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The Predictor Value of Neutrophil Lymphocyte Ratio on 30-day Mortality after Transcatheter Aortic Valve Implantation

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Abstract

Aim: Neutrophil lymphocyte ratio (NLR) has been found to be an independent predictor of prognosis in coronary artery disease and valvular diseases. Current knowledge about the relation of NLR with prognosis after transcatheter aortic valve implantation (TAVI) is not sufficient. The aim of this study is to investigate if neutrophil lymphocyte ratio (NLR) is an independent predictor of 30-day mortality after TAVI.

Material and methods: A total of 196 patients who underwent TAVI between October 2010 and December 2016 were screened and 184 patients were included in the study. The cut off value for NLR was determined by ROC analysis. The cut off value for postoperative 3rd day NLR (NLR Postop 3) was defined as 7.93. The study population was divided into two groups: those who have higher and lower than this cut off value as "high NLR" and "low NLR" respectively. Baseline, peroperative, and postoperative clinical features, echocardiographic and laboratory findings of high and low NLR groups were analyzed by univariate and multivariate analyses.

Results: One hundred thirteen (61.4%) of the patients were female and mean age was 79.41 ± 7.88. Sixteen patients died within 30 days follow up after the TAVI. Three patients died within 24-72 hours. Mortality was found to be significantly higher in the high NLR group [12 (22.2%) versus 1 (0.8%), p <0.001]. In Kaplan-Meier survival analysis, 30-day survival was lower in the high NLR group (Log-rank, p <0.001). In multivariate Cox regression analyses, NLR Postop 3 [Hazard Ratio (HR): 1.168, 95% Confidence Interval (CI): 1.09- 1.251 p<0.001], acute kidney injury (AKI) [HR: 6.58, 95% CI: 1.360-31.875 p = 0.019] and preoperative peak gradient [HR: 1.045, 95% CI: 1.008-1.084 p = 0,018] were found to be independent predictors of 30-day mortality after TAVI.

Conclusion: In this study, NLR Postop 3 was found to be an independent predictor of 30-day mortality after TAVI.

Key Words: Aortic stenosis, transcatheter aortic valve implantation, neutrophil lymphocyte ratio, mortality

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Introduction

Aortic valve stenosis (AS) is the obstruction of the left ventricular outflow tract (LVOT) by several mechanisms (1). It is a progressive disease with long latent period, mortality and morbidity. After symptoms appear, progression occurs quickly (2). Although several mechanisms can cause AS, in developed countries the most frequent type is senile AS and it is the most common encountered type of acquired valvular disease (3). 50-60 % of the patients who are not treated surgically die within 2 years (4-5). In severe AS, surgical aortic valve replacement (SAVR) is the most important therapy strategy to improve the symptoms and decrease the mortality (6). Transcatheter aortic valve implantation (TAVI) is the well developed and successfully performed procedure for the high risk patients who have co-morbidities, advanced age and impaired left ventricular function (7).

Nowadays, neutrophil lymphocyte ratio (NLR) which is easily accessible and calculable from the routine blood test, is a highly evaluated inflammatory marker for the prediction of the cardiovascular disease mortality and morbidity (8,9). NLR was found to be a helpful marker for the mortality prediction of chronic stabile angina, acute coronary syndrome and coronary bypass surgery (10,11). The literature results show a statistically significant relationship between NLR and cardiovascular mortality and morbidity but current literature doesn't contain sufficient data of NLR for predicting the mortality in TAVI patients. The aim of the study is to evaluate the predictive value of NLR for in hospital and 30-day mortality of TAVI patients retrospectively.

Materials and Methods

Study population

This single-center retrospective study was carried out at a tertiary heart care center. A total of 196 consecutive patients with symptomatic severe AS who underwent TAVI between October 2010 and December 2016 were reviewed. Data were obtained after a systematic review of the patients' hospital records. Verbal and written informed consent was obtained from each study participant and the study protocol was approved by the Local Ethics Committee.

Patient selection

The decision for TAVI was rendered for the symptomatic severe AS patients by a consensus of the heart team and preoperative risk was assessed on the basis of the European System for Cardiac Operative Risk Evaluation (EuroSCORE) or the Society of Thoracic Surgeons (STS) risk calculator systems. Intraoperative period was defined as 0-24 hours after procedure, early postoperative period was defined as 24-72 hours after procedure.

The inclusion criteria

Symptomatic severe AS (NYHA class III or IV) who met these transthoracic echocardiographic

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criteria : - Mean gradient > 40 mmHg or velocity > 4.0 m/s Aortic valve area < 1 cm2
In impaired left ventricular function; with dobutamin stress test, mean gradient > 40 mmHg or velocity > 4.0 m/s or Aortic valve area < 1 cm2 or indexed valve area < 0.6 cm2/m2
Due to other contraindications to surgical valve replacement, high-risk status was defined as EuroSCORE >20% or an STS score >10%.

The exclusion criteria
Exitus during TAVI procedure or in first 24 hours (intraoperative)
Patients who underwent urgent SAVR due to failed procedure

Procedural details

The severity of AS, the aortic valve structure, the aortic root, degree of calcification and ascending aorta were evaluated by transthoracic echocardiography (TTE) and transeosophageal echocardiography (TEE). Multislice computed tomography (CT) was performed for the assessment of valve measurements,aortic root-arch calcification, diameters of the femoral and iliac arteries, and calcifications and tortuocities. Selection of self-expandable or balloon-expandable valves were done after all these measurements. Edwards Sapien [Edwards Lifesciences Corp.Irvine, CA] valves were mostly used on our TAVI procedures (79.9% of all the procedures). The other valves were Core Valve [Medtronic, Dublin 2, Ireland] .

The TAVI procedure was performed in a sterile environment in the catheterization laboratory. The procedure can be done under local anesthesia, sedation anesthesia or general anesthesia. Our procedures were done under general anesthesia. In our hospital, we usually chose transfemoral (TF) approach. But for the patients who were not eligible for the TF approach, transapical (TA) and transsubclavian approaches were used.

In TF approach, before the femoral artery punction which will carry the delivery system, two sheaths were placed in the contralateral femoral artery and femoral vein for placement of a pigtail catheter in the aorta and a pacemaker lead in the right ventricle, respectively. In most of our patients, preimplant balloon dilatations was carried out with overdrive pacing (200/min) .Bioprosthetic valve was implanted to the native valve level according to the suitable techniques. The aortic valve, valvular or paravalvular leak and peripheral arteries were evaluated after the deployment of the valve by the aortography and peripheral angiography. Punction site was closed by surgically or percutaneous techniques (Proglide [Abbott. Abbott Park, Illinois, U.S.A] or Prostar [Abbott. Abbott Park, Illinois, U.S.A]). Proglide [Abbott. Abbott Park, Illinois, U.S.A] and Prostar [Abbott. Abbott Park, Illinois, U.S.A] closure devices placed femoral punction zone before valve transport system advanced into the femoral artery. Both of these devices were used to occlude femoral

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punction zone by percutaneous techniques.

After the procedure, patients were transferred to the intensive care unit and typically extubated within early postoperative period (first 6 hours). In intensive care unit, patients were followed by laboratory tests and ECG. TTE was performed to evaluate the complications and the function of the bioprosthetic aortic valve. The postoperative anti-platelet regimen consisted of clopidogrel 75 mg daily for 6 months and aspirin 100 mg daily indefinitely. Patients with atrial fibrillation or other indications for anticoagulation received warfarin and aspirin without clopidogrel.

Definitions

Neutrophil lymphocyte ratio (NLR) was calculated from peripheral blood as neutrophil count/ lymphocyte count. Preoperative NLR was defined as 'NLR Basal'. Intraoperative NLR value was defined as 'NLR Intraop'. Postoperative 1st day NLR was defined as 'NLR Postop 1'. Postoperative 3rd day NLR was defined as 'NLR Postop 3'. Left ventricular dysfunction was defined as ejection fraction (EF) < 50 % . Chronic renal failure was defined as glomerular filtration rate (GFR) < 60 ml/dk .

Statistical analysis

Continuous variables are expressed as means ± SD, and categorical variables are expressed as percentages. Initially, univariate analyses (using the $\chi 2$ statistic for categorical variables

Mortality according to the NLR was analyzed by Kaplan-Meier, statistical significance was compared with Log Rank test. Then multivariate logistic regression model was carried out to assess the independent relationship between NLR and 30-day mortality after TAVI. For all tests, 2-sided *p* values <0.05 were considered as significant.

Results

A total of 196 consecutive patients underwent TAVI between October 2010 and December 2016 were screened. After exclusion of 12 patients, final study population consisted of 184 patients. 7 patients died in the first 24 hour after the procedure, 3 patients requiring immediate conversion to SAVR because of procedure failure. Success of the procedure was stated as 93.88 %. During follow-up, 16 patients of 184 were died in postoperative 24 hours - 30 days. 30-day mortality of TAVI was 8.69 %. The characteristics of study population summarized on Table 1.

Table 1: The characteristics of study population

Characteristics	Mean ± SD	Number, n	Percentage, %
Age	79.41± 7.882		
Woman		113	61.4
Man		71	38.6
EuroScore	32.6873± 15.38		

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STS Score	12.0443± 5.038		
NYHA Class III		108	58.7
NYHA Class IV		65	35.3
Coronary Artery Disease		114	62
Chronic obstructive pulmonary disease		112	60.9
Diyabetes Mellitus		74	40.2
Chronic Kidney Disease		54	29.3
Hypertension		151	82.1
CABG		44	23.9
Pulmonary Hypertension		124	67.4
Peripheral Artery Disease		68	37
Cerebro Vascular Disease		8	4.3
Atrial Fibrillation		30	16.3
Pacemaker		7	3.8

CABG: Coronary Artery Bypass Grafting , NYHA: New York Heart Association, STS: Society of Thoracic Surgeons

Preoperative and postoperative values were evaluated with ROC anaylsis to find out the value of NLR to predict 30 day mortality after TAVI (Figure- 1).

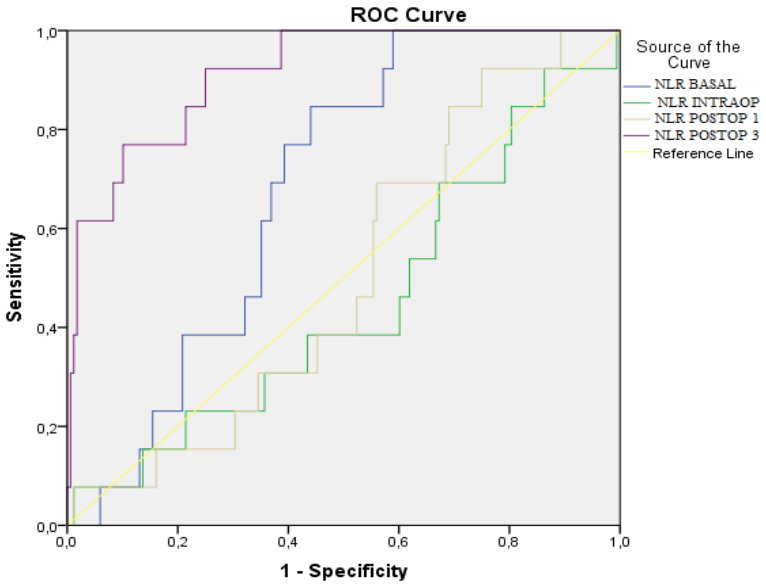

Figure 1: NLR ROC curves (AUC)
NLR BASAL: Preoperative Neutrophil Lymphocyte Ratio. NLR INTRAOP: Intra- operative Neutrophil Lymphocyte Ratio. NLR POSTOP 1: Postoperative 1st day Neutrophil Lymphocyte Ratio. NLR POSTOP 3: Postoperative 3rd day Neutrophil Lymphocyte Ratio.

Diagnostic power of results were compared with Area Under the Curve (AUC).

NLR Basal and NLR Postop 3 AUCs were 0.681 (p: 0.030) and 0.914 (p<0.001) respectively and they were found to be statistically significant.

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The values with highest spesifity and sensitivity were stated as cut off value. NLR basal ve NLR postop 3 values calculated by positive likelihood ratio which evaluates the spesifity and sensitivity together were 1.694 and 3.640, respectively.

As a result of ROC analysis most precious NLR value to predict 30 day mortality after TAVI was found as postop 3 NLR value [AUC: 0.914 ($p<0.001$), cut off value: 7.929, sensitivity:91%, spesifity: 75% ve +LHR: 3.64](Table 2). Although NLR Basal was not strong as NLR postop 3 for diagnosis, NLR basal is a pre-operative value which increases the clinical importance, had moderate diagnostic power for 2.058 cut off value with 100% sensitivity and 41% spesifity.

Table 2: NLR limit values calculated by ROC analysis.

Area Under the Curve [AUC]							
	AUC	**p value**	**95% Confidence Interval (CI)** *Lower-Upper*	**Cut off value**	**Sensitivity, %**	**Specificity, %**	**+LHR**
NLR Basal	0.681	0.030	0.580- 0.782	2.058	100	41	1.694
NLR Intraop	0.449	0.538	0.286- 0.612	1.998	92	13	1.057
NLR Postop 1	0.501	0.987	0.363- 0.640	6.614	92	25	1.226
NLR Postop 3	0.914	<0.001	0.846- 0.982	7.929	91	75	3.640

NLR BASAL: Preoperative Neutrophil Lymphocyte Ratio. NLR INTRAOP: Intra- operative Neutrophil Lymphocyte Ratio. NLR POSTOP 1: Postoperative 1st day Neutrophil Lymphocyte Ratio. NLR POSTOP 3: Postoperative 3rd day Neutrophil Lymphocyte Ratio. +LHR: Positive Likelihood Ratio.

Study patients' mortality causes, mortality days and last measured NLR summarized on table 3. Three patients died at postoperative day 2, so they weren't included to the NLR postop 3 analysis. But the last measured NLRs were found to be higher than the NLR postop 3 cutoff value. All the NLR values of died patients were higher than the cut off value which was determined with ROC analysis.

Table 3: Study patients' mortality causes, mortality days and last measured NLR

Mortality Cause	**Mortality Day**	**Last NLR**
Tamponade	2	15.77
Ventricular Tachycardia	2	10.61

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Cardiogenic Shock	2	30.49
Cerebrovascular event	3	14.07
Cardiogenic Shock	3	14.02
Atrioventricular Block	3	7.99
Ventricular Tachycardia	3	8.38
Cardiogenic Shock	4	28.09
Cardiogenic Shock	4	19.37
Pulmonary Edema/ Respiratory Failure	4	8.32
Cardiogenic Shock	5	21.32
Cardiogenic Shock	6	23.06
Septic Shock	18	12.2
Acute Kidney Injury	22	11.36
Septic Shock	27	18.3
Septic Shock	28	9.22

Study population was divided into two groups according to the cut off value; high NLR group (NLR≥ cut off value), low NLR group (NLR< cut off value). Two groups were compared according to demographic, clinical and echocardiagraphic data and there was no statistically significance. NLR Bazal and NLR Postop 3 were significantly higher in high NLR group for 30 day mortality. ['NLR Bazal' Ki kare: 10.27 (p: 0.001), 'NLR Postop 3' Ki Kare: 26.113 (p<0.001)] (Table 4).

Table 4: Relationship between 30 day mortality after TAVI and low NLR, high NLR groups divided according to NLR cut off value

		TOTAL NUMBER	NUMBER OF MORTALITY	NUMBER OF SURVIVAL	PERCENT OF SURVIVAL %	Pearson Chi Square
NLR BASAL	LOW NLR	68	0	68	100.0	10.27
	HIGH NLR	116	16	100	86.2	(*p* value: 0.001)
	OVERALL	184	16	168	91.3	
NLR INTRAOP	LOW NLR	23	1	22	95.7	0.626
	HIGH NLR	161	15	146	90.7	(*p* value: 0.429)
	OVERALL	184	16	168	91.3	
NLP POSTOP 1	LOW NLR	43	1	42	97.7	2.86
	HIGH NLR	141	15	126	89.4	(*p* value: 0.09)
	OVERALL	184	16	168	91.3	
NLR POSTOP 3	LOW NLR	127	1	126	99.2	26.113
	HIGH NLR	54	12	42	77.8	(*p* value< 0.001)
	OVERALL	181	13	168	92.8	

NLR BASAL: Preoperative Neutrophil Lymphocyte Ratio [LOW NLR<2.058, HIGH NLR>2.058].
NLR INTRAOP: Intra- operative Neutrophil Lymphocyte Ratio [LOW NLR<1.998, HIGH NLR>1.998].
NLR POSTOP 1: Postoperative 1st day Neutrophil Lymphocyte Ratio [LOW NLR<6.614, HIGH NLR>6.614].
NLR POSTOP 3: Postoperative 3rd day Neutrophil Lymphocyte Ratio [LOW NLR<7.929, HIGH NLR>7.929].

30 day survival of both high and low NLR groups were evaluated with Kaplan Meier analysis. Log Rank Ki Kare for NLR Basal and 'NLR Postop 3' were found 10.061 (p value: 0.002) and 27.18 (p value< 0.001) respectively. These parameters were shown to be significantly associated with 30 day survival after TAVI (Figure 2).

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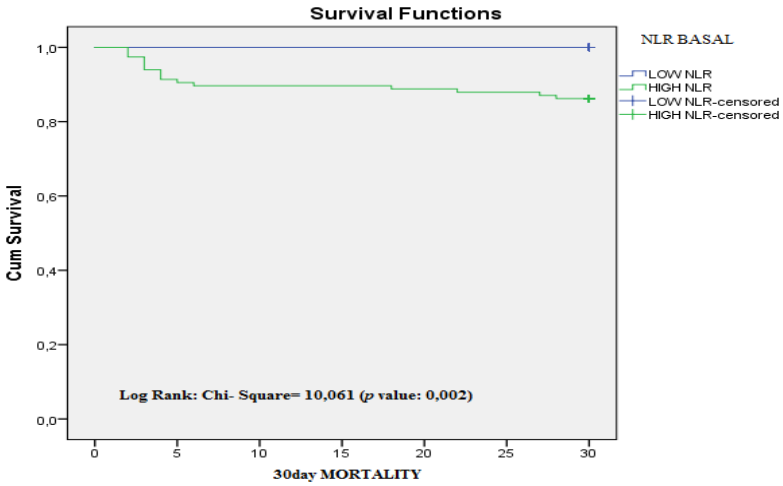

Figure 2a: Graphic for Kaplan Meier analysis of 30 day survival of high and low NLR groups divided according to the basal cut off value

NLR BASAL: Preoperative Neutrophil Lymphocyte Ratio. LOW NLR: NLR< 2,058, HIGH NLR: NLR> 2,0587

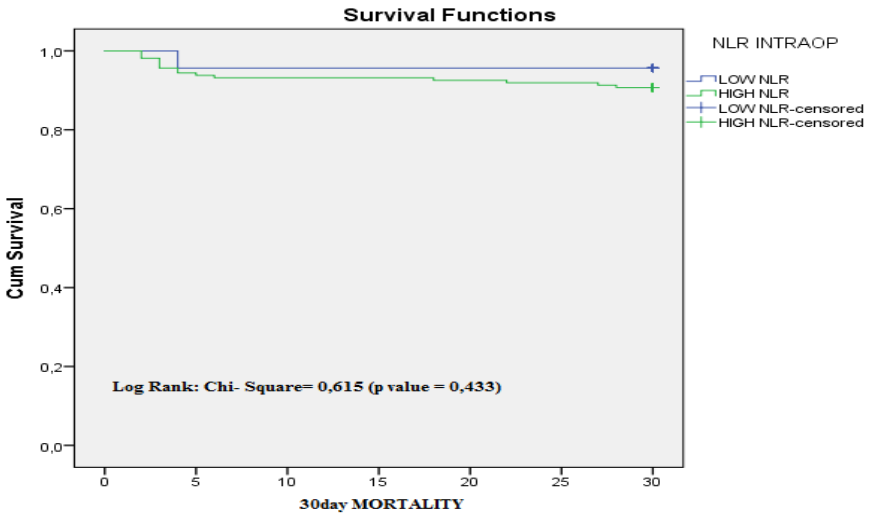

Figure 2b: Graphic for Kaplan Meier analysis of 30 day survival of high and low NLR groups divided according to the intraoperative cut off value

NLR INTRAOP: Intra- operative Neutrophil Lymphocyte Ratio [LOW NLR<1.998, HIGH NLR>1.998].

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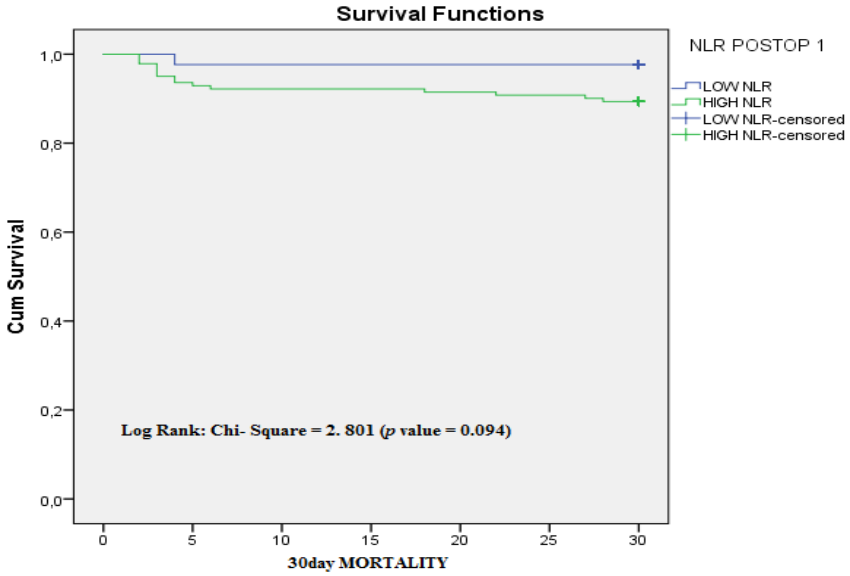

Figure 2c: Graphic for Kaplan Meier analysis of 30 day survival of high and low NLR groups divided according to the postoperative 1 cut off value

NLR POSTOP 1: Postoperative 1st day Neutrophil Lymphocyte Ratio [LOW NLR<6.614, HIGH NLR>6.614].

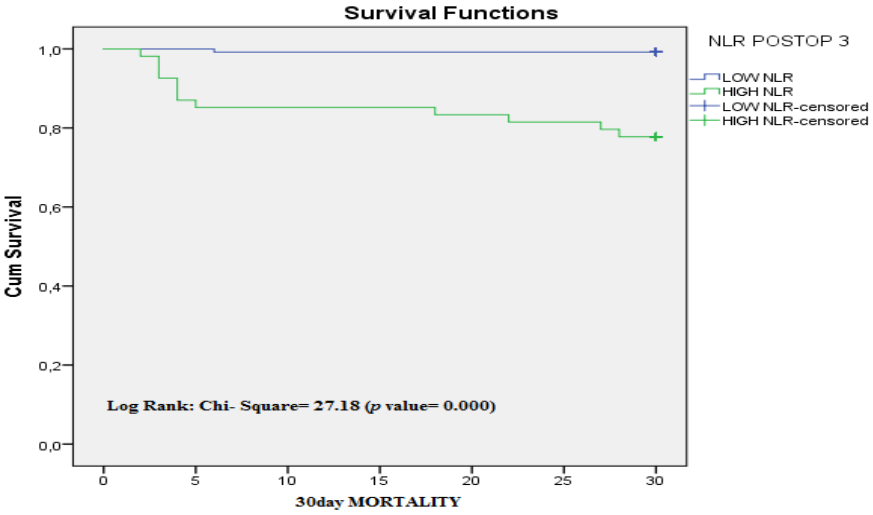

Figure 2d: Graphic for Kaplan Meier analysis of 30 day survival of high and low NLR groups divided according to the postoperative 3 cut off value

NLR POSTOP 3: Postoperative 3rd day Neutrophil Lymphocyte Ratio [LOW NLR<7.929, HIGH NLR>7.929].

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All data were evaluated with univariate analysis to find out the independent risk factors for 30 day mortality after TAVI (Table 5). According to the results of univariate analysis, a model was produced with "Coronary Artery Disease, Diabetes Mellitus, Hypertension, Chronic Kidney Disease, Basal Platelet Count and Preoperative Peak Gradient" (Model Omnibus test p value is 0.001). Preoperative and postoperative NLR values were evaluated with univariate analysis to find out if they were independent risk factors for the 30 day mortality after TAVI. When adjusted with produced model, it was shown that NLP postop 3 increased the mortality 1.168 times (p value < 0.001, CI: 1.09- 1.251) and was an independent risk factor for the 30 day mortality after TAVI (Table 6).

Acute Kidney Injury (AKI) [HR:6.583 , 95% CI: 1.360- 31.875 ; *p*: 0.019], preoperative Chronic Kidney Disease [HR: 3.664, 95% CI: 1.104-12.161; *p:* 0.034] and preoperative peak gradient [HR: 1.045 95%, CI: 1.008-1.084 , *p*:0.018] were found to be independent predictors on mortality.

As a result, although NLR Basal was a preoperative, highly clinical valued parameter, it had moderate power to predict the 30 day mortality after TAVI. NLR postop 3 had high diagnostic power for mortality and was an independent risk factor for the 30 day mortality.

Table 5: Univariate analysis of all study data by Cox regression analysis

Characteristics	***p* Value**	**Univariate Hazard Ratio**	**95% CI (Confidence Interval)**	
Age	0.841	0.994	0.935	1.056
Gender	0.251	0.515	0.166	1.597
Euro Score	0.346	0.983	0.949	1.019
STS Score	0.314	1.042	0.962	1.129
Coronary Artery Disease	0.107	2.252	0.838	6.047
Diabetes Mellitus	0.070	2.548	0.926	7.012
Hypertension	0.044	2.833	1.030	7.796
Coronary Artery Bypass Grafting	0.119	5.014	0.662	37.959
Chronic Kidney Disease	0.065	2.591	0.941	7.129
Basal Platelets	0.015	1.004	1.001	1.007
Postoperative 1st Day Platelets	0.018	1.003	1.001	1.006
Postoperative 3rd Day Platelets	0.032	1.006	1.001	1.012
Preoperative Peak Gradient	0.076	1.018	0.998	1.039
Acute Kidney Injury	<0.001	8.226	2.856	23.693

STS: Society of Thoracic Surgeons

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Table 6: Univariate and multivariate analysis to evaluate the effect of NLR on 30 day mortality after TAVI

Characteristics	*p* Value	Univariate Hazard Ratio	95% CI (Confidence Interval)	*p* Value	Multivariate Hazard Ratio	95% CI (Confidence Interval)
NLR BASAL	0.581	1.047	0.889- 1.233	0.674*	1.065	0.795- 1.425
NLR INTRAOP	0.591	0.974	0.885- 1.072	0.537*	0.962	0.850- 1.088
NLP POSTOP 1	0.989	1.000	0.948- 1.055	0.694*	1.012	0.954- 1.074
NLR POSTOP 3	0.000	1.205	1.135- 1.280	0.000*	1.168	1.09- 1.251

NLR BASAL: Preoperative Neutrophil Lymphocyte Ratio. NLR INTRAOP: Intra- operative Neutrophil Lymphocyte Ratio. NLR POSTOP 1: Postoperative 1st day Neutrophil Lymphocyte Ratio. NLR POSTOP 3: Postoperative 3rd day Neutrophil Lymphocyte Ratio

*Adjusted with parameters of Coronary Artery Disease, Diabetes Mellitus, Hypertension, Chronic Kidney Disease, Basal Platelet Count and preoperative Peak Gradient (Model Omnibus test p value is 0.001)

Table 7: Mean and percentage values of NLR.

Characteristics	Overal l Mean	Mean of Survival Paiens	Mean of Exitus Patiens	Overall 25% percentage	Overall 50% percentage	Overall 75% percentage
NLR BASAL	2,964	2,949	3,278	1,829	2,386	3,208
NLR INTRAOP	6,739	6,770	5,973	2,834	4,923	8,302
NLP POSTOP 1	13,176	13,181	13,188	6,693	10,680	17,077
NLR POSTOP 3	7,292	6,405	18,759	3,495	5,147	8,573

NLR BASAL: Preoperative Neutrophil Lymphocyte Ratio. NLR INTRAOP: Intra- operative Neutrophil Lymphocyte Ratio. NLR POSTOP 1: Postoperative 1st day Neutrophil Lymphocyte Ratio. NLR POSTOP 3: Postoperative 3rd day Neutrophil Lymphocyte Ratio

Table 8: Multivariate analysis for predictors of 30day mortality after TAVI

Characteristics	Hazard Ratio(%95 Confidence Interval)	*p value*
Diabetes Mellitus*	2,564(0,604-10,881)	0,202
Preoperative Peak Gradient*	1,045(1,008-1,084)	0,018
Acute Kidney Injury**	6,583(1,360- 31,875)	0,019
NLR Postop 3*	1.168 (1.09- 1.251)	<0.001
Coronary Artery Disease*	1.832 (0.607- 5.525)	*0.282*
Hypertension*	2.493 (0.774- 8.03)	*0.126*
Chronic Kidney Disease*	3.664 (1.104- 12.161)	*0.034*

NLR POSTOP 3: Postoperative 3rd day Neutrophil Lymphocyte Ratio

*Adjusted with parameters of Coronary Artery Disease, Diabetes Mellitus, Hypertension, Chronic Kidney Disease, Basal Platelet Count and preoperative Peak Gradient (Model Omnibus test *p value* is 0.001)

**Adjusted with parameters of Coronary Artery Disease, Diabetes Mellitus, Hypertension, Basal Platelet Count and preoperative Peak Gradient (Model Omnibus test *p value* is 0.001)

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Discussion

A total of 196 patients were screened and 12 of them were excluded according to the exclusion criteria. Our study showed; intraoperative mortality was 2.55%, procedure associated mortality was 6.12% and procedure success was 93.87%. 16 of 184 successfully TAVI performed patients died within 30 days. 30-day mortality was 8.69%.

In Crawford et al study which analyzed the mortality of surgical AVR and TAVI comparatively, includes 240 TAVI patients. When we catagorized the our mortality data according to the that study; preoperative mortality was 2 (7.14%), intraoperative mortality was 3 (0.7%), postoperative first 24 hour intensive care unit mortality was 7 (25%) and postoperative 24hour-30day mortality was 16 (57%) (12). According to the literature intraoperative mortality dispersion was good but postoperative mortality dispersion was found to be high. In Crawford et al study, the mean STS score of TAVI group was 9.7, survivors' mean STS score was 9.3 and died patients' mean STS score was 14.7. In our study, our patients' mean STS score was 12.04, survivors' mean STS score was 11.92 and died patients' mean STS score was 15.98. STS score is calculated according to preoperative comorbidities of patients and is widely used as a predictor of procedural mortality for surgical procedures. It has been shown that STS score was an independent predictor of inhospital and 30 day mortality after TAVI (13,14). High STS score in severe AS means SAVR has high mortality and morbidity and it is important to make a decision of TAVI. In Rose VEE et al study which evaluated the relationship between STS score and TAVI mortality, mean STS score was 20.7 and the 30 day mortality was 13.5% (14). High STS score increases the mortality as shown in our study. Our postoperative mortality was found significantly higher than the literature data, it can be explained with higher mortality and morbidity risks of our study population.

In our study's model, we used the data that Tamburino et al found as an independent risk factor for 30 day and 1 year mortality in 663 TAVI patients (15). They showed systolic dysfunction [LVEF < 40%], previous balloon valvuloplasty and DM were independent predictors for 30 day mortality. In our study we defined the LV systolic dysfunction as LVEF<50%. 26.4% of our patients' LVEF<50% and just the three of our died patients' LVEF was less than 50%. In our study we didn't find LV systolic dysfunction as an independent predictor of mortality, maybe due to the limited study population. In our study none of our patients had aortic balloon valvuloplasty, so we didn't evaluated this parameter in analysis. We found important difference that DM increased the mortality 2.564 times but it was not found to be statistically significant (95% CI:0.604-10.881; *p*: 0.202) in 30-day mortality. Our study was designed as 30 day mortality but in that study they showed that history of cerebrovascular event

(CVE) , preoperative pulmonary edema, chronic renal failure (CRF) were associated with 1 year mortality. We had 8 patients with previous CVE history who survived in 30 day follow up after TAVI. Due to short follow up period, we didn't find relationship between CVE and 30 day mortality. Also preoperative plumonery edema didn't found to be associated with mortality due to limited population. Our study showed that CRF was an independent risk factor for mortality *(p: 0.034).* and increased the 30 day mortality 3.664 times (%95 CI: 1.104-12.161).

Preoperative peak gradient [OR: 1.045 95%, CI: 1.008-1.084; *p*:0.018] was found to be statistically significant in 30-day mortality. AVA and mean gradient are important parameters for severe AS diagnosis but they were not found to be independent risk factors for 30 day mortality after TAVI.

Bagur, Sinning, Wessely and Nuis et al studies investigated the effect of AKI development to after TAVI on 30-day mortality and found that AKI development is an independent risk factor on 30-day mortality(16-19). Due to AKI development, Bagur found 4,14 times (95% CI: 1.42-12.13), Sinning found 4.9 times (95% CI: 1.2-20.4), Wessely found 16.4 times (95% CI: 1.3–197.8) and Nuis found 5.47 times (95% CI: 1.23-24.21) increased 30-day mortality risk. Acute kidney injury (AKI) and hemodialysis frequency were significantly higher in high NLR group. AKI [OR:6.583, 95% CI: 1.360-31.875 ; *p*: 0.019] was found to be statistically significant in 30-day mortality.

Condado et al analyzed the relation between NLR, platelet lymphocyte ratio (PLR) and 30-day early safety outcome, 1 year survival in 520 TAVI patients. They found high NLR was not able to predict the 30-day mortality or 30-days re-hospitalization separately but able to predict the composite early safety outcome. High NLR can effect 1 year survival negatively [HR 1.22, 95% CI 1.04–1.44] (20). Also they found a statistical association between change in NLR and 1-year readmission or 1-year mortality in unadjusted and adjusted analysis. But they didn't give a cut off value or mean value for NLR. They reported 22 of 520 patients died but NLR values weren't mentioned. Also when compared to our study population, their mean STS scores were lower than ours. This is the reason why our mortality was slightly higher. They compared the data according to quarters that were formed by NLR values and they performed the analysis according to NLR basal values. When we compared the our 25%, 50% ve 75% quarters cut off values and their value, our mean NLR was found to be lower. But it didn't negavitely effect the value of NLR basal for predicting the mortality after TAVI. Our results for relation between NLR basal and mortality and their results for 30 day mortality and morbidity with ROC analysis were similar. They used basal values while performing NLR analysis to predict the 30 day mortality and early safety

outcomes. Composite early safety outcomes included all cause mortality, CVE, CAD, life threathining bleeding, vascular complications, acute renal failure and reoperation due to valvular dysfunction. They found no statistically significant relationship between NLR basal values and 30 day mortality but the relation between 30 day composite early safety outcomes found to be statistically significant. Alteration in preoperative and postoperative NLR was used a parameter to evaluate the 1 year results and mortality. In our study NLR basal had moderate value with 1.694 posivite likelihood ratio to predict 30 day mortality after TAVI and NLR basal was not found as an independent precidtor for mortality as well as Condado et al. Study. We evaluated the relationship between NLR in different days and mortality. NLR postop 3 is a valuable parameter with 3.64 positive likelihoos ratio, high sensitivity and specifity to predict 30 day mortality after TAVI. NLR postop 3 was found to be an independent predictor for mortality with multivariate analysis. However it seems a technical problem to name a postoperative day 3 data as a "predictor", the cut off value for NLR postop 3 was lower than the patients who died before postoperative day 3. This adds to the mortality prediction in these patients.

When compared to preoperative values, it was showned that inpostoperative perior NLR tended to increase and this increase finished at postoperative day 3 and started to discrease. When survivors and died patients' mean NLRs were compared, especially NLR basal and NLR postop 3 values were found significantly increased in died patients (Table 7).

As a conclusion, postoperative 3rd day NLR, preoperative peak gradient and AKI were found to be independent predictors on 30-day mortality after TAVI procedure.

Study limitations

Our study was designed as a single center and retrospective study. Edwards Sapien valves were used in 79,9% of our patients. This can be a limitation for adaptation of other centers which use other valve types. While investigating the independent risk factors of 30-day mortality, we used literature and our clinical experience, so this can lead missing some other independent risk factors. In our study we evaluated NLR as an independent risk factor for 30 day mortality after TAVI but NLR shows systemic inflamation and it can be effected by any other factor during or after the TAVI procedure. For example general anesthesia increases the inflamation and all of our patients underwent to general anesthesia. A control group which is consist of TAVI patients who underwent sedation can increase the impact of study. But in our center we don't have a big size population for TAVI patients who underwent sedation. This is the limitation of our study.

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