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Neutrophil Percentage to Albumin Ratio Is Associated With In-Hospital Mortality in Patients With Acute Type A Aortic Dissection

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Keywords: acute type A aortic dissection | in-hospital mortality | neutrophil percentage-to-albumin ratio | neutrophils | prognosis

ABSTRACT

The neutrophil percentage to albumin ratio (NPAR) has been associated with prognosis of various cardiovascular diseases, but its role in acute type A aortic dissection (AAAD) mortality remains unclear. The aim of this study was to investigate the relationship between preoperative NPAR and in-hospital mortality in AAAD patients. Clinical data from patients who underwent AAAD surgery at the Cardiac Medical Center of Fujian Province between January 2020 and April 2024 were retrospectively analyzed. Patients were categorized into three groups based on NPAR tertiles. Univariate and multivariate logistic regression analyses were employed to identify factors contributing to in-hospital mortality. The predictive performance of NPAR was assessed using ROC curve analysis. The results revealed that out of 813 AAAD patients meeting the inclusion criteria, 137 (16.9%) died in hospital. Multivariate logistic regression analysis indicated that compared to the low tertile group, the odds ratios (95% CI) for in-hospital mortality in the middle and high tertile groups were (OR 3.041, 95% CI: 1.502–6.158, $p = 0.002$) and (OR 6.586, 95% CI: 3.324–13.049, $p<0.001$), respectively. Additionally, cardiopulmonary bypass time (OR 1.010, 95% CI: 1.007-1.013, $p<0.001$) and mechanical ventilation time (OR 1.115, 95% CI: 1.082–1.150, $p<0.001$) were also independently associated with in-hospital mortality in AAAD patients. The area under the curve for NPAR was 0.708 (95% CI: 0.676–0.739) ($p<0.001$), with an optimal cut-off value of 24.105, yielding a sensitivity of 73.7% and a specificity of 64.8%. In conclusion, higher preoperative NPAR may be independently associated with increased in-hospital mortality, suggesting its potential as a novel indicator for monitoring AAAD patients.

1 | Introduction

Acute type A aortic dissection (AAAD) is a fatal cardiovascular event involving the ascending aorta [1]. It is caused by a tear in the intimal layer, and has an acute onset, rapid progress, and high mortality [1]. It is reported that the mortality rate of AAAD patients within 48 h after onset is 1%–2% [2]. At present, emergency surgical repair remains the only effective treatment for AAAD patients [3]. The guidelines of the American Heart Association also recommend, as early as possible, surgical

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intervention for AAAD patients [3]. In spite of advances in surgical management and techniques of AAAD, the in-hospital mortality of AAAD patients receiving surgical treatment remains high, about 18%–25% [4]. Timely and accurate prediction of adverse prognosis is essential for better management of AAAD. Thus, it is important to find reliable and easily accessible predictive biomarkers to help clinicians identify high-risk AAAD patients for early interventions, thereby reducing in-hospital mortality and improving prognosis.

Inflammatory reaction is the main pathophysiological feature of the occurrence and development of AAAD [5]. As a typical effector, neutrophils can participate in the inflammatory process by secreting matrix metalloproteinases (MMP), which leads to further deterioration of aortic dissection (AD) [6]. Albumin has a variety of capabilities, including regulating osmotic pressure, antioxidation and anti-inflammatory, is a significant inhibitor of platelet activation and aggregation, and is linked to the regulation of AD inflammatory state [7, 8]. Recent research combined the two indicators and proved that the neutrophil percentage to albumin ratio (NPAR) could be used as a predictor of the prognosis of many cardiovascular diseases. Recent studies have shown that admission NPAR was an independent predictor of all-cause mortality in acute myocardial infarction (AMI) [9]. In another study, NPAR was independently associated with all-cause mortality in heart failure patients [10]. In addition, studies have shown that higher NPAR was independently associated with increased risk of 30-day, 60-day, and 365-day all-cause mortality in coronary heart disease (CHD) patients [11]. However, no study has examined how NPAR level on admission relates to in-hospital mortality in AAAD patients. Therefore, it was the purpose of this study to determine whether NPAR has potential value in predicting the in-hospital mortality of AAAD patients.

2 | Methods

2.1 | Study Population

Records of patients over 18 years old who were diagnosed as AAAD by computed tomographic angiography (CTA) or magnetic resonance angiography (MRA) and underwent surgical repair at the Cardiac Medical Center of Fujian Province from January 2020 to April 2024 were analyzed retrospectively in this study. The exclusion criteria for this study were as follows: (1) Have been used drugs that affect blood cell counts, like aspirin, antibiotics and glucocorticoids in the past 2 weeks; (2) Previous history of malignant tumor; (3) Combined with chronic liver and kidney failure; and (4) Suffering from autoimmune diseases. All patients were admitted to the intensive care unit (ICU) postoperatively. This study was approved by the Ethics Committee of Fujian Medical University Union Hospital (Approval No: 2019KY019) and was in accordance with the Declaration of Helsinki. Informed consent waivers were obtained because the data were anonymous.

2.2 | Data Collection and Definition

The demographic information, vital signs on admission, complications, intraoperative conditions, laboratory indicators, mechanical ventilation time, and postoperative complications of all enrolled patients were collected from electronic medical records. There was a collection of demographic information, including age, gender, body mass index (BMI), history of cardiac surgery, smoking, and drinking. Admission vital signs include systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate. Complications included hypertension, diabetes mellitus, CHD, and Marfan's syndrome. Intraoperative conditions included operating time, CPB time, aortic cross-clamping clamp time, and surgical type. Laboratory indicators were obtained from the first laboratory results after admission, including neutrophil percentage, albumin, hemoglobin (Hb), lymphocyte, platelet (PLT), white blood cell (WBC), alanine aminotransferase (ALT), aspartate transferase (AST), creatinine (Cr), and blood urea nitrogen (BUN).

The percentage of neutrophils was defined as the percentage of neutrophils in white blood cells. A neutrophil percentage divided by serum albumin concentration was used to calculate NPAR. The calculation formula was as follows: neutrophil percentage (%) × 100/albumin (g/dL). In-hospital mortality was the primary outcome measure of the current study, and the postoperative complications, such as gastrointestinal bleeding, pulmonary infection, acute renal injury (AKI), multiple organ dysfunction syndrome (MODS), and arrhythmia, were the secondary outcome measures. In addition, the length of stay in ICU and length of hospital stay were recorded. In-hospital mortality was defined as any death during postoperative hospital stay after AAAD surgery [12]. In cases of gastrointestinal bleeding, fecal occult blood tests or vomit that contains blood were used for diagnosis [13]. Pulmonary infection referred to the presence of pneumonia, or atelectasis on radiograph, and positive sputum bacterial culture [14]. AKI was defined as an increase in serum creatinine by ≥0.3 mg/dl within 48 h, a ≥1.5-fold increase from baseline within 7 days, or a reduction in urine output to <0.5 mL/kg/h for 6 h or longer [15]. MODS was defined as a sequential organ failure assessment (SOFA) ≥ 6 over 2 successive days, at least 48 h after hospital admission [16]. Arrhythmia referred to any clinically significant cardiac arrhythmia, such as atrial fibrillation, supraventricular tachycardia, or cardiac arrest [17].

2.3 | Study Endpoints

The primary endpoint was in-hospital mortality. The secondary endpoints were postoperative complications and the duration of ICU and hospital stays. The postoperative complications consisted of gastrointestinal hemorrhage, pulmonary infection, AKI, MODS, and arrhythmia.

2.4 | Statistical Analysis

SPSS Version 25.0 and MedCalc version 19.2.1 were used for statistical analysis. The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. Variables with a Kolmogorov–Smirnov test result of $p \geq 0.05$ were considered normally distributed. If the continuous variables in this study were normally distributed, they were expressed as mean ± standard deviation (SD), and the difference between groups was analyzed using a one-way analysis of variance (ANOVA). If the variable did

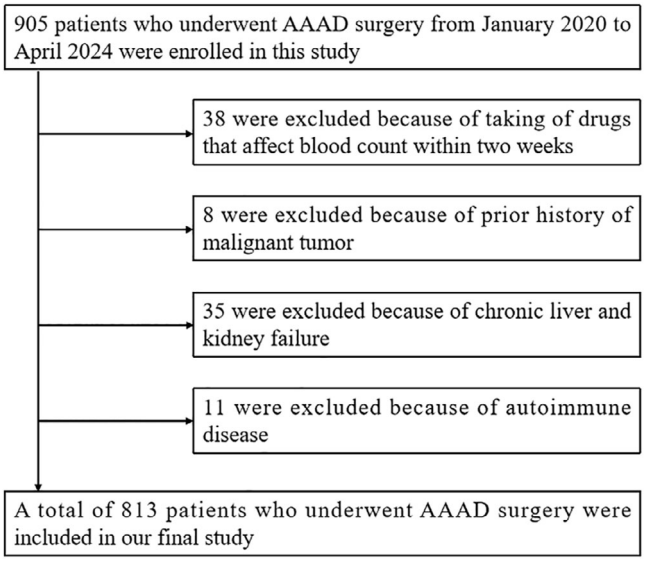

FIGURE 1 | The flow chart for the selection process of patients with AAAD. AAAD, acute type A aortic dissection.

not follow a normal distribution, it was indicated by median and quartile range, and comparisons between groups were conducted using Kruskal–Wallis tests. A frequency or percentage was used to express categorical variables, and for comparing groups, the Chi-square test or Fisher's exact test were used. After adjusting for possible confounding factors, we used multivariate logistic regression analysis to determine the independent correlation between NPAR and in-hospital mortality. These confounding factors were judged by statistical significance and clinical judgment in univariate analysis. The first tertile was defined as reference, odds ratio (OR) and 95% confidence interval (CI) have been used to calculate the results. The study also conducted subgroup analysis on the relationship between NPAR and in-hospital mortality, and calculated the p value for interaction to confirm whether the relationship between NPAR and in-hospital mortality was different in each subgroup classified by demographic information (such as age and BMI), complications (such as hypertension), vital signs (such as SBP, DBP, heart rate), and laboratory test results (such as Hb, lymphocytes, PLT, WBC, ALT, AST, Cr, BUN). ROC curves were used to evaluate the predictive value of neutrophil percentage, albumin and NPAR in predicting in-hospital mortality of AAAD patients. Area under curve (AUC), sensitivity and specificity were calculated. In order to compare AUC between different indicators, we used the Delong test. All tests were two-sided, and the differences were considered statistically significant when $p<0.05$.

3 | Results

3.1 | Subject Characteristics

This study included 813 AAAD patients (Figure 1). This study included 629 males and 184 females, with a mean age of 52.50 ± 11.55 years. Using tertiles of admission NPAR, patients were split into three groups (T1:<21.87; T2: 21.87–24.81; T3:>24.81). The baseline characteristics for patients stratified by NPAR tertiles were summarized in Table 1. A total of 269 patients were included in T1 group, 274 patients in T2 group, and 270 patients in T3 group. In comparison with T1 and T2 groups, T3 patients were older ($p<0.001$), had longer mechanical ventilation ($p<0.001$), had less hypertension ($p = 0.009$), and had lower SBP ($p = 0.007$). In the laboratory test results, compared with T1 and T2 groups, patients in T3 group had lower Hb ($p<0.001$) and PLT ($p<0.001$), higher WBC counts ($p<0.001$), and higher Cr levels ($p = 0.028$). There were no significant differences among the three groups in BMI, diabetes, CHD, Marfan's syndrome, history of cardiac surgery, smoking, drinking, DBP, heart rate, surgical type, operating time, CPB time, aortic cross-clamping time, ALT, AST, and BUN ($p>0.05$).

3.2 | Relationship between NPAR Values and In-Hospital Outcomes

As shown in Table 2, 137 patients died during hospitalization (in-hospital mortality 16.9%). Compared with T1 and T2 groups, T3 group had a higher in-hospital mortality of 33.0% ($p <0.001$). In addition, the incidence of AKI ($p <0.001$) and MODS ($p = 0.004$) in T3 group was significantly higher than that in T1 and T2 groups, and the stay time in ICU was significantly longer ($p <0.001$). The overall incidence of postoperative pulmonary infection was 27.3% (222 out of 813). Specifically, the incidence was 25.7% (69 out of 269) in group T1, 26.6% (73 out of 274) in group T2, and 29.6% (80 out of 270) in group T3. However, the difference in incidence among the three groups was not statistically significant ($p >0.05$). Additionally, no significant differences were observed among the three groups in the incidence of postoperative gastrointestinal hemorrhage, arrhythmia and hospital length of stay ($p >0.05$).

3.3 | Univariate and Multivariate Logistic Regression Analysis

The univariate logistic regression analysis of in-hospital mortality of AAAD patients showed that age, operating time, CPB time, aortic cross-clamping time, mechanical ventilation time, PLT, WBC, AST, and NPAR were the factors related to in-hospital mortality ($p <0.05$). After adjusting for all covariates, multivariate logistic regression analysis revealed that CPB time (OR 1.010, 95% CI: 1.007–1.013, $p <0.001$), mechanical ventilation time (OR 1.115, 95% CI: 1.082–1.150, $p <0.001$), NPAR were significantly correlated with in-hospital mortality. With group T1 as a reference, the OR (95% CI) values of group T2 and group T3 were 3.041 (1.502–6.158) ($p = 0.002$) and 6.586 (3.324–13.049), respectively ($p <0.001$). In addition, the p value of NPAR trend was less than 0.001, indicating that as NPAR increases, in-hospital mortality increases as well. A summary of the results was shown in Table 3.

3.4 | Subgroup Analysis

In order to verify the consistency of the correlation between NPAR and in-hospital mortality, a subgroup analysis was conducted on AAAD patients. Interaction analysis showed that there was no significant interaction between subgroups classified by age, BMI, hypertension, SBP, DBP, heart rate, Hb, lymphocytes, PLT, WBC, ALT, AST, Cr, and BUN ($p >0.05$). The results were shown in Table 4.

TABLE 1 | Baseline characteristics stratified by preoperative NPAR.

Variable	NPAR			p
	T1 (<21.87) N = 269	T2 (21.87–24.81) N = 274	T3 (>24.81) N = 270	
Age (years)	49.78 ± 11.75	53.05 ± 11.07	54.64 ± 11.33	**<0.001**
Male	227 (84.4)	221 (80.7)	181 (67.0)	**<0.001**
BMI (kg/m^2)	25.26 ± 4.30	24.97 ± 3.90	24.44 ± 3.92	0.059
Hypertension	158 (58.7)	136 (49.6)	124 (45.9)	**0.009**
Diabetes mellitus	14 (5.2)	9 (3.3)	7 (2.6)	0.249
CHD	2 (0.7)	1 (0.4)	4 (1.5)	0.359
Marfan's syndrome	15 (5.6)	13 (4.7)	13 (4.8)	0.887
Previous cardiac surgery	18 (6.7)	16 (5.8)	12 (4.4)	0.522
Smoker	140 (52.0)	130 (47.4)	124 (45.9)	0.334
Drinker	119 (44.2)	110 (40.1)	100 (37.0)	0.232
SBP (mmHg)	144.39 ± 27.82	138.27 ± 27.18	137.10 ± 31.34	**0.007**
DBP (mmHg)	76.19 ± 15.91	75.15 ± 16.77	73.79 ± 15.97	0.228
Heart rate	82.34 ± 16.05	81.59 ± 15.92	81.71 ± 17.00	0.850
Operating time (min)	290.0 (255.0–335.0)	301.0 (263.0–348.0)	310.0 (265.0–365.0)	0.254
CPB time (min)	150.0 (118.0–185.0)	153.0 (122.0–190.0)	151.0 (124.0–185.0)	0.727
Aortic cross-clamping time (min)	65.0 (48.0–98.0)	75.0 (53.0–102.0)	69.0 (50.0–96.0)	0.520
Mechanical ventilation time (days)	1.8 (0.9–3.4)	2.0 (1.1–4.4)	2.9 (1.5–8.3)	**<0.001**
Surgical type				0.365
Simple aortic surgeries	249 (92.6)	255 (93.1)	256 (94.8)	
Combined CABG	11 (4.1)	15 (5.5)	9 (3.3)	
Combined valve surgery	9 (3.3)	3 (1.1)	4 (1.5)	
Combined CABG and valve surgery	0	1 (0.4)	1 (0.4)	
Laboratory tests				
Neutrophil percentage (%)	76.60 (65.50–83.50)	86.30 (81.40–90.40)	91.40 (86.90–97.80)	**<0.001**
Albumin (g/dL)	4.01 ± 0.52	3.69 ± 0.31	3.29 ± 0.34	**<0.001**
Hb (g/dL)	13.16 ± 1.98	12.98 ± 1.75	12.22 ± 2.01	**<0.001**
Lymphocyte (10^9/L)	1.30 (0.92–1.74)	0.92 (0.68–1.31)	0.95 (0.63–1.86)	**<0.001**
PLT (10^9/L)	198.93 ± 69.61	184.41 ± 68.44	170.64 ± 72.18	**<0.001**
WBC (10^9/L)	11.63 ± 4.22	12.35 ± 3.60	12.95 ± 4.56	**0.001**
ALT (IU/L)	27.00 (19.00–36.00)	27.00 (17.00–38.00)	27.00 (19.00–41.00)	0.074
AST (IU/L)	24.00 (19.00–38.50)	26.00 (20.00–39.00)	27.00 (20.00–43.00)	0.148
Cr (μmol/L)	87.00 (70.00–119.00)	85.50 (69.00–118.50)	89.00 (69.00–131.00)	**0.028**
BUN (mmol/L)	5.40 (4.30–7.00)	6.50 (5.20–8.60)	7.30 (5.30–9.80)	0.083

The values in bold indicate statistically significant p-values, meaning $p < 0.05$.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; CHD, coronary heart disease; CPB, cardiopulmonary bypass; Cr, creatinine; DBP, diastolic blood pressure; Hb, hemoglobin; NPAR, neutrophil percentage to albumin ratio; PLT, platelet; SBP, systolic blood pressure; WBC, white blood cell.

3.5 | Sensitivity and Specificity of Neutrophil Percentage, Albumin, and NPAR in Predicting In-Hospital Mortality

The predictive values of neutrophil percentage, albumin, and NPAR for in-hospital mortality of AAAD patients were shown in Table 5 and Figure 2. Results indicated that the AUC of NPAR was 0.708 (95% CI: 0.676–0.739) (p <0.001), the optimal cutoff value was 24.105, with a sensitivity of 73.7% and a specificity of 64.8%. The AUC of neutrophil percentage and albumin were 0.649 (95% CI: 0.615–0.682) (p<0.001) and 0.622 (95% CI: 0.588–0.656) (p<0.001), respectively. Based on the Delong test results, the AUC of NPAR was significantly higher than that of neutrophil percentage (p = 0.004) and albumin (p<0.001),

TABLE 2 | In-Hospital Outcomes stratified by preoperative NPAR.

Variable	Total	NPAR			*p*
		T1 (<21.87) *N* = 269	T2 (21.87–24.81) *N* = 274	T3>24.81 *N* = 270	
In-hospital mortality	137 (16.9)	6 (2.2)	42 (15.3)	89 (33.0)	**<0.001**
Gastrointestinal hemorrhage	78 (9.6)	23 (8.6)	26 (9.5)	29 (10.7)	0.687
Pulmonary infection	222 (27.3)	69 (25.7)	73 (26.6)	80 (29.6)	0.558
AKI	175 (21.5)	36 (13.4)	52 (19.0)	87 (32.2)	**<0.001**
MODS	28 (3.4)	2 (0.7)	10 (3.6)	16 (5.9)	**0.004**
Arrhythmia	17 (2.1)	3 (1.1)	4 (1.5)	10 (3.7)	0.074
ICU stay (days)	6.0 (4.0–10.0)	5.0 (4.0–9.0)	6.0 (4.0–10.0)	8.0 (4.0–15.0)	**<0.001**
hospital length of stay (days)	20.0 (15.0–27.0)	19.0 (15.0–26.0)	20.0 (15.0–26.0)	21.0 (15.0–29.0)	0.069

The values in bold indicate statistically significant *p*-values, meaning $p < 0.05$.

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; MODS, multiple organ dysfunction syndrome; NPAR, neutrophil percentage to albumin ratio.

and NPAR showed higher predictive value in predicting hospital mortality.

4 | Discussion

As far as we know, this is the first study to examine the relationship between NPAR and in-hospital mortality in AAAD patients. The results of our study were summarized below. First, AAAD patients had a 16.9% in-hospital mortality rate, which was similar to previous studies [18]. Patients with higher preoperative NPAR have higher incidence of AKI and MODS, and longer ICU stay. Second, after adjusting for potential confounders, AAAD patients with higher preoperative NPAR had an increased risk of in-hospital mortality. From the results of subgroup analysis, there were no significant interactions between the subgroups of patients. In addition, CPB time and mechanical ventilation time also correlated with in-hospital mortality of AAAD patients. Finally, the ROC curves showed that in comparison with the percentage of neutrophils or albumin alone, NPAR was a better predictor of in-hospital mortality.

NPAR is a comprehensive reflection of the neutrophil percentage and albumin. In this study, AAAD patients with higher preoperative NPAR had a significantly higher risk of in-hospital mortality than those with lower NPAR, which was consistent with the findings of NPAR in the prognostic value of acute myocardial infarction, heart failure, and CHD [9–11]. The underlying mechanism for NPAR levels in association with in-hospital mortality in AAAD patients is unclear. According to previous studies, inflammation plays a crucial role in the occurrence, progression and prognosis of AD [2]. Lafçi et al. [19] found that neutrophil-to-lymphocyte ratio (NLR) as an indicator of inflammation was also independently associated with mortality in AAAD patients, thereby underscoring the pivotal role of the inflammatory response in the progression of AD.

As a result of inflammation, the media layer of the aorta degenerates and arterial walls remodel, resulting in a fragile aortic wall and an increased risk of rupture. As an inflammatory marker, NPAR was closely related to the inflammatory process. Thus, we tried to explain the relationship between NPAR levels and in-hospital mortality in AAAD. Neutrophils were the major type of WBC [20], as a classic cellular effector, neutrophils played a crucial role in mediating inflammatory responses of AD [21]. Previous studies have shown that high neutrophil-to-platelet ratio (NPR) and NLR were independently linked to poor prognosis in acute aortic dissection (AAD) [22, 23]. A study by Liu et al. [24] revealed that neutrophil count was linked to in-hospital mortality in AAAD patients. There are probably several reasons for that. First, neutrophils play a pivotal role in mediating the inflammatory response during the acute phase of AAAD [23]. The aortic wall dissection induces localized ischemia and necrosis, which triggers the release of damage-associated molecular patterns (DAMPs) and activates Toll-like receptors (TLRs) and the NF-κB signaling pathway, consequently promoting neutrophil infiltration [23]. Second, activated neutrophils secrete matrix metalloproteinases (MMPs) such as MMP-9, along with reactive oxygen species (ROS) and pro-inflammatory cytokines including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) [24, 25]. These mediators contribute to the degradation of the aortic wall's extracellular matrix (ECM), thereby compromising vascular structural integrity [24, 25]. Furthermore, the generation of neutrophil extracellular traps (NETs) exacerbates endothelial injury and promotes thrombotic complications [26]. Finally, neutrophil activation leads to the production of substantial reactive oxygen intermediates, which induce apoptosis in aortic smooth muscle cells and further degrade the ECM [27]. This cascade of events exacerbates vascular endothelial injury, thereby heightening the risk of aortic dissection and coarctation, and consequently, elevating the in-hospital mortality rate [27].

The protein albumin is a major component of plasma and plays various roles such as anti-inflammatory, antioxidant, anticoagulant, and antiplatelet aggregation [28]. Albumin levels were associated with poor prognosis in a wide range of cardiovascular diseases. A previous study found that lower albumin levels were independently associated with increased in-hospital mortality in both type A and type B AAD [29]. A previous study on first episode acute myocardial infarction (AMI) showed that low albumin level at admission was independently correlated with

TABLE 3 | Univariate and multivariate analysis of variables associated with in-hospital mortality.

Variable	Univariate		Multivariate	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Age (years)	1.030 (1.013–1.047)	**0.001**	1.006 (0.986–1.026)	0.569
Male	1.272 (0.834–1.939)	0.264		
BMI (kg/m^2)	1.027 (0.983–1.074)	0.235		
Hypertension	0.717 (0.496–1.038)	0.078		
Diabetes mellitus	0.986 (0.371–2.624)	0.978		
CHD	1.988 (0.382–10.354)	0.414		
Marfan's syndrome	1.017 (0.441–2.344)	0.969		
Previous cardiac surgery	0.454 (0.160–1.288)	0.138		
Smoker	0.743 (0.513–1.077)	0.116		
Drinker	0.984 (0.677–1.431)	0.933		
SBP (mmHg)	0.995 (0.989–1.002)	0.156		
DBP (mmHg)	1.004 (0.992–1.015)	0.536		
Heart rate	1.008 (0.997–1.020)	0.132		
Surgical type				
Simple aortic surgeries	1.0 (ref)			
Combined CABG	1.682 (0.790, 3.580)	0.177		
Combined valve surgery	1.402 (0.446, 4.409)	0.563		
Combined CABG and valve surgery	—	0.999		
Operating time (min)	1.005 (1.003–1.007)	**<0.001**		
CPB time (min)	1.009 (1.006–1.012)	**<0.001**	1.010 (1.007–1.013)	**<0.001**
Aortic cross-clamping time (min)	1.004 (1.001–1.007)	**0.025**		
Mechanical ventilation time (days)	1.141 (1.109–1.175)	**<0.001**	1.115 (1.082–1.150)	**<0.001**
Laboratory tests				
Hb (g/dL)	0.966 (0.881–1.059)	0.463		
Lymphocyte (10^9/L)	0.974 (0.916–1.035)	0.392		
PLT (10^9/L)	0.994 (0.991–0.997)	**<0.001**	0.999 (0.996–1.002)	0.516
WBC (10^9/L)	1.064 (1.021–1.109)	**0.004**	1.031 (0.979–1.086)	0.248
ALT (IU/L)	1.004 (0.998–1.011)	0.216		
AST (IU/L)	1.006 (1.001–1.011)	**0.027**	1.004 (0.997–1.010)	0.235
Cr (μmol/L)	1.001 (0.999–1.003)	0.384		
BUN (mmol/L)	1.003 (0.995–1.011)	0.529		
NPAR				
<21.87	1.0 (ref)		1.0 (ref)	
21.87–24.81	3.297 (1.755–6.194)	**<0.001**	3.041 (1.502–6.158)	**0.002**
>24.81	7.806 (4.294–14.191)	**<0.001**	6.586 (3.324–13.049)	**<0.001**
p for trend		**<0.001**		**<0.001**

The values in bold indicate statistically significant *p*-values, meaning $p < 0.05$.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; CHD, coronary heart disease; CPB, cardiopulmonary bypass; Cr, creatinine; DBP, diastolic blood pressure; Hb, hemoglobin; NPAR, neutrophil percentage to albumin ratio; PLT, platelet; SBP, systolic blood pressure; WBC, white blood cell.

TABLE 4 | Subgroup analysis of the associations between preoperative NPAR and in-hospital mortality.

Variable	*N*	NPAR			*p* for interaction
		<21.87	21.87–24.81	>24.81	
Age (years)					0.289
<53	398	1.0 (ref)	1.806 (0.747–4.367)	6.579 (2.973–14.560)	
≥53	415	1.0 (ref)	5.437 (2.029–14.571)	9.478 (3.643–24.658)	
BMI (kg/m^2)					0.642
<24	338	1.0 (ref)	4.341 (1.408–13.387)	8.500 (2.903–24.889)	
24≤BMI<28	313	1.0 (ref)	2.735 (0.940–7.963)	9.794 (3.631–26.417)	
≥28	162	1.0 (ref)	3.293 (1.080–10.041)	6.321 (2.088–19.135)	
Hypertension					0.183
No	395	1.0 (ref)	6.210 (2.097–18.387)	11.167 (3.870–32.223)	
Yes	418	1.0 (ref)	1.973 (0.864–4.507)	6.540 (3.103–13.783)	
SBP (mmHg)					0.171
<140.00	405	1.0 (ref)	6.386 (2.159–18.889)	11.733 (4.075–33.786)	
≥140.00	408	1.0 (ref)	1.939 (0.848–4.433)	6.299 (2.979–13.317)	
DBP (mmHg)					0.572
<74.00	393	1.0 (ref)	3.275 (1.340–8.008)	6.765 (2.898–15.794)	
≥74.00	420	1.0 (ref)	3.317 (1.363–8.073)	8.967 (3.859–20.834)	
Heart rate					0.338
<80.00	387	1.0 (ref)	2.750 (1.175–6.437)	4.620 (2.039–10.470)	
≥80.00	426	1.0 (ref)	3.972 (1.545–10.210)	12.854 (5.284–31.269)	
Hb (g/dL)					0.154
<12.90	380	1.0 (ref)	2.689 (1.030–7.021)	5.739 (2.342–14.066)	
≥12.90	433	1.0 (ref)	3.765 (1.630–8.697)	10.312 (4.579–23.226)	
Lymphocyte (10^9/L)					0.140
<1.05	406	1.0 (ref)	2.534 (1.064–6.032)	6.078 (2.619–14.106)	
≥1.05	407	1.0 (ref)	3.140 (1.196–8.242)	8.010 (3.377–18.998)	
PLT (10^9/L)					0.477
<176.00	404	1.0 (ref)	5.784 (1.942–17.225)	13.502 (4.719–38.637)	
≥176.00	409	1.0 (ref)	2.202 (0.980–4.947)	4.933 (2.284–10.656)	
WBC (10^9/L)					0.295
<12.06	406	1.0 (ref)	3.610 (1.490–8.746)	6.847 (2.882–16.266)	
≥12.06	407	1.0 (ref)	2.986 (1.215–7.338)	8.286 (3.600–19.070)	
ALT (IU/L)					0.499
<27.00	393	1.0 (ref)	7.037 (2.030–24.390)	16.370 (4.878–54.934)	
≥27.00	420	1.0 (ref)	2.273 (1.061–4.869)	5.395 (2.659–10.945)	
AST (IU/L)					0.208
<26.00	387	1.0 (ref)	4.354 (1.406–13.479)	10.236 (3.454–30.335)	
≥26.00	426	1.0 (ref)	2.795 (1.294–6.035)	6.363 (3.085–13.125)	
Cr (μmol/L)					0.986
<87.00	399	1.0 (ref)	3.024 (1.234–7.409)	6.243 (2.640–14.759)	
≥87.00	414	1.0 (ref)	3.592 (1.479–8.725)	9.333 (4.050–21.511)	
BUN (mmol/L)					0.197
<6.3	406	1.0 (ref)	2.208 (0.831–5.866)	7.667 (3.204–18.349)	
≥6.3	407	1.0 (ref)	3.512 (1.479–8.339)	6.633 (2.877–15.291)	

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; Cr, creatinine; DBP, diastolic blood pressure; Hb, hemoglobin; NPAR, neutrophil percentage to albumin ratio; PLT, platelet; SBP, systolic blood pressure; WBC, white blood cell.

TABLE 5 | Diagnostic value of neutrophil percentage, albumin, and NPAR for in-hospital mortality.

Variable	AUC	95% CI	Cut-off value	Sensitivity (%)	Specificity (%)
Neutrophil percentage (%)	0.649	0.615–0.682	85.108	78.1	51.6
Albumin (g/dL)	0.622	0.588–0.656	3.705	77.4	48.5
NPAR	0.708	0.676–0.739	24.105	73.7	64.8

Abbreviations: AUC, area under the curve; NPAR, neutrophil percentage to albumin ratio.

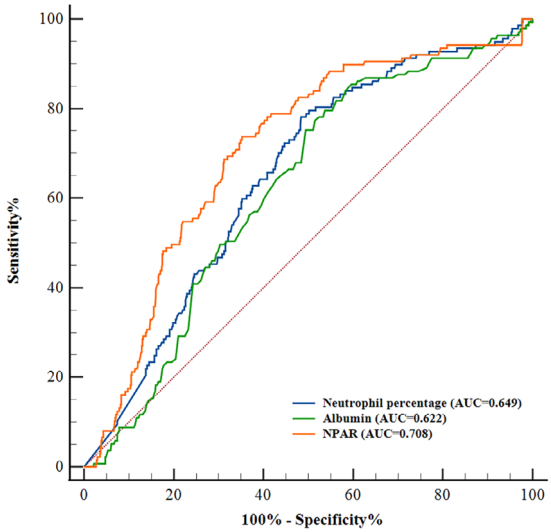

FIGURE 2 | ROC curves of neutrophil percentage, albumin, and NPAR for in-hospital mortality. AUC, the area under the curve; NPAR, neutrophil percentage to albumin ratio; ROC curve, the receiver operating characteristic curve.

all-cause mortality [30]. A meta-analysis demonstrated that low serum albumin levels were at high risk for all-cause mortality among patients with acute coronary syndrome (ACS), even after adjusting for the confounding factors [31]. This may be due to the following reasons: First, albumin functions as a primary circulating antioxidant, effectively scavenging reactive oxygen species (ROS) and protecting the vascular endothelium against oxidative stress-induced damage [32]. Consequently, diminished albumin levels may augment oxidative damage to the aortic wall [32]. Second, albumin plays a crucial role in inhibiting platelet aggregation and augmenting antithrombin III activity. A reduction in albumin levels may elevate the risk of thrombosis, thereby exacerbating aortic false lumen thrombosis or postoperative thrombotic events [33]. Furthermore, albumin serves as an essential nutritional biomarker and modulates vascular permeability through maintenance of colloid osmolality [34]. Low albumin levels may signify malnutrition, peripheral edema, or organ dysfunction in patients [34]. Finally, lower albumin levels may reflect more severe blood loss and catabolic reactions and lower potential to scavenge oxygen free radicals, likewise suggesting the presence of microcirculatory dysfunction and tissue damage after CPB [35, 36]. These states are strongly associated with an increased risk of death in AAAD [35, 36].

On the other hand, we found that patients who had higher preoperative NPAR were more likely to experience AKI and MODS, and longer stays in the ICU, which was similar to the results of another study [37]. This may be because the occurrence of AKI and MODS is inextricably linked to the activation of inflammatory cells, oxidative stress and the increase of oxygen free radicals, and NPAR can reflect the severity of inflammation and oxidative stress reaction to a certain extent [38]. Existing literature has established that mortality in patients with AAAD is primarily driven by two interrelated factors: progression of the underlying aortic pathology and postoperative multi-organ failure [39]. In our study, while no statistically significant correlation between the NPAR and pulmonary infections was observed, there was an observable trend indicating a higher incidence of infections in the cohort with elevated NPAR. This suggested that systemic inflammatory responses may exacerbate postoperative immune imbalances, thereby heightening susceptibility to infection [40]. In addition, we noticed that in addition to NPAR, CPB time and mechanical ventilation time were also independent predictors of in-hospital mortality among AAAD patients, which was consistent with the study of Bhamidipati et al. [41] This may be due to the existence of inflammation and ischemia-reperfusion during CPB. In this case, the function of important organs such as lung, liver and kidney will deteriorate due to cell damage, vasodilation and increased capillary filtration [42, 43]. Moreover, patients with long mechanical ventilation had worse physical condition and were often accompanied by weakness and cognitive decline [44]. These factors may increase the in-hospital mortality risk among AAAD patients.

It was found that NPAR could better predict in-hospital mortality in AAAD than neutrophil percentage or albumin alone. As a potential novel biomarker, NPAR can be obtained from admission laboratory results quickly and conveniently, which is practical and simple. Existing literature has established CRP and NLR as biomarkers closely linked to systemic inflammatory responses, demonstrating prognostic value in cardiovascular disease outcomes [45]. However, CRP alone reflects only the intensity of inflammation, and NLR is limited to cellular ratios without accounting for the organism's nutritional status [45]. The NPAR emerges as a novel composite indicator, uniquely integrating acute inflammatory status with nutritional reserve capacity. A decrease in albumin is often accompanied by increased oxidative stress, coagulation disorders, and inadequate organ perfusion, mechanisms that are closely linked to postoperative complications of AAAD, such as AKI and multiple organ dysfunction syndrome MODS. Consequently, this comprehensive feature may render NPAR more advantageous in evaluating systemic inflammatory load and the risk of organ damage in AAAD patients. In light of its inexpensive cost, high availability, and ability in predicting in-hospital mortality, NPAR may be a suitable clinical risk assessment tool for AAAD. Therefore, it is recommended that this indicator be included in risk stratification when making a clinical monitoring protocol.

This present study had some potential limitations. First, this was a single-center retrospective study, which may result in selection bias. In the future, there is still a need for multicenter prospective studies to validate the conclusions of this study. Second, the percentage of neutrophils and the concentrations of serum albumin for our study were obtained through the first blood test after admission. However, since these indicators were dynamic, random error was inevitable from using only the first blood results, which made it impossible to dynamically observe NPAR. Additionally, this study did not account for the potential influence of additional inflammatory biomarkers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). It is advisable for future research to investigate the synergistic effects of these markers in conjunction with the NPAR to further substantiate the independent predictive value of NPAR and to comprehensively evaluate the influence of inflammatory status on the prognosis of AAAD. Finally, the study only discussed how NPAR was associated with poor prognosis of AAAD patients during hospitalization, and there is a need for additional long-term follow-up studies to determine whether preoperative NPAR predicts long-term patient outcome.

5 | Conclusions

This study demonstrated that elevated NPAR on admission was independently related to the increased risk of in-hospital mortality of AAAD patients. In addition, the practicability, availability and low cost of NPAR make it a valuable biomarker, which plays a critical rolein predicting the in-hospital mortality of AAAD patients. For AAAD patients with high preoperative NPAR, more attention and closer monitoring should be given in clinical practice.

Author Contributions

We would like to acknowledge the valuable contributions made by each author to this article. Liangwan Chen and Yanjuan Lin conceived the whole study. Xuecui Zhang drafted the original manuscript and prepared the tables and figures. Lingyu Lin and Yanchun Peng were responsible for reviewing and editing the manuscript. Sailan Li and Xizhen Huang were in charge of data collecting. Xuecui Zhang and Lingyu Lin analyzed the data. All authors have contributed to the revision and refinement of the article, ensuring its clarity, coherence, and accuracy. We would like to express our gratitude to each author for their dedication, hard work, and invaluable contributions to this article.

Ethics Statement

This study was approved by the Ethics Committee of Fujian Medical University Union Hospital (Approval No: 2019KY019) and was by the Declaration of Helsinki.

Consent

Informed consent waivers were obtained because the data were anonymous.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data Availability Statement

Full data set available from the corresponding author. However, reanalysis of the full data needs to be approved by Fujian Medical University Union Hospital.

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