A Cross- sectional Study on the Association of Red Cell Distribution Width and Acute Coronary Syndrome Among Patients admitted to the Bataan General Hospital and Medical Center

Monica B. Alagon, MD[1] and Almalyn C. Sevilla, MD[2]

Abstract

Introduction. Red cell distribution width (RDW) is a parameter that is readily available as part of a standard complete blood count (CBC). Studies have shown that an elevated RDW is associated with increased cardiovascular events including acute coronary syndrome (ACS). This cross- sectional retrospective study was conducted to determine the association of RDW in patients with ACS admitted to Bataan General Hospital and Medical Center (BGHMC).

Methods. A cross-sectional study was performed in a 500-bed tertiary care hospital in Bataan, Philippines. The clinical medical records of patients with ACS were analyzed retrospectively. A total of 811 patients was admitted as cases of ACS from January 2017 to December 2019. Using Slovin's formula, the computed sample size was 261 patients. However, only 205 cases were included in the study in accordance to the eligibility criteria. The baseline RDW were recorded from the CBC obtained upon admission of patients with ACS.

Results. Based on the data collected from January 2017 to December 2019 from patients admitted to BGHMC, there was no significant association between RDW and in-house morbidity and mortality and classification of ACS.

Conclusions. There were no significant association between RDW and in-house morbidity and mortality and classification of ACS. The authors recommend to conduct the study for a longer duration to have more population included and to include other parameters such as cardiac enzymes, electrocardiogram (ECG) changes and presence of co-morbidities.

Keywords. Red cell distribution width, Acute coronary syndrome, Unstable angina, ST segment elevation myocardial infarction, non-ST segment elevation myocardial infarction

Introduction

Red cell distribution width (RDW) is a parameter that is readily available as part of a standard complete blood count. It measures variation in red blood cell size or red blood cell volume. It is elevated in accordance with variation in red cell size (anisocytosis). The reference range for RDW is as follows; RDW-SD = 39-46 femtoliters (fl), and RDW-CV = 11.6-14.6%.[1]

Red cell distribution width coefficient of variation (RDW-CV) represents the coefficient of variation of erythrocyte volume around mean corpuscular volume (MCV). It is calculated as follows: RDW-CV (%) = 1 SD (fl)/MCV x 100, where 1 SD = 1 SD in relation to MCV, which is obtained by height of 68.2% above the base of the erythrocyte volume distribution histogram. Red cell distribution width standard deviation (RDW-SD) is determined from the width of erythrocyte volume distribution curve at level 20% above baseline and is expressed in femtoliters.[2]

ACS refers to a spectrum of clinical presentations ranging from those for ST-segment elevation myocardial infarction (STEMI) to presentations found in non-ST-segment elevation myocardial infarction (NSTEMI) or in unstable angina (UA). It is almost always associated with

[1] 3rd Year Internal Medicine Resident, Department of Internal Medicine, Bataan General Hospital and Medical Center
[2] Medical Specialist III Department of Internal Medicine, Bataan General Hospital and Medical Center

Corresponding Author: Monica B. Alagon, MD eMail: moniquealagon@yahoo.com

rupture of an atherosclerotic plaque and partial or complete thrombosis of the infarct related artery.[3]

Vedanthan et.al, stated that ischemic heart disease (IHD) is the greatest single cause of mortality and loss of disability-adjusted life years (DALYs) worldwide, accounting for roughly 7 million deaths and 129 million DALYs annually.[4] Cardiovascular disease exerts a significant economic toll, accounting for one-third of a projected US$47 trillion in economic losses to non-communicable diseases (NCDs) over the next 20 years.

According to the European Society of Cardiology, cardiovascular diseases cause approximately one-third of all deaths in the world, of which 7.5 million deaths are estimated to be due to IHD.[5] ACS and sudden death cause most IHD-related deaths, which represent 1.8 million deaths per year. The incidence of IHD in general, and of ACS, increases with age, and on average, occurs 7–10 years earlier in men compared with women. According to the WHO, 120 out of every 100,000 Filipinos died of IHD, or coronary, heart disease (CAD) in 2019, up from 103 per 100,000 population in 2015, the worst record among Southeast Asian countries that listed the ailment as its top cause of death.[6]

Previous studies have shown that an elevated RDW is associated with increased cardiovascular events including ACS.

This cross- sectional retrospective study was conducted to determine the association of RDW in patients with ACS in BGHMC. A total of 811 patients were admitted as a case of ACS from January 2017 to December 2019. Among these patients, 205 were included in this study. The researchers did a chart review and obtained the baseline RDW and classified the patient as to STEMI, NSTEMI, UA and associate the level of RDW with patients' outcome.

Objectives:

General objective. To determine the association of RDW in patients with ACS in BGHMC.

Specific objectives: (a) To determine the RDW of patients with ACS, (b) To determine the association between RDW and in-house mortality and in-house morbidity of patients with ACS, and (c) To define the association between RDW and ACS.

Methodology

Study Design. This is a retrospective cross-sectional study.

Study Setting, Population, Sampling Method and Sample Size. The study was conducted in BGHMC in Balanga City, Bataan, Philippines. BGHMC is a tertiary hospital that caters to people not only from Bataan but also from neighboring provinces.

The researchers coordinated with the in-patients record section to identify the number of ACS patients admitted from January 2017 to December 2019. The number of patients were identified to be 811 gleaned from the electronic database. After that, the researchers asked permission from the Medical Center Chief to borrow the charts to do manual chart review.

A total of 811 patients were admitted as a case of ACS from January 2017 to December 2019. Using Slovin's formula, the computed sample size was 261 patients. However, only 205 cases were included in the study in accordance to the eligibility criteria.

To avoid selection bias, all charts were borrowed and reviewed by the researchers.

Inclusion and Exclusion Criteria. All patients admitted from January 2017 to December 2019 as a case of ACS with complete parameters of the CBC results were included.

Excluded were patients with incomplete parameters for CBC, patients with previous history of ACS and those with chronic kidney disease and end stage renal disease.

Data Collection and Statistical Plan. A chart review was done and determined the distribution of ACS by age and sex, ACS classification and Sex, Age and ACS classification, and Hospital length of stay (LOS) and ACS classification. The classification of ACS was divided into STEMI, NSTEMI, and UA. The researchers also determined the comparison of RDW in STEMI, NSTEMI, and UA among survivors and non survivors, as well as the percentage of alive, and in-house mortality according to ACS classification.

The patients were classified to STEMI based on electrocardiogram abnormality and a rise in serum biomarkers. For NSTEMI patients, those with ST segment depression or T-wave inversion on electrocardiogram and a rise in serum biomarkers. For patients under UA, those with myocardial ischemia but with normal cardiac biomarkers. In this study, patients were categorized according to ACS classification based on the diagnosis stated in the chart since it is a retrospective study.

Data collected were tabulated using Microsoft Excel®. The data collected were processed and analyzed using Statistical Package for the Social Sciences (*SPSSS™ v23*). Only the researcher, adviser and statistician had access to these data.

The difference of the means of two samples were tested for statistical significance using *t-test*. *Chi square* was used to determine whether there is significant association between RDW and ACS, and the patients' outcomes. Significance level lower than *0.05* is considered statistically significant.

Definition of Terms

1. Red cell distribution width (RDW)- a parameter that is readily available as part of a standard CBC. It measures variation in red blood cell size or red blood cell volume. It is elevated in accordance with variation in red cell size (anisocytosis). The reference range for RDW is as follows; RDW-SD = 39-46 fl and RDW-CV = 11.6-14.6%.[1]

Table I. Distribution of ACS patients by Classification (STEMI, NSTEMI, UA), Age, and Sex

Variables	STEMI	NSTEMI	Unstable Angina	Total	Fisher's Exact p-value
	No. (%)	No. (%)	No. (%)	No. (%)	
Age					
< 50 years old	9 (16.1)	20 (16.13)	5 (20)	34 (16.6)	0.565
50-59 years old	14 (25)	23 (18.55)	6 (24)	43 21)	
60-69 years old	19 (33.9)	36 (29.03)	8 (32)	63 (30.7)	
70-90 years old	14 (25)	44 (35.48)	5 (20)	63 (30.7)	
≥ 91 years old	0	1 (0.81)	1 (4)	2 (1)	
TOTAL	56	124	25	205	
Sex					0.483
Male	38 (30.2)	74 (58.7)	14 (11.1)	126	
Female	18 (22.8)	50 (63.3)	11 (13.9)	79	

Table II. Distribution of ACS patients by Classification (STEMI, NSTEMI, UA) and Length of Hospital Stay

Length of hospital stay	STEMI	NSTEMI	Unstable angina	Total
1-5 days	22	47	13	82
6-10 days	28	54	8	90
11-15 days	3	15	2	20
16-20 days	1	4	1	6
21-25 days	2	2	0	4
26-30 days	0	1	0	1
31 days and above	0	1	1	2
TOTAL	56	124	25	205
Mean (+ SD)	1.80 ± 0.903	1.93 ± 1.053	1.84 ± 1.344	1.88 + 1.051
Median	2	2	1	2
One-way F- test	*p = 0.66*			

2. Acute coronary syndrome (ACS)- refers to a spectrum of clinical presentations ranging from STEMI to presentations found in NSTEMI or in UA. It is almost always associated with rupture of an atherosclerotic plaque and partial or complete thrombosis of the infarct related artery.[3]

3. STEMI - the presence of symptoms of myocardial ischemia/injury along with persistent electrocardiogram ST segment elevation in addition to the presence of cardiac biomarkers.[10]

4. Non-ST elevation ACS - further divided into UA and NSTEMI. These two conditions resemble each other very closely. UA is distinguished from NSTEMI by the absence of an elevation of cardiac biomarker levels.[11]

5. In-hospital morbidity and mortality - patients who had complications and had longer hospital stay and those who expired.

Results

Table I shows the distribution of ACS patients by classification and age. Majority of ACS patients have NSTEMI (124 patients) followed by STEMI with 56 patients and the least have unstable angina with 25 patients. Among those with NSTEMI, majority belong to the age group of 70 to 90 years old with 35.48% (44 patients) and the least belong to 91 years old and above with 0.81% (1 patient). For patients who have STEMI, 33.9% (19 patients) belong to the age group of 60 to 69 years old and the least belong to the age group of 91 years old and above with 0%. Like the patients with STEMI, majority of patients with UA belong to the age group of 60 to 69 years old and the least with 4% (1 patient) from the 91 years old and above age group. Overall, majority of the ACS patients belong to the age group of 60 to 69 years old and 70 to 90 years old with 30.7% (63 patients). Using *chi-square test*, the classification of ACS is not significantly affected by age (*0.565 > 0.05*).

Also in *Table I* is the distribution of ACS patients by classification and sex. There were 205 ACS patients which is comprised of 79 females and 126 males. Majority of female patients have NSTEMI with 63.3% (50 patients) followed by STEMI with 22.8% and UA with the least percentage of 13.9% (11 patients). Like the female patients, majority of male ACS patients have NSTEMI with 58.7% (74 patients) and the least belongs to UA with 11.1% (14 patients). In general, the majority of the population have NSTEMI with 60.5% (124 patients) and the least percentage have UA with 12.2% (25 patients). Using the *chi-square test*, the classification of ACS is not significantly affected by sex (*0.483 > 0.05*).

Also in *Table I* is the distribution of ACS patients by age and sex. Among the 205 patients, 79 are females and 126 are males. Majority of the 79 female ACS patients dominated the age group of 70 to 90 years old by 38% (30 patients) and the least percentage was from the age group of 91 years old and above with 1.3% (1 patient). Among the male patients, 31.7% (40 patients) dominated the 60 to 69 years old and the least percentage is from 91 years old and above with 0.8% (1 patient). Overall, majority of ACS patients was dominated by the age group 60 to 69 years old and 70 to 90 years with 30.7% (63 patients). Comparing the mean age of the two by sex, female patients have a greater mean or older age which is 64 years old compared with 62 years old for male patients. Using *t-test* for independent sample with 95% confidence level, the value obtained was not significant (*0.087 > 0.05*), therefore age group between male and female is not a factor in ACS patients.

Table III. Comparison of Red Cell Distribution Width in STEMI, NSTEMI, and UA

RDW	STEMI	NSTEMI	UA	Total
0.100- 0.110	0	1	0	1
0.111- 0.120	6	11	4	21
0.121- 0.130	25	53	10	88
0.131- 0.140	12	29	4	45
0.141- 0.150	5	17	6	28
0.151- 0.160	4	3	0	7
0.161- 0.170	2	2	0	4
0.171- 0.180	0	3	0	3
0.181- 0.190	1	1	0	2
0.191- 0.200	0	1	0	1
≥ 0.201	1	3	1	5
TOTAL	**56**	**124**	**25**	**205**
Mean ± SD	0.368 ± 1.759	0.272 ± 1.506	0.748 ± 3.094	0.356 ± 1.831
Median	2	1	2	2
One-way F-test	*p = 0.495*			

Table IV. Comparison of Red Cell Distribution Width in STEMI, NSTEMI, Unstable angina among survivors and non- survivors

RDW (RDW-CV)	Survivors	Non-survivors	Total
0.100- 0.110	1	0	1
0.111- 0.120	19	2	21
0.121- 0.130	77	11	88
0.131- 0.140	38	7	45
0.141- 0.150	22	6	28
0.151- 0.160	4	3	7
0.161- 0.170	4	0	4
0.171- 0.180	1	2	3
0.181- 0.190	1	1	2
0.191- 0.200	1	0	1
≥ 0.201	7	0	5
TOTAL	**173**	**32**	**205**
Mean ± SD	3.85 ± 1.795	4.31 ± 1.712	3.92 ± 1.786
Median	3	4	3
One-way F-test	*p = 0.126*		

Table V. Percentage of Alive and In- hospital Mortality in STEMI, NSTEMI, and UA

Outcome	STEMI	NSTEMI	UA	Total
	No. (%)	No. (%)	No. (%)	No. (%)
Alive	49 (87.5)	101 (81.5)	23 (92)	173 (84.4)
Died	7 (12.5)	23 (18.5)	2 (8)	32 (15.6)
Total	**56**	**124**	**25**	**205**
Fisher's Exact test	*p = 0.316*			

Table II shows the distribution of ACS patients by classification and length of hospital stay. Among the 124 patients with NSTEMI, majority (54 patients) stayed in the hospital for 6 to 10 days and the least belong to 26 to 30 days and 31 days and above hospital stay, both with a single patient. For patients with STEMI, majority (28 patients) belong to 6 to 10 days hospital stay in contrast with 26 to 30 days and 31 days and above hospital stay with zero patient. For those with UA, majority (13 patients) stayed for 1 to 5 days and the least with no patient belongs to 21 to 25 days and 26 to 30 days hospital stay. In conclusion, among the 205 ACS patients, majority stayed in the hospital for 6 to 10 days. Only two patients stayed for 31 days and above. In relation to the classification of ACS and length of hospital stay, NSTEMI have the highest mean of 1.93 days followed by UA with 1.84 days and the last is STEMI with 1.8 days. Using the *chi-square test*, the classification of ACS is not significantly affected by the length of hospital stay (*0.660 > 0.05*).

Table III shows the comparison of RDW and Classification of ACS (NSTEMI, STEMI, UA). Among the 205 patients, UA has the least number of patients (25 patients) as compared to NSTEMI with 124 patients, the highest among the ACS classification. Based on RDW, majority of STEMI patients (25 patients) have RDW of 0.121 to 0.130 fl, same with NSTEMI with 53 patients and UA with 10 patients. Overall, most of the population (88 patients) have RDW of 0.121 to 0.30 fl. Using the one-way ANOVA, RDW has no significant effect on the classification of ACS (*0.495 > 0.05*).

Table IV shows the comparison of RDW in patients with NSTEMI, STEMI, UA among survivors and non-survivors, with 173 patients and 32 patients respectively. Among the 173 survivors, majority (77 patients) have RDW of 0.121 to 0.130. Similar with the survivors, majority (11 patients) of the non-survivors have RDW of 0.121 to 0.130. Using *t-test* with independent sample, it shows that the RDW and patient's outcome (survival and non-survival) has no significant association (*0.126 > 0.05*).

Table V shows the percentage of alive and in-hospital mortality with classification of ACS. Among the 124 NSTEMI patients, majority survived with 81.5% (101 patients) compared with non-survivors with 18.5% (23 patients). For the 56 patients with STEMI, majority survived with 87.5% (49 patients) compared to non-survivors with 12.5% (7 patients). Lastly, for the 25 patients with UA, majority survived with 84.4% (173 patients) compared to non-survivors with 15.6% (32 patients). With the use of *chi-square test*, it shows that there is no significant association between patient's outcome and the classification of ACS (*0.316 > 0.05*).

Discussion

The study was conducted to determine the association of RDW and ACS among patients admitted at BGHMC. IHD is common in people aged 80 years or older, and is a major cause of morbidity and mortality in this age group worldwide. As this patient group grows, with an increase in life expectancy of up to 10 years or more, the absolute prevalence of cardiovascular disease is expected to increase.[7]

Women are more likely to have worse health status than are men at the time of ACS. Smoking and diabetes may be stronger risk factors among women compared to

men. Smoking cardiovascular (CV) risk is highest among young and middle-aged women. Sex difference in socioeconomic status, psychological burden, and mental health may contribute to CV risk among women.

Evidence suggests that depression and perceived stress are predictive of CV risk in young and middle-aged women.[8] However, in this study, results showed that age group and sex were not factors in ACS patients.

Limited studies were done regarding the duration of hospital stay depending on the classification of ACS. In this study, it showed that classification of ACS is not affected by the length of hospital stay.

RDW is reported to be associated with all-cause mortality and cardiovascular mortality in patients with STEMI, NSTEMI, or stable CAD. Increased values of these parameters are associated with greater numbers of comorbidities and a higher likelihood of complications among patients with CAD treated via percutaneous coronary intervention.[9] Comparing it with our study, it showed that RDW has no significant effect on the classification of ACS and patients' outcomes. The study also determined that there is no association between patients' outcomes and the classification of ACS.

The authors suggest to do further study for a longer duration with a larger population included. In addition, further work up is suggested and to include other parameters such as cardiac enzymes, electrocardiogram changes and the presence of comorbidities.

Conflict of Interest. There is no conflict of interest in this study. No funding is needed to conduct the study.

References

1. Choladda Vejabhuti Curry, MD. (2015). Red Cell Distribution Width (RDW) test. Accessible at: https://emedicine.medscape.com/article/2098635-overview
2. Caporal, Fernando Augusto, & Comar, Samuel Ricardo. (2013). Evaluation of RDW-CV, RDW-SD, and MATH-1SD for the detection of erythrocyte anisocytosis observed by optical microscopy. *Jornal Brasileiro de Patologia e Medicina Laboratorial*, *49*(5), 324-331. Accessible at: https://dx.doi.org/10.1590/S1676-24442013000500005
3. David L Coven, MD, PhD. (2018). Acute Coronary Syndrome. Accessible at: https://emedicine.medscape.com/article/1910735-overview
4. Vedanthan R, Seligman B, Fuster V. Global perspective on acute coronary syndrome: a burden on the young and poor [published correction appears in Circ Res. 2014 Aug 1;115(4):e8]. *Circ Res*. 2014;114(12):1959–1975. doi:10.1161/CIRCRESAHA.114.302782
5. James, Stefan, and Héctor Bueno (ed.), 'Epidemiology of acute coronary syndromes', in A. John Camm and others (eds), The ESC Textbook of Cardiovascular Medicine, 3 edn, The European Society of Cardiology Series (Oxford, 2018; online edn, ESC Publications, 1 July 2018). Accessible at: https://doi.org/10.1093/med/9780198784906.003.0305
6. Jovic Yee. (2020, December 13). WHO: Heart disease in the Philippines worst in Southeast Asia. *Philippine Daily Inquirer*. Accessible at: https://newsinfo.inquirer.net/1371108/heart-disease-in-ph-worst-in-sea
7. Bjorn Bendz, et. Al (2020, August). Acute coronary syndrome in older patients: does older age matter? *The Lancet* volume 396, Issue 10251, p585-587. Accessible at: https://doi.org/10.1016/S0140-6736(20)31317-9
8. Ahmed Haider, Susan Bengs, Judy Luu, Elena Osto, Jolanta M Siller-Matula, Taulant Muka, Catherine Gebhard, Sex and gender in cardiovascular medicine: presentation and outcomes of acute coronary syndrome, *European Heart Journal*, Volume 41, Issue 13, 1 April 2020, Pages 1328–1336. Accessible at: https://doi.org/10.1093/eurheartj/ehz898
9. Bujak K, Wasilewski J, Osadnik T, Jonczyk S, Kołodziejska A, Gierlotka M, Gąsior M. The Prognostic Role of Red Blood Cell Distribution Width in Coronary Artery Disease: A Review of the Pathophysiology. Dis Markers. 2015;2015:824624. doi: 10.1155/2015/824624. Epub 2015 Aug 26. PMID: 26379362; PMCID: PMC4563066.
10. O'Gara PT, Kushner FG, Ascheim DD, et al. American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report to American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013 Jan 29. 127 (4):e362-425.
11. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014 Dec 23. 130 (25):e344-426.