Original Article

"Correlation of red blood cell distribution width with the severity of coronary artery disease—A single center study"

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A B S T R A C T

Objective: Coronary Artery Disease (CAD) is the leading cause of morbidity and mortality all around the world. We evaluated the correlation of Red blood cell Distribution Width (RDW) with the severity of lesion on coronary angiography as assessed by Modified Gensini score (MGS) in CAD patients.
Methods: A total of 576 consecutive patients admitted in Department of Cardiology over a period of one year, who underwent coronary angiography after diagnosis of CAD or presence of angina like chest pain and/or positive treadmill test were enrolled in the study (August 2014–May 2015). Patients were divided into two groups, with CAD (Group A) and without CAD (Group B). The RDW Cofficience of variance (RDW CV) and RDW standard deviatiton (RDW SD) of each patient, and their correlation with severity of CAD was assessed.
Results: Of the total 576 patients enrolled, 438 were in Group A and 138 were in Group B. The mean age of presentation in Group A and Group B was (53.64 ± 10.36 vs 49.4 ± 9.73) years ($p < 0.0001$). The Male and Female ratio overall was 2.42:1. Patients in Group A had significantly elevated RDW CV and RDW SD levels compared with those in Group B [(14.59 ± 1.04)% vs (13.6 ± 0.68)%, $p < 0.0001$], [(45.78 ± 4.76) vs (40.77 ± 3.01), $p < 0.0001$ respectively]. A significant positive correlation between RDW CV, RDW SD and MGS was noted ($r = 0.33$, $p < 0.0001$) ($r = 0.43$, $p < 0.0001$) respectively. On multivariate logistic regression analysis, RDW was demonstrated to be an independent predictor for angiographic CAD ($OR = 4.17$, 95% CI 3.05–5.69, $p < 0.0001$). On receiver operating characteristic curve (ROC) analysis, an RDW value of 14.3% was identified as an effective cut off point in diagnosing CAD with a sensitivity of 58.9% and specificity of 84.8%.
Conclusions: RDW is an independent predictor of CAD and severity of coronary stenosis, suggesting that it can be a readily available marker for prediction and severity of CAD.

1. Introduction

Coronary Artery Disease, due to atherosclerosis is the most common cause of death worldwide. Atherosclerosis is a chronic inflammatory disorder with long asymptomatic period for years and usually manifests as acute coronary events with occlusion of coronaries. RDW, a measure of heterogeneity of red blood cell size, is usually used in the differential diagnosis of anemia.[1] In the recent years, there is increased interest in the role of increased RDW as a risk marker of various cardiovascular diseases for example heart failure[2] and coronary artery disease.[3] We have

assessed the RDW in patients presenting with chest pain and correlated its relation with severity of lesion as assessed by Modified Gensini score (MGS) on angiography.

2. Methods

2.1. Study population

The study was carried out in Department of Cardiology, Osmania General Hospital, Hyderabad between August 2014–March 2015. After analyzing 1835 patients presenting with chest pain, a total of 576 consecutive patients have been enrolled in the study.

2.2. Inclusion criteria

Patients with Age >18 years, with diagnosis of

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1 Acute Coronary Syndrome (ACS) **[ST segment Elevation Myocardial Infarction (STEMI), Non ST elevation Acute Coronary Syndrome (NSTEACS)]**
ACS was defined as presentation with symptoms of ischemia in association with ECG changes (ST segment deviation elevation or depression, T wave inversion, and new Qwave), positive cardiac enzymes and regional wall motion abnormalities on echocardiography (absent in patients with unstable angina,with intracoronary lesion on angiography in most of the cases).

2 Typical Angina, described as substernal chest discomfort lasting for less than 20 min precipitated by stress and relived by rest or nitroglycerin

3 Atypical angina with conventional risk factors (i.e. diabetes mellitus, hypertension, obesity, family history of CAD, chronic smoking, chronic alcohol intake) or

4 Chest pain with treadmill test positive for inducible ischemia (i.e. new ST depression at the start of exercise, new ST depression >2 mm in multiple leads, hypotensive response to exercise, development of heart failure or sustained ventricular arrhythmias during the study, prolonged interval after exercise (>5 min) before the ischemic changes return to baseline) were included in the study.

2.3. Exclusion criteria

Patients with anemia i.e with Hemoglobin level of < 12gm/dl in males and < 11gm/dl in females were excluded.[4]

The patients with previous history of Percutaneous Coronary Intervention (PCI), Coronary Artery Bypass Grafting (CABG) surgery, Valvular Heart Disease, Bleeding disorders, Chronic Kidney Disease (CKD), on Estrogen Replacement Therapy (ERT), Anemia and Blood transfusions, Liver disease, Pregnancy, Thrombotic Thrombocytopenic Purpura were excluded from the study.

Institutional ethical committee has approved the study.

Each patient has been enrolled after obtaining written and informed consent.

A detailed evaluation of demographic data of each patient, presence of risk factors (hypertension, diabetes mellitus, smoking, alcohol intake, family history of premature CAD, obesity) clinical examination, with electrocardiography (ECG), echocardiography (2d ECHO) and the treadmill test whenever required i.e in patients without ACS has been done. Venous blood sample for RDW has been collected at the time of admission from the antecubital vein by atraumatic puncture and value was assessed by SYSMEX 2.0 analyzer within an hour of collection of sample. Blood was collected in a tube containing EDTA for measurement of red cell indices. The reference value of RDW in our laboratory was 11.5–13.5%. Transthoracic echocardiography was performed with Phillips I3 machine using 3–5 MHz transducer on each patient after admission to the intensive cardiac care unit. Each patient underwent coronary angiography either by transradial or trans-femoral route using 5F Optitorque catheter in the former and 6F Judkins catheters in the latter within 24 h after hospital admission. The severity of lesion on angiography has been assessed by MGS.

After coronary angiography patients were divided into two groups, those with CAD (Group A) and those without CAD (Group B). Angiographic CAD was defined as the diameter of the stenosis in a vessel reaching more than or equal to 50%. Severity of lesion is by MGS, based upon the total added value of the eight proximal segments of coronary arterial tree. Maximum score is 32 and minimum is 4. Mild, moderate, severe is for scores of 1–6, 7–13 and >13 respectively (**Appendix A.1**). The RDW CV, RDW SD values were correlated with MGS.

2.4. Statistical analysis

Statistical analysis was carried out using Medcalc (Belgium). Continuous variables are expressed as mean ± standard deviation (SD). Categorical variables are expressed as percentages. Students t-test or analysis of variance was used to compare parametric continuous variables. To compare categorical variables, the chi-square (χ2) test was used. Correlation of two variables were examined by Pearson r correlation coefficient. Receiver operating characteristic (ROC) curves for RDW values were plotted to determine the optimal cut off point for use in clinical decision making. Multivariate logistic regression analysis was used to identify the independent predictors of angiographic CAD. A p value <0.05 was considered significant statistically. Tables, bar diagrams, pie diagrams were illustrated wherever possible.

3. Results

Total number of patients included in the study were 576. In CAD group (hereby Group A) there were 438 patients and in without CAD group (hereby Group B) were 138. The mean age of presentation in the whole cohort was 52.6 ± 10.38 years. The range of age of patients was 22 years to 84 years. On group analysis, the mean age of presentation in Group A was 53.64 ± 10.36 years whereas in Group B was 49.4 ± 9.73 years ($p < 0.0001$). Males were predominant than the females (70.8% vs 29.2%) with a sex ratio of 2.42:1. The difference in mean hemoglobin levels between the two groups was statistically insignificant(13.66 ± 0.71 vs 13.63 ± 0.54, p = 0.65). In Group A, the most common risk factor was hypertension seen in 287 (65.5%), followed by smoking in 243 (55.5%) and diabetes in 189 (43.2%) patients. Patients in Group A had significantly elevated RDW CV levels compared to Group B [(14.59 ± 1.04)% vs (13.6 ± 0.68)%, $p < 0.0001$]. The RDW SD levels were also significantly elevated [(45.78 ± 4.76) vs (40.77 ± 3.01), $p < 0.0001$]. The red cell indices when analysed showed no significant difference in the mean hematocrit (Hct) and mean corpuscular hemoglobin (MCH) values between the two groups but significant difference with regards to mean values of the mean corpuscular volume (MCV), and mean corpuscular hemoglobin concentration (MCHC). The baseline characteristics of patients in both groups are shown in Table 1.

The most common diagnosis in Group A was Anterior wall STEMI in 180 (42%), the next common diagnosis was NSTEACS seen in 112 (26%) patients (Table 2). The patients in CAD group were stratified according to the MGS and the baseline characteristics along with the RDW CV and RDW SD have been analysed (Table 3). The RDW CV value increased along the score values of 1–6, 7–13 and >13 (14.53 ± 0.88, 14.55 ± 1.07, 14.68 ± 1.10) respectively ($p < 0.0001$). A significant positive correlation between RDW CV for the presence or absence of angiographic CAD (n = 576, r = 0.40, $p < 0.0001$) and with severity of CAD (n = 438, r = 0.33, $p < 0.0001$) was seen on Pearson correlation analysis. The correlation of hemoglobin levels in the whole cohort with RDW CV was − 0.109, a weak negative correlation noted.

On subgroup analysis in CAD group (Group A) according to the diagnosis in comparison with group B (n = 138, 13.60 ± 0.68), the RDW CV was increased in all subgroups i.e AWSTEMI (n = 180,14.79 ± 4.86,p = 0.0041), NSTEACS (n = 112,14.65 ± 1.02, p = 0.0001), IW STEMI (n = 72, 14.84 ± 5.46,p = 0.0091), Stable angina (n = 65, 14.25 ± 2.46,p = 0.0089).

In multivariate logistic regression analysis, RDW was demonstrated to be an independent predictor for angiographic CAD (OR = 4.17, 95% CI 3.05–5.69, $P < 0.0001$) (Table 4). On ROC analysis, an RDW value of 14.3% was identified as an effective cut off point in diagnosing CAD with a sensitivity of 58.9% and specificity of 84.8%