The Correlation of Platelet-to-Lymphocyte Ratio Levels With Clinical Outcomes in Acute Coronary Syndrome Patients Admitted in a Tertiary Hospital From January 2011 to December 2020

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Abstract

BACKGROUND: Studies have shown that inflammation plays a role in the pathogenesis of acute coronary syndrome (ACS). The use of platelet-to-lymphocyte ratio (PLR) as a marker for inflammatory conditions such as malignancy, systemic lupus erythematosus, and rheumatoid arthritis has been demonstrated in several studies. The aim of this study is to determine whether an elevated PLR taken on admission is associated with in-hospital mortality and major adverse cardiac events among ACS patients.

METHODS: This is a single-center, retrospective correlational study. It included all ACS ST-segment elevation myocardial infarction and non–ST-segment elevation myocardial infarction adult patients admitted from January 2011 to December 2020. Complete blood count on admission was used to derive the PLR. Patient's course in the ward was reviewed for development of adverse clinical outcomes such as in-hospital mortality, arrhythmias, heart failure, cardiogenic shock, and reinfarction. Primary outcome for this study was in-hospital mortality, and the secondary outcomes were the development of other complications previously mentioned. Optimal cutoff value associated with in-hospital mortality was determined using receiver operating characteristic curve.

RESULTS: A total of 342 patients were included in the study. Forty-three (12.57%) of the sample had in-hospital mortality and was noted to have higher PLR compared with patients who did not develop complications. Univariate logistic regression analysis showed a significant relationship between a high PLR and occurrence of in-hospital mortality ($P = 0.0039$). The optimal cutoff value of PLR that can predict in-hospital mortality is 165, with 52.17% sensitivity, 56.76% specificity, and an area under the curve of 59.69%. On the other hand, a high PLR did not show association with the development of complications during the hospital stay.

CONCLUSION: A PLR of >165 is a cheap, readily available marker that can be used to predict in-hospital mortality among Filipino patients with ACS.

KEYWORDS: acute coronary syndrome, platelet-to-lymphocyte ratio

INTRODUCTION

Ischemic heart disease is a condition wherein an imbalance between oxygen supply and demand causes ischemia to a portion of myocardium. It is most commonly due to atherosclerosis.[1] According to the Philippine Statistics Authority, despite the COVID-19 pandemic, ischemic heart disease is still the leading cause of mortality in the Philippines, comprising 56,760 cases or 18.7% of total deaths in the country in January to June 2021.[2]

Acute coronary syndrome (ACS) encompasses ST-segment elevation myocardial infarction (STEMI), non–ST-segment elevation myocardial infarction (NSTEMI), and unstable angina. It is due to coronary atherosclerosis with concomitant coronary thrombosis, which occurred due to atherosclerotic plaque rupture or erosion.[3] Studies have shown that inflammation plays an important in the atherosclerotic process. During inflammation, proatherogenic and antiatherogenic immune networks are activated. Once an imbalance between the two occurs, ACS develops.[4] Moreover, an inflammation in the myocardium can also cause inflammation in the atherosclerotic plaque, predisposing them to disrupt and provoke thrombosis.[3]

Platelets have a key role in the pathophysiology of ACS. It is responsible in the formation of thrombotic vascular occlusion. Furthermore, it plays a role in plaque progression and inflammatory reactions.[5] On the other hand, lymphocytes modulate the inflammatory process and inhibits the development or progression of atherosclerosis.[6] Platelet-to-lymphocyte ratio has been used as a prognostic marker in cardiovascular conditions.[7-15]

Working in an environment with only one PCI-capable institution with limited resources in terms of management of ACS patients, the use of PLR as an economical and readily available test may greatly help in identifying the risk of Filipino patients to develop complications. In addition, this study will also greatly benefit the health care team in deciding for the urgency in doing invasive procedure.

The PLACS study conducted in PGH last 2017 was the first and only available data we have in the Philippines regarding the use of PLR. Locally, no study was conducted regarding this matter. With the addition of this study and with enrollment of more patients with ACS in Negros Oriental, we aim to determine the correlation of PLR levels with clinical outcomes in ACS patients.

METHODOLOGY

Study Design and Population

This was a single-center, retrospective cross-sectional study done at Silliman University Medical Center Foundation, Inc (SUMCFI). The study included all ACS STEMI and NSTEMI patients older than 18 years diagnosed within 24 hours of admission and admitted from January 2011 to December 2020. Patients with any of the following exclusion criteria were not included in the study: (a) diagnosed with any infection, acute inflammatory condition, autoimmune disease, tuberculosis, renal failure and hematologic disease; (b) initially treated or managed in another hospital during the first 24 hours of symptom onset; and (c) incomplete medical record.

Slovin's formula with a 95% level of confidence was used to determine the target sample size of at least 341 patients.

Procedures

A transmittal letter was sent to the medical director of SUMCFI, coursed through the chair of the Department of Internal Medicine and its training officer. The research protocol was then submitted for ethical review to the Research Ethics Board. A letter was sent to the head of medical records of SUMCFI for permission to access the patient's data through chart review.

Data collection was done from February 2021 to September 2022. Medical records were gathered, reviewed, and sorted according to the inclusion criteria.

A total of 659 medical records were reviewed. Three hundred forty-two patients were included in the study. Three hundred seventeen patients were then excluded for the following reasons: 117 due to infection (37%), 95 developed MI not during admission (30%), 52 had renal failure (16%), 22 had incomplete medical records (7%), 18 were initially treated in another hospital (6%), 5 had hematologic condition (1%), 5 had tuberculosis (1%), and 3 had no CBC taken on admission (1%). See Figure 1.

Complete blood count taken on admission was used in this study. The PLR values were computed as follows: platelet count divided by lymphocyte count. Subsequent patient's course in the ward was reviewed for development of adverse clinical outcomes such as in-hospital mortality, arrhythmias, heart

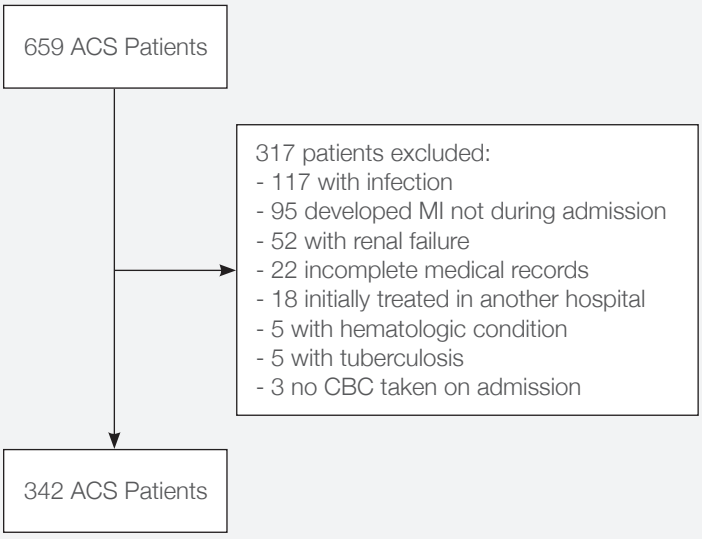

Figure 1. Study population.
ACS=acute coronary syndrome; CBC=complete blood count; MI=myocardial infarction.

Table 1. Baseline Clinical Characteristics

Demographics	All Patients	In-hospital Mortality	Discharged With Complications	Discharged Without Complications
	(n = 342)	(n = 43)	(n = 152)	(n = 147)
	Frequency (%) or Mean ± SD			
Age, y	65 ± 13.04	67 ± 12	66 ± 13	62.41 ± 13.32
Sex				
Female	126 (36.84%)	15 (34.88%)	59 (38.82%)	52 (35.37%)
Male	216 (63.16%)	28 (65.12%)	93 (61.18%)	95 (64.63%)
Diabetes	146 (42.69%)	23 (53.49%)	65 (42.76%)	58 (39.46%)
Hypertension	246 (71.93%)	27 (62.79%)	118 (77.63%)	101 (68.71%)
Dyslipidemia	100 (29.24%)	8 (18.60%)	37 (24.34%)	55 (37.41%)
Smoker	155 (45.32%)	18 (41.86%)	69 (45.39%)	68 (46.26%)
Prior MI	47 (13.74%)	11 (25.58%)	20 (13.16%)	16 (10.88%)
Diagnosis				
NSTEMI	243 (71.05%)	30 (69.77%)	114 (75%)	99 (67.35%)
STEMI	99 (28.95%)	13 (30.23%)	38 (25%)	48 (32.65%)
Platelet count (/mm^3)	245,088 ± 86,264.53	259,000 ± 111,465	248,309 ± 95,478	237,687.07 ± 65,232.97
WBCs (/mm^3)	11,416 ± 4635.26	13,097 ± 6398	11,908 ± 4542	10,414.56 ± 3869.68
Lymphocytes (/mm^3)	18 ± 10.75	13.91 ± 10	16.59 ± 10	20.74 ± 10.62
ALC (/1000 mm^3)	1829 ± 1043.03	1573.8 ± 1018	1804.7 ± 1176	1929.83 ± 884.65
PLR	183 ± 146.32	251.6 ± 214	194.49 ± 162	150.10 ± 84.34

ALC=absolute lymphocyte count; MI=myocardial infarction; NSTEMI=non–ST-segment elevation myocardial infarction; PLR=platelet-to-lymphocyte ratio; STEMI=ST-segment elevation myocardial infarction; WBCs=white blood cells.

failure, cardiogenic shock, and reinfarction. Primary outcome for this study was in-hospital mortality. Secondary outcome was the development of complications previously mentioned.

Operational Definition of Terms

Acute coronary syndrome—Patients diagnosed with STEMI and NSTEMI

Platelet-to-lymphocyte ratio—Derived by dividing the platelet count with the lymphocyte count

Discharged with complications—Patients diagnosed with ACS who developed MACE such as heart failure, arrhythmia, reinfarction, and cardiogenic shock during the hospital stay

Discharged without complications—Patients diagnosed with ACS who did not develop MACE during the hospital stay

Statistical Analysis

Descriptive statistics was used to describe the clinical profile of ACS patients in the study. Univariate logistic regression analysis was then used to determine the correlation between a high PLR and the clinical outcome of the patient. Receiver operating characteristic (ROC) curve was also utilized to determine the cutoff for the PLR that can predict in-hospital mortality.

RESULTS

Among the 342 patients included in the study, the mean age was 65 ± 13.04 years. The population mainly composed of male (63.16%), nondiabetic (57.31%), hypertensive (71.93%), nondyslipidemic (70.76%), and nonsmoker (54.68%) patients. On admission, 71.05% had NSTEMI, whereas 28.95% were diagnosed with STEMI. Table 1 shows the clinical profile of the patients.

Table 2 shows the clinical outcomes of the patients. Forty-three patients (12.57%) had in-hospital mortality, 152 patients (44.44%) developed complications while admitted, and 147 patients (42.98%) were discharged without complications.

Among patients who had in-hospital mortality, most of them were male (65.12%), had diabetes (53.49%), had hypertension (62.79%), was nondyslipidemic (81.4%), was nonsmoker (58.14%), and was diagnosed with NSTEMI on admission (69.77%). The PLR in these patients who had in-hospital mortality was noted to be higher at 251.6 ± 214 compared with patients who were discharged without complications.

In the study, among patients who were discharged with complications, majority of them were male (61.18%), nondiabetic (57.24%), hypertensive (77.63%), nondyslipidemic (75.66%), and nonsmoker (54.61%). Based in Table 3, the most common complication among patients was development of heart failure (32.75%).

Table 2. Clinical Outcomes

Outcome	All Patients (n= 342)
	Frequency (%)
In-hospital mortality	43 (12.57)
Discharged with complications	152 (44.44)
Discharged without complications	147 (42.98)

Table 3. Complications of Acute Coronary Syndrome

Complication	All Patients (n= 342)
	Frequency (%)
Heart failure	112 (32.75)
Arrhythmia	9 (2.63)
Cardiogenic shock	18 (5.26)
Heart failure and arrhythmia	10 (2.92)
Cardiogenic shock and arrhythmia	3 (0.88)
Reinfarction	0

Among patients who were discharged without complications, majority of them were male (64.63%), nondiabetic (60.54%), hypertensive (68.71%), nondyslipidemic (62.59%), and nonsmoker (53.74%). The PLR in patients who did not develop complication was noted to be lower at 150.10 ± 84.34 compared with those who had complications and in-hospital mortality.

Result of univariate logistic regression analysis shown in Table 4 demonstrated that PLR has a significant correlation with in-hospital mortality (P = 0.0039) with an odds ratio of 1.0027. A history of prior myocardial infarction also showed a significant relationship with in-hospital mortality (P = 0.0189) with an odds ratio of 2.5113.

As shown in Table 5, PLR was not found to be significantly associated with development of complication (P = 0.18577). On the other hand, age (P = 0.02525) and hypertension (P = 0.03671) had been demonstrated to have significant relationship with development of complications. Furthermore, lymphocyte count has been shown to be associated with occurrence of complication (P = 0.02731) and in-hospital mortality (P = 0077).

Using the ROC curve shown in Figure 2, PLR of >165 had 52.17% sensitivity and 56.76% specificity to predict in-hospital mortality with an area under the curve of 59.69%.

Table 4. Univariate Logistic Regression (In-hospital Mortality)

Independent Variables	Estimate	SE	Odds Ratio	Lower Bound	Upper Bound	*P*
PLR	0.0027	0.0009	1.0027	1.0009	1.0046	0.0039*
Age	0.0157	0.0127	1.0158	0.9910	1.0419	0.2184
Male sex	0.0972	0.3416	1.1021	0.5715	2.2006	0.7759
Diabetes	0.4981	0.3275	1.6455	0.8661	3.1507	0.1284
Hypertension	–0.4838	0.3415	0.6164	0.3186	1.2252	0.1565
Dyslipidemia	–0.6650	0.4114	0.5143	0.2147	1.0996	0.1060
Smoker	–0.1609	0.3302	0.8514	0.4401	1.6184	0.6261
Prior MI	0.9208	0.3921	2.5113	1.1253	5.3014	0.0189*
STEMI	0.0707	0.3558	1.0733	0.5189	2.1153	0.8425
Platelet count	0.0000	0.0000	1.0000	1.0000	1.0000	0.2618
WBCs	0.0001	0.0000	1.0001	1.0000	1.0001	0.0127*
Lymphocyte	–0.0511	0.0192	0.9502	0.9130	0.9845	0.0077*
ALC	–0.0003	0.0002	0.9997	0.9993	1.0000	0.0851

*Statistically significant.

ALC=absolute lymphocyte count; MI=myocardial infarction; PLR=platelet-to-lymphocyte ratio; STEMI=ST-segment elevation myocardial infarction; WBCs=white blood cells.

Table 5. Univariate Logistic Regression (Discharged With Complications)

Independent Variables	Estimate	Std. Error	Odds Ratio	Lower Bound	Upper Bound	*P*
PLR	0.00101	0.00077	1.00102	0.99954	1.00259	0.18577
Age	0.01910	0.00854	1.01928	1.00253	1.03673	0.02525*
Male sex	–0.15243	0.22529	0.85862	0.55192	1.33627	0.49867
Diabetes	0.00538	0.22000	1.00539	0.65262	1.54735	0.98050
Hypertension	0.51943	0.24865	1.68107	1.03788	2.75685	0.03671*
Dyslipidemia	–0.43296	0.24386	0.64859	0.39974	1.04178	0.07583
Smoker	0.00531	0.21859	1.00532	0.65451	1.54325	0.98062
Prior MI	–0.08916	0.31740	0.91470	0.48590	1.69748	0.77879
STEMI	–0.34967	0.24338	0.70492	0.43514	1.13186	0.15079
Platelet count	0.00000	0.00000	1.00000	1.00000	1.00000	0.53728
WBC	0.00004	0.00002	1.00004	1.00000	1.00009	0.08069
Lymphocyte	–0.02337	0.01059	0.97690	0.95637	0.99703	0.02731*
ALC	–0.00004	0.00011	0.99996	0.99975	1.00016	0.69453

*Statistically significant.
ALC=absolute lymphocyte count ; MI=myocardial infarction; NSTEMI=non–ST-segment elevation myocardial infarction; PLR=platelet-to-lymphocyte ratio; STEMI=ST-segment elevation myocardial infarction; WBCs=white blood cells.

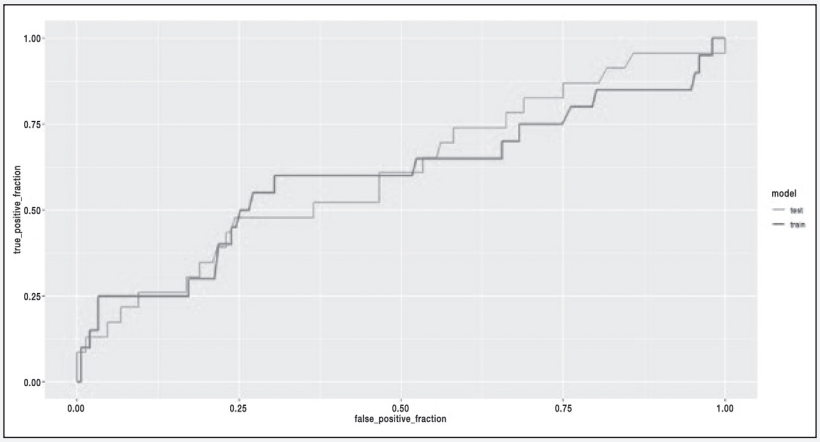

Figure 2. Receiver operating characteristic curve of PLR to predict in-hospital mortality in ACS.
ACS=acute coronary syndrome; PLR=platelet-to-lymphocyte ratio.

DISCUSSION

In this study, majority of the patients who were diagnosed with ACS were noted to be male, hypertensive, nondiabetic, and nonsmoker. This finding is similar to the studies done by Zheng et al[16] on Asian ACS patients who were on long-term antithrombotic treatment and Abrahan et al[15] on association of PLR with outcomes of Filipino ACS patients.

Patients who had in-hospital mortality in this study were mostly male and had diabetes and hypertension. The PLRs in these patients were higher compared with patients who were discharged without complications.

Based on the univariate logistic analysis, it has been found that a high PLR is significantly associated with occurrence of in-hospital mortality.[15] The association of high PLR with mortality in ACS patients was also demonstrated in other studies by Oylumlu et al,[10] Willim et al,[11] Hudzik et al,[12] and Ugur et al.[13] History of prior myocardial infarction was also noted to be significantly related with in-hospital mortality. The study showed that patients with a history of prior myocardial infarction is 2.5 times more likely to die.

Using the ROC curve analysis, the study was able to demonstrate a PLR >165 as an optimal cutoff value to predict

in-hospital mortality with a 52.17% sensitivity and 56.76% specificity. This is comparable to the PLACS study done by Abrahan et al[15] at UP-PGH. The PLR cutoff value derived in this study was higher than the one derived in Poland and China and lower compared with the value derived in Turkey.[12,13]

In terms of secondary outcome, it did not show significant relationship between a high PLR and development of complication, which is consistent with the findings in the PLACS study.[15] On the other hand, age has been found to be significantly related to development of complications: the older the patient, the more likely to develop complications during the hospital stay. Moreover, patients with hypertension are also 1.68 times more likely to develop complications.

This study also showed that increasing lymphocyte count decreases the risk of primary outcome of in-hospital mortality and secondary outcome of developing complications. This is consistent with the study by Zafrir et al[17] published in the European Heart Journal that showed lymphopenia is associated with long-term mortality.

LIMITATIONS AND RECOMMENDATIONS

The study was conducted in only one center. To better assess the correlation of PLR and ACS outcomes, other hospitals in the province should be included to have a larger sample. For future studies, incorporating laboratory profile of ACS patients and risk scoring systems into PLR can further assess the sensitivity and specificity of PLR.

CONCLUSION

A PLR of >165 is a cheap, readily available marker that can be used to predict in-hospital mortality among Filipino patients with ACS. This tool can be included in the risk stratification of the patient and can help in the decision-making of the health care team in terms of aggressiveness of therapeutic intervention.

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