



Prognostic Efficacy of Red Cell Distribution Width and Neutrophil/Lymphocyte in Cardiac Surgery

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ABSTRACT

Objectives: This study aimed to examine the effect of neutrophil-to-lymphocyte ratio (NLR) and red cell distribution width (RDW) values on postoperative mortality and morbidity in patients who underwent off-pump cardiac surgery.

Methods: This study included patients who underwent off-pump coronary artery bypass surgery from January 1, 2018 to January 1, 2020. Correlations between the preoperative NLR and RDW values and postoperative complications, extubation time, length of intensive care unit stay, and length of hospital stay were evaluated.

Results: A total of 68 patients were evaluated. No correlation was found between preoperative RDW and NLR values and age, ejection fraction, extubation time, or length of hospital stay. The length of stay in the intensive care unit did not correlate with the preoperative RDW value but was correlated with the NLR value ($p=0.042$). In six patients, postoperative complications were observed. No statistically significant difference was found between patients with and without complications in terms of preoperative RDW and NLR values.

Conclusion: In this study, a high preoperative NLR value was associated with a prolonged intensive care unit stay, one of the early complications of cardiac surgery. However, the preoperative RDW value did not have a predictive relationship with early postoperative complications.

Keywords: Neutrophil-to-lymphocyte ratio, off-pump cardiac surgery, red cell distribution width

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Introduction

In the general population, an increased prevalence of coronary heart disease has been observed, which is the leading cause of mortality worldwide. Coronary artery bypass grafting (CABG) remains the standard and optimal treatment for patients with diffuse coronary artery disease. "Off-pump" CABG (OPCABG) is a cardiac surgical technique in which physiological circulation is preserved without the need for aortic or right atrial cannulation or extracorporeal circulation.^[1]

Red cell distribution width (RDW) is a measurement of the change in circulating red blood cell (RBC) volume and is traditionally used to differentiate causes of anemia. An increased RDW value indicates greater heterogeneity in circulating RBC size (anisocytosis).^[2] The neutrophil-to-

lymphocyte ratio (NLR) is a marker of host inflammation, which is calculated by dividing the number of neutrophils by the number of lymphocytes.^[3]

RDW and NLR are inexpensive, simple, quantitative parameters routinely measured using automated complete blood count analysis. Both parameters are associated with cardiovascular diseases.^[2,3]

In this study, we aimed to explore the effects of NLR and RDW values on postoperative mortality and morbidity in patients undergoing OPCABG.

Methods

The study was initiated after receiving approval from the local ethics committee (approval number: 14.01.2020/13).

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The study was conducted in line with the 2008 Helsinki Declaration principles. This retrospective study included all patients who underwent OPCABG from January 1, 2018 to January 1, 2020. Patients with anemia (hemoglobin below 13 g/dL), liver or kidney failure, an ejection fraction (EF) value of 30, active infection, and unavailable data were excluded from the study.

In this study, the patients' sex, age, body mass index, comorbidities (diabetes mellitus [DM], hypertension, chronic obstructive pulmonary disease [COPD], and asthma), EF, number of grafted vessels, extubation time, length of intensive care unit (ICU) stay, length of hospital stay, presence of postoperative complications (cerebrovascular event, postoperative new atrial fibrillation [AF], postoperative dialysis requirement, bleeding, surgical revision, and myocardial infarction), and preoperative RDW and NLR values were recorded. Data were obtained from patient files, anesthesia records, and perfusion charts. Patients with missing data were excluded from the study.

In the statistical analyses, variables with continuous values were presented as mean, standard deviation, minimum, and maximum values, and those with categorical values were shown as frequency and percentages. The Shapiro–Wilk test was used to examine the conformity of the data to the normal distribution. The Mann–Whitney U test was conducted to compare groups that did not satisfy the normal distribution in the two groups. To determine the direction and size of the correlation between variables and for variables that did not conform to the normal distribution, Spearman correlation coefficients were calculated. Statistical significance was set at a p value <0.05 .

Results

Of the 85 patients who underwent OPCABG, 68 were included in the study. Eighteen (26.5%) patients were female and 50 (73.5%) were male. The mean age was 63.6 ± 10 years. A total of 32 (47.1%) patients had DM, one (1.5%) had COPD, and 44 (47%) patients had hypertension. One vessel graft was employed to 16 (23.5%) patients, two vessel grafts to 43 (64.2%) patients, and three vessel grafts to nine (13.2%) patients. In the study, the mean EF of the patients included was 50.3 ± 10.8 . The mean extubation time was 266.0 ± 78.0 min, the mean length of ICU stay was 2.66 ± 0.908 days, and the mean length of hospital stay was 8.40 ± 3.46 days (Table 1).

Correlations between the preoperative RDW and NLR values and age, EF, extubation time, length of ICU stay, and length of hospital stay were evaluated. Neither RDW nor NLR correlated with age ($p=0.052$ and 0.289 , respectively), EF ($p=0.967$ and 0.286 , respectively), extubation time ($p=0.648$ and 0.347 , respectively), or length of hospital stay ($p=0.930$ and 0.409 , respectively). Furthermore, no statistically

significant correlation was noted between the preoperative RDW value and the length of ICU stay ($p=0.477$). However, the preoperative NLR value was significantly correlated with the length of ICU stay ($p=0.042$) (Table 2). The mean NLR value was 3.68 ± 1.63 for patients who stayed in the ICU for 4 days or longer and 2.96 ± 0.98 for those with a shorter ICU stay, indicating a statistically significant difference ($p=0.038$). The longer ICU stay was attributed to the hemodynamic instability found in 42% of patients and the requirement for blood product replacement in 34%.

Postoperative complications were observed in six patients (bleeding without revision requirement and need for replacement in two patients, bleeding requiring revision in one patient, one-time dialysis in one patient, and inotropic agent requirement for longer than 12 h in two patients). When the relationship between the preoperative RDW and NLR values and the development of postoperative complications was evaluated, no statistically significant correlation was found ($p=0.815$ and 0.208 , respectively). The mean RDW value was $13.80\% \pm 1.568\%$ in patients with complications and $13.46\% \pm 1.19\%$ in those without complications, whereas the mean NLR values of these subgroups were determined to be 2.44 ± 0.825 and 3.54 ± 3.37 , respectively (Table 3).

Table 1. Demographic data

	n	%
Sex		
Female	18	26.5
Male	50	73.5
Diabetes mellitus		
Absent	36	52.9
Present	32	47.1
COPD		
Absent	67	98.5
Present	1	1.5
Hypertension		
Absent	23	34.3
Present	44	65.7
Number of vessels grafted		
1	16	23.5
2	43	64.2
3	9	13.2
	Mean±SD	Min-Max
Age	63.6 ± 10.5	38–82
Ejection fraction	50.3 ± 10.8	24–65
Extubation time (minute)	266 ± 78	60–480
Length of ICU stay (day)	2.66 ± 0.908	2–7
Length of hospital stay (day)	8.40 ± 3.46	4–30

COPD: Chronic obstructive pulmonary disease; SD: Standard deviation; ICU: Intensive care unit.

Table 2. Correlation between preoperative RDW and NLR

r p	Age	EF	Extubation time	Length of ICU stay	Length of hospital stay
RDW	0.237	0.005	0.056	-0.088	-0.011
	0.052	0.967	0.648	0.477	0.930
NLR	0.130	0.131	-0.116	0.247	-0.103
	0.289	0.286	0.347	0.042*	0.409

Spearman's correlation test, *p<0.05. RDW: Red cell distribution width; NLR: Neutrophil-to-lymphocyte ratio; EF: Ejection fraction.

Table 3. Comparison of patients with and without complications

	Patients with complications (n=6)	Patients without complications (n=62)	p
RDW (%)	13.80±1.568	13.46±1.19	0.815
NLR	2.44±0.825	3.54±3.37	0.208

Mann-Whitney U test.

Discussion

In addition to genetic, environmental, and behavioral factors, inflammation plays a role in cardiovascular disease development. Inflammatory cells and signaling pathways are involved in atherosclerosis development.^[4] Inflammatory response is a sequelae of chronic exposure to numerous factors that cause endothelial damage, and neutrophils play a major role in this response. Reactive products generated via neutrophil activation both damage the vascular endothelial wall and induce thrombosis with platelet activation. Lymphocytes also accumulate at the site of inflammation and contribute to chronic inflammation.^[5] Since the recognition of the effects of inflammatory markers on atherosclerosis, studies have been conducted on the use of these markers as predictive agents in cardiac diseases. A recently published meta-analysis reported that perioperative NLR was an independent predictor of short- and long-term postoperative mortality in CABG surgery involving cardiopulmonary pump use.^[6] Similar results were acquired from studies in which OPCABG was used.^[7,8]

In this study, the correlation between preoperative NLR values and early complications and mortality in patients who underwent OPCABG was evaluated. However, we found no statistically significant difference in NLR between patients with and without postoperative complications. Previous studies have demonstrated that preoperative NLR values are higher in patients with complications than in those without complications.^[9] Conversely, in our study, preoperative NLR values were found to be higher in the group without complications (2.44±0.825 vs. 3.54±3.37). Additionally, a correlation was found between the preoperative NLR value and the length of ICU stay, with the former being statistically significantly higher among

patients with a longer ICU stay. High preoperative NLR values prolong the duration of ICU stay in connection with hemodynamic instability and the need for blood product replacement, which are among the early complications. Haran et al.,^[10] in their evaluation of 1,694 patients, reported that patients with preoperative NLR values of 3.23 had a longer ICU stay, delayed extubation, and a higher rate of newly diagnosed neurological conditions. In the current study, the preoperative NLR value was above the previously reported value of 3.23 (3.68) in patients with a longer ICU stay.

A high RDW causes microcirculation impairment, although its pathogenesis remains unclear.^[11] RDW is an indicator of a patient's physiological reserve or the ability of cells to defend against hypoxic stress. Moreover, an increased RDW value reflects a low physiological reserve.^[12]

In a cohort study assessing the role of preoperative RDW in the prediction of acute kidney injury after on-pump cardiac surgery, a high preoperative RDW value might be an independent prognostic factor for acute renal failure, with a 0.1% increase in the RDW value increasing the risk by 1.1%.^[13] In another study assessing 150 patients and the role of preoperative RDW in predicting in-hospital mortality in patients undergoing OPCABG, the authors elucidated that a high preoperative RDW value could be used for this purpose. Moreover, among the many factors evaluated, a preoperative RDW value above 14% was the only independent prognostic factor for mortality.^[14] Other researchers have also reported that RDW values during admission may be useful for predicting long-term morbidity and mortality, especially in non-anemic patients undergoing off-pump cardiac surgery.^[15] In our study, unlike previous research, no statistically significant correlation was found

between the preoperative RDW values and extubation time, length of ICU stay, or length of hospital stay. Of the patients with complications, only two had RDW values above 14%. In our study, only early complications were assessed, and the correlation between major cardiovascular complications and RDW in the long term (after 30 days) was not evaluated. In a study in which 500 patients were evaluated in terms of late complications after on-pump surgery, a significant correlation was found with high RDW values.^[16] In another study involving 93 patients who underwent off-pump surgery, the relationship between preoperative RDW and the development of postoperative AF was explored, and the results revealed no statistically significant difference or independent factor.^[17] The limitations of our study include the single-center and retrospective design, small sample size, and evaluation of early complications only.

In conclusion, many studies have examined the correlation between RDW and NLR levels with postoperative complications, albeit with different results. Our study findings show that preoperative NLR and RDW levels did not exhibit definite predictive value for early postoperative complications. We think that further studies with many patients are warranted to determine the role of NLR and RDW, which are routinely obtained via a simple and inexpensive complete blood count examination in the preoperative evaluation of high-risk patients for OPCABG in clinical practice.

Disclosures

Ethics Committee Approval: The study was approved by The Eskisehir Osmangazi University Non-Interventional Clinical Research Ethics Committee (Date: 14/01/2020, No: 13).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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