Original article

The impact of the Naples Prognostic Score on the short- and long-term prognosis of patients undergoing transcatheter aortic valve implantation

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Background Preoperative systemic inflammation and nutritional status have been shown to affect prognosis in patients undergoing transcatheter aortic valve implantation (TAVI). In this study, we investigated the effect of the Naples Prognostic Score (NPS), which consists of four different parameters including these two components on short- and long-term prognosis in patients undergoing TAVI.

Methods In 343 patients (mean age 78.1 ± 8.4 years, 51.3% female) who underwent TAVI, the NPS score was calculated from the blood tests obtained before the procedure and the study population was divided into three according to the NPS value: those with 0 and 1 were divided into Group-1, those with 2 into Group-2, and those with 3 and 4 into Group-3. The relationship between NPS group and in-hospital adverse events and long-term survival was evaluated.

Results Systolic pulmonary artery pressure, STS score, presence of chronic lung disease and being in NPS Group-3 [adjusted odds ratio (adjOR): 3.93, 95% confidence interval (CI) (1.02–15.17), $P = 0.047$] were found to be independent predictors of in-hospital mortality. According to the multivariate Cox-regression model, both Group-2 NPS [adjusted hazard ratio (adjHR): 4.81, 95% CI (1.09–21.14), $P = 0.037$] and Group-3 NPS [adjHR: 10.1, 95% CI (2.31–43.36), $P = 0.002$] was an independent predictor of 2-year all-cause mortality after TAVI. There was no significant difference in perioperative adverse events between the groups except for postprocedural acute kidney injury. According to receiver-operating characteristic analysis, the optimal predictive value of NPS for in-hospital and long-term mortality was 2.5.

Conclusion In patients who will be candidates for TAVI, NPS is a simple and effective tool for determining both short- and long-term prognosis.

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Keywords: aortic stenosis, inflammation, malnutrition, Naples Prognostic Score, transcatheter aortic valve implantation

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Introduction

Aortic stenosis (AS) is a prevalent cardiac valvular disease among the elderly, primarily driven by age-related degenerative changes in the aortic valve.[1] These changes are often accelerated by cardiovascular risk factors such as hypertension, dyslipidemia, atherosclerosis, and chronic kidney disease, leading to a progressive narrowing of the aortic valve area through senile degeneration, calcification, and chronic inflammation.[2] A critical juncture in the clinical trajectory of AS is the onset of symptoms, marking a significant escalation in disease severity. This transition is associated with a marked increase in adverse outcomes. Thus, the onset of symptoms in AS is a vital indicator for timely and appropriate therapeutic interventions.[3] In the elderly population, particularly those aged 75 years and above, transcatheter aortic valve implantation (TAVI) has emerged as an effective and safe long-term treatment option for severe AS.[3,4] The success of TAVI in this demographic underscores the importance of precise patient selection and rigorous risk stratification. While traditional risk classification systems like the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) and EuroSCORE II are commonly employed, these were initially developed for patients undergoing open-heart surgery and may not fully address the unique predictive needs of the TAVI patient group.[5,6] Consequently, the inclusion of additional prognostic tools, such as specific imaging and laboratory parameters, is crucial in enhancing the accuracy of risk assessment and patient selection for TAVI.[7–10]

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Implication of Naples Prognostic Score

The Naples Prognostic Score (NPS) is a composite scoring system based on four laboratory parameters that assess patients' systemic inflammation and nutritional status. Initially validated in various chronic inflammatory and oncologic diseases, its utility has extended into the field of cardiovascular diseases.[11–16] Recent research has explored the efficacy of NPS in prognosticating outcomes and assessing disease severity in heart failure, coronary artery disease, and pulmonary embolism, thereby broadening its application beyond its traditional scope.[17–20]

Background and objective

The most common form of AS, senile degenerative AS, often treated with TAVI, is characterized by progressive fibro-calcific remodeling and thickening of the aortic valve leaflets due to a combination of genetic factors, lipoprotein accumulation and oxidation, prolonged inflammation and osteoblastic transformation of interstitial cells in the heart valve.[21] In this group of elderly patients, comorbid systemic diseases, decreased physical capacity and mental dysfunction in some patients may lead to malnutrition. Indeed, impaired nutritional indices have been associated with poor prognosis in patients undergoing TAVI.[22]

The aim of this study was to determine the association of NPS, which is calculated from preoperative blood tests and represents the level of systemic inflammation and nutritional status, with both in-hospital and 2-year long-term mortality in patients undergoing TAVI for severe AS.

Methods

Study population and design

This retrospective analysis focuses on a cohort of 396 patients, treated with TAVI for symptomatic severe AS at a tertiary care center from 2015 to 2021. We carefully applied exclusion criteria, eliminating individuals with active infections ($N=13$), significant anemia (hemoglobin levels $<$ 8 g/dl, $N=7$), advanced chronic renal [glomerular filtration rate (GFR) $\leq$30 ml/min/1.73 m^2] or Child-Pugh class C hepatic insufficiencies ($N=21$), autoimmune inflammatory disorders ($N=7$), and those under continuous corticosteroid therapy ($N=5$). This selection process resulted in a final study population of 343 patients. Each patient underwent a comprehensive preprocedural evaluation, including detailed transthoracic echocardiography (TTE) performed by seasoned cardiologists (Vivid E9, GE, Milwaukee, USA), aligning with contemporary imaging standards, to affirm the diagnosis of severe AS.[23] Additionally, a thorough documentation of preprocedural clinical, demographic, electrocardiographic, additional imaging features, and laboratory findings was conducted for all participants.

Transcatheter aortic valve implantation and postoperative follow-up

Experienced interventional cardiologists performed TAVI using balloon-expandable valves such as Edwards SAPIEN S3 and XT (Edwards Lifesciences Corporation, CA, USA), Myval (Meril Life Sciences, India), and self-expandable valves like Medtronic CoreValve Evolut R System (Medtronic, Minneapolis, USA) and Portico (St. Jude Medical, Minneapolis, USA). These procedures were predominantly conducted under deep sedation using a transfemoral approach and achieved high success rates. The Perclose ProGlide system (Abbott Vascular, CA, USA) or Angioseal (St. Jude Medical, St. Paul, MN, USA) were employed for hemostasis at the femoral artery access point. Patients were closely monitored for intraoperative and postoperative potential complications, with adverse events documented according to Valve Academic Research Consortium (VARC-3) criteria.[24] Patients who survived the hospital stay were discharged with appropriate medical treatment and followed up every 6 months for 2 years.

Definition of the Naples Prognostic Score

NPS, the pivotal metric in this study, was calculated based on blood tests conducted after eight hours of fasting during the last five days before the procedure. NPS comprises four blood parameters assessing systemic inflammation and nutritional status of the patients. These parameters are defined as total cholesterol (TC) $\leq$180 mg/dl, serum albumin $<$4 g/dl, neutrophil–lymphocyte ratio (NLR) $>$2.96, and lymphocyte–monocyte ratio (LMR) $\leq$4.44. Patients received one point for each parameter, resulting in a total NPS score ranging from 0 to 4. In this study, patients with NPS $=$ 0 and 1 were categorized as Group-1, those with NPS $=$ 2 as Group-2, and patients with NPS $=$ 3 and 4 were classified as Group-3 (Fig. 1).

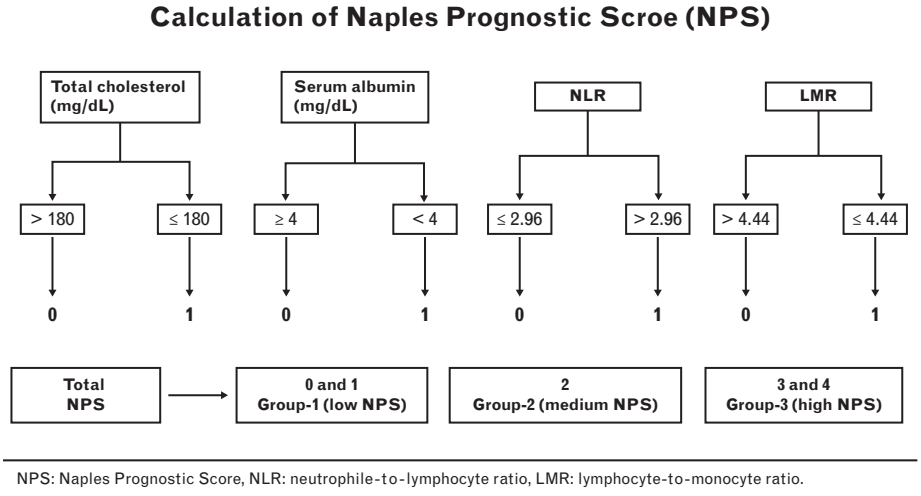
Primary endpoints

The study's two primary endpoints are in-hospital mortality and overall 2-year long-term all-cause mortality.

Data collection and ethics

Clinical data for all included patients were retrospectively collected from the hospital database. Written consent was obtained from patients undergoing interventional treatment, and ethical approval was granted by the Ethics Committee of Istanbul Medipol University. The study was conducted in accordance with the Declaration of Helsinki.

Fig. 1



The Naples Prognostic Score, which includes four different components derived from preoperative blood tests.

Statistical analyses

The assessment of continuous variables for normal distribution was undertaken through the Kolmogorov–Smirnov test, supplemented by histogram curve analyses. Variables conforming to a normal distribution were delineated as mean ± standard deviation in the tables, whereas those deviating from normality were represented as median and interquartile range (25–75). Categorical variables were given in numerical counts and percentages. The cohort was stratified into three distinct groups based on NPS, as detailed in Tables 1 and 2. Comparative statistical analyses among these groups utilized ANOVA and Kruskal–Wallis tests for parametric variables and chi-square and Fisher's exact tests for categorical variables, respecting a *P*-value threshold of 0.05 for statistical significance. Unadjusted (unadj) odds ratios (ORs) and their 95% confidence intervals (CIs) for variables associated with in-hospital mortality were determined with binary logistic regression analysis. Independent predictors of in-hospital mortality and their adjusted (adj) ORs and 95% CIs were calculated with the multivariate model generated by including variables that reached statistical significance ($P < 0.05$) in the univariate analysis. Similarly, Cox-regression analysis was harnessed to identify the independent predictors of 2-year long-term mortality, quantifying their hazard ratios (HRs). Two-year Kaplan–Meier survival curves for each group were plotted and assessed using the log-rank test for *P*-value computation. Additionally, receiver-operating characteristic (ROC) curves were utilized to determine the optimal cut-off values for NPS in predicting both in-hospital and long-term mortality. All statistical analyses were executed using IBM SPSS Statistics, version-26 (IBM Corporation, NY, USA).

Results

Characteristics of the study population according to the Naples Prognostic Score

Demographic, echocardiographic, procedural and laboratory characteristics of the study population stratified into three distinct groups on the basis of NPS are given in Table 1. A notable observation was the younger age profile of patients in Group-1 compared with the other groups ($P = 0.036$). Parameters such as body mass index, comorbid conditions, and STS scores showed no significant differences across the groups.

In-depth preoperative TTE assessments revealed that Group-1 patients exhibited superior left ventricular ejection fraction (LVEF) ($P = 0.039$) and lower systolic pulmonary artery pressure (sPAP) ($P = 0.001$). Other TTE parameters did not show significant differences. Furthermore, intraoperative features and hospital stay durations were comparably consistent across all groups.

Blood test analyses prior to TAVI unveiled a correlation between increasing NPS group and a decrease in hemoglobin levels ($P = 0.036$), accompanied by a rise in white blood cell count ($P < 0.001$). Statistically significant disparities were also evident across the groups concerning NLR, LMR, serum albumin, triglycerides, and cholesterol levels ($P < 0.001$). Notably, a progressive decrease in mean GFR values was observed as one moved from Group-1 to Group-3 ($P = 0.003$).

Table 1 Comparison of basic clinical, echocardiographic, procedural and laboratory data, dividing the study population into three different groups based on the Naples Prognostic Score

	Group-1 (low NPS) ($N=98$, 28.6%)	Group-2 (medium NPS) ($N=137$, 39.9%)	Group-3 (high NPS) ($N=108$, 31.5%)	Overall population ($N=343$)	*P*-value
Baseline characteristics					
Age	76.4 ± 9.5	79.3 ± 7.9	77.9 ± 7.8	78.1 ± 8.4	0.036
Gender (female)	53 (54.1%)	74 (54%)	49 (45.4%)	176 (51.3%)	0.328
BMI (kg/m^2)	27.5 ± 3.9	27.2 ± 4.7	27.6 ± 4.1	27.4 ± 4.3	0.704
Hypertension	85 (86.7%)	118 (86.1%)	91 (84.3%)	294 (85.7%)	0.865
Diabetes	36 (36.7%)	48 (35%)	41 (38%)	125 (36.4%)	0.892
Atrial fibrillation	35 (35.7%)	42 (30.7%)	45 (41.7%)	122 (35.6%)	0.202
COPD	37 (37.8%)	56 (40.9%)	45 (41.7%)	138 (40.2%)	0.833
Previous stroke	4 (4.1%)	8 (5.8%)	5 (4.6%)	17 (5%)	0.814
CAD	68 (69.4%)	94 (68.6%)	70 (64.8%)	232 (67.6%)	0.745
Previous CABG	12 (12.2%)	27 (19.7%)	15 (13.9%)	54 (15.7%)	0.246
STS score	8 (5.7–13)	8 (6–14)	9 (6.2–12)	9 (6–13)	0.528
Echocardiographic measures					
LVEF (%)	53.2 ± 11.9	49.9 ± 12.3	49 ± 12.9	50.6 ± 12.4	0.039
Aortic peak gradient (mmHg)	73.8 ± 20.8	73.2 ± 21.1	72.4 ± 19.4	73.1 ± 20.4	0.889
Aortic mean gradient (mmHg)	47.9 ± 13.4	46.4 ± 14.1	46.5 ± 13.1	46.9 ± 13.5	0.673
Aortic valve area (m^2)	0.72 ± 0.14	0.71 ± 0.15	0.71 ± 0.15	0.71 ± 0.15	0.738
Moderate to severe AR	51 (52%)	61 (44.5%)	44 (40.7%)	156 (45.5%)	0.255
Moderate to severe MR	76 (77.6%)	88 (64.2%)	72 (66.7%)	236 (68.8%)	0.08
Moderate to severe TR	73 (74.5%)	108 (78.8%)	92 (85.2%)	273 (79.6%)	0.157
sPAP (mmHg)	40.9 ± 9.9	45.7 ± 11.8	46.5 ± 11.2	44.6 ± 11.3	0.001
LA diameter (cm)	4.2 ± 0.5	4.3 ± 0.5	4.4 ± 0.7	4.3 ± 0.6	0.066
Procedural features					
VIV TAVI	3 (3.1%)	9 (6.6%)	4 (3.7%)	16 (4.7%)	0.385
General anesthesia	8 (8.2%)	8 (5.8%)	10 (9.3%)	26 (7.6%)	0.584
Self-expanding THV	68 (69.4%)	97 (70.8%)	69 (63.9%)	234 (68.2%)	0.492
THV size (mm)	29 (26–29)	29 (26–29)	27 (26–29)	29 (26–29)	0.621
THV implantation success	96 (98%)	133 (97.1%)	107 (99.1%)	336 (98%)	0.549
Sheath size (F)	16 (14–18)	16 (14–18)	16 (14–18)	16 (14–18)	0.699
Hospitalization (days)	4 (3–6)	4 (3–7)	4 (3–8)	4 (3–7)	0.582
Laboratory					
Hemoglobin (g/dl)	11.9 ± 1.6	11.4 ± 1.8	11.2 ± 1.9	11.5 ± 1.8	0.036
Hematocrit (%)	35.5 ± 4.3	34.2 ± 5.3	33.8 ± 5.3	34.4 ± 5.1	0.035
RBC count (×10^6/μl)	4.24 ± 0.62	4.06 ± 0.65	4.01 ± 0.66	4.11 ± 0.65	0.029
WBC count (×10^3/μl)	6.91 ± 1.84	8.21 ± 2.62	8.64 ± 2.91	7.97 ± 2.61	<0.001
Platelet count (×10^3/dl)	219.7 ± 69.6	221.1 ± 74.1	230.8 ± 78.3	223.8 ± 74.2	0.490
Neutrophil (×10^3/μl)	4.09 ± 1.33	5.92 ± 2.54	6.48 ± 2.74	5.57 ± 2.52	<0.001
Lymphocyte (×10^3/μl)	1.96 ± 0.64	1.38 ± 0.64	1.28 ± 0.58	1.51 ± 0.68	<0.001
Monocyte (×10^3/μl)	0.61 ± 0.21	0.65 ± 0.24	0.66 ± 0.31	0.64 ± 0.25	0.278
NLR	2.13 (1.75–2.58)	4.01 (2.91–6.23)	4.79 (3.63–7.34)	3.49 (2.33–5.63)	<0.001
LMR	3.17 (2.47–4.56)	2.05 (1.39–3.06)	1.89 (1.42–2.75)	2.32 (1.64–3.27)	<0.001
Serum albumin (g/dl)	4.6 ± 0.6	4.5 ± 0.6	3.9 ± 0.6	4.3 ± 0.7	<0.001
LDL (mg/dl)	144.6 ± 29.5	137.8 ± 33.6	99.1 ± 37.4	127.6 ± 38.9	<0.001
HDL (mg/dl)	43.3 ± 13.3	41.9 ± 11.7	35.9 ± 9.8	40.4 ± 12.1	<0.001
Triglyceride (mg/dl)	175.4 ± 56	157.6 ± 50.3	140.1 ± 38.3	157.2 ± 50.4	<0.001
Total cholesterol (mg/dl)	223.1 ± 34.1	211.3 ± 41.9	163.2 ± 41.5	199.5 ± 46.9	<0.001
Creatinine (mg/dl)	1.1 ± 0.3	1.1 ± 0.4	1.2 ± 0.4	1.1 ± 0.4	0.005
GFR (ml/min/1.73 m^2)	75.5 ± 22.6	67.4 ± 22.6	64.9 ± 23.4	68.9 ± 23.2	0.003

AR, aortic regurgitation; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; F, French; GFR, glomerular filtration rate; HDL, high-density lipoprotein; LA, left atrium; LDL, low-density lipoprotein; LMR, lymphocyte-to-monocyte ratio; LVEF, left ventricle ejection fraction; MR, mitral regurgitation; NLR, neutrophil-to-lymphocyte ratio; NPS, Naples Prognostic Score; RBC, red blood cell; sPAP, systolic pulmonary artery pressure; STS, Society of Thoracic Surgeons; THV, transcatheter heart valve; TR, tricuspid regurgitation; VIV TAVI, vale-in-valve transcatheter aortic valve implantation; WBC, white blood cell.

Adverse events in terms of Naples Prognostic Score

Based on NPS, the study populations of Group-1, Group-2, and Group-3 exhibited in-hospital mortality rates of 3.1% ($N=3$), 4.4% ($N=6$), and 13.9% ($N=15$), respectively ($P=0.003$). In the 2-year long-term follow-up of patients who achieved in-hospital survival, a statistically significant worsening in prognosis was observed with increasing NPS group ($P<0.001$). Rates of periprocedural bleeding, vascular complications, permanent pacemaker implantation (PPI), and post-TAVI paravalvular

Table 2 In-hospital and long-term adverse event rates in terms of Naples Prognostic Score

	Group-1 (low NPS) ($N=98$, 28.6%)	Group-2 (medium NPS) ($N=137$, 39.9%)	Group-3 (high NPS) ($N=108$, 31.5%)	Overall population ($N=343$)	*P*-value
In-hospital mortality	3 (3.1%)	6 (4.4%)	15 (13.9%)	24 (7%)	0.003
Mortality during follow-up	2 (2%)	19 (13.9%)	23 (21.3%)	44 (12.8%)	<0.001
Overall 2-year mortality	5 (5.1%)	25 (18.2%)	38 (35.2%)	68 (19.8%)	<0.001
Minor bleeding	16 (16.3%)	21 (15.3%)	17 (15.7%)	54 (15.7%)	0.979
Major bleeding	12 (12.2%)	26 (19%)	15 (13.9%)	53 (15.5%)	0.320
Overall vascular complication	19 (19.4%)	37 (27%)	19 (17.6%)	75 (21.9%)	0.163
Minor vascular complication	7 (7.1%)	22 (16.1%)	7 (6.5%)	36 (10.5%)	0.023
Major vascular complication	10 (10.2%)	15 (10.9%)	12 (11.1%)	37 (10.8%)	0.975
Contrast induced AKI	9 (9.2%)	19 (13.9%)	23 (21.3%)	51 (14.9%)	0.047
PPM implantation	6 (6.1%)	11 (8%)	9 (8.3%)	26 (7.6%)	0.809
Moderate to severe PVAR	29 (30.5%)	41 (31.3%)	24 (25.8%)	94 (29.5%)	0.650

AKI, acute kidney injury; PPM, permanent pacemaker; PVAR, paravalvular aortic regurgitation.

aortic regurgitation (PVAR) were similar across all three groups ($P>0.05$). However, there was a statistical difference in the development of acute kidney injury (AKI) postprocedure among the groups ($P=0.047$) (Table 2).

Predictors of in-hospital mortality

According to the model including age, sPAP, GFR, STS score, presence of chronic obstructive pulmonary disease (COPD) and 3-categorized NPS variables, the independent predictors of in-hospital mortality were sPAP [adjOR: 1.04, 95% CI (1.01–1.08), $P=0.049$], STS score [adjOR: 1.12, 95% CI (1.02–1.23), $P=0.016$], COPD [adjOR: 2.93, 95% CI (1.16–7.37), $P=0.022$] and categorical NPS (Table 3). Additionally, transition from Group-1 to Group-2 did not demonstrate a significant mortality change [adjOR: 0.91, 95% CI (0.21–3.95), $P=0.89$], but progression to Group-3 markedly increased mortality risk [adjOR: 3.93, 95% CI (1.02–15.17), $P=0.047$].

Long-term prognosis

The Cox-regression model used to analyze the determinants of long-term mortality included age, LVEF, sPAP, GFR, STS score, presence of COPD, moderate-severe PVAR, and three categories of NPS. The independent predictors of 2-year all-cause mortality were identified as sPAP [adjHR: 1.04, 95% CI (1.01–1.07), $P=0.001$], moderate-severe PVAR [adjHR: 1.94, 95% CI (1.03–3.65), $P=0.041$], medium NPS (Group-2) [adjHR: 4.81, 95% CI (1.09–21.14), $P=0.037$], and high NPS (Group-3) [adjHR: 10.1, 95% CI (2.31–43.36), $P=0.002$] (Table 4). Kaplan–Meier survival curves based on NPS groups also showed a clear separation, with a 3.8-fold increase in overall mortality risk between Group-2 and Group-1, and an 8.2-fold increase between Group-3 and Group-1 ($P<0.001$) (Fig. 2).

Receiver-operating characteristic curve analysis

The ROC curves constructed to evaluate capability of NPS at predicting in-hospital and long-term mortality are presented in Fig. 3a and b. According to the analysis, a NPS value of 2.5 predicts in-hospital mortality with 62.5% sensitivity and 70.8% specificity [area under the curve (AUC): 0.708, 95% CI (0.594–0.822), $P=0.001$], and long-term mortality with 55.9% sensitivity and 74.5% specificity [AUC: 0.721, 95% CI (0.655–0.786), $P<0.001$].

Table 3 Univariate and multivariate logistic regression analyses for in-hospital mortality

	In-hospital mortality			
	Univariate		Multivariate	
Variable	Unadjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Age	1.06 (1.01–1.13)	0.041	1.06 (0.98–1.14)	0.103
sPAP (mmHg)	1.04 (1.01–1.08)	0.011	1.04 (1.01–1.08)	0.049
GFR (ml/min/1.73 m^2)	0.97 (0.96–0.99)	0.029	0.99 (0.97–1.01)	0.994
STS score	1.14 (1.05–1.23)	0.001	1.12 (1.02–1.23)	0.016
COPD	2.65 (1.12–6.25)	0.025	2.93 (1.16–7.37)	0.022
Low NPS (Group-1) (reference)	–	–	–	–
Medium NPS (Group-2) (categorical)	1.45 (0.35–5.94)	0.605	0.91 (0.21–3.95)	0.891
High NPS (Group-3) (categorical)	5.11 (1.43–18.22)	<0.001	3.93 (1.02–15.17)	0.047

COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; NPS, Naples Prognostic Score; sPAP, systolic pulmonary artery pressure; STS, Society of Thoracic Surgeons.

Table 4 Univariate and multivariate Cox-regression analyses for overall 2-year mortality

	Long-term mortality			
	Univariate		Multivariate	
Variable	Unadjusted HR (95% CI)	*P*-value	Adjusted HR (95% CI)	*P*-value
Age	1.05 (1.01–1.08)	0.003	1.04 (0.99–1.09)	0.099
LVEF (%)	0.97 (0.96–0.99)	0.019	0.99 (0.97–1.01)	0.495
sPAP (mmHg)	1.05 (1.03–1.07)	<0.001	1.04 (1.01–1.07)	0.001
GFR (ml/min/1.73 m^2)	0.97 (0.96–0.98)	<0.001	0.98 (0.97–1.01)	0.091
STS score	1.08 (1.03–1.13)	0.001	1.01 (0.94–1.08)	0.661
COPD	1.71 (1.06–2.76)	0.026	1.48 (0.81–2.71)	0.195
Moderate to severe PVAR	2.35 (1.31–4.25)	0.005	1.94 (1.03–3.65)	0.041
Low NPS (Group-1) (reference)	–	–	–	–
Medium NPS (Group-2) (categorical)	3.82 (1.46–9.98)	0.006	4.81 (1.09–21.14)	0.037
High NPS (Group-3) (categorical)	8.26 (3.25–21.1)	<0.001	10.1 (2.31–43.36)	0.002

COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; LVEF, left ventricle ejection fraction; NPS, Naples Prognostic Score; PVAR, paravalvular aortic regurgitation; sPAP, systolic pulmonary artery pressure; STS, Society of Thoracic Surgeons.

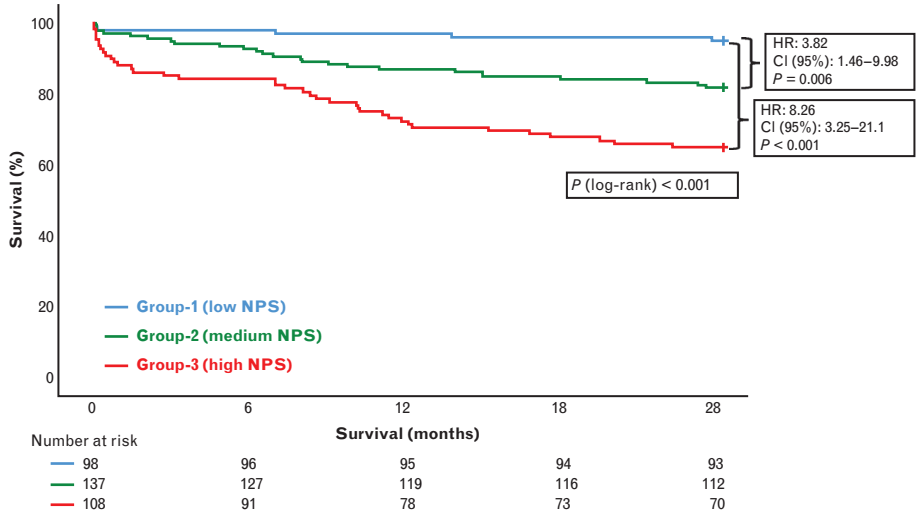
Discussion

Brief outcomes of the study

This single-center, retrospective study delved into the prognostic significance of NPS in patients undergoing TAVI for severe AS. The foremost finding of this investigation is the association of a high NPS with an elevated rate of in-hospital mortality, underscoring the score's relevance in acute patient outcomes post-TAVI. In a more extended scope, the study discerned that preoperative NPS serves as an independent predictor of survival, demonstrably affecting the 2-year long-term prognosis. According to our multivariate analysis, patients classified under medium NPS (Group-2) exhibited a 4.8-fold increase in mortality risk, whereas those with high NPS (Group-3) encountered a 10.1-fold escalation in 2-year long-term mortality risk.

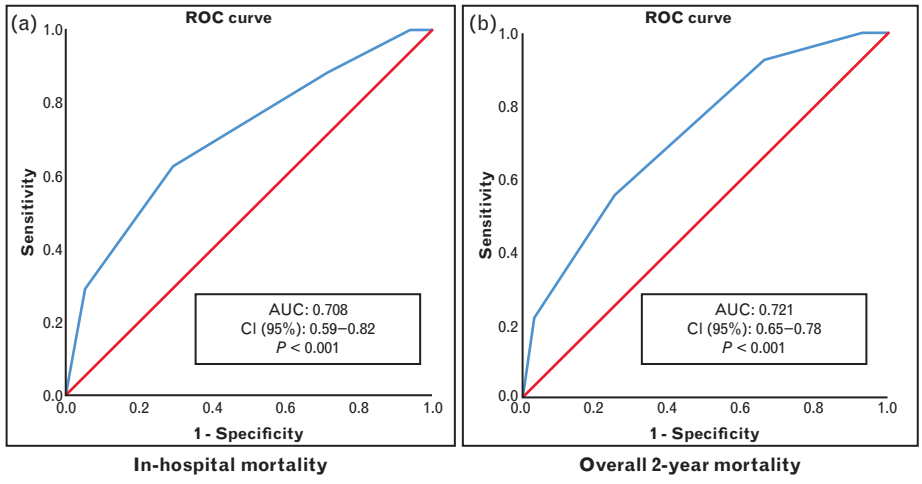
Furthermore, the analysis pinpointed 2.5 as the optimal cut-off value for NPS in predicting both short-term and long-term mortality rates, as deduced from ROC curve assessments. This finding enhances the clinical utility of NPS as a prognostic tool, allowing more nuanced risk stratification in the TAVI patient population. Finally, in this series, it was observed that patients with high NPS were associated with severe cardiac and renal impairment such as lower LVEF, GFR and higher sPAP. As an indirect consequence of this, the incidence of postprocedural AKI was higher in parallel with the increase in NPS.

Fig. 2



24-month Kaplan–Meier survival plots for each group based on Naples Prognostic Score (NPS).

Fig. 3



ROC curves of Naples Prognostic Score for in-hospital (a) and 2-year long-term (b) mortality prediction. AUC, area under curve; CI, confidence interval.

Rationale for clinical use of Naples Prognostic Score

NPS is an established and effective scoring system utilized across a wide range of clinical scenarios to determine the severity and prognosis of diseases. Its ease of calculation from routine blood tests provides both clinical convenience and cost-effectiveness, making it a valuable tool in various healthcare settings.

Initially, in 2017, NPS was used to evaluate the long-term survival of patients operated on for colorectal cancer.[25] The prognostic effectiveness of NPS has been studied in subsequent years across various malignancies and chronic disease populations. In a meta-analysis including lung cancer patients, a low NPS was found to be associated with increased overall survival and disease-free survival.[14] Similarly, another meta-analysis in gastrointestinal cancer patients found that a high NPS was a predictor of increased mortality and poor prognosis.[26] Subsequently, limited studies have investigated the power of NPS in determining prognosis in cardiovascular diseases. Notably, NPS was shown to affect both in-hospital and mid-term mortality and rehospitalization in patients hospitalized with functional class-3 and -4 heart failure due to decompensated heart failure.[19] Similarly, in coronary artery disease, which is fundamentally based on chronic inflammation, NPS is thought to be associated with atherosclerotic burden.[27] Indeed, in two different studies with a high number of patients treated for ST-elevation myocardial infarction (STEMI), high NPS was documented to significantly increase both in-hospital and long-term mortality during a median follow-up of 43 months.[17,28] In another study involving 2901 STEMI patients treated with primary percutaneous intervention, the NPS score was claimed to predict postprocedural AKI.[29] Indeed, in our current study, the frequency of AKI after TAVI was found to be 9.2%, 13.9% and 21.3% in Group-1, -2 and -3 patients, respectively ($P = 0.047$). Although NPS does not include any renal function parameter, high systemic inflammation, hypoalbuminemia and malnutrition can be considered as indirect indicators of impaired renal function. Moreover, NPS has been validated as an efficient predictor of 30-day mortality in acute pulmonary embolism, demonstrating its versatility and reliability as a prognostic tool in a wide array of clinical settings.[18]

The effect of systemic inflammation and frailty on prognosis in patients undergoing transcatheter aortic valve implantation

Chronic inflammation plays a pivotal role in the progression of degenerative AS. Extensive research has focused on systemic inflammation markers to predict outcomes in patients undergoing TAVI. A notable study, incorporating basal blood tests and flow-cytometric analyses, has linked elevated levels of high-sensitivity C-reactive protein, interleukin-6, decreased T-helper-2, and increased T-helper-17 to higher 1-year mortality and impaired left ventricular reverse remodeling after TAVI.[30] Moreover, the NLR, a component of NPS and an indicator of systemic inflammation, has been identified as an independent predictor of long-term survival in TAVI patients.[31–33]

In the elderly with severe AS, numerous factors such as prolonged inflammation, appetite loss, decreased physical capacity, reduced muscle mass, impaired mental functions, and coexisting comorbidities often contribute to malnutrition. Hypoalbuminemia, a marker of malnutrition,

is associated with increased in-hospital and long-term mortality in patients with dilated caridyomyopathy.[34] This nutritional deficiency markedly increases frailty in patients, adversely impacting their prognosis. Various scoring systems, assessing nutrition and physical status, have been utilized in extensive global studies, consistently associating functional and metabolic frailty with poor outcomes.[35–37] A comprehensive national cohort study in the United States revealed that malnutrition is a predictor of increased post-TAVI mortality, infection rates, procedural complications, hospital readmissions, and high treatment costs.[38]

Additionally, the prognostic capacities of widely used indices like the Controlling Nutritional Status (CONUT) score, Prognostic Nutritional Index (PNI), and Geriatric Nutritional Risk Index (GNRI) have been explored. A comparative study suggested that CONUT and PNI might surpass GNRI in predicting 1-year mortality.[39] In a meta-analysis of 6785 patients including 13 observational studies, the 1-year mortality risk was found to be 2.7, 1.79, and 1.17 times higher according to CONUT, GNRI, and PNI systems, respectively. In addition, a low GNRI score was associated with postprocedural AKI, while a low PNI score was associated with vascular complications.[22] In our current study, however, no substantial correlation was found between NPS and specific complications such as post-TAVI bleeding, vascular complications, PPI and PVAR. This finding suggests that other anatomical and procedural factors may be more influential in predicting these particular complications. Nevertheless, the link between systemic inflammation, oxidative stress, and the development of post-TAVI AKI, as supported by our study's findings, aligns with the observed proportional relationship between NPS scores and AKI risk.[40]

Naples Prognostic Score as a composite determinant

As mentioned above, heightened inflammation and malnutrition significantly increase metabolic and physical frailty in patients undergoing TAVI, consequently raising the risk of both peri-procedural and long-term adverse events. NPS, constituted by combining TC, serum albumin levels, NLR and LMR, has emerged as a rapid, cost-effective, and easy-to-use method requiring no extensive clinical experience, particularly beneficial in this patient demographic. To date, few studies have investigated the prognostic power of NPS in patients with TAVI. A retrospective, single-center study by Cetin *et al.* analyzed 370 patients, categorizing them into two groups as low and high based on their NPS. While no significant differences were observed in in-hospital and 1-month mortality rates between the NPS groups, the high NPS group demonstrated a statistically higher mortality rate at the 1-year follow-up.[41] In another recent retrospective study reported by Demirci *et al.* consisting of 400 patients with a median follow-up of 40.6 months, patients undergoing TAVI were divided into two groups according to preoperative NPS and an association was found between NPS and long-term all-cause mortality.[42] Our series, with a patient population similar to those in these two studies, replicated long-term outcomes, albeit with differences in study design and certain endpoints. A primary distinction in our series is the stratification of the patient population into three NPS categories: low, medium, and high. This design facilitates a more comprehensive understanding of the linear progression of NPS and its correlation with clinical outcomes and endpoints. For instance, while the study by Cetin *et al.* did not find a relationship between NPS and in-hospital mortality, our analysis revealed no significant difference in in-hospital mortality rates between low and medium NPS groups; however, the high NPS group exhibited a 3.9-fold increase in mortality risk compared with the low NPS group [95% CI (1.02–15.17), $P=0.047$]. Meanwhile, Demirci *et al.* did not report in-hospital adverse events. Similarly, when examining long-term outcomes, a statistically significant incremental increase in mortality risk was observed with the rise in NPS from Group-1 to -2 and from Group-2 to -3. Moreover, the extended follow-up duration in our series (24 months) and Demirci *et al.* contributed to more robust and satisfactory long-term outcomes.

This study highlights the significance of NPS as an independent predictor of in-hospital mortality in patients undergoing TAVI, providing valuable insights. Although numerous studies in the current literature have investigated the prognostic impacts of systemic inflammation and nutrition indices in TAVI patients, they predominantly focus on mid- and long-term mortality or readmissions rather than in-hospital mortality. Currently, the STS score and EuroSCORE II are globally recognized as strong predictors of in-hospital mortality in TAVI patients. Although a direct comparison of NPS with these scores may not be appropriate, its simplicity in calculation and the absence of imaging data requirements render it a practical alternative. The exclusion of variables such as age, LVEF, GFR, and sPAP suggests that NPS independently influences prognosis in TAVI patients, even in the presence of these critical prognostic factors. Multivariate analyses reveal that NPS remains an independent predictor of both in-hospital and 2-year long-term mortality, even when these parameters are included. However, the current literature does not support using NPS alone for prognosis determination. Focus should be placed on identifying the optimal cut-off value for mortality prediction using NPS, necessitating support through multicenter, prospective studies. For now, the NPS score can be considered a clinically supportive tool alongside established systems in daily practice, offering guidance in patient selection for clinicians.

Conclusions

In predicting both in-hospital and 2-year long-term mortality for TAVI candidates, NPS, which objectively reflects systemic inflammation and nutritional status, has emerged as an effective and practical alternative method. Preoperative assessment of NPS can be a supportive tool in accurate patient selection, a critical component for short- and long-term success in TAVI. It is hoped that this study will inspire more comprehensive research protocols to further investigate the efficacy and reliability of NPS.

Study limitations

Despite being a pioneering study in its field, it possesses certain limitations. Firstly, its retrospective and single-center nature limits the generalizability of its findings and leads to various interpretations. Additionally, the focus solely on preprocedure NPS, without examining changes in NPS postprocedure in both the early and long-term phases, narrows the scope of the study. This omission results in a lack of crucial information about the impact of postprocedure NPS changes on long-term prognosis. The reliance on ROC analysis alone to determine the optimal cut-off value of NPS is a methodological limitation of the study. sPAP, a predictor of in-hospital and long-term mortality, was measured only by TTE in this study. The lack of cardiac catheterization may compromise the accuracy of sPAP values. Moreover the patients included in the study were heterogeneous in terms of the type of valve implanted. In this context, it was not mentioned whether there is a difference in outcomes according to the type of valve preferred. In addition, different results may arise with new-generation valves from other companies that were not used in the study. Another notable limitation of the study is the lack of consideration of the anatomical features of the aortic root, annulus and leaflets, which are important determinants of PVAR after TAVI. Finally, a larger patient cohort and longer follow-up periods could have strengthened the study's outcomes.

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Conflicts of interest

There are no conflicts of interest.

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