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ORIGINAL RESEARCH

Evaluation of prognosis by complete blood parameters in patients with acute pulmonary embolism

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Abstract

Background: Acute pulmonary embolism is associated with high death and morbidity. During a pulmonary embolism, neutrophils infiltrate the right ventricular wall, inflammatory mediators are released, and necrosis develops. This study aimed to compare the effectiveness of whole blood parameters mean platelet volume (MPV), mean platelet volume to platelet ratio (MPVPR), neutrophils (NEU), neutrophil-to-lymphocyte platelet ratio (NLPR), neutrophil to lymphocyte ratio (NLR), neutrophil to platelet ratio (NPR), platelets (PLT), platelet mass index (PMI), and systemic immune-inflammatory index (SII) in predicting mortality in patients with acute pulmonary embolism. **Methods**: We retrospectively analyzed 112 patients diagnosed with acute pulmonary embolism at Dicle University Hospital's emergency department between January 2016 and December 2022. Receiver operating characteristic (ROC) curve analysis was used to examine the diagnostic decision properties of the variables used in mortality prediction. **Results**: 103 (91.96%) of the patients survived and 9 (8.04%) died. As a result, the best parameters for predicting mortality outcomes were NLPR (area under the curve (AUC): 0.887, sensitivity: 88.89%, specificity: 84.47%, positive predictive value (PPV): 33.33%, negative predictive value (NPV): 98.86%), NPR (AUC: 0.828, sensitivity: 77.78%, specificity: 91.26%, PPV: 43.75%, NPV: 97.92%), NLR (AUC: 0.803, sensitivity: 88.89%, specificity: 60.19%, PPV: 16.33%, NPV: 98.41%) respectively. **Conclusions**: This study found that NLPR, NPR and NLR were the most accurate complete blood parameters for predicting mortality in acute pulmonary embolism patients admitted to the emergency department.

Keywords

Acute pulmonary embolism; Neutrophil-to-lymphocyte platelet ratio (NLPR); Neutrophil to lymphocyte ratio (NLR); Neutrophil to platelet ratio (NPR); Mortalite

1. Introduction

Acute pulmonary embolism (APE) has high mortality and morbidity rates, with an annual incidence between 39 and 115 people per hundred thousand [1].

Experimental animal studies have shown that right ventricular pressure increases during pulmonary embolism, neutrophils infiltrate the right ventricular wall early on, inflammatory mediators are released, and necrosis occurs. Autopsy studies in patients who died from massive pulmonary embolism prove that leukocytes play important roles in right ventricular wall damage [2]. Several whole blood parameters have been studied in APE patients, including leukocytes, white blood cells (WBC), neutrophil to lymphocyte ratio (NLR), mean platelet volume (MPV), platelet to lymphocyte ratio (PLR) and platelet mass index (PMI); these parameters have been shown to predict mortality [2–6]. APE patients have not been studied for mean platelet volume to platelet ratio (MPVPR), neutrophil-to-lymphocyte platelet ratio (NLPR), neutrophil to platelet ratio (NPR), or parameters obtained by complete blood count.

This study aimed to examine the effectiveness of whole blood parameters MPV, MPVPR, neutrophils (NEU), NLPR, NLR, NPR, platelets (PLT), PMI, systemic immune-inflammatory index (SII) in predicting hospital mortality in APE patients.

2. Material and methods

2.1 Place of study and ethics committee approval

In this study, patients with acute pulmonary embolism admitted to the Dicle University Hospital emergency room were retrospectively analyzed. Patient information was obtained from the hospital registration system.

2.2 Emergency department management

Patients were examined in the emergency department and a detailed history was taken. We collected peripheral venous blood samples for a complete blood count, placed them in calcium- ethylenediamine tetraacetic acid (EDTA) tubes, and analyzed them in the lab. Clinical decision rules based on Wells criteria or revised Geneva scores were used for patients with suspected APE. In accordance with clinical probability, computed tomography pulmonary angiography (CTPA) was performed to make the diagnosis [1]. Patients with APE were administered unfractionated heparin intravenously or subcutaneously at therapeutic doses. Thrombolytic treatment was initiated in hemodynamically unstable pulmonary embolism patients unless contraindicated [1]. Hospitalization and follow-up treatment were provided to patients.

2.3 Study population, including and excluding criteria

285 patients with APE diagnosed in Dicle University Hospital emergency room from January 2016 to December 2022 were consecutively analyzed.

Inclusion criteria: Patients over 18 who were admitted to the emergency room with an APE diagnosis.

Exclusion criteria: (1) Patients who are referred to another centre after diagnosis.

(2) Patients using thrombolytics, anticoagulants, corticosteroids, immunosuppressive therapy, or transfusions within the last two weeks.

(3) Patients with comorbidities: hematologic diseases, active infections, inflammatory diseases, malignancies, kidney diseases, liver diseases, diabetes mellitus, hypertension, acute coronary syndrome and ischemic heart diseases, congestive heart failure, cerebrovascular disease, and chronic obstructive pulmonary disease.

Therefore, 173 out of 285 patients were rejected for inclusion in this study. An analysis of 112 patients who met the study criteria was conducted (Fig. 1).

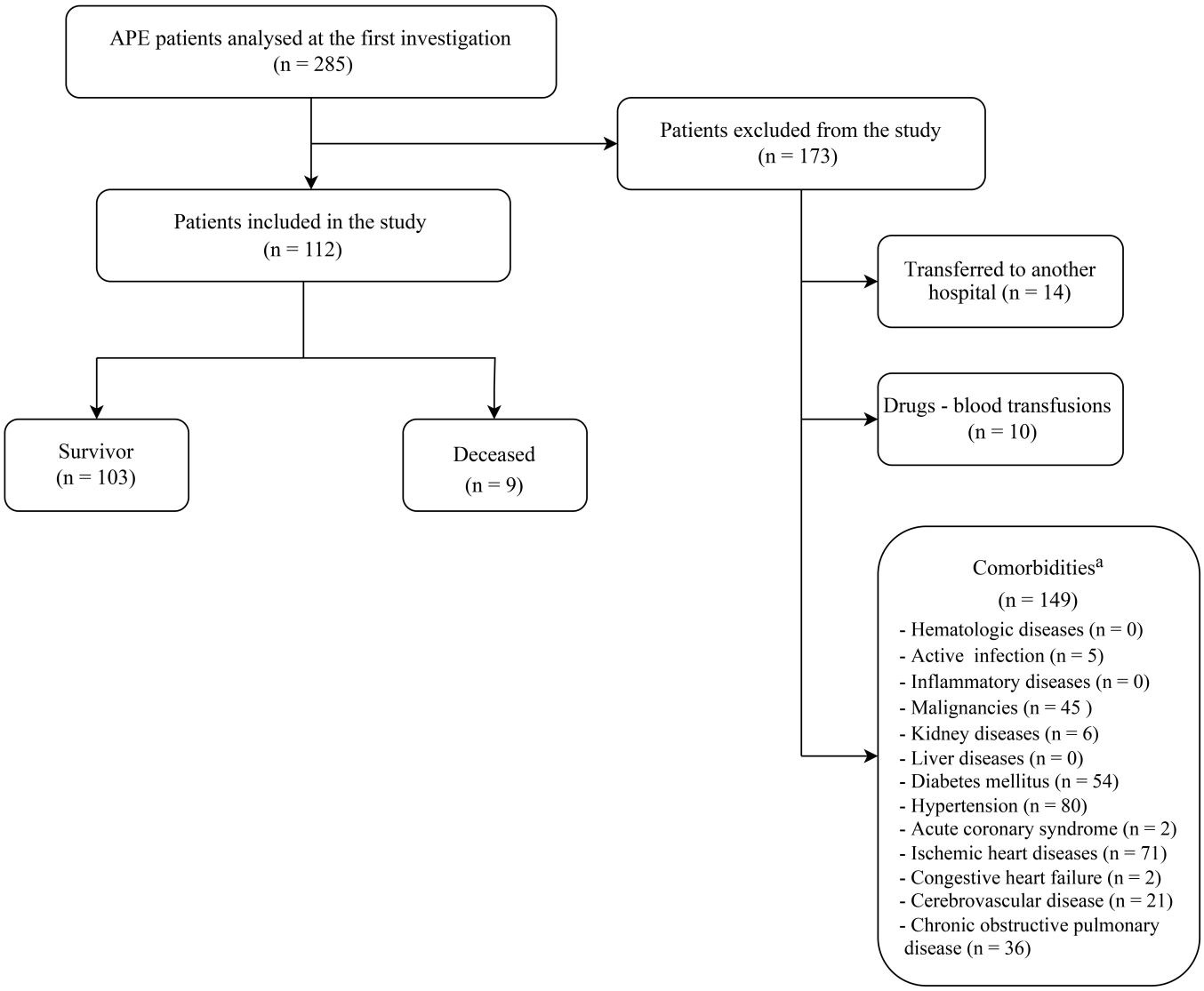

FIGURE 1. Flow chart. Abbreviation: a: Some patients had multiple comorbidities. APE: Acute pulmonary embolism.

2.4 Complete blood parameters and variables

The variables used in this study were derived from blood samples taken at the time of admission to the emergency room. We examined WBC, NEU, lymphocytes (LYM), PLT, MPV, MPVPR, NLPR, NLR, NPR, PMI, SII, which we believed would be effective in predicting mortality. According to the complete blood count, variables were calculated using the following formulas.

MPVPR = MPV/PLT
NLPR = NEU/(LYM × PLT)
NLR = NEU/LYM
NPR = NEU/PLT
PMI = PLT × MPV
SII = PLT × NEU/LYM

2.5 Statistical analysis

Continual variables with numerical anomalous dispersion were presented as a median, interquartile range (IQR, q1–q3). Mann-Whitney U-test was performed on these data. Categorical values were presented as frequency, percent. Chi-square test (χ^2) was performed on these data. ROC curve analysis was used to examine the diagnostic decision-making features of MPV, MPVPR, NEU, NLPR, NLR, NPR, PLT, PMI, SII in estimating death rates in APE patients. Data accuracy in predicting death consequences is measured by the area under the curve (AUC). Adjustments were made to the best cut-off point, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). All tests were two-way. $p < 0.05$ indicates statistically significant differences. Data anlalysis was performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1 Clinical features

The study evaluated 112 patients. The patients survived in 103 (91.96%) survived and died in 9 (8.04%). Patients with pulmonary embolism had an average age of 44 years (33–63) and age was not a determinant affecting death rate ($p = 0.352$). Syncope, tachycardia, massive embolism, heart rate, systolic blood pressure, diastolic blood pressure, and intensive care unit (ICU) admission showed significant differences in life-death (p values were: 0.003, 0.001, 0.001, 0.001, 0.001, 0.007, 0.009, 0.001, respectively). Table 1 presents clinical characteristics. The length of hospital stay was 10 (7.25–13) days for all patients, 10 (8–13) days for living patients and 8 (4.5–15.5) days for deceased patients. Mortality did not differ according to hospitalization duration ($p = 0.747$). Patients died due to massive embolism and intensive care unit complications.

3.2 Complete blood parameters and mortality

WBC, NEU, PLT, MPV, MPVPR, NLPR, NLR, NPR, SII were different in mortality (p values respectively: 0.010, 0.016, 0.006, 0.044, 0.003, <0.001, 0.003, 0.001, 0.036) (Table 2).

3.3 Evaluation of complete blood parameters for predicting mortality by ROC analysis

As a consequence of ROC analysis, MPV, MPVPR, NEU, NLPR, NLR, NPR, PLT values had diagnostic value in predicting mortality. However, the descriptive value of PMI and SII values is found to be weak. AUC, 95% confidence interval (CI): lower bound-upper bound, p values; MPV (AUC: 0.703, 95% CI: 0.482–0.925, $p = 0.044$), MPVPR (AUC: 0.786, 95% CI: 0.650–0.923, $p = 0.004$), NEU (AUC: 0.744, 95% CI: 0.541–0.947, $p = 0.016$), NLPR (AUC: 0.887, 95% CI: 0.755–1.000, $p < 0.001$), NLR (AUC: 0.803, 95% CI: 0.667–0.938, $p = 0.003$), NPR (AUC: 0.828, 95% CI: 0.630–1.000, $p = 0.001$), PLT (AUC: 0.777, 95% CI: 0.615–0.939, $p = 0.006$), PMI (AUC: 0.693, 95% CI: 0.489–0.897, $p = 0.056$), SII (AUC: 0.620, 95% CI: 0.420–0.821, $p = 0.233$). AUC values were highest for NLPR, NPR and NLR among whole blood parameters in predicting mortality (Table 3). ROC curves for patients with pulmonary embolism are shown in Fig. 2.

4. Discussion

APE patients' mortality can be predicted using whole blood parameters [3–7]. Using whole blood parameters in addition to whole blood parameters previously studied in APE patients, this study evaluated the predictive power of mortality in APE patients with different variables derived from whole blood parameters. Whole blood parameters were negatively affected by many conditions including drug use and comorbidities. Hence, in this study, all patients whose drug use and comorbidities affected whole blood parameters were excluded, and whole blood parameters were tested for their direct effect on mortality in APE patients. A good predictive power was found for NLPR, NPR and NLR and the highest for NLPR in this study.

Venetz *et al.* [3] identified WBC count as an independent predictive tool affecting mortality in APE patients. Obradovic *et al.* [8] showed that the WBC count is significant in determining the prognosis in patients with intermediate-high level risk pulmonary embolism and in patients receiving thrombolysis treatment. APE patients presenting to the emergency room with an increase in WBC and NEU counts were found to be a good predictor of mortality, with high sensitivity and specificity.

APE mortality was not significantly associated with PLT or MPV in most studies [5, 9, 10]. PLT, however, influenced mortality according to Kundi *et al.* [11]. MPV is associated with thrombosis, but hypertension, dyslipidemia, heart disease, and cerebrovascular disorders also affect MPV [12]. Even though patients with factors affecting MPV were excluded from this study, MPV had a borderline significant effect on mortality in APE. In APE, MPVPR was a good predictor of mortality.

NLR was effective in estimating mortality in studies of APE [13]. Kayrak *et al.* [14] examined mortality in APE and found 68.6% sensitivity, 80.5% specificity, and 0.75 AUC value for NLR cut-off value >9.2. Another study examining mortality in APE found 69.7% sensitivity, 47.5% specificity, and 0.604 AUC for the NLR cut-off value >7.3. Ma *et al.* [5]

TABLE 1. Clinical characters in acute pulmonary embolism patients.

Variables	Total (n = 112)	Survival (n = 103)	Mortality (n = 9)	*p*-value*
Age, yr[1]	44 (33.00–63.00)	44 (32.00–63.00)	50 (36.50–70.50)	0.352
Sex[2]				
Female	63 (56.20)	60 (58.30)	3 (33.30)	0.176
Male	49 (43.80)	43 (41.70)	6 (66.70)	
Symptoms[2]				
Chest pain	78 (69.60)	71 (68.90)	7 (77.80)	0.720
Dyspnea	106 (94.60)	97 (94.20)	9 (100.00)	1.000
Syncope	5 (4.50)	2 (1.90)	3 (33.30)	0.003
Tachycardia	28 (25.00)	21 (20.40)	7 (77.80)	0.001
Hemoptysis	28 (25.00)	25 (24.30)	3 (33.30)	0.688
Unilateral leg pain	47 (42.00)	45 (43.70)	2 (22.20)	0.299
Vital signs[1]				
Heart rate (beats/min)	84 (76.00–98.00)	84 (76.00–96.00)	122 (99.00–132.00)	0.001
Systolic blood pressure (mmHg)	110 (100.00–120.00)	110 (100.00–120.00)	90 (85.00–111.50)	0.007
Diastolic blood pressure (mmHg)	70 (60.00–80.00)	70 (60.00–80.00)	60 (50.00–65.00)	0.009
Embolism location[2]				
Massive	19 (17.00)	13 (12.60)	6 (66.70)	0.001
Segmental	91 (81.30)	85 (82.50)	6 (66.70)	0.366
Subsegmental	48 (42.90)	45 (43.70)	3 (33.30)	0.730
ICU admission[2]	27 (24.10)	20 (19.40)	7 (77.80)	0.001

*Abbreviations: ICU: intensive care unit. [1]: The values of variables are given as median (interquartile range), and analyzed with Mann-Whitney U-test. [2]: The values of variables are given n (%), and analyzed with Chi-square test (χ^2). *: p value compares survival and mortality.*

TABLE 2. Mortality and complete blood parameters in patients with acute pulmonary embolism.

Variables[1]	Total (n = 112)	Survival (n = 103)	Mortality (n = 9)	*p*-value*
WBC, (10^3/μL)	9.26 (7.35–13.35)	9.17 (7.20–12.20)	14.20 (12.22–18.80)	0.010
NEU, (10^3/μL)	6.93 (4.82–10.09)	6.70 (4.81–9.00)	11.20 (8.10–15.00)	0.016
LYM, (10^3/μL)	1.84 (1.47–2.18)	1.84 (1.47–2.19)	1.58 (1.00–2.48)	0.363
PLT, (10^3/μL)	268.50 (210.50–351.00)	275.00 (221.00–356.00)	182.00 (141.00–262.00)	0.006
MPV	7.84 (7.12–8.91)	7.79 (7.11–8.79)	9.22 (7.87–9.59)	0.044
MPVPR	0.03 (0.02–0.04)	0.03 (0.02–0.04)	0.05 (0.03–0.06)	0.003
NLPR	0.01 (0.01–0.02)	0.01 (0.01–0.02)	0.04 (0.03–0.08)	<0.001
NLR	3.48 (2.48–5.56)	3.29 (2.41–5.34)	7.13 (4.06–13.89)	0.003
NPR	0.03 (0.02–0.03)	0.02 (0.02–0.03)	0.07 (0.04–0.08)	0.001
PMI	2111.54 (1747.00–2640.52)	2127.36 (1772.77–2642.58)	1792.70 (981.78–2435.25)	0.056
SII	912.42 (588.45–1707.00)	905.60 (564.20–1690.75)	954.71 (660.50–2786.64)	0.036

*Abbreviations: WBC: white blood cell, NEU: neutrophils, LYM: lymphocytes, PLT: platelets, MPV: mean platelet volume, MPVPR: mean platelet volume to platelet ratio, NLPR: neutrophil-to-lymphocyte platelet ratio, NLR: neutrophil to lymphocyte ratio, NPR: neutrophil to platelet ratio, PMI: platelet mass index, SII: systemic immune-inflammation index. [1]: The values of variables are given as median (interquartile range), and analyzed with Mann-Whitney U-test. *: p value compares survival and mortality.*

TABLE 3. Effectiveness of complete blood parameters at predicting mortality in acute pulmonary embolism patients.

Predictor	Optimal Cut Point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
MPV	9.05	77.78	84.47	30.43	97.75	0.703
MPVPR	0.04	66.67	85.44	28.57	96.70	0.786
NEU	10.40	66.67	80.58	23.08	96.51	0.744
NLPR	0.02	88.89	84.47	33.33	98.86	0.887
NLR	4.06	88.89	60.19	16.33	98.41	0.803
NPR	0.05	77.78	91.26	43.75	97.92	0.828
PLT	199.00	66.67	83.50	26.09	96.63	0.777
PMI	1375.60	44.44	94.17	40.00	95.10	0.693
SII	2661.29	33.33	94.17	33.33	94.17	0.620

Abbreviations: NPV: negative predictive value, PPV: positive predictive value, AUC: area under the curve, MPV: mean platelet volume, MPVPR: mean platelet volume to platelet ratio, NEU: neutrophils, NLPR: neutrophil-to-lymphocyte platelet ratio, NLR: neutrophil to lymphocyte ratio, NPR: neutrophil to platelet ratio, PLT: platelets, PMI: platelet mass index, SII: systemic immune-inflammation index.

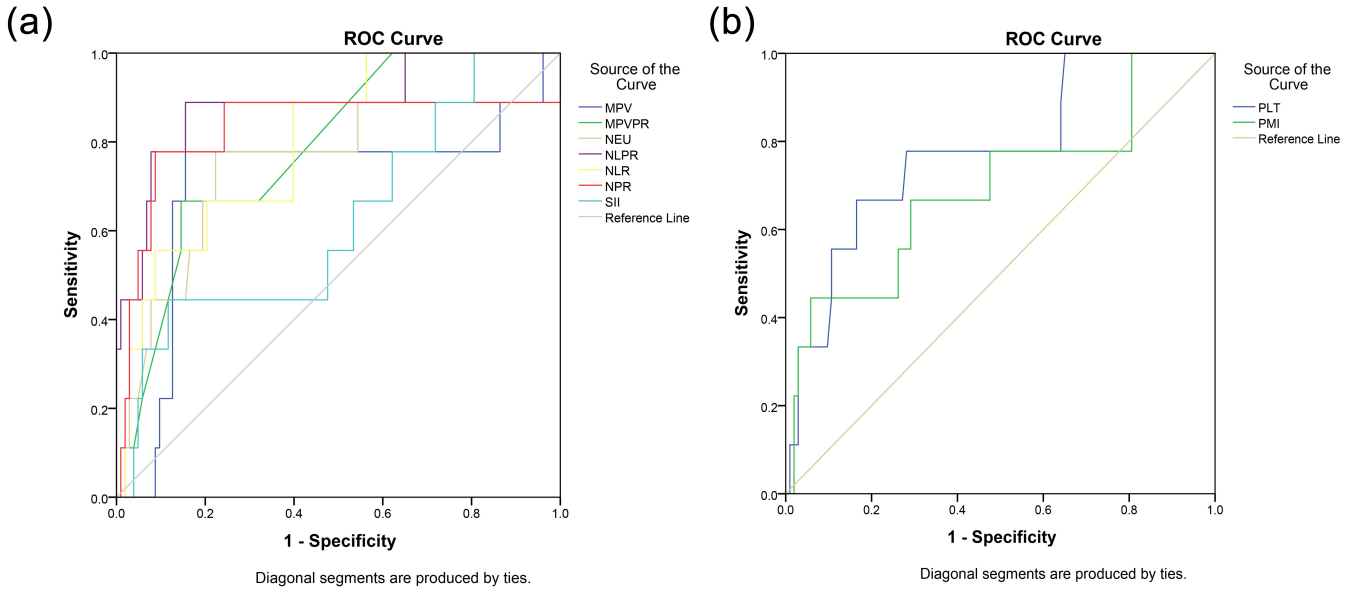

FIGURE 2. ROC curve of complete blood parameters at predicting mortality in acute pulmonary embolism patients. (a) ROC curve of MPV, MPVPR, NEU, NLPR, NLR, NPR, SII. (b) ROC curve of PLT, PMI. ROC: receiver operating characteristic, MPV: mean platelet volume, MPVPR: mean platelet volume to platelet ratio, NEU: neutrophils, NLPR: neutrophil-to-lymphocyte platelet ratio, NLR: neutrophil to lymphocyte ratio, NPR: neutrophil to platelet ratio, SII: systemic immune-inflammation index, PLT: platelets, PMI: platelet mass index.

reported 80% sensitivity, 66.75% specificity, and 0.792 AUC for NLR cut-off value 5.99 is effective in predicting mortality in patients with APE, but its sensitivity and specificity differ from previous studies. This may be due to the different mortality duration, exclusion criteria and population in the studies.

NLPR was effective in predicting the seriousness of the disease and reception to the intensive care unit in COVID-19 patients [15, 16]. NLPR was associated with sepsis development in pyogenic liver abscess [17]. In another study, NLPR was associated with poor long-term outcomes in patients with acute ischemic stroke [18]. For COVID-19 patients, the AUC value for NLPR cut-off value >0.044 was 0.807, sensitivity 71.1%, and specificity 82.3%, according to Ghobadi *et al.* [19]. Patients with COVID-19 are able to predict disease severity using NPR [20]. At three years after ST elevation myocardial infarction, NPR was independently associated with all causes of mortality [21]. However, no studies examining NLPR and NPR in APE patients were found. Nevertheless, NLPR and NPR are superior to conventional parameters in predicting mortality in APE patients. In this study, the most effective variable for predicting mortality in APE patients was

NLPR, followed by NPR.

A study by Suwadi *et al*. [22] reports that SII can be used as a strong marker for detecting mortality and severity of APE patients. Siddiqui *et al*. [23] observed that SII was effective in predicting major bleeding and mortality, with an AUC value of 0.696 for mortality in patients with venus thromboembolism. In this research, SII predictive power for mortality in APE patients was consistent with the literature.

This study has some limitations. It is a sectional and retrospective study; prospective investigations are needed for validation. Whole blood parameters are affected by a variety of factors. Due to these factors, all patients who met the exclusion criteria were excluded from the study. Due to interregional differences, this study was monocentric and needs to be powered by global multicenter studies. In addition, since NLPR and NPR were used for the first time to predict mortality in APE patients, no comparisons could be made with other studies. It will therefore need to be supported by other studies.

5. Conclusions

In emergency departments, whole blood parameters and variables are always available. NLPR, NPR, and NLR were found to be more effective whole blood parameters for predicting mortality in APE patients presenting to the emergency room. NLPR, NPR and NLR can be used as helpful parameters to predict poor prognosis in APE patients in emergency rooms.

AVAILABILITY OF DATA AND MATERIALS

The data generated and analysed during the study can be obtained from the corresponding author.

AUTHOR CONTRIBUTIONS

Mİ—made conception and design, data collection analysis and interpretation of data, drafting the manuscript, writing, critical revision; VT—made analysis and interpretation of data. All of the authors approved the final version to be published.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Permission to study was obtained from The Ethics Committee of Dicle University Faculty of Medicine with registration number 14.06.2023/204. Due to the retrospective nature of the study, informed consent was waived by The Ethics Committee of Dicle University Faculty of Medicine.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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