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The Association of Demographic Data and Hematological Parameters with Causes of Death in Patients Following Cardiopulmonary Resuscitation in the Emergency Department

Acil Serviste Kardiyopulmoner Resüsitasyon Sonrası Kaybedilen Hastaların Demografik Verileri ve Hematolojik Parametrelerinin Ölüm Nedenleri ile İlişkisi

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Abstract

Background: Cardiopulmonary arrest, marked by the cessation of breathing and circulation, has high mortality rates. Cardiopulmonary resuscitation (CPR) outcomes are influenced by factors like arrest duration and underlying conditions. Inflammatory markers such as platelet-lymphocyte ratio (PLR), lymphocyte-monocyte ratio (LMR), and red cell distribution width (RDW) may predict mortality.

Materials and Methods: This retrospective study analyzed 142 patients who died after CPR in the Emergency Department of Harran University Training and Research Hospital (between January 1, 2018, and December 31, 2020) and 150 healthy controls. Hematological indices (WBC, PLR, LMR, RDW) and clinical data were compared using statistical tests, including ROC analysis.

Results: The patient group had a mean age of 58.99 ± 19.28 years. Heart failure (7.5%) and acute myocardial infarction (6.8%) were the leading causes of death. WBC, LMR, and RDW were significantly higher in the patient group, while PLR and platelet counts were lower ($p<0.05$). ROC analysis identified RDW (AUC: 0.670) and LMR (AUC: 0.707) as significant prognostic markers.

Conclusions: Elevated LMR and RDW values and reduced PLR and platelet counts may predict mortality in CPR patients.

Keywords: Cardiopulmonary Resuscitation, Mortality Inflammatory Markers, Lymphocyte-Monocyte Ratio, Red Cell Distribution Width

ÖZ

Amaç: Kardiyopulmoner arrest, solunum ve dolaşımın durmasıyla karakterize olup yüksek mortalite oranlarına sahiptir. Kardiyopulmoner resüsitasyon sonuçları, arrest süresi ve altta yatan hastalıklar gibi faktörlerden etkilenir. Trombosit-lenfosit oranı, lenfosit-monosit oranı ve eritrosit dağılım genişliği gibi inflamatuar belirteçlerin mortaliteyi öngörmede etkili olabileceği düşünülmektedir.

Gereç ve Yöntem: Bu retrospektif çalışmada, Harran Üniversitesi Eğitim ve Araştırma Hastanesi Acil Servisi'nde CPR sonrası hayatını kaybeden 142 hasta (1 Ocak 2018 ile 31 Aralık 2020 arasında) ile 150 sağlıklı kontrol grubu karşılaştırılmıştır. Hematolojik parametreler (WBC, PLR, LMR, RDW) ve klinik veriler istatistiksel testler ve ROC analizi kullanılarak değerlendirilmiştir.

Bulgular: Hasta grubunun ortalama yaşı 58,99 ± 19,28 yıl olarak tespit edilmiştir. En sık ölüm nedenleri %7,5 ile kalp yetmezliği ve %6,8 ile akut miyokard enfarktüsü olmuştur. Hasta grubunda WBC, LMR ve RDW değerleri anlamlı derecede yüksek, PLR ve trombosit değerleri ise düşüktür ($p<0,05$). ROC analizinde RDW (AUC: 0,670) ve LMR (AUC: 0,707) önemli prognostik belirteçler olarak bulunmuştur.

Sonuç: Yüksek LMR ve RDW değerleri ile düşük PLR ve trombosit değerleri, CPR hastalarında mortaliteyi öngörmede kullanılabilir.

Anahtar kelimeler: Kardiyopulmoner Resüsitasyon, Mortalite, İnflamatuar Belirteçler, Lenfosit-Monosit Oranı, Eritrosit Dağılım Genişliği

Highlights

- The role of inflammatory markers in predicting post-CPR mortality was examined
- Elevated RDW and LMR, along with decreased PLR and platelet counts, were identified as significant prognostic indicators.
- These markers may aid in improving post-CPR patient management.

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Introduction

Cardiopulmonary arrest is characterized by the cessation of the patient's breathing and circulation and is among the medical emergencies with a high mortality rate. Cardiopulmonary resuscitation (CPR) refers to a series of interventions aimed at restoring these vital functions (1). Sudden cardiac death accounts for 15-20% of all deaths and represents a significant public health issue (2). The success of CPR depends on various factors, including the duration of arrest, the patient's age, cardiac rhythm, and underlying conditions (3,4).

During cardiac arrest, ischemia triggers a systemic inflammatory response in tissues. With the onset of reperfusion, this inflammation intensifies, leading to extensive tissue damage. This process, known as 'reperfusion injury,' significantly impacts patient prognosis (3). Platelets play a critical role in this inflammatory process. By secreting mediators such as adenosine diphosphate, thromboxane, and von Willebrand Factor, platelets act as initiators and regulators of vascular inflammation. These properties highlight the central role of platelets in understanding the interaction between inflammation and reperfusion injury (3).

The inflammatory effects of platelets can be assessed through hematological parameters. The literature identifies key inflammatory markers, including platelet-lymphocyte ratio (PLR), lymphocyte-monocyte ratio (LMR), and red cell distribution width (RDW), which reflect the severity and systemic impact of inflammation. These markers have also been reported to be associated with sudden cardiac death and other causes of mortality (5-9).

This study aims to evaluate the historical records of patients who died after CPR in the Emergency Department of Harran University Training and Research Hospital to identify the causes of death and demographic characteristics. Furthermore, the study seeks to investigate the association of inflammatory markers such as PLR, LMR, and RDW with mortality in resuscitated patients.

Material and Methods

This retrospective study included 142 patients who died between January 1, 2018, and December 31, 2020, in the Emergency Department of Harran University Training and Research Hospital, forming the patient group. Inclusion criteria consisted of adult, in-hospital cardiac arrest cases with available laboratory data. Data collected included age, gender, province of residence, date of death, and primary and secondary diseases contributing to death, recorded systematically in a standardized data collection form.

The control group comprised 150 healthy individuals who visited the emergency clinic during the same period for non-cardiac and non-inflammatory complaints. Hematological indices including NLR, PLR, LMR, and RDW were compared retrospectively between the patient and control groups. NLR was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. PLR was calculated as the absolute platelet count divided by the absolute lymphocyte count, and LMR was determined by dividing the absolute lymphocyte count by the absolute monocyte count. RDW, a measure of red blood cell size variation expressed as a percentage, was obtained from complete blood count results.

Patients aged <18 years, those with traumatic cardiac arrest, cases lacking sufficient laboratory data, and individuals with prior diagnoses of leukemia, myelodysplastic syndrome, or myelofibrosis were excluded. Laboratory data for the patient group were collected during their hospital stay, while data for the control group were obtained under standard health check protocols. The study was approved by the Ethics Committee of Harran University Training and Research Hospital (Number: HRU/21.04.03 Date: 15.02.2024). All data were anonymized, and the study was conducted in compliance with the Declaration of Helsinki.

Statistical Analysis

All statistical analyses performed using the SPSS 21.0 software package (SPSS Inc., Chicago, IL, USA). Numerical variables expressed as mean ± standard deviation for normally distributed data. Qualitative variables presented as frequencies and percentages. To evaluate the differences between groups for qualitative variables, the chi-square test employed. For numerical variables, differences between the two groups assessed using the independent student t-test. The predictive ability of significant parameters for mortality was assessed using receiver operating characteristic (ROC) analysis, and the area under the curve (AUC) was calculated. The threshold for statistical significance will be set at $p<0.05$.

Results

The patient group included 142 individuals who underwent CPR in the emergency department, and the control group consisted of 150 healthy individuals. Of the patient group, 63.4% were male and 36.6% female, while the

control group had 60% male and 40% female participants. The mean age of the patient group was 58.99 ± 19.28 years, significantly higher than the control group's mean age of 58.65 ± 7.12 years (p=0.001) **(Table 1)**.

Table 1. Distribution of Patient and Control Groups by Age

Parameter	Patient Group n=142	Control Group n=150	p
Age, years / Mean ± SD	58.99 ± 19.278	58.65 ± 7.124	0.001

Among the causes of death in the patient group, heart failure (7.5%) and acute myocardial infarction (6.8%) were the most common, followed by trauma-related causes, including traffic accidents and gunshot wounds **(Table 2)**. Respiratory arrest and cardiac arrest were also frequently presenting complaints, with rates of 39.4% and 26.8%, respectively **(Table 3)**. Comorbidities such as hypertension (61.7%) and coronary artery disease (55.6%) were prevalent in the patient group **(Table 4)**.

Table 2: Causes of Death of Patients

Cause of Death	n	%	Cause of Death	n	%
Traumatic Subarachnoid Hemorrhage	1	0.3	**Fall from Height**	2	0.7
Heart Failure	22	7.5	**Electric Shock**	2	0.7
Acute Myocardial Infarction	20	6.8	**Gastrointestinal Bleeding**	2	0.7
Traffic Accident	16	5.5	**Mixed-Type Acidosis**	2	0.7
Sudden Cardiac Death	16	5.5	**Kidney Failure**	1	0.3
Cardiac Arrest	13	4.5	**Multiple Organ Failure**	1	0.3
Gunshot Wound	8	2.7	**Epidural Bleeding**	1	0.3
Diabetic Coma	8	2.7	**Cardiogenic Shock**	1	0.3
Respiratory Arrest	7	2.4	**Sharp Object Injury**	1	0.3
Pulmonary Embolism	6	2.1	**Pneumothorax**	1	0.3
General Condition Disorder	3	1.0	**Sepsis**	1	0.3
Liver Failure	3	1.0	**Stroke**	1	0.3
Pneumonia	3	1.0			

Table 3: Complaints of Patients Presenting to the Emergency Department

Complaint	n	%	Complaint	n	%
Respiratory Arrest	55	39.4	**General Condition Disorder**	5	3.5
Cardiac Arrest	38	26.8	**Abdominal Pain**	4	2.8
Chest Pain	10	7.0	**Traffic Accident**	3	2.1
Shortness of Breath	10	7.0	**Nausea and Vomiting**	2	1.4
Blurred Consciousness	7	4.9	**Fall from Height**	1	0.7
Syncope	6	4.2			

Table 4. Distribution of Comorbidities in the Patient Group

Comorbidity	Present n, (%)	Absent n, (%)	Comorbidity	Present n, (%)	Absent n, (%)
Hypertension	87(61.7)	54(38.3)	**ALS**	1(0.7)	141(99.3)
CAD	79(55.6)	63(44.4)	**Hepatitis B**	1(0.7)	141(99.3)
Diabetes Mellitus	42(29.6)	100(70.4)	**COPD**	12(8.5)	130(91.5)
Myasthenia Gravis	1(0.7)	141(99.3)	**Epilepsy**	1(0.7)	141(99.3)
Venous Insufficiency	1(0.7)	141(99.3)	**Heart Failure**	10(7.0)	131(93.0)
Hyperlipidemia	6(4.2)	136(95.8)	**Asthma**	5(3.5)	137(96.5)
Acute Renal Failure	1(0.7)	141(99.3)	**Stroke**	7(4.9)	135(95.1)
CKD	1(0.7)	141(99.3)	**Dysrhythmia**	1(0.7)	141(99.3)
Schizophrenia	1(0.7)	141(99.3)	**Osteoporosis**	1(0.7)	141(99.3)
CLD	1(0.7)	141(99.3)	**BPH**	4(2.8)	138(97.2)

Abbreviations: COPD: Chronic Obstructive Pulmonary Disease ALS: Amyotrophic Lateral Sclerosis BPH: Benign Prostatic Hyperplasia, CAD: Coronary Artery Disease, CKD:Chronic Kidney Disease, CLD: Chronic Liver Disease

Laboratory comparisons revealed statistically significant elevations in neutrophil count (9.94 ± 9.15, $p<0.001$), lymphocyte count (4.91 ± 3.41, $p<0.001$), WBC count (16.92 ± 17.42, $p<0.001$), LMR (7.82 ± 7.31, $p<0.001$), NLR (4.31 ± 8.23, $p<0.001$), and RDW (14.25 ± 2.84, $p<0.001$) in the DG compared to the control group **(Table 5)**. Conversely, PLT and PLR were significantly lower in the patient group than in the control group ($p<0.05$).

Table 5. Comparison of Hematological Parameters Between Patient and Control Groups

Parameters	Patient Group (Mean ± SD)	Control Group (Mean ± SD)	p
WBC (10^9/L)	16.92 ± 17.42	9.27 ± 3.43	<0.001
Neutrophil (10^9/L)	9.94 ± 9.15	6.18 ± 3.22	<0.001
Lymphocyte (10^9/L)	4.91 ± 3.41	2.22 ± 0.94	<0.001
PLT (10^9/L)	187.31 ± 116.30	286.32 ± 88.91	0.017
MON (10^9/L)	1.60 ± 9.35	0.98 ± 4.20	0.269
LMR	7.82 ± 7.31	3.94 ± 1.88	<0.001
PLR	86.26 ± 174.08	78.19 ± 7.31	0.097
NLR	4.31 ± 8.23	3.53 ± 8.23	<0.001
MPV (fL)	7.82 ± 1.15	7.67 ± 1.69	0.020
RDW (%)	14.25 ± 2.84	12.77 ± 2.84	<0.001

Abbreviations: WBC: White Blood Cell (total leukocyte count), PLT: Platelet count, MON: Monocyte count, LMR: Lymphocyte-Monocyte Ratio, PLR: Platelet-Lymphocyte Ratio, NLR: Neutrophil-Lymphocyte Ratio, MPV: Mean Platelet Volume, RDW: Red Cell Distribution Width

ROC analysis demonstrated that LMR, RDW, PLR, and PLT had significant predictive value for mortality, with AUC values indicating moderate to good discrimination **(Table 6, Figure 1)**. Specifically, RDW and LMR were the most predictive markers, supporting their potential utility as prognostic indicators in patients undergoing CPR.
This analysis highlights the role of hematological parameters, such as elevated RDW and LMR and reduced PLR and PLT, in reflecting systemic inflammation and predicting mortality in resuscitated patients. These findings underscore the importance of incorporating these parameters into the clinical assessment and follow-up of critically ill patients.

Table 6. Predictive Value of Hematological Parameters for Mortality

Parameter	AUC (95% CI)	Cut-off	p	Sensitivity (%)	Specificity (%)
PLT (10^9/L)	0.207 (0.153-0.261)	3.3	0.001	78	89.4
LMR	0.707 (0.645-0.770)	5.4	0.001	80.7	40.1
RDW (%)	0.670 (0.608-0.732)	14.47	0.001	86	65.5
PLR	0.147 (0.096-0.197)	4.3	0.001	2.0	57.7

Abbreviations: PLT: Platelet count (109/L10^9/\text{L}109/L), **LMR:** Lymphocyte-Monocyte Ratio, **RDW:** Red Cell Distribution Width (%), **PLR:** Platelet-Lymphocyte Ratio, **AUC:** Area Under the Curve, **CI:** Confidence Interval

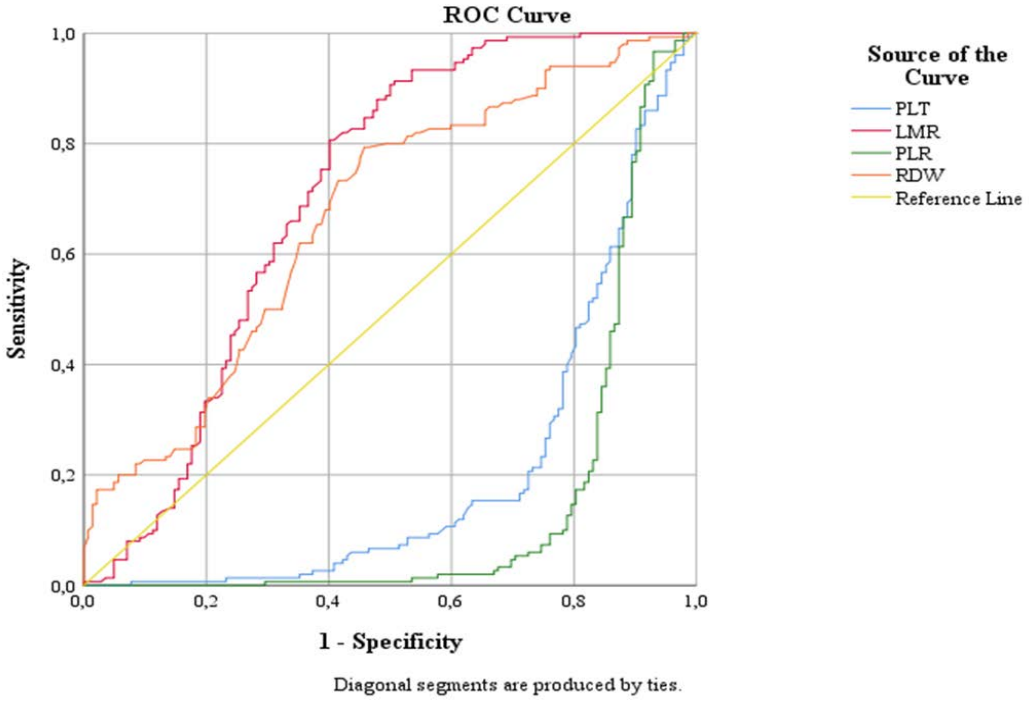

Figure 1. Distribution of laboratory results of the patient and control groups according to ROC analysis

Discussion

Cardiopulmonary resuscitation success is influenced by factors such as arrest duration, age, cardiac rhythm, and underlying conditions (3). Understanding the characteristics of patients undergoing CPR may improve resuscitation outcomes. However, despite these efforts, approximately 1 million people die annually from cardiac-related issues, with 350,000 of these attributed to cardiac causes (10,11).
In our study, most resuscitated patients were male, consistent with findings in the literature (12,13). This gender disparity may be explained by the higher prevalence of cardiovascular and respiratory diseases in men, increasing their likelihood of experiencing cardiac arrest (14).

The OPALS (Ontario Prehospital Advanced Life Support) study by Petrie et al. reported a mean age of 68 years for cardiac arrest cases (15). In contrast, the mean age in our study was 58.9 years for the patient group and 58.6 years for the control group. This lower age range may reflect the inclusion of younger trauma patients, as our hospital is a trauma center serving a region with high trauma incidence.

The most common causes of death in our study were heart failure (7.5%) and acute myocardial infarction (6.8%). These findings align with the study by Qingting Lin et al., which reported heart failure (41.5%) and AMI (24.7%) as the leading causes of death (16). The differences in rates may stem from variations in prehospital and in-hospital resuscitation protocols and the profile of resuscitated patients.

Trauma was also a significant cause of mortality in our study, reflecting its status as a major global public health issue with rising mortality rates (17). Karataş et al. identified trauma as the third leading cause of death (13.7%) (9), while Heymann et al. found trauma to be the second leading cause of death in their emergency department (18). Our hospital's proximity to the Syrian border and location along a busy trade route likely contributes to the high proportion of trauma cases.

Elevated white blood cell counts have been associated with poor CPR outcomes (16). In our study, WBC values were significantly higher in the patient group compared to controls, consistent with the literature. Platelets, as key mediators of vascular inflammation, play a critical role in prognosis (19). Endothelial damage and activation, common in cardiac arrest, lead to platelet adhesion and depletion, resulting in thrombocytopenia. Studies by Kim et al. and Bilge et al. have linked low platelet counts to higher mortality rates (20). In our study, platelet counts were significantly lower in the patient group, and ROC analysis indicated their potential as a prognostic marker.

Platelet-lymphocyte ratio values were also lower in deceased patients compared to controls, consistent with findings by Han SI et al. (21). PLR has been associated with inflammatory processes and excessive thrombus activity in conditions like heart failure and malignant tumors (22). Despite limited investigation into PLR's role in cardiac arrest, our results support its potential as a marker of microcirculatory dysfunction and systemic ischemia/reperfusion injury (23).

Lymphocyte-monocyte ratio has emerged as a simple and cost-effective marker in cardiovascular and inflammatory diseases. Increased monocyte and decreased lymphocyte counts have been linked to atherosclerosis and poor prognosis in coronary artery disease (24). In our study, LMR was significantly higher in the patient group, highlighting its association with mortality.

Red cell distribution width, reflecting heterogeneity in red blood cell size, is another marker of systemic inflammation and oxidative stress (25). Elevated RDW values have been associated with increased mortality in acute coronary syndrome and critically ill patients (26). Our study found significantly higher RDW levels in deceased patients, reinforcing its prognostic value.

In summary, patients who died after CPR had significantly higher WBC, lymphocyte, neutrophil, LMR, and RDW values, and significantly lower PLR and PLT values compared to controls. LMR, RDW, and PLR may reflect systemic inflammation and serve as useful markers in the follow-up of resuscitated patients.

Study limitations

The limitation of this study is the retrospective design, which prevented access to prehospital data known to influence CPR outcomes. Additionally, missing data led to the exclusion of some patients, which, while not compromising statistical power, limits comprehensive analysis. Prospective studies would better address this issue by ensuring more complete data collection.

Conclusion

In our emergency department, heart failure, acute myocardial infarction, and trauma were the leading causes of death. Elevated LMR and RDW values and reduced PLR and PLT values may guide the prognosis of resuscitated patients.

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Ethical Approval: *This Study approval was obtained from the Harran University Faculty of Medicine, Non-Interventional Clinical Research Ethics Committee (number:* HRU/21.04.03. *date: 15.02.2024).*

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