Association of the Platelet–Lymphocyte Ratio (PLR) with Outcomes in Patients Admitted for Acute Coronary Syndrome: The PLACS Study

Lauro L. Abrahan IV, M.D.*; Jaime Alfonso M. Aherrera, M.D.*; John Daniel A. Ramos, M.D.*; Paul Ferdinand Reganit, M.D.**; Felix Eduardo Punzalan, M.D.**

Abstract

Introduction: Patients with acute coronary syndrome (ACS) exhibit a wide spectrum of early risk of death (one to 10 percent). High platelet counts may indicate a propensity for platelet-rich thrombi. Lymphocyte counts drop during ACS due to stress-induced cortisol release. Combining these two markers, recent studies have found that the platelet-to-lymphocyte ratio (PLR) is associated with adverse cardiac events among patients with ACS, but local data is limited. The objective of this study is to determine if an elevated PLR taken on admission is associated with higher rates of adverse cardiac events.

Methods: A retrospective cohort of adult patients with ACS admitted at the UP-Philippine General Hospital was analyzed. Leukocyte and platelet counts were measured by an automated hematology analyzer. The PLR values of these patients were computed, and they were stratified into two groups after determining the optimal cut-off from the receiver operating characteristic curve (ROC) curve. The primary outcome was in-hospital mortality. Secondary outcomes included development of heart failure, cardiogenic shock, reinfarction, and significant arrhythmias.

Results: A total of 174 Filipinos with ACS were included. In-hospital mortality occurred in 30 patients (17%). These patients had a higher PLR compared to those who were discharged alive (*p*-value <0.0001). The optimal cutoff value of PLR to predict in-hospital mortality is 165, with a sensitivity of 77% and specificity of 70% (area under the ROC curve of 0.766). On multiple logistic regression analysis, a high PLR was an independent predictor of in-hospital mortality (RR 8.52; *p* 0.003) after controlling for the effect of other variables. The development of the predetermined secondary outcomes did not correlate with PLR on multivariate analysis.

Conclusion: Among Filipino patients with ACS, an elevated PLR taken within 24 hours of admission is a useful marker to predict in-hospital mortality, thus providing vital information for risk stratification and more aggressive management strategies.

Keywords: platelet-lymphocyte ratio, acute coronary syndrome

Introduction

Inflammation plays a central role in the atherosclerotic process that underlies coronary artery disease (CAD).[1] Platelets, in particular, have a crucial part in the pathogenesis of atherosclerosis. They interact with endothelial cells and white blood cells (WBCs), releasing chemoattractant substances that facilitate monocyte transmigration through the vessel wall. [2,3] Low-grade inflammation, through a variety of mediators, also induces thrombocytosis.[4] Several studies have demonstrated the association of thrombocytosis with decreased survival and poor clinical outcomes following an acute coronary event.[5,6,7,8]

Lymphocytes, on the other hand, have been implicated in regulating the inflammatory response during the development of atherosclerotic lesions,[9] and low lymphocyte counts have been correlated with higher mortality and low ejection fraction (EF) in patients with acute coronary syndrome (ACS).[10,11] It is theorized that high cortisol levels from the stress of ACS leads to lymphopenia via apoptosis. [12,13]

Combining platelet count with the lymphocyte count yields the platelet-lymphocyte ratio (PLR), and several foreign studies have already substantiated the use of PLR as a prognostic marker (Appendix A, Table I). Given the generally limited resources in our healthcare system, the PLR may be a useful but inexpensive tool for risk stratification in Filipino patients with ACS, and may have improved discriminative capability compared to either platelet or lymphocyte count alone. Prognostication is a vital element in the ACS treatment pathway, since patients known to have high risk features and increased mortality rates will likely benefit from more aggressive and/or invasive strategies such as early percutaneous coronary intervention. To our knowledge, this is the first study examining this simple but reliable tool in our local setting.

*Fellow in training, Section of Cardiology, Department of Medicine, University of the Philippines-Philippine General Hospital
**Consultant, Section of Cardiology, Department of Medicine, University of the Philippines-Philippine General Hospital

*Corresponding author: Lauro L. Abrahan IV, M.D., University of the Philippines – Philippine General Hospital, Manila, Philippines
Email: s.abrahan@gmail.com*

Research Question:

Among patients diagnosed with ACS in the Philippine General Hospital (PGH), is an elevated PLR taken within 24 hours of admission associated with higher rates of cardiovascular mortality and morbidity?

Objectives

General Objective

1. To determine if PLR taken within 24 hours of hospital admission is associated with adverse outcomes in patients diagnosed with ACS

Specific Objectives

1. To describe the clinical and laboratory profile of patients admitted for ACS
2. To determine the optimal cut-off value of PLR for predicting in-hospital mortality in patients diagnosed with ACS
3. To determine if there is a correlation between a high PLR on admission and the occurrence of adverse outcomes
    a. Primary outcome: in-hospital mortality
    b. Secondary outcomes: development of heart failure (or worsening of chronic compensated heart failure), reinfarction, arrhythmias, cardiogenic shock
4. To enumerate other predictors of adverse cardiovascular outcomes in ACS

Methods

This study is a single-center, retrospective cohort study conducted at the UP-PGH. All admitted adult patients with a diagnosis of ACS (UA, NSTEMI, STEMI) at UP-PGH within a span of seven months were screened. The diagnosis of ACS was independently verified by two of the investigators using the universal definition of ACS (Appendix B). Patients who met any of the following exclusion criteria were not included in the study: any form of infection on admission, any acute inflammatory/autoimmune condition (including, but not limited to, acute renal failure, gout in flare, lupus in flare, etc.), active tuberculosis, any hematologic disease, bleeding of any form, managed at a different facility prior to UP-PGH, and onset of symptoms more than 24 hours prior to admission.

The complete blood count on admission (sent to our centralized laboratory utilizing the automated Beckman Coulter® UniCel DxH 800 Cellular Analysis System) of these patients was recorded in the standardized data sheet (Appendix C). The PLR values of these patients were computed: platelet count divided by lymphocyte count. Their in-hospital course was then monitored for the development of the predetermined outcomes. The primary outcome for this study was in-hospital death (cardiac or non-cardiac). Secondary outcomes were the following: development or worsening of heart failure, reinfarction, significant arrhythmias (excluding premature atrial or ventricular complexes), and cardiogenic shock.

Descriptive analysis was done by obtaining the mean and standard deviation of quantitative variables. Proportions and frequencies were reported for qualitative variables. For quantitative variables, T-test of two independent samples was used to determine if there was a statistically significant difference. For categorical variables, the Z-test was used. The optimal cut-off for the PLR to predict adverse outcomes (in-hospital mortality) was determined using the receiver operating characteristic (ROC) curve. After determining the optimal cut-off, the population was divided into those with a high PLR versus a low PLR.

Logistic regression analysis was used to find correlation between a high PLR and the subsequent development of cardiovascular events with or without adjustments for potentially confounding baseline variables. Age, male sex, obesity (BMI >25 kg/m^2), high risk TIMI scores, elevated WBC, and occurrence of adverse cardiovascular events were also considered. A p-value < 0.25 was considered as a statistically significant association in univariate analysis. All significant variables were included in the final model of multivariate analysis to determine the association with the predetermined outcomes.

The protocol was submitted for ethical review to the University of the Philippines Manila Research Ethics Board (UPMREB) prior to data collection, and the study was carried out only upon ethical approval of the protocol. There is no conflict of interest in this study which may arise from financial, familial, or proprietary considerations of the primary and co-investigators or the study site. The investigators shouldered the cost of this research.

Results

Clinical Profile of Patients with ACS

In total, 174 patients recruited over a span of seven months were included in the analysis. The mean age was 59 ± 12 years, and 72% of the sample population was male. The baseline characteristics of these patients are summarized in Table I, classified according to the primary outcome of in-hospital mortality, which occurred in 30 patients (17.2%). Patients who died were older (p=0.001), predominantly male (p=0.034), and had a higher proportion of chronic kidney disease (CKD) as a co-morbidity (p=0.011). There were no significant differences in terms of other individual risk factors for ACS. Diagnosis on admission was unstable angina (26%), NSTEMI (34%), and STEMI (40%). Mortalities had higher TIMI risk scores and faster heart rates on admission.

Table I. Baseline clinical characteristics

Variables	Total (n=174)	Mortalities (n=30)	Survivors (n=144)	*p*-value
Age (mean ± SD)	59.05 ± 12.59	65.87 ± 13.01	57.63 ± 12.07	0.0010
Sex				
Male	48 (27.59)	13 (43.33)	35 (24.31)	
Female	126 (72.41)	17 (56.67)	109 (75.69)	0.0339
BMI (mean ± SD)	24.94 ± 3.34	25.25 ± 4.18	24.87 ± 3.15	0.5754
Co-Morbidities and Risks				
Diabetes	54 (31.03)	7 (23.33)	47 (32.64)	0.3162
Hypertension	127 (72.99)	24 (80.00)	103 (71.53)	0.3417
Dyslipidemia	67 (38.51)	12 (40.00)	55 (38.19)	0.8533
Smoker	71 (40.80)	11 (36.67)	60 (41.67)	0.6122
Chronic Kidney Disease	22 (12.64)	8 (26.67)	14 (9.72)	0.0111
Prior Angina	65 (37.36)	12 (40.00)	53 (36.81)	0.7421
Prior MI	49 (28.16)	10 (33.33)	39 (27.08)	0.4887
New York Functional Class				
I or II	172 (98.85)	29 (96.67)	143 (99.31)	
III or IV	2 (1.15)	1 (3.33)	1 (0.69)	0.2174
Prior Revascularization	12 (6.90)	3 (10.00)	9 (6.25)	0.4609
Documented CAD	19 (10.92)	3 (10.00)	16 (11.11)	0.8591
Diagnosis				
UA	45 (25.86)	3 (10.00)	42 (29.17)	
NSTEMI	59 (33.91)	16 (53.33)	43 (29.86)	0.0220
STEMI	70 (40.23)	11 (36.67)	59 (40.97)	
% Risk of Mortality Based on TIMI (mean ± SD)	13.95 ± 10.44	24.63 ± 10.43	11.72 ± 8.99	<0.0001
High Risk TIMI Score *	65 (37.36)	21 (70.00)	44 (30.56)	<0.0001
Heart Rate (mean ± SD)	81.26 ± 20.22	101.13 ± 22.40	77.12 ± 17.11	<0.0001
Admission Heart Rate >100 bpm	27 (15.52)	16 (53.33)	11 (7.64)	<0.0001

*TIMI Score: A high risk TIMI score was >3 points for UA/NSTEMI and >5 points for STEMI. Components of the score include age, diabetes/hypertension/angina, systolic BP ≥100, heart rate > 100, Killip class, weight, anterior ST elevation or LBBB on ECG, and time to treatment for STEMI; and age ≥65, ≥3 traditional risk factors for vascular disease, known coronary stenosis ≥50%, presence of >0.5 mm ST segment deviation on admission ECG, angina episodes within the last 24 hours, positive biomarkers, and use of ASA in the last 7 days for UA/NSTEMI.

Table II. Patient laboratory findings

Variables	Total (n=174)	Mortalities (n=30)	Survivors (n=144)	*p*-value
Hemoglobin (mean ± SD)	130.22 ± 22.36	123.40 ± 21.93	131.65 ± 22.26	0.0660
WBC (mean ± SD)	11.73 ± 9.00	15.28 ± 16.47	10.99 ± 6.31	0.0170
Platelet (mean ± SD)	253.27 ± 82.73	265.93 ± 99.09	250.63 ± 79.04	0.3583
Lymphocyte (mean ± SD)	20.13 ± 10.71	12.03 ± 6.91	21.82 ± 10.61	<0.0001
PLR (mean ± SD)	160.05 ± 102.91	242.10 ± 128.78	142.96 ± 87.99	<0.0001
Trop I (n=129, mean ± SD)	18.19 ± 27.08	10.22 ± 17.18	20.10 ± 28.70	0.1014
CKMB (n=53, mean ± SD)	72.09 ± 106.69	39.10 ± 31.34	79.76 ± 116.46	0.2819
Creatinine (n=169, mean ± SD)	149.84 ± 160.83	239.52 ± 263.45	131.26 ± 123.52	0.0008

Table III. In-hospital adverse cardiovascular events

Variables	Total (n=174)	Mortalities (n=30)	Survivors (n=144)	*p*-value
Reinfarction	26 (14.94)	11 (36.67)	15 (10.43)	0.0002
Severe CHF	61 (35.06)	28 (93.33)	33 (22.92)	<0.0001
Arrhythmia	31 (17.82)	12 (40.00)	19 (13.19)	0.0005
Cardiogenic Shock	54 (31.03)	21 (70.00)	33 (22.92)	<0.0001

Laboratory Profile of Patients with ACS

Table II describes the laboratory parameters for the patients in this study. PLR was demonstrated to be significantly higher for patients in the mortality group ($p< 0.0001$). The mean PLR of patients who died was 242.10, while the mean PLR of patients who survived was 142.96. Of note, there was no significant statistical difference between mean platelet counts of non-survivors and survivors (265.93 vs. 250.63, $p=0.358$). There was also no significant difference between the two groups in terms of levels of cardiac enzymes (whether troponin I or CKMB). Creatinine levels were higher in patients who expired.

Outcomes

Thirty patients (17%) experienced the primary outcome of mortality. Table III shows that the occurrence of the other secondary adverse cardiovascular events was all significantly higher for the patients who expired.

Optimal Cut-Off of PLR to Predict In-Hospital Mortality

In the ROC analysis (Figure 1), a PLR >165 had 76.7% sensitivity and 70.1% specificity to predict death, with an area under the curve or C-statistic of 0.766. A cut-off PLR of >165 is therefore associated with higher risk for mortality.

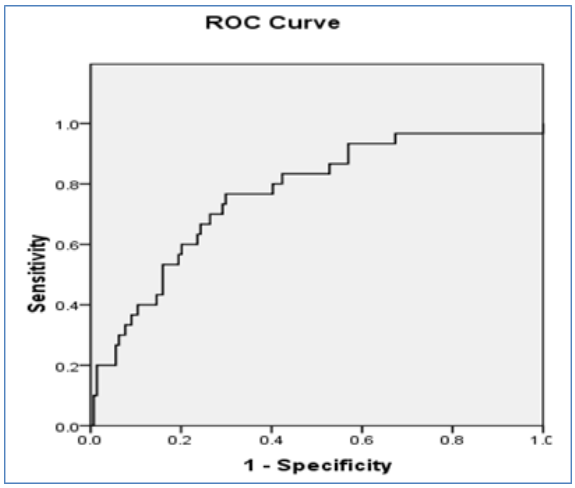

FIGURE 1. ROC curve for PLR to predict in-hospital mortality in ACS.

Table IV. Univariate analysis: predictors of in-hospital mortality

Variables	Relative Risk	*p*-value
Age > 50 years	2.41 (0.79 – 7.36)	0.121
Male Sex	0.42 (0.19 – 0.95)	0.037
BMI > 25 kg/m^2	1.60 (0.73 – 3.53)	0.244
High Risk TIMI Score	5.30 (2.25 – 12.50)	<0.001
PLR > 165.35	7.72 (3.08 – 19.33)	<0.001
WBC > 12 x 109/L	1.04 (1.00 – 1.08)	0.072
Occurrence of Complications		
Reinfarction	4.98 (1.99 – 12.43)	0.001
Severe CHF	47.09 (10.65 – 208.16)	<0.001
Arrhythmia	4.39 (1.83 – 10.53)	0.001
Cardiogenic Shock	7.85 (3.28 – 18.78)	<0.001

Table V. Multivariate analysis: independent predictors of in-hospital mortality

Variables	Relative Risk	*p*-value
Severe CHF	28.12 (5.40 – 146.31)	<0.001
High PLR > 165.35	8.52 (2.06 – 35.21)	0.003
High Risk TIMI Score	4.81 (1.29 – 17.93)	0.019
BMI > 25 kg/m^2	4.09 (1.06 – 15.74)	0.040

Predictors of In-Hospital Mortality (Primary Outcome)

Univariate logistic regression analysis determined the association of certain variables with in-hospital mortality: age >50 years, male sex, obesity (BMI >25 kg/m^2), high risk TIMI scores, high PLR (>165), elevated WBC (>12 x 109), and occurrence of adverse cardiovascular events. Table IV shows the results of univariate analysis. On multivariate analysis (Table V), a high PLR value of > 165 was demonstrated as an independent predictor of in-hospital mortality (RR 8.52; $p= 0.003$), after adjusting for other factors. Other significant predictors include HR >100 beats/min. (RR 10.46; $p=0.001$), severe CHF (RR 28.12; $p < 0.001$), high risk TIMI score (RR 4.81; $p = 0.019$) and obesity (RR 4.09; $p=0.04$). The relative risk of mortality in patients with an elevated PLR (>165) is 8.52 times higher than those with lower PLR values (CI 2.06 – 35.21, $p=0.003$), thus supporting our hypothesis that there is indeed a statistically significant correlation between a high PLR and mortality in ACS patients.

Table VI. Multivariate analysis: independent predictors of secondary outcomes

Outcome	Independent Predictors
Heart Failure	Shock, reinfarction, age > 50, male sex
Cardiogenic Shock	Severe CHF, high risk TIMI score, age > 50
Reinfarction	Severe CHF
Arrhythmia	Shock, male sex

Predictors of Secondary Outcomes

The secondary outcomes (development of heart failure, cardiogenic shock, reinfarction, and significant arrhythmias) did not correlate with PLR on multivariate analysis. Other variables such as male sex and age >50 were more prominent as independent predictors for these complications of ACS (Table VI).

Discussion

Our present study examined the relationship between PLR on admission and in-hospital mortality in ACS patients. Baseline clinical characteristics between mortalities and survivors were mostly similar, with the exception of age, sex, and presence of CKD. The higher TIMI risk scores in patients who died is supported by previous studies that examined the use of the TIMI score as a prognostic tool for patients with ACS.[14,15,16] A notable finding is that the level of cardiac enzymes (troponin, CKMB) did not differ significantly between the two groups, which can be partly explained by incomplete sampling and non-standardized timing of serum collection (ranging from one hour to three days). Faster heart rates on admission were also seen in the mortality group, which highlights the importance of adequate heart rate control in the early post-MI period.

In our multivariate logistic regression analysis, we demonstrated that high PLR is a statistically significant and independent predictor of in-hospital mortality in patients with ACS. Interestingly though, mean platelet count was not significantly different between mortalities and survivors (265.9 x 10^9/L vs. 250.6 x 10^9/L, p=0.338), implying that PLR may actually be a more reliable marker for prognosis than platelet count alone. From the ROC analysis of our data set, we have determined a PLR >165 as the optimal cut-off value for predicting in-hospital mortality in ACS (sensitivity of 76.70% and specificity of 70.10%, area under the curve 0.766). The mechanism behind this association of elevated PLR with increased mortality may be explained by a higher degree of antiplatelet drug resistance and/or more platelet-rich thrombi in atherosclerotic plaques.[17]

Our findings are consistent with other studies in foreign literature that have reviewed the relationship of PLR with various cardiovascular surrogate and clinical outcomes. The most similar to our study was that of Oylumlu et al.[17], albeit with a slightly lower optimal PLR cut-off value of 142. Azab et al.[18] found PLR to be an independent predictor of four-year mortality in NSTEMI patients. Also examining NSTE-ACS patients, Bekler et al.[13] showed that PLR correlated well with poor LV systolic function on echocardiography. The studies by Hudzik et al.[19], Temiz et al.[20], and Ugur et al.[21] focused on STEMI patients, and they all successfully demonstrated high PLR to be a predictor of mortality for this subset of ACS. In terms of angiographic grading for CAD, Kurtul et al.[22] and Yüksel et al.[23] showed that higher PLR correlated with higher SYNTAX and Gensini scores, respectively. Finally, Gary et al.[24] found high PLR to be an independent marker for critical limb ischemia in patients with PAD. The major findings of these studies are summarized in Appendix A.

There is a mild degree of variation in the optimal PLR value used as a cut-off for the aforementioned publications as well as our own study, ranging from 111 to 176. These may be accounted for by racial differences in the study populations, together with some permutations as to the exact subset of ischemic heart disease included for the studies (NSTE-ACS vs. STEMI vs. stable CAD). In addition, some studies examined surrogate outcomes such as left ventricular ejection fraction on echocardiography and lesion severity on coronary angiography instead of patient mortality. Nevertheless, these studies all generally agree that high PLR values portend a poorer prognosis for patients with atherosclerotic disease.

In terms of the secondary outcomes, PLR failed to significantly correlate with any of the adverse cardiovascular morbidities that were monitored for this study (reinfarction, severe HF, significant arrhythmias, and cardiogenic shock). This seeming disparity may be explained by limitations in the study design, particularly the short follow-up duration. Patients were only monitored during their hospital confinement, and major adverse CV events may have occurred after hospital discharge.

Limitations and Recommendation

This study represented a single-center experience and only examined in-hospital mortality and outcomes. Recommendations for future studies include involvement of other major health centers to enlarge the sample size, as well as long-term follow-up that extends even beyond hospital discharge.

Conclusion

Among patients with ACS, a high PLR >165 taken within 24 hours of presentation is a useful and readily available marker to predict in-hospital mortality. The PLR values of ACS patients who died (PLR 242.10) were significantly higher compared to

the survivors (PLR 142.96). For this cohort, however, PLR did not correlate with the development of other major adverse cardiovascular outcomes, such as worsening heart failure, reinfarction, arrhythmias, and cardiogenic shock. Other independent predictors of mortality among ACS patients included the development of severe heart failure, high risk TIMI scores, and BMI > 25 kg/m^2. Used in conjunction with clinical judgment and other risk scoring systems, a high PLR in ACS patients may reflect the need for more aggressive therapeutic interventions. This paper represents the first endeavor to investigate the utility of PLR in Filipino ACS patients, and can pave the way for future studies.

References

1. **Hansson GK**. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med 2005; 352: 1685-95.
2. **Gawaz M, Langer H, May AE**. Platelets in inflammation and atherogenesis. J Clin Invest 2005; 115: 3378-84.
3. **Lindemann S, Kramer B, Seizer P, Gawaz M.** Platelets, inflammation and atherosclerosis. J Thromb Haemost 2007; 5: 203-11.
4. **Alexandrakis MG, Passam FH, Moschandrea IA, Christophoridou AV, Pappa CA, Coulocheri SA, et al**. Levels of serum cytokines and acute phase proteins in patients with essential and cancer-related thrombocytosis. Am J Clin Oncol 2003; 26: 135-40.
5. **Iijima R, Ndrepepa G, Mehilli J, Bruskina O, Schulz S, Schomig A, et al**. Relationship between platelet count and 30 day clinical outcomes after percutaneous coronary interventions. Pooled analysis of four ISAR trials. Thromb Haemost 2007; 98: 852-7.
6. **Nikolsky E, Grines CL, Cox DA, Garcia E, Tcheng JE, Sadeghi M, et al**. Impact of baseline platelet count in patients undergoing primary percutaneous coronary intervention in acute myocardial infarction (from the CADILLAC trial). Am J Cardiol 2007; 99: 1055-61.
7. **Jakl M, Sevcik R, Ceral J, Fatorova I, Horacek JM, Vojacek J. Mean** platelet volume and platelet count: overlooked markers of high on-treatment platelet reactivity and worse outcome in patients with acute coronary syndrome. Anadolu Kardiyol Derg 2014; 14: 85-6.
8. **Ly HQ, Kirtane AJ, Murphy SA et al**: Association of platelet counts on presentation and clinical outcomes in ST-elevation myocardial infarction (from the TIMI Trials). Am J Cardiol, 2006; 98: 1–5.
9. **Mallat Z, Tedgui A**. Immunomodulation to combat atherosclerosis: The potential role of immune regulatory cells. Expert Opin Biol Ther. 2004 Sep;4(9):1387-93.
10. **Nuñez, J, Sanchiz J, Bodí V, et al**. Relationship between low lymphocyte count and major cardiac events in patients with acute chest pain, a non-diagnostic electrocardiogram and normal troponin levels. Atherosclerosis. 2009 Sep;206(1):251-7.
11. **Blum A, Sclarovsky S, Rehavia E, Shohat B**. Levels of T-lymphocyte sub-populations, interleukin-1 beta, and soluble interleukin-2 receptor in acute myocardial infarction. Am Heart J 1994;127:1226-30.
12. **Gupta S, Agrawal A, Agrawal S, Su H, Gollapudi S**. A paradox of immunodeficiency and inflammation in human aging: lessons learned from apoptosis. Immun Ageing 2006; 3: 5.
13. **Bekler A, Gazi E, Yılmaz M, et al.** Could elevated platelet-lymphocyte ratio predict left ventricular systolic dysfunction in patients with non-ST elevated acute coronary syndrome? Anadolu Kardiyol Derg. 2014 Apr 16.
14. **Antman EM, Cohen M, Bernink PJ, et al**. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. JAMA. 2000 Aug 16;284(7):835-42.
15. **Hess EP, Agarwal D, Chandra S, et al.** Diagnostic accuracy of the TIMI risk score in patients with chest pain in the emergency department: a meta-analysis. CMAJ. 2010 Jul 13;182(10):1039-44.
16. **Morrow DA, Antman EM, Charlesworth A, et al**. TIMI risk score for ST-elevation myocardial infarction: A convenient, bedside, clinical score for risk assessmentat presentation: An intravenous nPA for treatment of infarcting myocardium early II trial substudy. Circulation. 2000 Oct 24;102(17):2031-7.
17. **Oylumlu M, Yıldız A, Oylumlu M, et al.** Platelet-to-lymphocyte ratio is a predictor of in-hospital mortality patients with acute coronary syndrome. Anadolu Kardiyol Derg. 2014 Apr 8.
18. **Azab B, Shah N, Akerman M, et al.** Value of platelet/lymphocyte ratio as a predictor of all-cause mortality after non-ST-elevation myocardial infarction. J Thromb Thrombolysis. 2012 Oct;34(3):326-34.
19. **Hudzik B, Szkodzinski J, Gorol J, et al.** Platelet-to-lymphocyte ratio is a marker of poor prognosis in patients with diabetes mellitus and ST-elevation myocardial infarction. Biomark Med. 2015 Mar;9(3): 199-207.
20. **Temiz A, Gazi E, Güngör Ö, et al.** Platelet/lymphocyte ratio and risk of in-hospital mortality in patients with ST-elevated myocardial infarction. Med Sci Monit. 2014 Apr 22;20:660-5.
21. **Ugur M, Gul M, Bozbay M, et al.** The relationship between platelet to lymphocyte ratio and the clinical outcomes in ST elevation myocardial infarction underwent primary coronary intervention. Blood Coagul Fibrinolysis. 2014 Dec;25(8):806-11.
22. **Kurtul A, Murat SN, Yarlioglues M, et al.** Association of platelet-to-lymphocyte ratio with severity and complexity of coronary artery disease in patients with acute coronary syndromes. Am J Cardiol. 2014 Oct 1;114(7):972-8.
23. **Yüksel M, Yıldız A, Oylumlu M, et al.** The association between platelet/lymphocyte ratio and coronary artery disease severity. Anadolu Kardiyol Derg. 2014 Jul 11.
24. **Gary T, Pichler M, Belaj K, et al.** Platelet-to-lymphocyte ratio: a novel marker for critical limb ischemia in peripheral arterial occlusive disease patients. PLoS One. 2013 Jul 2;8(7):e67688.
25. **Cannon CP, Battler A, Brindis RG, et al.** American College of Cardiology key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes: a report of the American College of Cardiology Task Force on Clinical Data Standards (Acute Coronary Syndromes Writing Committee). J Am Coll Cardiol 2001;38:2114-30.

APPENDIX A

Summary of published literature involving PLR in atherosclerotic disease

Author	Population	Outcome	Results
Oylumlu et al. (2014)	587 ACS patients	In-hospital mortality	High PLR is an independent predictor of mortality in ACS patients OR = 1.012 (1.005-1.087, *p* = 0.027) ROC: PLR > 142 had 69% sensitivity, 63% specificity
Azab et al. (2012)	619 NSTEMI patients	four-year all-cause mortality	High PLR is an independent predictor of 4-year mortality in NSTEMI patients For patients with PLR > 176, those on dual antiplatelets had lower mortality than single antiplatelet (*p* = 0.0018).
Bekler et al. (2014)	220 NSTE-ACS patients	LV systolic dysfunction(EF ≤ 40%)	High PLR is an independent predictor of LV systolic dysfunction in NSTE-ACS patients OR = 2.88 (1.39-5.95, *p* = 0.004)
Hudzik et al. (2015)	523 STEMI patients with DM	In-hospital & one-year mortality	High PLR is an independent predictor for in-hospital and 1-year mortality in STEMI patients with DM ROC: optimal cut-off value for predicting early mortality was higher than that for late mortality (PLR > 155 vs. 146)
Temiz et al. (2014)	636 STEMI patients	In-hospital mortality	High PLR is an independent predictor of mortality in STEMI HR = 2.16 (1.16-4.0, *p* = 0.014) ROC: PLR > 144 had 51% sensitivity, 69% specificity
Ugur et al. (2014)	639 STEMI patients (s/p PCI)	six-month all-cause mortality	High PLR is an independent predictor of 6-month mortality in STEMI patients who undergo PCI OR = 2.51 (1.058-5.95, *p* = 0.03)
Kurtul et al. (2014)	1016 ACS patients (s/p CA)	SYNTAX score	High PLR is an independent predictor of higher SYNTAX score in ACS patients who undergo urgent CA OR = 1.018 (1.013-1.023, *p* < 0.001) ROC: PLR ≥ 116 had 71% sensitivity and 66% sensitivity
Yüksel et al. (2014)	388 CAD patients	Severity of atherosclerosis (Gensini score)	High PLR is an independent predictor of severe atherosclerosis ß = 0.141 (*p* = 0.004) ROC: PLR > 111 had 61% sensitivity, 59% specificity
Gary et al. (2013)	2121 PAD patients	Critical limb ischemia (CLI)	High PLR is an independent predictor of CLI in PAD patients OR = 1.9 (1.7-2.1, *p* < 0.001) ROC: PLR > 150 optimal cut-off value

APPENDIX B
Operational Definitions

Myocardial Infarction	Defined by the presence of symptoms suggestive of ischemia or infarction, with either electrocardiographic evidence (new Q waves in two or more leads) or cardiac-marker evidence of infarction, according to the standard Thrombolysis in Myocardial Infarction (TIMI) and American College of Cardiology definition[25]
Unstable Angina	Defined as ischemic discomfort at rest for at least 10 minutes prompting rehospitalization, combined with one of the following: ST-segment or T-wave changes, cardiac-marker elevations that were above the upper limit of normal but did not meet the criteria for myocardial infarction, or a second episode of ischemic chest discomfort lasting more than 10 minutes and that was distinct from the episode that had prompted hospitalization[25]
Cardiogenic Shock	Defined as a systolic arterial pressure of less than 80 mm Hg for a duration of at least 30 minutes with evidence of organ hypoperfusion (clouded sensorium, cold extremities, oliguria, acidosis) and/or low urine output (<0.5ml/kg/hr) and with a pulse rate >60 beats per minute with or without evidence of pulmonary congestion
Heart Failure (HF)	Defined as development of signs/symptoms of systolic dysfunction such as dyspnea, orthopnea, neck vein engorgement, rales/crackles, edema, pulmonary congestion on chest X-ray, or ejection fraction < 50% on echocardiography • Mild HF: Rales in 50% or less of the lung fields • Severe HF: Rales in more than 50% of the lung fields / evidence of pulmonary edema
Decompensation of Chronic Heart Failure	Defined as development of worsening signs/symptoms of systolic dysfunction (as above) from a patient with a known diagnosis of congestive heart failure prior to present admission
Reinfarction	Defined by development of recurrence of symptoms during the admission after initial management. It may be an ST elevation or non-ST elevation myocardial infarction

APPENDIX C
DATA COLLECTION SHEET

GENERAL DATA

Number								
Location		**Age / Sex**		**Weight / Height**			**BMI**	
RISKS		Diabetes	**RISKS**	Prior Angina	**PRIOR MEDS**		Beta Blocker	
		Hypertension		Prior MI			Antiplatelets	
		Dyslipidemia		Prior CHF			Anticoagulants	
		PAD		Previous PCI / CABG			ARB/ACEi	
		Former Smoking		Documented CAD			Calcium Ch Block	
		Current Smoker		History of CVD/TIA			Statins	
		CKD		Others:			Nitrates	
		Family History: CAD					Digoxin	
		Others:					Non Compliant	
							Others:	

Date of Admission			**Date Discharged**				
Admission Diagnosis		**STEMI**		**NSTEMI**		**Unstable Angina**	
Basis of Diagnosis	☐ Symptoms ☐ Cardiac Enzymes ☐ ECG						
Time from Symptom Onset							
Other Diagnosis							
ECG Reading	Rate:	aVR Elevation?	QT / QTc:	EF (2.264 avr) + (age x 0.645):			
	Final Reading:						
Complete Blood Count	Hemoglobin		Neutrophils				
	WBC Count		Lymphocytes				
	Platelet Count		Monocytes				
Laboratory Work Up on Admission	Trop I:		CKMB				
	EF Teicholz		EF Simpsons				
	LVEDD		Creatinine				
	Cholesterol		HDL				
	LDL		TG				
Management	**Medical**				**Reperfusion**		
		Beta Blocker		Calcium Ch Blck		PCI	
		Antiplatelets		Statins		CABG	
		Anticoagulants		Nitrates		Thrombolysis	
		ARB/ACEi		Digoxin			

OUTCOMES (If No Complications occurred, may Disregard this part)

Complications During Present Admission		Death from Cardiac Cause Date of Death: Cause of Death:
		Death from Non-Cardiac Cause Date of Death: Cause of Death:
		Heart Failure Mild Severe
		Shock
		Re-Infarction NSTEMI STEMI
		Development of High Risk Pneumonia
		Development of Dialysis requiring renal failure
		CP arrest, but survived
		Arrhythmia (Bradyarrhythmia, Tachyarrhythmia): _____
Complications After Discharge **(within 30 day period)**		Death from Cardiac Cause Date of Death: Cause of Death:
		Death from Non-Cardiac Cause Date of Death: Cause of Death:
		Heart Failure
		Re-Hospitalization – Indicate Reason:
		Others (enumerate):