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RED CELL DISTRIBUTION WIDTH, AN INFLAMMATORY MARKER OF ACUTE ST SEGMENT ELEVATION MYOCARDIAL INFARCTION (STEMI) SEVERITY; ECHOCARDIOGRAPHIC ASSESSMENT

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ABSTRACT

Background: Increasing value of Red cell distribution width (RDW) is documented to be linked to worse clinical outcomes so that it can be considered as a prognostic indicator in states like acute myocardial infarction coupled with other inflammatory markers taking in consideration its easy availability. **Aim of the study:** This study aimed to assess the relationship of RDW and echocardiographic parameters especially systolic and diastolic dysfunction in patients with ST-elevation myocardial infarction (STEMI). **Patients and methods:** In this study 60 {38 (63%) were males and 22 (37%) females} consecutive patients who had acute ST elevation myocardial infarction (STEMI) at Rozhalat hospital, Erbil, Iraq were included, RDW was obtained during the event of STEMI and the levels obtained where analyzed according to measures of systolic and diastolic dysfunction calculated by transthoracic echocardiophic study. **Results:** RDW was found to be increasing in patients with impaired systolic and diastolic functions (ejection fraction of the left ventricle <50%, diastolic filling wave (E/A)<1 , peak early transmitral velocity over early diastolic annular velocity [E/E'] >10 , and more obviously with combined E/A < 1 and E/E' > 10 (P **<0.01**). The best cut off value of RDW was **13%** with sensitivity (75.9%) and specificity (61.3%) and this is obtained applying ROC curve analysis according to echocardiography ejection fraction 50%. **Conclusion:** Elevated RDW can be considered as a new biomarker of poor outcome in patients acute STEMI patients as it is associated with diastolic as well as and to a lesser extent systolic dysfunction in patients with STEMI even after adjustment of several confounding factors.

INTRODUCTION

Globally, ST-segment elevation myocardial infarction (STEMI) continues to be an utmost important etiology of cardiac mortality and morbidity and so it is crucial to specify the patients with increased risk who is in need for more intensive care and follow-up.[1,2] Echocardiogram is one of the important investigations for evaluating patients after acute ischemic events, the access to echocardiography is quite easy at city and peripheral hospitals and medical centers but there are a lot of obstacles including being time consuming and operator dependent procedure and this possibly mandates a need of easily interpretable and low cost marker by which we can predict the disturbance of left ventricular ejection fraction (LVEF) at early assessment of patient with acute myocardial infraction.[3]

Recently many studies showed an association between adverse outcome of cardiovascular diseases and elevated RDW and so it can be considered as a respectful parameter for both diagnostic application and prediction for outcome in various settings of cardiovascular issues.[3,4]

Felker et al. (2007) study was one of the earliest studies to assess the role of RDW in diseases of cardiovascular system , where by a prognostic value of RDW in patients with heart failure (HF) was observed.[4] The same result was shown in states other than heart failure, as in acute coronary syndromes.[5,6,7,8] further more many researches documented a relation of RDW with the echocardiographic features of systolic as well as diastolic dysfunction in many cardiovascular conditions.[9,10,11,12]

AIM OF THE STUDY

This study aimed to assess the relationship of RDW and echocardiographic parameters especially systolic and diastolic dysfunction in patients with ST-elevation myocardial infarction (STEMI) ascertaining its predictive values taking in consideration these and more other echocardiographic parameters.

PATIENTS AND METHODS

This is a single-center, cross sectional observational study done at Department of Emergency Medicine, Rozhalat hospital, Erbil, Iraq from June 15th, 2022 to June 14th, 2024. 60 (patients with acute myocardial infarction were assessed, all these patients had no other important cardiac or respiratory illness and patients with a history of chronic hematological and inflammatory conditions were excluded from the study.

Echocardiography: Echocardiography through transthoracic access was done and all measurements were taken by one expert echocardiographer and using the same equipment. LVEF along with wall motion abnormalities and valvular pathologies were recorded for each patient.

The measurements were recorded from 3 consecutive cycles, and the mean values were considered for the study. The test was performed at the first week after the STEMI. The echocardiography was performed by the echocardiography machine (Vivid E9, GE Healthcare, Horten, Norway) with a 1.5—4 MHz sector transducer probe.

The following parameters were recorded; Fractional shortening (FS %): (LV diameter at end of diastole - LV diameter at end of systole)/LV diameter at end diastole (25%—43%: male, 27-45%: female). Left ventricular ejection fraction (LVEF %) applying the Modified Simpson method(52%—72%: male, 54-74%: female).[13]

LV end-systolic diameter and LV end-diastolic diameter obtained by M-mode
End-diastolic interventricular septal thickness.
End-diastolic LV posterior wall thickness.

LV diastolic filling patterns were assessed by Doppler examination of the inflow pulsed wave of mitral valve, best obtained through the view of apical 4-chamber.[14]

The diastolic measures were taken by three beats and defined as. E-wave: early maximal flow velocity transmitral.
A-wave: peak velocity at late diastole during atrial contraction
E/A ratio: ratio between (E) and (A).

According to age group Left ventricular diastolic dysfunction was documented as E/A is <1.3 (at ages 45-49 years), <1.2 (at ages 50-59 years), <1.0 (at ages 60-69 years), and <0.8 (70 years and older).[15]

Statistical analysis

IBM Statistical Package of Social Science (SPSS) Statistics. Independent sample t-test, Chi-squared test ($\chi 2$) were applied as indicated. Numerical variables optimal cut-off values was analysed according to Receiver operating characteristic (ROC). Logistic regression test was applied for Multivariate analyses to document the presence of systolic and diastolic dysfunction. ($p \leq 0.05$) was considered a statistically significant. Ethical approval was obtained from ethical committee of scientific researchs of the Iraqi board of internal medicine.

RESULTS

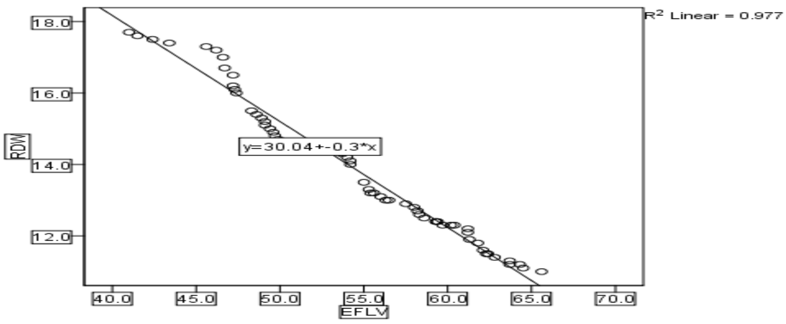
In this study 60 patients (38 (63%) males and 22 (37%) females) were included, the patients' echocardiographic features are shown in Table 1. The mean left ventricular ejection fraction (LVEF) of studied participants was 52.5±6.9 %; 23 (38.3%) of them had LVEF of less than 50%. The mean peak velocity of the early diastolic filling wave (E) of the patients was 0.64±0.19 and the mean peak velocity of the late diastolic filling wave (A) was 0.71±0.12. While 41 (68.3%) patients had peak velocity flow in early diastole to peak velocity flow in late diastole (E/A) of less than 1, the mean E/A ratio of the participants was 0.9±0.25. The mean early transmitral velocity and early diastolic annular velocity ratio (E/E') of the participants was 9.5±2, and 39(65%) of them had E/E' ratio of more than 10. The combination of E/A<1 and E/E'>10 was detected in 28 (46.7%) patients. According to these results, a significant association between low LVEF (<50%) and high RDW levels ($p<0.006$) was observed. The mean **A** of the high RDW group was higher than the mean A of the next group ($p<0.001$). A highly significant association was observed between **E/A ratio** <1 and high RDW levels ($p<0.001$). There was a dramatically significant association between patients with E/E'>10 and high RDW levels ($p<0.001$). The mean E/E' of high RDW group was higher compared to mean E/E' of low RDW group ($p<0.001$). Significantly higher RDW readings were documented in patients with **E/E'** >10. A highly significant association was observed between patients with E/A<1 and E/E'>10 and high RDW levels ($p< 0.001$). RDW values detected in patients with E/A < 1 combined with E/E' > 10 were shown to be higher.

There was no important differences between both groups regarding mean LVEF, LVEDD , LVESD , E value, and tricuspid annular plane systolic excursion TAPSE .

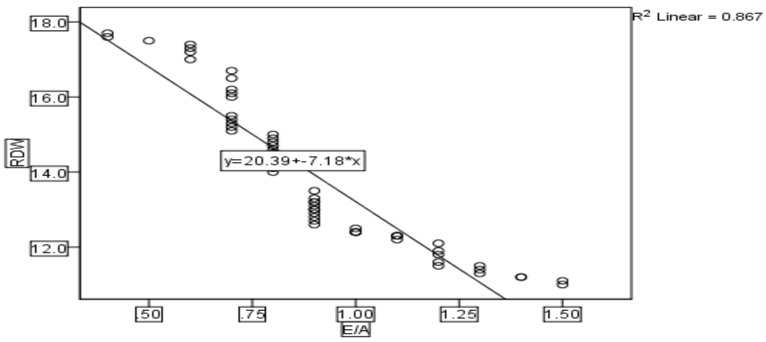
Table 1: Echocardiographic characteristics of the two groups.

Variables	All patients N=60	Patient with low RDW N=32	Patients with high RDW N=28	P value
LVEF mean±SD	52.5±6.9 %	54.8±7.5	51.3±10.3	0.073**N S
LVEF<50%	23(38.3)	9(28.1)	14(50.0)	**0.006**
LVEDD **mean±SD**	51±4.3	51.9±2.4	50.9±1.9	0.09** NS
LVESD **mean±SD**	36.5±4.4	37.3±2.4	37.6±2.3	0.6** NS
E mean±SD	0.64±0.19	0.64±0.1	0.63±0.2	0.8** NS
A mean±SD	0.71±0.12	0.63±0.09	0.78±0.09	**<0.001**** S
E/A mean±SD	0.9±0.25	1.1±0.2	0.7±0.17	**<0.001**** S
E/A<1	41(68.3)	14(43.8)	27(96.4)	**<0.001*** S
E/E' mean±SD	9.5±2	7.9±0.8	11.1±1.5	**<0.001**** S
E/E' >10	39(65)	19(59.3)	21(75.4)	**<0.001*** S
TAPSE mean±SD	19.5±1.13	19.4±1	19.6±1.2	0.4** NS
Combination of E/A<1 and E/E>10	28(46.7)	8(25)	20(71.4)	**<0.001**

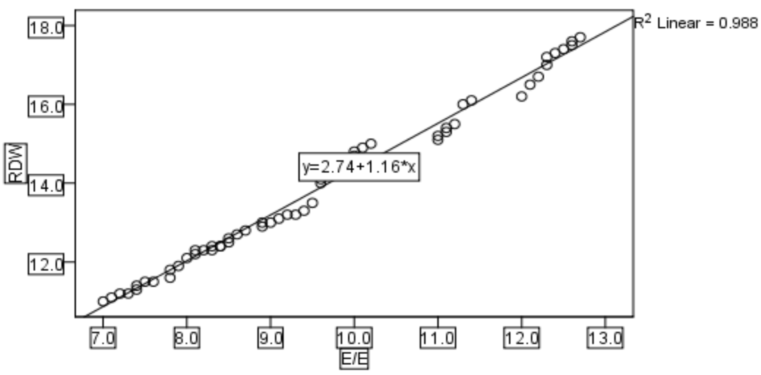
Using bivariate correlations analysis, RDW values have negative correlation with LVEF (P<0.01, Rho= - 1.0) and E/A (P<0.01, Rho=-0.99), and a positively significant association with E/E' (P=0.01, Rho= 1.0), as shown in Figure 1 (A–C). A positive association between RDW and A (P<0.001, Rho=0.36) was observed (D).



A



B



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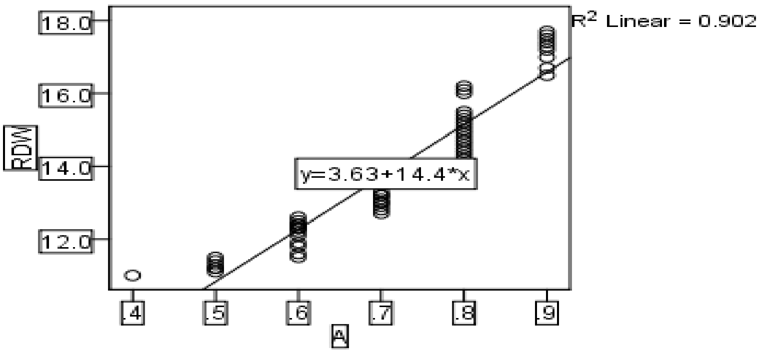


D

Figure 1: Correlation of values of RDW with LVEF, E/A ratio and E/E ratio. (A) RDW values were correlated negatively with LVEF, (B) Correlated negatively with E/A ratio,(C) Correlated positively with E/E'.(D) Positive correlation with A.

Using receiver operating characteristic (ROC) curve analysis, we ascertained practical cutoff points of RDW to differentiate patients having systolic/diastolic dysfunction from others (Fig2. A–D).

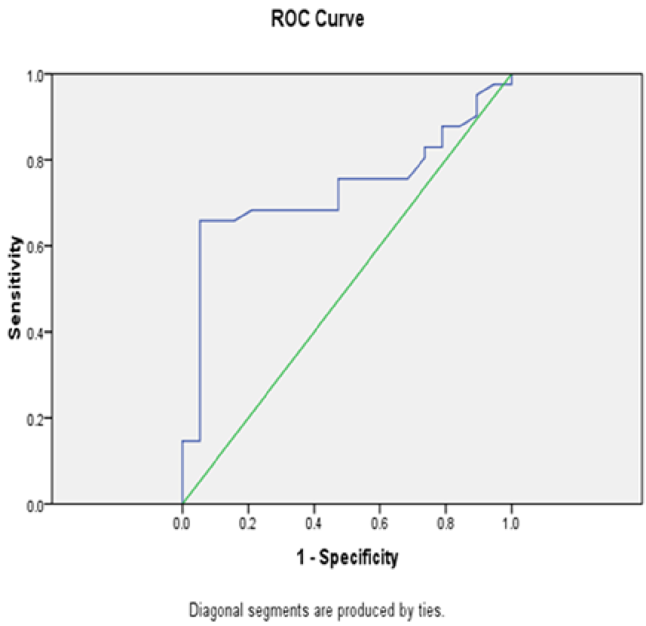
Cutoff RDW values of 13% were applied to ascertain patients with **LVEF < 50%** (AUC 0.7, P<007) with acceptable validity results (a sensitivity of 76%, a specificity of 61%, a positive predictive value (PPV) of 60%; and a negative predictive value (NPV) of 79% and accuracy 70%), figure 2.

The acceptable cut off points and the corresponding validity values for RDW values in prediction of E/A<1(AUC 0.73, P<.001) were shown in table 2 and figure 2. RDW values of 14 % were perfect to document patients with **E/A < 1** with a sensitivity of 63.4%; a specificity of 94.7%; a positive predictive value (PPV) of 67%; and a negative predictive value (NPV) of 93% and accuracy 75%.

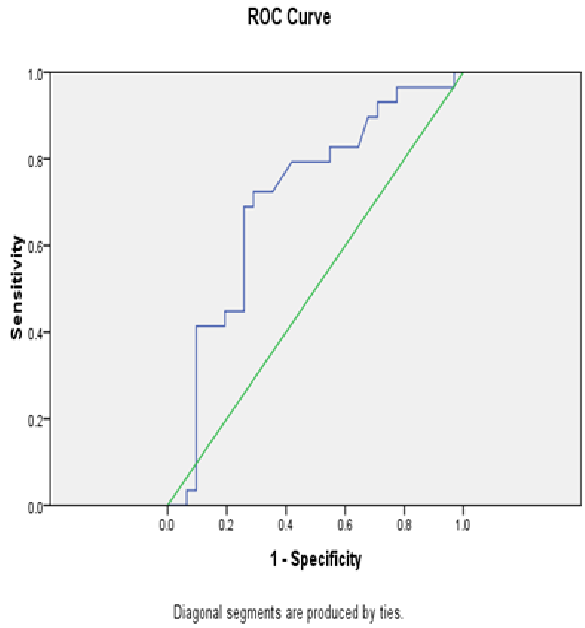
The acceptable cut off points and the corresponding validity values for RDW level in prediction of **E/E'>10**(AUC 0.88, P<.001) was shown in table 2 and figure 2, values of 14 had acceptable validity results (94.7% sensitivity, 78% specificity, 72.8%PPV, 93% NPV and accuracy 85%) for the prediction of E/E'>10.

RDW values of 14% were regarded to ascertain patients featuring **both E/A < 1 and E/E' > 10** (AUC 0.88, P<.001) with a sensitivity of 94.7%; a specificity of 78%; a positive predictive value (PPV) of 72.8%; and a negative predictive value (NPV) of 93% and accuracy 85%.

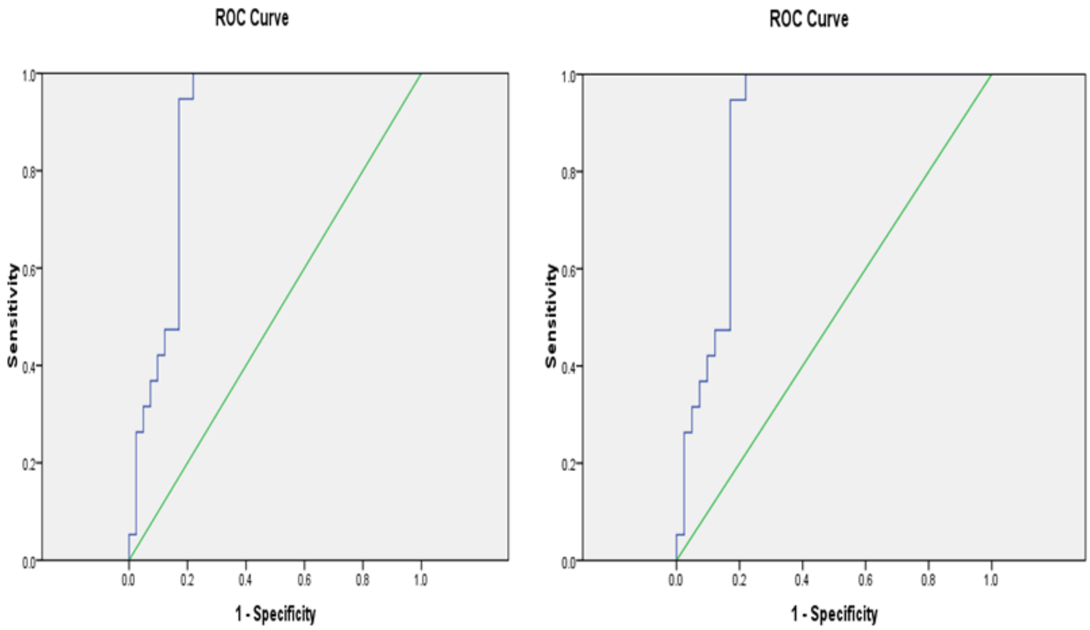
The acceptable cutoff point for predicting diastolic heart failure (DHF) was 14%. (Table 2).



A) ROC for RDW prediction of E/A<1 (AUC=0.73).



B) ROC for RDW prediction of EFLV<50% (AUC=0.7).



C) ROC for RDW prediction of E/E'>10 (AUC=0.88). D) ROC for RDW prediction of E/A<1 and E/E'>10 (AUC=0.88).

Figure 2: Receiver operating characteristic curve analysis for RDW in assessing patients with (A) E/A < 1 (B) EFLV < 50%, (C) E/E' > 10, and (D) Combined E/A < 1 and E/E' >10.

Table 2: ROC coordinates for prediction of low EFLV<50%, E/A<1, E/E'>10andcombined E/A<1 and E/E'>10 by RDW.

Cutoff point low EFLV<50%	Sensitivity	Specificity	PPV	NPV	Accuracy
12%	93.1%	28.6%	45.4%	83.2%	58%
13%	**75.9%**	**61.3%**	**60.2%**	**78.5%**	**70%**
14%	65.5%	74.2%	72.8%	63%	69%
Cutoff point E/A<1	Sensitivity	Specificity	PPV	NPV	Accuracy
12	82.9%	21.1%	31.8%	73.4%	48%
13	68.3%	68.4%	66.7%	68.5%	67%
14	**63.4%**	**94.7%**	**66.7%**	**93%**	**75%**
Cutoff point E/E'>10	Sensitivity	Specificity	PPV	NPV	Accuracy
12	100%	26.8%	21.2%	93.4%	38%
13	100%	36.8%	31.2%	94.4%	48%
14	**94.7%**	**78%**	**72.8%**	**93%**	**85%**
Cutoff point E/A<1 and E/E'>10	Sensitivity	Specificity	PPV	NPV	Accuracy
12	100%	27.2%	25.7%	98.0%	43%
13	100%	46.9%	41.1%	96.2%	57.6%
14	**94.7%**	**78%**	**72.8%**	**93%**	**85%**

DISCUSSION

RDW was approved to be the predictor of all cause mortalities in two large studies.[16,17] RDW was concluded to be a good indicator for expecting worse outcome in heart failure patients.[18,19] RDW predicts independently one-year mortality following acute heart failure attacks regardless of anemia status,[20,21] other studies documented that increasing RDW levels are associated significantly with a bad results in patients of acute myocardial infarction and patients undergoing percutaneus coronary intervention.[3,22,23]

Bujak et al. assessed the importance of RDW in CAD as a prognostic indicator, predicting that such a rule primarily results from the effect of oxidative stress of inflammation and deficiency of vitamin D3 and iron on erythropoiesis in bone marrow[24], this is supported by multiple studies documenting that inflammatory factors, as interleukin 6, WBC count, fibrinogen level and Creactive protein (CRP) affects homeostasis of erythrocyte and leading possibly to increased values of RDW by decreasing red blood cell survival through impairment of iron manipulation , and affecting the release or the effect of erythropoietin.[25,26]

In this work, increasing RDW predicts both systolic and diastolic dysfunction after STEMI, RDW correlated with diastolic more precisely than systolic dysfunction; and 14% values of RDW may be valuable for excluding a combined E/A<1andE/E' >10 situation due to a significant good negative predictive value. RDW, In multivariate analyses constantly shown to be precisely associated with values of both systolic and diastolic dysfunction (EF < 50%, E/A < 1, E/E' > 10) as a single existence or combined in a multiple logistic regression models after adjustment of several confounders as age, gender, TIMI score, and consistent with this study, Karakas found that raised RDW at admission was associated with systolic dysfunction after STEMI[9] and this is consistent with our results. Van Kimmenade et al.[7] also featured that the increment of RDW in patients with acute cardiac failure was independent of nutritional status, inflammation or history of transfusion. Additionally, Allen et al. in a recent research found that raised RDW may point to inflammatory stress and impairment of iron mobilization in heart failure patients.[28]

In the management of coronary disease the analysis of diastolic dysfunction as well as systolic one also has a rule in both diagnosis and prognosis.[29,30] Inconsistence with many recent studies, subclinical diastolic dysfunction is expected in a good percent of patients[12], according to Kitzman et al.[31] neurohormonal changes resembling those documented in systolic heart failure occur in diastolic one.

The positive relation between increased RDW and E/E', in this study indicates that rise in left ventricular filling pressure (LVFP) may be the initiative for the increase in RDW in patients with DHF. Oh et al.[32] documented a relation between RDW elevation and E/E' in patients with acute cardiac failure, and the most appropriate cutoff value of RDW for predicting E/E' > 15 is suggested to be 13.45%.

An important finding in this study was that increasing RDW may reflect exaggerated myocardial injury in patients with either STEMI or ACS, and it can regarded as a marker of occurrence of events of coronary heart disease in different cardiovascular conditions and of all-cause mortality.[33,34] Cavusoglu et al., observed that the RDW was also documented to be a relevant factor that is independent of all-cause mortality in patients sustained ACS[22], this is documented in this study where by Patients with RDW >13.9 had significantly higher TIMI risk scores and ASCVD.

CONCLUSIONS

Elevated RDW can be considered as a new marker of poor outcome in patients acute STEMI as it associated with diastolic as well as and to a lesser extent systolic dysfunction in patients with STEMI even after adjustment of several confounding factors.

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