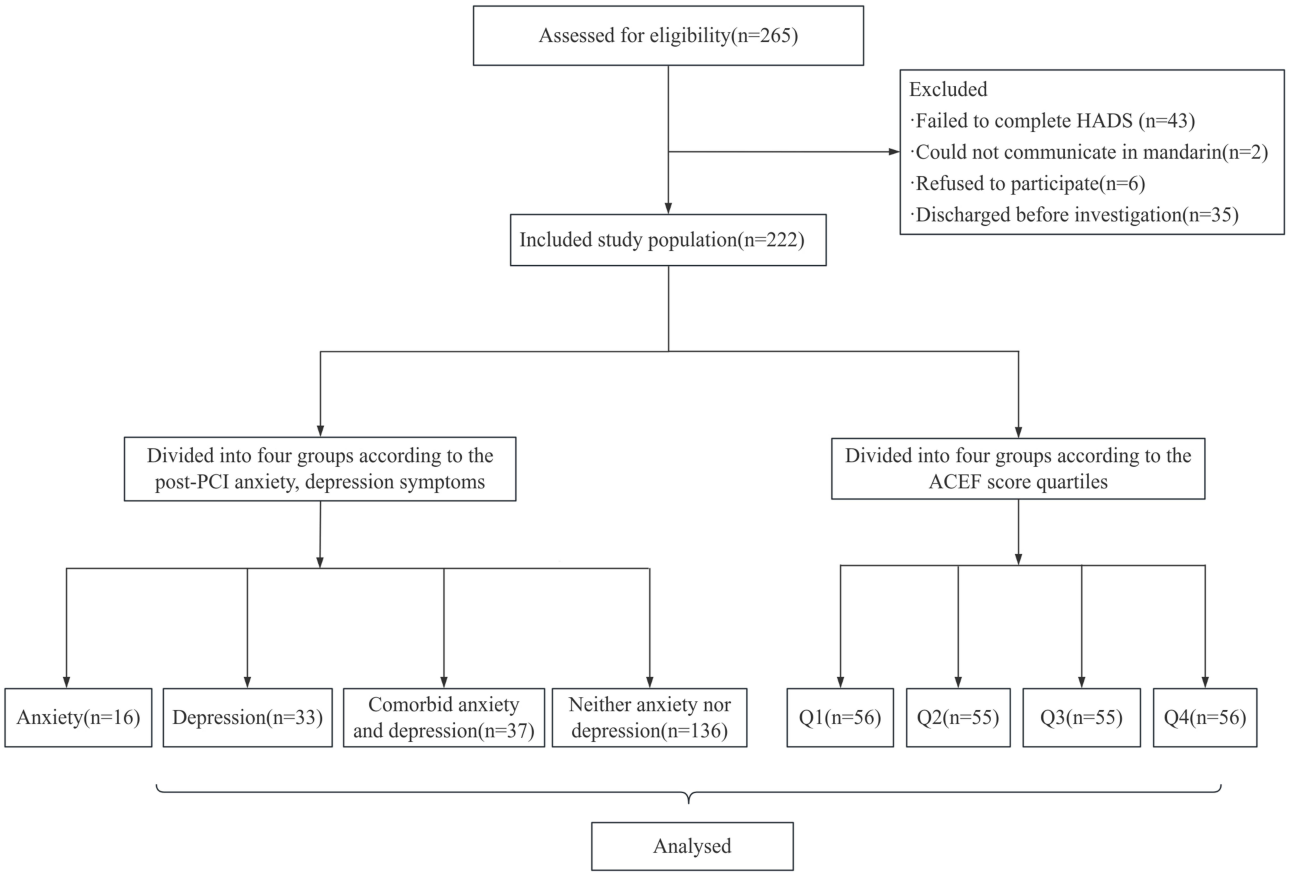


**Figure 1** Flow chart of the study.

diuretics, LVEF, ACEF score among the patients with different quartiles were statistical significantly different (all $P < 0.05$). Other characteristics had no statistically significant differences according to the quartiles.

In addition, we compared the proportions of post-PCI anxiety, depression and comorbid anxiety and depression symptoms among patients stratified by ACEF quartiles. The ratios of post-PCI anxiety, depression and comorbid anxiety and depression

**Table 1** The Demographic Characteristics of Patients According to Anxiety and Depression Symptoms

| | Neither Anxiety Nor Depression | Anxiety | Depression | Comorbid Anxiety and Depression | *P* value[†] |
|---|---|---|---|---|---|
| **Number of patients** | **N=136** | **N=16** | **N=33** | **N=37** | |
| Age, mean ±SD | 59.58±10.64 | 58.31±12.71 | 60.18±11.32 | 64.27±11.30 | 0.159 |
| Female | 16(11.8%) | 4(25.0%) | 9(27.3%) | 10(27.0%) | 0.121 |
| Married | 132(97.1%) | 15(93.8%) | 31(93.9%) | 36(97.3%) | 0.785 |
| Education levels | | | | | 0.302 |
| Illiterate | 3(2.2%) | 1(6.3%) | 2(6.1%) | 3(8.1%) | |
| Primary | 15(11.0%) | 2(12.5%) | 9(27.3%) | 6(16.2%) | |
| Junior | 43(31.6%) | 6(37.5%) | 13(39.4%) | 15(40.5%) | |
| Senior | 46(33.8%) | 4(25.0%) | 4(12.2%) | 9(24.3%) | |
| College | 29(21.3%) | 3(18.8%) | 5(15.2%) | 4(10.8%) | |
| CAD risk factors | | | | | |
| Hypertension | 82(60.3%) | 10(62.5%) | 19(57.6%) | 16(43.2%) | 0.463 |
| Diabetes mellitus | 48(35.3%) | 8(50.0%) | 16(48.5%) | 15(40.5%) | 0.589 |
| Smoking | 83(61.0%) | 11(68.8%) | 17(51.5%) | 20(54.1%) | 0.692 |

(*Continued*)

**Table 1** (Continued).

| | Neither Anxiety Nor Depression | Anxiety | Depression | Comorbid Anxiety and Depression | *P* value† |
|---|---|---|---|---|---|
| **Number of patients** | **N=136** | **N=16** | **N=33** | **N=37** | |
| Emergency PCI | 66(48.5%) | 9(56.3%) | 23(68.7%) | 25(67.6%) | 0.611 |
| Killip | | | | | 0.113 |
| I | 80(58.8%) | 6(37.5%) | 18(54.5%) | 18(48.6%) | |
| II | 42(30.9%) | 8(50.0%) | 7(21.2%) | 7(18.9%) | |
| III | 8(5.9%) | 1(6.3%) | 6(18.2%) | 9(24.3%) | |
| IV | 6(4.4%) | 1(6.1%) | 2(6.2%) | 3(8.1%) | |
| Culprit vessel | | | | | 0.121 |
| RCA | 44(32.4%) | 3(18.8%) | 8(24.2%) | 11(29.7%) | |
| LAD | 69(50.7%) | 12(75.0%) | 23(69.7%) | 18(48.6%) | |
| LCX | 22(16.2%) | 1(6.3%) | 2(6.1%) | 5(13.5%) | |
| D | 1(0.7%) | 0(0.0%) | 0(0.0%) | 3(8.1%) | |
| Number of stents | | | | | 0.113 |
| 0 | 22(16.2%) | 0(0.0%) | 10(30.0%) | 10(27.0%) | |
| 1 | 64(47.1%) | 7(43.8%) | 9(27.3%) | 20(54.1%) | |
| 2 | 39(28.7%) | 8(50.0%) | 10(30.3%) | 7(18.9%) | |
| ≥3 | 11(8.1%) | 1(6.3%) | 4(12.1%) | 0(0.0%) | |
| Medication | | | | | |
| Aspirin | 122(89.7%) | 14(87.5%) | 29(87.9%) | 23(62.2%) | 0.010 |
| Clopidogrel | 50(62.2%) | 6(45.5%) | 15(43.2%) | 16(36.8%) | 0.785 |
| Ticagrelor | 86(63.2%) | 10(62.5%) | 18(54.5%) | 21(56.8%) | 0.785 |
| Diuretics | 25(18.4%) | 5(31.3%) | 5(15.2%) | 18(48.6%) | 0.010 |
| Statins | 132(97.1%) | 16(100.0%) | 32(97.0%) | 32(86.5%) | 0.121 |
| Beta-blockers | 117(86.0%) | 15(93.8%) | 26(78.8%) | 31(83.8%) | 0.691 |
| ACEIs/ARBs | 97(70.6%) | 11(68.8%) | 19(57.6%) | 24(64.9%) | 0.691 |
| Laboratory findings | | | | | |
| Creatinine (mg/dL) | 0.84(0.26) | 0.76(0.28) | 0.79(0.25) | 0.87(0.55) | 0.245 |
| LVEF (%) | 59(11) | 54(14) | 55(13) | 50(15) | 0.004 |
| ACEF score | 1.03(0.32) | 1.13(0.55) | 1.15(0.34) | 1.25(0.36) | 0.002 |

**Notes**: †*P* value was corrected for multiplicity by *Benjamini-Hochberg*.

**Table 2** Baseline Characteristics of Post-PCI Patients in ACEF Quartiles

| **Variables** | **ACEF Quartiles** | | | | |
|---|---|---|---|---|---|
| | **Quartile 1 (<0.923)** | **Quartile 2 (0.923–1.116)** | **Quartile 3 (1.116–1.259)** | **Quartile 4 (≥1.259)** | ***P* value** † |
| Number of patients | 56(25.2%) | 55(24.8%) | 55(24.8%) | 56(25.2%) | |
| Age, mean ±SD | 48.63±6.96 | 58.93±7.277 | 65.20±8.97 | 68.75±8.72 | 0.003 |
| Female gender | 2(3.6%) | 11(20.0%) | 13(23.6%) | 13(23.2%) | 0.043 |
| Married | 53(94.6%) | 55(100.0%) | 51(92.7%) | 55(98.2%) | 0.271 |
| Education levels | | | | | 0.004 |
| Illiterate | 0(0.0%) | 0(0.0%) | 5(9.1%) | 4(7.1%) | |
| Primary | 5(8.9%) | 5(9.1%) | 11(20.0%) | 11(19.6%) | |
| Junior | 9(16.1%) | 20(36.4%) | 22(40.0%) | 26(46.4%) | |
| Senior | 21(37.5%) | 19(34.5%) | 13(23.6%) | 10(17.9%) | |
| College | 21(37.5%) | 11(20.0%) | 4(7.3%) | 5(8.9%) | |

(*Continued*)


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**Table 2** (Continued).

| Variables | ACEF Quartiles | | | | |
|---|---|---|---|---|---|
| | Quartile 1 (<0.923) | Quartile 2 (0.923–1.116) | Quartile 3 (1.116–1.259) | Quartile 4 (≥1.259) | *P* value † |
| CAD risk factors | | | | | |
| Hypertension | 34(60.7%) | 35(63.6%) | 28(50.9%) | 30(53.6%) | 0.580 |
| Diabetes mellitus | 20(35.7%) | 20(36.4%) | 23(41.8%) | 24(42.9%) | 0.826 |
| Smoking | 44(78.6%) | 31(56.4%) | 26(47.3%) | 30(53.6%) | 0.011 |
| Emergency PCI | 29(51.8%) | 30(54.5%) | 28(50.9%) | 36(64.3%) | 0.466 |
| Killip | | | | | 0.004 |
| I | 38(67.9%) | 41(74.5%) | 29(52.7%) | 14(25.0%) | |
| II | 12(21.4%) | 14(25.5%) | 20(36.4%) | 18(32.1%) | |
| III | 3(5.4%) | 0(0.0%) | 6(10.9%) | 15(26.8%) | |
| IV | 3(5.4%) | 0(0.0%) | 0(0.0%) | 9(16.1%) | |
| Culprit vessel | | | | | 0.373 |
| RCA | 14(25.0%) | 16(29.1%) | 23(41.8%) | 13(23.2%) | |
| LAD | 33(58.9%) | 31(56.4%) | 22(40.0%) | 36(64.3%) | |
| LCX | 8(14.3%) | 7(12.7%) | 10(18.2%) | 5(8.9%) | |
| D | 1(1.8%) | 1(1.8%) | 0(0.0%) | 2(3.6%) | |
| Number of stents | | | | | 0.580 |
| 0 | 11(19.6%) | 6(10.9%) | 10(18.2%) | 15(26.8%) | |
| 1 | 25(44.6%) | 26(47.3%) | 28(50.9%) | 21(37.5%) | |
| 2 | 17(30.4%) | 16(29.1%) | 14(25.5%) | 17(30.4%) | |
| ≥3 | 3(5.4%) | 7(12.7%) | 3(5.5%) | 3(5.4%) | |
| Medication | | | | | |
| Aspirin | 53(94.6%) | 51(92.7%) | 44(80.0%) | 40(71.4%) | 0.006 |
| Clopidogrel | 17(30.4%) | 16(29.1%) | 29(52.7%) | 25(44.6%) | 0.064 |
| Ticagrelor | 39(69.6%) | 39(70.9%) | 26(47.3%) | 31(55.4%) | 0.054 |
| Diuretics | 6(10.7%) | 1(1.8%) | 15(27.3%) | 31(55.4%) | 0.004 |
| Statins | 55(98.2%) | 52(94.5%) | 53(96.4%) | 52(92.9%) | 0.624 |
| Beta-blockers | 49(87.5%) | 46(83.6%) | 43(78.2%) | 51(91.1%) | 0.373 |
| ACEI /ARB | 41(73.2%) | 33(60.0%) | 35(63.6%) | 41(73.2%) | 0.438 |
| Laboratory findings | | | | | |
| Creatinine (mg/dL) | 0.84(0.24) | 0.83(0.26) | 0.80(0.28) | 0.87(0.47) | 0.248 |
| LVEF (%) | 60.00(6.00) | 58.00(9.00) | 56.00(11.00) | 45.00(11.00) | 0.002 |
| ACEF score | 0.82(0.10) | 1.02(0.08) | 1.18(0.07) | 1.5(0.29) | 0.002 |

**Notes**: †*P* value was corrected for multiplicity by *Benjamini-Hochberg*.

symptoms increased with ascending quartiles of ACEF score ($P_{for\ trend}$ <0.001). The numbers of patients with post-PCI anxiety symptoms were 2(3.6%) in Q1, 3(5.5%) in Q2, 5(9.1%) in Q3 and 6(10.7%) in Q4. Numbers of patients with post-PCI depression symptoms were 6(10.7%) in Q1, 8(14.5%) in Q2, 8(14.5%) in Q3 and 11 (19.6%) in Q4. Post-PCI comorbid anxiety and depression symptoms were 4(7.1%) in Q1, 3(5.5%) in Q2, 8(14.5%) in Q3 and 22 (39.3%) in Q4 (Figure 2).

## Logistic Regression Between ACEF Score Levels and Post-PCI Anxiety, Depression Symptoms

As shown in Table 3, elevated ACEF score levels were dose-dependently associated with higher risks of post-PCI anxiety and depression symptoms across progressively adjusted models. In the fully adjusted Model 3, patients in the highest ACEF quartile (Q4) had 7.7-fold increased odds of anxiety symptoms (OR = 7.70; 95% CI: 1.61–36.77) and 6.2-fold increased odds of depression symptoms (OR = 6.17; 95% CI: 1.61–28.03) compared to the lowest quartile (Q1). Statistically significant positive trends were observed for both outcomes ($P_{\text{for trend}} < 0.008$ for anxiety symptoms and <0.009 for depression symptoms).

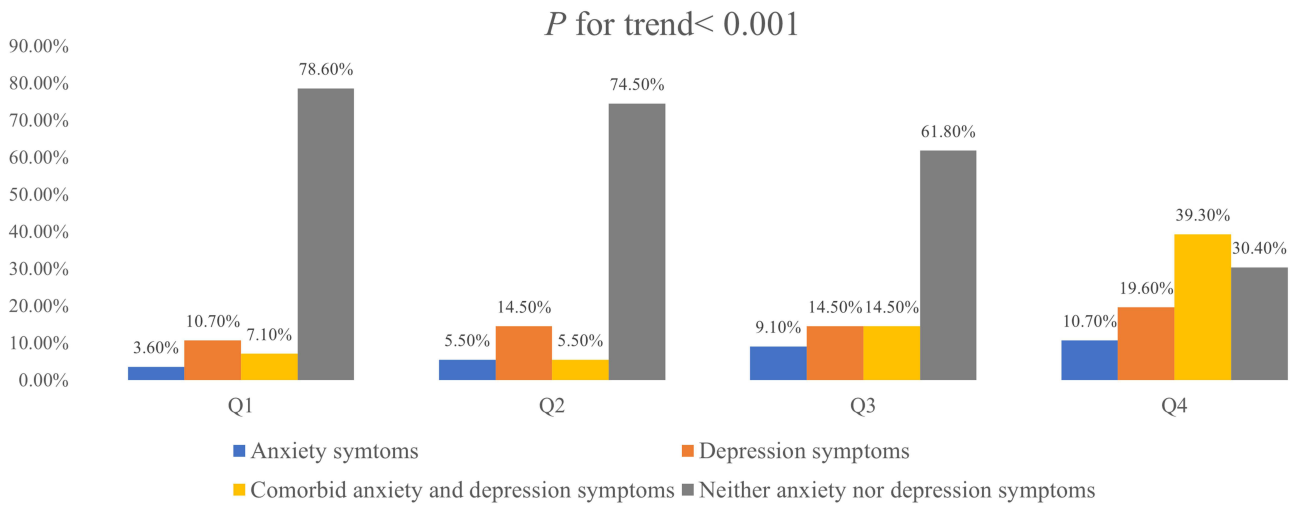


**Figure 2** The proportion of post-PCI anxiety, depression and comorbid anxiety and depression symptoms for the quartiles of ACEF score.

## Linear Regression Between ACEF Score and Post-PCI Anxiety, Depression Score

In Table 4, higher ACEF scores were statistically significant associated with increased anxiety score and depression score after PCI. In fully adjusted models (Model 3), each 1-unit elevation in the ACEF score corresponded to a 3.50-point increase in anxiety score (95% CI: 1.36–5.64; $P = 0.001$) and a 3.45-point increase in depression score (95% CI: 0.93–5.99; $P = 0.008$). These associations remained statistically robust across progressively adjusted models, indicating a linear relationship between ACEF score and psychological symptom burden.

From a non-linear perspective, the positive correlations between ACEF score and anxiety score and depression score were further corroborated by smooth curve fitting (based on the penalized spline method) (Figure 3).

**Table 3** Multivariate Adjusted Odds Ratios for the Association Between ACEF Levels and Post-PCI Anxiety and Depression Symptoms

| Variable | Quartiles of ACEF Score | | | | |
|---|---|---|---|---|---|
| | Q1 | Q2 | Q3 | Q4 | $P_{\text{for trend}}$ [e] |
| Median | 0.815 | 1.017 | 1.185 | 1.500 | |
| Anxiety symptoms | | | | | |
| Unadjusted | 1.00(Reference) | 1.379(0.471–3.979) | 2.167(0.791–5.931) | 5.250(2.025–13.609) | < 0.001 |
| Model 1[a] | 1.00(Reference) | 1.716(0.523–5.624) | 3.787(1.089–13.173) | 11.556(3.056–43.702) | < 0.001 |
| Model 2[b] | 1.00(Reference) | 1.761(0.514–6.035) | 2.861(0.768–10.681) | 8.166(1.758–37.931) | 0.005 |
| Model 3[c] | 1.00(Reference) | 1.743(0.507–5.990) | 2.775(0.730–10.549) | 7.701(1.613–36.766) | 0.008 |
| Depression symptoms | | | | | |
| Unadjusted | 1.00(Reference) | 1.616(0.627–4.164) | 3.225(1.315–7.909) | 4.862(2.007–11.781) | < 0.001 |
| Model 1 | 1.00(Reference) | 1.947(0.682–5.558) | 4.524(1.477–13.857) | 9.870(2.922–33.343) | < 0.001 |
| Model 2[d] | 1.00(Reference) | 1.983(0.655–6.006) | 3.789(1.143–12.563) | 7.511(1.845–30.582) | 0.005 |
| Model 3 | 1.00(Reference) | 1.967(0.644–6.006) | 3.591(1.055–12.222) | 6.173(1.608–28.028) | 0.009 |

**Notes**: [a]Model 1: adjusted for age, sex. [b]Model 2: adjusted for covariates from Model 1 and further adjusted for variables with $P < 0.05$ in univariate analysis (Education level, Killip, Aspirin, Diuretics and Depression symptoms). [c]Model 3: adjusted for covariates from Model 2 and further adjusted for conventional confounding factors (Smoking, Hypertension, Diabetes mellitus). [d]Model 2: adjusted for covariates from Model 1 and further adjusted for variables with $P < 0.05$ in univariate analysis (Education level, Killip, Aspirin, Diuretics and Anxiety symptoms). [e]Test for trend based on variable containing median value for each quartile.


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**Table 4** Multivariate Linear Analysis for the Association Among ACEF Score and Post-PCI Anxiety, Depression Score

| ACEF Score | Anxiety Score | | Depression Score | |
|---|---|---|---|---|
| | *β* (95% CI) | *P* | *β* (95% CI) | *P* |
| Unadjusted | 3.351(2.000–4.702) | < 0.001 | 4.018(2.437–5.600) | < 0.001 |
| Model 1[a] | 4.717(2.966–6.469) | < 0.001 | 5.097(3.035–7.158) | < 0.001 |
| Model 2[b] | 3.647(1.539–5.755) | < 0.001 | 3.601(1.113–6.089) | 0.005 |
| Model 3[c] | 3.503(1.364–5.641) | 0.001 | 3.452(0.926–5.987) | 0.008 |

**Notes**: [a]Model 1: adjusted for age, sex. [b]Model 2: adjusted for covariates from Model 1 and further adjusted for variables with $P < 0.05$ in univariate analysis (Education level, Killip, Aspirin and Diuretics). [c]Model 3: adjusted for covariates from Model 2 and further adjusted for conventional confounding factors (Smoking, Hypertension, Diabetes mellitus).

## ROC Curve of ACEF Score in Predicting Post-PCI Anxiety, Depression and Comorbid Anxiety and Depression Symptoms

The ROC curve analysis demonstrated that ACEF score presented ideal accuracy as predictors of in-hospital post-PCI anxiety, depression and comorbid anxiety and depression symptoms (Figure 4). For anxiety symptoms, the AUC of ACEF score was 0.666 (95% CI: 0.578–0.753, $P < 0.001$). For depression symptoms, the AUC of ACEF score was 0.662, (95% CI: 0.584–0.740, $P < 0.001$) and for comorbid anxiety and depression symptoms, it was 0.701 (95% CI: 0.608–0.794, $P < 0.001$) (Table 5).

# Discussion

This work, originally reporting on the association between ACEF score and post-PCI anxiety and depression symptoms, has the following findings: a) the incidences of post-PCI anxiety, depression and comorbid anxiety and depression symptoms were 16 (7.2%), 33 (14.9%) and 37 (16.7%); b) higher levels of ACEF score were significantly related to post-PCI anxiety and depression symptoms even adjusting for potential confounders; c) ACEF score has an ideal accuracy in predicting the anxiety and depression symptoms of patients after PCI.

Our study revealed that the ACEF score could predict the occurrence of anxiety and depression symptoms. Previously, the ACEF score was mainly used for risk assessment in cardiac patients. To our knowledge, this is the first study to explore the associations between ACEF scores and the risk of experiencing post-PCI anxiety and depression symptoms.

The underlying mechanism between the ACEF score and post-PCI depression and anxiety symptoms might involve the following aspects. First, regarding age, in our study, the participants in the anxiety, depression and comorbid anxiety and depression symptoms groups were older, and this age-related vulnerability to depression and anxiety might be explained by dysfunction of the hypothalamic–pituitary–adrenal (HPA) axis. The HPA axis is an essential modulator of endocrine and behavioural responses to stress. Thus, malfunction of the HPA axis, mainly characterized by the abnormal

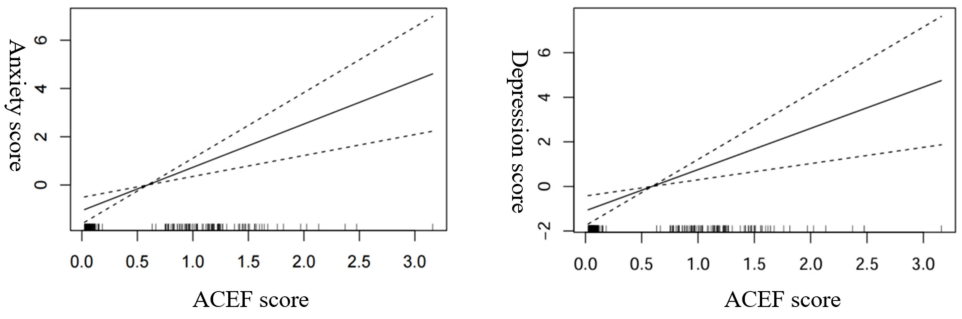


**Figure 3** The fitted smooth curve between ACEF score, anxiety score and depression score.

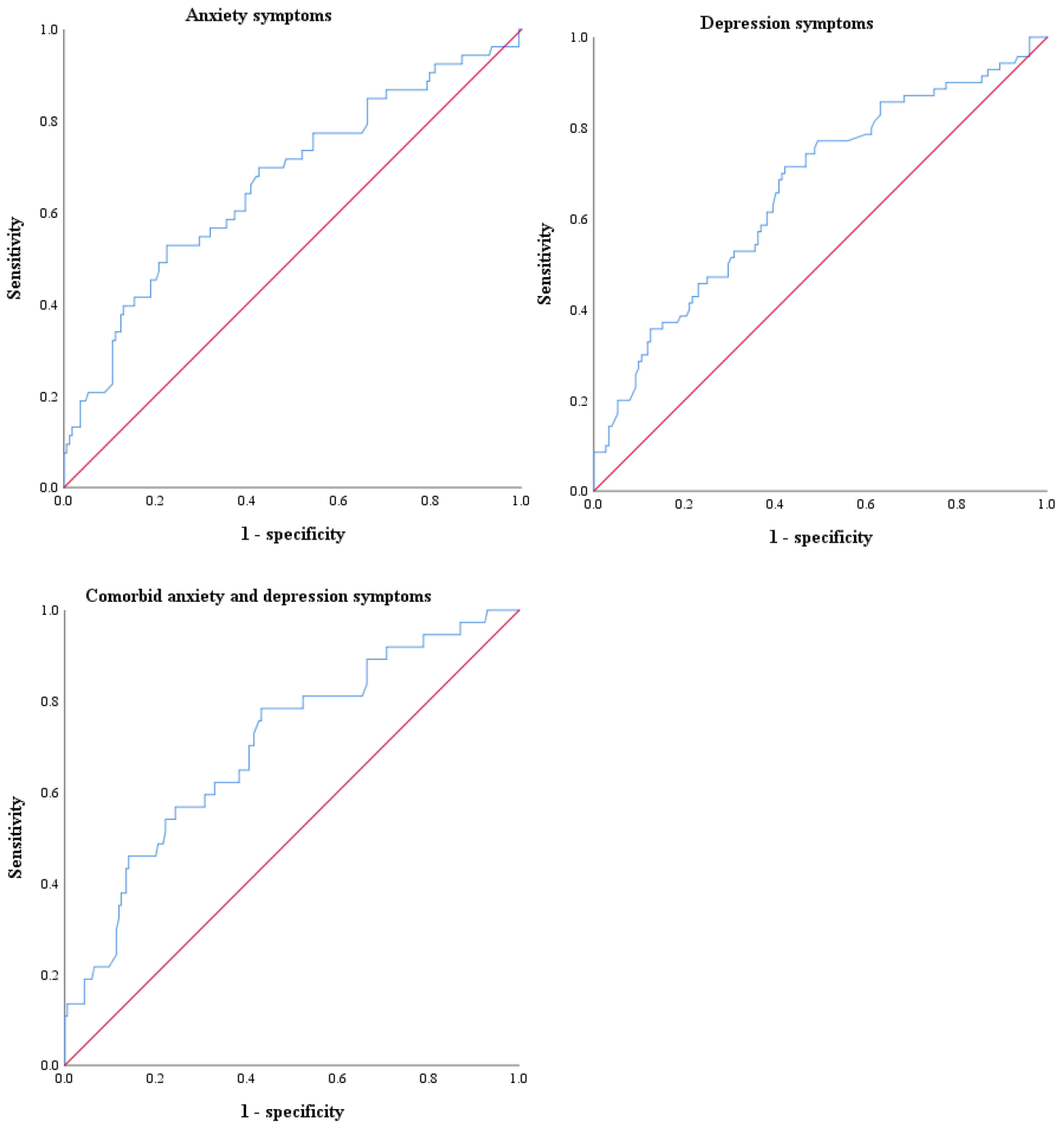


**Figure 4** ROC curves for post-PCI anxiety, depression and comorbid anxiety and depression symptoms.

secretion of glucocorticoids (GCs), could lead to the development of a variety of stress-dependent and age-related diseases. With ageing, the amplitude of the diurnal rhythmic activity of the HPA axis dampens,[13,14] and evening and night cortisol (CORT) secretion might increase in humans and primates.[13,15] The activities of the HPA axis both under basal conditions and in response to stress exposure are dependent on circadian rhythms.[16] Thus, numerous publications have demonstrated that circadian dysregulation increases the risk of various ageing-related diseases, especially anxiety, depression and cardiovascular diseases.[13,17,18] The research by Goncharova et al[19] used young adult and aged female rhesus monkeys as models to characterize the HPA axis in response to acute stress exposure under chronic constant light


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**Table 5** Characteristics of ROC Curve

| | AUC | *P* | 95% CI | Cut-Off Value | Sensitivity | Specificity |
|---|---|---|---|---|---|---|
| Anxiety symptoms | 0.666 | < 0.001 | 0.578–0.753 | 1.229 | 52.8% | 77.5% |
| Depression symptoms | 0.662 | < 0.001 | 0.584–0.740 | 1.102 | 71.4% | 57.9% |
| Comorbid anxiety and depression symptoms | 0.701 | < 0.001 | 0.608–0.794 | 1.124 | 78.4% | 56.8% |

**Abbreviations**: AUC, area under curve; Max, maximum.

conditions, and a significant decrease in the increase in CORT levels in response to acute stress exposure was observed, with an age-dependent mechanism. In addition, CORT levels were also associated with cardiovascular risk. Degroote et al[20] reported that reductions in total daytime CORT production independently predict increased cardiovascular risk, as evidenced by increased levels of biomarkers of atherothrombotic risk. Therefore, in light of the above mechanisms and experiments, it could be speculated that older patients with coronary artery diseases are more likely to have mental disorders.

Second, the relationships between creatinine and depression and anxiety are controversial. Previous studies have confirmed that depression and anxiety are linked to metabolic abnormalities of peripheral body systems, such as lipid, fatty acid and fluid balance abnormalities.[21,22] Bernhardsen et al[23] reported on prospective data from the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) Study comparing serum metabolic biomarkers in depression and control groups and revealed that creatinine was positively correlated with subsequent depression symptoms. The West China Health and Ageing Trend (WCHAT) study, a large multiethnic sample, divided participants into four groups according to comorbid anxiety and depression, anxiety only, depression only and neither, and significantly differed in creatinine compared with the healthy group.[24] A meta-analysis of 23 distinctly distributed metabolites from 46 studies in individuals with major depressive disorder (MDD) and controls suggested that MDD patients had lower creatinine levels.[25] Rather, another study based on data from the Korea National Health and Nutrition Examination Survey demonstrated that creatinine levels were greater in females in the depression group.[26] However, in other metabolomic profile studies, no associations existed,[27,28] which is in accordance with this study. In our study, the creatinine component was rarely triggered (>2.0 mg/dL in only 1.4%), making it a non-contributing factor in most cases. We further added a linear regression analysis comparing the performance of the full ACEF score versus a modified score excluding creatinine. In the fully adjusted model, modified ACEF score outperformed the full ACEF score (Supplement 2). But its inclusion in ACEF retains clinical relevance for following reasons: Even subthreshold creatinine values may reflect early renal dysfunction, which synergizes with age and LVEF to amplify cardiovascular risk. In populations with higher renal impairment prevalence (eg, advanced heart failure), creatinine's contribution to ACEF may be more pronounced. Future validation in cohorts with broader renal function profiles to dissect the relative contributions of ACEF components was needed.

Third, in terms of LVEF, Van Melle et al[11] assessed 1989 patients from the Myocardial Infarction and Depression-Intervention Trial (MIND-IT) and demonstrated that there was a significant relationship between LV dysfunction and depression symptoms, both during hospitalization and at 3, 6, 9, and 12 months of follow-up in post-MI patients (ie, the lower the LVEF was, the greater the proportion of depression symptoms). Frasure-Smith et al[29] enrolled 896 patients and dichotomized the LVEF with a cut-off of 35%, showing a marked association between LVEF and depression scores. A meta-analysis of 10,175 MI patients reached the same conclusion, but such a correlation existed only in male patients.[30] However, in contrast to the above large-sample studies, statistically significant differences were observed among the 222 patients in this study, which might be explained by the fact that the study explored the state of depression and anxiety symptoms during hospitalization and that the patients might still be in a state of acute stress.

Overall, it is reasonable to believe that the ACEF score is a reliable predictor of anxiety and depression symptoms after PCI. Previously there have also been composite objective parameters to predict post-PCI depression and anxiety symptoms. Li et al based on the theory that the inflammatory system was a potential pathological mechanism for the development of depression symptoms, they found that NLR index might be useful inflammatory markers to predict post-PCI depressive symptoms at 1 month (AUC: 0.716, 95% CI: 0.641–0.791).[31] Recently, a nomogram based on the

2005–2018 National Health and Nutrition Examination Surveys (NHANES) database was constructed to accurately and objectively predict post-PCI depression, the simplified model variables including age, smoking, poverty to income ratio, and insomnia (AUC: 0.772,95% CI: 0.732–0.812).[32] Another nomogram predicting the occurrence of post-PCI depression in acute coronary syndrome patients included female, hypertension history, Gensini score, neutrophil to lymphocyte ratio ≥ 3.24, palate to lymphocyte ratio ≥ 147.74 (AUC: 0.881,95% CI: 0.824–0.938).[33] The ACEF score in present study was as accurate a predictor of post-PCI anxiety and depression symptoms as the predictive models described above, with an AUC and 0.666 (95% CI: 0.578–0.753) and 0.662 (95% CI: 0.584–0.740), respectively. And, after multivariable adjusting, individuals in the highest quartile of ACEF score had a 7.701-fold and 6.173-fold higher risk of post-PCI anxiety and depression than those with the lowest quartile.

What's more, although we have excluded patients who had a history of depression disorders, anxiety disorders or other mental illnesses, it is important to note that anxiety and depression symptoms may have existed prior to PCI in some patients. Given the well-established association between psychological disorders and cardiovascular risk, pre-existing anxiety and depression may exacerbate cardiovascular damage through multiple pathophysiological pathways (eg, chronic inflammation, autonomic dysfunction, or endothelial dysfunction), thereby influencing components of the ACEF score (such as age-related HPA axis dysregulation, abnormal creatinine metabolism, or reduced left ventricular function). Thus, these psychological conditions could act both as triggers for cardiovascular diseases and as contributing factors to elevated ACEF scores, forming a bidirectional association with postoperative psychological symptoms. Future studies should systematically assess patients' psychological status at baseline to further clarify the interplay between pre-procedural anxiety/depression and the ACEF score.

## Clinical Implications

The ACEF score, derived from routinely collected clinical parameters (age, creatinine, and ejection fraction), offers a pragmatic advantage over dedicated psychological screening tools like HADS. Specifically, ACEF does not require additional patient-reported data or dedicated staff time, making it inherently scalable in resource-constrained settings. Clinicians could leverage this score to flag high-risk patients for targeted mental health assessments, particularly in populations where formal anxiety/depression screening is underutilized.

## Limitations

This study has several limitations. First, this is a heterogenous population with a relatively small cohort of patients. The heterogeneity reflects real-world clinical diversity, as our study aimed to capture a broad spectrum of patients undergoing PCI in routine practice. This approach enhances ecological validity but may introduce variability. Larger, multicenter validation studies were needed. And our study included a predominantly male cohort (82.4%), with only 17.6% female participants. This imbalance limits the statistical power to detect meaningful gender differences in outcomes. Future studies with balanced gender representation are needed to explore potential sex-specific associations between ACEF scores and psychological morbidity.

Second, in this study, ACEF score was only used to predict post-PCI anxiety and depression status during hospitalization, given that anxiety and depression are considered state indicators and may change over time and conditions. Future studies incorporating serial assessments at 1-month, 6-month and 1-year intervals are needed to evaluate whether ACEF scores predict sustained psychological morbidity or serve as dynamic markers of mental health trajectories.

Third, we included all comers who underwent PCI, whereas psychological preparation might be different for patients undergoing emergency vs elective PCI. In our study, emergency PCI patients exhibited higher anxiety scores, and statistically significant was observed. While depression scores were numerically higher in acute PCI patients, the difference between the two groups did not reach statistical significance, which may be attributed to factors such as the time window of assessment, measurement tools and sample size limitations (Supplement 1).

Finally, the use of the Hospital Anxiety and Depression Scale (HADS) to assess anxiety and depressive symptoms. Although HADS is widely adopted in clinical practice, the validity of its two-factor structure remains controversial, which may compromise the independent distinction between anxiety and depression symptoms. Future research could

employ multidimensional psychological assessment tools (eg, PHQ-9 and GAD-7, or combined clinical interviews) to further validate the current findings and enhance the robustness of the results. Additionally, exploring the consistency of associations between ACEF scores and psychological symptoms across different scales would help clarify the generalizability of its predictive value.

## Conclusion

ACEF, a simple and objective score, can be a valid predictor of anxiety and depression symptoms during hospitalization after PCI, and higher ACEF score is positively correlated with the prevalences of depression and anxiety symptoms.

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## Disclosure

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## References

1. Madhavan MV, Kirtane AJ, Redfors B, et al. Stent-related adverse events >1 year after percutaneous coronary intervention. *J Am Coll Cardiol*. 2020;75(6):590–604. doi:10.1016/j.jacc.2019.11.058
2. Zhang WY, Nan N, Song XT, et al. Impact of depression on clinical outcomes following percutaneous coronary intervention: a systematic review and meta-analysis. *BMJ Open*. 2019;9(8):e026445. doi:10.1136/bmjopen-2018-026445
3. Lichtman JH, Bigger JT, Blumenthal JA, et al. Depression and coronary heart disease: recommendations for screening, referral, and treatment: a science advisory from the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Psychiatric Association. *Circulation*. 2008;118(17):1768–1775. doi:10.1161/CIRCULATIONAHA.108.190769
4. Saini RK, Chaudhury S, Singh N, et al. Depression, anxiety, and quality of life after percutaneous coronary interventions. *Ind psychiatry j*. 2022;31(1):6–18. doi:10.4103/ipj.ipj_126_21
5. Park JH, Tahk SJ, Bae SH. Depression and anxiety as predictors of recurrent cardiac events 12 months after percutaneous coronary interventions. *J Cardiovasc Nurs*. 2015;30(4):351–359. doi:10.1097/JCN.0000000000000143
6. Hou Y, Zhang D, Zhu J, et al. Short report: depression and anxiety symptoms as predictors of adverse cardiovascular events in Chinese patients after percutaneous coronary intervention. *Psychol Health Med*. 2021;26(9):1126–1133. doi:10.1080/13548506.2020.1837388
7. Ranucci M, Castelvecchio S, Menicanti L, et al. Risk of assessing mortality risk in elective cardiac operations: age, creatinine, ejection fraction, and the law of parsimony. *Circulation*. 2009;119(24):3053–3061. doi:10.1161/CIRCULATIONAHA.108.842393
8. Wijns W, Kolh P, Danchin N, et al. Guidelines on myocardial revascularization. *Eur Heart J*. 2010;31(20):2501–2555. doi:10.1093/eurheartj/ehq277
9. Lee JH, Bae MH, Yang DH, et al. Prognostic value of the age, creatinine, and ejection fraction score for 1-year mortality in 30-day survivors who underwent percutaneous coronary intervention after acute myocardial infarction. *Am J Cardiol*. 2015;115(9):1167–1173. doi:10.1016/j.amjcard.2015.02.001
10. Yang XL, Xie WY, Cai YM, et al. Investigation of the negative emotions exhibited in patients with coronary heart disease after PCI and any influencing factors. *Psychol Res Behav Manag*. 2022;15:3027–3037. doi:10.2147/PRBM.S379422
11. Van Melle JP, De Jonge P, Ormel J, et al. Relationship between left ventricular dysfunction and depression following myocardial infarction: data from the MIND-IT. *Eur Heart J*. 2005;26(24):2650–2656. doi:10.1093/eurheartj/ehi480
12. Bjelland I, Dahl AA, Haug TT, et al. The validity of the hospital anxiety and depression scale. An updated literature review. *J Psychosom Res*. 2002;52(2):69–77. doi:10.1016/S0022-3999(01)00296-3
13. Rao R, Androulakis IP. The physiological significance of the circadian dynamics of the HPA axis: interplay between circadian rhythms, allostasis and stress resilience. *Horm Behav*. 2019;110:77–89. doi:10.1016/j.yhbeh.2019.02.018
14. Gaffey AE, Bergeman CS, Clark LA, et al. Aging and the HPA axis: stress and resilience in older adults. *Neurosci Biobehav Rev*. 2016;68:928–945. doi:10.1016/j.neubiorev.2016.05.036
15. Goncharova ND, Oganyan TE, Smelkova SA. Effect of aging on stress reactivity of the adrenal cortex in laboratory primates. Dependence on the time of day. *Bull Exp Biol Med*. 2006;141(3):368–371. doi:10.1007/s10517-006-0173-5
16. Goncharova ND. The HPA axis under stress and aging: individual vulnerability is associated with behavioral patterns and exposure time. *BioEssays*. 2020;42(9):e2000007. doi:10.1002/bies.202000007
17. Hood S, Amir S. Neurodegeneration and the circadian clock. *Front Aging Neurosci*. 2017;9:170. doi:10.3389/fnagi.2017.00170
18. Saad L, Washington I. Can vitamin A be improved to prevent blindness due to age-related macular degeneration, stargardt disease and other retinal dystrophies? *Adv Exp Med Biol*. 2016;854:355–361.
19. Goncharova N, Chigarova O, Oganyan T. Age-related and individual features of the HPA axis stress responsiveness under constant light in nonhuman primates. *Front Endocrinol*. 2022;13:1051882. doi:10.3389/fendo.2022.1051882

20. Degroote C, Von Känel R, Thomas L, et al. Lower diurnal HPA-axis activity in male hypertensive and coronary heart disease patients predicts future CHD risk. *Front Endocrinol*. 2023;14:1080938. doi:10.3389/fendo.2023.1080938
21. Otte C, Gold SM, Penninx BW, et al. Major depressive disorder. *Nat Rev Dis Prim*. 2016;2:16065. doi:10.1038/nrdp.2016.65
22. De Kluiver H, Jansen R, Milaneschi Y, et al. Metabolomic profiles discriminating anxiety from depression. *Acta Psychiatr Scand*. 2021;144 (2):178–193. doi:10.1111/acps.13310
23. Bernhardsen GP, Thomas O, Mäntyselkä P, et al. Metabolites and depressive symptoms: network- and longitudinal analyses from the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study. *J Affect Disord*. 2024;347:199–209. doi:10.1016/j.jad.2023.11.070
24. Liu X, Zhao W, Hu F, et al. Comorbid anxiety and depression, depression, and anxiety in comparison in multi-ethnic community of west China: prevalence, metabolic profile, and related factors. *J Affect Disord*. 2022;298(Pt A):381–387. doi:10.1016/j.jad.2021.10.083
25. Pu J, Liu Y, Zhang H, et al. An integrated meta-analysis of peripheral blood metabolites and biological functions in major depressive disorder. *Mol Psychiatry*. 2021;26(8):4265–4276. doi:10.1038/s41380-020-0645-4
26. Lee BJ. Association of depressive disorder with biochemical and anthropometric indices in adult men and women. *Sci Rep*. 2021;11(1):13596. doi:10.1038/s41598-021-93103-0
27. Bot M, Milaneschi Y, Al-Shehri T, et al. Metabolomics profile in depression: a pooled analysis of 230 metabolic markers in 5283 cases with depression and 10,145 controls. *Biol Psychiatry*. 2020;87(5):409–418. doi:10.1016/j.biopsych.2019.08.016
28. Hamidifard S, Fakhari A, Mahboob S, et al. Plasma levels of lipoprotein (a) in patients with major depressive disorders. *Psychiatry Res*. 2009;169 (3):253–256. doi:10.1016/j.psychres.2008.06.033
29. Frasure-Smith N, Lespérance F, Juneau M, et al. Gender, depression, and one-year prognosis after myocardial infarction. *Psychosom Med*. 1999;61 (1):26–37. doi:10.1097/00006842-199901000-00006
30. Doyle F, Mcgee H, Conroy R, et al. Systematic review and individual patient data meta-analysis of sex differences in depression and prognosis in persons with myocardial infarction: a MINDMAPS study. *Psychosom Med*. 2015;77(4):419–428. doi:10.1097/PSY.0000000000000174
31. Li C, Wan S, Li W, et al. Higher neutrophil to lymphocyte ratio at admission is association with post-PCI depressive symptoms in patients with ACS. *Neuropsychiatr Dis Treat*. 2022;18:2981–2990. doi:10.2147/NDT.S387582
32. Wang D, Jia S, Yan S, et al. Development and validation using NHANES data of a predictive model for depression risk in myocardial infarction survivors. *Heliyon*. 2022;8(1):e08853. doi:10.1016/j.heliyon.2022.e08853
33. Li G, Lyu J, Wan S, et al. Nomogram prediction model of depressive symptoms risk in patients with acute coronary syndrome after interventional treatment. *Chin Mental Health J*. 2023;37(9):771–779. doi:10.3969/j.issn.10006729.2023.09.007