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ORIGINAL RESEARCH

Study Of Red Cell Distribution Width (RDW) As Prognostic Marker In Heart Failure With Reduced Ejection Fraction (HFrEF)

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ABSTRACT

Objective: To evaluate RDW as a prognostic marker in HFrEF. **Materials and Methods:** A prospective study was conducted among 50 patients who attended Guru Nanak Dev Hospital, Amritsar in the medicine department for various symptoms and signs related to Heart Failure. The sample population was selected based on a brief history, ECG, and 2echo. RDW was measured using an automated hemolyser. **Results:** Among 50, 26 were males and 24 were females. Most of the participants in the sample hadan ejection fraction in the range of 20-30%. The sample size with RDW >13.6 was 70% and with ≤13.6, it was30%. Among the participants, samples with higher ejection fractions were associated with good outcomes (NYHA 1 & 2), and those with lower ejection fractions were associated with bad outcomes (NYHA 3 & expired). Sample with higher RDW were associated with bad prognoses and lower RDW with good prognoses. **Conclusion:** Sample with RDW <13.6, were associated with 100% good outcome. Participants with RDW > 13.6, 48.6% had a good outcome (NYHA1 & 2) and 51.4% had a bad outcome (NYHA 3& expired) with a p-value is highly significant (p = 0.001).Themean RDW was 14.84 and SD 2.25 and 64 % had good outcomes, 36% had bad outcomes.

Key Words: Red Cell Distribution Width (RDW), Heart Failure with Reduced Ejection Fraction (HFrEF), good outcome (NYHA1&2), bad outcome (NYHA3 & expired).

INTRODUCTION

According to the American College of Cardiology and American Heart Association (ACC/AHA) 2022 definition, heart failure (HF) is a complex clinical disease whose symptoms and signs such as fatigue, dyspnea, decreased exercise intolerance, PND, and edema. These are mostly caused by anomalies in the structure and/or function of the heart, which lead to decreased cardiac output and/or increased intracardiac pressures.[1] Ever since HF was classified as a new epidemic in 1997, the epidemiology of this disease has drawn constant attention.[2] Over the past 20 years, India has experienced rapid urbanization and lifestyle changes, which have increased the country's burden of coronary risk factors. Estimates of prevalence range from 1.3 million to 4.6 million, with 4,91, 600–1.8 million yearly incidents, suggesting that the burden of HF in India appears significant.[3] Epidemiological transition is going on in India, in which communicable diseases are decreasing slowly and noncommunicable diseases are increasing rapidly, leading to a dual burden. In India, coronary heart disease (CHD) prevalence has increased fourfold in the last forty years. This can be due to increased cardiovascular risk factors. The HF pathophysiology is complex and includes neurohumoral, structural, molecular, and cellular mechanisms activation to maintain physiologic functioning. The performance of left ventricle function and stroke volume is under the control of preload, myocardial contractility, and afterload explained by the Frank-Starling curve. To diagnose HF, there is no gold standard diagnostic criteria, complete clinical history is the first step to diagnose. The Framingham[4], Duke[5], and Boston[6] were established criteria before non-invasive techniques to assess diastolic and systolic dysfunction became widely available. HF patients are categorized into different categories based on ejection fraction and

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NYHA classes based on functional limitation.[7] Assessment of patients with chronic HF has been improved with biomarkers and clinical evaluation. Over the last decade, several biomarkers have emerged in heart medicine like uric acid, neurohormones, high-sensitive C-reactive protein (hs-CRP), BNP, and many other pro-inflammatory cytokines that help in the diagnosis and also prognosis of HF. Recently red cell distribution width (RDW) was found to be elevated in many HF cohorts. It is considered a measure of variability in the size of RBC.

RED CELL DISTRIBUTION WIDTH

A mature RBC commonly has a disc shape, a central pale, a diameter of 6-8 μm, and a mean corpuscular volume (MCV) of 80-100 fl (femtolitres). RBCs with very high or low quantities are referred to as macrocytic or microcytic, respectively.[8]Adult blood has a physiological variation in size, expressed in terms of RDW. Most modern hematologicalanalyzers are capable of evaluating anisocytosis. Telomere length shortening, oxidative stress, inadequate nutrition, dyslipidemia, hypertension, and inflammation are all linked to these abnormalities.[9]RDW is calculated as the standard deviation (SD) expressed in absolute value (i.e., RDW-SD) or, as the coefficient of variation (RDWCV) (SD/MCV × 100). A low RDW indicates a more uniform population of RBC sizes, while an elevated RDW indicates a significant range in RBC size (anisocytosis).Recently, the clinical significance of RDW in non-hematologic disorders, such as liver diseases[10], autoimmune diseases[11], respiratory diseases[12], cerebrovascular accidents (stroke)[13], illness critically[14], and heart diseases[15]has been investigated extensively.

MATERIAL AND METHOD

This prospective study was conducted among 50 patients who attended Guru Nanak Dev Hospital, Government Medical College, Amritsar, in the medicine department for various symptoms and signs related to HF. The study population comprised all the patients admitted to the medicine department with HF. The sample population was selected based on a brief history, ECG, and based on inclusion and exclusion criteria. The study was carried out after seeking permission from the Institutional Ethics Committee, Government Medical College, Amritsar.

Written informed consent was obtained from the patients.

Duration of study: 16 months. The sample included the population aged >18 years, excluding patients with AKI, CKD, Thyroid disorder, Stroke, Thalassemia., Sickle cell disease

All cases were subjected to a detailed history taking and clinical examination based on a simple questionnaire which included complaints like dyspnoea, chest pain, orthopnoea, paroxysmal nocturnal dyspnea (PND), nocturnal cough, syncope, palpitations, etc. All risk factors like smoking, alcoholism, hypertension, DM, dyslipidemia, and coronary artery disease were taken into account. NYHA functional class will be applied and patients will be classified into 4 classes of heart failure. Clinical features like rales, jugular venous distension, edema, and S3 gallop were noted. Random blood glucose, blood urea, serum creatinine, serum electrolytes, bilirubin, liver enzymes, albumin, total serum protein, and lipid profile were measured in all these patients. ECG, X-ray chest, and 2-D echo were done for all these patients. USG abdomen was also done. Based on history, examination, and investigation results, complete blood counts with RDW were done for all 50 patients who met the inclusion criteria.

STATISTICAL ANALYSIS:

The results were analyzed using SPSS software. The association between variables was analyzed using the chi-square test. Its benefits include data dissemination, computational simplicity, comprehensive information obtained from the test, and adaptability when managing data from one or more groups.

RESULTS

The present study was conducted in the medicine department, Guru Nanak Dev Hospital attached to the Government Medical College, Amritsar to study RDW as a prognostic marker in HFrEF. This was a prospective study done on 50 HFrEF patients divided into RDW >13.6 and <13.6.

The age of all patients included in the study varied between 33-90 years. Most of the study participants are 50-59 yearsand 60-69 years, constituting 34% and 30% of the total sample, respectively. The mean age was 58.46±1.71. Males were 52% and females were 48%.

Prevalence of various risk factors among the participants with heart failure were smoking and alcohol (26%), DM is the most prevalent risk factor, affecting 54% of the individuals. Hypertension is also significant, present in 44% of the participants. Additionally, dyslipidemia is present in 36% of the individuals.

Prevalence of symptoms and signs with which HF patients presented were dyspnea the most prevalent, orthopnea (62%), chest pain (44%), and PND (30%).

Participants were categorized according to NYHA. 64% were in class 4, 22% were in class 3 and 14% were in class 2. Patients were classified into 3 groups based on EF, <20%, 20-30%, and >30% which comprised 6%, 52%, and 42% respectively, and also based on RDW with ≤13.6 (30%) and >13.6 (70%).

The patients` age was compared with HF which was not significant and also compared with the outcome which was significant with higher age ranges shown

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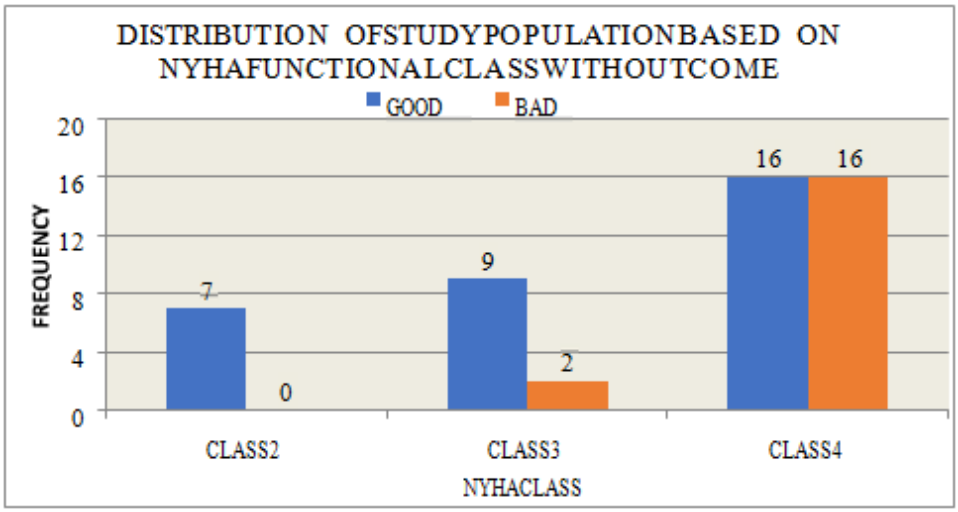
bad prognosis. There is no significant association between outcome and gender.

DISTRIBUTION OF STUDY POPULATION BASED ON NYHA FUNCTIONAL CLASS WITH OUTCOME

			Outcome category		Total
			Good (NYHA 1&2)	Bad (NYHA3 & Expired)	
NYHA functional class	2	Count	7	0	7
		%	100.00%	0.00%	100.00%
	3	Count	9	2	11
		%	81.80%	18.20%	100.00%
	4	Count	16	16	32
		%	50.00%	50.00%	100.00%
Total		Count	32	18	50
		%	64.00%	36.00%	100.00%

Chi-Square Test; p=0.017*

Table showed, participants with NYHA Class 2, 100% had a good outcome. In NYHA Class 3, 81.8% had a good outcome while 18.2% had a bad outcome. For those in NYHA Class 4, the outcomes were evenly split, with 50% having a good outcome and 50% experiencing a bad outcome. These differences were statistically significant, with a p-value of 0.017, indicating that the severity of the NYHA functional class is significantly associated with the outcomes.



Distribution Of Study Population Based On RDW With Outcome

			Outcome category		Total
			Good (NYHA 1&2)	Bad (NYHA3 & Expired)	
RDW	≤13.6	Count	15	0	15
		%	100.00%	.0%	100.00%
	>13.6	Count	17	18	35
		%	81.80%	51.4%	100.0%
Total		Count	32	18	50
		%	64.0%	36.0%	100.0%

Chi-Square Test; p=0.001* (highly significant)

This table shows that in patients with RDW value ≤13.6, 100% of participants had a good outcome. Conversely, in patients with RDW >13.6, only 48.6% had a good outcome, while 51.4% had a bad outcome. This association was observed to be statistically highly significant (p=0.001*)

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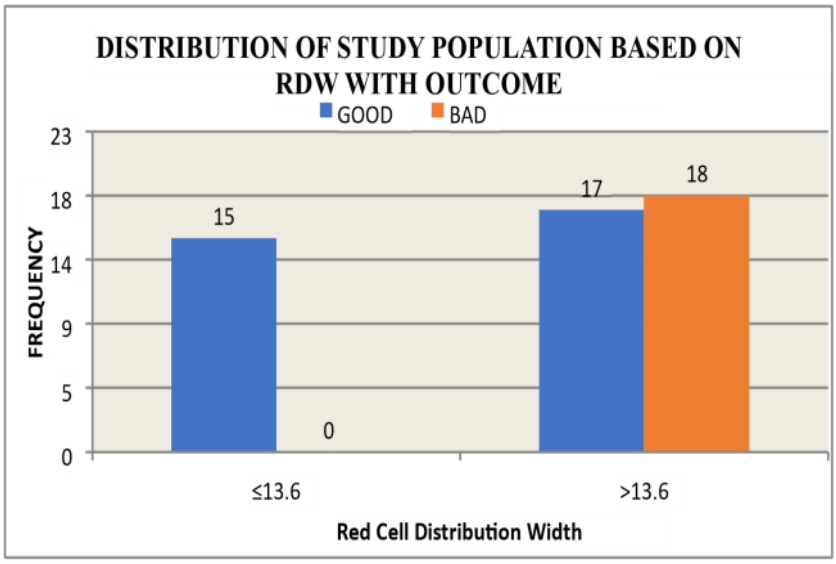


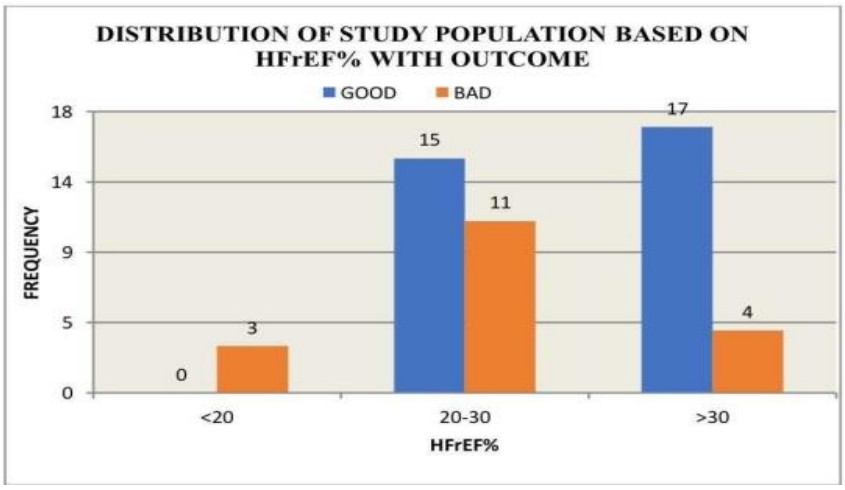
Distribution Of Study Population Based On Hfref% With Outcome

			Outcome category		Total
			Good (NYHA 1& 2)	Bad (NYHA 3 &Expired)	
HFrEF category	<20	Count	0	3	3
		%	0.00%	100.00%	100.00%
	20-30	Count	15	11	26
		%	57.70%	42.30%	100.00%
	>30	Count	17	4	21
		%	81.00%	19.00%	100.00%
Total		Count	32	18	50
		%	64.00%	36.00%	100.00%

Chi-Square Test; p=0.015*

Table shows that for patients with an HFrEF% <20%, 100% had a bad outcome (NYHA 3 & expired), with none experiencing a good outcome (NYHA 1&2). In the 2030% HFrEF category, 57.7% had a good outcome, while 42.3% had a bad outcome. Among those with an HFrEF > 30%, 81.0% had a good outcome, and 19.0% had a bad outcome. This association was observed to be statistically significant (p=0.015*)

These findings highlight that higher ejection fractions are associated with better outcomes, while very low ejection fractions (<20%) are strongly linked to bad outcomes.



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ComparisonBiochemical Findings With Rdw

BIOCHEMICAL FINDINGS	≤13.6 (RDW) (N=15)		>13.6 (RDW) (N=35)		P VALUE
	MEAN	SD	MEAN	SD	
ALBUMIN	3.386	0.34	3.10	0.521	0.05*
SODIUM	137.47	4.27	136.29	5.05	0.433
POTASSIUM	4.086	0.601	4.154	0.615	0.722
TOTAL BILIRUBIN	0.860	0.403	1.12	0.54	0.02*
SGOT	53.06	69.62	89.08	52.95	0.05*
SGPT	43.40	44.80	91.97	78.10	0.02*
UREA	35.13	5.93	34.34	7.09	0.707
CREATININE	0.946	0.255	1.09	0.218	0.04*
Hb	12.62	0.601	11.89	1.61	0.098
MCV	87.93	3.32	91.4	4.76	0.013*
TOTAL SERUM PROTEIN	6.58	0.427	6.76	0.606	0.303

This table shows a significant association between RDW and albumin, total bilirubin, OT, PT, creatinine, MCV.

BIOCHEMICAL FINDINGS WITH OUTCOME

BIOCHEMICAL FINDINGS	GOOD OUTCOME		BAD OUTCOME		P value
	MEAN	SD	MEAN	SD	
Albumin	3.43	0.53	3.31	0.35	0.393
Sodium	136.75	4.41	136.44	5.61	0.934
Potassium	4.21	0.54	4.01	0.70	0. 256
Total Bilirubin	0.77	0.35	1.34	1.34	0.025*
SGOT	45.38	48.82	129.00	205.74	0.032*
SGPT	44.88	38.06	135.22	241.62	0.042*
Urea	36.53	5.16	31.11	7.86	0.005*
Creatinine	0.96	0.23	0.87	0.21	0.183
Hb	12.18	1.22	11.98	1.76	0.103
MCV	88.00	1.00	90.56	5.22	0.053*
Total Serum Protein	6.67	0.47	6.77	0.71	0.620

This table shows a significant association between outcome and total bilirubin, OT, PT, urea, MCV.

COMPARING MEAN RDW AMONG DIFFERENT RISK FACTORS

RISK FACTOR	PRESENT (mean RDW±sd)	ABSENT (mean RDW ±sd)	P value
SMOKING	53.38±5.516	49.17±6.93	0.05*
ALCOHOL	54.92±4.522	50.55±6.88	0.045*
DIABETES	53.00±7.382	49.20±5.56	0.042*
HYPERTENSION	50.61±4.803	52.44±7.84	0.334
DYSLIPIDEMIA	54.29±5.599	50.24±7.15	0.043*

This table shows a significant association between risk factors such as alcohol, smoking, diabetes, dyslipidemia and RDW

RISK FACTORS WITH OUTCOME

RISK FACTOR		GOOD OUTCOME (NYHA1&2)	BAD OUTCOME (NYHA3& expired)	P value
SMOKING	NO	27 (73.0%)	10 (27.0%)	0.025*
	YES	5 (38.5%)	8 (61.5%)	
ALCOHOL	NO	27 (73.0%)	10 (27.0%)	0.025*
	YES	5 (38.5%)	8 (61.5%)	
DIABETES	NO	20 (87.0%)	3 (13.0%)	0.001*
	YES	12 (44.4%)	15 (55.6%)	

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HYPERTENSION	NO	23 (82.1%)	5 (17.9%)	0.002*
	YES	9 (40.9%)	13 (59.1%)	
DYSLIPIDEMIA	NO	25 (78.1%)	7 (21.9%)	0.005*
	YES	7 (38.9%)	11 (61.1%)	

This table shows a significant association between outcome and risk factors.

DISCUSSION

The mean age of the study participants was 58.46±1.71years with the majority of the participants within the age ranges of 50-59 years and 60-69 years, constituting 34% and 30% respectively. The gender distribution showed a slight male (52%) predominance over females (48%).

The demographic characteristics of our study population are consistent with **Patyk Szlacheta et al.**[16]

RISK FACTORS

In the present study, we observed that DM emerged as the most prevalent risk factor, affecting 54% of the participants followed by hypertension, which was present in 44%. Significant correlations between these risk variables and clinical outcomes in HF patients were found in our investigation

These findings are consistent with existing literature, **Felker et al**.[17] emphasized the significant role of DM and hypertension in the development and progression of HF and also showedsignificant association with outcome.

NYHA CLASS

In our study, 64% of participants were classified into Class 4, 22% as Class 3, and 14% as Class 2. This distribution highlights the severity of HF. In terms of ejection fraction, the majority of our participants (52%) had an ejection fraction between 2030%, 42% had an ejection fraction greater than 30%, and only 6% had an ejection fraction of less than 20%. This distribution is indicative of significant cardiac dysfunction.

Our findings were consistent with **Patryk Szlacheta et al.**[16]

Further, in the present study, the outcomes based on the NYHA class showed statistically significant, with a p-value of 0.017, indicating that the severity of the NYHA functional class is significantly associated with patient outcomes. These findings emphasize the importance of NYHA functional classification as a prognostic tool in HF management. The clear correlation between higher NYHA classes and worse outcomes highlights the need for targeted interventions and close monitoring of patients with higher NYHA classes.

RDW

In the present study, the mean RDW was 14.84 with a standard deviation of 2.55, ranging from 10.00 to 24.00. Notably, 70% of the study population had an RDW greater than 13.6, while 30% had an RDW of 13.6 or less.

Further, in the present study focused on the outcome of patients in correlation with RDW, we referenced a study by **Atac Celik et al**[18]. Who took an RDW cut-off of 13.6 for predicting HF. Therefore, we divided our patients into two groups: those with RDW ≤ 13.6 and those with RDW > 13.6. We found that in patients with RDW value ≤13.6, 100% of participants had a good outcome. Conversely, in patients with RDW >13.6, only 48.6% had a good outcome, while 51.4% had a bad outcome. This association was observed to be statistically highly significant (p=0.001*).

In the present study, we further compared the relationship between RDW and various biochemical findings. We observed that participants with RDW ≤13.6 had a mean albumin level of 3.386±0.34, whereas those with RDW >13.6 had a lower mean of 3.10±0.521, with the difference being statistically significant (p=0.05). Similarly, the mean total bilirubin was significantly higher in participants with RDW >13.6 (1.12±0.54) compared to those with RDW ≤13.6 (0.860±0.403) (p-value 0.02). Apart from this, other biochemical parameters, including, SGOT, SGPT, creatinine, and mean corpuscular volume (MCV) were also compared and showed statistically significant differences between participants with RDW ≤13.6 and those with RDW >13.6. These findings are supported by previous research highlighting the prognostic value of RDW in HF.

Our findings, the association between RDW with risk factors like smoking, DM and also with the biochemical parameters like creatinine, urea, albumin, MCV, and transaminases were consistent with the study done by **J.H. Butt et al**.[19]

Van Deursen et al. (2014) similarly reported that elevated liver enzymes, such as SGOT and SGPT, correlate with increased mortality in HF patients, reflecting hepatic congestion and impaired liver function.[20]

In the present study, we observed significant associations between RDW and various risk factors in HF patients. Participants who smoked, consumed alcohol, or had DM, dyslipidemia exhibited significantly higher RDW levels, indicating that these conditions are linked to increased RDW due to factors like oxidative stress and metabolic disturbances.

Alem MM et al. found that RDW is a significant and independent predictor for secondary endpoints, supporting its use as a prognostic indicator for adverse cardiovascular outcomes in the Saudi population with chronic HF.[21]

CONCLUSION

The present study aimed to determine red cell distribution width (RDW) as a prognostic marker in

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HF with reduced ejection fraction (HFrEF). The current guidelines use expensive parameters like NT-proBNP, BNP, and 2Decho to evaluate HF patients. In this study, we conclude that elevated RDW is a novel and significant predictor of symptoms and death in HF patients. RDW, a variable not fully considered by physicians/cardiologists in HF cases shows a stronger independent link to outcome than many other clinical and laboratory indicators.

REFERENCES

1. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, et al.ESC Scientific Document Group . 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016; 37:2129-2200.
2. Braunwald E. Shattuck lecture–cardiovascular medicine at the turn of the millennium: triumphs, concerns, and opportunities.N Engl J Med. 1997; 337:1360–1369.
3. Hajouli S, Ludhwani D. Heart Failure and Ejection Fraction.
4. [Updated 2022 Dec 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK553115/.
5. McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. N Engl J Med. 1971;285:1441-6.
6. Harlan WR, Oberman A, Grimm R, Rosati RA. Chronic congestive heart failure in coronary artery disease: clinical criteria. Ann Intern Med. 1977;86:133-8
7. Carlson KJ, Lee DC, Goroll AH, Leahy M, Johnson RA. An analysis of physicians' reasons for prescribing long-term digitalis therapy in outpatients. J Chron Dis. 1985;38:733-9.
8. https://www.heart.org/en/health-topics/heart-failure/what-isheart-failure/classes-of-heart-failure
9. Dzierzak E, Philipsen S. Erythropoiesis: development and differentiation. Cold Spring Harb PerspectMed.2013;3:a011601. doi: 10.1101/cshperspect.a011601
10. Lippi G, Cervellin G, Sanchis-Gomar F. Red blood cell distribution width: A marker of anisocytosis potentially associated with atrial fibrillation. World J Cardiol 2019; 11(12): 292-304
11. Lou Y, Wang M, Mao W. Clinical usefulness of measuring red blood cell distribution width in patients with hepatitis B. PLoS One. 2012;7:e37644
12. Hu ZD, Chen Y, Zhang L, Sun Y, Huang YL, et al. Red blood cell distribution width is a potential index to assess the disease activity of systemic lupus erythematosus. Clin Chim Acta.2013;425: 202–205.
13. Nathan SD, Reffett T, Brown AW, Fischer CP, Shlobin OA, et al. The red cell distribution width as a prognostic indicator in idiopathic pulmonary fibrosis. Chest. 2013;143(6):1692-8.
14. Ani C, Ovbiagele B. Elevated red blood cell distribution width predicts mortality in persons with known stroke. Journal of the neurological sciences. 2009;277(1-2):103-8.
15. Wang F, Pan W, Pan S, Ge J, Wang S, et al. Red cell distribution width as a novel predictor of mortality in ICU patients. Annals of medicine. 2011;43(1):40-6.
16. Montagnana M, Cervellin G, Meschi T, Lippi G. The role of red blood cell distribution width in cardiovascular and thrombotic disorders. Clin Chem Lab Med. 2012;50:635–41
17. Szlacheta P, Malinowska-Borowska J, Nowak JU, Buczkowska M, Kulik A, et al. Long-term prognostic scores may underestimate the risk of death in patients with heart failure with reduced ejection fraction in whom red cell distribution width is elevated. Polish archives of internal medicine. 2023 Nov 29;133(11):16494.
18. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJ, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. J Am Coll Cardiol. 2007;50:40–47.
19. Atac Celik, Fatih Koc, Hasan Kadi, Koksal Ceyhan, Unal Erkorkmaz, et al. evaluated the relationship between red cell distribution width and echocardiographic parameters in patients with diastolic HF. TheKaohsiungJournalofMedicalSciencesVolume28,Issue3, March 2012, Pages 165-172.
20. Butt JH, McDowell K, Kondo T, Desai AS, Lefkowitz MP, et al. Heart failure with preserved ejection fraction, red cell distribution width, and sacubitril/valsartan. ESC Heart Failure. 2024 Feb;11(1):65-77.
21. Vincent M. Van Deursen, Christopher Edwards,
22. Davison, Kevin Damman, Michael Felker, et al. evaluated the Liver function, in-hospital, and post-discharge clinical outcomes in patients with acute heart failure.JournalofCardiacFailureVolume 20, Issue 6, June 2014, Pages 407- 413.
23. Kim M, Lee CJ, Kang HJ, Son NH, Bae S, et al. Red cell distribution width as a prognosticator in patients with heart failure. ESC Heart Failure. 2023 Apr;10(2):834-45.