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Effects of mean platelet volume, mean corpuscular hemoglobin concentration and neutrophil-to-lymphocyte ratio on mortality in patients undergoing coroner artery bypass graft surgery

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Abstract

Background/Aim: Laboratory tests play a vital role in diagnosing, monitoring, treating, and determining the prognosis of diseases. Several parameters, including mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), mean corpuscular volume (MCV), platelet distribution width (PDW), platelet count (PLT), plateletcrit (PCT), neutrophil count (NEU), platelet/lymphocyte ratio (PLR), and neutrophil/lymphocyte ratio (NLR), have been investigated in various diseases. This study aims to explore whether these parameters can predict mortality in patients undergoing coronary artery bypass graft surgery (CABG).

Methods: The study was conducted as a retrospective cohort study, analyzing 2478 patients who underwent CABG in the cardiovascular surgery clinic of our hospital between January 2013 and November 2020. Preoperative blood count parameter values (PLT, PCT, PDW, MPV, MCHC, MCV, PLR, NEU, NLR, and MCHC/MCV) were compared between 80 patients who died after the operation (Group 1) and 80 patients who were discharged from the hospital (Group 2).

Results: The analysis revealed that PLT and MCV were significantly lower in Group 1, while MPV, NEU, NLR, and MCHC/MCV were significantly higher. In the receiver operating characteristic (ROC) analysis, the positive probability rate of PLT in predicting mortality (cut-off >260.2, +LR: 2.44, 95% CI: 0.605–0.754) was higher than that of MPV (cut-off ≤7.53, +LR: 2, 95% CI: 0.584–0.735), MCV (cut-off ≤82.21, +LR: 1.26, 95% CI: 0.513–0.671), NEU (cut-off ≤68.2, +LR: 2.03, 95% CI: 0.640–0.785), NLR (cut-off ≤2.66, +LR: 2.58, 95% CI: 0.571–0.724), and MCHC/MCV (cut-off ≤0.4, +LR: 1.45, 95% CI: 0.551–0.706).

Conclusion: Preoperative PLT, MCV, MPV, NEU, NLR, and MCHC/MCV values are effective parameters for predicting mortality in CABG patients.

Keywords: coronary artery disease, coronary artery bypass graft operation, mortality, blood count parameters

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Ethics Committee Approval
The study was approved by Adıyaman University Non-Invasive Clinical Research Ethics Committee (17/11/2020, 2020/10-11).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Introduction

The purpose of coronary artery bypass graft surgery (CABG).can be summarized as improving the quality and duration of life, relieving angina, and reducing the occurrence of recurrent ischemic events, such as myocardial infarction, by decreasing the need for subsequent procedures. Despite being considered one of the most life-saving surgeries, the mortality rate for CABG ranges from approximately 1.48% to 2.67%, depending on the surgical technique employed and the surgeon's experience [1,2].

By identifying and addressing preventable factors contributing to mortality, it may be feasible to further reduce this rate. In the contemporary healthcare, laboratory tests are crucial in disease diagnosis, prognostic evaluation, and treatment selection.

Hematologic parameters, including mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW), platelet/lymphocyte ratio (PLR), and mean corpuscular hemoglobin concentration (MCHC), can be determined through cost-effective laboratory tests. The literature reports these parameters' utilization in the diagnosis and treatment of numerous diseases. For instance, MPV has been identified as an independent parameter associated with well-known risk factors such as dyslipidemia, hypertension, increased fibrinogen levels, and elevated white cell count. Moreover, a significant correlation has been observed between MPV and atherothrombosis [3].

Research has demonstrated the utility of PCT and PLR as markers for identifying heightened thrombotic status and inflammatory response in individuals with morbid obesity [4]. Additionally, a separate study indicated a correlation between NLR and acute coronary syndromes [5].

This study aims to examine whether MPV, PCT, PDW, PLR, MCHC, mean corpuscular volume (MCV), and MCHC/MCV can serve as predictors of mortality in CABG patients.

Materials and methods

The study commenced after obtaining approval from the Local Ethics Committee (TC. Non-Interventional Ethics Committee of Adiyaman University) on November 17, 2020, with session number 2020/10-11. A total of 3,478 patients who underwent CABGO and were diagnosed with coronary artery disease (CAD) between January 2013 and November 2020 were included in the study, along with 80 randomly selected patients who were discharged with recovery. The data were collected electronically from the hospital's data recording system. An equal number of male and female patients were randomly selected as the control group. The patients who died were categorized as Group 1, while the control patient group was referred to as Group 2. The preoperative PLT, PCT, PDW, MPV, MCHC, MCV, PLR, NEU, NLR, and MCHC/MCV values of these groups were compared. Blood samples were analyzed using the Abbott Cell-Dyn Ruby (USA) hematology analyzer.

Patients who underwent additional operations other than CABGO and emergency surgeries were excluded from the study. Furthermore, patients with hematologic diseases, active infections, and liver dysfunction were also excluded. To mitigate gender bias, an equal number of male and female patients were selected in this study, matching the number in the control group.

Statistical analysis

Statistical analysis was conducted using SPSS 15.0 for Windows (SPSS Inc.) and Medcalc v.9.4.4.0. The one-sample Kolmogorov-Smirnov test was employed to assess the normal distribution of the data. Group comparisons were performed using the Independent Two Samples t-test or the Mann-Whitney U test, as appropriate. Results were presented as mean, standard deviation and median (min-max). Non-parametric data were compared using the Chi-square test and reported as numbers or percentages. Pearson correlation coefficients were utilized for continuous variables. Multivariate binary logistic regression analysis was conducted to determine predictive factors for ex-subjects considering statistically relevant confounding variables. The receiver operating characteristics (ROC) curve was employed for evaluating clinical parameters. A *P*-value <0.05 was considered statistically significant.

Results

Randomly selected patients who underwent CABGO with a diagnosis of CAD and subsequently died after surgery were included in the study. Group 1 consisted of 40 males and 40 females, while Group 2 comprised 40 men and 40 women. The study was conducted between January 2013 and November 2020. The mean age of Group 1 was 66.49 (9.99) years, whereas Group 2 had a mean age of 63.30 (8.34) years (*P*=0.030). No significant differences were observed in comorbidity between the two groups (Table 1). Table 1 provides a summary of the demographic, clinical, and laboratory characteristics of the patients.

Table 1: Demographic, clinical and laboratory characteristics of the patients.

Variables		Group 1 (n=80) Exitus (Deceased)		Group 2 (n =80) Discharge		
		Mean (SD) n(%)	Median (Min-Max)	Mean (SD) n(%)	Median (Min-Max)	*P*-value
Age		66.49 (9.99)	65.00 (45.00-89.00)	63.30 (8.34)	63.00 (46.00-81.00)	0.030 $^{\Phi}$
Gender	Male	40 (50%)		40 (50%)		1.000 $^{\Psi}$
	Female	40 (50%)		40 (50%)		
Smoking		21 (26.25%)		19 (23.75%)		0.710 $^{\Psi}$
Hypertension		29 (36.25%)		26 (32.50%)		0.614 $^{\Psi}$
Alcohol		11 (13.75%)		10 (12.5%)		0.807 $^{\Psi}$
Diabetes Mellitus		20 (25%)		22 (27.5%)		0.715 $^{\Psi}$
PLT		229.69 (64.2)	229.69 (87.32-481.0)	276.82 (92.43)	269.5 (116.2-747.1)	<0.001 $^{\tau}$
MPV		8.40 (1.63)	8.16 (5.37-12.65)	7.50 (1.47)	7.2 5.11-11.74	<0.001 $^{\Phi}$
PCT		0.22 (0.1)	0.20 (0.10-0.63)	0.19 (0.06)	0.18 (0.09-0.41)	0.095 $^{\tau}$
PDW		18.40 (3.36)	19.27 (9.60-24.84)	17.70 (3.95)	18.57 (8.50-24.70)	0.228 $^{\Phi}$
MCHC		33.27 (1.64)	32.90 (29.62-37.66)	32.86 (1.49)	33.04 (29.26-36.39)	0.105 $^{\Phi}$
MCV		85.03 (5.93)	85.7 (70.64-99.62)	86.88 (4.23)	86.72 (73.41-100.30	0.025 $^{\Phi}$
NEU		69.53 (11.77)	69.70 (46.63-92.40)	60.88 (8.11)	60.34 (42.81-78.39)	<0.001 $^{\Phi}$
LYM		26.56 (7.82)	27.75 (9.40-42.96)	29.09 (6.38)	28.50 (16.04-45.60)	0.143 $^{\Phi}$
NLR		3.01(1.4)	2.76 (1.30-7.37)	2.22 (0.75)	2.17 (0.14-3.93)	<0.001 $^{\tau}$
PLR		9.71 (5.1)	8.40 (3.51-29.66)	10.07 (5.5)	9.0 (0.52-46.58)	0.187 $^{\tau}$
MCHC/MCV		0.393 (0.03)	0.39 (0.37-0.42)	0.382 (0.02)	0.38 (0.32-0.70)	0.002 $^{\Phi}$

$^{\Psi}$ Chi-Square test was used, $^{\Phi}$ Independent two sample t-test was used, $^{\tau}$ Mann-Whitney U test was used. SD: Standard deviation, Min: Minimum, Max: Maximum, PLT: Platelet, MPV: Mean platelet volume, MCV: Mean corpuscular, PCT: Plateletcrit, PDW: Platelet distribution width, MCHC: Mean corpuscular hemoglobin concentration, MCV: Mean corpuscular volume, NEU: Neutrophil, LYM: Lymphocyte, NLO: Neutrophil-to-lymphocyte ratio, PLO: Platelet-to-lymphocyte ratio, MCHC/MCV: Mean corpuscular hemoglobin concentration to mean corpuscular volume ratio

Based on the file scans, it was determined that all patients who experienced mortality had died prior to the follow-up period in the ward after being in the Intensive Care Unit.

Significant differences were observed between Group 1 and Group 2 in terms of PLT levels from laboratory data (P<0.001). Furthermore, Group 1 exhibited significantly higher values of MPV, MCV, NEU, NLO, and MCHV/MCV compared to Group 2 (P<0.001, P=0.025, P<0.001, P<0.001, and P=0.002, respectively). The results of the Multivariate Binary Logistic Regression Analysis are presented in Table 2. According to these findings, elevated PLR values were associated with increased mortality, whereas decreased MPV, PCT, PDW, NLR, and MCVC/MCV rates were associated with decreased mortality. The analysis revealed that MPV (OR: 0.653, 95% CI: 0.493–0.864, P=0.003), PCT (OR: 0.004, 95% CI: 0.000–1.000, P=0.003), PDW (OR: 0.885, 95% CI: 0.787–0.996, P=0.042), NLR (OR: 0.197, 95% CI: 0.102–0.381, P<0.001), and PLR (OR:1.310, 95%CI: 1.124–1.526, P=0.001) values were independent predictive factors for mortality (Table 2). Pearson Correlation Analysis was performed to examine the relationships between the predictive parameters and other variables (Table 3). In the deceased group (Group 1), PLR exhibited significant positive correlations with PLT (r=0.560, P<0.001), NEU (r=0.296, P<0.001), and NLR (r=0.778, P<0.001), while demonstrating a significant negative correlation with LYM (r=-0.724, P<0.001). NLR showed a significant positive correlation with NEU (r=0.632, P<0.001) but a negative and significant correlation with LYM (r= -0.922, P<0.001). PDW displayed a positive and significant correlation with MCHC (r=-0.224, P<0.001). No significant correlations were observed between MPV and PCT predictive parameters and other variables (P=0.095). In Group 2, PDW exhibited a negative and significant correlation with PCT (r=-0.224, P=0.05), while the other measurements were similar to those of the deceased group.

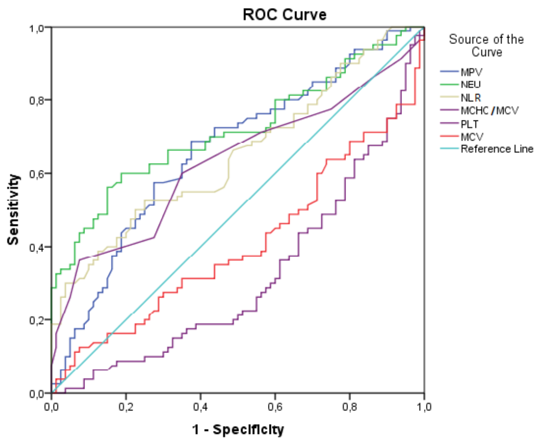
Table 2: The multivariate binary logistic regression analysis to identify predictors of mortality

Variables	B	S.E.	*P*-value	OR	95% CI	
					Lower	Upper
MPV	-0.427	0.143	0.003	0.653	0.493	0.864
PCT	-5.590	2.852	0.050	0.004	0.000	1.000
PDW	-0.122	0.060	0.042	0.885	0.787	0.996
NLR	-1.625	0.337	<0.001	0.197	0.102	0.381
PLR	0.270	0.078	0.001	1.310	1.124	1.526
MCHC/MCV	-23.555	7.684	0.002	0.000	0.000	0.000

B: Beta coefficient, SE: Standard error, OR: Odds Ratio, CI: Confidence Interval, Hosmer–Lemeshow goodness-of-fit test: X^2: 12.32, P=0.138, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet Distribution Width, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet- lymphocyte ratio, MCHC/MCV: Mean corpuscular hemoglobin concentration to mean corpuscular volume ratio

ROC curve analysis was conducted to assess the diagnostic performance and characteristics of the variables found to be significant in Table 1. The results revealed that the predictive capacity of probable positivity rate in predicting mortality (cut-off >260.2, +LR: 2.44, 95% CI: 0.605–0.754) was higher compared to MPV (cut-off ≤7.53, +LR: 2, 95% CI: 0.584–0.735), MCV (cut-off ≤82.21, +LR: 1.26, 95% CI: 0.513–0.671), NEU (cut-off ≤68.2, +LR: 2.03, 95% CI: 0.640–0.785), NLR (cut-off ≤2.66, +LR: 2.58, 95% CI: 0.571–0.724), and MCHC/MCV (cut-off ≤0.4, +LR: 1.45, 95% CI: 0.551–0.706). Consequently, the PLT value with a cut-off of 260.2 exhibited a more accurate diagnostic value in predicting mortality (AUC: 0.683, 95% CI: 0.605–0.754) (Table 3). The ROC chart illustrated that MPV, NLR, and MCHC/MCV were significantly higher in Group 1 than in Group 2, as indicated by their positioning above the reference line (Figure 1). Conversely, PLT and MCV were significantly lower in Group 1 than Group 2, causing them to be situated below the reference line.

Figure 1: Receiver operating characteristic curve of group variables to estimate the likelihood of mortality



MPV: Mean platelet volume, NEU: Neutrophil, NLR: Neutrophil-to-lymphocyte ratio, MCHC/MCV: Mean corpuscular hemoglobin concentration to mean corpuscular volume ratio, PLT: Platelet, MCV: Mean corpuscular volume

Table 3: Receiver operating characteristics curve analysis

Variables	Cut-off	Sensitivity (95% CI)	Specificity 95% CI	+LR 95% CI	-LR 95% CI	AUC (95% CI)	*P*-value
PLT	>260.2	55 (43.5 - 66.1)	77.5 (66.8 - 86.1)	2.44 (1.9 - 3.1)	0.58 (0.4 - 0.9)	0.683 (0.605 - 0.754)	<0.001
MPV	≤7.53	62.5 (51.0 - 73.1)	68.75 (57.4 - 78.6)	2 (1.6 - 2.5)	0.55 (0.4 - 0.8)	0.662 (0.584 - 0.735)	<0.001
MCV	>82.21	90 (81.2 - 95.6)	28.75 (19.2 - 40.0)	1.26 (0.9 - 1.8)	0.35 (0.2 - 0.7)	0.594 (0.513 - 0.671)	0.037
NEU	≤68.02	81.25 (71.0 - 89.1)	60 (48.4 - 70.8)	2.03 (1.7 - 2.5)	0.31 (0.2 - 0.5)	0.716 (0.640 - 0.785)	<0.001
NLR	≤2.66	75 (64.1 - 84.0)	52.5 (41.0 - 63.8)	1.58 (1.2 - 2.0)	0.48 (0.3 - 0.7)	0.651 (0.571 - 0.724)	0.001
MCHC/MCV	≤0.4	92.5 (84.4 - 97.2)	36.25 (25.8 - 47.8)	1.45 (1.1 - 2.0)	0.21 (0.09 - 0.5)	0.631 (0.551 - 0.706)	0.003

+LR: positive likelihood ratio, −LR: negative likelihood ratio, PLT: Platelet, MPV: Mean platelet volume, MCV: Mean corpuscular volume, NEU: Neutrophil, NLR: Neutrophil-to-lymphocyte ratio, MCHC/MCV: Mean corpuscular hemoglobin concentration to mean corpuscular volume ratio

Discussion

Despite advancements in cardiac surgery and cardiac anesthesia techniques, the mortality rate attributed to various complications remains around 2%, even in top-tier medical centers [2]. A thorough examination of the factors influencing mortality reveals that multiple variables, including body mass index, age, gender, aortic clamp time, and total cardiopulmonary bypass time, contribute to increased risk [6].

This study aimed to examine preoperative laboratory values and identify factors influencing mortality, excluding obvious factors. Multivariate Binary Logistic Regression Analysis was conducted to compare patients who died in the intensive care unit of cardiovascular surgery with those who were discharged, considering matching numbers and genders. The results revealed that PLT, MPV, PCT, PDW, and NLR were independent predictive factors for mortality. Specifically, low preoperative PLT and MCV levels, along with elevated MPV, NLR, and MCHC/MCV ratios, were found to significantly impact mortality.

MPV serves as an approximate indicator of platelet activation and has been utilized for risk assessment and prognostic evaluation in cardiovascular diseases [7]. However, no significant correlations were observed between Group 1 (patients who died) and Group 2 (patients who were discharged) in our study. Previous research has demonstrated that MPV is an independent risk factor in individuals with acute coronary syndrome and is closely linked to complications following acute myocardial infarction and restenosis post-stent placement in percutaneous coronary interventions [8]. Additionally, Smyth et al. conducted a separate study revealing elevated MPV levels in patients who experienced restenosis after successful single-vein angioplasty [9]. Our study found that low platelet (PLT) count and elevated MPV were associated with increased mortality.

A separate study highlighted the potential of MPV and MCHC as cost-effective and influential parameters for prognostic evaluation in three vascular coronary artery diseases [8]. MCV and MCHC were initially introduced by Wintrobe in 1929 to assess the size of red blood cells and the amount of hemoglobin. These values, referred to as red cell indices, were initially utilized solely for diagnosing specific types of anemia and understanding their underlying causes [10]. Subsequent clinical trials have emphasized that MCHC, in particular, could serve as a determinant of mortality in CAD and may also predict acute mortality in patients presenting at the emergency department [11-13].

Our study revealed that both MCV and MCHC/MCV ratios significantly impacted mortality. A low MCV value below the cut-off of 82.21, as well as an MCHC/MCV ratio below the cut-off of 0.4, were identified as significant determinants of mortality.

Atherosclerosis, diabetes mellitus, hypertension, dyslipidemia, and smoking are interconnected risk factors contributing to the complex systemic disease known as CAD [14]. Recent research findings indicate that the development of atherosclerosis involves not only passive vascular damage triggered by blood lipoproteins and other elements within the arterial wall but also a significant contribution from white blood cells in the inflammatory process [15,16]. Neutrophils, in particular, have been shown to play various roles, from atherosclerosis progression to plaque stabilization [14]. As a result, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been extensively studied as inflammation biomarkers, with NLR specifically linked to the severity and prognosis of CAD [14,17,18].

Our study evaluated the preoperatively calculated NLR using Multivariate Binary Logistic Regression and ROC Analysis. The results demonstrated that NLR independently served as a risk factor for predicting mortality in patients undergoing coronary artery bypass grafting (CABG).

Limitations

Our study had several limitations that should be acknowledged. Firstly, it was a single-center retrospective study, which inherently restricts the generalizability of the findings. The patient population included in the study was relatively small, further limiting the statistical power of the analysis. Another limitation is that most patients underwent interventional procedures such as coronary angiography, catheter insertion, and urinary probe placement at the cardiology clinic, and many were on anticoagulant and antiplatelet therapy. These procedures and medications can potentially induce inflammatory responses, which may have influenced the inflammatory parameters measured. It is important to recognize that inflammatory parameters can be influenced by various factors, and therefore, a multicenter study considering all relevant prospective influencing factors is necessary to provide a more comprehensive understanding.

The primary limitation of our study is its single-center design, which may restrict the generalizability of the findings to a broader population. Additionally, our study is retrospective in nature, which introduces inherent limitations such as potential bias and limited control over data collection. However, our study has notable strengths, including a relatively large sample size compared to similar studies and the novelty of being the first single-center study reporting on these specific findings in the literature.

Conclusion

In summary, our study demonstrated the significant impact of inflammatory parameters, including preoperative MPV, NEU, NLR, MCHC/MCV, PLT, and MCV, on mortality in patients who underwent CABG. These findings align with existing literature regarding the influence of inflammatory markers on CAD and surgical mortality. Notably, these parameters offer several advantages, such as cost-effectiveness, quick availability (results in less than 20 minutes), and ease of repeatability.

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