ORIGINAL ARTICLE

Neutrophil/lymphocyte ratio as a predictor of mortality among aortic dissection patients in the emergency department

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ABSTRACT

BACKGROUND: Aortic dissection (AD) is a serious cardiovascular condition associated with high mortality rates. The systemic inflammatory response can influence the prognosis of AD, and in this context, the neutrophil-to-lymphocyte ratio (NLR) emerges as a simple and rapid inflammatory biomarker.

METHODS: This retrospective cohort study included 103 patients diagnosed with AD and treated in the emergency department between 2018 and 2023. Patient demographics, clinical features, and laboratory results were evaluated. Multivariate logistic regression analysis was performed to adjust for potential confounders such as age, mean systolic blood pressure, oxygen saturation, hemoglobin, lactate values, and the presence of coronary artery disease. The ability of NLR to predict mortality was analyzed using receiver operating characteristic (ROC) analysis.

RESULTS: The study population was divided into two groups: non-survivors (68% mortality rate) and survivors (32% survival rate). The non-survivor group had significantly higher NLR values compared to the survivor group (median NLR 7.66 vs. 2.5, p<0.001). Multivariate logistic regression analysis identified NLR as an independent predictor of in-hospital mortality (adjusted odds ratio [OR] 2.33, 95% confidence interval [CI] 1.42-3.82, p<0.001). ROC analysis for NLR demonstrated high discriminative power with an area under the ROC curve (AUROC) of 0.851 (95% CI 0.768-0.914). The determined cut-off point was >5.08 with a sensitivity of 77.14% and specificity of 81.82%.

CONCLUSION: The findings indicate that high NLR is strongly associated with increased mortality risk in patients with AD and can be used in emergency clinical settings to predict mortality.

Keywords: Aortic dissection; mortality; neutrophil-to-lymphocyte ratio.

INTRODUCTION

Aortic dissection (AD) is a separation within the layers of the aortic wall and is one of the most serious and common types of acute aortic syndromes.[1-3] AD is one of the leading causes of sudden death and requires urgent diagnosis and treatment, which are critical factors in determining patient survival.4

This pathology is usually associated with fundamental pathophysiological processes such as aortic aneurysm or hypertension; however, recent years have suggested that a systemic inflammatory response could play a significant role in the development and progression of AD. Inflammation, resulting from damage to the aortic wall, can emerge and accelerate the progression of the disease, increasing the risk of complications.[5-7]

Biomarkers can reflect signs of inflammation and disease ac-

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tivity, and it has been suggested that these markers may play an important role in determining the prognosis of diseases such as acute cardiovascular events.[8-10] The neutrophil-to-lymphocyte ratio (NLR) has been particularly notable among these markers. NLR represents the ratio of neutrophil to lymphocyte levels in the bloodstream and is considered an indicator of systemic inflammation.[11] A high NLR can indicate an increased level of inflammation in the body, which could potentially be useful in assessing the severity of various cardiovascular diseases and predicting their prognosis.[12,13]

The aim of this study is to evaluate the effects of NLR on mortality in patients diagnosed with AD.

MATERIALS AND METHODS

Approval for this study was granted by the Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital on April 27, 2023, with the decision number 2023/514/248/18, in accordance with the ethical principles outlined in the Declaration of Helsinki for research involving human subjects.

A retrospective cohort analysis was conducted on patients diagnosed with AD in the emergency department of Kartal Dr. Lütfi Kırdar City Hospital between January 2018 and January 2023. The inclusion criteria are as follows: patients must be 18 years of age or older, presenting to the emergency department, and diagnosed with AD through diagnostic imaging methods. The exclusion criteria include patients with missing or incomplete data and those with other acute aortic pathologies besides AD. The diagnosis of AD is based on the patient's clinical history, physical examination findings, and imaging methods, including computed tomography (CT) and echocardiography.

Data were collected from hospital records and electronic health record systems. The data analyzed include patients' age, gender, vital signs, comorbidity status, and laboratory values. The primary outcome of the study has been determined as in-hospital mortality.

Statistical Analysis

Statistical analyses will be performed using SPSS software for Windows (Version 29, Chicago, IL, USA). The normal distribution of the data was assessed using the Shapiro-Wilk test, and non-normally distributed continuous variables were expressed using the median and interquartile range (IQR), while normally distributed variables were expressed using the mean and standard deviation. Receiver operating characteristic (ROC) analysis was conducted to evaluate the effectiveness of NLR in predicting in-hospital mortality. The Youden index was used to determine the cutoff value. The area under the ROC curve (AUC) was used to assess the discriminative power of NLR in predicting mortality. To account for potential confounders, a multivariate logistic regression analysis was conducted, including age, mean systolic blood pressure, oxygen saturation, hemoglobin, lactate values, and the presence of coronary artery disease as covariates. This analysis aimed to determine the independent predictive value of NLR for mortality. In the study, a p-value of <0.05 was considered statistically significant.

RESULTS

The study included 103 patients diagnosed with aortic dissection, categorized into survivor (32%, n=33) and non-survivor (68%, n=70) groups based on their outcomes. The mean age of the study cohort was 73.9±13.5 years, with the non-survivor group having a significantly higher mean age (76.2±13 years) compared to the survivor group (69.1±13.3 years), showing an average difference of 7.2 years (95% confidence

Table 1. Comparison of various characteristics between survivor and non-survivor groups

Variables	All (n=103)	Survivors (n=33)	Non-survivors (n=70)	p value	Mean Difference (95% CI)
Age	73.9±13.5	69.1±13.3	76.2±13	0.012	7.2 (1.6-12.8)
Sex (Male)	78 (75.7%)	24 (72.7%)	54 (77.1%)	0.626	
Pulse Rate (/min)	90 (76.8-125.3)	88.5 (77-138.8)	90 (73.8-120)	0.960	
Systolic BP (mmHg)	105.4±41.7	122.8±38.4	97.5±41	0.004	25.3 (8.3-42.3)
Diastolic BP (mmHg)	80.7±25.9	86.4±22.7	78.1±27	0.056	
Oxygen Saturation (%)	96 (94-98)	97 (95.3-98)	96 (92.8-97)	0.002	
Hypertension	52 (50.5%)	15 (45.5%)	37 (52.9%)	0.483	
Diabetes Mellitus	12 (11.7%)	3 (9.1%)	9 (12.9%)	0.578	
Chronic Kidney Disease	11 (10.7%)	4 (12.1%)	7 (10%)	0.745	
Coronary Artery Disease	22 (21.4%)	13 (39.4%)	9 (12.9%)	0.002	
Stanford A	27 (26.2%)	8 (24.2%)	19 (27.1%)	0.755	
Stanford B	76 (73.8%)	25 (75.8%)	51 (72.9%)	0.755	

interval [CI] 1.5-12.8, p=0.012) (Table 1).

The gender distribution of the study cohort was determined to be 75.7% male (n=78), with no statistically significant difference observed in gender frequencies between the groups (p=0.626). While no significant differences were found in median pulse rate and mean diastolic blood pressure between the groups (p=0.960, p=0.0.56, respectively), the non-survivor group exhibited a significantly lower mean systolic blood pressure (97.5±41 mmHg) compared to the survivor group (122.8±38.4 mmHg), with a mean difference of 25.3 mmHg (95% CI 8.3-42.3, p=0.004). Conversely, the median peripheral oxygen saturation was significantly lower in the non-survivor group (96% [IQR 92.8-97%]) compared to the survivor group (97% [IQR 95.3-98%], p=0.002) (Table 1).

There were no statistically significant differences in the frequencies of hypertension, diabetes mellitus, and chronic kidney disease between the groups (p=0.483, p=0.578, p=0.745, respectively). However, the prevalence of coronary artery disease was significantly higher in the survivor group (39.4%, n=13) compared to the non-survivor group (12.9%, n=9, p=0.002).

Stanford A type aortic dissection was observed in 26.2% (n=27) of the study cohort, while Stanford B type was observed in 73.8% (n=76), with no statistically significant difference observed between the groups in terms of aortic dissection types (p=0.755) (Table 1).

While no significant difference was observed in mean white blood cell count between the groups (p=0.218), the non-survivor group had a significantly higher mean neutrophil count (10.5±4.7 103/μL) compared to the survivor group (7.8±3.8 103/μL), with a mean difference of 2.7 (95% CI 1-4.5) 103/μL, p=0.002. On the other hand, the survivor group had a significantly higher mean hemoglobin level (12.8±1.8 g/dL) compared to the non-survivor group (11.3±2.5 g/dL), with a mean difference of 1.5 (95% CI 0.7-2.4) g/dL. There was no statistically significant difference in mean platelet count between the groups (p=0.736); however, the non-survivor group had a significantly lower mean lymphocyte count (1.5±0.9 103/μL) compared to the survivor group (2.9±1.5 103/μL), with a mean difference of 1.5 (95% CI 1-1.9) 103/μL, p<0.001. While no significant differences were observed in median urea and creatinine values between the groups (p=0.865, p=0.068, respectively), the median lactate level was significantly higher in the non-survivor group (3.7 [IQR 2.35-8.05] mmol/L) compared to the survivor group (2.3 [IQR 1.5-3.25] mmol/L), p<0.001 (Table 2).

The median NLR was significantly higher in the non-survivor group (7.66 [IQR 5.12-12.77]) compared to the survivor group (2.5 [IQR 1.47-4.79]), p<0.001 (Table 2). The diagnostic performance analysis for NLR in predicting mortality in patients with aortic dissection revealed an area under the receiver operating characteristic curve (AUROC) of 0.851 (95% CI 0.768-0.914), p<0.001. The Youden index identified a cutoff value of >5.08, with a sensitivity of 77.14% (95% CI 65.6-93) and specificity of 81.82% (95% CI 64.5-93), a positive likelihood ratio of 4.24 (95% CI 2.03-8.85), and a nega-

Table 2. Comparison of laboratory values between survivor and non-survivor groups

	All (n=103)	Survivor (n=33)	Non-survivors (n=70)	p value	Mean Difference (95% CI)
White blood cell count (103/μL)	12.8±5	12±4	13.2±5.3	0.218	
Hemoglobin (g/dL)	11.8±2.4	12.8±1.8	11.3±2.5	<0.001	1.5 (0.7-2.4)
Neutrophil Count (103/μL)	9.66±4.6	7.8±3.8	10.5±4.7	0.002	2.7 (1-4.5)
Lymphocyte Count (103/μL)	1.96±1.3	2.9±1.5	1.5±0.9	<0.001	1.5 (1-1.9)
Platelet Count (103/μL)	226.5±90	230.7±83	224.5±93.6	0.736	
Urea (mg/dL)	28 (23-42.3)	31 (19.5-42)	28 (23-42.5)	0.865	
Creatinine (mg/dL)	1.2 (0.96-1.66)	1.19 (0.73-1.57)	1.2 (0.98-1.77)	0.068	
Lactate (mmol/L)	3.1 (1.88-6.8)	2.3 (1.4-3.25)	3.7 (2.35-8.05)	<0.001	
Neutrophil-to-Lymphocyte Ratio	6.37 (2.81-10.2)	2.5 (1.47-4.79)	7.66 (5.12-12.77)	<0.001	

Table 3. Predictive performance of neutrophil-to-lymphocyte ratio in terms of mortality among aortic dissection patients

AUROC (95% CI)	p	Cut-Off	Sensitivity (95% CI)	Specificity (95% CI)	+LR	-LR
0.851 (0.768-0.914)	<0.001	>5.08	77.14 (65.6-86.3)	81.82 (64.5-93)	4.24 (2.03-8.85)	0.28 (0.18-0.44)

AUROC: Area Under the Receiver Operating Characteristic; +LR: Positive Likelihood Ratio; -LR: Negative Likelihood Ratio.

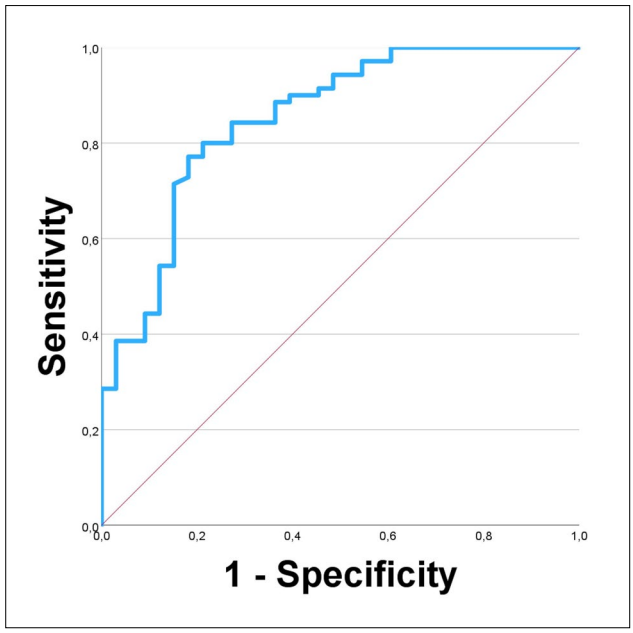

Figure 1. Area under the curve analysis for the neutrophil-to-lymphocyte ratio in predicting mortality.

Table 4. Multivariate logistic regression analysis of predictors of in-hospital mortality in aortic dissection patients

Predictors	p	OR (95% CI)
Age (in years)	0.258	1.04 (0.97-1.12)
Systolic Blood Pressure (mmHg)	0.479	1.01 (0.99-1.03)
Diastolic Blood Pressure (mmHg)	0.782	1.01 (0.96-1.05)
Oxygen Saturation (%)	0.182	0.68 (0.38-1.2)
Coronary Artery Disease	0.509	0.48 (0.01-1.36)
Hemoglobin (g/dL)	0.817	1.06 (0.65-1.74)
Lactate (mmol/L)	0.134	1.59 (0.94-2.45)
Neutrophil-to-Lymphocyte Ratio	<0.001	2.33 (1.42-3.82)

CI: Confidence Interval; OR: Odds Ratio.

tive likelihood ratio of 0.28 (95% CI 0.18-0.44) (Fig. 1, Table 3). The multivariate logistic regression analysis demonstrated that NLR remains a significant predictor of mortality even after adjusting for confounders (adjusted odds ratio [OR]: 2.33, 95% CI: 1.42-3.82, p<0.001). The model showed good calibration and discrimination with a Hosmer-Lemeshow test p-value of 0.951 and a C-statistic of 0.750. The model achieved an accuracy rate of 92% (Table 4).

DISCUSSION

In this study, the effectiveness of the NLR in predicting mortality in patients with AD was investigated. Our findings indicate that NLR is an independent predictor of mortality in patients with aortic dissection, even when considering confounding factors such as age, blood pressure, oxygen saturation, hemoglobin, lactate levels, and coronary artery disease. This reinforces the utility of NLR as a simple and rapid biomarker for risk stratification in the emergency department.

Inflammation plays a critical role in acute cardiovascular events like AD. Specifically, neutrophils are considered one of the primary mediators of vascular damage and subsequent inflammatory processes. Neutrophils rapidly migrate to infected or damaged tissues and form the first line of inflammation.[14] These cells destroy pathogens through phagocytosis and the release of destructive enzymes and reactive oxygen species, aiding in tissue clearance. However, the excessive production of these reactive species can damage surrounding tissues, contributing to the progression of the disease and increasing the complications associated with AD.[15] This dual effect of neutrophils holds significant importance in the pathophysiology of AD. The elevated neutrophil levels observed in patients with AD indicate that these cells are actively involved in the inflammatory process, which may be directly related to the severity of the disease. In this context, NLR emerges as a strong indicator reflecting the intensity of inflammation and the overall status of the inflammatory response in the body.

Lymphocytes are fundamental components of the adaptive immune response in the body and provide protection against both viral and bacterial infections.[16] In serious vascular events such as AD, lymphocytes play critical roles in the immune regulation and repair processes in damaged tissues. These cells proliferate in response to specific antigens and develop specialized immune responses to modulate inflammation. Particularly, T-lymphocytes help prevent harmful autoimmune responses through their inflammation-limiting and tissue-protective effects, while B-lymphocytes neutralize pathogens through antibody production.[17] The functions of lymphocytes can be decisive in the progression and outcomes of AD. A decrease in lymphocyte levels, known as lymphopenia, often indicates immune suppression in cases of severe infection or systemic inflammation. In this context, the NLR, characterized by high neutrophil levels and low lymphocyte counts, can objectively measure the severity of the inflammatory process and stress on tissues. High NLR values in patients with AD indicate a disruption of this balance and an increased risk of mortality, thus making NLR an important indicator in clinical decision-making processes.

There are numerous studies in the literature regarding the prognostic value of NLR in AD. In a study conducted by Dönmez and colleagues, it was noted that an increased NLR in patients with AD is significantly associated with mortality, indicating that a high NLR could be related to the severity of the disease.[18] A meta-analysis concluded that preoperative NLR could be a practical tool in predicting in-hospital mortality in patients with AD.[19] Li and colleagues investigated the diagnostic value of NLR and fibrinogen in patients with Type B AD, finding that NLR showed high specificity and could be

a valuable tool in diagnosing Type B AD.[20] Consequently, the findings of our study are in alignment with the data presented in the literature, supporting that NLR is a strong and reliable indicator of mortality risk in patients with AD. This consistency demonstrates that NLR could play a critical role in the prognostication of AD and potentially benefit clinical decision-making processes.

This study has several limitations. Firstly, due to its retrospective design, some important variables may not have been recorded, which could affect the outcomes. Secondly, the study was conducted at a single center, which may limit the generalizability of the findings. Thirdly, we did not examine the role of other inflammatory markers besides NLR, which limits the scope of the study. Lastly, the applicability of the findings to other populations may be limited due to the demographic characteristics of the study population.

CONCLUSION

In conclusion, this study demonstrates that a high NLR is associated with an increased risk of mortality in patients with AD, and that NLR can be used as an effective predictor of mortality. These findings are applicable to clinical practice and can contribute to the development of early intervention strategies in emergency departments.

Ethics Committee Approval: This study was approved by the Kartal Lutfi Kirdar City Hospital Ethics Committee (Date: 27.04.2023, Decision No: 2023/514/248/18).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: İ.U.; Design: İ.U.; Supervision: G.A.U., İ.U.; Resource: İ.U.; Materials: İ.U.; Data collection and/or processing: İ.U.; Analysis and/or interpretation: G.A.U.; Literature search: G.A.U.; Writing: G.A.U., İ.U.; Critical reviews: G.A.U., İ.U.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Acil servise başvuran aort diseksiyonu hastalarında mortalitenin belirleyicisi olarak nötrofil/lenfosit oranı

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AMAÇ: Aort diseksiyonu (AD), yüksek mortalite oranlarıyla ilişkili ciddi bir kardiyovasküler durumdur. Sistemik enflamatuvar yanıt AD'nin prognozunu etkileyebilir ve bu bağlamda nötrofil-lenfosit oranı (NLR) basit ve hızlı bir enflamatuvar biyobelirteç olarak ortaya çıkmaktadır.

GEREÇ VE YÖNTEM: Bu retrospektif kohort çalışmaya 2018-2023 yılları arasında AD tanısı konulan ve acil serviste tedavi gören 103 hasta alındı. Hastaların demografik özellikleri, klinik özellikleri ve laboratuvar sonuçları değerlendirildi. Yaş, ortalama sistolik kan basıncı, oksijen doygunluğu, hemoglobin, laktat değerleri ve koroner arter hastalığının varlığı gibi potansiyel karıştırıcıları ayarlamak için çok değişkenli lojistik regresyon analizi yapıldı. NLR'nin mortaliteyi tahmin etme yeteneği, alıcı işletim karakteristiği (ROC) analizi kullanılarak analiz edildi.

BULGULAR: Çalışma popülasyonu iki gruba ayrıldı: Hayatta kalmayanlar (%68 ölüm oranı) ve hayatta kalanlar (%32 hayatta kalma oranı). Hayatta kalmayan grup, hayatta kalan gruba kıyasla anlamlı derecede daha yüksek NLR değerlerine sahipti (medyan NLR 7.66'ya karşı 2.5, p<0.001). Çok değişkenli lojistik regresyon analizi, NLO'yu hastane içi mortalitenin bağımsız bir belirleyicisi olarak tanımladı (düzeltilmiş OR 2.33, %95 GA 1.42-3.82, p<0.001). NLR için ROC analizi, ROC eğrisi altındaki alan (AUROC) 0.851 (%95 GA 0.768-0.914) ile yüksek ayırt edici güç gösterdi. Belirlenen kesme noktası >5.08 olup duyarlılığı %77.14, özgüllüğü %81.82 idi.

SONUÇ: Bulgular, yüksek NLR'nin AD'li hastalarda artan mortalite riskiyle güçlü bir şekilde ilişkili olduğunu ve acil klinik ortamlarda mortaliteyi tahmin etmek için kullanılabileceğini göstermektedir.

Anahtar sözcükler: Aort diseksiyonu; mortalite; nötrofil-lenfosit oranı.

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