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Original Research Article

Correlation between red cell distribution width and coronary artery disease in patients undergoing elective coronary angiography

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ABSTRACT

Background: Coronary artery disease (CAD) is the primary cause of death in developed countries and is one of the leading causes of disease burden in developing countries.
Methods: This descriptive cross-sectional study included 124 purposively selected patients who underwent elective CAG in the department of cardiology, Chittagong medical college hospital, Chattogram, from July 2020 to June 2021. SPSS 23.0 software was used for processing and analysis at the end of the data collection period.
Results: According to the Gensini score, patients were categorized into two groups (score <30 and ≥30). There were no significant differences between the two groups concerning BMI, smoking, hypertension, DM, F/H of CAD, statin or beta-blocker use, or the levels of hemoglobin, hematocrit, MCV, MCH MCHC, and creatinine. However, the mean age was older, and there were more males in the severe CAD group. The percentage of dyslipidemia was significantly higher in patients with Gensini score ≥30 than in patients with <30. RDW (OR: 2.629; 95% CI: 1.425-4.484; p=0.002) and age (OR: 1.058; 95%CI: 1.00-1.111; p=0.027) were independently correlated with the severity of CAD. The AUROC for red cell distribution width (RDW) was 0.915 with a p<0.001 for predicting CAD on CAG. It indicated a statistically significant association of RDW with the presence of CAD. A cut-off value of 13.65% RDW had a sensitivity of 80% and specificity of 84.2% for the prediction of CAD. There were no significant differences between patients with and without angiographic CAD for BMI, hypertension, DM, statin, or beta-blocker use, or of the levels of hemoglobin, hematocrit, MCV, MCH, MCHC, and creatinine. However, the mean age was older, and there were more males in the CAD group. The percentage with dyslipidemia, smoking, and F/H of CAD was significantly higher in patients with CAD than in patients without CAD. The data indicate that only RDW was independently correlated with the presence of CAD (OR: 2.593; 95% CI: 1.347-4.989; p=0.004).
Conclusions: RDW is associated with the presence of CAD and suggests that it might be a readily available test for predicting coronary artery diseases.

Keywords: CAD, CAG, RDW, Gensini score

INTRODUCTION

Coronary artery disease (CAD) is characterized by atherosclerotic plaque accumulation in the epicardial arteries. The dynamic nature of the CAD process results in various clinical presentations, which can be categorized as either acute coronary syndrome (ACS) or chronic coronary syndrome (CCS). ACS is further classified into ST-elevation myocardial infarction (STEMI) and Non-ST elevation-acute coronary syndrome (NSTE-ACS), which consists of non-ST elevation MI (NSTEMI), and Unstable angina (UA).[1] CAD is the

primary cause of death in developed countries and is one of the leading causes of disease burden in developing countries. According to the world health organization estimates, CAD was responsible for more than nine million deaths globally in 2016. Three-fourths of fatalities occurred in low and middle-income countries.[2] Coronary atherosclerosis, the significant cause of CAD, is a chronic inflammatory process that leads to an acute clinical event by plaque rupture and arterial thrombosis. Inflammation and oxidative stress drive all phases of atherosclerosis, including initiation, progression, and thrombotic complications of the lesion.[3] The RDW is a standard component of a routine complete blood count test. RDW quantifies the variation of individual red blood cell (RBC) volumes. It is elevated when an excess of reticulocytes is released into circulation. Therefore, an increase in RDW corresponds to a decrease in mean RBC volume (MCV), an increase in RBC volume variance, or both. Alongside its role in evaluating anemia, RDW is an important prognostic marker in patients with cardiovascular disorders.[4] Several hypotheses have been proposed for explaining this role. One of the most probable mechanisms is inflammation.[5-7] Several inflammatory markers, such as C-reactive protein (CRP), and interleukin-6 are closely related to the severity of CAD.[8,9] Elevated RDW levels, either at the time of admission, during the stay in the hospital, or at the time of discharge, significantly correlate with the increased all-cause mortality among congestive heart failure and CAD patients. An author found that increased RDW is an independent prognostic predictor for heart failure.[10] A correlation between RDW and stable CAD has also been receiving more attention. A study reported that RDW was associated with all-cause mortality and adverse cardiovascular events in patients with stable CAD without heart failure symptoms.[11] This study aimed to analyze the correlation between RDW and CAD in patients undergoing elective coronary angiography.

Objectives

General objective

General objective was to determine the correlation between RDW and CAD in patients undergoing elective coronary angiography.

Specific objectives

Specific objectives were to describe the demographic characteristics of the patients, to calculate the optimal cutoff point of RDW for the presence or absence of CAD and to determine the correlation between RDW and Gensini score.

METHODS

This descriptive cross-sectional study included 124 patients who underwent elective CAG in the department of cardiology, Chittagong medical college hospital, Chattogram, from July 2020 to June 2021. A pretested structured case record form containing all the variables of interest was used for data collection. Written informed consent was obtained from all subjects. All necessary laboratory investigations including-RDW, Hb%, MCV, HbA1c, and lipid profile were done. Continuous data were expressed as mean ± standard deviation (SD) for normally distributed data or median and 25-75% interquartile range for non-normally distributed data. Categorical variables were presented as percentages (%) or proportions. Differences in variables were analyzed using student t-tests or the Mann-Whitney U tests. Categorical data were evaluated by the Chi-square test or Fisher exact test, as appropriate. A p value of less than 0.05 was considered significant statistically. SPSS 23.0 software was used for data processing and analysis. Ethical clearance was obtained from the ethical review committee of Chittagong medical college.

Inclusion criteria

Patients scheduled for elective CAG for their symptoms related to CAD, patients who had given consent to participate in the study were included in the study.

Exclusion criteria

Patients with pregnancy, patients of iron deficiency anemia, megaloblastic anemia, thalassemia, or on treatment for anemia, such as receiving supplemental iron, folate, or erythropoiesis-stimulating agent and patients who did not give consent to participate in the study were excluded from the study.

RESULTS

The age of the patients ranged from 32-75 years with a mean (±SD) age of 53.4 (±9.9) years. The majority of the patients (83.1%) were male with a male-to-female ratio of 4.9:1 (Table 1). According to the Gensini score, patients were categorized into two groups (score <30 and ≥ 30). There were no significant differences between the two groups concerning BMI, smoking, hypertension, DM, F/H of CAD, statin or beta-blocker use, or the levels of hemoglobin, hematocrit, MCV, MCH MCHC, and creatinine. However, the mean age was older, and there were more males in the severe CAD group. The percentage of dyslipidemia was significantly higher in patients with Gensini score ≥30 than in patients with <30 (Table 2). RDW (OR: 2.629; 95%CI: 1.425-4.484; p=0.002) and age (OR: 1.058; 95% CI: 1.00-1.111; p=0.027) were independently correlated with the severity of CAD (Table 3). A positive correlation between RDW and coronary artery disease severity in terms of Gensini score (r=0.393). With the increase of RDW, the Gensini score increases. It was found statistically significant (p≤0.001) by Pearson's correlation test (Figure 1). The AUROC for RDW was 0.915 with a p<0.001 for predicting CAD on CAG. It indicated a statistically significant association of RDW with the presence of CAD. A cut-off value of 13.65% RDW had a sensitivity

of 80% and specificity of 84.2% for the prediction of CAD (Figure 2). There were no significant differences between patients with and without angiographic CAD for BMI, hypertension, DM, statin, or beta-blocker use or of the levels of hemoglobin, hematocrit, MCV, MCH, MCHC, and creatinine. However, the mean age was older, and there were more males in the CAD group. The percentage with dyslipidemia, smoking, and F/H of CAD was significantly higher in patients with CAD than in patients without CAD (Table 4). Variables that were statistically significant in univariate analyses, included age, male gender, smoking history, family history, dyslipidemia, RDW, total cholesterol, TG, LDL-C, HDL-C, and HbA1C were entered into multivariate logistic regression analysis. The data indicate that only RDW was independently correlated with the presence of CAD (OR: 2.593; 95% CI: 1.347-4.989; p=0.004) (Table 5).

Table 1: Demographic characteristics of the patients, (n=124).

Variables	Response
Age (Years)	
Mean (±SD)	53.4±9.9
Range	32-75
Sex, n (%)	
Male	103 (83.1)
Female	21 (16.9)

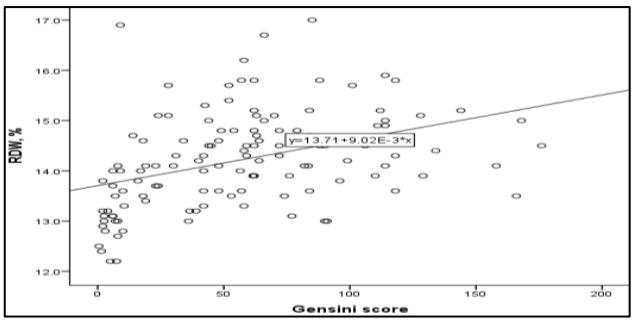

Figure 1: Correlation between RDW and Gensini score by Pearson's correlation test.

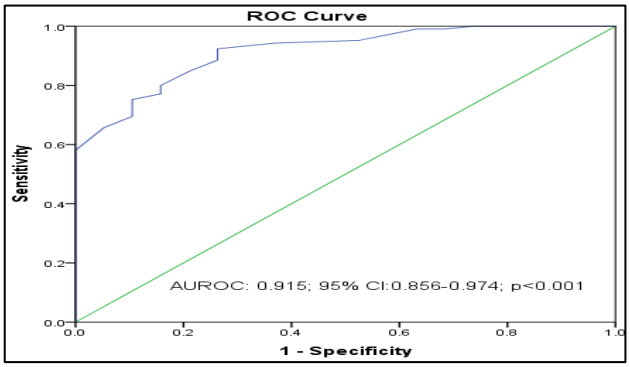

Figure 2: ROC curve analysis of RDW for predicting CAD on angiography.

Table 2: Comparison of demographic, clinical, and laboratory parameters between patients with or without severe CAD (Gensini score ≥30), (n=124).

Variables	Severity of CAD, n (%)		P value
	Gensini score <30, (n=38)	Gensini score ≥30, (n=86)	
Age (Years)	49.6 (±10.3)	54.9 (±9.4)	0.005*
Male sex	27 (71.1)	76 (88.4)	0.018†
Smoker	14 (36.8)	47 (54.7)	0.067†
Hypertension	15 (39.5)	39 (45.3)	0.543†
Diabetes mellitus	10 (26.3)	30 (34.9)	0.347†
Dyslipidemia	23 (60.5)	69 (80.2)	0.021†
F/H of CAD	14 (36.8)	39 (45.3)	0.377†
Statin use	8 (21.1)	29 (33.7)	0.155†
Beta blocker use	4 (10.5)	22 (26.6)	0.058†
BMI (kg/m^2)	22.4 (±1.6)	22.6 (±2.4)	0.498*
Haemoglobin (mg/dl)	13.9 (±0.8)	14.1 (±0.9)	0.201*
Hematocrit (%)	46.8 (±10.3)	44.7 (±3.2)	0.080*
MCV (fl)	91.9 (±5.0)	89.3 (±10.9)	0.151*
MCH (pg/cl)	29.0 (±2.2)	29.2 (±2.5)	0.685*
MCHC (gm/dl)	31.6 (±1.7)	31.6 (±1.8)	0.925*
RDW (%)	13.6 (±0.9)	14.5 (±0.8)	<0.001*
HbA1C (%)	5.9 (±1.2)	6.6 (±1.3)	0.012*
Total cholesterol (mg/dl)	177.2 (±24.0)	195.5 (±29.8)	0.001*
Triglyceride (mg/dl)	165.1 (±47.8)	213.7 (±73.1)	<0.001*
LDL-C	96.4 (±19.1)	112.4 (±21.3)	<0.001*
HDL-C	41.8 (±4.3)	39.5 (±3.4)	0.001*
Serum creatinine	1.0 (±0.2)	1.1 (±0.2)	0.625*

P value was derived from *Independent samples t-test; †Chi-square test.

Table 3: Predictors of severe angiographic CAD (Gensini score ≥30) in multivariate logistic regression analysis.

Variables of interest, (n=124)	B	SE.	OR	95% CI for OR		P value
				Lower	Upper	
RDW (%)	0.967	0.312	2.629	1.425	4.848	0.002
Age (Years)	0.056	0.025	1.058	1.007	1.111	0.027
Dyslipidemia	-0.651	0.680	0.522	0.138	1.978	0.339
HbA1C (%)	0.236	0.216	1.266	0.830	1.931	0.274
Total cholesterol (mg/dl)	0.016	0.012	1.017	0.993	1.041	0.169
Triglyceride (mg/dl)	0.004	0.006	1.004	0.992	1.015	0.509
LDL-C (mg/dl)	0.013	0.018	1.013	0.978	1.050	0.477
HDL (mg/dl)	-0.115	0.083	0.891	0.757	1.049	0.166

OR: Odds ratio; CI: Confidence interval.

Table 4: Comparison of demographic, clinical, and laboratory parameters between patients with and without angiographic CAD, (n=124).

Variables	CAD on angiogram		P value
	Absent, (n=19)	Present, (n=105)	
Age (Years)	48.5 (±9.8)	54.2 (±9.8)	0.021
Male sex	7 (36.8)	14 (13.3)	0.012†
Smoker	4 (21.1)	57 (54.3)	0.008‡
Hypertension	6 (31.6)	48 (45.7)	0.253‡
Diabetes mellitus	4 (21.1)	36 (34.3)	0.256‡
Dyslipidemia	9 (47.4)	83 (79.0)	0.004†
F/H of CAD	3 (15.8)	50 (47.6)	0.010‡
Statin use	5 (26.3)	32 (30.5)	0.715‡
Beta blocker use	2 (10.5)	24 (22.9)	0.224‡
BMI (kg/m^2)	22.4 (±1.4)	22.6 (±2.3)	0.745*
Hemoglobin (mg/dl)	14.0 (±0.9)	14.0 (±0.8)	0.955*
Hematocrit (%)	46.9 (±10.7)	45.0 (±5.3)	0.240*
MCV (fl)	92.9 (±4.9)	89.6 (±10.1)	0.166*
MCH (pg/cl)	29.4 (±2.2)	29.1 (±2.4)	0.567*
MCHC (gm/dl)	31.9 (±1.6)	31.5 (±1.8)	0.366*
RDW (%)	13.1 (±0.6)	14.4 (±0.9)	<0.001*
HbA1C (%)	5.8 (±1.0)	6.6 (±1.3)	0.010*
Total cholesterol (mg/dl)	171.8 (±24.4)	193.2 (±29.0)	0.003*
Triglyceride (mg/dl)	152.5 (±33.8)	207.2 (±71.5)	0.001*
LDL-C	88.4 (±15.1)	110.9 (±21.0)	<0.001*
HDL-C	43.1 (±4.8)	39.6 (±3.4)	0.001*
Serum creatinine	0.9 (±0.2)	1.1 (±0.2)	0.162*

P value was derived from *Independent samples t-test; †Chi-square test or Fisher exact test.

Table 5: Predictors of angiographic CAD in multivariate logistic regression analysis, (n=124).

Variables of interest	B	SE.	OR	95% CI for OR		P value
				Lower	Upper	
Age (Years)	0.058	0.030	1.060	0.999	1.125	0.055
Male	-1.442	0.752	4.230	0.968	18.484	0.055
Smoking	-0.058	0.601	0.944	0.291	3.065	0.924
Dyslipidemia	-0.467	0.717	0.627	0.154	2.557	0.515
F/H of CAD	0.342	0.579	1.407	0.452	4.382	0.555
RDW (%)	0.953	0.334	2.593	1.347	4.989	0.004
HbA1C (%)	0.196	0.225	1.216	0.783	1.889	0.383
Total cholesterol (mg/dl)	0.019	0.012	1.019	0.995	1.043	0.121
Triglyceride (mg/dl)	0.005	0.006	1.005	0.993	1.017	0.411
LDL-C	0.006	0.018	1.006	0.971	1.042	0.747
HDL-C	-0.105	0.089	0.900	0.756	1.072	0.237

DISCUSSION

Regarding the demographic and clinical presentation of the patients undergoing elective CAG, most patients (83.1%) in the present study were male with a mean age of around 54 years. The mean age of the current study population was similar to another study, but the age was earlier than in the developed countries.[12-14] CAG is the gold standard for the clinical judgment of CAD, and the Gensini score is a quantitative indicator for estimating coronary artery stenosis based on CAG. Gensini score is a widely used angiographic scoring system for quantifying the severity of CAD.[15] A positive correlation between RDW and Gensini score was found in the present study. With the increase of RDW, the Gensini score increased, indicating more severe CAD. In the current study correlation coefficient between RDW and Gensini score was r=0.393 ($p \leq 0.001$). This positive correlation was in agreement with other similar studies. A study demonstrated a positive correlation between RDW and Gensini score in patients with CAD (r=0.37, $p<0.001$).[16] Another study demonstrated a similar positive correlation (r=0.464 $p<0.001$) between RDW and the severity of CAD (measured by SYNTAX score).[14] Another study reported a statistical correlation between RDW values and coronary artery calcium scoring (r=0.53; $p<0.001$).[17] All these results, including the present study, indicated that RDW is a marker for CAD. In addition, in the ROC curve analysis of the present study, the results showed that RDW had a sensitivity of 80.0% and a specificity of 84.2% for diagnosing CAD when the cutoff value of RDW was 13.65%. These data were inconsistent with previous investigations and provided new information regarding the role of RDW in cardiovascular diseases in the Bangladeshi population.[12,16] One of those studies reported that an RDW value of 12.85% was a practical cutoff point in the segregation of the presence or absence of CAD (AUC=0.61, 95% CI: 0.56-0.66) with a sensitivity of 50.0% and a specificity of 65.2%, and another study described the cutoff value of RDW as 14.3% for diagnosing CAD with a sensitivity of 58.9% and specificity of 84.8%.[12,16] These findings indicated that the cutoff point of RDW for CAD diagnosis on angiography varies, which justifies more studies involving a larger population from multiple centers in Bangladesh. In addition to the cutoff value for identifying CAD, the present study also determines another cutoff value of RDW for the segregation of the presence or absence of severe CAD (Gensini score ≥30). The present study findings had important clinical implications. Diagnosis of CAD is principally based on CAG and other cardiovascular imaging modalities. However, these tools are expensive and time-consuming with potential unwanted effects such as exposure to radiation. Therefore, RDW, which is cheap and easily obtainable, could be used as an initial filter criterion, especially in small centers, to determine the need for further imaging modalities in assessing CAD. RDW can be easily incorporated into the laboratory routine, and it practically does not involve an additional cost. Unlike other inflammatory biomarkers, RDW is an inexpensive and widely available test that provides an extra level of risk scores in predicting coronary artery stenosis. RDW was a good indicator in different cardiovascular, cerebro-vascular and infectious conditions.[18,19]

Limitations

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. Moreover, it was done among the patients of ACS, so the results cannot be applied to the overall patients of CAD.

CONCLUSION

This study concluded that RDW is associated with the presence of CAD and suggested that it might be a readily available test for predicting coronary artery diseases.

Recommendation

Along with previous international recommendations, the present study supports the use of RDW as a widely available, inexpensive test to predict individuals at risk of coronary artery disease. Moreover, further studies should be conducted involving a large sample size and multiple centers.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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