

The Effect of White Blood Cell and Platelet Values on Mortality in Patients With Abdominal Aortic Aneurysm

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Abstract

Background: In this study, we aimed to investigate the relationship between preoperative inflammatory markers, length of hospital stay, and mortality in patients with abdominal aortic aneurysm (AAA) who underwent surgical repair.

Materials and methods: A total of 83 patients diagnosed with AAA were included in the study. A complete blood count (CBC) was performed on the first visit (pre-op 0-1 hour) in all patients. Non-ruptured cases (AAA) and ruptured cases (AAA-R) were compared.

Result: 14.5% (n=12) of the patients died. Higher White blood cells and neutrophils were obtained in patients who died than in surviving patients (respectively, $p=0.0002$, $p=0.001$). Higher WBC and NALP in AAA-R patients were determined.

Conclusion: WBC and Neu's values were higher in AAA patients who died post-operatively and who were detected rupture pre-operatively but PLT and HB values were similar. Normal or near-normal HB and PLT values that will be seen in the first examination of AAA cases in the emergency department may mislead clinicians or cause them to display a more optimistic attitude.

Keywords: Abdominal aortic aneurysm, Mortality, White blood cell, Neutrophil

Introduction

An abdominal aortic aneurysm (AAA) is a disease that occurs where the aortic wall is weak and is characterized by enlargement of the vessel diameter (>1.5 times). Structural changes in the wall and arterial pressure lead to thinning of the wall and separation of the extracellular matrix [1]. Despite significant advances in diagnostic methods, surgical repair, and anesthesia techniques, aortic aneurysms remain serious and early diagnosis is important [2]. The frequency of diagnosis of aortic aneurysms is increasing day by day due to the increase in life expectancy and the developments in imaging techniques worldwide. AAA is a disease mostly seen in the elderly and men, the most important risk factor being smoking [4]. Other risk factors include atherosclerosis, hypertension, hyperlipidemia, and genetic factors (it has great importance) [4]. AAA is difficult to diagnose clinically and is usually detected during imaging for other purposes. Ultrasound and CT are commonly used diagnostic methods [5, 6]. While the risk of rupture is quite low in small AAAs, it is higher in large AAAs [7]. There are two main methods

for the management of AAAs, open surgery and endovascular aneurysm repair (EVAR) [6, 8]. Despite new procedures, mortality in FMF remains high despite improved therapies [9].

Aneurysm formation results from a complex process characterized by infiltration of the aortic wall by inflammatory cells [10]. Neutrophilia has been implicated in several mechanisms potentially relevant for aneurysmal disease, including the secretion of proinflammatory mediators, induction of endothelial cell damage, and prothrombotic states [11, 12]. In addition, neutrophilia has been associated with a significantly increased risk of major adverse cardiovascular events [13].

Lymphopenia is mainly due to the margination and redistribution of lymphocytes within the lymphatic system associated with an increase in apoptosis [14, 15]. Lymphopenia indicates a generalized state of immunosuppression and has been identified as a predictor of mortality in patients with chest pain and a prognostic marker in patients with coronary heart disease or advanced heart failure [14]. However, its significance in patients with AAA has not been adequate-

ly studied so far. Several studies have emphasized the role of lymphocytes in the pathogenesis of aneurysms [15]. It revealed an increase in lymphocytes in aneurysms [16].

The platelet/lymphocyte ratio (PLR) represents a marker of the systemic inflammatory response [17, 18]. The relationship with inflammatory indices has been investigated in atherosclerosis and various cardiovascular diseases[19]. In addition, studies are showing that PLR predicts 30-day morbidity in ruptured AAA[20].

Our study aimed to investigate the relationship between preoperative inflammatory markers, length of hospital stay, and mortality in patients with AAA who underwent EVAR or open surgical operation.

Materials and methods

The study was carried out in the Emergency Medicine and Cardiovascular surgery departments of Abant İzzet Baysal University. Ethics committee approval was obtained from the local ethics committee. Records of AAA cases who underwent open or endovascular repair between January 2015 and February 2022 were reviewed retrospectively.

Study Population

A total of 83 patients diagnosed with AAA were included in the study.

Inclusion criteria

Patients with a large aortic diameter (abdominal aortic diameter >5.5 cm for men and >4.5 for women), rupture detected, patients who are scheduled for emergency or elective operation (EVAR or open surgical repair).

Exclusion criteria

Patients with a previous history of hematological disease and malignancy were excluded from the study.

Demographic and clinical characteristics of the patients were noted, taking into account the patient's statements, medical records, and treatment. In all patients, the diagnosis was confirmed by computed tomography scanning, which is the gold standard diagnostic method. The patients were divided into two groups ruptured or non-ruptured aneurysms. Complete blood count(CBC) was performed on the first visit (pre-op 0-1 hour) in all patients, WBC: White Blood Cell, HGB: Hemoglobin, PLT: Platelet, RDW: Red Cell Distribution width LYM: Lymphocyte, MONO: Monocytes, NEU: Neutrophil, PDW: Platelet Distribution Width, MPV: Mean Platelet Volume, PCT: Procalcitonin, CRP: C Reactive Protein ALBM: Albumin, NLR: Neutrophil/Lymphocyte ratio, LMR: Lymphocyte /Monocytes ratio, PLR: Platelet/Lymphocyte ratio V, RDW*MPV: Red cell distribution width/Mean Platelet Volume, PDW*MPV: Platelet Distribution width/Mean Platelet Volume, CRP/Alb: C Reactive Protein /Albumin values were recorded. PLR is the number

of Platelets/ lymphocyte count. NLR is the neutrophil count/ lymphocyte count. The NALP score was calculated with the formula neutrophil x albumin x lymphocyte/platelet. Post-operative results such as mortality and length of stay were recorded. Data were collected using electronic or manual files. Imaging data were collected from the hospital information system. Non-ruptured cases (AAA) and ruptured cases (AAA-R) were compared.

Statistical Analysis

CBC parameters and index values of the patients in both groups were analyzed with the Mann-Whitney U test. The relationship with the length of stay was evaluated with the Spearman (rho) correlation coefficient. The performances of CBC parameters and indices for mortality estimation and diagnosis discrimination were investigated by ROC analysis. AUC values were compared with the DeLong test. R (version 4.1.0) program pROC (version 1.17.0.1) package was used for ROC analysis. Statistical software SPSS version 23 (SPSS Inc., Armonk, NY) was used for all other analyses. The significance level was determined as $p < 0.05$.

Results

The median age of AAA patients included in the study was 71 (63-77) and 80.7% (n:67) were male. There was a weak negative correlation was found between age and MPV. Higher hemoglobin [10.15 (9.32-12.53), 11.7 (10.4-13.8)], CRP [2.6 (0.23-14.25), 17.4 (3.9-35)] and CRP/Alb ratio [respectively,] in male patients than in female patients. 0.1 (0.01-0.4), 0.45 (0.1-1.09)] (respectively, $p=0.029$, $p=0.030$, $p=0.048$) (Table 1).

The patients presented with abdominal pain [n=34 (40%)], chest pain [and=27 (32.5%)], back pain [n=13 (15.7%)] and other reasons [n=9 (11.8%)]. 21 (25.3%) patients applied to the emergency department [rupture was detected in 15 of the patients (71.4% of ED visits), 10 of these patients died], and others admitted to the cardiovascular surgery outpatient clinic. 31 (37.3%) of the patients were treated with EVAR, while the others underwent open surgical procedures.

14.5% (n=12) of the patients died. Higher WBC [9.68 (7.61-14.9), 16.34 (12.91-22.88), respectively) and NEU (7.38 [4.57-12.6), 13.65 (8.78-20.24, respectively)] were obtained in patients who died than in surviving patients (respectively, $p=0.0002$, $p=0.001$). NALP [1.8 (0.9-2.8, 4.7 (3.4-5), respectively)] values were higher in patients who died than in surviving patients, while PLR [151.7 (99.4-247.2), 105.7 (75.8-133.3, respectively)] values were lower ($p= 0.00004$, $p=0.008$) (Table 2). The area under the curve (AUC) values were found to be 0.871 for NALP, 0.832 for WBC, 0.793 for NEU, and 0.739 for PLR (Figure 1). Although the highest AUC value was obtained for NALP, the difference between the AUC values of WBC, NEU and PLR

Table 1: Comparative data on genders

	Age		Gender		p
	r	p	Female (n=16) Med (IQR)	Male (n=67) Med (IQR)	
Hemogram					
WBC	-0.08	0.491	9.3 (5.85-15.26)	10.8 (8.03-16.26)	0.315
HGB	-0.01	0.927	10.15 (9.32-12.53)	11.7 (10.4-13.8)	0.029
PLT	-0.04	0.701	219.5 (160.25-245.5)	188 (153-241)	0.583
RDW	0.17	0.114	15.65 (14.03-16.88)	15.4 (13.7-16.6)	0.544
LYM	0.01	0.930	1.5 (0.52-2.32)	1.5 (0.96-2.03)	0.926
MONO	-0.12	0.284	0.59 (0.4-1)	0.64 (0.45-0.94)	0.858
NEU	-0.09	0.431	6.98 (4.4-12.02)	9.18 (4.99-13.9)	0.258
PDW	0.01	0.913	15.9 (11.13-17.43)	17.3 (12.7-18.2)	0.078
MPV	-0.26	0.019	9.64 (7.52-10.7)	8.64 (7.55-10.4)	0.544
PCT	-0.21	0.054	0.18 (0.15-0.23)	0.17 (0.13-0.22)	0.347
CRP	0.07	0.542	2.6 (0.23-14.25)	17.4 (3.9-35)	0.030
Albm	-0.18	0.103	31.7 (30-38)	36 (32-41)	0.164
Ratios					
NLR	-0.03	0.755	6.27 (2.17-14.94)	7.34 (2.82-12.63)	0.844
LMR	0.12	0.291	2.73 (1.02-4.09)	2.49 (1.3-3.59)	0.917
CLR	0.05	0.665	5.18 (0.16-15.28)	10.5 (2.08-32.81)	0.100
PLR	-0.05	0.658	161.36 (95.21-391.24)	135.14 (98.54-205.26)	0.426
Indexes					
RDW*MPV	-0.21	0.057	138.94 (126.89-162.35)	137.5 (118.4-147)	0.356
PDW*MPV	0.06	0.567	239.59 (177.78-284.68)	271.44 (178.56-295.48)	0.329
CRP/Alb	0.09	0.392	0.1 (0.01-0.4)	0.45 (0.1-1.09)	0.048
NALP	-0.07	0.542	1.59 (0.81-2.59)	2.09 (1.14-3.93)	0.170
Length of stay*	-0.26	0.028	17.5 (10-22.25)	11 (6-16)	0.016

IQR: Interquartile range (25th-75th percentiles). Mann-Whitney u testi, r: Spearman (rho) correlation coefficient.

WBC: White Blood Cell, HGB: Hemoglobin, PLT: Platelet, RDW: Red Cell Distribution width, LYM: Lymphocyte, MONO: Monocytes, NEU: Neutrophil, PDW: Platelet Distribution Width, MPV: Mean Platelet Volume, PCT: Procalcitonin, CRP: C Reaktif Protein, ALBM: Albumin, NLR: Neutrophil/Lymphocyte ratio, LMR: Lymphocyte/Monocytes ratio, PLR: Platelet/Lymphocyte ratio, RDW*MPV: Red cell distribution width/Mean Platelet Volume, PDW*MPV: Platelet Distribution width/Mean Platelet Volume, CRP/Alb: C Reaktif Protein /Albumin

were not statistically significant (DeLong test: $p=0.238$, $p=0.128$, $p=0.073$, respectively). The cut-off points for the classification of surviving and deceased patients were determined as 2.99 for NALP, 12.24 for WBC, 7.19 for NEU, and 144.52 for PLR (Table 3).

The median length of stay in surviving patients is 12 (7-18) days. There was a weak negative correlation between the age of these patients and their length of stay ($r=-0.26$,

$p=0.028$). This period. Female patients were approximately 7 days [17.5 (10-22.25) - 11 (6-16)] and were hospitalized longer than males ($p=0.016$) (Table 1). There was a very weak negative correlation between hospitalization times and hemoglobin and platelet values, and a weak positive correlation between MPV and RDW*MPV values ($r=-0.24$, $p=0.043$, $r=-0.24$, $p=0.044$, $r=0.30$, $p=0.010$, $r=0.356$, $p=0.002$) (Table 4).

Table 2: Effect of all parameters on mortality

	All Cases		p
	Discharge (n=71)	Exitus (n=12)	
Age, Year, Med (IQR)	69 (62-77)	72 (70.25-77.25)	0.193
Gender - Male, n (%)	57 (80.28)	10 (83.33)	1.000 ^a
Hemogram Med (IQR)			
WBC	9.68 (7.61-14.9)	16.34 (12.91-22.88)	0.0002
HGB	11.6 (10.20-13.30)	10.9 (7.84-13.08)	0.271
PLT	197 (157-240)	200.5 (140.5-253.25)	0.646
RDW	15.4 (13.8-16.6)	15.8 (14.38-16.75)	0.560
LYM	1.41 (0.79-2.03)	1.73 (1.22-2.61)	0.091
MONO	0.64 (0.45-0.91)	0.64 (0.46-1.14)	0.766
NEU	7.38 (4.57-12.6)	13.65 (8.78-20.24)	0.001
PDW	17.2 (12.7-18.1)	16.8 (11-19.2)	0.887
MPV	8.64 (7.56-10.4)	9.6 (7.02-10.85)	0.693
PCT	0.17 (0.14-0.22)	0.17 (0.1-0.26)	0.641
CRP	10 (2.2-35.7)	19 (1.68-26.23)	0.776
Albm	36 (31.5-41)	33.2 (26.48-37)	0.075
Ratios Med (IQR)			
NLR	7.1 (2.7-13.3)	10.1 (3.9-11.7)	0.560
LMR	2.5 (1.3-3.3)	2.7 (1.1-5.3)	0.468
CLR	8.5 (1.7-50.9)	12.3 (1.2-17.6)	0.669
PLR	151.7 (99.4-247.2)	105.7 (75.8-133.3)	0.008
Indexes Med (IQR)			
RDW*MPV	137.5 (122.5-147.6)	139.6 (117.3-164.3)	0.578
PDW*MPV	270.8 (178.6-289)	260.1 (175.4-310.1)	0.641
CRP/Alb	0.3 (0.1-1.1)	0.5 (0.1-0.8)	0.948
NALP	1.8 (0.9-2.8)	4.7 (3.4-5)	0.00004

IQR: Interquartile range (25th-75th percentiles).

Mann-Whitney U testi, ^a: Fisher'in Kesin (Exact) testi.

There was no difference in age and gender between the AAA and AAA-R diagnostic groups, (p=0.563, p=0.724, respectively). It was observed significantly more frequently in AAA-R patients (n=10, 66.7%) than in others (p<0.01) (Table 1). Higher WBC and NALP in AAA-R patients were determined (Table 5).

Discussion

In this study, we investigated the relationship between preoperative CBC parameters, the ratios, and indices of these

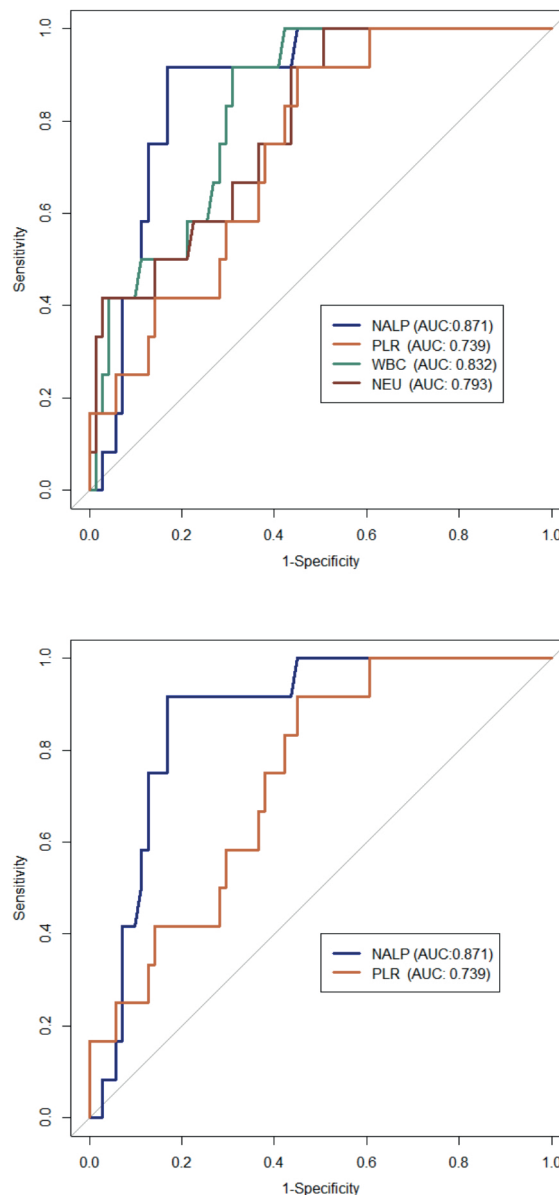


Figure 1: ROC curves and AUC values for mortality classification

parameters, and postoperative mortality in AAA patients. We found higher WBC and neutrophil counts in patients with preoperative rupture and patients with postoperative death. However, we found that hemoglobin and platelet counts did not help detect preoperative rupture and predict postoperative mortality.

An aneurysm can induce an inflammatory response by leukocytosis and platelet activation [21]. Platelets can induce thrombosis and also release inflammatory molecules. Neutrophils can promote inflammatory responses, cause damage to the blood-brain barrier, and release inflammatory mediators [12]. It can interact with monocytes, platelets, and endothelial cells to support inflammatory and prothrombotic pathways [22]. In contrast, lymphocytes play an important

Table 3: Cut-off points and performance measures for mortality classification

	Cut-off	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
NALP	2.99	91.7	83.1	47.8	98.3
PLR	144.52	91.7	54.9	25.6	97.5
WBC	12.24	91.7	69.0	33.3	98.0
NEU	7.19	100	49.3	25.0	100.0

Table 4: The relationship of hemogram parameters, rates and indices with length of stay in discharged patients

	All Cases	
	r	p
Hemogram		
WBC	-0.02	0.859
HGB	-0.24	0.043
PLT	-0.24	0.044
RDW	-0.04	0.768
LYM	-0.12	0.319
MONO	-0.09	0.472
NEU	-0.01	0.939
PDW	-0.10	0.426
MPV	0.30	0.010
PCT	-0.04	0.711
CRP	-0.09	0.433
Albm	-0.19	0.111
Ratios		
NLR	0.08	0.503
LMR	0.002	0.990
CLR	-0.07	0.577
PLR	0.01	0.909
Indexes		
RDW*MPV	0.356	0.002
PDW*MPV	-0.06	0.642
CRP/Aib	-0.08	0.500
NALP	-0.02	0.849

r: Spearman (rho) correlation coefficient.

role in the anti-inflammatory response [15]. In a study conducted by Ko et al., it was shown that mortal cases in Open Repair of Abdominal Aortic Aneurysms had higher neutrophil counts and lower hemoglobin values preoperatively [23]. Nejm et al. showed that patients with a preoperative WBC value of >10000 had a larger aneurysm and were more mortal [24]. Domanovits et al. found that the CRP and WBC values of patients with ruptured AAA were not different, but

hemoglobin values were lower [25]. In another study, a cohort of 252 patients undergoing thoracic endovascular aortic repair for degenerative AAA revealed that preoperative leukocytosis independently predicted the risk of late mortality [26]. In this study, higher WBC and neutrophil counts were detected in ruptured AAA cases and post-op mortal cases. However, no difference was observed between hemoglobin levels and platelet counts.

It is known that neutrophils also play a role in coagulation apart from their antimicrobial activities [25]. Activated neutrophils exhibit important procoagulant properties; neutrophils stimulate coagulation by the release of tissue factor; it has been found that they can activate platelets, factor X, factor XII, and prothrombin, and contribute to the stabilization of the fibrin clot [25]. It is seen that neutrophils play an active role in limiting bleeding that develops in this way. This information may explain the higher neutrophil monitoring in ruptured patients detected in our study.

Although there was a correlation between mortality and low PLR in our study, high PLR and decreased LMR were associated with poor clinical outcomes in some other aneurysmatic diseases [27]. Ntalouka MP et al. in the group of patients who underwent EVAR, NLR and PLR values were found to be significant in showing postoperative kidney damage and major adverse cardiovascular events (MACE) [17]. Lareyre et al. reported that high NLR values may be an indicator for a ruptured thoracic aortic aneurysm [28]. In this study, which included 83 patients with FMF, no significant difference was observed in terms of preoperative PLR value in terms of postoperative hospital stay.

Conclusion

Although the incidence and prevalence of abdominal aortic aneurysm has decreased in the last years globally, it is one of the life-threatening emergencies [29]. Therefore, new markers are needed to determine the prognosis. WBC and Neu's values were higher in AAA patients with preoperative rupture, but PLT and HB values were similar. High mortality was observed in patients with rupture. WBC and Neu's values were higher in AAA patients who died post-operatively,

Table 3: Comparison of cases with and without rupture

	AAA (n=68)	AAA-R (n=15)	P
Age, Year, Med (IQR)	70 (61.2-78)	71 (68-75)	0.563
Gender - Male, n (%)	54 (79.4)	13 (86.7)	0.724 ^a
Mortality, n (%)	2 (2.9)	10 (66.7)	<0.00001 ^a
Hemogram, Med (IQR)			
WBC	9.66 (7.61-14.11)	17.3 (13.1-23.82)	0.00005
HGB	11.65 (10.13-13.53)	10.9 (9.9-12.6)	0.362
PLT	186 (153.25-237.5)	234 (170-255)	0.142
RDW	15.35 (13.9-16.58)	15.8 (13.7-16.6)	0.795
LYM	1.43 (0.8-1.98)	1.63 (1.14-2.7)	0.100
MONO	0.64 (0.45-0.93)	0.59 (0.45-1.32)	0.767
NEU	7.23 (4.63-10.96)	15.2 (9.7-21)	0.0001
PDW	17.15 (12.7-18.08)	17.4 (10.2-18.9)	0.657
MPV	8.72 (7.6-10.5)	8.99 (6.94-9.85)	0.459
PCT	0.17 (0.14-0.21)	0.2 (0.13-0.26)	0.442
CRP	11.35 (2.2-35.93)	16.7 (2.2-22.1)	0.519
Albm	9.66 (7.61-14.11)	17.3 (13.1-23.82)	0.145
Ratios, Med (IQR)			
NLR	6.72 (2.62-13.22)	9.62 (3.49-11.8)	0.344
LMR	2.53 (1.23-3.52)	2.48 (1.43-3.72)	0.661
CLR	8.69 (1.76-52.25)	11.95 (0.77-15.08)	0.485
PLR	146.84 (98.77-239.12)	124.29 (85.89-172.66)	0.115
Indexes, Med (IQR)			
RDW*MPV	138.56 (122.98-150.09)	129.69 (115.2-147)	0.326
PDW*MPV	268.66 (179.23-288.91)	288.84 (144-313.74)	0.485
CRP/Alb	0.28 (0.06-1.33)	0.4 (0.09-0.7)	0.636
NALP	1.75 (0.9-2.83)	4.71 (2.09-6.17)	0.0001

IQR: Interquartile range (25th-75th percentiles).

Mann-Whitney U test, a: Fisher's Exact tests.

but PLT and HB values were similar. Normal or near-normal HB and PLT values that will be seen in the first examination of AAA cases in the emergency department may mislead clinicians or cause them to display a more optimistic attitude. Therefore, high WBC and Neu values should alert clinicians to possible rupture or mortality.

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