Section: Miscellaneous

Original Research Article

CORRELATION OF RED CELL DISTRIBUTION WIDTH AND NEUTROPHIL TO LYMPHOCYTE RATIO WITH LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN PATIENTS WITH ACUTE STEMI: A CROSS-SECTIONAL OBSERVATIONAL STUDY

Sana Sajid[1], Irshad Ahmad Wani[2], Zeeba Sidique[1], Bashir Ahmad Mir[2], Nishat I Iram[3], Abhishek Gupta[1]

[1]*Department of Medicine, Era Medical College, Lucknow-226003, Uttar Pradesh, India.*
[2]*Department of Cardiology, Era Medical College, Lucknow-226003, Uttar Pradesh, India.*
[3]*Department of Pathology, Era Medical College, Lucknow-226003, Uttar Pradesh, India.*

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Corresponding Author:
Dr. Bashir Ahmad Mir,
Department of Cardiology, Era Medical College, Sarfarzjung Lucknow-226003, Uttar Pradesh, India.
Email: mirbashir849@gmail.com

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ABSTRACT

Background: To assess the correlation of red cell distribution width (RDW) and neutrophil-to-lymphocyte ratio (NLR) in patients with left ventricular systolic dysfunction (LVSD) and acute ST-segment elevation myocardial infarction (STEMI).

Materials and Methods: In this retrospective, hospital-based, observational study, 120 patients admitted with acute STEMI were consecutively included. All the patients underwent echocardiography for the assessment of left ventricle function (ejection fraction, systolic and diastolic functions, and regional wall motion abnormalities). Patients were divided into two groups based on the left ventricle systolic function (LVSD): left ventricle ejection fraction (LVEF)<50% and normal LVEF ≥50%. Hematological (hemoglobin, total leucocyte count, differential leukocyte count, RDW and NLR), renal (serum creatinine and serum urea), lipid parameters (triglyceride, cholesterol, low-density lipoprotein, high-density lipoprotein or very-low-density lipoprotein) were measured and their relationship with LVSD were studied.

Results: The prevalence of LVSD in the study population was 40.8%. Triglyceride (232.35 ± 64.18 vs 187.75 ± 85.22; P=0.002), cholesterol (155.86 ± 23.57 vs 144.39 ± 26.40; P=0.016), VLDL (46.47 ± 12.84 vs 37.55 ± 17.04; P=0.002), and RDW (14.44 ± 0.64 vs 13.93 ± 1.03; P=0.003) were significantly higher in the LVSD group than the normal LVSD group. RDW was a significant predictor of LVSD at a cut-off of ≥14.05 [area under the curve (AUC): 0.644, 95% CI: 0.547-0.741, P=0.007), with 69.4% sensitivity and 53.5% specificity, while NLR was a non-significant predictor of LVSD (AUC: 0.527, 95% CI=0.421-0.633, P=0.614).

Conclusion: The study showed that simple hematological parameters like RDW could be considered as additional markers to assess patients with STEMI.

Keywords: Cholesterol; hematologic tests; LV dysfunction; trigylcerides; very low-density lipoproteins.

Significance: Red cell distribution width (RDW) and neutrophil-to-lymphocyte ratio (NLR) are inflammatory markers and are used as a predictor in different cardiovascular settings. The study shows a significant difference in the RDW values between patients with LVSD and patients with normal LV function. Therefore, RDW could be used as an additional marker to assess patients with STEMI.

INTRODUCTION

Atherosclerosis, one of the leading causes of cardiovascular disease and inflammation is the primary cause in the pathogenesis of atherosclerosis. A meta-analysis suggested that higher levels of inflammatory biomarkers like high-sensitivity C-reactive protein, interleukin-6 are significant risk factors for cardiovascular events.[1] Red cell distribution width (RDW) and neutrophil-to-lymphocyte ratio (NLR) are two newer inflammatory markers that are used as a predictor in different cardiovascular settings.

The RDW could illustrate how erythrocyte volume is distributed. Higher RDW levels reduce blood flow and oxygen delivery; hence, they are associated with more serious and unfavourable outcomes.[2] Elevated RDW has shown to predict outcomes in patients with specific cardiovascular diseases like heart failure, acute coronary syndrome (ACS) and atrial fibrillation.[3] Moreover, studies have proven that the rise in RDW has a positive correlation with the mortality not only in patients with acute/chronic illness but also in healthy population.[4]

Neutrophil-to-lymphocyte ratio (NLR) is a simple ratio of the absolute number of neutrophils and lymphocytes and is one of the inflammatory markers which has been recently introduced as a prognostic marker in patients with cardiovascular disease.[5,6] Recent studies have determined the prognostic significance of NLR in ACS, which suggested that the higher the NLR value, the worse the prognosis of ACS patients.[7] NLR was shown to be prognostic factor for hospitalizations and long-term prognosis in patients with ST elevated myocardial infarction (STEMI) receiving percutaneous coronary intervention (PCI) in two meta-analyses that included more than 10,000 patients each.[8]

Left ventricular ejection fraction (LVEF) is the most important echocardiographic measure for the assessment of left ventricular (LV) systolic function. It has been proven as an efficacious predictor of prognosis following acute myocardial infarction (AMI).[9] The association between RDW and NLR, as determined by complete blood count during initial hospital admission with LV systolic dysfunction (LVSD) has been studied. Against this background, the present study sought to assess the correlation of RDW and NLR with LVSD in patients with acute STEMI.

MATERIALS AND METHODS

This was a retrospective, hospital-based, observational study of 120 STEMI patients who were admitted to a tertiary care hospital during the period of six months, from October 2021 to March 2021.

2.1. Inclusion and exclusion criteria

Eligible participants were aged 18 to 80 years and presented with acute STEMI. Patients with age > 80 years, anemia, pancytopenia, severe renal dysfunction, active infection, cardiogenic shock, and post-cardiopulmonary resuscitation status were excluded.

2.2. Data collection

Echocardiographic measures for LV functions (ejection fraction, LV systolic and diastolic functions, and regional wall motion abnormality) were assessed. Patients were divided into two groups based on the LVEF systolic function: LVSD (LVEF <50%) or normal left ventricular systolic function (LVEF ≥50%). Hematological (hemoglobin, total leucocyte count, differential leukocyte count, RDW and NLR), renal (serum creatinine and serum urea), lipid parameters [(triglyceride, cholesterol, low-density lipoprotein, high-density lipoprotein or very-low-density lipoprotein (VLDL)] were measured and their relationship with LVSD were studied.

2.3. Ethical statement

Patients were given primary treatment in the form of primary PCI or thrombolysis. The study protocol was approved by the Institutional Ethical Committee (IEC) [RGH, EC/2019/143] and was conducted according to the Declaration of Helsinki. All patients gave written informed consent.

2.4. Statistical analysis

The statistical analysis was done using the SPSS-15 package. Categorical data were reported as frequency and percentages and compared using the chi-square test. Continuous data were presented as a mean and standard deviation and compared using an independent sample t-test. $P<0.05$ indicated statistical significance and the confidence level (CI) of the study was kept at 95%. Receiver operating characteristics (ROC) curve analysis and area under the curve (AUC) calculations of NLR and RDW were used to calculate their effectiveness in predicting LVSD. Cut-off values of the predictor parameters were recorded with the most appropriate % specificity and % sensitivity.

RESULTS

One hundred twenty STEMI patients were evaluated, of which, 49 (40.8%) had LVSD and 71 (59.2%) patients had normal LV systolic function. The mean age was (54.0 ± 9.7) years (range: 28-68) and 83 (69.2%) patients were males. Table 1 outlines the baseline and clinical characteristics of the included STEMI patients. The differences in smoking, family history of coronary artery disease, diabetes, diastolic blood pressure, and body mass index were significant between the two groups. Systolic blood pressure was significantly higher in the LVSD group than in the normal LV function group [(132.45 ± 8.04) mmHg vs (123.92 ± 11.41) mmHg; $P<0.001$]. [Table 1]

The renal, lipid, and hematological profiles is outlined in Table 2. Triglyceride (232.35 ± 64.18 vs 187.75 ± 85.22; P=0.002), cholesterol (155.86 ± 23.57 vs 144.39 ± 26.40; P=0.016), VLDL (46.47 ± 12.84 vs 37.55 ± 17.04; P=0.002), and RDW (14.44 ± 0.64 vs 13.93 ± 1.03; P=0.003) were significantly higher in the LVSD group than the normal LV function group. The majority of patients [34 (69.4%) patients] in the LVSD group had RDW ≥14.05%, whereas almost all cases [38 (53.5%) patients] in the normal LV function group had RDW <14.05. The difference between the two groups was significant (P=0.013).

ROC analysis for the prediction of LVSD shows an RDW cut-off of ≥14.05 with an AUC of 0.644 (95% CI: 0.547-0.741; P=0.007), with 69.4% sensitivity and 53.5% specificity, while NLR was a non-significant predictor of LVSD (AUC: 0.527; 95% CI: 0.421-0.633; p=0.614). [Figure 1]

Table 1: Baseline and clinical characteristics (n=120)

Variables	Total	LVSD (n=49)	Normal LV systolic function (n=71)	t /x^2	P
Age (years, mean ± SD)	54.0±9.7	53.5 ± 10.1	54.4 ± 9.4		0.591
Male (n, %)	83 (69.2)	34 (69.4)	49 (69.0)		0.965
Smoking (n, %)	83 (69.2)	38 (77.6)	30 (42.3)		<0.001
Family history of CAD (n, %)	68 (56.7)	37 (75.5)	20 (28.2)		<0.001
Diabetes (n, %)	55 (45.8)	33 (67.3)	22 (31.0)		<0.001
Systolic blood pressure (mmHg, mean ± SD)	127.40 ± 10.97	132.45 ± 8.04	123.92 ± 11.41		<0.001
Diastolic blood pressure (mmHg, mean ± SD)	78.18 ± 8.29	80.20 ± 6.92	76.79 ± 8.90		0.026
Body mass index (kg/m^2, mean ± SD)	25.56 ± 1.99	26.47 ± 0.97	24.94 ± 2.26		<0.001

CAD, Coronary artery disease; LV, Left ventricle; LVSD, LV systolic dysfunction.

Table 2: Association of left ventricle systolic dysfunction with renal, lipid, and hematological profile

Variables	LVSD (n=49)	Normal LV systolic function (n=71)	t/U/x^2	P
Serum creatinine (mg/dL, mean ± SD)	0.90 ± 0.21	0.85 ± 0.20		0.178
Serum urea (mg/dL, mean ± SD)	29.71 ± 7.57	29.08 ± 8.49		0.677
Triglyceride (mg/dL, mean ± SD)	232.35 ± 64.18	187.75 ± 85.22		0.002
Cholesterol (mg/dL, mean ± SD)	155.86 ± 23.57	144.39 ± 26.40		0.016
High-density lipoprotein (mg/dL, mean ± SD)	37.59 ± 5.38	37.96 ± 7.50		0.77
Very-low-density lipoprotein (mg/dL, mean ± SD)	46.47 ± 12.84	37.55 ± 17.04		0.002
Low-density lipoprotein (mg/dL, mean ± SD)	71.80 ± 17.31	68.89 ± 20.60		0.419
Haemoglobin (g/dL, mean ± SD)	13.62 ± 0.95	13.48 ± 0.97		0.434
Neutrophils/ (mL, mean ± SD)	75.69 ± 9.93	75.59 ± 10.57		0.958
Lymphocytes (/mL, mean ± SD)	20.63 ± 8.78	21.76 ± 8.80		0.491
Total leucocyte count (/mm^3, mean ± SD)	8 118.37 ± 1784.62	7 897.75 ± 2131.79		0.553
Red cell distribution width (mean ± SD)	14.44 ± 0.64	13.93 ± 1.03		0.003
Neutrophil to lymphocyte ratio (median, Q1, Q3)	4.43 ± 2.75	4.61 ± 4.15		0.785
Red cell distribution width (n, %)				
≥14.05	34 (69.4)	33 (46.5)		0.013
<14.05	15 (30.6)	38 (53.5)		

DISCUSSION

The present study revealed that levels of lipid parameters (triglyceride, cholesterol, and VLDL) and RDW were significantly higher in LVSD patients with acute STEMI, and can serve as a prognostic marker for adverse clinical outcomes. Moreover, The difference in NLR was not significant. In contrast to our finding, Wang et al,[10] found that total triglycerides and total cholesterol were significantly low in the groups with <50% LVEF as compared to the ≥50% LVEF group. Karakas et al,[11] found that upon admission RDW levels were higher in LVSD patients following STEMI and subsequent PCI. Similarly, in a study by Karabulut et al,[12] it was reported that a high RDW level was independently associated with increased long-term cardiovascular mortality, elevated risk during hospitalization, and worse reperfusion in STEMI patients undergoing primary PCI. Gündoğmuş et al,[13] confirmed that RDW might be useful to estimate LV reverse remodeling. Additionally, we found that RDW values of ≥14.05 may be effective in ruling out LVSD in acute STEMI patients. Cemin et al,[14] also presented that RDW was a significant predictor of AMI at a 13.7% cut-off value, with sensitivity and specificity of 0.75 and 0.52, exhibiting an AUC of 0.61 (95% CI: 0.54-0.68). However, it's important to note that these cut-off values should be interpreted in the context of other clinical factors and diagnostic tests, as RDW can be influenced by a variety of factors, and the diagnosis of LVSD should be based on a comprehensive evaluation. Further research is

needed to determine the optimal cut-off value for RDW in ruling out LVSD.

The exact mechanism through which RDW is directly linked to ventricular dysfunction remains unknown, although some possible indirect associations have been proposed. Several studies have demonstrated a strong correlation between age and increased RDW levels in the general population.[9,15,16] Both cardiovascular risk factors and RDW may be indicative of a high risk for developing cardiovascular incidents and STEMI, even in individuals with positive lifestyle habits.

Neutrophils secrete inflammatory mediators that can cause vascular wall degeneration. Conversely, lymphocytes regulate the inflammatory response and thus have an antiatherosclerosis role. Therefore, NLR has been proposed as an inflammatory biomarker and potential predictor of risk and prognosis in cardiovascular disease. Horne et al,[17] was among the first to observe the significance of NLR in stable CAD patients. Mayyas et al,[18] demonstrated that the plasma NLR was negatively associated with LVEF at baseline and the 30-day follow-up in the study cohort comprising STEMI and NSTEMI (non-ST-elevation myocardial infarction) patients. Consistent with these findings, one published study found that higher NLR was associated with a higher incidence of LVSD in STEMI patients who underwent primary PCI.[19] Many studies reported that NLR is a strong predictor of myocardial damage in AMI patients[.20,21] High NLR has been associated with myocardial dysfunction in all patients. By contrast, we found that NLR was lower in the LVSD group than in the normal LV function group, and the difference was not significant.

Our study had certain limitations. It was a retrospective, single-center, hospital-based study with a small sample size. In the future study, we will include multi-center data.

CONCLUSION

In conclusion, RDW value is associated with myocardial damage and can be obtained at no additional cost. Therefore, RDW could be considered as additional markers to assess patients with STEMI.

Conflict of interest statement

The authors report no conflict of interest.

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This study received no extramural funding.

Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

Author's contributions

SS performed a literature search, data acquisition, and experimental studies and prepared manuscript; IAW conducted clinical studies, data analysis, and manuscript preparation; ZS conducted the study and prepared the manuscript; BAM contributed to study design, data acquisition, and manuscript preparation; NII led the concept, clinical studies, data analysis, and manuscript preparation; AG conducted a literature search, performed analysis, and prepared the manuscript. All authors approved the final draft and are accountable for the manuscript's content.

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