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ORIGINAL RESEARCH

# The Prognostic Role of Naples Prognostic Score in Patients with Coronary Artery Disease

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**Background and Objective:** The Naples Prognostic Score (NPS) is a tool for assessing inflammation and nutrition, widely used in outcome evaluation. However, its association with adverse outcomes in patients with coronary artery disease (CAD) has not been explored. This study aims to investigate the prognostic value of NPS in CAD patients.

**Methods:** This retrospective cohort study included 2453 patients with CAD who visited the Fujian Heart Medical Center between 2017 and 2022. Patients were divided into three groups based on NPS. The NPS was calculated based on serum albumin, total cholesterol, neutrophil-to-lymphocyte ratio, and lymphocyte-to-monocyte ratio. Univariate and multivariate regression analyses, along with Cox models, were used to assess the impact of NPS on adverse outcomes. Receiver operating characteristic (ROC) curves evaluated NPS's accuracy in predicting all-cause in-hospital mortality.

**Results:** Patients with lower NPS scores are less likely to have comorbidities such as hyperlipidemia and chronic kidney disease. Additionally, they tend to use fewer medications for treatment. Multivariate analysis revealed that elevated NPS levels were independently associated with poorer clinical outcomes. Compared to group 1, the risk of all-cause mortality was significantly higher in groups 2 and 3 [group 2, adjusted odds ratio (aOR)=0.33; group 3, aOR=1.82; $P$=0.037], the risk of acute myocardial infarction was higher (group 2, aOR=2.41; group 3, aOR=4.05; $P$<0.001), and the risk of stroke was also higher (group 2, aOR=1.26; group 3, aOR=1.80; $P$=0.039). ROC curve analysis showed that NPS could independently predict the risk of all-cause mortality in patients with CAD.

**Conclusion:** This study suggests that the NPS, a novel metric integrating inflammation and nutritional status, is closely associated with the prognosis of CAD.

**Keywords:** naples prognostic score, outcomes, coronary artery disease, prognosis

## Introduction

Atherosclerotic cardiovascular disease (ASCVD) is a major non-communicable chronic disease that significantly threatens the health and life expectancy of China's population. It is characterized by high incidence, disability, mortality, and economic burden.[1,2] Coronary artery disease (CAD), which accounts for approximately 40%–50% of total ASCVD cases, is a leading contributor. In 2019, CAD was responsible for 1.87 million deaths in China, making it the second leading cause of death.[3,4] With an aging population and the ongoing prevalence of risk factors, the challenges of CAD prevention and control are intensifying. Despite the increasing use of percutaneous coronary intervention (PCI) as an essential treatment for CAD, numerous studies have shown that while PCI can improve long-term outcomes, the short-term risks of adverse events such as contrast-induced nephropathy and major adverse cardiovascular and cerebrovascular events (MACCEs) remain high. These complications significantly elevate patient mortality and hospital readmission rates.[5,6] Wang et al conducted a one-year follow-up study of PCI patients and reported a 41.5% incidence of MACCEs post-procedure.[7] Given this, identifying reliable markers that can predict patient outcomes is crucial for early intervention in high-risk individuals, with the aim of reducing complications and improving patients' quality of life.

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Inflammation plays a key role in the onset and progression of CAD, contributing to endothelial dysfunction, cytokine production, and immune cell activation.[8–10] Several inflammation-related markers, such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR), have been proposed as potential biomarkers for the severity and prognosis of CAD.[11–16] While elevated total cholesterol (TC), particularly low-density lipoprotein cholesterol (LDL-C), is traditionally considered a major risk factor for atherosclerotic cardiovascular disease, emerging evidence suggests that low TC may also be associated with adverse outcomes in certain clinical settings.[17] This paradox may be explained by the fact that low TC can reflect underlying malnutrition or systemic inflammation, both of which are linked to poor prognosis. For instance, studies in patients with chronic heart failure and coronary slow flow have shown that lower cholesterol levels are associated with higher mortality, potentially due to cholesterol's involvement in immune regulation and cellular repair.[18] Nevertheless, findings across studies remain inconsistent, and the optimal cut-off values for these biomarkers have not been clearly established. In addition to inflammatory indices, nutritional markers—such as the prognostic nutritional index and the triglyceride-glucose index—have also been associated with the risk and complications of CAD.[19,20] Nevertheless, the causal associations between these indices and CAD are not well-established, and the underlying mechanisms remain poorly understood. Thus, it is essential to further investigate the roles of inflammation and nutritional markers in CAD and assess their prognostic value. Individual inflammatory markers such as NLR, MLR, and PLR, as well as nutritional indicators like the prognostic nutritional index and the triglyceride-glucose index, typically reflect only isolated aspects of a disease and fail to provide a comprehensive assessment of a patient's overall physiological condition. This limitation highlights the need for a more integrated approach, such as the NPS, to better capture the multifaceted nature of a patient's health status. The NPS is a novel multidimensional assessment system that integrates both inflammatory and nutritional status based on four parameters: albumin, total cholesterol, NLR, and lymphocyte-to-monocyte ratio (LMR).[21] The NPS offers several advantages over relying on individual biomarkers. By combining inflammatory and nutritional parameters, NPS provides a more comprehensive view of a patient's health, capturing interactions between these factors that may not be apparent when assessed separately. While biomarkers like NLR, MLR and PLR offer valuable insights into specific aspects of a patient's condition, they may not fully reflect the complexity of the overall prognosis.[11–16] As a composite score, NPS has been shown to offer superior prognostic accuracy, better predicting patient outcomes than individual markers. Additionally, NPS simplifies clinical decision-making by providing a single, easy-to-interpret score, reducing the need to monitor multiple parameters. Thus, NPS enhances both the reliability and practicality of patient risk assessment, making it a valuable tool in clinical practice. Currently, The NPS has been validated in various cancers and non-malignant conditions. In patients with ampullary carcinoma and colorectal cancer, NPS independently predicts both short-term and long-term outcomes, with higher scores correlating with poorer survival. Additionally, in adult asthma patients, elevated NPS scores are associated with an increased risk of acute exacerbations and poorer disease control. These findings demonstrate that NPS not only holds prognostic value in cancer but also effectively predicts outcomes in non-malignant diseases, highlighting its broad potential for clinical application.[21–23] However, its prognostic value in CAD has not yet been explored.

Therefore, this study aims to evaluate the predictive value of the NPS, as a novel multidimensional inflammatory and nutritional assessment tool, for the prognosis of CAD. By providing a more precise assessment, the NPS may help identify high-risk patients with poor outcomes, facilitating more accurate and timely clinical decision-making.

# Methods

## Study Design and Population

This retrospective study included 2,453 hospitalized patients diagnosed with CAD at the Fujian Heart Medical Center in Fuzhou, China, between May 2017 and December 2022. The inclusion criteria were: (1) patients aged 18 years or older; (2) all patients met the diagnostic criteria for CAD, defined as having at least one major coronary artery (left main coronary artery, left anterior descending artery, circumflex artery, or right coronary artery) or its branches with a lumen diameter stenosis of ≥70%, along with indications for interventional therapy.[24] The exclusion criteria were: (1) patients with severe underlying diseases or major complications; (2) chronic liver disease or abnormal liver function suggestive of hepatic insufficiency; (3) incomplete clinical data; and (4) those diagnosed with COVID-19 (Figure 1).

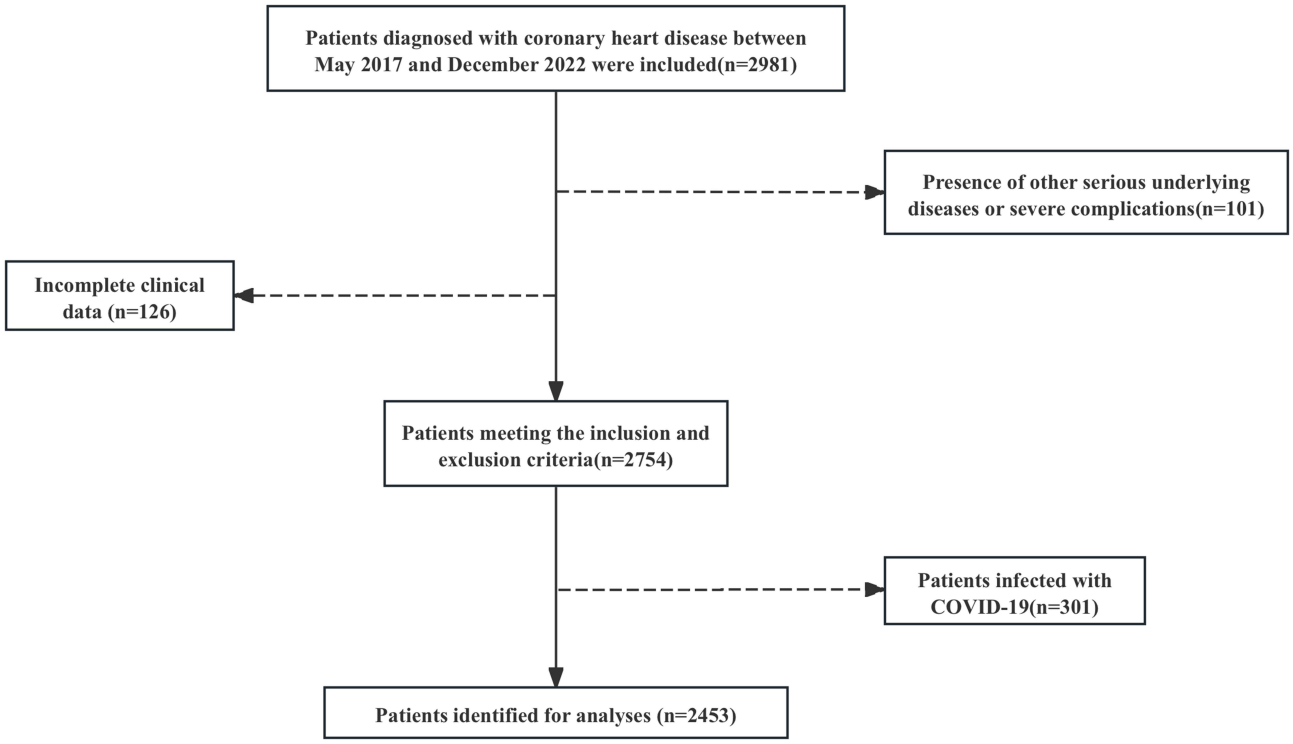


**Figure 1** Inclusion/exclusion flowchart for the study group.

## Data Collection

Venous blood samples were collected within 24 hours of hospital admission, with all samples drawn after fasting for more than 8 hours. If multiple blood tests were performed within the 24-hour window, the results from the first test were used. All laboratory data included in this study were measured by the clinical laboratory of Fujian Medical University Union Hospital, and the data were obtained from the hospital's electronic medical record system. Baseline data comprised demographic information, admission and discharge diagnoses, laboratory results, medications, surgical procedures, and discharge status.

## Definition of the NPS

The NPS is defined based on the levels of serum albumin, total cholesterol, NLR, and LMR.[21,25] the scoring system assigns points as follows: a serum albumin level ≥4 mg/dL is assigned 0 points, while <4 mg/dL is assigned 1 point. For total cholesterol, a concentration >180 mg/dL is assigned 0 points, and ≤180 mg/dL is assigned 1 point. A NLR ≤2.96 receives 0 points, while >2.96 is assigned 1 point. For LMR, values >4.44 are given 0 points, and ≤4.44 are assigned 1 point. The NPS total score is calculated as the sum of these parameter scores. Based on the NPS, patients are classified into three groups: low NPS, moderate NPS, and high NPS. The low NPS group has a total score of 0, the moderate NPS group scores between 1 and 2, and the high NPS group scores between 3 and 4. Serum albumin, total cholesterol, NLR and LMR values were calculated from untreated admission reports (Figure 2).[26]

## Outcomes Measured

The primary endpoint of this study was the occurrence of MACCEs, which included all-cause in-hospital mortality, new-onset atrial fibrillation (AF), acute myocardial infarction (AMI), and stroke. All-cause in-hospital mortality was defined as death from any cause during hospitalization. New-onset AF was characterized by the absence of prior atrial fibrillation history and was diagnosed through routine electrocardiograms (ECG), Holter monitoring, or bedside ECG monitors during outpatient or inpatient care. AMI was defined as elevated serum cardiac enzyme levels, accompanied by symptoms of myocardial ischemia and hypoxia, along with electrocardiographic changes. The diagnosis of acute

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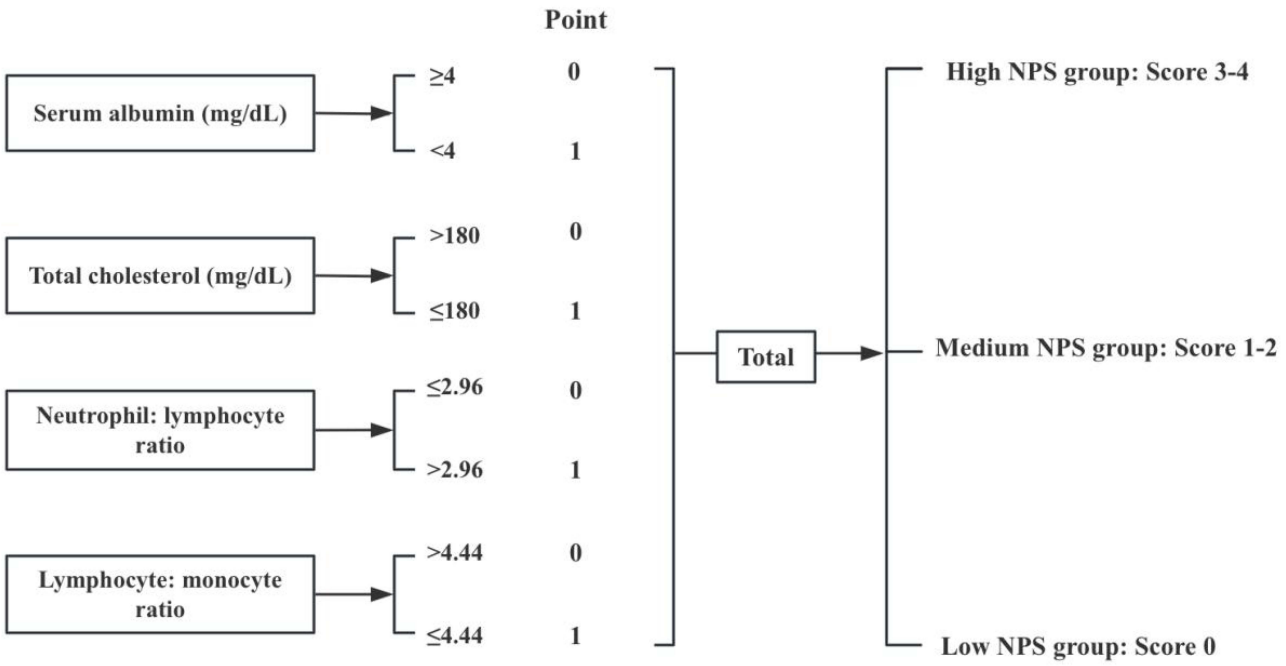


**Figure 2** The formula for the Naples prognostic score.
**Abbreviation**: NPS, Naples Prognostic Score.

myocardial infarction (AMI) is based on elevated cardiac enzyme levels, including troponin I/T (above the 99th percentile) and CK-MB (greater than twice the upper limit of normal), in conjunction with clinical symptoms of myocardial ischemia and electrocardiographic changes, such as ST-segment elevation or new left bundle branch block.[27] Stroke diagnosis is based on clinical neurological symptoms (eg, sudden onset of weakness or speech difficulties), confirmed through brain imaging with either CT or MRI. Ischemic stroke is characterized by hypodense areas on CT or hyperintense lesions on diffusion-weighted MRI, while hemorrhagic stroke is diagnosed by the presence of blood on either CT or MRI scans.[28] Secondary endpoints included all-cause readmission rates. Readmission events for any cause were confirmed by reviewing medical records or contacting the patient or their treating physician. The average follow-up period for this study was one year.

## Statistical Analysis

Continuous variables were presented as weighted means±standard deviations (SD), while categorical variables were expressed as frequencies (percentages). Group differences were assessed using Student's *t*-test, Mann–Whitney *U*-test, and $\chi^2$-test, as appropriate. Univariate and multivariate regression analyses, along with Cox proportional hazards models, were employed to evaluate the association between NPS, all-cause mortality, and other adverse outcomes. To reduce potential confounding, sensitivity analyses were performed by adjusting for covariates in a stepwise manner (Model 1–2). Model 1 was adjusted for age and sex, while Model 2 further accounted for smoking history, previous interventions, BMI, hypertension, length of hospital stay, hyperlipidemia, medication use (calcium channel blockers, statins, dual antiplatelet therapy, diuretics), triglycerides, HDL cholesterol, LDL cholesterol, serum potassium, serum sodium, blood glucose, glomerular filtration rate, hemoglobin, total cholesterol (TC), cardiac ejection fraction, and serum creatinine. Time-dependent receiver operating characteristic (ROC) curve analysis and the area under the curve (AUC) were used to assess the accuracy of NPS in predicting all-cause in-hospital mortality risk in coronary artery disease patients. Subgroup analyses explored the association between NPS and mortality, as well as its interaction across different subgroups. In the subgroup analysis, due to the lack of widely accepted standardized cutoff values, all continuous variables were divided based on their median values. All statistical analyses were conducted using SPSS version 26.0, with statistical significance set at $P<0.05$.

## Ethical Approval and Informed Consent

This study received approval from the Ethics Committee of Fujian Medical University Union Hospital (No: 2023KY032). Given that the research solely involved the retrospective collection of anonymized patient data from electronic medical records, the Ethics Committee waived the requirement for informed consent. The use of research data began on May 28, 2023. Throughout the data collection process, the authors did not have access to any information that could identify individual participants. This study adhered to the principles outlined in the revised Declaration of Helsinki from 2013.

# Results

## Baseline Characteristics of the Study Population

This study included a total of 2,453 patients with an average age of 64.50±10.59 years. Among these patients, 530 (21.6%) were female, 943 (38.4%) had hypertension, and 1,573 (64.1%) had a history of diabetes. Based on the NPS, the patients were categorized into three groups: low NPS (n=177), moderate NPS (n=1,132), and high NPS (n=1,144). From a demographic perspective, patients in the low NPS group generally exhibited higher body mass index (BMI) and ejection fraction, shorter hospital stays, and a lower proportion of prior PCI compared to those in the high NPS group. Additionally, individuals in the low NPS group were less likely to be smokers. In terms of comorbidities, the low NPS group had a lower likelihood of hyperlipidemia and chronic kidney disease. Regarding medication history, patients in the high NPS group were prescribed a greater number of medications, including diuretics, antihypertensives, statins, and dual antiplatelet therapy (DAPT). Biochemical analyses revealed that the low NPS group had higher levels of hemoglobin, serum albumin, total cholesterol, and triglycerides, along with a tendency for elevated high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels, as well as higher concentrations of serum sodium and potassium. Conversely, the high NPS group exhibited higher serum creatinine (Scr) and blood glucose levels, alongside a lower estimated glomerular filtration rate (eGFR) (Table 1).

## Association Between NPS and the Risk of Adverse Outcomes in Patients with CAD

In the study population, the incidence of MACCEs was relatively high. Specifically, 33 patients (1.3%) experienced all-cause mortality, 845 patients (34.4%) had acute AMI, and 285 patients (11.6%) suffered a stroke (Table 2).

**Table 1** Baseline Characteristics in Patients with Coronary Heart Disease

| Characteristics | Overall (n=2453) | Naples Prognostic Score | | | *P*-Value |
|---|---|---|---|---|---|
| | | Low(0) (n=175) | Medium(1–2) (n=1125) | High(3–4) (n=1153) | |
| **Demographic and clinical characteristics** | | | | | |
| Age, years, M (SD) | 64.50±10.59 | 61.95±10.07 | 62.75±10.44 | 66.61±10.42 | <0.001 |
| Female, n (%) | 530 (21.6) | 60 (33.9) | 284 (25.1) | 186 (16.3) | <0.001 |
| Current smoking, n (%) | 896 (36.5) | 53 (29.9) | 432 (38.2) | 411 (35.9) | 0.006 |
| Current drinking, n (%) | 192 (7.8) | 9 (5.1) | 84 (7.4) | 99 (8.7) | 0.302 |
| BMI, kg/m$^2$, M (SD) | 24.30±2.99 | 24.65±4.15 | 24.47±3.05 | 24.08±2.70 | 0.003 |
| EF (%), M (SD) | 59.46±11.78 | 63.68±9.61 | 61.24±10.67 | 57.07±12.62 | <0.001 |
| LOS, days, M (SD) | 9.56±7.74 | 8.96±6.82 | 8.47±6.43 | 10.73±8.82 | <0.001 |
| History of PCI, n (%) | 507 (20.7) | 24 (13.6) | 251 (22.2) | 232 (20.3) | 0.028 |
| History of CABG, n (%) | 58 (2.4) | 2 (1.1) | 28 (2.5) | 28 (2.4) | 0.532 |
| **Complication** | | | | | |
| Hypertension, n (%) | 1573 (64.1) | 103 (58.2) | 710 (62.7) | 760 (66.4) | 0.042 |
| DM, n (%) | 943 (38.4) | 62 (35.0) | 419 (37.0) | 462 (40.4) | 0.160 |
| Hyperlipemia, n (%) | 843 (34.4) | 101 (57.1) | 435 (38.4) | 307 (26.8) | <0.001 |
| Chronic heart failure, n (%) | 74 (3.0) | 0 (0.0) | 22 (1.9) | 52 (4.5) | <0.001 |
| COPD, n (%) | 58 (2.4) | 4 (2.3) | 19 (1.7) | 35 (3.1) | 0.095 |

(*Continued*)

**Table 1** (Continued).

| Characteristics | Overall (n=2453) | Naples Prognostic Score | | | *P*-Value |
|---|---|---|---|---|---|
| | | Low(0) (n=175) | Medium(1–2) (n=1125) | High(3–4) (n=1153) | |
| **Medications** | | | | | |
| Diuretics, n (%) | 549 (22.4) | 23 (13.0) | 221 (19.5) | 305 (26.7) | <0.001 |
| CCB, n (%) | 636 (25.9) | 53 (29.9) | 322 (28.4) | 261 (22.8) | 0.004 |
| ACEI/ARB/ARNI, n (%) | 827 (33.7) | 53 (29.9) | 387 (34.2) | 387 (33.8) | 0.536 |
| β-blockers, n (%) | 1343 (54.7) | 95 (53.7) | 627 (55.4) | 621 (54.3) | 0.831 |
| Statins, n (%) | 1950 (79.2) | 149 (84.2) | 928 (82.0) | 865 (75.6) | <0.001 |
| DAPT, n (%) | 1950 (79.5) | 155 (87.6) | 946 (83.6) | 849 (74.2) | <0.001 |
| **Laboratory findings** | | | | | |
| ALB, g/L, M (SD) | 39.38±4.35 | 43.90±2.48 | 40.99±3.64 | 37.09±3.93 | <0.001 |
| GFR, mL/min, M (SD) | 75.44±22.68 | 78.79±23.53 | 79.30±24.45 | 71.10±19.75 | <0.001 |
| Scr, μmol/L, M (SD) | 91.72±65.54 | 79.28±22.28 | 81.89±40.44 | 103.39±85.18 | <0.001 |
| Total cholesterol, mmol/L, M (SD) | 4.28±1.29 | 5.82±1.61 | 4.46±1.29 | 3.87±0.99 | <0.001 |
| Triglycerides, mmol/L,MED (IQR) | 1.80±2.01 | 1.79 (1.26, 2.59) | 1.50 (1.10, 2.11) | 1.31 (0.97, 1.77) | <0.001 |
| HDL-C, μmol/L, M (SD) | 1.03±0.28 | 1.17±0.39 | 1.04±0.27 | 0.99±0.27 | <0.001 |
| LDL-C, μmol/L, M (SD) | 2.77±1.12 | 3.97±1.03 | 2.90±1.18 | 2.46±0.89 | <0.001 |
| K, mmol/L, M (SD) | 4.03±0.44 | 4.14±0.39 | 4.02±0.42 | 4.02±0.46 | 0.004 |
| Na, mmol/L, M (SD) | 140.59±2.92 | 140.98±2.88 | 140.94±2.37 | 140.18±3.33 | <0.001 |
| Blood glucose, mmol/L, M (SD) | 6.34±2.63 | 6.28±3.37 | 6.18±2.37 | 6.61±3.10 | 0.001 |
| Hemoglobin, g/L, M (SD) | 133.08±18.77 | 141.13±15.07 | 136.22±16.83 | 128.03±20.64 | <0.001 |
| Platelets, 10^9/L, M (SD) | 229.97±71.38 | 235.41±54.98 | 231.14±63.78 | 227.87±80.11 | 0.253 |
| NLR, M (SD) | 3.40±3.13 | 1.62±0.52 | 2.40±1.85 | 4.75±3.89 | <0.001 |
| LMR, M (SD) | 3.84±1.83 | 6.18±1.57 | 4.58±1.80 | 2.72±0.99 | <0.001 |

**Abbreviations**: BMI, body mass index; EF, ejection fraction; LOS, length of stay; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CCB, Calcium Channel Blockers; ACEI /ARB/ARNI, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers or angiotensin receptor–neprilysin inhibitors; DAPT, dual antiplatelet therapy; ALB, albumin; GFR,glomerular filtration rate; Scr, serum creatinine; HDL-C, High density lipoprotein cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; NLR, neutrophil-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio.

**Table 2** The Risk of Clinical Outcomes in Patients with Coronary Heart Disease

| Main outcomes | Model | Naples Prognostic Score | | | *P*-value |
|---|---|---|---|---|---|
| | | Low(0) (n=177) | Medium(1–2) (n=1132) | High(3–4) (n=1144) | |
| **MACCEs** | | | | | |
| All-cause in-hospital mortality | All-cause in-hospital mortality | 1 (0.6) | 4 (0.4) | 28 (2.4) | <0.001 |
| | Model 1 | Reference | 0.66 (0.07, 5.99) | 5.27 (0.70, 39.54) | <0.001 |
| | Model 2 | Reference | 0.33 (0.03,3.41) | 1.82 (0.20, 16.66) | 0.037 |
| Atrial fibrillation | AF | 15 (8.5) | 82 (7.2) | 134 (11.7) | 0.001 |
| | Model 1 | Reference | 0.78 (0.43,1.40) | 1.04 (0.58, 1.85) | 0.161 |
| | Model 2 | Reference | 0.47 (0.24,0.95) | 0.41 (0.18,0.96) | 0.095 |
| Acute myocardial infarction | Acute myocardial Infarction | 18 (10.2) | 287 (25.4) | 540 (47.2) | <0.001 |
| | Model 1 | Reference | 3.03 (1.83, 5.03) | 8.44 (5.09, 14.00) | <0.001 |
| | Model 2 | Reference | 2.41 (1.35, 4.32) | 4.05 (2.07, 7.93) | <0.001 |
| Stroke | Stroke | 12 (6.8) | 105 (9.3) | 168 (14.7) | <0.001 |
| | Model 1 | Reference | 1.32 (0.71, 2.47) | 1.84 (0.99, 3.41) | 0.018 |
| | Model 2 | Reference | 1.26 (0.66, 2.38) | 1.80 (0.92, 3.50) | 0.039 |

(*Continued*)

**Table 2** (Continued).

| Main outcomes | Model | Naples Prognostic Score | | | *P*-value |
|---|---|---|---|---|---|
| | | Low(0) (n=177) | Medium(1–2) (n=1132) | High(3–4) (n=1144) | |
| **Secondary outcomes** | | | | | |
| All-cause readmission | All-cause readmission | 76 (42.9) | 470 (41.5) | 450 (39.3) | 0.459 |
| | Model 1 | Reference | 0.98 (0.76,1.25) | 0.98 (0.76,1.26) | 0.982 |
| | Model 2 | Reference | 1.04 (0.78,1.38) | 1.00 (0.71,1.43) | 0.882 |

**Notes**: Model 1 was adjusted for age and sex; Model 2 was adjusted for Model 1 plus other risk factors.
**Abbreviation**: MACCEs, major adverse cardiovascular and cerebrovascular events.

The study demonstrated a strong positive association between NPS levels and the risk of all-cause mortality. ($P$<0.001). In the unadjusted model (Model 1), each unit increase in NPS was associated with a 4.27-fold increase in the risk of all-cause mortality in CAD patients (OR=5.27, 95% CI=0.70–39.54, $P$<0.001). In the fully adjusted model (Model 2), patients in the high NPS group had an 82% higher risk of all-cause mortality compared to those in the low NPS group (OR=1.82, 95% CI=0.20–16.66, $P$<0.001). Although we controlled for multiple confounding factors through adjusted analyses, some of the adjusted odds ratios (aORs) exhibit wide 95% confidence intervals due to the limited sample size. This wide confidence interval is typically a result of the small number of death events (Table 2).

Additionally, there was a significant positive association between NPS levels and the risk of acute myocardial infarction (10.2% vs 25.4% vs 47.2%, $P$<0.001). After adjusting for confounding factors in Model 1, this association remained unchanged, indicating that a higher NPS was associated with an increased risk of AMI. Notably, even after controlling for all confounding factors in Model 2, the association remained statistically significant (OR=4.05, 95% CI=2.07–7.93, $P$<0.001) (Table 2).

Moreover, NPS levels were independently associated with the risk of stroke, with patients in the high NPS group having the highest risk of stroke, and there was a statistically significant difference between the groups (6.8% vs 9.3% vs 14.7%, $P$<0.001). After adjusting for confounders in Model 1, it was observed that a higher NPS was associated with an increased risk of stroke. Compared to the low NPS group, the moderate NPS group and high NPS group had a 82% (OR=1.82, 95% CI=0.71–2.47, $P$<0.05) and 84% (OR=1.84, 95% CI=0.99–3.41, $P$<0.05) higher risk of all-cause mortality, respectively. After full adjustment for confounders, multivariable logistic regression further confirmed this association. (OR=1.80, 95% CI=0.92–3.50, $P$<0.05) (Table 2).

It is worth noting that our study found no difference in the risk of atrial fibrillation and all-cause readmission among patients with coronary artery disease across the three different NPS levels. This conclusion was further confirmed after adjusting for confounding factors ($P$>0.05) (Table 2).

## Predictive Value Between NPS and Risk of All-Cause Mortality in Patients with CAD

ROC analysis was used to evaluate the predictive value of the NPS for all-cause mortality in CAD patients. The results demonstrated that NPS could independently predict the risk of all-cause mortality in these patients, with a moderate discriminative ability. The AUC was 0.739 (95% CI, 0.660–0.817, $P$<0.001) (Figure 3).

## Subgroup Analysis Between NPS and Risk of Adverse Outcomes in Patients with CAD

A subgroup analysis of high-risk patients for all-cause mortality indicated that statin use was associated with a 6% reduction in the risk of death compared to those not using statins. Furthermore, a left ventricular ejection fraction (LVEF) ≥59.74% was identified as a protective factor against all-cause mortality, whereas a blood glucose level ≥5.48 mmol/L was linked to an increased risk of mortality. Additionally, each extra day of hospitalization was associated with a 4% increase in the risk of all-cause mortality. Elevated serum creatinine levels (≥79 μmol/L) were also found to be a significant risk factor for all-cause mortality (Figure 4).

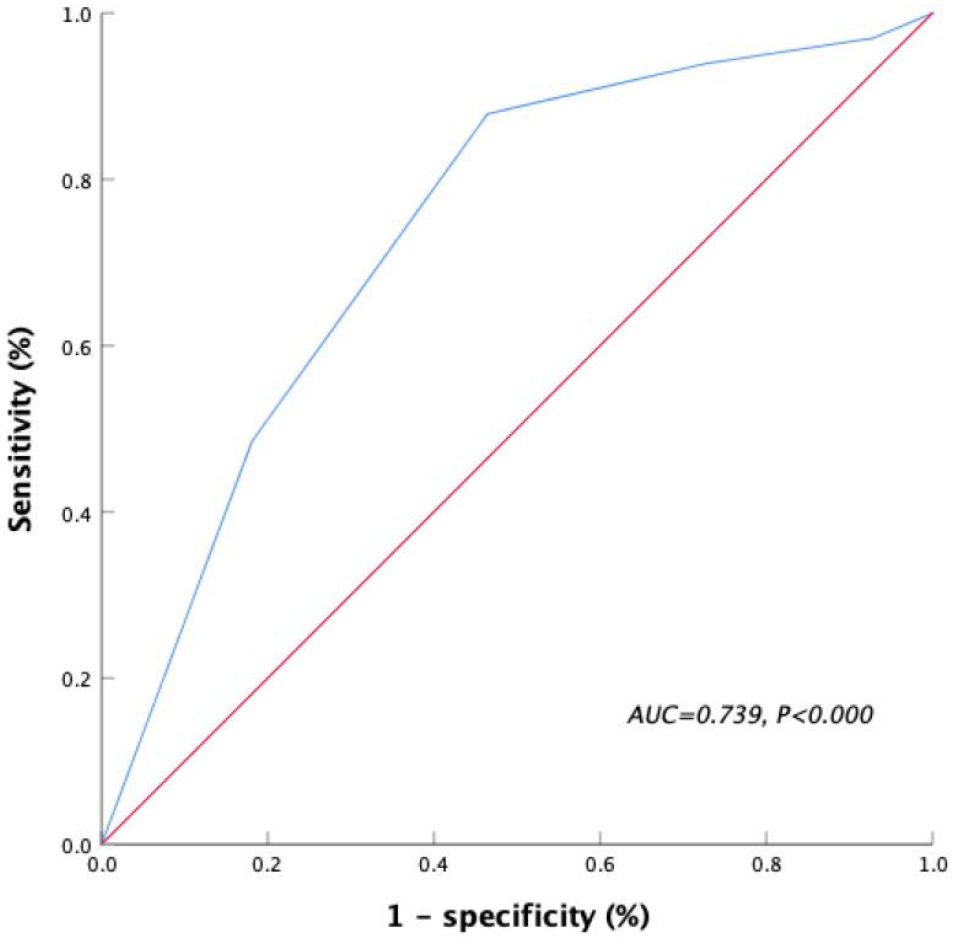


**Figure 3** Estimation of mortality by ROC curve of NPS.
**Abbreviations** AUC, area under the curve; NPS, Napoli prognostic score; ROC, receiver operating characteristic.

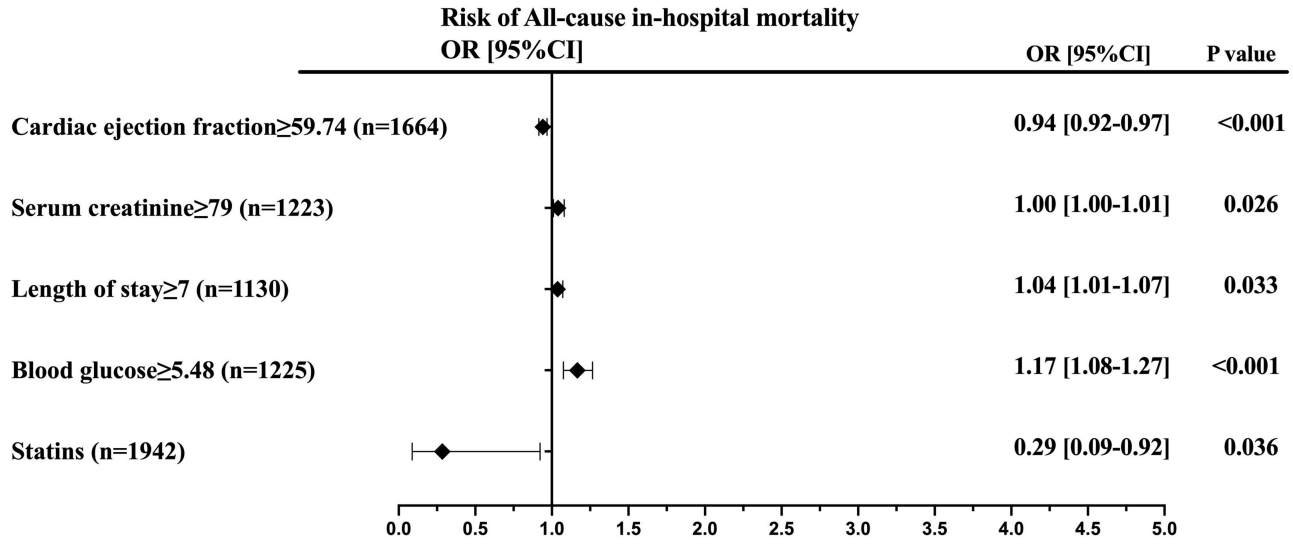


**Figure 4** Forest plot for the effects sizes of individual predictors of all-cause mortality risk in patients with coronary heart disease.

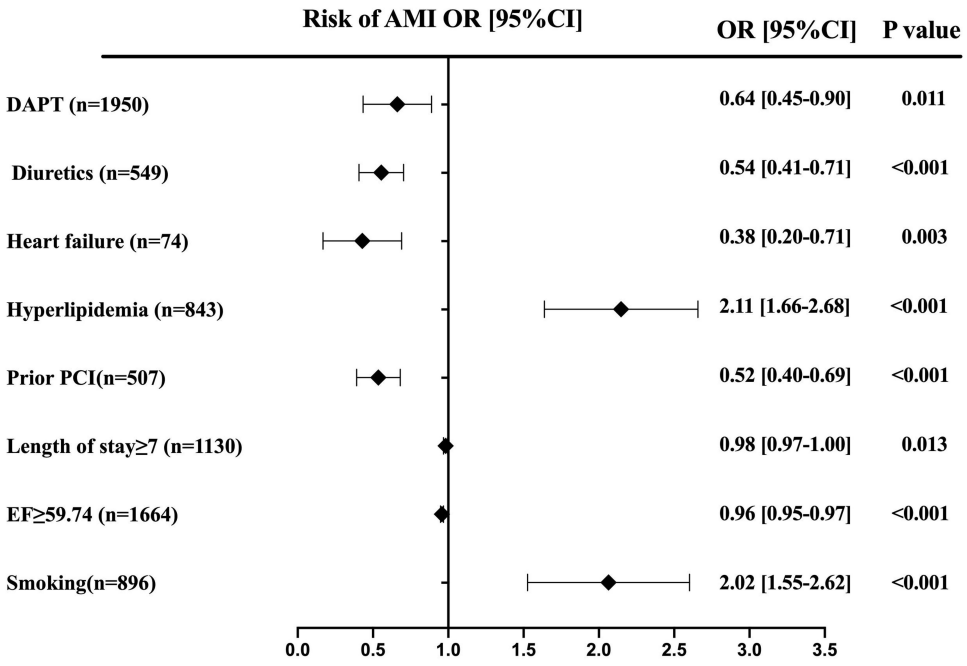


**Figure 5** Forest plot for the effects sizes of individual predictors of AMI risk in patients with coronary heart disease.
**Abbreviations**: AMI, acute myocardial infarction; DAPT, dual antiplatelet therapy; PCI, percutaneous coronary intervention; EF, ejection fraction.

In the stratified analysis by age, sex, smoking status, and history of hypertension, a significant association was observed between the NPS score and the risk of AMI in CAD patients. Smoking and hyperlipidemia were identified as risk factors for AMI, whereas the use of DAPT, diuretics, a history of chronic heart failure, prior PCI, hospital stays ≥7 days, and LVEF ≥59.74% were found to be protective factors (Figure 5).

Moreover, the association between NPS score and stroke risk remained consistent after subgroup analysis. The analysis of stroke risk factors revealed several key findings. Hyperlipidemia and prior PCI history were not significantly associated with stroke risk. In contrast, the use of CCBs was strongly associated with an increased risk of stroke, suggesting that CCBs may be a significant risk factor. Additionally, a LVEF ≥59.74% was modestly associated with an increased risk of stroke, while age ≥ 65 years showed a consistent, significant increase in stroke risk. These findings highlight the importance of age, LVEF, and CCB use in stroke risk assessment, with age over 65 and CCB use standing out as key risk factors. Further research is needed to explore the underlying mechanisms, particularly regarding CCB use and LVEF in stroke outcomes (Figure 6).

## Discussion

To our knowledge, this is the first large-scale study to assess the prognostic value of the novel NPS in patients with acute myocardial infarction. Based on 2,453 CAD cases, our findings suggest that NPS may serve as a practical tool for risk stratification and outcome prediction in this population.

The pathogenesis of CAD mainly involves atherosclerosis and coronary spasm, with atherosclerosis being the key driver.[29] Inflammation contributes to plaque formation and poor outcomes.[30] NLR and LMR are well-established inflammatory markers for prognosis, but single markers may be affected by confounders.[31,32] A combined approach offers better predictive value. Nutritional status also impacts CAD progression. Serum albumin (SA) and TC are linked to disease severity.[33,34] Low albumin reflects malnutrition and systemic inflammation and is associated with poor outcomes,[35,36] likely due to its anti-inflammatory, antioxidant, and antithrombotic properties.[37–41] Elevated TC has also been linked to increased CAD mortality.[34] Thus, both serum albumin and TC can serve as indicators of nutritional status in patients with CAD. It is worth noting that, although high TC, particularly LDL-C, is traditionally recognized as a risk factor for cardiovascular disease, decreased TC levels in certain patients may reflect malnutrition or an underlying


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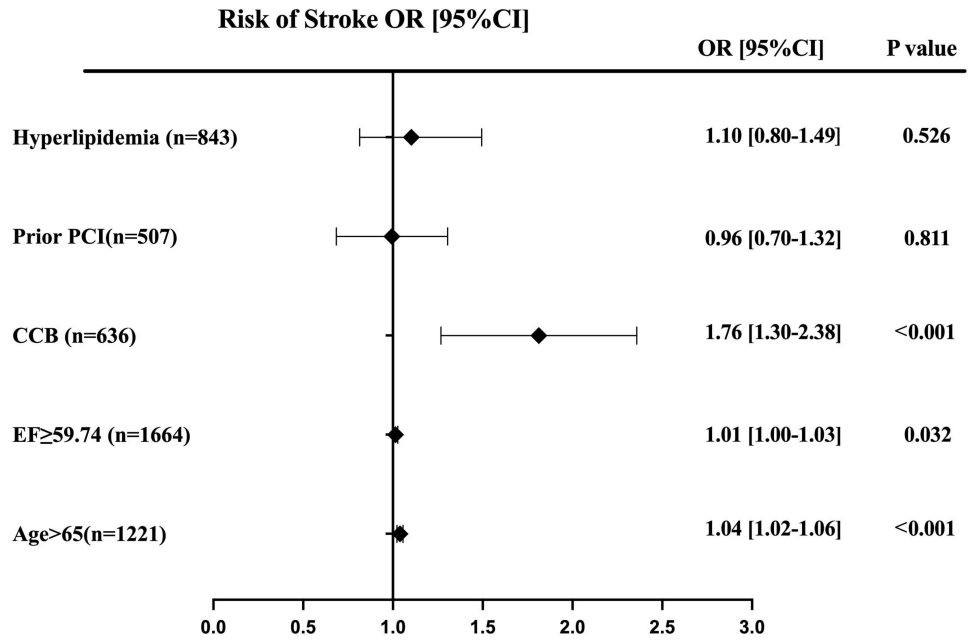


**Figure 6** Forest plot for the effects sizes of individual predictors of stroke risk in patients with coronary heart disease.
**Abbreviations**: PCI, percutaneous coronary intervention; CCB, Calcium Channel Blockers; EF, ejection fraction.

inflammatory state—both of which are associated with poor prognosis. This paradox is captured in the NPS, where lower TC is associated with higher risk. Recent studies employing modified NPS models, including those involving patients with coronary slow flow, support this interpretation and suggest that in the context of systemic illness, low TC may serve as a marker of vulnerability rather than protection.[18]

Our study shows that patients in moderate and high NPS groups face increased all-cause mortality risk compared to those in the low NPS group, aligning with previous findings.[42,43] This risk may reflect reduced SA and TC, elevated NLR, and decreased LMR—indicating systemic inflammation and poor nutrition. SA, a negative acute-phase reactant, declines during inflammation and is associated with markers like CRP and WBC.[44–46] TC also plays a complex role; while generally linked to higher mortality, paradoxically, hypercholesterolemia may lower short-term mortality after myocardial infarction.[47] NLR and LMR reflect multiple inflammatory cell types, offering better prognostic accuracy than individual markers.[48,49] Although each NPS component has been used to assess STEMI risk, combining them into a single, calculable score may improve short-term mortality prediction. Subgroup analysis further found statin use reduced mortality risk. Statins, as HMG-CoA reductase inhibitors, improve lipid control and plaque stability, contributing to CAD mortality reduction.[50,51] These findings emphasize the value of NPS and the need for closer surveillance of high-risk patients.

This study found that AMI incidence increases with higher NPS scores; each one-unit rise in NPS corresponds to a 3.05-fold increased AMI risk in CAD patients. AMI is closely linked to immune and inflammatory responses, with inflammation intensity associated with infarct size and adverse ventricular remodeling.[52,53] Malnutrition, common in CAD, is also linked to poor outcomes,[54] and low serum albumin reflects both poor nutrition and systemic inflammation in atherosclerosis.[55,56] Thus, NPS—a composite of inflammatory and nutritional markers—can be a useful indicator for AMI risk. Interestingly, subgroup analysis revealed that, contrary to conventional expectations, the presence of heart failure appeared to exert a protective effect against AMI. This finding may be partially attributed to the fact that patients with comorbid heart failure often receive more intensive monitoring and timely medical interventions during hospitalization, which could reduce the risk of AMI. In addition, the limited sample size and the heterogeneity of heart failure, including variations between acute and chronic conditions as well as differences in ejection fraction levels, may have influenced the observed outcomes. Further research is needed to investigate the potential mechanisms behind this association.

In our cohort of 2,453 CAD patients, elevated NPS levels were significantly associated with an increased risk of in-hospital stroke. Neuroinflammation plays a key role in stroke pathophysiology, where ischemic injury triggers neuronal

death and DAMPs release, activating immune responses and promoting inflammatory cell infiltration into the brain.[57–60] Peripheral immune cells, especially lymphocytes, may exert complex effects—some studies suggest neurotoxicity, while others report potential protective roles.[61,62] Nutritional status is also closely linked to stroke risk. Cholesterol fluctuations may destabilize atherosclerotic plaques, increasing stroke susceptibility.[63] Serum albumin, known for its antioxidant and anti-inflammatory properties, helps maintain vascular volume and reduce cerebral edema, contributing to better stroke outcomes.[64,65] Thus, NPS, integrating inflammatory and nutritional markers, may serve as a useful predictor for stroke in CAD patients. Subgroup analysis found short-acting CCB use to be a stroke risk factor. Literature suggests that such formulations can induce reflex sympathetic activation and BP variability, increasing the risk of plaque rupture and subsequent stroke events.[66] These findings merit further investigation into the mechanisms linking NPS and stroke risk.

Traditional CAD risk assessment relies on single indicators like blood pressure and cholesterol,[67] which may not fully capture a patient's overall condition. In contrast, the NPS—a composite score based on albumin, cholesterol, NLR, and LMR—offers a more holistic view of inflammatory and nutritional status, both of which are key drivers of CAD progression.[11,19] In clinical settings, NPS allows for more accurate risk stratification. High NPS scores identify patients at greater risk, prompting early intervention with anti-inflammatory therapy, nutritional support, and close monitoring. Conversely, patients with low scores may benefit from less intensive management. Beyond prognosis, NPS also informs treatment decisions, as elevated scores are linked to higher readmission and mortality rates. Incorporating NPS into routine assessment may improve outcomes by guiding personalized therapy focused on inflammation and nutrition.

Our study benefits from a large sample size and rigorous adjustment for confounders. As NPS is calculated from routine tests such as blood count, albumin, and cholesterol, it can be easily integrated into primary care workflows, supporting early detection and follow-up of CAD patients in community settings. Nonetheless, several limitations should be considered. First, the retrospective single-center design may introduce residual confounding, even after statistical adjustments. Second, the limited number of mortality events led to wide confidence intervals for some adjusted odds ratios, which may affect the precision of the estimates. Third, the study did not explore the relationship between NPS and other relevant biomarkers that could provide additional insights into underlying mechanisms. Fourth, although the NPS showed prognostic value, it was not directly compared with widely used risk stratification tools such as the GRACE or SYNTAX scores. This is a recognized limitation, and we are currently planning comparative validation studies. Finally, the NPS was assessed only at admission, which restricts interpretation regarding its changes over time and their clinical implications. Further prospective, multicenter research is needed to validate and extend these findings.

## Conclusion

The NPS serves as a comprehensive indicator for multidimensional assessments of nutritional and inflammatory status. This study highlights its potential as an easily accessible, cost-effective, and reliable prognostic tool for patients with CAD. These findings provide a valuable addition to existing prognostic indicators for CAD, enhancing risk stratification and improving integrated management strategies. Ultimately, the implementation of NPS may help prevent adverse outcomes in this patient population.

## Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request (Please contact Yanjuan Lin, fjxhyjl@163.com).

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. Yan Jiang and Yaqin Chen should be considered joint first authors.

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## Disclosure

No potential conflict of interest was reported by the author(s).

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