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Predictors of In-hospital Death in Patients with Stanford Type B Acute Aortic Dissection

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Abstract

Background: Even with immediate surgical intervention, acute aortic dissection (AAD) is a cardiovascular emergency with a high mortality rate. The purpose of this study was to look at the relationship between in-hospital mortality and red cell distribution width (RDW)/lymphocyte ratio (RLR), monocyte/lymphocyte ratio (MLR), and systemic immune inflammation index (SII) in patients with type B acute aortic dissection (BAAD).

Materials and methods: 59 BAAD patients who presented to the emergency room of a tertiary hospital were included in this cross-sectional study. The predictive ability and cut-off value of biomarkers for mortality were evaluated using Receiver Operating Characteristic (ROC) analysis. The variables believed to be connected to in-hospital mortality were subjected to multiple regression analysis, and the odds ratio was calculated.

Results: The study consisted of 59 patients in total, 44 of whom (74.6%) were male. 17 of these patients died in the hospital. In terms of predicting in-hospital mortality in BAAD patients, MLR, and neutrophil/lymphocyte ratio (NLR) have excellent diagnostic power (AUC: 0.826, 0.822, respectively), while platelet/lymphocyte ratio (PLR), RLR, and SII have acceptable diagnostic power (AUC: 0.758-0.786). Increased NLR, PLR, MLR, RLR, and SII were found to be independent predictors of in-hospital mortality in patients with BAAD (odss ratio: 9.16, 7.68, 9.33, 6, 8.57, respectively).

Conclusion: MLR, RLR, and SII are valuable parameters for estimating in-hospital mortality in adult BAAD patients. Increased NLR, PLR, MLR, RLR, and SII in BAAD patients are independent predictors of in-hospital mortality.

Keywords: RDW to lymphocyte ratio, monocyte to lymphocye ratio, acute aortic dissection type B, in-hospital death, systemic immune inflammation index.

Introduction

Even with immediate surgical intervention, acute aortic dissection (AAD) is a cardiovascular emergency with a high mortality rate[1]. According to the Stanford system, aortic dissections are classified as type A or type B depending on whether or not the ascending aorta is involved[2]. Age, hypotension/shock, history of cardiac and renal surgery, and mesenteric or myocardial ischemia are all independent risk factors for AAD mortality, per the International Registry of Acute Aortic Dissection[3]. Furthermore, biomarkers such as inflammation, thrombosis, and vascular injury have been investigated as potential contributors to AAD diagnosis or risk estimation tools[4,5].

Recent research has found that inflammatory indices like and red cel distribution width (RDW) platelet ratio (RPR), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), and lymphocyte monocyte ratio (LMR), which can be easily calculated from routine blood tests, can predict mortality[6–9].

There have been no research has looked at the relationship between inflammatory biomarkers like RDW lymphocyte ratio (RLR), monocyte lymphocyte ratio (MLR), and systemic immune inflammation index (SII) and patients with AAD who have a mortal course. The relationship between mortality in Stanford Type B Acute Aortic Dissection (BAAD) patients has not been thoroughly revealed.

The purpose of this study was to look at the relationship between in-hospital mortality and RLR, MLR, and SII in patients with type B acute aortic dissection (BAAD).

Materials and Methods

This cross-sectional study included 59 BAAD patients who presented to a tertiary hospital emergency department between April 18, 2020 and April 18, 2022. The local ethics committee approved the study and waived the requirement for informed consent (protocol code:120, decision no:120, issue:E-48670771-514.99 date:18 April 2022). The current study was carried out in accordance with the Helsinki Declaration.

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Post-study power analysis

According to the cross-sectional study design, the NLR value, which is the main outcome variable, was used to determine the reliability assessment (post-study power) of the number of patients included in the groups. While NLR was 9.37±5.79 in-hospital deaths, it was 5.39±2.78 in survivors. According to the difference in NLR levels between the independent group averages, the post-study power was 94.47%. According to the difference in the secondary outcome variables PLR, MLR, RLR, and SII, the post-study power was above 80%.

Study Protocol

Following ethical committee approval, data from the hospital's data network were analyzed retrospectively. The diagnosis of BAAD was confirmed by aortic angiography with multi-detector computed tomography (CT) scanning. Patients over the age of 18 who were diagnosed with BAAD inside of 24 hours of onset were included in the investigation. Patients who had missing clinical, laboratory, or radiographic data, were pregnant, had peripheral vascular disease, heart failure, hematologic disease, or liver disease, were on anticoagulants or steroids, had other acute or chronic infections, or had a history of aortic dissection were excluded from the study. BAAD patients were split into two groups: those who died in the hospital and those who survived. Demographic data of the groups (gender, age, etc.) and laboratory findings obtained at the first admission to the emergency department were recorded. The cardiovascular surgeons at our hospital determined the patients' treatment approach (the reason for and strategy of surgical techniques).

Laboratory analyses

The complete blood count (CBC) was measured with an automated hematological analyser. Hematological parameters white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM), monocyte (MON), platelet (PLT), RDW, NLR, PLR, MLR, SII, and RLR values were recorded.

Primary purpose

To assess the predictive value of RLR, MLR, and SII in BAAD patients.

Statistical analysis

Parametric tests were used without the normality test due to the compatibility of the Central Limit Theorem10. The mean and standard deviation, as well as the minimum and maximum values of the features, were used in the data analysis while performing continuous data statistics. Categorical variables were defined using frequency and percentage values. The student's t-test was used to compare the means of two independent groups. Chi-square test statistics were used to examine the relationships among categorical variables. The cut-off in diagnostic value measurements was ascertained using Receiver Operating Characteristic (ROC) analysis. The statistics of specificity, sensitivity, positive predictive value (PPV), and negative predictive value (NPV) were used to determine statistical significance. An AUC of 0.5 to 0.6 was interpreted as poor, 0.6 to 0.7 as fair, 0.7 to 0.8 as acceptable, 0.8 to 0.9 as excellent, and greater than 0.9 as outstanding. The variables believed to be linked to in-hospital mortality were subjected to multiple regression analysis, and the odds ratio was calculated. The level of statistical significance of the data is considered $p<0.05$. The www.e-picos.com New York software and the MedCalc statistical package program were used to analyze the data.

Results

A total of 59 patients with type B AAD were included in this study, 44 of whom (74.6) were male. The average age of the patients was 63.2±13.3 years. The in-hospital mortality rate was 29% (17 of 59 patients). Table 1 shows the mean values of all patients' laboratory results in detail. While there was no significant difference in PLT, HGB, HTC, RDW, NEU, and MON group averages ($p>0.05$), there was a significant difference in LYM, NLR, PLR, MLR, SII, and RLR group averages (p0.05) (table 1).

In Table 2, the diagnostic accuracy of prognostic parameters used to predict type B AAD related in-hospital mortality in ROC analysis is given in detail (table 2, figure 1).

In predicting in-hospital mortality in patients with BAAD, MLR and NLR have excellent diagnostic power (AUC: 0.826, 0.822, respectively), while PLR, RLR and SII have acceptable diagnostic power (AUC: 0.758-0.786).

When the probability ratio of the variables thought to be associated with in-hospital mortality was evaluated; Increased NLR, PLR, MLR, RLR and SII were found to be independent predictors of in-hospital mortality in BAD (Odss ratio: 9.16, 7.68, 9.33, 6, 8.57, respectively) ($P<0.05$) (Table 3).

Discussion

Emergency physicians are constantly on the lookout for non-invasive, dependable, and easily accessible tools to detect life-threatening conditions in patients. This study showed that MLR, RLR and SII are valuable parameters in predicting in-hospital mortality in adult patients with BAAD in the emergency department. Furthermore, in-hospital mortality was found to be high in patients with high MLR, RLR, and SII at admission. This is the first study in the literature, as far as we know. These results indicate that MLR, RLR, and SII may be used as biomarkers in future BAAD risk classifications.

BAAD is responsible for roughly one-third of all AAD cases. Predicting the prognosis of each BAAD patient is difficult due to the variety of clinical features of

Table 1: Comparison of clinical characteristics of the study population

		Total (n=59)	Survivors (n=42)	In-hospital death (n=17)	P-value	
Features		**x̄±SD**	**x̄±SD**	**x̄±SD**		
Age		63.2±13.3	63.2±13.8	63.1±12.2	0.97	
PLT (10^3mcL)		328.39±62.08	300±57.93	324.41±73.11	0.76	
HGB (g/L)		12.95±2.29	13.02±2.43	12.8±1.96	0.74	
HTC (%)		39.11±6.31	39.23±6.59	38.8±5.73	0.81	
RDW (fL)		14.39±1.71	14.38±1.79	14.42±1.52	0.95	
NEU (10^3mcL)		8.5±3.42	8.39±3.76	8.77±2.51	0.71	
LYM (10^3mcL)		1.53±0.62	1.71±0.61	1.09±0.39	**<0.001**	
MON (10^3mcL)		0.58±0.19	0.57±0.15	0.61±0.26	0.65	
NLR		6.53±4.25	5.39±2.78	9.37±5.79	**0.01**	
PLR		253.49±133.22	214.17±73.86	350.67±190.44	**0.01**	
MLR		0.43±0.17	0.36±0.12	0.58±0.19	**<0.001**	
RLR		11.79±8.94	9.67±4.06	17.01±14.39	**0.05**	
SII(PLT*NLR)		2106.23±1221.53	1763.14±956.76	2953.85±14.11	**0.004**	
		n(%)	**n(%)**	**n(%)**		
Gender	Female	15 (25.4)	12 (28.6)	3 (17.6)	0.38	-
	Male	44 (74.6)	30 (71.4)	14 (82.4)		

Student's t-test, Chi-Square test (p<0.05 significance)

PLT: Platelets, **HGB:** Hemoglobin, **HCT:** Hematocrit, **RDW:** Red Cell Distribution Width, **NEU:** Neutrophil, **LYM:** lymphocyte, **MON:** monocyte, **NLR:** neutrophil to lymphocyte ratio, **PLR:** platelet to lymphocyte ratio, **MLR:** monocyte to lymphocyte ratio, **RLR:** RDW to lymphocyte ratio,
SII: Systemic immune-inflammation index

BAAD[11]. Recent research has revealed that inflammation plays a prominent role in aortic dissection. Lymphocytes, macrophages, and neutrophils contribute to the apoptosis of smooth muscle cells in the aortic artery and ultimately lead to medial degradation. This is widely accepted as the fundamental mechanism of aortic dissection[5].

Nunez et al. discovered a link between lower lymphocyte counts and higher monocyte counts and poorer cardiovascular outcomes[12]. Lin et al. found that LMR with a cut-off value of 1.43 (around 0.7 AUC) in patients with type A AAD (AAAD) could predict in-hospital mortality[4]. Chen et al. found an AUC of 0.575 and a cut-off value of 1.435 for LMR in predicting 30-day mortality (sensitivity 49%, specificity 64%)[13]. Our study found that an equivalent of LMR, MLR, is an independent predictor of mortality.

Variability in circulating erythrocyte size, as measured by red cell distribution width (RDW), is a risk factor for cardiovascular mortality. RDW indicates an underlying inflammatory condition leading to impaired erythrocyte maturation[14]. RLR is a new biomarker. Wu et al. demonstrated high sensitivity and specificity of RLR in predicting hepatic impairment in patients with hepatitis E virüs[15]. Moreover, RLR was shown to have acceptable diagnostic power in the detection of acute appendicitis in pediatric patients[16]. RLR

Table 2: Diagnostic accuracy of prognostic parameters to predict type B AAD related in-hospital mortality with the best predictive cut-offs.

	AUC	Cut-off	Sensitivity %	Specificity%	AUC 95% CI	P	PPV %	NPV%
NLR	0.82	>6.32	76.47	78.57	0.70-0.91	<0.001	59.1	89.2
PLR	0.77	>241.38	70.6	78.6	0.65-0.87	<0.001	57.1	86.8
MLR	0.83	>0.44	82.35	73.81	0.71-0.91	<0.001	56	91.2
RLR	0.76	>10.72	70.59	71.43	0.63-0.86	<0.001	50	85.7
SII(PLT*NLR)	0.78	>2579.85	58.82	88.10	0.65-0.87	<0.001	64.3	82.2

AUC, Area under curve; SE, Standard error; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval;

NLR: neutrophil to lymphocyte ratio, **PLR:** platelet to lymphocyte ratio, **RDW:** Red Cell Distribution Width, **RLR:** RDW to lymphocyte ratio,
MLR: monocyte to lymphocyte ratio, **PLT:** Platelet, **SII:** Systemic immune-inflammation index

Table 3: Multiple regression analysis of risk factors affecting in-hospital mortality associated with type B AAD

Variables	Odds ratio	95% CI	P-value
NLR	9.16	2.46-34.11	0.001
PLR	7.68	2.17-7.13	0.002
MLR	9.33	2.3-37.94	0.002
RLR	6	1.74-20.73	0.005
SII(PLT*NLR)	8.57	2.35-31.33	0.001

CI: confidence interval, **NLR:** neutrophil to lymphocyte ratio, **PLR:** platelet to lymphocyte ratio, **MLR:** monocyte to lymphocyte ratio, **RLR:** Red Cell Distribution Width (RDW) to lymphocyte ratio, **SII:** Systemic immune-inflammation index, **PLT:** Platelet

was found to be an independent predictor of mortality in BAAD patients in our study.

SII is a new inflammatory index that comprehensively reflects the host immune and inflammatory state balance[17]. It has even been proposed that SII is more useful than NLR and PLR alone in predicting inflammatory status and prognosis in a variety of clinical scenarios[18]. A high SII score has been linked to poor outcomes in cancer patients, heart failure, and coronary artery disease[19]. Therefore, we thought that patients with BAAD might show a similarly poor prognosis. In the light of our study results, we can conclude that SII is a new predictor of mortality in BAAD.

In cases of increased inflammation, the neutrophil count increases rapidly, while the lymphocyte count decreases, thus significantly increasing NLR. In patients with AAAD, Karakoyun et al. showed a specificity of 74%, and a sensitivity of 77% for the prediction of in-hospital mortality with an NLR value >8.51 (AUC: 0.829)[20]. Bedel et al. observed that a cut-off point of 9.74 (AUC 0.746) accurately predicted in-hospital mortality in type A AAD with 70.6 percent sensitivity and 76.8 percent specificity in AAAD[21]. When compared to the AAAD literature, NLR had a higher predictive power of mortality (AUC: 0.822) in BAAD, with a lower cut-off value (6.32).

PLR has been linked to the magnitude of inflammation in recent studies[22]. In the study of Du et al. in patients with BAAD, both elevated and decreased PLRs were independently associated with in-hospital mortality[23]. Contrary to this study, in the logistic regression analysis performed by Li et al in patients with BAAD, PLR was an independent predictor of all-cause mortality (hazard ratio 6.14, 95% CI:1.401-26.895, P: 0.02). PLR 9.16 (CI: 2.46-34.11, P: 0.001) predicted mortality with odds ratio in our study.

Limitations

Our study has several limitations. This is a single-center retrospective study. We used the laboratory results of the first application for analysis and could not include follow-up values. Serial follow-up of these indices we studied can also predict mortality. Therefore, our findings cannot be generalized but may be informative and supportive for future studies for more reliable and conclusive results.

Conclusion

MLR, RLR, and SII are valuable parameters in predicting in-hospital mortality in adult patients with BAAD. In patients with BAAD, increased NLR, PLR, MLR, RLR, and SII are independent predictors of in-hospital mortality.

Ethics Committee Approval: *The local ethics committee approved the study and waived the requirement for informed consent (protocol code:120, decision no: 120, issue: E-48670771-514.99 date: 18 April 2022). The current study was carried out in accordance with the Helsinki Declaration.*

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