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The performance of the NAPLES prognostic score in predicting one-year mortality and major adverse cardiovascular events after transcatheter aortic valve implantation in patients with severe aortic stenosis

Short title: Impact of Naples score on one-year outcomes in TAVI patients

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WHAT'S NEW?

This study introduces a pioneering approach in transcatheter aortic valve implantation patient risk assessment by incorporating the Naples Prognostic Score (NPS), a composite marker of nutritional and inflammatory status. Unlike traditional risk scores, the NPS has shown a strong correlation with one-year mortality and major adverse cardiovascular events in our analysis of 222 patients. Its ability to act as an independent predictor of mortality and major adverse

cardiovascular events positions it as a potentially transformative tool for enhancing patient selection, guiding clinical decisions, and improving communication regarding procedural risks. The integration of NPS into risk stratification models represents a significant advancement in personalized interventional cardiology.

ABSTRACT

Background: Existing risk scores for transcatheter aortic valve implantation (TAVI) may not fully capture patient complexity. Combining nutritional and inflammatory markers, the NPS (the NAPLES prognostic score) might improve outcome prediction.

Aims: This study investigated the associations of the NPS with one-year mortality and major adverse cardiovascular events (MACEs) in TAVI patients.

Methods: This retrospective analysis included 222 patients with severe aortic stenosis who underwent TAVI. The NPS was calculated based on the serum albumin concentration, cholesterol concentration, lymphocyte/monocyte ratio, and neutrophil/lymphocyte ratio. The patients were subsequently categorized into two groups: the low-NPS group (NPS 0–2) and the high-NPS group (NPS 3–4).

Results: A high NPS significantly associated with increased one-year mortality (4.8% vs. 23.7%; $P < 0.001$) and MACE rates (7.2% vs. 35.9%; $P < 0.001$). Cox regression analysis revealed that a high NPS was an independent predictor of both mortality (HR, 5.94; 95% CI, 2.03–17.37; $P = 0.001$) and MACE (HR, 5.09; 95% CI, 2.15–12.02; $P < 0.001$).

Conclusions: The NPS emerged as a potential predictor of long-term mortality and MACEs in TAVI patients. Further validation through larger, multicenter studies is warranted. This research contributes valuable data on the role of the NPS in TAVI risk stratification.

Key words: aortic valve stenosis, major adverse cardiac events, mortality, prognostic factors, transcatheter aortic valve implantation

INTRODUCTION

Aortic stenosis (AS) is a prevalent valvular heart disease in older adults and is associated with high morbidity and mortality if left untreated. Transcatheter aortic valve implantation (TAVI) is currently considered the standard treatment for patients older than 75 years of age with native severe AS. TAVI has emerged as a valid alternative method offering a less invasive approach for this group of patients. Additionally, TAVI is a safe and effective option for patients with

failed surgical and transcatheter prostheses, reducing the need for re-do surgery in high-risk patients. However, surgical aortic valve replacement (SAVR) remains the standard treatment method, especially for low-risk and younger populations [1]. Many studies have shown that TAVI is noninferior or superior to SAVR in reducing mortality, stroke and heart failure and improving quality of life in different surgical risk categories. Therefore, TAVI has become the preferred treatment modality for AS patients [2, 3].

Numerous prognostic scoring models, including the Society of Thoracic Surgeons score and the EuroSCORE II, have been established to predict clinical outcomes subsequent to TAVI [4, 5]. These instruments are routinely employed to categorize patients, evaluate their eligibility for surgical or percutaneous interventions, and appraise the risk of mortality both intrahospitally and within 30 days postdischarge, with a particular emphasis on the risk of surgical mortality. However, these scores have limitations in capturing the complexity and heterogeneity of the patient population, which has a high burden of comorbidities and may not benefit from valve replacement alone. Additional determinants, such as the overall cardiovascular profile, noncardiac comorbidities, and the degree of frailty, can exert a significant impact on the enduring outcomes of TAVI, extending beyond the scope of valvular pathology [6–8]. Therefore, additional indicators that complement surgical risk scores are needed to improve the prediction of outcomes and optimize patient care after TAVI.

AS is a disease that shares a pathophysiology similar to that of atherosclerosis, including calcification, lipoprotein accumulation, and chronic inflammation. This is not only a consequence of aging, but also a dynamic inflammatory process. Therefore, the use of inflammatory biomarkers may be useful in predicting the outcomes of patients undergoing TAVI. Furthermore, malnutrition is a marker of frailty in elderly patients and a predictor of adverse outcomes in patients with severe AS. Low serum albumin levels, which could indicate malnutrition, inflammation, or cachexia, have been associated with the development of coronary artery disease and increased cardiovascular mortality risk in TAVI patients [9, 10].

The NPS is a novel scoring system that assesses the nutritional and inflammatory status of patients. The NPS is derived from biochemical markers such as the serum albumin level, total cholesterol level, lymphocyte/monocyte ratio (LMR) and neutrophil/lymphocyte ratio (NLR) [11, 12]. The NPS has been used as a prognostic score for various cancers in recent years [13–15]. The NPS has also been found to predict follow-up mortality in heart failure and myocardial infarction patients [16–18]. The role of the NPS in predicting mortality and major adverse cardiac event (MACE) risk after TAVI is unclear. This study aimed to examine the

performance of the NPS in predicting one-year mortality and MACE risk after TAVI in patients with severe AS.

METHODS

Study design

This study is a retrospective analysis of patients who were diagnosed with severe AS and who underwent transfemoral TAVI, and self-expandable CoreValve Evolut valve implantation during the procedure, at the Dicle University Medicine Faculty, Department of Cardiology, between January 2015 and March 2022.

Before undergoing either elective or emergency TAVI procedures, the patients were evaluated by a multidisciplinary cardiac team. Experienced interventional cardiologists performed the valve implantations and followed up with the patients.

We screened a total of 268 patients. 6 patients who died during the TAVI procedure, 14 patients who were lost to clinical follow-up before one year, 3 patients with severe anaemia, 10 patients with chronic renal failure, 5 patients who had valve-in-valve TAVI and 8 patients with missing hospital medical records were excluded. Thus, 222 patients were included in the study.

A total of 222 patients were included in the study after excluding those with missing medical records, those with missing follow-up records, and those who did not meet the predetermined inclusion criteria.

Patients who had undergone previous pacemaker implantations, surgical aortic valve replacements, TAVI procedures, balloon-expandable TAVI procedures, valve-in-valve procedures, or bicuspid aortic valves were excluded.

After the procedure, all patients were retrospectively evaluated at the time of in-hospital discharge, as well as at 1-month and 1-year follow-up intervals. Demographic, physical, echocardiographic, and laboratory data were obtained from the hospital's database. The vital status of all patients was confirmed through the Turkish National Death Indices.

This study was conducted according to the principles of the Helsinki Declaration and was approved by the Institutional Ethics Committee of the Batman Training and Research Hospital (Approval Number: 23/01/2024-373). Additionally, institutional permission was obtained from the chief physician of the Dicle University Faculty of Medicine and the head of the Department of Cardiology for the archive records of the patients included in our study.

Periprocedural imaging and the TAVI procedure

Transthoracic echocardiographic images were taken before the TAVI procedure to assess the severity of AS. Twelve-lead standard electrocardiography was also performed for each patient. Computed tomography scans were performed to evaluate the anatomy of the aorta and the aortic valve. Analyses were performed according to the Valve Academic Research Consortium 3-criteria Guidelines (VARC-3) [19]. The procedures were carried out with conscious sedation and transfemoral access and anticoagulation with unfractionated heparin. Rapid pacing was utilized during the procedure, and vascular closure devices were employed for hemostasis at the access site.

Clinical endpoints

The effectiveness of the aortic valve replacement procedure was measured by evaluating the technical success of the procedure as the clinical endpoint. Any complications that occurred were classified according to the VARC-3 consensus report [19], which included issues such as left bundle branch block, periprocedural myocardial injury, arrhythmia, renal failure, hemorrhage, paravalvular regurgitation, duration of hospitalization, pericardial tamponade, and MACE (CV death, vascular complications, coronary obstruction, and periprocedural MI). Additionally, the study evaluated MACE and all-cause death during hospitalization, and at one month, and one year.

Assessment of the NPS

The NPS score was calculated as follows: The NPS was based on the NLR, LMR, serum albumin concentration and total cholesterol concentration. According to Galizia et al. [11] method (the cutoff values of NLR and LMR were defined by MaxStat analysis), a serum total cholesterol level ≤ 180 mg/dl, an albumin level < 40 g/l, an LMR ≤ 44 or a NLR > 2.96 were each assigned 1 point; otherwise, they were assigned 0 points. The patients were subsequently categorized into two groups: the low-NPS group (NPS 0–2) and the high-NPS group (NPS 3–4).

Statistical analysis

We used SPSS 21.0 (IBM Corporation) for the analyses. To assess the normality of continuous variables, we utilized the Kolmogorov–Smirnov test. Continuous variables are presented as the mean (standard deviation) or median (interquartile range), depending on the variable distribution and were compared using either Student’s t- test or the Mann–Whitney U test, as needed. Categorical variables are expressed as numbers and percentages (%) and were

compared using either the χ^2 test or Fisher's exact test, as appropriate. We plotted survival curves using the Kaplan–Meier method and compared them with the log-rank test. To estimate the HR and 95% CI for mortality and MACE predictors, we used both univariable and multivariable Cox proportional hazards models. Parameters associated with mortality and MACE were included in the univariable regression analysis. Variables with significant P values in the univariable analysis were further analyzed in the multivariable regression. The analysis results were also displayed with the forest plot graph. We considered $P < 0.05$ to indicate statistical significance.

RESULTS

A total of 222 patients with severe AS who underwent TAVI were included in the study. The mean age of the patients was 79.2 (6.4) years, and 124 (55.8%) were female. Overall, 83 (37.4%) patients were in the low NPS group, and 139 (62.6%) patients were in the high NPS group. There was no significant difference between the two groups in terms of age, sex or disease history. However, neutrophil (4.85 [1.54] vs. 5.77 [1.98]; $P < 0.001$) and NLR (2.57 [1.15] vs. 3.91 [1.89]; $P < 0.001$) levels were greater in the high NPS group. The baseline demographic and clinical characteristics of the two groups are shown in [Table 1](#). Both one-year total mortality (4.8% vs. 23.7%; $P < 0.001$) and one-year total MACE (7.2% vs. 35.9%; $P < 0.001$) were greater in the high NPS group than in the low NPS group ([Table 2](#)).

We performed a comprehensive analysis using univariable and multivariable Cox regression analysis to determine the factors predicting one-year mortality and MACEs. Following a multivariable Cox regression analysis, it was found that high NPS, heart failure, and post-TAVI major bleeding independently predicted one-year mortality (HR, 5.94; 95% CI, 2.03–17.37; $P = 0.001$; HR, 0.386; 95% CI, 0.17–0.88; $P = 0.024$; HR, 5.147; 95% CI, 2.14–12.37; $P < 0.001$, respectively) ([Table 3](#) and [Figure 1](#)). Additionally, high NPS and heart failure were identified as independent predictors of one-year MACE (HR, 5.09; 95% CI, 2.15–12.02; $P < 0.001$; HR, 0.511; 95% CI, 0.27–0.98; $P = 0.04$, respectively) ([Table 4](#) and [Figure 1](#)).

In this study, we performed a Kaplan–Meier survival analysis to investigate the potential association between high NPS and mortality. Survival at the one-year follow-up was greater in the low NPS group than in the high NPS group (log-rank $P < 0.001$) ([Figure 2](#)).

DISCUSSION

Our study underscores the potential of the Naples Prognostic Score (NPS) as a significant predictor of long-term outcomes in patients undergoing TAVI for severe AS. By exploring the

association between NPS and one-year clinical outcomes, we provide new insights into its role in risk stratification, which could enhance decision-making processes and ultimately improve patient management in this high-risk population. These findings contribute to the growing body of evidence supporting the integration of nutritional and inflammatory markers into cardiovascular risk assessment models.

The prevalence of malnutrition is greater in TAVI patients than in those with other cardiovascular diseases, and malnutrition is correlated with increased mortality [20]. Various nutritional indices, such as the Mini Nutritional Assessment Short Form (MNA-SF), Controlling Nutritional Status (CONUT), Prognostic Nutritional Index (PNI), Nutritional Risk Index (NRI), and Geriatric Nutritional Risk Index (GNRI), have been investigated in TAVI patients and have demonstrated prognostic value in predicting outcomes [21, 22]. In a study by Kazemian et al. [23], a high incidence of malnutrition, as indicated by objective nutritional indices (CONUT, GNRI, NRI, PNI), was observed among TAVI patients, with malnutrition being linked to an increased risk of one-year all-cause mortality. In a study by Sudo et al. [24], it was found that a low total cholesterol-to-brachial index, indicative of right heart overload symptoms, increased the risk of three-year mortality, and the addition of the total cholesterol-to-brachial index to the EuroSCORE II improved the predictive value for all-cause mortality. In a study by Kucukosmanoglu et al. [25], other nutritional indices, such as the GNRI, PNI, and CONUT, were evaluated in TAVI patients and were associated with one-year all-cause mortality. In a study by Mas-Peiro et al. [26], the PNI was identified as a useful and practical nutritional marker strongly predictive of one-year survival in TAVI patients, showing superior predictive value compared to the GNRI and body mass index. Furthermore, according to a study by He et al. [27], the PNI was associated with short-term survival and fewer post-TAVI complications. These findings suggest that nutritional indices can offer valuable insights for risk stratification and outcome prediction in patients undergoing TAVI.

Albumin has been studied in various medical conditions to assess its association with mortality. In patients with acute heart failure, the use of albumin was found to be associated with lower 30-day mortality, especially in males, those with heart failure with reduced ejection fraction, and those without sepsis [28]. In patients with severe COVID-19, low serum albumin levels were found to be associated with severe disease and poor prognosis, with the neutrophil/albumin ratio, C-reactive protein/albumin ratio and blood urea nitrogen/albumin ratio being more valuable predictors of prognosis [29]. Serum albumin is a multifunctional protein that may have direct or indirect effects on mortality in TAVI patients [30].

The NPS is a contemporary method for assessing malnutrition, that considers the serum ALB concentration, total cholesterol level, LMR, and NLR. The NPS is unique in that it considers both inflammation and nutritional status concurrently. The results of our study are consistent with the results of many previous studies investigating the relationships of the NPS with mortality and long-term outcomes in different patient groups. Researchers have noted the correlation between the NPS and long-term prognostic outcomes, as well as mortality rates, in patients who have undergone surgery for colorectal cancer [11]. Moreover, the NPS has been shown to be a reliable indicator of postoperative complications in patients who have undergone colectomy for diverticulitis [31]. The NPS has proven to be a valuable tool for predicting outcomes in patients with heart failure. Studies have shown that it is linked to both short- and medium-term mortality as well as hospital readmissions [32]. Furthermore, it has been found to be significantly associated with long-term mortality in patients experiencing STEMI [33].

In a study conducted by Çetin et al. [34], the one-year total mortality in TAVI patients was found to be 8.6% (5% in the low NPS group vs. 13% in the high NPS group; $P = 0.006$). In another study conducted by Demirci et al. [35], total mortality was found to be 62% in TAVI patients in their 40-month long-term follow-up (42% in the low NPS group vs 87.9% in the high NPS group; $P < 0.001$). These two studies support our study in terms of NPS being a predictor of mortality. However, our study is important in terms of showing the additional predictive effect of NPS in terms of MACEs in addition to mortality.

However, there are currently insufficient data in the literature regarding the association of the NPS with mortality and morbidity in patients with severe AS undergoing TAVI. We believe that our study adds new data to clarify this uncertainty. Patients with higher NPS may benefit from closer monitoring, and correcting inadequate nutrition/malnutrition and limiting inflammation may help improve survival in patients undergoing TAVI.

There are several limitations in our study. First, it is primarily retrospective and involves a restricted patient sample size. Furthermore, we cannot determine the extent to which the exclusion of patients with data limitations may have affected the study results. Another limitation is our inability to establish a correlation between the NPS and other inflammatory markers and nutritional indices. The study investigated the NAPLES risk score upon patients' admission. However, it is essential to acknowledge potential uncertainties related to dynamic changes in albumin levels and other blood parameters over time, the possibility of dehydration at admission, and variations in nutritional status.

CONCLUSIONS

In conclusion, the NPS is a key predictor of long-term mortality and MACE in patients with severe aortic stenosis undergoing TAVI. As a measure of inflammation and malnutrition, NPS enhances risk stratification and guides clinical decisions. Further multicenter and randomized controlled trials are needed to confirm these findings and explore their broader applicability.

Article information

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Table 1. Baseline demographic and clinical characteristics of the patients

Variables	Total (n = 222)	Low NPS (n = 83)	High NPS (n = 139)	<i>P</i> -value
Age, years	79.2 (6.4)	78.5 (6.7)	79.6 (6.2)	0.24
Gender (male), n (%)	98 (44.1)	30 (36.1)	68 (48.9)	0.06
BMI (kg/cm ²)	21.8 (1.7)	21.4 (1.4)	22.0 (1.8)	0.01
Hypertention, n (%)	122 (54.9)	47 (56.6)	75 (53.9)	0.69
Diabetes mellitus, n (%)	54 (24.3)	24 (28.9)	30 (21.6)	0.22
Hyperlipidemia, n (%)	60 (27.0)	28 (33.7)	32 (23.0)	0.08
Prior PCI, n (%)	72 (32.4)	33 (39.7)	39 (28.1)	0.07
Prior CABG, n (%)	28 (12.6)	12 (14.5)	16 (11.5)	0.52
Heart failure, n (%)	82 (36.9)	36 (43.4)	46 (33.1)	0.15
Peripheral artery disease, n (%)	5 (2.3)	1 (1.2)	4 (2.9)	0.65
Cerebrovascular disease, n (%)	4 (1.8)	2 (2.4)	2 (1.4)	0.63
COPD, n (%)	22 (9.9)	9 (10.8)	13 (9.3)	0.82
CKD, n (%)	59 (26.6)	17 (20.5)	42 (30.2)	0.12
Anemia, n (%)	116 (52.3)	35 (42.2)	81 (58.3)	0.03
Atrial fibrillation, n (%)	49 (22.1)	16 (19.3)	33 (23.7)	0.51
Smoking, n (%)	51 (22.9)	17 (20.5)	34 (24.4)	0.52
LVEF, %	50.9 (40.0-60.0)	49.7 (40.0-60.0)	51.6 (45.0-60.0)	0.25
Aortic valve area, cm ²	0.67 (0.18)	0.68 (0.20)	0.67 (0.18)	0.85
STS risk score	9.40 (7.0-11.0)	8.86 (7.0-10.0)	9.72 (7.0-11.0)	0.25
Angular angle	48.10 (8.83)	48.90 (9.56)	47.63 (8.41)	0.43

Valve size, mm	28.73 (3.39)	28.29 (3.45)	28.99 (3.35)	0.14
GFR, ml/min/1.73 m ²	73.15 (25.12)	80.87 (30.07)	72.61 (27.82)	0.005
WBC, ×1000/μl	7.85 (2.21)	7.55 (1.89)	8.03 (2.37)	0.12
Haemoglobin, g/l	12.18 (1.89)	12.41 (2.01)	12.04 (1.79)	0.16
Lymphocyte, 10 ⁹ /l	1.77 (0.59)	2.05 (0.66)	1.61 (0.49)	<0.001
Neutrophil, 10 ⁹ /l	5.42 (1.87)	4.85 (1.54)	5.77 (1.98)	<0.001
Monocyte, 10 ⁹ /l	0.62 (0.19)	0.58 (0.17)	0.64 (0.21)	0.05
Platelet, 10 ⁹ /l	242.3 (79.7)	258.1 (87.5)	232.9 (73.5)	0.02
Creatinine, mg/dl	1.03 (0.70-1.10)	0.92 (0.64-0.99)	1.09 (0.73-1.24)	0.11
Total cholesterol, mg/dl	182.44 (39.16)	207.23 (34.46)	167.64 (34.07)	<0.001
LDL, mg/dl	109.98 (36.89)	123.62 (41.58)	102.68 (31.96)	<0.001
HDL, mg/dl	44.08 (12.57)	45.76 (10.19)	43.02 (13.81)	0.12
Albumin, g/dl	35.95 (4.33)	38.26 (3.56)	34.58 (4.18)	<0.001
NLR	3.41 (1.77)	2.57 (1.15)	3.91 (1.89)	<0.001
LMR	3.07 (1.16)	3.69 (1.23)	2.70 (0.94)	<0.001
AST (iu/l)	28.30 (17.0-32.0)	27.02 (17.0-31.0)	29.06 (17.0-33.8)	0.54
ALT (iu/l)	18.99 (10.95-20.0)	19.00 (11.0-21.0)	18.99 (10.8-20.0)	0.99

P <0.05 was considered statistical significant. Values are presented as n (%) or mean (standard deviation), or median (interquartile range), depending on the variable distribution

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; HDL, high-density lipoprotein; LVEF, left ventricular ejection fraction; LDL, low-density lipoprotein; LMR, lymphocyte monocyte ratio; NLR, neutrophil lymphocyte ratio; NPS, Naples prognostic score; PCI, percutaneous coronary intervention; STS, the society of thoracic surgery risk score; WBC, white blood cell count

Table 2. Procedural complications and clinical endpoints of the patients

Variables	Total (n = 222)	Low NPS (n = 83)	High NPS (n = 139)	<i>P</i> -value
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Major vascular complication, n (%)	14 (6.3)	6 (7.2)	8 (5.7)	0.78
Major bleeding, n (%)	14 (6.3)	3 (3.6)	11 (7.9)	0.26
Pacemaker implantation, n (%)	20 (9.0)	5 (6.0)	15 (10.8)	0.33
Cerebrovascular event, n (%)	8 (3.6)	1 (1.2)	7 (5.0)	0.26
Acute kidney injury, n (%)	11 (4.9)	2 (2.4)	9 (6.5)	0.22
Post-TAVI MACEs, n (%)	25 (11.3)	5 (6.0)	20 (14.4)	0.08
One-month MACEs, n (%)	32 (14.4)	5 (6.0)	27 (19.4)	0.006
One-year MACEs, n (%)	56 (25.2)	6 (7.2)	50 (35.9)	<0.001
In-hospital death, n (%)	16(7.2)	3 (3.6)	13 (9.3)	0.18
One-Month death, n (%)	24 (10.8)	4 (4.8)	20 (14.4)	0.03
One-year death, n (%)	37 (16.6)	4 (4.8)	33 (23.7)	<0.001

P <0.05 was considered statistical significant. Values are presented as n (%)

Abbreviations: MACEs, major adverse cardiovascular events; NPS, Naples prognostic score; TAVI, transcatheter aortic valve implantation

Table 3. Independent predictors of one-year mortality in univariable and multivariable Cox regression analysis

Parameters	Univariable analysis		Multivariable analysis	
	HR (95% CI)	<i>P</i> -value	HR (95% CI)	<i>P</i> -value
Age	1.029 (0.980–1.081)	0.25		
Gender (male)	0.857 (0.457–1.606)	0.63		
Diabetes mellitus	1.015 (0.497–2.070)	0.97		
Hypertension	0.933 (0.505–1.725)	0.83		
Heart failure	0.325 (0.144–0.733)	0.007	0.386 (0.169–0.883)	0.024
Body mass index	1.089 (0.916–1.293)	0.33		
Prior PCI	1.591 (0.854–2.962)	0.14		
Anemia	1.948 (1.021–3.717)	0.04	1.079 (0.526–2.211)	0.84
Platelets count	1.003 (0.999–1.006)	0.11		

Glomerular filtration rate	0.983 (0.971–0.994)	0.004	0.993 (0.981–1.006)	0.15
NAPLES prognostic score	7.052 (2.507–19.837)	<0.001	5.936 (2.028–17.372)	0.001
Post-TAVI major vascular complications	3.161 (1.328–7.522)	0.009	2.055 (0.768–5.494)	0.15
Post-TAVI major bleeding	7.343 (3.571–15.099)	<0.001	5.142 (2.138–12.370)	<0.001
Post-TAVI pacemaker implantation	0.769 (0.237–2.492)	0.66		
Post-TAVI cerebrovascular event	2.456 (0.756–7.982)	0.35		
Post-TAVI acute kidney injury	3.349 (1.311–8.556)	0.012	0.691 (0.210–2.271)	0.54

$P < 0.05$ was considered statistical significant

Abbreviations: CI, confidence interval; HR, hazard ratio; PCI, percutaneous coronary intervention; TAVI, transcatheter aortic valve implantation

Table 4. Independent predictors of one-year MACE in univariable and multivariable Cox regression analysis

Parameters	Univariable analysis		Multivariable analysis	
	HR (95% CI)	<i>P</i> -value	HR (95% CI)	<i>P</i> -value
Age	1.047 (1.003–1.093)	0.03	1.040 (0.993–1.090)	0.09
Gender (male)	0.954 (0.560–1.626)	0.86		
Diabetes mellitus	0.948 (0.510–1.763)	0.86		
Hypertension	0.927 (0.548–1.567)	0.77		
Heart failure	0.424 (0.224–0.802)	0.008	0.511 (0.267–0.979)	0.04

Body mass index	1.054 (0.903–1.230)	0.51		
Prior PCI	1.080 (0.616–1.893)	0.79		
Anemia	2.186 (1.247–3.832)	0.006	1.472 (0.812–2.669)	0.20
Platelets count	1.002 (0.999–1.005)	0.29		
Glomerular filtration rate	0.983 (0.973–0.993)	0.001	0.990 (0.980–1.001)	0.06
NAPLES prognostic score	6.679 (2.858–15.610)	<0.001	5.085 (2.151–12.017)	<0.001
Post-TAVI pacemaker implantation	0.950 (0.379–2.380)	0.91		
Post-TAVI acute kidney injury	3.695 (1.669–8.180)	0.001	1.702 (0.720–4.022)	0.22

P <0.05 was considered statistical significant

Abbreviations: CI, confidence interval; HR, hazard ratio; PCI, percutaneous coronary intervention; TAVI, transcatheter aortic valve implantation

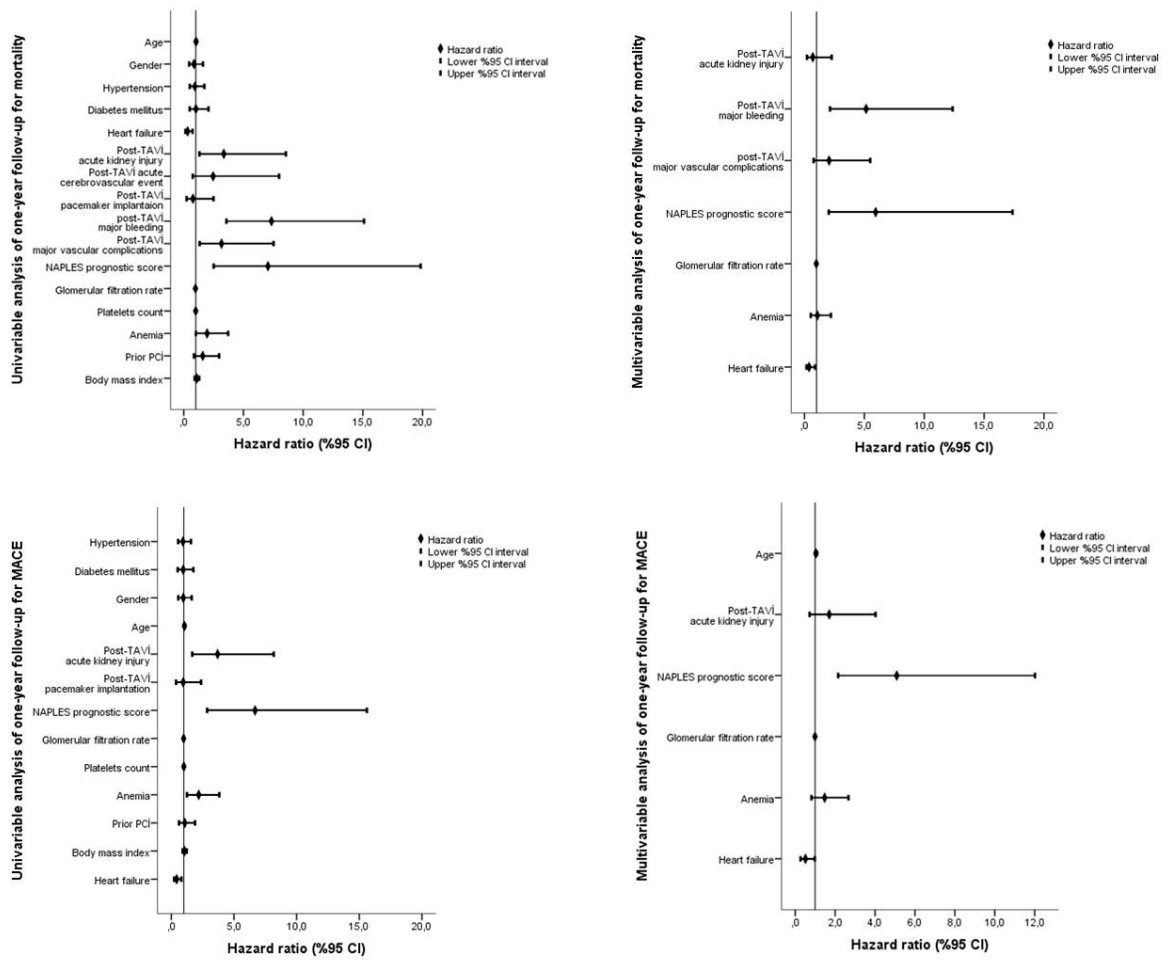
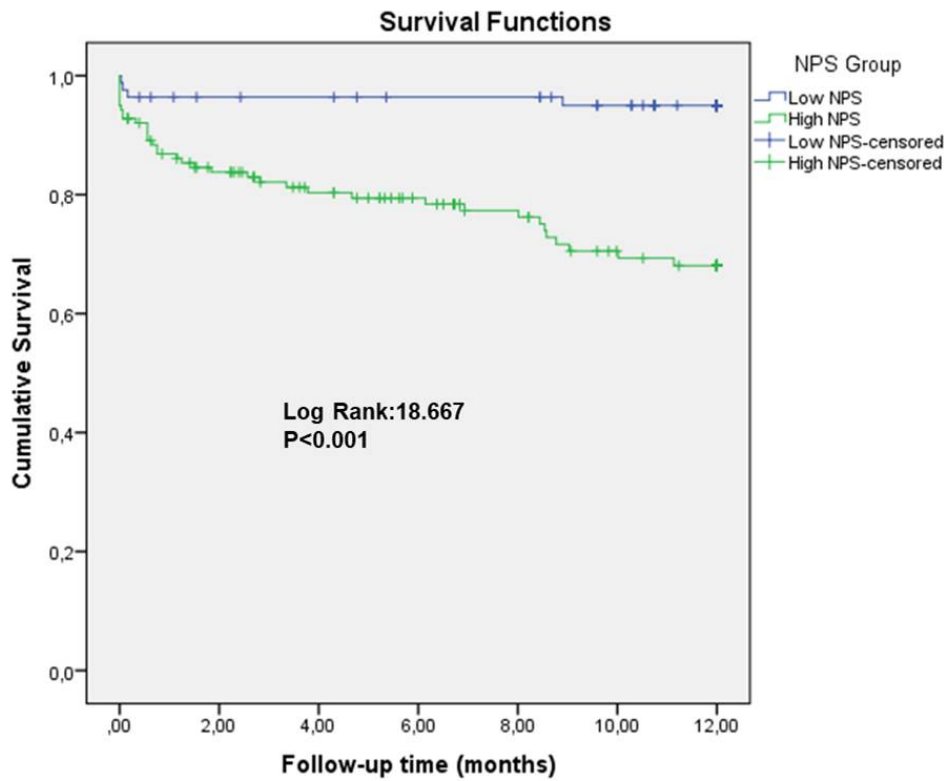


Figure 1. Forest plot showing the univariate and multivariate Cox regression analysis results for mortality and major adverse cardiovascular event at one-year follow-up



	0. Day	In Hospital	1. Month	6. Month	12. month
Low NPS	83	80	79	79	79
High NPS	139	126	119	111	106

Figure 2. Kaplan–Meier survival curve for one-year mortality stratified by the Naples Prognostic Score (NPS)