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# Prognostic Value of Four Objective Nutritional Indices in Predicting Long-Term Prognosis in Elderly Patients with Atrial Fibrillation: A Retrospective Cohort Study

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**Background:** Several objective and comprehensive nutritional assessment methods have been used for predicting adverse outcomes in elderly patients with various diseases. However, their predictive value for long-term adverse outcomes in elderly patients with atrial fibrillation (AF) is unclear. This study aimed to explore the prognostic significance of the four nutritional indices, namely Prognostic Nutritional Index (PNI), Geriatric Nutritional Risk Index (GNRI), Controlling Nutritional Status (CONUT), and High-Sensitivity Modified Glasgow Prognostic Score (HS-mGPS), in evaluating the long-term prognosis in elderly patients with AF.

**Methods:** This retrospective study was conducted at a single center and included a total of 261 elderly patients with AF from December 2015 to December 2021. Patients were divided into all-cause death and survival groups based on the follow-up results. Kaplan–Meier analysis and COX regression were conducted to explore the relationship between all-cause mortality and nutritional scores. In addition, Receiver Operating Characteristic (ROC) curves were used to compare the predictive value of the four nutritional screening tools for the endpoint event.

**Results:** During the follow-up period, 119 cases (45.59%) of all-cause mortality were recorded. The cumulative incidence of all-cause death was significantly higher in participants with a lower PNI, lower GNRI, higher CONUT, and higher HS-mGPS levels. And the low PNI (HR 1.325, 95% CI 1.032–2.857, P=0.025) and the high HS-mGPS (HR 2.166, 95% CI 1.281–4.326, P=0.023) groups were independently and significantly associated with increased risk of all-cause death analyzed by multivariate COX regression. Additionally, PNI showed the best area under the curve value (AUC: 0.696, 95% CI 0.632–0.760 P < 0.001) for the prediction of all-cause mortality compared with the other nutritional indices.

**Conclusion:** Among the four nutritional risk screening tools, PNI might be a simple and useful indicator in predicting the long-term prognosis of elderly patients with AF.

**Keywords:** atrial fibrillation, AF, aged, mortality, nutrition, prognosis

## Introduction

Atrial fibrillation (AF) is one of the most prevalent cardiac rhythm disorders, associated with an elevated risk of stroke, heart failure, and mortality.[1] A recent epidemiological survey indicated that the incidence of AF increased rapidly and estimated that at least 12.1 million people would have AF in the United States by 2030.[2] Despite the significant progress in antiarrhythmic drugs, ablation procedures, and stroke-prevention strategies, AF remains an important cause of death and disability in middle-aged and elderly individuals by increasing the risk of heart failure, stroke, myocardial infarction, and so on.[3] According to the Global Burden of Disease data (GBD), 287,241 deaths were attributed to AF globally in

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2017.[4] Therefore, AF is a significant burden for cardiovascular health worldwide. It is important to identify and avoid risk factors to reduce complications and mortality in elderly patients with AF.

A significant proportion of hospitalized elderly patients experience malnutrition, which significantly increases the risk of adverse clinical events.[5,6] Recent studies have demonstrated that malnutrition is strongly correlated with an increased incidence of AF, poor prognosis, and higher risks after surgery, particularly in the elderly population.[7–9] In the development of malnutrition, increased levels of many cytokines and interleukins involved in inflammation have been found, which could accelerate inflammatory processes in AF and cause chaotic contraction.[9,10] Therefore, nutritional assessment methods might be useful to identify and screen for poor nutritional status in elderly patients with AF. And it could also stratify the risks for elderly patients with AF, and thus prevent adverse outcomes, as well as improve long-term prognosis.

Although many tools are available for nutritional risk screening, there is no gold standard at present. The application of some nutritional assessment tools such as the Mini Nutritional Assessment (MNA) and Subjective Global Assessment (SGA) is restricted due to low sensitivity and specificity.[5] Therefore, novel nutritional scores have been developed to integrate objectively measurable parameters including albumin, lymphocyte count, body weight, total cholesterol, and additional variables for a comprehensive and objective assessment. Currently, four objective nutritional scores have been widely used in previous studies to evaluate the prognosis of patients with several diseases. These scores include the Prognostic Nutritional Index (PNI), Geriatric Nutritional Risk Index (GNRI), Controlling Nutritional Status (CONUT), and High-Sensitivity Modified Glasgow Prognostic Score (HS-mGPS). Recent clinical data indicated that PNI, GNRI, CONUT, and HS-mGPS scores were widely used in nutritional assessments for various clinical conditions, including cancer, heart failure, and myocardial infarction.[11–15] However, the correlation between nutritional status and long-term prognosis in elderly patients with AF is largely unknown. Consequently, our study aimed to evaluate the value of these novel nutritional indices in predicting the long-term prognosis of elderly AF patients and explored the most suitable nutritional screening tool, allowing for providing clinicians with a reference for early clinical decision-making and intervention.

# Materials and Methods

## Study Population

This retrospective study consecutively included 857 patients with AF hospitalized in the Cardiovascular Department of the Air Force Medical Center from December 2015 to December 2021. The survival status of participants was followed up to December 31, 2023. Inclusion criteria: (1) AF can be diagnosed on a standard 12-lead electrocardiogram or a single-lead electrocardiogram of ≥30 seconds with no obvious repetitive P waves and irregular R-R intervals, following the 2020 European Society of Cardiology (ESC) criteria;[16] (2) Age ≥65 years. Exclusion criteria: (1) Severe infections, severe anemia, significant hemorrhage, malignant tumors, hematological diseases, and other non-cardiac diseases that lead to poor prognosis; (2) Valve structure abnormalities or damage diagnosed by ultrasound upon admission, leading to poor prognosis of cardiac diseases; (3) Loss to follow-up or accidental death; (4) Incomplete medical record data. According to the inclusion and exclusion criteria, a total of 261 elderly patients with AF were ultimately enrolled (specific screening process see Figure 1), including 176 males and 85 females, aged 65–100 years. This retrospective study was conducted in accordance with the Declaration of Helsinki and relevant guidelines/regulations. It was approved by the Ethics Review Board of the Air Force Medical Center of the Chinese People's Liberation Army (2023–034-PJ01). The Institutional Review Board of the Air Force Medical Center granted a waiver of informed consent due to the fully de-identification of data without any patient identifiers and the retrospective nature of the study.

## Data Collection and Endpoint Definitions

Data was collected by trained physicians from the electronic medical record system, including: (1) Basic clinical characteristics: age, gender, height, weight, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse, CHA2DS2-VASc score, where BMI is defined as weight (kg) / [height $(m)^2$]; (2) Past medical history: hypertension, diabetes, chronic kidney disease (CKD), stroke, hyperuricemia, hyperlipidemia; (3) Laboratory

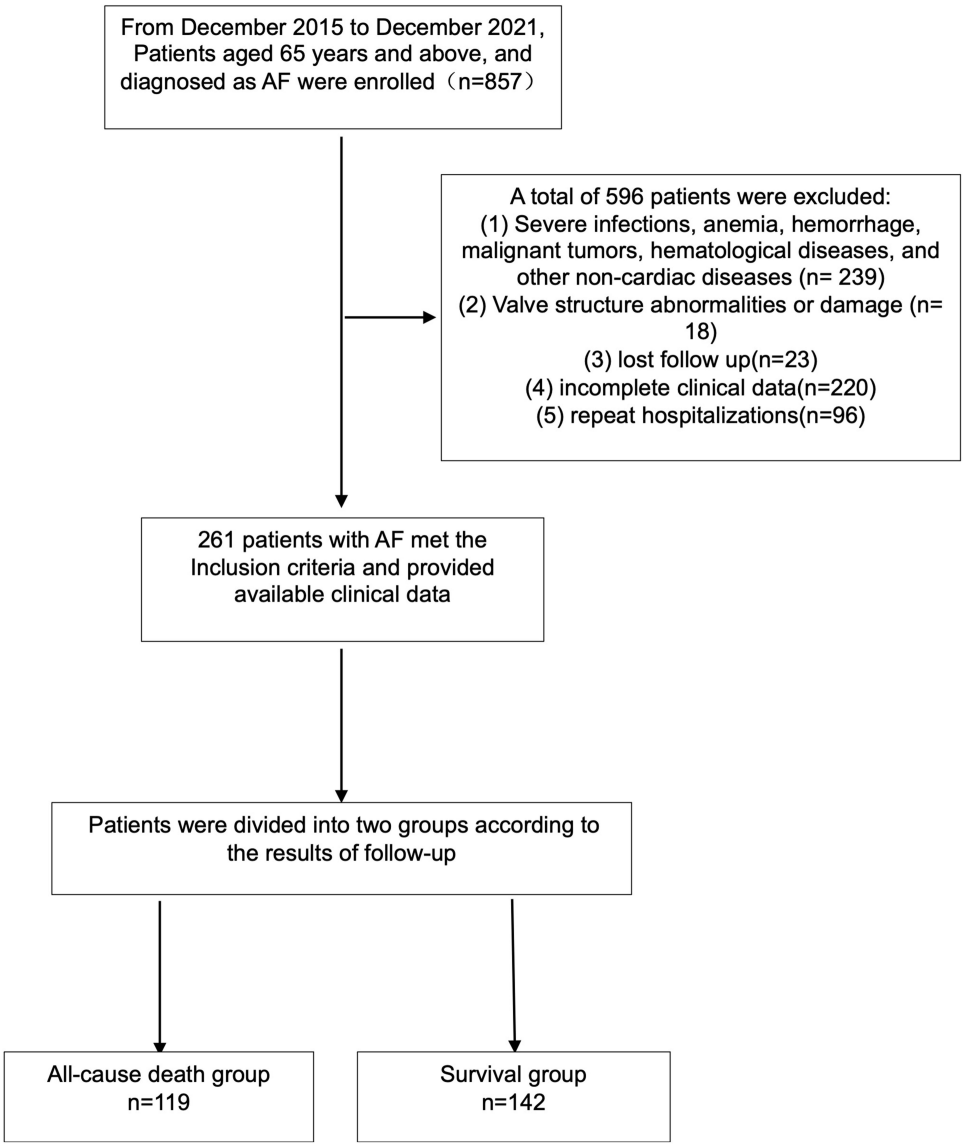


**Figure 1** Flowchart indicating patients in this study.

tests and ultrasound examinations within 24 hours of admission: triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), B-type natriuretic peptide (BNP), lymphocyte count (LYM), white blood cell count (WBC), neutrophil count, monocyte count, C-reactive protein (CRP), hemoglobin, platelet count, blood creatinine, serum albumin (ALB), fasting blood glucose (FPG), sodium (Na), potassium (K), left ventricular ejection fraction (LVEF); these tests were performed on fasting overnight (>8h) peripheral venous blood; (4) Medication use: beta-blockers, calcium channel blockers (CCB), digoxin, statins, antiplatelet drugs, anticoagulants; (5) Objective nutritional indicators: PNI, GNRI, CONUT, and HS-mGPS, all of which were calculated using their respective formulas or scoring standards.

The first day of admission was taken as the starting time point for follow-ups, and the survival status of participants was followed up to December 31, 2023. The study obtained clinical outcomes primarily through telephone follow-up or patient medical record reports. This included monitoring for the occurrence of main outcome events and noting the time of their occurrence. All-cause mortality was defined as death from any cause. The primary outcome event under observation was all-cause death. Overall survival was expressed in months and defined as the time from the date of admission until death or censored if alive at follow-up analysis (31 December 2023).

## Definitions and Subgroups of PNI, GNRI, CONUT and HS-mGPS

The four nutritional status assessment tools, including PNI, GNRI, CONUT, and HS-mGPS, are composite indices based on ALB, LYM, TC, body weight, CRP, and height.

1. PNI is calculated based on ALB and LYM count: PNI = ALB (g/L) + 5 × LYM ($10^9$/L); PNI nutritional assessment values are divided into tertiles: low group (PNI < 41.85), median group (41.85 ≤ PNI < 51.40), and high group (PNI ≥ 51.40).
2. GNRI is calculated using height, body weight, ideal body weight, and ALB: GNRI = (1.489) × ALB (g/L) + 41.7 × (weight / ideal weight); tertiles are determined for grouping: low group (GNRI < 90.45), median group (90.45 ≤ GNRI < 102.01), and high group (GNRI ≥ 102.01). The ideal body weight for males is calculated as (height [cm] - 100 - [height [cm] - 150] / 4), and for females as (height [cm] - 100 - [height [cm] - 150] / 2). When the actual weight is greater than the ideal weight, the ratio of weight to ideal weight is set to 1.
3. The CONUT score is calculated by the sum of the scores derived from ALB, TC, and LYM count: For ALB ≥ 3.5 g/dL, 3.0–3.49 g/dL, 2.5–2.99 g/dL, and < 2.5 g/dL, scores of 0, 2, 4, and 6 are assigned, respectively. For TC ≥ 180 mg/dL, 140–179 mg/dL, 100–139 mg/dL, and < 100 mg/dL, scores of 0, 1, 2, and 3 are assigned, respectively. For LYM count ($10^9$/L) ≥ 1.6, 1.2–1.59, 0.8–1.19, and < 0.8, scores of 0, 1, 2, and 3 are assigned, respectively. CONUT nutritional scores are grouped into tertiles: low group (CONUT ≤ 2), median group (2 < CONUT ≤ 4), and high group (CONUT > 4).
4. The HS-mGPS score is an inflammation-nutrition index based on CRP and ALB scores: HS-mGPS is calculated as 0 (CRP ≤ 3 mg/L and ALB ≥ 3.5 g/dL), 1 (CRP > 3 mg/L and ALB ≥ 3.5 g/dL, or CRP ≤ 3 mg/L and ALB < 3.5 g/dL), or 2 (CRP > 3 mg/L and ALB < 3.5 g/dL). HS-mGPS nutritional scores are grouped as: low group (HS-mGPS= 0), median group (HS-mGPS= 1), and high group (HS-mGPS= 2).

## Statistical Analysis

Continuous variables with a normal distribution were expressed as the mean ± standard deviation and compared between groups using independent samples *t*-test. Non-normally distributed variables were expressed as median (25th quartile, 75th quartile), and compared between groups using the Mann–Whitney *U*-test. Categorical variables are represented as frequencies and percentages, which are compared using the chi-square test or Fisher's exact test.

Kaplan–Meier survival curves were used to determine the differences in the cumulative rates of all-cause mortality and the survival data was compared using the Log rank test among four risk-stratified groups.

Univariate and multivariate COX regression were used to analyze the impact of PNI, GNRI, CONUT, and HS-mGPS scores on long-term prognosis. The model 1 solely included the nutritional index without any further adjustments. In Model 2, adjustments were made for medication use, laboratory tests and comorbidities such as hyperlipidemia, CKD, and antiplatelet drugs. Model 3 incorporated further adjustments for some relevant laboratory variables. Additionally, a correlation matrix was generated for these variables, and a multicollinearity analysis was performed to exclude variables with variance inflation factor (VIF) >10 or tolerances < 0.1.

To assess the predictive efficacy of PNI, GNRI, CONUT, and HS-mGPS scores on all-cause mortality in elderly patients with AF, receiver operating characteristic (ROC) curve analyses were performed to compare these four nutritional indexes. The differences in the area under the curve (AUC) between the two ROC curves were analyzed using the DeLong test.

All tests were two-sided, and P < 0.05 was regarded as statistically significant. All statistical analyses were performed using R (version 4.2.3), GraphPad Prism (version 9.5.1), and SPSS (version 26.0) software.

# Results

## Baseline Characteristics

A total of 857 patients were screened and 261 patients met the entry criteria and were enrolled in the study for final analysis, 119 patients died for various reasons, and 142 survived as shown in Figure 1. These patients were categorized based on follow-up outcomes as either all-cause mortality or survival. Patient characteristics are shown in Table 1. The

**Table 1** Baseline Characteristics of Different Groups

| Variables | Total (n=261) | All-Cause Mortality Group (n=119) | Survival Group (n=142) | P-value |
|---|---|---|---|---|
| **Basic clinical characteristics** | | | | |
| Age (years) | 83.02±7.85 | 83.08±8.00 | 82.98±7.75 | 0.921 |
| Gender (male%) | 176(67.43) | 82(68.91) | 94(66.20) | 0.642 |
| Height (cm) | 165.62±8.24 | 166.08±8.37 | 165.23±8.14 | 0.407 |
| Weight (kg) | 65.90±11.86 | 66.25±12.03 | 65.61±11.74 | 0.666 |
| BMI ($kg/m^2$) | 23.97±3.61 | 23.96±3.71 | 23.98±3.54 | 0.981 |
| SBP (mmHg) | 139.26±22.05 | 137.07±22.16 | 141.09±21.86 | 0.142 |
| DBP (mmHg) | 73.17±12.72 | 71.78±12.59 | 74.34±12.77 | 0.106 |
| Pulse (beats/min) | 75.00(68.00, 86.00) | 74.00(65.00, 86.00) | 75.7(68.00, 86.25) | 0.295 |
| LVEF (%) | 56.00(54.00, 58.00) | 57.00(54.00, 58.00) | 57.00(54.00, 59.00) | 0.007 |
| $CHA_2DS_2$-VASc score | 4.00(4.00, 5.00) | 4.00(4.00, 5.00) | 4.00(4.00, 5.00) | 0.738 |
| **Past medical history** (%) | | | | |
| Hypertension | 213(81.60) | 97(81.51) | 116(81.69) | 0.971 |
| Diabetes | 80(30.65) | 39(32.77) | 41(28.87) | 0.496 |
| CKD | 66(25.29) | 42(35.29) | 24(16.90) | 0.001 |
| Stroke | 47(18.01) | 19(15.97) | 28(19.72) | 0.432 |
| Hyperuricemia | 29(11.11) | 17(14.29) | 12(8.45) | 0.135 |
| Hyperlipidemia | 99(37.93) | 37(31.09) | 62(43.66) | 0.037 |
| **Laboratory tests results** | | | | |
| TG (mmol/L) | 1.13(0.87, 1.52) | 1.12(0.80, 1.48) | 1.14(0.88, 1.58) | 0.489 |
| TC (mmol/L) | 3.78(3.15, 4.42) | 3.90(2.41, 5.39) | 3.73(2.51, 4.95) | 0.100 |
| LDL-C (mmol/L) | 2.09(1.64, 2.67) | 2.25(1.71, 2.80) | 2.02(1.59, 2.57) | 0.093 |
| HDL-C (mmol/L) | 1.06(0.90, 1.29) | 1.05(0.87, 1.30) | 1.06(0.91, 1.29) | 0.750 |
| BNP (pg/Ml) | 220.80(102.65, 454.35) | 294.00(129.10, 771.20) | 193.95(90.93, 333.55) | < 0.001 |
| LYM ($\times 10^9$ /L) | 1.20(0.90, 1.67) | 1.10(0.80, 1.50) | 1.38(0.90, 1.81) | 0.001 |
| WBC ($\times 10^9$ /L) | 6.90±2.72 | 6.94±2.59 | 6.86±2.84 | 0.810 |
| Neutrophil count ($\times 10^9$ /L) | 4.25(3.30, 5.74) | 4.11(3.30, 5.60) | 4.45(3.30, 6.07) | 0.257 |
| Monocyte count ($\times 10^9$ /L) | 0.46(0.35, 0.60) | 0.46(0.33, 0.60) | 0.47(0.33, 0.60) | 0.656 |
| CRP (mg/L) | 8.00(3.00, 20.30) | 17.00(6.92, 38.00) | 4.94(2.58, 9.00) | < 0.001 |
| Hemoglobin (g/L) | 116.95±21.39 | 110.24±22.41 | 122.57±18.80 | < 0.001 |
| Platelet count ($\times 10^9$ /L) | 180.20±62.90 | 179.21±67.51 | 181.03±58.98 | 0.817 |
| Blood creatinine (μmol/L) | 93.00(72.00, 129.50) | 106.00(79.00, 173.00) | 83.00(64.00, 112.5) | < 0.001 |
| ALB (g/L) | 39.70±3.84 | 38.52±3.96 | 40.68±3.46 | < 0.001 |
| FPG (mmol/L) | 5.80(5.00, 7.30) | 5.80(5.00, 7.50) | 5.80(5.00, 7.10) | 0.491 |
| Na (mmol/L) | 139.00(137.00, 141.00) | 139.00(136.00, 141.00) | 139.20(137.00, 142.00) | 0.023 |
| K (mmol/L) | 4.10(3.80, 4.40) | 4.20(3.80, 4.60) | 4.10(3.80, 4.30) | 0.013 |
| **Medication use (%)** | | | | |
| Beta-blockers | 143(54.79) | 59(49.58) | 84(59.15) | 0.122 |
| CCB | 121(46.36) | 53(44.54) | 68(47.88) | 0.589 |
| Digoxin | 31(11.88) | 13(10.92) | 18(12.68) | 0.663 |
| Statins | 166(63.60) | 57(47.90) | 109(76.76) | < 0.001 |
| Antiplatelet drugs | 141(54.02) | 54(45.38) | 87(61.27) | 0.010 |
| Anticoagulants | 51(19.547) | 17(14.29) | 34(23.94) | 0.050 |
| **Nutritional indicators** | | | | |
| PNI | 46.25±5.08 | 44.39±4.67 | 47.81±4.90 | < 0.001 |
| GNRI | 99.88±6.43 | 98.24±6.61 | 101.25±5.95 | < 0.001 |
| CONUT | 3.00(2.00, 4.00) | 3.00(2.00, 4.00) | 3.00(2.00, 4.00) | 0.006 |
| Hs-mGPS | 1.00(0.95, 1.00) | 1.00(1.00, 1.00) | 1.00(0.00, 1.00) | < 0.001 |

**Notes**: Values are given as median and interquartile range or numbers and percentages.

**Abbreviations**: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; CKD, chronic kidney disease; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; BNP, B-type natriuretic peptide; LYM, lymphocyte conut; WBC, white blood cell conut; CRP, C-reactive protein; ALB, serum albumin; FPG, fasting blood glucose; Na, sodium; K, potassium; CCB, calcium channel blockers; PNI, the prognostic nutritional index; GNRI, geriatric nutritional risk index; CONUT, controlling nutritional status; HS-mGPS, high-sensitivity modified Glasgow prognostic.

average age of the study population was 83.02±7.85 years, including 176 male patients (67.43%). Compared with the survival group, the prevalence of CKD and hyperlipidemia was higher in the all-cause mortality group. Additionally, this group showed increased levels of BNP, CRP, blood creatinine, sodium, potassium, CONUT, and HS-mGPS scores, but decreased levels of LYM, hemoglobin, ALB, LVEF, PNI, and GNRI, and lower usage rates of antiplatelet drugs and statins, with statistically significant differences. Other variable indicators were compared between the two groups, and no significant differences were detected.

## Comparison of Groups with Different Outcomes and Subgroups with Different Nutritional Indicator Levels

During a median follow-up period of 41.00 months [interquartile range (IQR): 22.50–62.00], a total of 119 cases (45.59%) of all-cause mortality were recorded. The comparison of all-cause mortality among the four nutritional assessment tools is shown in Figures 2 and 3.

The participants were stratified according to the nutritional values tertiles as follows: the low-value group, the middle-value group, and the high-value group. As shown in Figure 2, the median group showed the highest proportion of all-cause mortality due to the largest number of people. According to the result, 61.3% of the all-cause mortality was in the median PNI group, 56.3% was in the median GNRI group, 47.1% was in the median CONUT group, and 71.4% was in the median HS-mGPS group. Notably, the all-cause mortality rate was significantly higher in the low PNI and GNRI

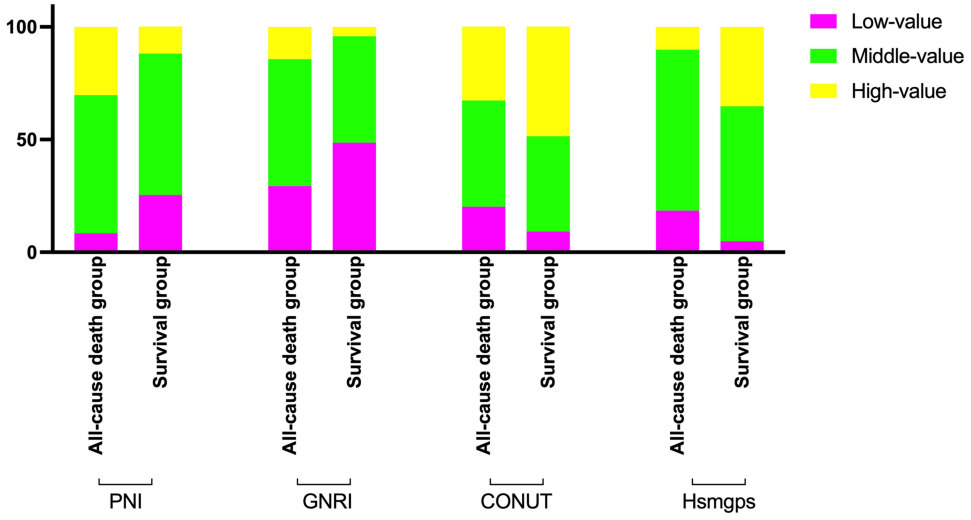


**Figure 2** The proportion of the low value, middle value and high value tertiles of four objective nutritional indices in all-cause death and survival groups.
**Abbreviations**: PNI, Prognostic Nutritional Index; GNRI, Geriatric Nutritional Risk Index; CONUT, Controlled Nutrition Score; HS-mGPS, High-Sensitivity Modified Glasgow Prognostic Score.

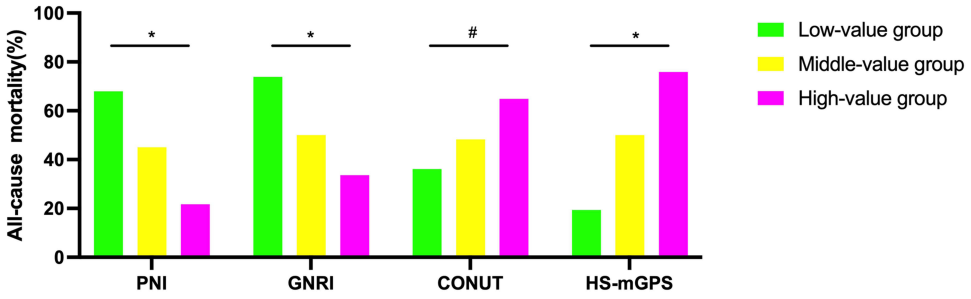


**Figure 3** Comparison of the low value, middle value and high value tertiles of all-cause mortality among patients in different nutritional index groups.
**Notes**: A hash symbol (#) indicates a significance level of $p < 0.05$. An asterisk (*) denotes a significance level of $p < 0.001$ in the comparison among three groups.
**Abbreviations**: PNI, Prognostic Nutritional Index; GNRI, Geriatric Nutritional Risk Index; CONUT, Controlled Nutrition Score; HS-mGPS, High-Sensitivity Modified Glasgow Prognostic Score.

groups compared to the median and high groups. On the contrary, the all-cause mortality rate was significantly higher in the high CONUT and HS-mGPS groups as shown in Figure 3.

## Association Between Four Nutritional Scores and All-Cause Mortality

The Kaplan-Meier curves in Figure 4 revealed the incidence of all-cause death among different groups. Overall, the cumulative incidence of all-cause mortality was significantly higher in patients with a lower PNI and GNRI or higher COUNT and HS-mGPS scores. In addition, PNI showed better performance on grading and risk assessment than other nutritional scores.

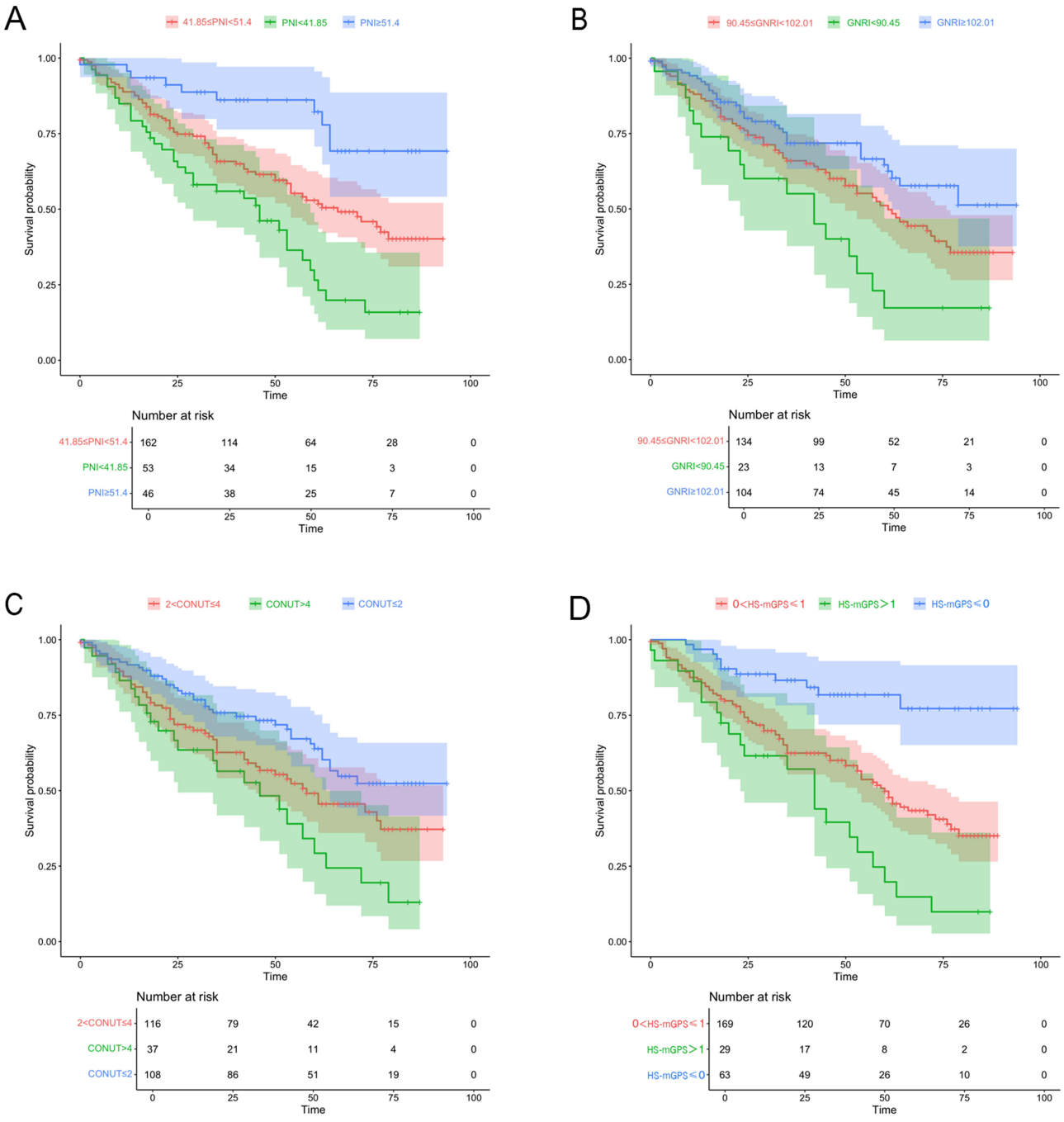


**Figure 4** Kaplan-Meier survival curve analysis of all-cause mortality based on four nutritional scores (**A**): PNI; (**B**) GNRI; (**C**) CONUT; (**D**) HS-mGPS. Time: months.
**Abbreviations**: PNI, Prognostic Nutritional Index; GNRI, Geriatric Nutritional Risk Index; CONUT, Controlled Nutrition Score; HS-mGPS, High-Sensitivity Modified Glasgow Prognostic Score.

## Univariate and Multivariate COX Proportional Hazards Models for All-Cause Mortality

According to the nutritional indices calculated by each equation as the categorical variable grouped previously mentioned, we performed the Cox proportional hazard models to analyze the four nutritional scores with all-cause mortality as shown in Table 2. In the univariate COX regression analysis (model 1), participants with the low GNRI group (HR 2.684, 95% CI 1.502–4.796, P=0.001) and the low PNI group (HR 3.548, 95% CI 2.251–7.189, P < 0.001), the median PNI group (HR 2.549, 95% CI 1.315–4.940, P=0.006), the median GNRI group (HR 1.517, 95% CI 1.008–2.285, P=0.046) and the median HS-mGPS group (HR 2.363, 95% CI 1.362–4.100, P=0.002), and the high CONUT group (HR 2.402, 95% CI 1.443–4.001, P=0.021) and the high HS-mGPS group (HR 3.094, 95% CI 2.133–6.855, P < 0.001) had increased risks of all-cause death. Model 2 adjusted for LVEF, CKD, hyperlipidemia, BNP, hemoglobin, blood creatinine, blood sodium, blood potassium, statin drugs, and antiplatelet drugs. Model 3 adjusted for LVEF, CKD, hyperlipidemia, BNP, hemoglobin, blood creatinine, blood sodium, blood potassium, statin drugs, antiplatelet drugs, and LYM, ALB, and CRP. For Model 2 and 3, the low PNI group (Model 2 hR 1.752, 95% CI 1.296–3.978, P=0.012; Model 3 hR 1.325, 95% CI 1.032–2.857, P=0.025) was associated with increased risk for all-cause mortality. And for HS-mGPS, the highest score was also found associated with increased all-cause mortality in Model 2 and 3. The low GNRI group (HR 1.627, 95% CI 1.125–3.761, P= 0.023) was significantly independently associated with all-cause mortality in Model 2. However, after adjustment for major confounders in model 3, there was no statistically significant difference.

## Comparative Analysis of the Predictive Value of the Four Objective Nutritional Indices

We conducted ROC curve analysis and Delong's test to compare the discrimination capacity of the four nutritional indices including PNI, GNRI, CONUT, and HS-mGPS in predicting all-cause mortality among elderly patients with AF (Figure 5; Table 3). In terms of the AUC for all-cause mortality, PNI demonstrated a higher AUC than both GNRI (P= 0.010) and CONUT (P < 0.001), showing a statistically significant difference. Although PNI exhibited a greater AUC for

**Table 2** Univariate and Multivariate COX Regression Analysis of All-Cause Mortality in Elderly Patients with AF

| Nutritional Score | Model 1 | | Model 2 | | Model 3 | |
|---|---|---|---|---|---|---|
| | HR (95% CI) | P | HR (95% CI) | P | HR (95% CI) | P |
| **PNI** | | | | | | |
| PNI<41.85 | 3.548(2.251, 7.189) | <0.001 | 1.752(1.296, 3.978) | 0.012 | 1.325(1.032, 2.857) | 0.025 |
| 41.85≤PNI<51.4 | 2.549(1.315, 4.940) | 0.006 | 1.182(0.897, 3.286) | 0.138 | 1.023(0.762, 2.328) | 0.256 |
| PNI≥51.4 | Ref | | Ref | | Ref | |
| **GNRI** | | | | | | |
| GNRI<90.45 | 2.684(1.502, 4.796) | 0.001 | 1.627(1.125, 3.761) | 0.023 | 1.013(0.895, 2.263) | 0.062 |
| 90.45≤GNRI<102.01 | 1.517(1.008, 2.285) | 0.046 | 1.007(0.609, 1.667) | 0.187 | 0.846(0.431, 1.663) | 0.228 |
| GNRI≥102.01 | Ref | | Ref | | Ref | |
| **CONUT** | | | | | | |
| CONUT≤2 | Ref | | Ref | | Ref | |
| 2<CONUT≤4 | 1.571(1.043, 2.365) | 0.051 | 0.667(0.328, 1.857) | 0.614 | 0.609(0.266, 1.393) | 0.630 |
| CONUT>4 | 2.402(1.443, 4.001) | 0.021 | 1.132(0.700, 1.832) | 0.264 | 1.139(0.672, 1.930) | 0.240 |
| **HS-mGPS** | | | | | | |
| HS-mGPS≤0 | Ref | | Ref | | Ref | |
| 0<HS-mGPS≤1 | 2.363(1.362, 4.100) | 0.002 | 2.043(1.087, 3.840) | 0.067 | 1.399(1.050, 2.805) | 0.095 |
| HS-mGPS>1 | 3.094(2.133, 6.855) | <0.001 | 2.576(1.477, 5.150) | 0.015 | 2.166(1.281, 4.326) | 0.023 |

**Notes**: Model 1 performed the univariate Cox regression analysis. Model 2 adjusted for LVEF, CKD, hyperlipidemia, BNP, hemoglobin, blood creatinine, blood sodium, blood potassium, statin drugs, and antiplatelet drugs. Model 3 adjusted for LVEF, CKD, hyperlipidemia, BNP, hemoglobin, blood creatinine, blood sodium, blood potassium, statin drugs, antiplatelet drugs, and LYM, ALB, and CRP. And the test indicates a statistically significant difference with p < 0.05.

**Abbreviations**: PNI, Prognostic Nutritional Index; GNRI, Geriatric Nutritional Risk Index; CONUT, Controlled Nutrition Score; HS-mGPS, High-Sensitivity Modified Glasgow Prognostic Score; CKD, chronic kidney disease; BNP, B-type natriuretic peptide; LYM, lymphocyte conut; ALB, serum albumin; CRP, C-reactive protein.

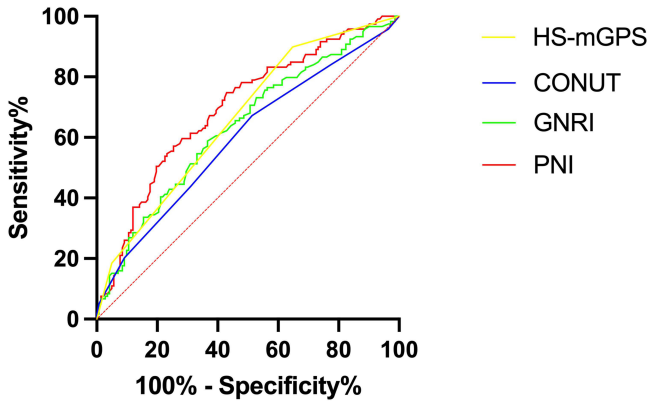


**Figure 5** Comparison of the ROC curves of four nutritional scores in predicting the long-term prognosis of AF in older adults.
**Abbreviations**: ROC, receiver operating characteristic; PNI, Prognostic Nutritional Index; GNRI, Geriatric Nutritional Risk Index; CONUT, Controlled Nutrition Score; HS-mGPS, High-Sensitivity Modified Glasgow Prognostic Score.

all-cause death than HS-mGPS, there was no statistically significant difference, as shown in Table 3 and Figure 5. Additionally, positive predictive value (PPV) of PNI: 0.730 was superior to GNRI, CONUT, and HS-mGPS, while negative predictive value (NPV) of HS-mGPS: 0.806 was better than GNRI, CONUT and PNI.

## Discussion

The present research was a single-center retrospective cohort study performed on elderly patients with AF. In this study, we first investigated the association between the four nutritional screening tools, including PNI, GNRI, CONUT, and HS-mGPS, and the occurrence of long-term all-cause mortality in elderly patients with AF. We then investigated which nutritional assessment indices were the independent predictive factor for long-term survival in elderly patients with AF. As a result, we demonstrate, for the first time, that PNI and Hs-mGPS were reliable and independent prognostic factors for elderly patients with AF. However, malnutrition assessments based on the CONUT score were not associated with increased risk for long-term all-cause mortality. Among the four nutritional indices, the AUC of PNI and HS-mGPS were significantly higher than CONUT and GNRI. From the AUC and PPV, PNI showed the greatest predictive value for long-term all-cause mortality in elderly patients with AF. From the AUC and NPV, it was found that Hs-mGPS predicted the survival rates better.

The mortality of AF is increasing year by year because of its complex risk factors and pathophysiologic mechanisms. Age is an important independent risk factor for AF, and the incidence of AF increases with age.[17] In addition, populations around the world are rapidly aging.[18] Previous studies have revealed the relationship between malnutrition and AF development.[9] The negative impact of malnutrition on the occurrence and development of AF could be attributed to cardiac cachexia, which activates proinflammatory cytokines, such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6).[19] These proinflammatory cytokines could contribute to increased oxidative stress and further accelerate morbidity

**Table 3** Comparison of the ROC Curves of the Four Nutritional Scores in Predicting All-Cause Mortality in Elderly Patients with AF

| Variation | AUC | 95% CI | Sensitivities | Specific | PPV | NPV | P-value | Vs PNI | Vs GNRI | Vs CONUT | vs HS-mGPS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| PNI | 0.696 | 0.632–0.760 | 0.570 | 0.748 | 0.730 | 0.593 | <0.001 | Ref | 0.010 | <0.001 | 0.365 |
| GNRI | 0.635 | 0.567–0.703 | 0.634 | 0.558 | 0.647 | 0.574 | <0.001 | 0.010 | Ref | 0.350 | 0.434 |
| CONUT | 0.596 | 0.528–0.665 | 0.672 | 0.486 | 0.523 | 0.639 | 0.003 | <0.001 | 0.350 | Ref | 0.072 |
| HS-mGPS | 0.663 | 0.610–0.717 | 0.899 | 0.352 | 0.538 | 0.806 | <0.001 | 0.365 | 0.434 | 0.072 | Ref |

**Notes**: The text indicates a statistically significant difference with a *p*-value less than 0.05.
**Abbreviations**: ROC, receiver operating characteristic; PNI, Prognostic Nutritional Index; GNRI, Geriatric Nutritional Risk Index; CONUT, Controlled Nutrition Score; HS-mGPS, High-Sensitivity Modified Glasgow Prognostic Score; PPV, Positive Predictive Value; NPV, Negative Predictive Value.

and mortality in AF.[20] Simultaneously, malnutrition could also cause neurohormonal dysfunction and a weakened protective effect of adipokines stemming from a reduced fat mass, which is associated with adverse events of AF.[8] Various studies have shown that malnutrition is a common and serious problem in the elderly population, which is significantly related to the increased risk of all-cause mortality.[21,22] Accordingly, it is important to investigate the predictors associated with the long-term prognosis and identify the high-risk patients in the early stage. The prevalence of malnutrition varied depending on the nutritional screening tools used. Therefore, it is recommended that a suitable and accurate nutritional screening approach for a specific population should be used to estimate malnutrition. There are few generally accepted and used methodologies for nutritional assessment and screening of patients with AF. In the past, although several nutritional screening scale tools have also been developed, including MNA, Malnutrition Screening Tool (MST), Nutritional Risk Screening 2002 (NRS2002), and SGA, the evaluating items are still lack of reliability and validity.[6] They are susceptible to interference from various factors and cannot comprehensively assess the overall nutritional status of patients, which limits their clinical application. Meanwhile, such items of screening tools collected in the form of scales are greatly affected by patients' subjective factors and cognitive disorders, so they are not suitable for elderly adults. In recent years, a variety of new screen simple, efficient, and comprehensive nutritional assessment indexes called objective nutritional screening tools, represented by PNI, GNRI, CONUT, and HS-mGPS, developed rapidly. The association of these nutritional risk indices with poor prognosis has been thoroughly compared and evaluated in some cardiovascular diseases, including acute myocardial infarction and heart failure.[23,24] A recent retrospective cohort study has shown that PNI demonstrates superior prognostic performance in heart failure with preserved ejection fraction (HFpEF) when compared to Triglyceride-Total Cholesterol-Body Weight Index (TCBI), GNRI, and COUNT.[25] In another study of patients with hypertension, GNRI and PNI showed greater predictive values for kidney events than TCBI and CONUT.[26] Nonetheless, it remains unclear which nutritional index is more suitable for the prognostic assessment of elderly patients with AF. Therefore, exploring the predictive value of the four Objective Nutritional Indices associated with the long-term prognosis of AF and early identifying the high-risk elderly patients with AF are effective strategies to deal with this problem.

The PNI is calculated based on serum albumin level and the peripheral blood lymphocyte count, both of which are easily accessible parameters in routine clinical practice. It emerges as a comprehensive reflection that encompasses nutritional and inflammatory states, which are critical in the pathophysiology of AF. Previous academic studies have emphasized the prognostic performance of the PNI in cardiovascular diseases, including heart failure and myocardial infarction.[11,27–29] Serum albumin exhibits several beneficial physiological properties including stabilizing oxidative stress reactions in the body and regulating inflammatory responses.[30,31] There is evidence that low albumin levels are significantly correlated with elevated inflammatory markers in the elderly population.[32] In addition, numerous studies have reported a significant correlation between low albumin levels and adverse outcomes in various diseases, such as acute myocardial infarction (AMI), coronary artery disease, peripheral arterial disease, and ischemic stroke.[33,34] However, serum albumin levels are not only determined by the nutritional status but also affected by the body's pathological conditions such as renal insufficiency, blood dilution, and severe illness. Thus, the predictive utility of PNI may be attributable to the fact that it is calculated based on patient lymphocyte counts and serum albumin levels, both of which are negative prognostic biomarkers in a variety of contexts.[35] Moreover, it is well known that low lymphocyte count can reflect a poorly regulated immune response. In addition, low lymphocyte count is a common phenomenon during the inflammatory reaction.[36] The protective effects of different types of lymphocytes in AF patients have been proven. CD4+ T cells can differentiate into helper T (TH) cell subsets and mediate the progression of AF by secreting interferon-γ.[37] Natural killer (NK) cells can prevent the development of cardiac fibrosis in AF patients by limiting excessive collagen production in fibroblasts, preventing excessive accumulation of profibrotic cells, and inhibiting apoptosis in cardiomyocytes.[38] Once peripheral lymphocyte counts are reduced, the protective function also decreases, especially in the elderly population. Previous studies have shown that low lymphocyte counts were associated with the adverse prognosis of cardiovascular diseases, such as heart failure and stroke, through mediating immune functions and concurrent infections in patients.[39,40] Compared with COUNT and Hs-mGPS scores using categorical variables, albumin, and lymphocyte count are used as continuous variables to calculate PNI, which minimizes the loss of information and better reflects the nutritional status. Meanwhile, they are more stable indicators of body composition during long-term follow-up. In summary, the reasons mentioned above might explain why PNI is a strong predictor of survival in elderly patients with AF.

The GNRI is proposed to emerge as an age-specific indicator to assess the nutritional status of elderly patients. It evaluates their nutritional risk by considering changes in body weight and the degree of appetite decline. Recent studies have suggested that the GNRI shows the predictive value for adverse outcomes in elderly patients with some diseases.[41,42] Given the high prevalence of AF in the elderly, the GNRI is relevant for identifying AF patients at risk of malnutrition and their associated prognosis. Additionally, the feature of the GNRI is the utilization of the ratio of body weight to ideal body weight, which could better reflect the deviation of the malnourished population from normal BMI. However, the weight may change substantially during long-term follow-up, which limits its predictive value in the general population. Furthermore, the accurate measurement of body weight is often influenced by several factors such as edema and bedridden. Fluid distribution in the body may make the measured weight of participants with edema higher than their actual weight. Many advanced-age AF patients were bedridden, so the feasibility and accuracy of collecting height and weight were not available, which would potentially confound researchers. Our results revealed that the survival rate was lower in the low GNRI groups compared to the middle and high GNRI group, which showed a negative correlation with all-cause mortality. Nevertheless, further analysis of multivariate COX proportional hazards models demonstrated that GNRI was not an independent risk factor for all-cause mortality in elderly patients with AF.

The CONUT score has been confirmed by many studies as an effective nutritional assessment method, and could emerge as a predictor of adverse outcomes in various types of cancer and cardiovascular diseases, such as lymphoma, esophageal cancer, hypertension and ischemic stroke.[26,43–45] However, our study found that the CONUT score performed the worst predictive value in predicting all-cause mortality in elderly patients with AF. Compared with PNI, it incorporates the influence of TC on nutritional status and uses categorical variables. Total cholesterol levels above 180 mg/dL (4.65 mmol/L) were regarded as normal. On one hand, high cholesterol levels are significantly associated with an increased risk of incident cardiovascular events. Therefore, patients who were considered to have a normal nutritional status based on the CONUT score may be at a higher risk. On the other hand, the use of statins could lower TC and TG but contribute to stabilizing atherosclerotic plaques and extending survival cycles. The CONUT score may be overestimated due to stain use in patients with hyperlipidemia. Moreover, compared with continuous variables, categorical variables might exacerbate the loss of information and cannot accurately reflect the nutritional status. These results suggested that CONUT might not be a suitable indicator for long-term all-cause mortality among older AF patients.

The HS-mGPS score, based on two parameters of CRP and albumin, can also reflect the patient's inflammatory and nutritional status. Compared with the other three nutritional indices, the advantage of HS-mGPS is that CRP has been widely proven to be a sensitive marker of inflammatory response, which is related to adverse outcomes of various diseases. Previous studies suggested that CRP could participate in the process of AF development by increasing the inward L-type calcium current of atrial myocytes, which is involved in the immunological process of atrial fibrosis.[46] Then, the intensified inflammatory response could accelerate the process of adverse prognosis of AF.[47] Several studies have reported that the HS-mGPS score, composed of CRP and serum albumin, showed superior predictive value in adverse outcomes of various diseases.[48,49] Consistent with previous results, the analysis of multivariate COX proportional hazards models showed that HS-mGPS was an independent risk factor for all-cause mortality, and its predictive efficacy was also more significant compared with CONUT and GNRI. However, compared with PNI, the predictive efficacy of HS-mGPS is lower, although there was no statistically significant difference. Considering that the HS-mGPS score treats albumin and CRP as categorical variables, we think this may be its great deficiency.

AF is a common disease among elderly persons, accompanied by a rapidly increasing prevalence with age. More and more patients older than 65 experience malnutritional problems, including frailty and sarcopenia which were never traditionally considered as a relevant issue but have become a major clinical challenge nowadays. Malnutrition may decrease immunity and antioxidant capacity and increase inflammation and blood viscosity, which may lead to the occurrence of adverse outcomes. The relationship between malnutrition and AF is very complex. However, there are relatively limited studies focusing on the relationship between the assessment of the nutritional status and the long-term prognosis of patients with AF. In our study, lower PNI and higher HS-mGPS scores were significant independent predictors of all-cause mortality in elderly patients with AF. In addition, since PNI showed the highest predictive value, we needed to focus more on the nutritional status assessed by PNI to reduce all-cause mortality in elderly patients with AF.

## Study Limitations

Our study has several limitations. First, this is a single-center, retrospective, and observational study, which was subject to the clinical data of patients to a certain extent. Second, the sample size of this paper is relatively small, which is subject to potential biases, including selection bias, information bias and confounding bias, and may be center-specific to the research results. Third, it only explores the relationship between nutritional scores and all-cause mortality, but it does not explore the correlation with other causes of death. Although we demonstrated the strong prognostic power of PNI in elderly patients with AF, it was unclear whether PNI can be used as a therapeutic target. To clarify the answer to this question, further longitudinal studies are needed to investigate whether nutritional intervention can improve the prognosis of AF.

## Conclusions

PNI and HS-mGPS are independent risk factors for long-term prognosis of elderly patients with AF, with PNI demonstrates superior predictive performance. Given these findings, we recommend integrating nutritional status assessment into the routine clinical care for elderly patients with AF, allowing for further risk stratification and guidance for intervention. However, further research will be necessary to validate these findings.

## Abbreviations

AF, atrial fibrillation; PNI, Prognostic Nutritional Index; GNRI, Geriatric Nutritional Risk Index; CONUT, Controlling Nutritional Status; HS-mGPS, High-Sensitivity Modified Glasgow Prognostic Score; ROC, Receiver Operating Characteristic; AUC, area under the curve; GBD, Global Burden of Disease data; MNA, Mini Nutritional Assessment; SGA, Subjective Global Assessment; ESC, European Society of Cardiology; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CKD, chronic kidney disease; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; BNP, B-type natriuretic peptide; LYM, lymphocyte count; WBC, white blood cell count; CRP, C-reactive protein; ALB, serum albumin; FPG, fasting blood glucose; Na, sodium; K, potassium; LVEF, left ventricular ejection fraction; CCB, calcium channel blockers; VIF, variance inflation factor; MST, Malnutrition Screening Tool; NRS2002, Nutritional Risk Screening 2002; AMI, acute myocardial infarction; Th, helper T; NK, Natural killer; TCBI, Triglyceride-Total Cholesterol-Body Weight Index (TCBI); PPV, Positive Predictive Value; NPV, Negative Predictive Value; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; HFpEF, heart failure with preserved ejection fraction.

## Data Sharing Statement

All data presented and analyzed in this study are included in this published article, further inquiries can be directed to the corresponding authors upon reasonable request.

## Ethics Approval and Informed Consent

This study has been approved by the Ethics Review Board of the Air Force Medical Center of the Chinese People's Liberation Army (2023-034-PJ01). The Institutional Review Board of the Air Force Medical Center granted a waiver of informed consent due to the fully de-identification of data without any patient identifiers and the retrospective nature of the study.

## Consent for Publication

All participants provided written informed consent for the publication of their data.

## 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 all 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.

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## Disclosure

All authors declare that they have no conflict of interest.

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