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PREOPERATIVE NEUTROPHIL TO LYMPHOCYTE RATIO AND PLATELET TO LYMPHOCYTE RATIO FOR PROGNOSIS AFTER EMBOLECTOMY

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ABSTRACT

Introduction: The neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR) are novel parameters that have been associated with inflammation in arterial embolism. This study aimed to evaluate NLR and PLR for the prediction of the prognosis in arterial embolism. **Methods:**197 patients admitted to the hospital with acute extremity embolism who underwent embolectomy with a Fogarty balloon catheter between February 2019 to March 2022 were included in the study. Receiver Operating Characteristics (ROC) curve analysis was generated for NLR and PLT to predict postoperative mortality and amputation. Patients were divided into two groups according to the NLR cut-off value (Low NLR group; High NLR Group). The Delong Test Was Used To Compare The Area Under The Curve (AUC) With Each Of These Parameters. *Results:* The mean age of the patients was 67.4 ± 15.9 years. The male population was 114 (57.9%). The median neutrophil/lymphocyte ratio was 5.8 (Q1: 3.3- Q3: 10.4), median platelet / lymphocyte ratio was 193.4 (Q1: 128.7- Q3: 298.1). Hospital mortality occurred in 73 patients. ROC curve analysis was performed with NLR to predict hospital mortality. The AUC value was 0.723 (95% CI 0.649 - 0.798, p <0.05). The cut-off for NLR was calculated as 5.97 by predicting hospital mortality (specificity = %66, sensitivity = %70, likelihood ratio: 2.06). **Conclusion:** High preoperative NLR is an independent mortality predictor for patients who underwent surgical embolectomy. Using NLR as a prognostic indicator for patients undergoing surgical embolectomy will be useful and cost-effective.

Keywords: Embolism; Embolectomy; Biomarkers

INTRODUCTION

Embolism and thrombosis such as acute arterial occlusion are life-threatening emergencies. Increased inflammation occurs due to atherosclerotic plaque rupture and acute arterial embolism [1, 2]. Severe inflammation is also initiated with the severity of embolism, thrombosis, and reperfusion injury [3, 4]. Altered neutrophil and platelet levels may initiate with inflammation. The neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR) are novel parameters that have been extensively researched and associated with inflammation [5-9]. However, there are not routinely evaluated in clinics [10]. NLR and PLR can be easily calculated in a complete blood count.

In this context, assessing the inflammation degree may be a key to assuming the predictive value of the prognosis in acute arterial ischemia. This study aimed to evaluate the relationship between preoperative NLR and PLR, and postoperative mortality and amputation in patients who underwent surgical embolectomy.

METHODOLOGY

Study Set Up and Data Collection:

The study was retrospectively all patients admitted to the hospital with acute extremity ischemia who underwent embolectomy with a Fogarty balloon catheter between February 2019 to March 2022 were included in the study. Patients with a history of major surgery in the last month (including aortobifemoral bypass, femoropopliteal bypass, cardiac or non-cardiac surgeries), patients with sepsis, patients younger than 18 years old, and patients with a hematological disease (except iron- deficiency anemia) were excluded from the study. 197 patients were enrolled and the demographic characteristics, blood tests, and outcomes were obtained from hospital The demographic characteristics of the patients were collected retrospectively. The last preoperative complete blood count was achieved for laboratory data from the hospital network data. Radiological data were obtained from computed tomographic angiography (CTA) or Doppler ultrasonography. The type of anesthesia, incision type, and operation technique was recorded. Postoperative data included postoperative mortality and postoperative amputation. This retrospective cohort study was conducted in accordance with the Declaration of Helsinki. The data of the study were collected after approval no: E1-22-2732 of the local ethics committee.

Definitions:

Diabetes mellitus was defined according to the 2019 ESC Guidelines on diabetes[11]. Renal impairment was defined as an estimated glomerular filtration rate <60 mL/min/1.73 m 2. Peripheral artery disease was defined by radiology reports showing more than 50% stenosis in the extremities or recorded ankle-brachial index (ABI)

≤0.90 before acute limb ischemia. The diagnosis of

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COPD was taken from the national disease registry system (E-nabız), not from spirometry tests, considering the emergency surgeries. Preoperative Covid-19 was defined as a positive PCR test within
1 month before the operation. Postoperative mortality was defined as death occurring before discharge from the hospital or within 30 days postoperatively. Amputation was defined as all extremity amputations proximal to the ankle and wrist.

Surgical Preparation and Technique: Electrocardiogram, laboratory tests, and detailed Doppler ultrasonography were performed in patients presenting with acute limb ischemia. CTA was performed in patients without renal failure. Transthoracic echocardiography (TTE) was performed in the preoperative period in patients with atrial fibrillation detected in ECG.TTE was performed on all other remaining patients in the postoperative period. According to Rutherford's classification, IIA and IIB patients were operated on. All operations were performed under local anesthesia. After the target artery was found, longitudinal or transverse arteriotomy was performed after 1 cc systemic heparinization. Embolectomy was performed with a Fogarty balloon catheter. An endarterectomy was performed as needed. Arteriotomy was closed with a primary or patch angioplasty technique. In patients without arterial retrograde flow, bypass graft operation was added to the procedure. Fasciotomy was performed against compartment syndrome as needed. The operational features were obtained from the hospital database and the operational history.

Statistical Analysis:

Shapiro – Wilk test was used to determine the normal distribution. Normally distributed continuous data were presented as mean and standard deviation (SD) and were compared by Student's t-test. Abnormally distributed continuous data were presented as median with interquartile range (Q1–Q3) and were compared by Mann- Whitney U test. Categorical data were presented as number of patients and ratio. Categorical variables were compared by a chi-squared analysis or Fisher's exact test. Receiver Operating Characteristics (ROC) curve analysis was generated for NLR and PLT to predict postoperative mortality and amputation. The AUC value was calculated for NLR and PLT to mortality and amputation. The cut-off values for postoperative mortality were calculated using the highest likelihood ratio. Postoperative amputation sensitivity and specificity were calculated using the mortality cut-off values. Patients were divided into two groups according to the NLR cut-off value (Low NLR group; High NLR group). The DeLong test was used to compare the area under the curve (AUC) with each of these parameters[12].Statistical tests were two-sided, and p-values < 0.05 were considered statistically significant. Statistical analyzes were performed using R version 4.0.3 (R Foundation for Statistical Computing).

RESULTS

Demographic characteristics of patients: The mean age of the patients was 67.4 ± 15.9 years. The male population was 114 (57.9%), female population was 83 (42.1%).The median neutrophil/lymphocyte ratio was 5.8 (Q1: 3.3- Q3: 10.4), median platelet /lymphocyte ratio was 193.4 (Q1: 128.7- Q3: 298.1).

Anatomical distribution of acute arterial occlusions:

The upper extremity was threatened in 32 patients; the lower extremity was threatened in 165 patients with acute arterial occlusion. Eleven patients were admitted to the hospital with acute ulnar or radial arterial occlusion, 21 patients with acute brachial or axillary arterial occlusion, 47 patients with acute popliteal arterial occlusion, 88 patients with acute femoral arterial occlusion, 28 patients with acute iliac arterial occlusion, and two patients with acute aortic arterial occlusion.

Postoperative mortality: Hospital mortality occurred in 73 patients. Roc curve analysis was performed with NLR to predict hospital mortality. The AUC value was 0.723 (95% CI 0.649 - 0.798, p <0.05). The cut-off for NLR was calculated as 5.97 by predicting hospital mortality (specificity = %66, sensitivity = %70, likelihood ratio: 2.06).

ROC curve analysis was performed with PNR to predict hospital mortality. The AUC value was 0.657 (95% CI 0.579 - 0.736, p <0.05). The cut-
off for PNR was calculated as 217 by predicting hospital mortality (specificity = %62, sensitivity =
%68, likelihood ratio: 1.79). NLR and PLR ROC analyses to predict hospital mortality were compared with the De- long test, no statistically significant difference was found between the ratios to predict hospital mortality(p:0.055).

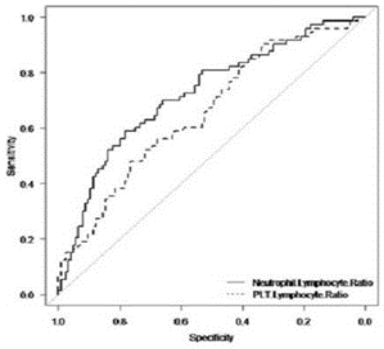

Fig 1: shows that ROC analysis of NLR and PLR to predict hospital mortality.

Amputation: Amputation was performed in 31 patients within 30 days postoperatively. In-hospital mortality occurred in 19 of 31 patients who underwent amputation. Roc curve analysis was performed with NLR to postoperative amputation. The AUC value was 0.655 (95% CI 0.556 - 0.754, p <0.05). The cut-off for NLR was calculated as 5.97 by predicting hospital mortality (specificity = %65, sensitivity = %56, likelihood ratio: 1.60).

ROC curve analysis was performed with PNR to predict postoperative. The AUC value was 0.623 (95% CI 0.519 - 0.727, p <0.05). The cut-off for PNR was calculated as 217 by predicting hospital mortality (specificity = %61, sensitivity = %63, likelihood ratio: 1.61). NLR and PLR

= %61, sensitivity = %63, likelihood ratio: 1.61). NLR and PLR ROC analyses to predict postoperative amputation were compared with the De- long test, no statistically significant difference was found between the ratios to predict hospital mortality(p:0.521).

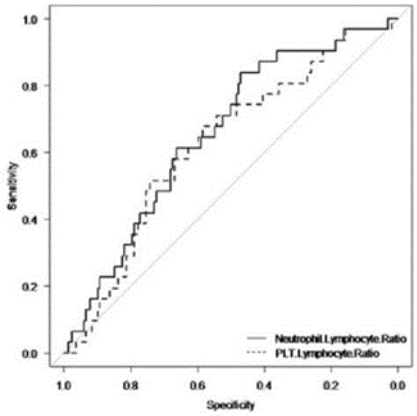

Figure 2 : shows that ROC analysis of NLR and PLR to predict postoperative amputation.

Characteristics and surgical outcomes of patients with low and high NLP:

This cohort included 105 patients with low NLR and 92 patients with high NLR (the cut-off value for NLR is 5.97). Patients in the high NLR group were older (p: 0.02). Hypertension and Covid - 19 history were more common in patients in the high NLR group (p:0.03;0.04, respectively). Popliteal artery occlusion was more common in the low LNR group (p:<0.01). Univariate and multivariate analysis of hospital mortality Univariate analysis was performed to evaluate risk factors for hospital mortality. Age, female gender, atrial fibrillation, DM, hypertension, and high NLR is statistically significant univariate risk factors for hospital mortality. Multivariate analysis was performed with risk factors that were significant in univariate analysis. Age, female gender, and high NLR were found statistically significant risk factors for hospital mortality in multivariate analysis.

DISCUSSION

Rutherford IIA-IIB extremities must be revascularized in the first 6 hours. Surgical embolectomy is the first revascularization option for most patients [13]. Acute arterial occlusion is associated with high amputation and mortality rates despite all advanced treatments. Determining the prognosis of patients with acute extremity ischemia remains a challenge for vascular surgeons. It has been reported that newly developed inflammation markers such as NLR and PLT have the ability to predict the prognosis of vascular diseases [14-16]. In this study, we evaluated the patients' prognosis that underwent surgical embolectomy, using preoperative NLR and PLR. The study found a significant relationship between preoperative high NLR and postoperative mortality and amputation in patients who underwent surgical embolectomy. Also, a similar but weaker relationship was found between PLRand postoperative mortality and amputation. Our results are in line with previous studies [6, 17, 18]. Neutrophils activate myeloperoxidase and oxygen- derived free radicals [19, 20]. High NLR and PLR in the preoperative period can cause more severe reperfusion injury postoperatively. Some types of lymphocytes suppress inflammation, and low lymphocyte counts are associated with malnutrition and frailty[21]. Lymphopenia has been shown to be an indicator of poor survival in surgeries[22]. There is no normal accepted range or cut-off value for PLR and NLR. In the study, we performed ROC analysis to evaluate the ability of NLR and PLR to predict postoperative outcomes. The ability of NLR to predict postoperative mortality was better than its ability to predict postoperative amputation. On the other hand, ROC analysis for NLR and PLR was compared with the Delong test, there is no statistically significant difference between the ability to predict postoperative mortality and amputation.

In the study, the NLR cut-off value was higher than in other similar studies. Taşoğlu et al. found that NLR > 5.2 was an independent risk factor for postoperative amputation. Similarly, Taurino et al. found that NLR >5 was an independent risk factor for mortality[6, 17]. Also, Coelho et al. calculated the NLR cut-off as 5.4, with 90.5% sensitivity and 73.6% specificity for 30-day death or amputation after revascularization for acute limb ischemia[18]. Postoperative mortality occurred in more than half of patients with high NLR. Also, more than one- fifth of high NLR patients required amputation. While, preoperative atrial fibrillation, diabetes mellitus, and hypertension were found to be significant risk factors for postoperative mortality in univariate analysis, there were not significant in the multivariate analysis. High preoperative NLR, age, and female gender are independent predictors of mortality in patients who underwent surgical embolectomy.

CONCLUSION

High preoperative NLR is one of the independent predictors of mortality in patients who underwent surgical embolectomy. Using NLR as a prognostic indicator in patients undergoing surgical embolectomy will be useful and cost-effective.

Limitations: Due to the nature of a retrospective study, all data were obtained from the hospital system. Therefore, there may be inaccessible or incorrectly evaluated data. Only patients treated with surgical embolectomy were included in the study. The outcomes of patients presenting with ALI who did not have a chance for surgical treatment (Rutherford classification III) were not analyzed. There are no prospective studies on the subject.

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