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Association Between Neutrophil Percentage-to-Albumin Ratio and 2-Year Mortality in Patients Undergoing Transcatheter Aortic Valve Replacement

ABSTRACT

Background: Transcatheter aortic valve replacement (TAVR) is the standard therapy for severe aortic stenosis, particularly in elderly patients with comorbidities. Simple biomarkers to predict mid-term mortality are still needed. This study evaluated the prognostic value of the preprocedural neutrophil percentage-to-albumin ratio (NPAR) for 2-year all-cause mortality after TAVR.

Methods: A total of 618 patients undergoing TAVR between 2013 and 2023 were retrospectively analyzed. NPAR was calculated as neutrophil percentage × 100 / albumin (g/dL), and patients were classified into tertiles. The prognostic role of NPAR was assessed using Cox regression, Kaplan–Meier survival analysis, and receiver operating characteristic curves.

Results: Baseline characteristics were similar across tertiles, but higher NPAR was associated with elevated inflammation and lower albumin levels. In multivariable Cox analysis, high NPAR independently predicted 2-year mortality (T3 vs. T1: hazard ratio [HR] 2.75, 95% CI 1.77-4.28; $P < .001$). In a model including both categorical NPAR and Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM), tertile 3 of NPAR (HR 2.49, 95% CI 1.61-3.85; $P < .001$) and STS-PROM (HR 1.31, 95% CI 1.12-1.53; $P = .001$) remained independent predictors, indicating incremental prognostic value of NPAR beyond established surgical risk scores. Kaplan–Meier curves showed the lowest survival in the highest tertile (35.9% mortality at 2 years). Receiver operating characteristic analysis confirmed NPAR had the best discriminatory ability (area under the curve = 0.703).

Conclusion: Preprocedural NPAR is an independent, low-cost, and readily available biomarker for predicting mid-term mortality after TAVR. Its integration into risk models may improve prediction accuracy and help guide patient management.

Keywords: Inflammation, mortality, neutrophils, prognostic value, serum albumin, transcatheter aortic valve replacement

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) is increasingly being used as an alternative to surgery in patients with severe symptomatic aortic stenosis. While current guidelines recommend TAVR for intermediate- and high-risk patients, studies demonstrating similar efficacy to surgery in low-risk groups have made it applicable to all risk groups.[1-4] While short-term procedural success rates are high thanks to increasing clinical experience and technological advancements, the observed mortality risk in the mid- and long-term remains a clinically significant problem.[5-9] In this context, predicting mortality risk with readily available, inexpensive, and reliable biomarkers before the procedure can contribute to personalized medical decisions in patient management.

In recent years, hematological and biochemical markers reflecting the relationship between systemic inflammation, nutritional status, and mortality have attracted attention.[10-12] Neutrophil percentage and serum albumin are 2 important parameters that provide information about inflammatory burden and nutritional reserve,

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respectively. The neutrophil percentage-to-albumin ratio (NPAR), combining these markers, has been proposed as a holistic indicator of inflammation and general health status, and has been associated with poor prognosis in cardiovascular conditions such as acute myocardial infarction, heart failure, and cardiogenic shock.[13-15] In contrast to the neutrophil-to-albumin ratio (NAR), which relies on the absolute neutrophil count, NPAR incorporates neutrophil percentage together with serum albumin. This distinct calculation may yield different prognostic insights. To the authors' knowledge, its prognostic relevance has never been explored in TAVR populations, positioning this study as the first to investigate this relationship.

Therefore, this study aimed to investigate the relationship between NPAR and 2-year all-cause mortality, and to evaluate the clinical utility of NPAR in predicting mortality after TAVR.

METHODS

Study Design and Population

A retrospective analysis was performed on consecutive patients who underwent TAVR at this institution, a tertiary cardiac center, from February 2013 to June 2023. The study was conducted in accordance with the Declaration of Helsinki and approved by the Local Ethics Committee (Date: August 19, 2025; Decision No.: 2025.07-75). Inclusion criteria were as follows: (1) TAVR was performed with a diagnosis of symptomatic severe aortic stenosis, (2) preprocedural complete blood count (CBC) and biochemistry data were available, and (3) at least 2 years of follow-up data were available. Exclusion criteria included active infection, malignancy, autoimmune disease, hematological malignancy, or use of immunosuppressive therapy, chronic liver disease, and patients referred to another center during follow-up or missing mortality data. Finally, a total of 618 eligible patients were included in the study (Figure 1).

Data Collection and Definitions

Study data were collected retrospectively through the hospital information system and patient follow-up files. Demographic characteristics (age, gender), comorbidities (hypertension, diabetes mellitus, coronary artery disease, peripheral artery disease, atrial fibrillation, stroke history), echocardiographic parameters (left ventricular ejection fraction [LVEF], aortic valve area, systolic pulmonary artery pressure [sPAP]), and preprocedure laboratory data (CBC, biochemistry, inflammatory markers) were systematically recorded.

Laboratory Analysis and Neutrophil Percentage-to-Albumin Ratio Calculation

All blood samples were collected within 24 hours before the TAVR procedure. Neutrophil percentage and serum albumin levels were measured from the same sample. Neutrophil percentage-to-albumin ratio, the ratio of these 2 variables, was calculated using the following formula: NPAR = Neutrophil percentage (%) × 100 / Albumin (g/dL). Neutrophil percentage-to-albumin ratio values were divided into 3 tertiles for use in statistical analyses in the study: low NPAR (Tertile 1), medium NPAR (Tertile 2), and high NPAR (Tertile 3).

Transcatheter Aortic Valve Replacement Procedure

All patients were thoroughly evaluated by a multidisciplinary cardiac team and considered candidates for TAVR after being determined to be at high risk for valve surgery. All TAVR procedures were performed in a fully equipped hybrid operating room using a transfemoral approach. The method of anesthesia (local or general) was made at the discretion of the operator and the anesthesiologist, considering the clinical indications. Valve type and size were determined according to manufacturer recommendations based on computed tomography and echocardiography findings. The following transcatheter valve designs were used: CoreValve Evolut R (Medtronic, Minneapolis, Minn, USA), Portico (St. Jude Medical, St. Paul, Minneapolis, Minn, USA), Acurate neo2 (Boston Scientific, Marlborough, MA, USA), Sapien XT/Sapien 3 (Edwards Lifesciences, Irvine, California, USA), and Myval (Meril Life Sciences Private Ltd., Gujarat, India). Predilation of the native aortic valve was performed at the operator's discretion. Postdilation under rapid pacing was considered in cases of moderate or severe paravalvular aortic regurgitation and/or underdilatation of the prosthesis. A percutaneous closure system (Perclose ProGlide; Abbott Laboratories, Abbott Park, Illinois) was used to close the vascular access site. A temporary pacemaker was placed as a backup for high-degree atrioventricular (AV) block when necessary. Postprocedural care was conducted in accordance with current guidelines.[1,2]

Follow-Up and Clinical Endpoints

Patients were followed up at outpatient clinic visits and by telephone when necessary. Death information was verified with the National Death Notification System and hospital records. All clinical endpoints were defined according to Valve Academic Research Consortium-3 (VARC-3) criteria.[16] The primary endpoint was 2-year all-cause mortality after TAVR. Secondary endpoints included 30-day stroke, major vascular complications, bleeding, acute kidney injury, myocardial infarction, and new permanent pacemaker implantation.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 24 software

HIGHLIGHTS

- Neutrophil percentage-to-albumin ratio (NPAR) provides a simple and low-cost biomarker for risk stratification in transcatheter aortic valve replacement (TAVR) patients.
- Higher NPAR levels are independently associated with increased all-cause mortality over 2 years.
- This study is the first to demonstrate the prognostic utility of NPAR in the TAVR population.
- Neutrophil percentage-to-albumin ratio offers incremental prognostic value beyond STS-PROM, supporting its integration into existing risk models.

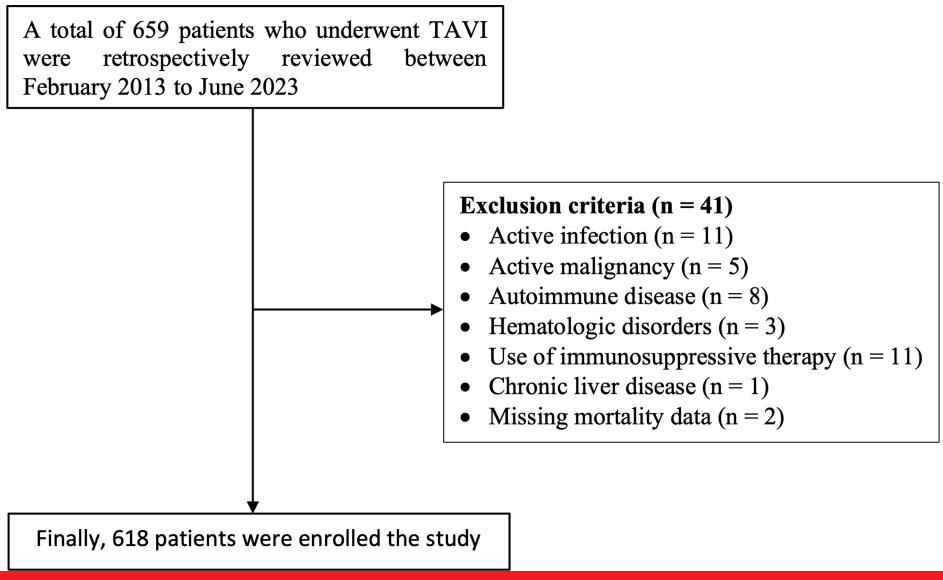

Figure 1. Flowchart of the study population.

package (SPSS Inc., Chicago, Illinois, USA). The normality of distribution of continuous variables was evaluated using both graphical (histograms) and numerical methods. Among numerical tests, both Kolmogorov–Smirnov and Shapiro–Wilk tests were performed to ensure robustness. As each group included more than 200 patients, the Kolmogorov–Smirnov test was considered more appropriate for evaluating normality. One-way ANOVA was used for normally distributed data, and the Kruskal–Wallis test was used for non-normally distributed data. Comparisons between categorical data were made using the Chi-square or Fisher's exact test. Continuous variables are presented as mean ± SD or median and interquartile range. Categorical variables are expressed as numbers (percentages). The predictive power of NPAR, neutrophil percentage, and albumin levels for mortality was assessed using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) for each parameter was calculated and reported with its 95% CI. The optimal cut-off value of NPAR for predicting 2-year all-cause mortality was determined using the Youden index. Comparisons between ROC curves were performed using the DeLong test. All-cause survival time was analyzed using the Kaplan–Meier method, and survival curves were plotted for the 3 NPAR groups. The difference between the groups was assessed using the log-rank test. Median survival time and event incidence rates were calculated separately for 30 days, 1 year, and 2 years. Cox proportional hazards regression analyses were performed to identify independent risk factors associated with 2-year mortality. Analyses were performed as follows: Univariable analysis for all available variables; Multivariable Model 1, including demographic, clinical, and laboratory variables with $P < .10$ in univariable analysis; and Multivariable Model 2, including Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) and categorical NPAR simultaneously to avoid multicollinearity with individual variables incorporated within STS-PROM. The model results are presented with hazard ratio (HR) and 95% CI. Statistical significance was set at $P < .05$.

RESULTS

Demographic and Clinical Characteristics

A total of 618 patients were included in this study. Demographic characteristics, comorbidities, laboratory, and echocardiographic parameters were compared among the 3 tertiles established according to NPAR (Table 1). The mean age was 78.5 ± 7.0 years, and 41.9% of the patients were male. The most common comorbidities were hypertension (76.4%), coronary artery disease (69.1%), and diabetes mellitus (45.1%). Demographic data and comorbidities were similar between the groups ($P > .05$). However, laboratory findings revealed that as NPAR increased, the neutrophil percentage increased, while albumin levels decreased ($P < .001$ for both). White blood cell and neutrophil counts were highest in the T3 group ($P = .032$ and $P < .001$), while the lymphocyte count was inversely proportional ($P < .001$). Hemoglobin levels were lowest in the T3 group ($P < .001$). The difference between groups for C-reactive protein (CRP) and creatinine was not statistically significant. Left ventricular ejection fraction and sPAP differed significantly with NPAR ($P = .001$ and $P = .041$).

Procedural Characteristics and Clinical Outcomes

A total of 66.8% of patients underwent TAVR under conscious sedation, and these rates were similar between the groups. There were no significant differences in procedure time, contrast amount, or the intensive care unit stay ($P > .05$). However, the length of hospitalization was longer in the high NPAR group (median 9 days; $P = .024$). No differences were observed between the groups in terms of valve type, size, or gradients. Clinical outcome data are summarized in Table 2. Significant increases in 30-day, 1-year, and 2-year mortality rates were observed with increasing NPAR levels ($P = .006$, $P < .001$, $P < .001$, respectively). Cardiovascular mortality was similarly associated with NPAR ($P = .006$). There were no significant differences in secondary endpoints.

Predictors of Mortality

In the multivariable Cox proportional hazards regression analysis, 2 separate models were constructed (Table 3): Model

Table 1. Baseline Characteristics According to Neutrophil Percentage-to-Albumin Ratio Tertiles

Variables	Total (n = 618)	Neutrophil Percentage-to-Albumin Ratio			P
		Tertile 1 ≤14 (n = 206)	Tertile 2 14-20 (n = 206)	Tertile 3 ≥20 (n = 206)	
Age (years)	78.50 ± 7.03	78.05 ± 7.46	78.39 ± 7.01	79.05 ± 6.61	.342
Sex (male), n (%)	259 (41.9)	87 (42.2)	83 (40.3)	89 (43.2)	.830
Comorbidities, n (%)					
Hypertension	472 (76.4)	165 (80.1)	154 (74.8)	153 (74.3)	.303
Diabetes mellitus	279 (45.1)	94 (45.6)	85 (41.3)	100 (48.5)	.327
Coronary artery disease	427 (69.1)	149 (72.3)	138 (67.0)	140 (68.0)	.458
Previous CABG	127 (20.6)	50 (24.3)	38 (18.4)	39 (18.9)	.268
Peripheral artery disease	114 (18.4)	37 (18.0)	35 (17.0)	42 (20.4)	.657
Chronic lung disease	196 (31.7)	59 (28.6)	66 (32.0)	71 (34.5)	.443
Chronic kidney disease	169 (27.3)	50 (24.3)	55 (26.7)	64 (31.1)	.292
Previous Stroke/TIA	35 (5.7)	13 (6.3)	9 (4.4)	13 (6.3)	.616
Paroxysmal or persistent atrial fibrillation	118 (19.1)	31 (15.0)	39 (18.9)	48 (23.3)	.103
Prior pacemaker	20 (3.2)	5 (2.4)	9 (4.4)	6 (2.9)	.511
STS-PROM score: mortality (%)	6.22 ± 0.80	6.12 ± 0.76	6.18 ± 0.90	6.35 ± 0.71	.010
Laboratory parameters					
Neutrophil percentage, %	63.1 ± 10.4	53.1 ± 7.2	63.5 ± 5.7	72.6 ± 7.1	<.001
Albumin, g/dL	3.90 ± 0.41	4.14 ± 0.33	3.96 ± 0.33	3.61 ± 0.38	<.001
NPAR	16.38 ± 3.51	12.83 ± 1.54	16.04 ± 0.75	20.28 ± 2.51	<.001
White blood cell, 10^9/L	7.54 ± 3.31	7.31 ± 2.52	7.28 ± 2.23	8.04 ± 4.62	.032
Hemoglobin, g/dL	11.35 ± 1.64	11.60 ± 1.57	11.54 ± 1.61	10.90 ± 1.66	<.001
Neutrophil, 10^9/L	4.87 ± 2.98	4.28 ± 1.89	4.63 ± 1.49	5.69 ± 4.45	<.001
Lymphocyte, 10^9/L	1.82 ± 1.23	2.17 ± 1.50	1.79 ± 1.28	1.49 ± 0.65	<.001
CRP, mg/L	6.5 (16.2)	4.0 (8.1)	6.0 (17.1)	11 (17.1)	.314
Creatine, mg/dL	1.14 ± 0.65	1.10 ± 0.60	1.11 ± 0.77	1.21 ± 0.54	.138
Total cholesterol, mg/dL	156 ± 73	160 ± 73	150 ± 76	156 ± 69	.467
Echocardiographic parameters					
LVEF (%)	60 (14)	60 (10)	60 (10)	55 (20)	.001
Aortic valve area (cm^2)	0.72 ± 0.16	0.73 ± 0.18	0.72 ± 0.14	0.70 ± 0.15	.268
Maximum aortic gradient (mm Hg)	77.27 ± 32.94	80.76 ± 47.60	76.71 ± 23.53	74.39 ± 20.74	.147
Mean aortic gradient (mm Hg)	48.12 ± 13.38	49.21 ± 13.49	47.73 ± 13.37	47.41 ± 13.27	.357
Aortic peak systolic velocity (m/s)	4.33 ± 0.61	4.37 ± 0.48	4.35 ± 0.68	4.27 ± 0.64	.362
Systolic pulmonary arterial pressure	42 ± 13.82	42.67 ± 14.25	40.72 ± 13.81	44.67 ± 13.26	.041

Continuous variables are presented as mean ± SD or median (interquartile range). Categorical variables are presented as number (percentage).
CABG, coronary artery bypass grafting; CRP, C-reactive protein; LVEF, left ventricular ejection fraction; NPAR, neutrophil-percentage-to-albumin ratio; STS, Society of Thoracic Surgeons; TIA, transient ischemic attack.

1: including demographic, clinical, and laboratory variables with $P < .10$ in univariable analysis (excluding STS-PROM). In this model, categorical NPAR remained an independent predictor of 2-year all-cause mortality. The risk of mortality was significantly higher in individuals in Tertile 3 compared to Tertile 1 (HR: 2.75; 95% CI: 1.77-4.28; $P < .001$). The increase in Tertile 2 showed borderline significance (HR: 1.59; 95% CI: 0.99-2.55; $P = .055$). Peripheral arterial disease (HR: 1.52; 95% CI: 1.03-2.25; $P = .034$) and serum creatinine level (HR: 1.26; 95% CI: 1.05-1.50; $P = .011$) were also independent factors increasing the risk of mortality. In contrast, previous CABG history was identified as an independent protective factor reducing mortality risk (HR: 0.52; 95% CI: 0.32-0.84; $P = .009$).

Model 2: including both categorical NPAR and STS-PROM. In this model, STS-PROM was independently associated with 2-year mortality (HR: 1.31; 95% CI: 1.12-1.53; $P = .001$). Among the NPAR categories, patients in Tertile 3 had a significantly higher risk of 2-year mortality compared with Tertile 1 (HR: 2.49; 95% CI: 1.61-3.85; $P < .001$), while Tertile 2 showed only a borderline association (HR: 1.55; 95% CI: 0.96-2.49; $P = .068$). These findings indicate that NPAR provides incremental prognostic value beyond STS-PROM, primarily driven by the highest NPAR tertile.

Survival Analysis

Kaplan–Meier survival curves for 2-year all-cause mortality showed a significant difference in survival between

Table 2. Procedural Characteristics and Primary/Secondary Clinical Outcomes According to Neutrophil Percentage-to-Albumin Ratio Tertiles

Variables	Total (n = 618)	Neutrophil Percentage-to-Albumin Ratio			*P*
		Tertile 1 ≤14 (n = 206)	Tertile 2 14-20 (n = 206)	Tertile 3 ≥20 (n = 206)	
Procedural characteristics, n (%)					
Conscious sedation	413 (66.8)	136 (66.0)	143 (69.4)	134 (65.0)	.613
Procedure time*, min	71 (35)	73 (39)	72 (36)	70 (34)	.573
Total contrast used (mL)	150 (90)	150 (88)	150 (94)	150 (90)	.386
ICU stay, days	2 (3)	2 (3)	2 (3)	2 (4)	.357
Discharge time, days	8 (7)	7 (5)	7 (6)	9 (5)	.024
Valve type, self	273 (44.2)	91 (44.2)	82 (39.8)	100 (48.5)	.203
Valve size	26.36 ± 2.82	26.41 ± 2.68	26.13 ± 2.83	26.56 ± 2.82	.283
Primary outcomes, n (%)					
30-day mortality	46 (7.4)	9 (4.4)	12 (5.8)	25 (12.1)	.006
1-year mortality	107 (17.3)	17 (8.3)	35 (17.0)	55 (26.7)	<.001
2-year mortality	147 (23.8)	28 (13.6)	45 (21.8)	74 (35.9)	<.001
Secondary outcomes, n (%)					
Cardiovascular mortality	76 (12.3)	16 (7.8)	23 (11.2)	37 (18.0)	.006
All stroke	18 (2.9)	4 (1.9)	5 (2.4)	9 (4.4)	.143
Bleeding and transfusions (≥Type 2)	138 (22.3)	51 (24.8)	47 (22.8)	40 (19.4)	.420
Major vascular and access-related complications	48 (7.8)	21 (10.2)	13 (6.3)	14 (6.8)	.276
Moderate or severe aortic regurgitation	20 (3.3)	7 (3.4)	5 (2.5)	8 (3.9)	.708
Acute kidney injury stage 3 or 4	24 (3.9)	4 (1.9)	7 (3.4)	13 (6.3)	.065
Myocardial infarction	6 (1.0)	2 (1.0)	1 (0.5)	3 (1.5)	.616
New permanent pacemaker	105 (17.0)	36 (17.5)	38 (18.4)	31 (15.0)	.639

Continuous variables are presented as mean ± SD or median (interquartile range). Categorical variables are presented as number (percentage).
ICU, intensive care unit.

NPAR tertiles (Figure 2). Patients in the highest tertile (Tertile 3) had the lowest cumulative survival, while those in the lowest tertile (Tertile 1) had the highest probability of survival. Event rates at the end of follow-up were 13.6%, 21.8%, and 35.9% for Tertiles 1, 2, and 3, respectively. Median survival time decreased to 666.0 days (95% CI: 640.5-691.5) in Tertile 1, 617.2 days (95% CI: 584.7-649.7) in Tertile 2, and 535.5 days (95% CI: 495.4-575.5) in Tertile 3. According to the log-rank test, there was a statistically significant difference in survival distributions between NPAR tertiles ($P < .001$).

Receiver Operating Characteristic Curve Analysis

The predictive power of NPAR, albumin, and neutrophil percentage for all-cause mortality was evaluated using ROC analyses. The ROC curves of the 3 variables are presented together in Figure 3. Receiver operating characteristic analysis yielded an AUC of 0.703, with an optimal cut-off value of NPAR = 16.07 (sensitivity 75.5%, specificity 58.2%) for predicting 2-year all-cause mortality ($P < .001$). The AUC for neutrophil percentage and albumin was 0.634 and 0.668, respectively, while NPAR showed the highest AUC (0.703) and was superior to both markers in predicting mortality (DeLong test, $P < .05$). These results indicate that NPAR provides moderate but superior discriminatory ability compared with traditional parameters.

DISCUSSION

This is the first study to evaluate the relationship between preprocedural NPAR and all-cause mortality in patients undergoing TAVR. Mortality rates were observed to gradually increase with increasing NPAR values. Receiver operating characteristic curve analysis demonstrated that NPAR had a higher predictive value than albumin levels and neutrophil percentage. Multivariable Cox regression analysis demonstrated that elevated NPAR was independently associated with mortality. These results suggest that NPAR can be used as a simple, inexpensive, and accessible prognostic marker in TAVR patients.

Neutrophil percentage is one of the main cellular components involved in the acute phase response to inflammation. Neutrophils are known to play a central role in the triggering of cardiovascular events and contribute to endothelial dysfunction and atherothrombotic processes.[17-20] A strong correlation has been demonstrated between elevated neutrophil percentage and mortality, particularly in conditions such as acute myocardial infarction, cardiogenic shock, and heart failure.[13-15,21,22] Excessive activation of neutrophils can increase myocardial damage through the release of inflammatory cytokines and procoagulant effects. On the other hand, serum albumin level is an important indicator

Table 3. Univariable and Multivariable Cox Proportional Hazards Regression Analyses of 2-Year All-Cause Mortality

Univariable analysis				
Variables	**HR (95% CI)**	**P**		
Age (years)	1.01 (0.99-1.04)	.131		
Sex (male)	1.29 (0.93-1.78)	.119		
Hypertension	0.80 (0.55-1.15)	.231		
Diabetes mellitus	1.23 (0.89-1.70)	.199		
Coronary artery disease	0.83 (0.59-1.17)	.304		
Previous CABG	0.56 (0.35-0.90)	.018		
Peripheral artery disease	1.39 (0.94-2.04)	.091		
Chronic lung disease	1.17 (0.83-1.64)	.365		
Chronic kidney disease	1.84 (1.32-2.56)	<.001		
Previous Stroke/TIA	1.48 (0.82-2.68)	.188		
Paroxysmal or persistent atrial fibrillation	1.01 (0.67-1.52)	.959		
Prior pacemaker	0.37 (0.09-1.50)	.164		
STS-PROM score	1.33 (1.15-1.54)	<.001		
LVEF	0.98 (0.97-0.99)	.007		
Systolic pulmonary arterial pressure	1.01 (0.99-1.02)	.137		
Neutrophil percentage	1.04 (1.02-1.05)	<.001		
Albumin	0.27 (0.19-0.40)	<.001		
NPAR		<.001		
Tertile 1	1.0 (reference)			
Tertile 2	1.68 (1.05-2.70)	.030		
Tertile 3	3.08 (1.99-4.76)	<.001		
White blood cell	1.00 (0.95-1.05)	.902		
Hemoglobin	0.92 (0.83-1.01)	.106		
CRP	1.00 (1.00-1.01)	.067		
Creatine	1.32 (1.12-1.55)	.001		
Total cholesterol	1.00 (0.99-1.00)	.946		
Valve type, self	1.17 (0.85-1.62)	.331		
Conscious sedation	0.79 (0.56-1.10)	.171		
Multivariable analysis				
Variables	**Model 1 for NPAR and clinical variables**		**Model 2 for NPAR and STS-PROM**	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***
Previous CABG	0.52 (0.32-0.84)	.009		
Peripheral artery disease	1.52 (1.03-2.25)	.034		
LVEF	0.98 (0.97-1.00)	.080		
CRP	1.00 (0.99-1.01)	.335		
Creatine	1.26 (1.05-1.50)	.011		
NPAR, categorical		<.001		<.001
Tertile 1	1.0 (reference)			
Tertile 2	1.59 (0.99-2.55)	.055	1.55 (0.96-2.49)	.068
Tertile 3	2.75 (1.77-4.28)	<.001	2.49 (1.61-13.85)	<.001
STS-PROM score			1.31 (1.12-1.53)	.001

CABG, coronary artery bypass grafting; CRP, C-reactive protein; HR, hazard ratio; LVEF, left ventricular ejection fraction; NPAR, neutrophil-percentage-to-albumin ratio; STS, Society of Thoracic Surgeons; TIA, transient ischemic attack.

of chronic inflammation, malnutrition, and liver function. Hypoalbuminemia has been associated with an increased risk of mortality in elderly patients and has been used as an independent prognostic marker in various cardiovascular conditions.[23-25] The antioxidant and anti-inflammatory properties of albumin play an important role in maintaining vascular integrity. Therefore, a decrease in albumin level may indicate advanced systemic inflammation and decreased physiological reserve. Neutrophil percentage-to-albumin ratio is the combination of these 2 parameters and is a composite biomarker that simultaneously reflects systemic inflammation, as indicated by neutrophil

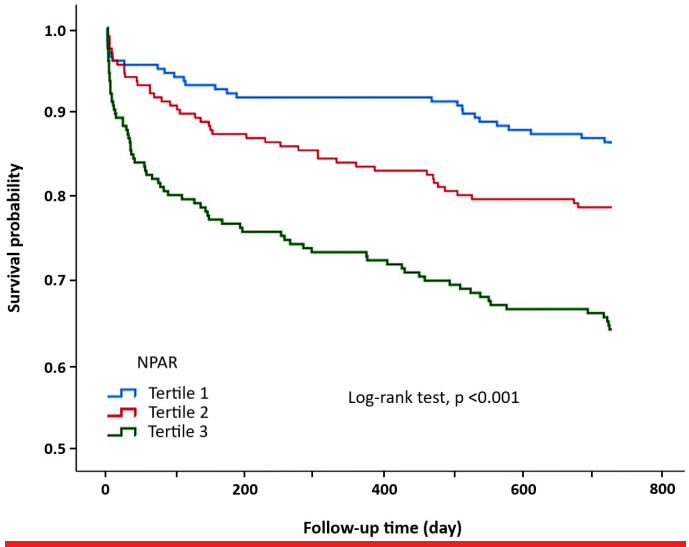

Figure 2. Kaplan–Meier curves of 2-year all-cause mortality according to NPAR tertiles. NPAR, neutrophil percentage-to-albumin ratio.

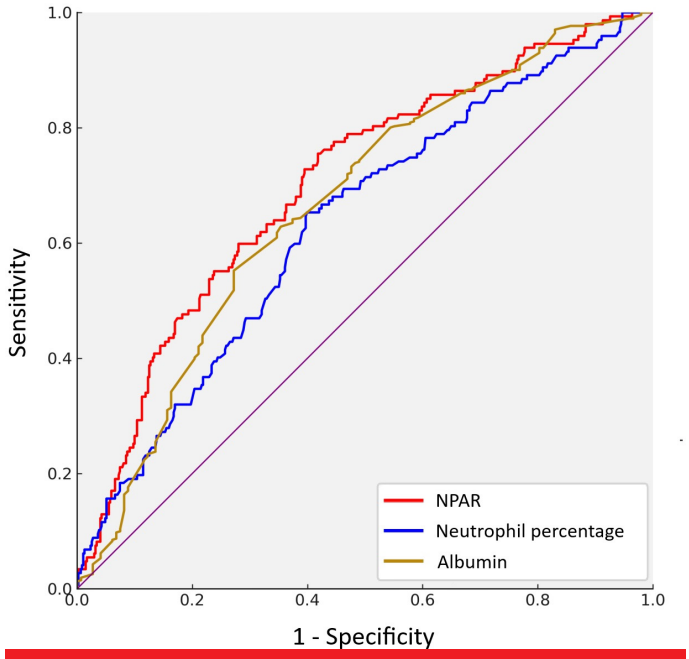

Figure 3. Receiver operating characteristic curves showing the predictive value of NPAR, neutrophil percentage, and albumin for the prediction of 2-year all-cause mortality. AUC for NPAR = 0.703, 95% CI 0.655-0.751, $P < .001$; AUC for neutrophil percentage = 0.634, 95% CI 0.582-0.685, $P < .001$; AUC for albumin = 0.668, 95% CI 0.616-0.719, $P < .001$. AUC, area under the curve; NPAR, neutrophil percentage-to-albumin ratio.

percentage, and nutritional/immune reserve, as indicated by albumin level.

The patient group undergoing TAVR generally consists of individuals with advanced age, a high comorbidity burden, and increased frailty. In this patient group, postoperative outcomes and prognosis are closely related not only to the correction of valvular pathology but also to parameters such as systemic inflammatory burden and nutritional status. Previous studies have investigated the prognostic role of other inflammation-based indices in TAVR populations. For example, both the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio have been associated with increased mortality and adverse cardiovascular events after TAVR, suggesting that systemic inflammation plays a central role in determining outcomes.[10,26] Similarly, the C-reactive protein/albumin ratio has been linked with poor prognosis, emphasizing the combined importance of inflammatory burden and nutritional reserve.[27] Taken together, these findings support the utility of composite biomarkers that integrate different biological dimensions. The current results with NPAR are consistent with this line of evidence, reinforcing the prognostic significance of systemic inflammation and nutritional status in TAVR patients.

It is important to distinguish NPAR from the NAR. While NAR uses the absolute neutrophil count, NPAR is derived from neutrophil percentage in combination with serum albumin.[28] This methodological difference may influence its prognostic implications, as percentage-based indices may better capture relative leukocyte distribution in systemic inflammation. To date, no study has evaluated NPAR in TAVR patients, making this work the first to address this gap in the literature. Importantly, in a dedicated model including both STS-PROM and NPAR, each variable remained independently associated with mortality, suggesting that NPAR provides incremental prognostic information beyond established surgical risk scores.

This study showed that as NPAR levels increased, 30-day, 1-year, and 2-year mortality rates increased significantly. Furthermore, Kaplan–Meier survival analysis revealed significantly shorter survival in the higher NPAR tertile. These findings suggest that NPAR is a strong predictor of clinical outcomes after TAVR. Kaplan–Meier survival analysis further confirmed that high NPAR levels were associated with significantly increased 2-year all-cause mortality. The approximately 22% difference in mortality rates across tertiles and the median survival time exceeding 130 days suggest that NPAR is a strong predictor of clinical outcome after TAVR.

In this study, patients with elevated NPAR experienced longer hospital stays following TAVR. This observation may reflect underlying biological mechanisms linking inflammation and frailty to adverse perioperative outcomes. Elevated systemic inflammation can impair wound healing and increase vulnerability to complications, while low albumin levels may signal impaired nutritional reserve and reduced physiological resilience.[23-25] Furthermore, frailty—a common feature in elderly TAVR candidates—may exacerbate these effects, contributing to delayed convalescence and extended hospitalization. Taken together, these findings suggest that NPAR not only predicts long-term mortality but may also be associated with short-term clinical trajectories, underscoring its potential relevance for perioperative management.

In the ROC analysis, the AUC value for NPAR (0.703) indicates moderate predictive power, which is higher than its

individual components, such as albumin (0.668) and neutrophil percentage (0.634). This finding suggests that composite markers such as NPAR may have stronger prognostic capacity than individual laboratory parameters, consistent with previous reports in patients with coronary artery disease and heart failure.[13,15,29] The ROC-derived threshold further supports the potential clinical applicability of NPAR, although its discriminatory ability remains moderate and should be interpreted with caution. While tertile-based categorization enabled exploratory risk stratification, the ROC cut-off provides a more practical benchmark for potential clinical use.

In multivariable Cox regression analysis, elevated NPAR remained an independent predictor of 2-year all-cause mortality, even after adjusting for classical risk factors such as age, LVEF, creatinine, and peripheral artery disease. Patients in the Tertile 3 group, in particular, had a 2.75-fold higher risk of mortality compared to the reference group (HR: 2.75; 95% CI: 1.77-4.28; $P < .001$). This finding highlights the robustness of NPAR as a prognostic marker and supports its potential integration into existing risk scoring systems. Additionally, high creatinine levels and peripheral artery disease negatively impacted survival, indicating that systemic vascular health plays a decisive role in prognosis after TAVR. Interestingly, prior CABG has been identified as a protective factor in terms of mortality. This suggests that myocardial perfusion achieved through revascularization may have a favorable contribution to mid-term prognosis. Importantly, in the current analysis, STS-PROM emerged as a significant predictor of mortality, consistent with prior literature.[30] To account for potential multicollinearity, a dedicated model including both STS-PROM and categorical NPAR was constructed. In this model, each variable remained independently associated with 2-year mortality, suggesting that NPAR provides incremental prognostic information beyond STS-PROM. This finding highlights the potential value of incorporating NPAR alongside established surgical risk scores in clinical decision-making.

Risk assessment in TAVR patients has traditionally relied on scores such as STS-PROM and EuroSCORE II, developed for surgical populations and currently widely used.[31-33] The STS-PROM score does include measurements of Hb, WBC, and platelet count in addition to a myriad of clinical characteristics, highlighting that these blood markers are important prognostic tools in the preoperative workup. In recent years, it has been demonstrated that inflammation-based indices such as NLR and platelet-to-lymphocyte ratio (PLR) can provide prognostic value equivalent to or even superior to established risk scores.[10,34,26] Consistent with these findings, the current study demonstrated that NPAR, which reflects both systemic inflammation and nutritional reserve, has prognostic value independent of STS-PROM. Neutrophil percentage-to-albumin ratio is an easily accessible and cost-effective indicator that can be calculated using standard biochemical parameters, providing an additional advantage in clinical practice. Integrating this parameter into risk models may contribute to more accurate identification and close monitoring of patients, particularly those with frailty or a high inflammatory burden. The prognostic value of NPAR has been previously demonstrated in acute myocardial infarction, congestive heart failure, cardiogenic shock, and intensive care populations, and the current study extends this knowledge specifically to TAVR patients.[14,21,22,35,36] In conclusion, these findings suggest that NPAR is an independent marker and may enhance the accuracy of prognostication in TAVR populations by complementing existing risk scores and clinical variables.

Study Limitations

This study has several limitations. First, due to its retrospective design, a causal relationship cannot be established. Second, it was conducted at a single center with a limited patient population, which may affect the generalizability of the results. In addition, the long inclusion period (2013-2023) coincided with significant advances in TAVR technology and practice that could have influenced outcomes. Moreover, other markers of inflammation [e.g., CRP, interleukin (IL)-6, tumor necrosis factor-α (TNF-α)] were not included, preventing a comprehensive evaluation of inflammatory processes. Finally, patients with malignancy or autoimmune disease were excluded, although they constituted only a relatively small subgroup. This exclusion was necessary to minimize potential confounding effects of systemic inflammation or cachexia on NPAR values and is therefore unlikely to have significantly impacted the overall findings. Nevertheless, the large patient number, mid-term follow-up period, and adjustment for numerous potential confounding factors represent important strengths of this study.

Future Directions

Future studies should aim to further evaluate the prognostic value of NPAR and support its integration into clinical decision-making. In particular, temporal changes in NPAR should be monitored, and their association with short- and mid-term outcomes after TAVR should be clarified. Moreover, randomized controlled trials assessing the impact of preoperative interventions targeting inflammation and nutritional optimization on survival in patients with high NPAR levels are warranted. Combining NPAR with existing risk scoring systems to develop novel prognostic models could further enhance individualized patient management.

In conclusion, this study demonstrates that NPAR is an independent, accessible, and low-cost biomarker for predicting mid-term all-cause mortality in patients undergoing TAVR. Incorporating NPAR into routine clinical assessment could help refine risk stratification and guide postprocedural management in this growing patient population.

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics (Committee date: August 19, 2025; Decision no: 2025.07-75).

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