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Relationship Between Abdominal Aortic Aneurysm and Inflammatory Markers

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Abstract

Objective: In this study, we aimed to investigate the relationship between abdominal aortic aneurysm and systemic immune inflammation index (SII), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and other inflammatory markers, especially those derived from complete blood count.

Methods: Retrospectively, 72 consecutive patients admitted to our clinic for Abdominal Endovascular Aneurysm Repair (EVAR) for abdominal aortic aneurysm (AAA) between January 2019 and January 2022 were included in the study. Routine blood samples were taken before EVAR operation. NLR, PLR, SII of the patients were calculated and, RDW, Mean Platelet Volume (MPV), C-reactive protein values and other laboratory tests were recorded. They were compared with an age-matched control group.

Results: The age of the patients included in the study was 67.7 ± 10.6 years and the majority were male. The frequency of hypertension and coronary artery disease was also higher. In the comparison of hematologic parameters with the control group, MPV was 10.4(9.6-11.2) versus 9.5(8.6-10.1), p<0.001; CRP was 5(1.625-42.135) versus 3.21(2.08-4.75), p=0.04, NLR was 3.46(2.15-6.69) versus 2.29(1.65-2.78), p<0.001. SII was 682.54(417.08-1522.72) versus 558.22(405.33-711.31), p=0.02. The most significant association with the presence of ascending aortic aneurysm was observed between NLR.

Conclusion: Inflammatory markers, CRP, SII, NLR, MPV are significantly higher in patients with AAA. In patients with AAA, the association between aneurysm and NLR appears to be better. When following up these patients, it may be especially useful to look at CRP, SII, NLR, MPV levels.

Keyword: Aortic Aneurysm, Systemic İmmune İnflammation İndex, Neurophil Lymphocyte Ratio

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INTRODUCTION

Aortic aneurysm is a progressive and degenerative disease characterised by an increase in the cross-sectional diameter of any segment of the aorta of at least 50% above the cross-sectional diameter required for the age and body surface area of the individual (1). Today, it is still increasing in frequency and continues to cause morbidity and mortality. The risk factors involved in aneurysm formation and development are quite similar to the risk factors associated with coronary artery disease (2).

There are many cytokines that have local and systemic effects in the etiopathogenesis of aortic aneurysm and have been shown to be associated with medial degenerative changes. In the pathogenesis, lymphocytes and protease activity, macrophages and IL 6 were found to be involved as the source of proinflammatory cytokines (3). Therefore, it is emphasized that aortic aneurysm is an inflammatory response. It has been observed that inflammation is important not only in the formation of cardiovascular diseases but also in the complications that may occur later (4). Therefore, we aimed to investigate the relationship between Systemic immune inflammation index (SII), Neutrophil-to-lymphocyte ratio (NLR), C Reactive Protein (CRP) and Platelet-to-lymphocyte ratio (PLR), MPW, RDW and abdominal aortic aneurysm.

METHODS

Baseline clinical data were obtained retrospectively by reviewing the records of 72 consecutive patients who underwent computed tomography angiography of the aorta, were diagnosed with abdominal aortic aneurysm (AAA) and scheduled for Abdominal Endovascular Aneurysm Repair (EVAR) between January 2019 and January 2022 in our center. Patients with active systemic infections, malignant tumors, hematopoietic system disorders or known autoimmune diseases that may affect peripheral blood cells were excluded.

Biochemical analysis

Complete blood counts and biochemical parameters were examined in the venous blood samples taken from the antecubital vein. Complete blood count analyzes were performed with the same device, which was checked and maintained at regular hourly intervals in the central laboratory. Blood samples were collected in standard tubes containing a fixed amount of ethyl diamine tetra acidic acid. A complete blood count was measured within one hour following blood sample collection.

Neutrophil to lymphocyte ratio (NLR) was calculated by dividing neutrophil count by lymphocyte count, and platelet to lymphocyte ratio (PLR) was calculated by dividing platelet count by lymphocyte count. Systemic immune inflammation index (SII) was calculated by

multiplying the platelet count by NLR (5). The data obtained were compared with the age-matched control group.

All patients included in the study undervent 2D transthoracic echocardiographic (TTE) evaluation performed by an experienced cardiologist. (Philips, iE33, the Netherlands). Left ventricular (LV) end-systolic dimension, end-diastolic dimension and wall thickness were measured according to the guidelines of the American Society of Echocardiography. LV end-systolic and end-diastolic volumes and ejection fraction were measured from the apical four--chamber view and two-chamber views using the modified Simpson's method.

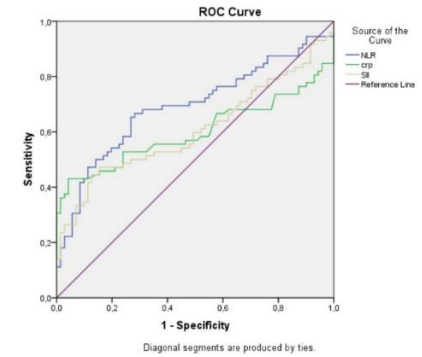
Our study was approved by the local ethics committee and institutional review board. In addition, our study was consistent with the Declaration of Helsinki.

Statistical analysis

Data were analyzed using SPSS 22.0 (SPSS Inc., Chicago, Illinois, USA). The categorical variables were expressed as the number with a percentage (n%). Chi-square analysis was used to compare categorical variables. The normality of the data was tested using the Kolmogorov Kolmogorov-Smirnov test. Variables are expressed as mean ± standard deviation (SD) and median (25th, 75th percentile) as appropriate. Significance test (independent t-test) and Mann-Whitney U test were used to compare the research and control groups based on the normality of the data. Receiver operating characteristic (ROC) curve analyses were performed to obtain the area under the curve (AUC) of NLR, CRP, and SII to determine the best diagnostic performance.

RESULTS

A total of 72 patients, 54 of whom were male, and 75 control groups were included in the study. The age of the patients was 67.7 ± 10.6 years, and the majority were male. The frequency of hypertension and coronary artery disease was also higher. Demographic data of the patient and control groups are summarized in Table 1. In the comparison of hematologic parameters with the control group, MPV was 10.4(9.6-11.2) versus 9.5(8.6-10.1), p<0.001; CRP was 5(1.625-42.135) versus 3.21(2.08-4.75), p=0.04, NLR was 3.46(2.15-6.69) versus 2.29(1.65-2.78), SII was 682.54(417.08-1522.72) versus 558.22(405.33-711.31), p=0.02 (Table 2). The most significant association with AAA was found to be with NLR (Figure 1.).



Area Under the Curve

Test Result Variable(s)	Area
NLR	,691
crp	,599
SII	,607

The test result variable(s): crp has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

Figure 1. Diagnoal segments are produced by ties

Table 1. Demographic data

Variable	EVAR +, n=72	Control, n=75	p value
Age (years)	67.7 ± 10.6	62.8 ± 11.5	0,112
Gender (male) n(%)	54 (75)	41 (54,7)	0,008
Hypertension n(%)	58 (80,6)	22 (31)	<0.001
DM, n(%)	20 (27,8)	25 (33,3)	0,219
Smoking n(%)	39 (54,2)	39 (52)	0,95
CAD n(%)	39 (54,2)	5(7)	<0.001

CAD: Coronary artery disease, DM: Diabetes mellitus, EVAR: Abdominal endovascular aneurysm repair

Table 2. Hematological and laboratory data of the study population

Variable	EVAR +, n=72	Control, n=75	p value
Hemoglobin (g/dl)	13.65(11.77-14.65)	14.3(12.8-15.6)	0,002
Hematocrit (%)	40.7(35.85-43.47)	42.9(38.2-46.4)	0,004
WBC (10^9/L)	8.42(7-10.54)	7.24(5.82-8.7)	0,01
Neutrophil (10^9/L)	6.13(3.75-8.39)	4.45(3.5-5.3)	<0.001
Lymphocyte (10^9/L)	1.6(1.055-2.27)	1.9(1.5-2.34)	0,03
Platelet (10^3/L)	194.5(155-253.75)	244(201-288)	0,002
MPV (fL)	10.4(9.6-11.2)	9.5(8.6-10.1)	<0.001
RDW (%)	13.85(13.2-14.6)	13.4(12.9-14.3)	0,066
Creatinine (mg/dl)	0.96(0.84-1.17)	0.86(0.73-0.94)	<0.001
CRP (mg/dl)	5(1,625-42,135)	3.21(2.08-4.75)	0,04
NLR	3.46(2.15-6.69)	2.29(1.65-2.78)	<0.001
PLR	130.18(96.55-176.88)	126.43(94.81-170.50)	0,552
SII	682.54(417.08-1522.72)	558.22(405.33-711.31)	0,02
EF (%)	60(51.5-60)	55(50-60)	0,378

WBC: White blood cell, MPV: Mean platelet volume, RDW: Red blood cell distribution width, CRP: C-reactive protein, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SII: Systemic inflammation index, EF: Ejection fraction

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DISCUSSION

When the results of our study were evaluated, CRP, MPV, NLR and SII were found to be significantly increased among inflammatory markers in patients with AAA. It suggests that these biomarkers have an impact on the development of AAA and may also guide its treatment.

Aneurysm advancement is multifactorial in nature, with both a genetic predisposition and natural components acting together to initiate a cascade of arterial degradation. An vital portion part of aneurysm improvement is the ubiquitous inflammatory cell infiltrate, which has been illustrated in all abdominal aortic aneurysms. In spite of the fact that this inflammation is more articulated in 'Inflammatory AAAs' current understanding favours one pathological process with changing degrees of inflammation rather than the distinct clinical entity first proposed by Walker. A modern think about has certified this hypothesis by illustrating indistinguishable HLA alleles working in both inflammatory and degenerative AAA, supporting the concept of a common immune-mediated pathogenesis.

Ordinary aortic tissue contains few on the off chance that any provocative cells in differentiate to AAA tissue extricate which demonstrate gross inflammatory changes. Koch et al. illustrated that aortic inflammation existed as a progressive continuum from generally

noninflammatory to inflammatory AAA. This more prominent understanding of the pathophysiology has fortified intrigued in focused on pharmacotherapy pointed at both lessening inflammation activity to diminish aneurysm growth.(6) These studies and hypotheses show the relationship between Inflammation and AAA, but also show the importance of our study.

In recent years, many studies have found that inflammatory markers, which are biomarkers that are easy to calculate from complete blood count data and require no additional cost, predict prognosis and survival in many different diseases. Previous studies have shown that AAA dilatation is associated with coronary artery disease, ischemic stroke, acute myocardial infarction, and cardiovascular mortality (7). Because of the similarity in the pathophysiology of these diseases, it is not surprising that there is evidence that AAA is an inflammatory process, including histologic evidence supporting the presence of lymphocytes and macrophages and inflammatory cytokines observed in the adventitia layer in patients with abdominal aortic aneurysms (8-9). In a study examining patients with AAA and chronic aortic dissection, elevated hs-CRP levels and increased white blood cell levels are another indicator of the presence of an inflammatory condition (10). Like these studies, in our study, CRP and white blood cells were significantly higher in patients with AAA.

Mean platelet volume (MPV) is considered an indicator of platelet activity and aggregation capacity (11). High MPV values have been found to be associated with atherothrombotic disorders such as atherosclerosis, myocardial ischemia, and cerebrovascular events (12). Many studies have shown that MPV can be used as a diagnostic marker for inflammatory disorders (13-14). In our study, the MPV value was significantly higher in patients with AAA. This finding seems to be important in confirming the relationship of AAA with inflammation.

Markers derived from complete blood count such as PLR, NLR, SII index have been found to be associated with cancer prognosis (15-16), cardiovascular diseases (17) and all-cause mortality (18-19).

In cardiovascular diseases, neutrophils secrete inflammatory mediators that can cause vessel wall degeneration (20). Neutrophilia has been associated with prothrombotic conditions accompanied by plaque disruption, direct endothelial cell damage and microvascular occlusion, increased blood viscosity and hypercoagulability (21). Additionally, there are some studies showing a negative correlation between neutrophil catalase activity and aortic size. This suggests that neutrophils have an important role in aneurysm formation (22). On the other hand, lymphocytes have an

antiatherosclerotic role as they regulate the inflammatory response (23). Low lymphocyte count reflects adverse physiological stress levels and is associated with worse cardiovascular outcomes (24). Considering these results in the literature, it is very valuable that the best association with AAA was determined by the NLR value in our study. In another study demonstrating the value of NLR in patients with AAA, Kordzadeh et al. showed that preoperative NLR was an independent predictor of 30-day morbidity, independent of gender, AAA size, blood loss, length of hospital stay, and comorbidities (25-26). One of our findings that will support these studies is that the SII index, calculated in relation to NLR, was found to be significantly higher in patients with AAA.

The limitations of our study are that it was retrospective as in many previous studies, it was single centered, and the number of patients was small.

CONCLUSION

In conclusion, beyond these limitations, our results suggest that CRP, NLR, MPV and SII are associated with AAA. It may be useful to evaluate these inflammatory markers derived from routine blood samples in the follow-up and treatment of patients.

Ethics Committee Approval: Ethics Committee Approval: Ethics approval for this study was obtained from the Ordu University Senate Ethics Committee (ethics committee date: 23.06.2023, ethics committee number: 172).

Peer-review: Externally peer-reviewed

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REFERENCES

1. Singh M, Koyfman A, Martinez JP. Abdominal Vascular Catastrophes. Emerg Med Clin North Am. 2016 May;34(2):327-39. doi: 10.1016/j.emc.2015.12.014.
2. Günay Ş, Güllülü NS. Yaşlılarda aort anevrizmalarına yaklaşım [Approach to aortic aneurysms in the elderly]. Turk Kardiyol Dern Ars. 2017 Sep;45(Suppl 5):93-95. Turkish. doi: 10.5543/tkda.2017.57034.
3. Pisano C, Balistreri CR, Ricasoli A, Ruvolo G. Cardiovascular disease in ageing: an overview on thoracic aortic aneurysm as an emerging inflammatory disease. Mediators Inflamm. 2017;2017:1274034.doi:10.1155/2017/1274034.

4. Gonzalez-Hidalgo C, De Haro J, Bleda S, Cañibano C, Michel I, Acin F. Differential mRNA expression of inflammasome genes NLRP1 and NLRP3 in abdominal aneurysmal and occlusive aortic disease. Ther Adv Cardiovasc Dis. 2018;12(4):123–9. doi:10.1177/1753944717750338.
5. Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W,et al., Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clin Cancer Res. 2014 Dec 1;20(23):6212-22. doi: 10.1158/1078-0432.CCR-14-0442.
6. Tang T, Boyle JR, Dixon AK, Varty K. Inflammatory abdominal aortic aneurysms. Eur J Vasc Endovasc Surg. 2005 Apr;29(4):353-62. doi: 10.1016/j.ejvs.2004.12.009. PMID: 15749035.
7. Gardin JM, Arnold AM, Polak J, Jackson S, Smith V, Gottdiener J. Usefulness of aortic root dimension in persons > or = 65 years of age in predicting heart failure, stroke, cardiovascular mortality, all-cause mortality and acute myocardial infarction (from the Cardiovascular health study). Am J Cardiol. 2006;97(2):270-5. doi:10.1016/j.amjcard.2005.08.039.
8. Ruvolo G, Pisano C, Candore G, Lio D, Palmeri C, Maresi E, et al. Can the TLR-4-mediated signaling pathway be "a key inflammatory promoter for sporadic TAA"? Mediators Inflamm. 2014;2014:349476. doi:10.1155/2014/349476.
9. Jia LX, Zhang WM, Zhang HJ, Li TT, Wang YL, Qin YW, et al. Mechanical stretch-induced endoplasmic reticulum stress, apoptosis and inflammation contribute to thoracic aortic aneurysm and dissection. J Pathol. 2015;236(3):373-83. doi:10.1002/path.4534.
10. Yuan SM, Shi YH, Wang JJ, Lü FQ, Gao S. Elevated plasma D-dimer and hypersensitive C-reactive protein levels may indicate aortic disorders. Rev Bras Cir Cardiovasc. 2011;26(4):573-81. doi:10.5935/1678-9741.20110047.
11. Bancroft AJ, Abel EW, McLaren M, Belch JJ. Mean platelet volume is a useful parameter: A reproducible routine method using a modified Coulter thrombocytometer. Platelets 2000;11:379 87. doi: 10.1080/09537100020008311.
12. Karaman H, Karakukcu C, Kocer D. Can mean platelet volume serve as a marker for prostatitis? Int J Med Sci. 2013 Aug 21;10(10):1387-91. doi: 10.7150/ijms.6126..
13. Canpolat F, Akpinar H, Eskioğlu F. Mean platelet volume in psoriasis and psoriatic arthritis. Clin Rheumatol. 2010 Mar;29(3):325-8. doi: 10.1007/s10067-009-1323-8.

14. Soydinc S, Turkbeyler IH, Pehlivan Y, Soylu G, Goktepe MF, Bilici M, et al. Mean platelet volume seems to be a valuable marker in patients with systemic sclerosis. Inflammation. 2014 Feb;37(1):100-6. doi: 10.1007/s10753-013-9716-x.
15. Moon G, Noh H, Cho IJ, Lee JI, Han A. Prediction of late recurrence in patients with breast cancer: elevated neutrophil to lymphocyte ratio (NLR) at 5 years after diagnosis and late recurrence. Breast Cancer. 2020 Jan;27(1):54-61. doi: 10.1007/s12282-019-00994-z.
16. Jomrich G, Gruber ES, Winkler D, Hollenstein M, Gnant M, Sahora K, et al. Systemic Immune-Inflammation Index (SII) Predicts Poor Survival in Pancreatic Cancer Patients Undergoing Resection. J Gastrointest Surg. 2020 Mar;24(3):610-618. doi: 10.1007/s11605-019-04187-z.
17. Bhutta H, Agha R, Wong J, Tang TY, Wilson YG, Walsh SR. Neutrophil-lymphocyte ratio predicts medium-term survival following elective major vascular surgery: a cross-sectional study. Vasc Endovascular Surg. 2011 Apr;45(3):227-31. doi: 10.1177/1538574410396590.
18. Hajibandeh S, Hajibandeh S, Hobbs N, Mansour M. Neutrophil-to-lymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: A systematic review and meta-analysis. Am J Surg. 2020 Jan;219(1):154-163. doi: 10.1016/j.amjsurg.2019.04.018.
19. Zhang HF, Ge YL, Wang HY, Zhang Q, Li WQ, Chen Y,et al. Neutrophil-to-Lymphocyte Ratio Improves the Accuracy and Sensitivity of Pneumonia Severity Index in Predicting 30-Day Mortality of CAP Patients. Clin Lab. 2019 Oct 1;65(10). doi: 10.7754/Clin.Lab.2019.190226.
20. Angkananard T, Anothaisintawee T, McEvoy M, Attia J, Thakkinstian A. Neutrophil Lymphocyte Ratio and Cardiovascular Disease Risk: A Systematic Review and Meta-Analysis. Biomed Res Int. 2018 Nov 11;2018:2703518. doi: 10.1155/2018/2703518.
21. Appleton ND, Bailey DM, Morris-Stiff G, Lewis MH. Neutrophil to lymphocyte ratio predicts perioperative mortality following open elective repair of abdominal aortic aneurysms. Vasc Endovascular Surg. 2014 May;48(4):311-6. doi: 10.1177/1538574413519713.
22. Dale MA, Ruhlman MK, Baxter BT. Inflammatory cell phenotypes in AAAs: their role and potential as targets for therapy. Arterioscler Thromb Vasc Biol. 2015 Aug;35(8):1746-55. doi: 10.1161/ATVBAHA.115.305269. Epub 2015 Jun 4.

23. Simpson E, Cantor H. Regulation of the immune response by subclasses of T lymphocytes. II. The effect of adult thymectomy upon humoral and cellular responses in mice. Eur J Immunol. 1975 May;5(5):337-43.
doi: 10.1002/eji.1830050509.
24. Gong S, Gao X, Xu F, Shang Z, Li S, Chen W, Yang J, Li J. Association of lymphocyte to monocyte ratio with severity of coronary artery disease. Medicine (Baltimore). 2018 Oct;97(43):e12813.
doi: 10.1097/MD.0000000000012813.
25. Kordzadeh A, Malietzis G, Browne T, Prionidis I, Panayiotopoulos YP. Neutrophil to lymphocyte ratio (NLR) of five predicts 30-day morbidity in ruptured abdominal aortic aneurysms (rAAA): a retrospective cohort study. Int J Surg. 2015 Mar;15:45-8.
doi: 10.1016/j.ijsu.2015.01.013.
26. Barnes M, Boult M, Maddern G, Fitridge R. A model to predict outcomes for endovascular aneurysm repair using preoperative variables. Eur J Vasc Endovasc Surg. 2008 May;35(5):571-9.
doi: 10.1016/j.ejvs.2007.12.003.