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Orgınal Article

Artificial Intelligence Evaluation of the Utility of HALP Score and Hematological Indicators in Estimating No-Reflow After Primary Percutaneous Coronary Intervention in Patients with ST-Segment Elevation Myocardial Infarction

ST Segment Yükselmeli Miyokard İnfarktüsü Olan Hastalarda Primer Perkütan Koroner Müdahale Sonrası Yeniden Akım Olmamasını Tahmin Etmede HALP Skoru ve Hematolojik Göstergelerin Faydasının Yapay Zeka ile Değerlendirilmesi

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Highlights

- In recent studies, artificial intelligence applications are increasingly used in cardiology clinical research.
- Hematological parameters are effective in estimating no-reflow in patients with ST-segment elevation myocardial infarction.

Abstract

Background: Acute Myocardial Infarction (AMI) is a leading cause of mortality globally, with ST-segment Elevation Myocardial Infarction (STEMI) being a specific type. The study aims to fill the gap in literature regarding the predictive utility of hematological parameters and the HALP score in the context of the "no-reflow" phenomenon in STEMI patients. To evaluate the predictive efficacy of hematological parameters and the HALP score in identifying the "no-reflow" phenomenon in STEMI patients undergoing Primary Percutaneous Coronary Intervention (PPCI) using Explainable AI (XAI) methodologies. **Material and Methods:** A retrospective observational design was used, involving 232 STEMI patients who underwent PPCI between January 2020 and September 2023. The cohort was subsequently dichotomized into two subsets based on the presence or absence of the no-reflow phenomenon. Data were collected on demographic variables, MI locations, and hematological parameters. The HALP score was calculated, and XGBoost machine learning models were developed and evaluated. **Results:** Statistically significant differences were observed in white blood cell count (WBC), monocyte (MO), neutrophil (NEU), platelet (PLT), albumin (ALB), and the MPV/LY ratio (MPVLR) between the 'NORMAL-REFLOW' and 'NO-REFLOW' categories. The XGBoost model showed good performance in the training set but had limitations in sensitivity in the test set. **Conclusion:** In this study, according to artificial intelligence analysis, the most important hematological parameter in predicting no-relow was MPVLR. However, in this study, HALP score was not found to be effective in predicting no-reflow. The study provides valuable insights into the predictive factors for reflow outcomes in STEMI patients.

Keywords: Acute Myocardial Infarction, ST-segment Elevation Myocardial Infarction, No-reflow Phenomenon, Hematological Indices, Explainable Artificial Intelligence.

ÖZ

Amaç: Akut Miyokard İnfarktüsü (AMI), dünya genelinde önde gelen ölüm nedenidir ve ST-segment elevasyonlu Miyokard İnfarktüsü (STEMI), akut myokard infartüsünün alt tipidir. Bu çalışma, STEMI hastalarında "yeniden akış olmaması" fenomeni bağlamında hematolojik parametrelerin ve HALP skorunun öngörücü faydasına ilişkin literatürdeki boşluğu doldurmayı amaçlamaktadır. Açıklanabilir Yapay Zeka (XAI) metodolojileri kullanılarak Primer Perkütan Koroner Müdahale (PPCI) uygulanan STEMI hastalarında "yeniden akış olmaması" fenomeninin öngörülmesinde hematolojik parametrelerin ve HALP skorunun öngörücü etkinliğini değerlendirmektir.

Gereç ve Yöntem: Ocak 2020 ile Eylül 2023 arasında PPCI uygulanan 232 STEMI hastasını içeren retrospektif bir gözlem tasarımı kullanıldı. Daha sonra kohort, yeniden akış olmaması fenomeninin varlığına veya yokluğuna dayalı olarak iki alt gruba ayrıldı. Demografik değişkenler, MI lokasyonları ve hematolojik parametrelere ilişkin veriler toplandı. HALP puanı hesaplandı ve XGBoost makine öğrenimi modelleri geliştirilip değerlendirildi. **Bulgular:** 'NORMAL YENİDEN AKIŞ' ve 'YENİDEN AKIŞ OLMAMASI' kategorileri arasında beyaz kan hücresi sayısı (WBC), monosit (MO), nötrofil (NEU), trombosit (PLT), albümin (ALB) ve MPV/LY oranında (MPVLR) istatistiksel olarak anlamlı farklılıklar gözlendi.. XGBoost modeli, eğitim setinde iyi bir performans gösterdi ancak test setinde hassasiyet konusunda sınırlamalar vardı. **Sonuçlar:** Bu çalışmada, yapay zeka analizlerine göre, yeniden akış olmamasını öngörmede en önemli hematolojik parametre MPVLR idi. Ancak bu çalışmada HALP skorunun yeniden akış olmamasını öngörmede etkili olmadığı görüldü. Çalışma, STEMI hastalarında yeniden akış sonuçlarının öngörücü faktörleri hakkında değerli bilgiler sağlıyor.

Anahtar Kelimeler: Akut Miyokard İnfarktüsü, ST-segment elevasyonlu Miyokard İnfarktüsü, Yeniden Akım Olmaması Olayı, Hematolojik İndeksler, Açıklanabilir Yapay Zeka.

Introduction

Acute Myocardial Infarction (AMI) remains a critical public health issue, serving as a leading cause of mortality worldwide. With an annual incidence exceeding three million cases, AMI presents a substantial burden on healthcare systems globally (1-3). The condition is primarily classified into two distinct categories: ST-segment Elevation Myocardial Infarction (STEMI) and Non-ST-segment Elevation Myocardial Infarction (NSTEMI). These classifications are based on the specific ischemic conditions they induce, which arise from either partial or complete cessation of coronary blood flow, culminating in irreversible myocardial damage (4). The clinical consequences of AMI are diverse and severe, ranging from systolic and diastolic cardiac dysfunction to the onset of life-threatening arrhythmias. Additionally, AMI can precipitate severe mechanical complications, such as left ventricular free wall rupture and heart valve dysfunction. The importance of timely coronary reperfusion has been empirically substantiated, showing significant reductions in these complications, particularly within the critical window of the first six hours post-onset (4).

In the specialized field of coronary angiography, the "no-reflow" phenomenon is characterized by a marked reduction in antegrade flow in the coronary artery. This is quantified by a Thrombolysis in Myocardial Infarction (TIMI) flow grade of ≤ 2 and occurs in the absence of any mechanical obstruction following recanalization (5-7). This phenomenon has been empirically linked to both short-term and long-term morbidity and mortality in patients diagnosed with STEMI who are undergoing Primary Percutaneous Coronary Intervention (PPCI).

The three main mechanisms that cause no-reflow are ischemic injury, reperfusion injury and distal embolization (8). First, ischemia causes degeneration of endothelial and myocardial cells. Endothelial cells show folds towards the lumen, bubbles form within the lumen, and the cells show swelling (9). This swelling causes obstruction in the microvascular structure. Necrosis in endothelial cells creates clefts between cells. Erythrocytes leaking from these slits put pressure on the vessels from the outside (10). Ischemia increases the expression of adhesion molecules on the endothelial surface, but decreases nitric oxide synthesis, impairing endothelium-dependent vasodilation. As a result, a thrombus-prone environment and vasospasm occur. The oxygen brought by blood returning to the environment through mechanical or pharmacological reperfusion is repeatedly reduced in the ischemic environment, causing the formation of free oxygen radicals (11). In addition, with the opening of the obstruction, abundant neutrophils cause an inflammatory environment and platelets cause a thrombotic environment. Neutrophils accelerate the production of free oxygen radicals. With the increase in adhesion molecules, neutrophils are taken into the endothelial lumen and reach the intercellular region and cardiac smooth muscle cells (12). Together with the erythrocytes leaking here, they cause interstitial bleeding and vascular compression. In addition, platelets and neutrophils, which come into the environment in large quantities, form microplugs in the capillary circulation. Fragments broken off from the thrombus formed in the lumen cause emboli in the distal vessels and capillaries (13). As a result, reflow cannot be achieved even though there is no mechanical obstruction.

Recent advancements in medical research have shed light on the prognostic utility of specific hematological indices, such as the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Mean Platelet Volume-to-Lymphocyte Ratio (MPVLR), in predicting adverse outcomes in STEMI patients (14-18). Concurrently, the Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score has emerged as a robust indicator of various clinical outcomes across a spectrum of diseases, including but not limited to, oncological conditions and cardiovascular diseases (19-22).

Despite these advancements, a significant gap exists in the current literature regarding the combined predictive utility of these hematological parameters and the HALP score in the context of no-reflow in STEMI patients. Moreover, no study to date has employed interpretable Artificial Intelligence (AI) methodologies to address this research question.

Machine learning (ML) is a branch of artificial intelligence (AI) that uses data-driven learning to create predictions about new data when exposed to new data. AI/ML approaches are one of the technologies that have seen widespread usage in illness detection and clinical decision support systems in recent years, and they have a wide range of applications. ML, which has a wide range of applications in health, is the foundation of applications in the determination of genetic illnesses, early detection of malignant diseases, and pattern recognition in medical imaging (23,24). ML methods, which are highly preferred in classification problems, will also be used in this study. The aim of this study is to classify the reflow status, which is the target variable, using the XGBoost ML method and to identify the risk factors affecting reflow with the help of variable importance values.

The objective of this study is to bridge this gap in the literature. Specifically, the study aims to employ Explainable AI (XAI) methodologies to evaluate the predictive efficacy of these hematological parameters and the HALP score for the no-reflow in STEMI patients undergoing PPCI.

Material And Methods

Study Design and Data

This investigation adopts a retrospective observational design, encompassing a cohort of STEMI patients who underwent PPCI at our medical institution between January 2020 and September 2023. The cohort was subsequently dichotomized into two subsets based on the presence or absence of the no-reflow phenomenon, totaling 232 individuals.

Ethical Considerations

Ethical clearance for this study was duly obtained from the institutional ethics committee, ensuring that the research adheres to established ethical guidelines (Date: 20.09.2023; Protocol number: 2023/17/10).

Inclusion and Exclusion Criteria

The inclusion criteria for this study were meticulously predicated on the 2017 European Society of Cardiology (ESC) Guidelines for the management of AMI in patients presenting with STEMI (25-27). Exclusion criteria were delineated to mitigate potential confounding variables and included age restrictions, drug interactions affecting complete blood count, and pre-existing medical conditions such as renal impairment or a recent history of cancer.

a) Age >18 years and 80 years.

The exclusion criteria from the study are given follow as:

a) Age <18 years and >80 years,
b) Patients use drugs known to affect the complete blood count,
c) Patients with a hemoglobin value of less than 10 g/dl,
d) Patients with active bleeding,
e) Patients with severe renal impairment
f) A history of cancer was detected within the previous year,
g) Patients with severe liver impairment.

Data Collection

Data pertaining to demographic variables, MI locations, and comorbidities were extracted from electronic medical records. Hematological and biochemical parameters were ascertained from venous blood samples obtained during the initial emergency department admission. Age, gender, MI locations, and underlying diseases were obtained from the medical records of the patients and the control group at the first admission to the hospital. At the same time, the hematological and biochemical laboratory results from the venous blood taken at the first application to the emergency department gathered from the groups were; urea (mg/dL), creatinine, albumine (Alb), c-reactive protein (CRP), aspartate transaminase (AST), alkaline phosphatase (ALT), troponin (Tn), hemoglobin (Hbg) values, hematocrit (Hct) values, mean corpuscular volume (MCV) values, mean corpuscular hemoglobin (MCH) values, mean corpuscular hemoglobin concentration (MCHC) value, red-cell distribution width-standard deviation (RDW-SD) values, RDW-coefficient of variation (RDW-CV) values, mean platelet volume (MPV) values, platelet width of distribution (PDW) values, procalcitonin (PCT) values, platelet (PLT) counts and white blood cell (WBC), neutrophil (NEU), lymphocyte (LY), NLR, basophil (BA), monocytes (MO) and eosinophil (EO) counts.

HALP Score Calculation

The HALP score was computed using a standardized formula: Hemoglobin (g/L) × Albumin (g/L) × Lymphocytes (/L) / Platelets (/L), serving as a key variable in the study's predictive model.

Machine Learning -XGBoost

Gradient Boost is a useful machine learning strategy for regression and classification issues in which weak prediction models commonly yield decision tree ensembles. Gradient Boost, which is based on the boosting approach, tries to build several weak learners sequentially and integrate them into a complicated model (28).

Extreme Gradient Boosting (XGBoost) is a supervised learning approach that uses gradient boosting machines (GBM). Its foundation is built on gradient boosting and decision tree methods. When compared to other algorithms, it offers a substantial speed and performance advantage. XGBoost is also highly predictive, ten times quicker than other algorithms, and incorporates a number of regularizations that boost overall performance while decreasing overfitting and over-learning. XGBoost can improve performance by managing the complexity of the trees through the use of various regularization approaches (29,30).

Machine Learning Modeling and Performance Evaluation

In the study, variable selection was made in order to determine the most prominent features affecting the dependent variable in the data set. Random Forest variable selection method was used as the variable selection method. In the current study, XGBoost was utilized in the modeling stage for the dataset. As a training and test dataset, the data set was divided 80:20. The n-fold cross-validation approach was used in the analyses. The data is separated into n parts in the n-fold cross-validation procedure, and the model is applied to n parts. One of the n components is utilized for testing, while the remaining n-1 components are used to train the model. In this study, 5-fold cross-validation was employed for the modeling process. Accuracy, balanced accuracy, sensitivity, selectivity, positive predictive value, negative predictive value, and F1-score were used as performance evaluation criteria. In addition, variable importances were calculated, which gives information about how much the input variables attach importance to the output variable.

Biostatistical Analysis

The numerical variables in the dataset are summarized with median (95% confidence interval for median) and mean±standard deviation. while the qualitative variables are summarized with count (percentage). The conformity of the data to a normal distribution was checked with the Shapiro-Wilk test. Depending on the data distribution. independent sample t-test or Mann-Whitney U test was used for statistical analysis. A $p \leq 0.05$ was considered statistically significant. Analyses were performed using IBM SPSS Statistics 25.

Results

A total of 232 patients were retrospectively included in the study, of which 173 (78.88%) were patients with normal-reflow and 49 (21.12%) were patients with no-reflow between January 2020 and September 2023. Of the participants, 72 (31.0%) were female and 160 (69.0%) were male. Descriptive statistics of the quantitative variables in the current study are given in Table 1.

Descriptive statistics of the qualitative variables in the study are given in Table 2.

Table 1: Descriptive statistics for quantitative variables

Variable	Median (95% confidence interval)
Age (years)	60(60-63)
White Blood Cell ($10^{9/L}$)	11.6(11.2-12)
Hemoglobin (g/dL)	14.1(13.8-14.5)
Red Blood Cell ($10^{12/L}$)	4.82(4.78-4.91)
Basophil ($10^{9/L}$)	0.06(0.06-0.08)
Eosinophil ($10^{9/L}$)	0.115(0.1-0.14)
Lymphocyte ($10^{9/L}$)	2.605(2.49-2.87)
Monocyte ($10^{9/L}$)	0.735(0.7-0.8)
Neutrophil ($10^{9/L}$)	7.235(6.72-7.77)
Mean Platelet Volume (pg)	9.35(9.1-9.5)
Platelet ($10^{9/L}$)	267(258-278)
Hematocrit (HCT)	41.70(41-42.60)
MCV	87.05(86.1-87.9)
RDW-SD	41.3(40.4-42)
RDW-CV	13.6(13.6-13.9)
MCH (pg)	29.5(29.1-29.8)
MCHC (g/dL)	33.9(33.7-34.1)
PDW (fL)	16.2(15.9-16.39)
PCT (%)	0.24(0.24-0.26)
Albumin (g/dL)	41(41-42)
HALP score	5.906(5.477-6.354)
MPV/LY ratio	3.4(3.215-3.714)
NEU/LY ratio	2.581(2.196-2.938)
PLT/LY ratio	95.567(89.607-106.923)

WBC: leukocyte; RBC: erythrocyte; HGB: hemoglobin; BA: basophil; EO: eosinophil; LY: lymphocyte; MO: monocyte; NEU: neutrophil; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; MPVLR: mean platelet volüme/lymphocyte ratio; LMR: lymphocyte/monocyte ratio; MPV: mean platelet volume; PLT: platelet; HCT: hematocrit; RDW-SD: red cell distribution width-standard deviation; RDW-CV: Red cell distribution width-coefficient of variation; MCH: mean erythrocyte hemoglobin; MCHC: mean corpuscular hemoglobin concentration; PDW: platelet distribution width; PCT: procalcitonin test.

Table 2: Descriptive statistics for qualitative variables

Variables	Categories	Count (%)
Reflow	NORMAL-REFLOW	183 (78.88)
	N0-REFLOW	49 (21.12)
Mi Location	Acute Inferior MI	135 (58.18)
	Acute Anterior MI	97 (41.82)
Gender	Female	72 (31.03)
	Male	160 (68.97)

Tablo 3: Statistical analysis results of normally distributed variables

Variables		REFLOW		*p*
		Normal-Reflow (N=183)	No-Reflow (N=49)	
		Mean±Standart Deviation		
Age (years)		59.858±9.8	58.939±11.4	0.577*
Variables	Categories	Count (%)		
MI Location	Acute inferior	104[a] (56.8)	31[b] (63.2)	0.063**
	Acute anterior	79 [a] (43.2)	18 [b] (36.8)	
Gender	Female	55 (30.1)	17 (34.7)	0.653**
	Male	128 (69.9)	32 (65.3)	

*: Independent sample t-test; **: Pearson chi-square test with Yates correction; myocardial infarction (MI); MI locations.

The results on whether there are statistical differences in demographic parameters in terms of the categories of the reflow variable are given in Table 3.

As a result of the analyses, no statistically significant difference was found between the categories of the reflow variable and the categories of the age variable, MI location variable, and gender variable. The results of whether there were statistical differences in the blood parameters in terms of the categories of the reflow variable are given in Table 4.

Tablo 4: Statistical analysis results of non-normally distributed variables

	REFLOW		*p*
Variables	**NORMAL-REFLOW(n=183)**	**NO-REFLOW(n=49)**	
	Median (95% confidence interval)		
White Blood Cell ($10^{9/L}$)	11.2(10.7-11.75)	13.5(12.2-14.35)	**<0.001***
Hemoglobin (g/dL)	14(13.6-14.5)	14.5(13.7-15.1)	0.521*
Basophil ($10^{9/L}$)	0.06(0.05-0.08)	0.07(0.05-0.1)	0.198*
Eosinophil ($10^{9/L}$)	0.11(0.1-0.15)	0.13(0.1-0.26)	0.801*
Lymphocyte ($10^{9/L}$)	2.6(2.48-2.89)	3.06(2.4-4.5)	0.060*
Monocyte ($10^{9/L}$)	0.7(0.7-0.79)	1(0.9-1.1)	**<0.001***
Neutrophil ($10^{9/L}$)	6.8(6.2-7.6)	8.69(8.11-9.36)	**0.001***
MPV (fL)	9.4(9.19-9.69)	9.3(8.5-9.8)	0.378*
Platelet ($10^{9/L}$)	265(252-275)	290(265-345)	**0.017***
MCV (fL)	87.3(86.6-88.3)	86.1(85-88.1)	0.282*
RDW-SD	41.2(40.3-42)	41.7(40-42.9)	0.700*
RDW-CV	13.5(13.4-13.7)	13.7(13.5-14.3)	0.124*
MCH (pg)	29.6(29.1-30.1)	29.5(28.3-30)	0.230*
MCHC (g/dL)	34(33.9-34.2)	33.7(33.5-34.2)	0.804*
PDW (fL)	16.2(15.8-16.39)	16.3(15.9-16.8)	0.346*
PCT (%)	0.24(0.24-0.26)	0.26(0.25-0.3)	0.059*
Albumin (g/dL)	41.3(41-42)	40(38-42)	**0.031***
HALP score	5.794(5.318-6.252)	6.464(5.338-8.409)	0.437*
MPV/LY ratio	3.511(3.269-3.855)	3.2(2.042-4.038)	**0.041***
NEU/LY ratio	2.445(2.168-2.85)	3.055(2.031-3.908)	0.667*
PLT/LY ratio	98(91.111-108.772)	85.946(73.786-112.162)	0.272*
	Mean ± Standard Deviation		
Red Blood Cell ($10^{12/L}$)	4.794±0.579	4.864±0.68	0.469**
Hematocrit (%)	41.384±4.629	41.598±5.185	0.779**

*:Mann Whitney U test, **:Independent sample t test, WBC: leukocyte; RBC: erythrocyte; HGB: hemoglobin; BA: basophil; EO: eosinophil; LY: lymphocyte; MO: monocyte; NEU: neutrophil; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; MPVLR: mean platelet volüme/lymphocyte ratio; MPV: mean platelet volume; PLT: platelet; HCT: hematocrit; RDW-SD: red cell distribution width-standard deviation; RDW-CV: Red cell distribution width-coefficient of variation; MCH: mean erythrocyte hemoglobin; MCHC: mean corpuscular hemoglobin concentration; PDW: platelet distribution width; PCT: procalcitonin test; HALP score (Hemaglobin*Albumin* Lymphocyte/Platelet).

As a result of the analyses, a statistically significant difference was observed in white blood cell (WBC), monocyte (MO), neutrophil (NEU), platelet (PLT), albumin, and MPV/LY variables in terms of the categories

of the reflow variable ($p<0.05$). For the other variables. no statistically significant difference was found in terms of the categories of the reflow variable.

The results of the performance metrics obtained for the test and training data as a result of modeling with XGBoost for the remaining variables and the reflow variable after the variable selection are given in Table 5.

Table 5: Results for performance metrics obtained from the XGBoost model

Metric	Training set Value	Test set Value
Accuracy	86.1	84.4
Balanced Accuracy	70.2	61.1
Sensitivity	42.5	22.2
Specificity	98	100
PPV	85	100
NPV	86.2	83.7
F1 score	56.7	36.4

In the training stage accuracy, balanced accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and F1 score obtained from the random forest model were 86.1%, 70.2%, 42.5%, 98%, 85%, 86.2%, and 56.7%, respectively. Also in the testing stage accuracy, balanced accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and F1 score obtained from the RF model were 84.4%, 61.1%, 22.2%, 100%, 100%, 83.7%, and 36.4%, respectively. Performance metrics are plotted for the XGBoost model in Figure 1.

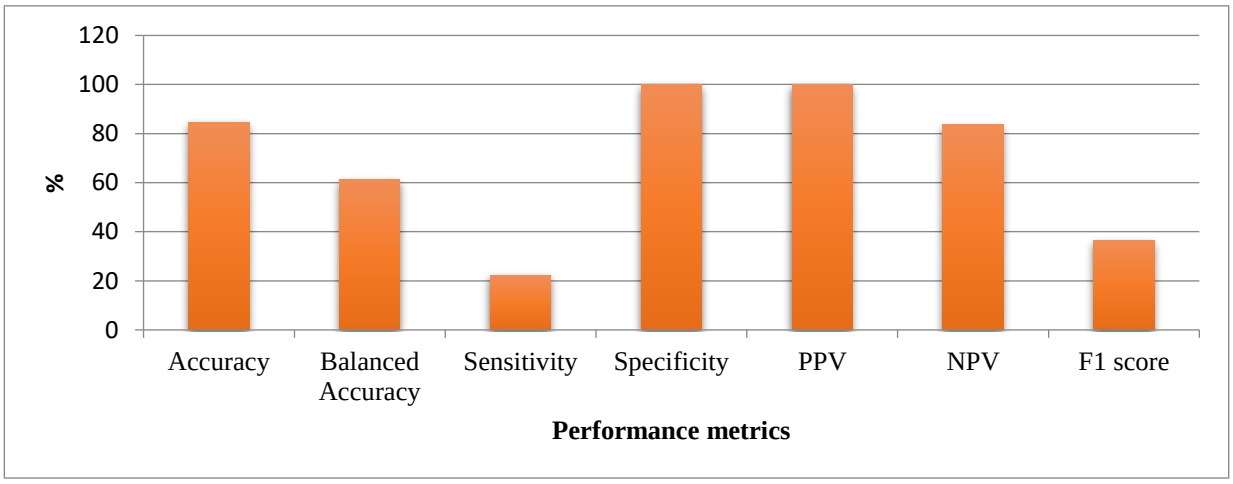

Figure 1: Graph of performance metrics

The graph of the variables associated with the output variable according to the variable importance obtained from the modeling is given in Figure 2.

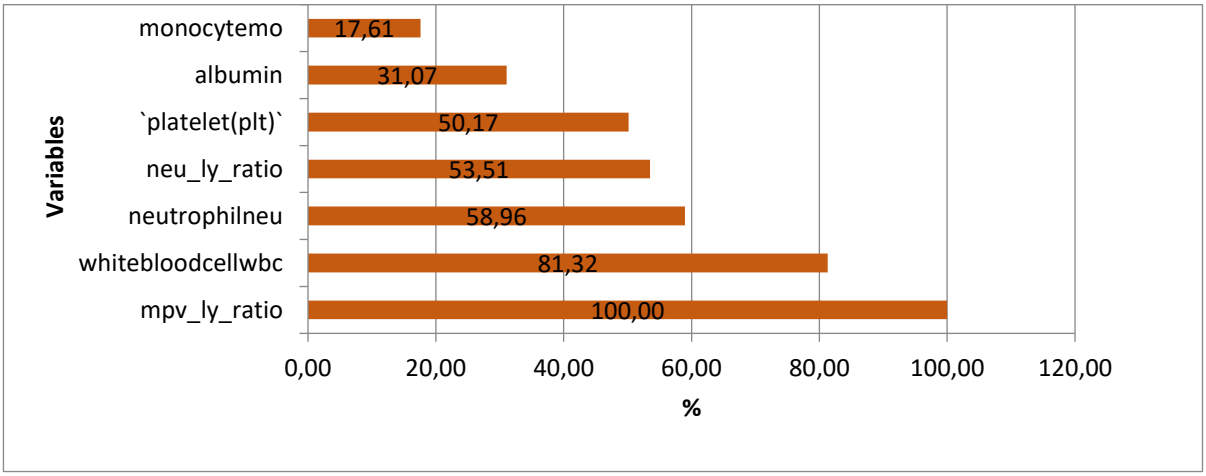

Figure 2: Variable importance graph

Discussion

The study presents a comprehensive analysis of both quantitative and qualitative variables related to blood parameters, demographic characteristics, and clinical outcomes. Descriptive statistics provide a snapshot of the central tendencies and variability within the dataset, while inferential statistics offer insights into the relationships between variables, particularly in terms of the 'reflow' categories.

In terms of blood parameters, significant differences were observed in white blood cell count (WBC), monocyte (MO), neutrophil (NEU), platelet (PLT), albumin, and the MPV/LY ratio when comparing the 'NORMAL-REFLOW' and 'NO-REFLOW' categories. These findings indicate that these specific blood parameters could serve as potential biomarkers for predicting reflow outcomes.

The XGBoost model demonstrated good performance in the training set with an accuracy of 86.1%, balanced accuracy of 70.2%, and an F1 score of 56.7%. However, the model's performance slightly declined in the test set, particularly in terms of balanced accuracy and sensitivity, which dropped to 61.1% and 22.2%, respectively. Despite the high specificity and positive predictive value (PPV) in both training and test sets, the low sensitivity in the test set suggests that the model may not be as effective in identifying 'NO-REFLOW' cases, which could be a limitation.

In comparison, the Random Forest (RF) model also showed a similar trend, with high accuracy but lower sensitivity and F1 score in the test set. This indicates that while the model is good at making correct predictions overall, it may struggle with identifying the less prevalent class in the dataset.

The study's findings have several clinical implications. The identification of specific blood parameters as potential biomarkers can guide clinicians in risk stratification and decision-making. However, the lower sensitivity in the test set suggests that the model may benefit from further tuning or the inclusion of additional features to improve its predictive power for 'NO-REFLOW' cases.

Future research could focus on incorporating more features or employing different machine learning algorithms to improve model performance. Additionally, external validation with a larger and more diverse dataset could provide more generalizable results.

This study used biostatistical analysis and XAI to investigate potential hematological indicators for predicting no-reflow. The observed results indicated that the WBC, MO, NEU, and PLT values of patients with no flow were statistically higher than those of the patients with normal flow (p<0.05). However, compared to patients with normal-flow, patients with no-reflow had significantly reduced albumin, and MPVLR levels (p<0.05). However, the HALP score was found to be statistically insignificant in both groups. In this study, according to artificial intelligence analysis, MPVLR, WBC, and NEU were most important hematological parameter in predicting no-relow.

A series of pathophysiological events occur in AMI that produce an intense inflammatory response mediated by myocardial ischemia. Neutrophils, white blood cells first detected at the infarct site due to oxidative stress. This is followed by white blood cells monocytes and lymphocytes, which then phagocytize the necrotic remnants by releasing proteo-enzymes and cytokines. In addition, activated platelets interact with neutrophils, monocytes, and lymphocytes, both acutely accelerating coronary artery occlusion and enhancing the inflammatory response. Previous studies have shown that the stronger this inflammatory response, the more severe the vascular thrombogenic state and the increased development of coronary no-reflow in invasive percutaneous coronary procedures, resulting in a worse prognosis in acute myocardial infarction (31-34). In our current study, according to the descriptive statistics results; WBC, NEU, and MO counts were found to be significantly higher in patients with no reflow than in patients with normal reflow (p<0.05). Similarly, artificial intelligence analysis; WBC, and NEU were some of the most important hematological parameters to predict no-reflow. The reason why the WBC and NEU numbers were higher in the no-reflow group compared to the normal-reflow group may be due to the more severe inflammatory response of myocardial ischemia in STEMI patients. As a result, this can lead to a poor AMI prognosis.

Recent studies have shed light on the prognostic utility of specific hematological indices, such as the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Mean Platelet Volume-to-Lymphocyte Ratio (MPVLR), in predicting adverse outcomes in STEMI patients (14-18). In another study, MPVLR was found to be moderately effective in demonstrating the no-relow (35). In this study, according to artificial intelligence analysis, the most important hematological parameter in predicting no-relow was MPVLR.

Previous studies have shown that high-sensitivity C-reactive protein (hs-CRP), neutrophil count, lymphocyte count, monocyte count, and albumin are important inflammatory markers in the inflammatory process of atherosclerosis, plaque development, and plaque progression (36,37). Adverse cardiovascular outcomes and the prevalence of atherosclerosis are significantly associated with high CRP levels (38). Additionally, another

study has shown that CRP/albumin ratio (CAR) is an important biochemical marker for predicting no reflow (39). In our study, albumin level was significantly lower in the non-reflow group. A study found that coronary artery disease and heart failure were more common in men, and rheumatic mitral valve disease and Takotsubo cardiomyopathy were more common in women (40). However, in the current study, the gender factor between the no-reflow and normal-reflow groups were statistically similar in both groups.

Limitations

The study has some limitations. First, the number of patients in the study limited. Second, our data source included patients from only 1 geographic region of Turkey, which limits generalizability and requires validation in other populations.

Conclusions

In our study, according to artificial intelligence analysis, the most important hematological parameter in predicting no-reflow was MPVLR. However, in this study, HALP score was not found to be effective in predicting no-reflow. The study offers valuable insights into the factors affecting reflow outcomes in patients, with specific blood parameters showing promise as predictive biomarkers. While the machine learning models employed show good predictive accuracy, there is room for improvement, particularly in enhancing the sensitivity of the models. Further research is needed to validate these findings and improve the predictive models.

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