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Original Article

Anemia at Admission and Clinical Outcomes in Patients With Acute ST-Segment-Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

Background: Anemia is common in ST-elevation myocardial infarction (STEMI) patients. The influence of anemia on the prognosis of STEMI patients remains unclear. Robust data are lacking regarding the outcome of patients with moderate-to-severe anemia who present with STEMI and who are treated via primary percutaneous coronary intervention (PCI). This study aimed to evaluate the effects of chronic anemia on major adverse cardiovascular and cerebral events (MACCE) in patients with STEMI undergoing primary PCI.

Methods: The present study recruited 330 consecutive STEMI patients who underwent primary PCI from November 2017 through October 2019 at our cardiology department. The study population was divided into 2 groups according to the hemoglobin level after primary PCI. The patients' baseline clinical characteristics and relationships between hemoglobin levels and the incidence of MACCE during a 1-year follow-up were recorded.

Results: Patients with a hemoglobin level of less than 11 g/dL were elderly, had a lower body mass index, a higher incidence rate of diabetes, a higher Killip class at presentation, and a higher incidence rate of MACCE. Anemia at admission was an independent predictor of MACCE during hospitalization and on post-primary PCI follow-ups at 30 days, 6 months, and 1 year after PCI (P=0.034, 0.028, 0.0032, and 0.0042, respectively).

Conclusions: Age, hypertension, and diabetes in STEMI patients with moderate-to-severe anemia were associated with an increased incidence rate of MACCE. Moderate-to-severe anemia at admission was an independent predictor of MACCE during hospitalization and on post-primary PCI follow-ups at 30 days, 6 months, and 1 year. ***(Iranian Heart Journal 2021; 22(2): 58-67)***

KEYWORDS: Myocardial infarction, Hemoglobin level, Primary PCI

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Primary percutaneous coronary intervention (PCI) is the preferred treatment option for patients with ST-segment-elevation myocardial infarction (STEMI). Following the procedure, patients are kept on antiplatelets and sometimes anticoagulants. [1] The latest guidelines recommend dual antiplatelet therapy for 1

year after acute coronary syndromes, regardless of the strategy of treatment. [2, 3] Several studies have correlated the presence of anemia in patients with acute coronary syndromes with the outcome, and it is deemed a good predictor of major bleeding. [4] Further, patients receiving dual antiplatelet therapy are at a high risk of bleeding. [5]

Anemia is present in about 15% of patients presenting with acute myocardial infarction (MI), with the percentage rising to 43% in elderly patients with acute MI. [6, 7] Anemia has the potential to worsen the myocardial ischemic effect in acute MI and acute coronary syndromes by decreasing the oxygen content of the blood supplied to the ischemic myocardium and by increasing myocardial oxygen demand through triggering a higher cardiac output to maintain enough systemic oxygen delivery. [8] The incidence of complications in patients with cardiovascular diseases such as uncontrolled hypertension, thromboembolic events, and bleeding complications may be correlated with anemia. [9, 10]

Patients with moderate-to-severe anemia have been excluded from hitherto-conducted trials testing the efficacy and safety of antiplatelets and anticoagulants. [3] Consequently, robust evidence-based data are lacking regarding their safety in this group of patients.

METHODS

From November 2017 to October 2019, 330 consecutive patients with STEMI who were admitted to our cardiology department were selected. All the patients were treated by primary PCI. The diagnosis of STEMI was based on the European guidelines. [2] The exclusion criteria were chronic kidney disease with an estimated glomerular filtration rate of less than 45 mL/min/1.73 m^2, a recent history of trauma or major surgery leading to significant blood loss over the preceding 3 months, cancer, contraindications to prolonged antiplatelet therapy, and unavailability of clinical or angiographic data.

The study population was classified into 2 groups according to the hemoglobin (Hb) level and the severity of anemia based on blood samples obtained immediately after primary PCI. Group I consisted of 170 patients with moderate-to-severe anemia [11] (Hb<11 g/dL) and Group II comprised 140 patients with Hb levels ranging between 11 g/dL and 16 g/dL. The level of Hb was measured from venous blood just after primary PCI. Also measured were biochemical indices, including serum creatinine, blood sugar, and blood lipid profile.

All the patients undergoing primary PCI were given aspirin (300 mg), clopidogrel (600 mg), or ticagrelor (180 mg) before the procedure and 70 IU/kg of unfractionated heparin during the procedure. The selection of the P2Y12 inhibitor was left to the discretion of the attending physician. After primary PCI, aspirin (100 mg, QD), ticagrelor (90 mg, BID), or clopidogrel (75 mg, QD) were administered, and the choice of the P2Y12 inhibitor was once again left to the discretion of the attending physician.

The patients were followed up at 1 month, 6 months, and 1 year following primary PCI either by clinical visits or by phone. The study endpoint was the occurrence of major adverse cardiovascular and cerebral events (MACCE) during the follow-up period. MACCE was considered to comprise all-cause mortality, MI, target vessel revascularization, unstable angina necessitating hospitalization, and heart failure.

Demographic data, medical history, clinical examination findings on admission, biochemical findings, angiographic findings, and echocardiogram data were recorded. An informed written consent form was signed by all the patients included in the study, and the protocol of the study was approved by the local research committee.

Statistical Analysis

The collected data were tabulated and statistically analyzed with the Prism 5 statistical computer package, version 5. The Kolmogorov–Smirnov test was utilized to test normal distribution among continuous data. Quantitative data were expressed as the mean ± the standard deviation (SD). Qualitative data were expressed as frequencies and percentages. For normally distributed data, the independent samples *t*-test of significance was used when 2 mean values were compared between the study groups. The χ^2 test of significance was employed to compare proportions between 2 qualitative parameters. Univariable and multivariable Cox proportional hazard models were used to identify the independent predictors of MACCE. Statistically significant parameters were selected for a multivariable analysis and expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). Survival was graphically presented through the Kaplan-Meier curves. Differences in survival rates were compared via the log-rank test. A *P* value of less than 0.05 was considered significant.

RESULTS

The study population consisted of 330 patients. The patients' baseline clinical data are presented in Table 1, and their biochemical, angiographic, and echocardiographic findings are shown in Table 2. Patients with an Hb level of less than 11 g/dL (Group I) were older than the patients in Group II (mean age=63.2±8.4 vs 60.1±9.6 y; *P*=0.003). Patients in Group I had a lower body mass index (BMI) than those in Group II (the mean BMI=23.20 vs 26.10; *P*=0.005). The incidence of diabetes was higher in Group I than in Group II (34% [n=48] vs 32% [n=55]).

There were more patients in Group I who were in a Killip class higher than I (23.5% [n=40] vs 19.2% [n=28]; *P*<0.001). Concerning biochemical data, there was no statistically significant difference between both groups except that Group I had higher mean random blood sugar and glycosylated Hb levels (*P*=0.01 and 0.047, respectively).

Apropos of the angiographic findings, the incidence of the use of thrombus aspiration during primary PCI was higher in Group I (*P*=0.071). On the other hand, echocardiographic parameters, biochemical tests, and medications at discharge showed no significant differences between the 2 groups (Table 2).

MACCE During Admission

During the hospital stay, the incidence of MACCE was significantly higher in Group I than in Group II (4.7% [n=8] vs 2.14% [n=3]; *P*=0.034) (Table 3).

MACCE During Follow-up

All the patients underwent clinical follow-ups after 1 month. Total MACCE was reported in 16 patients (9.4%) in Group I and 8 patients (5.71%) in Group II (*P*=0.028) (Table 3).

At the second follow-up, 6 months after primary PCI, total MACCE was reported in 21 patients (12.35%) in Group I and 11 patients (7.85%) in Group II (*P*=0.0032) (Table 3).

At the third follow-up, 12 months post PCI, total MACCE was reported in 24 patients (14.11%) in Group I and 13 patients (9.28%) in Group II (*P*=0.0042) (Table 3).

The log-rank test was used to compare survival between the 2 groups, and 1-year MACCE free survival for both groups is presented in a Kaplan–Meier curve in Figure 1. There was a statistically significant difference between the 2 groups, in favor of Group II, on follow-up at 1 month, 6

months, and 1 year (*P*=0.028, 0.0032, and 0.0042, respectively).

At 1 month's follow-up, a low Hb level (<11 g/dL [Group I]), age, the use of thrombus aspiration during PCI, and the ejection fraction were correlated with increased MACCE (Table 4).

A multivariable Cox proportional hazard model was used for the statistically significant parameters related to MACCE. The results revealed that low Hb levels (<11 g/dL [Group I)]) and age were independent predictors of MACCE at 30 days after primary PCI (*P*=0.03 and 0.001, correspondingly) (Table 4).

At 6 months' follow-up, low Hb levels (<11 g/dL [Group I]), age, hypertension, diabetes, and serum creatinine were related to increased MACCE. A multivariable Cox proportional hazard model was drawn upon for these parameters. The model demonstrated that low Hb levels (<11 g/dL [Group I]), age, hypertension, and diabetes were independent predictors of MACCE (*P*=0.019, 0.029, 0.042, and 0.021, respectively) (Table 5).

At 1 year's follow-up, low Hb levels (<11 g/dL [Group I]), age, hypertension, and diabetes were independent predictors of mortality (*P*=0.030, 0.025, 0.032, and 0.045, correspondingly) (Table 6).

Table 1: Baseline clinical and demographic characteristics of both groups

Characteristics	Group I (n=170)	Group II (n=140)	T/F value	*P* value
Age (y): mean±SD	63.2 ±8.4	60.1 ±9.6	2.9	0.003*
Gender, No. (M/F) (N/%)	108/62	106/34	0.53	0.75
BMI (kg/m) mean±SD	23.20 ±2.60	26.10 ±2.40	2.8	0.005*
Systolic BP mean±SD	136.20 ±16.00	135.20 ±14.80	0.56	0.57
Diastolic BP mean±SD	75.20 ±10.60	73.80 ±12.20	1.01	0.286
Heart rate (b/m) mean±SD	80.4 ±16.2	81.2± 17.1	0.442	0.763
Killip class>1 (N/%)	40 (23.5%)	27 (19.2%)	3.80	0.001*
Sudden cardiac arrest (N/%)	1 (0.6%)	1 (0.7%)	0.00	1.0
Smoker (N/%)	100 (58%)	90 (64%)	1.50	0.130
Hypertension (N/%)	98 (57%)	95 (67%)	0.44	0.650
Diabetes mellitus (N/%)	55 (32%)	48 (34%)	3.60	0.004*
Dyslipidemia (N/%)	58 (34%)	55 (38%)	1.28	0.201

MI, Myocardial infarction; BMI, Body mass index; BP, Blood pressure; M/F, Male/female,
* significant *P* value

Table 2: Biochemical and angiographic variables and echocardiographic results of both groups

Characteristics	Group I (n=170)	Group II (n=140)	T/F value	*P** value
Biochemical Indicators				
Hemoglobin , g/dL	9.40±2.20	12.20±2.80	4.70	0.001 *
Albumin, mg/dL	4.0±1.2	4.2±1.1	1.51	0.130
ALT, mg/dL	58.90±11.20	55.00±12.800	2.2	0.028
AST, mg/dL	44.00±10.30	40.40±11.80	2.07	0.039
CK, IU	115.90±11.80	113.70±12.00	1.52	0.122
CK-MB, mg/mL	28.40±9.20	30.30 ± 8.80	1.84	0.065
Cardiac troponin I, ng/mL	4.80± 2.60	5.20 ± 1.40	1.45	0.103
Glucose, mg/dL	130.10 ± 14.6	125.80± 16.40	2.44	0.015
Glycosylated hemoglobin%,	5.6±2.20	5.8±2.00	0.82	0.407
Creatinine, mg/dL	0.9.± 0.6	1.00 ±0.80	1.25	0.209
eGFR, mL/min	73.2±29.6	72.4±30.0	0.23	0.81
TC, mg/dL	180.20±10.80	178.50±12.40	1.29	0.19
LDL-C ,mg/dL	119.20± 8.10	120.400±6.800	1.39	0.164
Coronary angiography				
Successful PCI	160 (94.0%)	135 (96%)	1.54	0.122

Door-to-balloon time, min	60.5±20.2	64.2±20.0	1.61	0.108
Trans-radial	29 (17.0%)	28 (17.0%)	1.67	0.095
Triple-vessel disease	85 (50%)	80 (57%)	0.991	0.319
Thrombus aspiration	40 (23%)	25 (17.8%)	1.8	0.071
Echocardiography				
LVEF	50.00±2.400	48.60±8.200	1.71	0.088
RWMA	140 (82%)	122 (87%)	1.42	0.156
Medication Use at Discharge				
Aspirin	168 (98.8%)	139 (99%)	1.65	0.099
Clopidogrel/ Ticagrelor	170 (100%)	140 (100%)	1.67	0.095
Statin	160 (94%)	135 (96%)	1.54	0.122
Bet-blocker	130 (76%)	110 (78%)	1.88	0.060
ACEI/ARB	120 (70%)	110 (78.5%)	1.03	0.30

ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; CK, Creatine kinase; PCI, Percutaneous coronary intervention; eGFR, Estimated glomerular filtration rate; LDL-C, Low-density lipoprotein cholesterol; TC, Total cholesterol; LVEF, Left ventricular ejection fraction; ACEI/ARB, Angiotensin-converting enzyme inhibitor/ angiotensinogen receptor blocker; RWMA, Regional wall motion abnormalities
* significant *P* value

Table 3: Comparison of MACCE between the 2 groups

Characteristics	Group I (n=170)	Group II (n=140)	*P* value
MACCE Occurrence During Hospital Stay	8 (4.7%)	3 (2.14%)	0.034*
Myocardial re-infarction	1 (0.58%)	1 (0.7%)	
Post infarction angina	2 (1.17%)	1 (0.7%)	
Heart failure	3 (1.76%)	1 (0.70%)	
Death	1 (0.58%)	0 (0.0%)	
CVA (TIA or stroke)	1 (0.58)	0 (0.0%)	
MACCE Occurrence (30 days after PCI)	16 (9.4%)	8(5.71%)	0.028*
Myocardial infarction	2 (1.17%)	1 (0.7%)	
Unstable angina	5 (2.94%)	3 (2.14%)	
Heart failure	5 (2.94%)	3 (2.14%)	
Death	1 (0.58%)	0 (0.0%)	
CVA (TIA or stroke)	3 (1.76%)	1 (0.7%)	
MACCE Occurrence (6 months after PCI)	21 (12.35%)	11(7.85)	0.0032*
Myocardial infarction	3 (2.35%)	1 (0.7%)	
Unstable angina	6 (3.52%)	3 (2.14%)	
Heart failure	6 (4.11%)	4 (2.85%)	
Death	3 (1.76%)	1 (0.7%)	
CVA (TIA or stroke)	3 (1.76%)	2 (1.42%)	
MACCE Occurrence (12 months after PCI)	24 (14.11%)	13 (9.28%)	0.0042*
Myocardial infarction	4 (2.35%)	2 (1.40%)	
Unstable angina	6 (4.10%)	4 (2.85%)	
Heart failure	7 (4.70%)	4 (2.85%)	
Death	4 (2.94%)	1 (0.70%)	
CVA (TIA or stroke)	3 (1.76%)	2 (1.4%)	

MACCE, Major adverse cardiovascular and cerebral events; CVA, Cerebrovascular accident; TIA, Transient ischemic attack

Table 4: Univariable and Cox multivariable analyses for predictors of MACCE at 30 days

Variables	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Hb <11 g/dL	2.153	1.200-4.508	0.013*	2.503	1.095-4.691	0.030*
Age (y)	1.052	1.042–1.083	0.001*	1.045	1.033-1.054	0.001*
BMI (kg/m)	1.110	0.782-1.402	0.561			

Hypertension	1.564	1.403–2.301	0.072			
Diabetes mellitus	1.294	0.714-2.601	0.502			
Smoking	1.463	0.791-2.582	0.160			
Albumin	0.830	0.820-0.980	0.061			
Creatinine	1.010	0.900-1.102	0.081			
TC	0.796	0.625-1.103	0.094			
LDL-Cl	0.701	0.519-1.094	0.154			
Thrombus aspiration	0.503	0.290-0.971	0.029*	0.551	0.288-1.099	0.098
LVEF	0.268	0.045-0.508	0.016*	0.698	0.140-1.183	0.131
Trans-radial	0.883	0.795-1.18	0.681			

BMI, Body mass index; TC, Total cholesterol; LDL-C, Low-density lipoprotein cholesterol; LVEF, Left ventricular ejection fraction; Hb, Hemoglobin

Table 5: Univariable and Cox multivariable analyses for predictors of MACC at 6 months

Variables	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Hb<11 g/dL	1.893	1.195-3.281	0.015*	2.250	1.176-3.946	0.019*
Age (y)	1.107	1.010–1.165	0.012*	1.065	1.025-1.103	0.029*
BMI (kg/m)	1.088	0.912-1.356	0.421			
Hypertension	1.850	1.513–2.804	0.036*	1.972	1.642–2.903	0.042*
Diabetes mellitus	1.702	0.835-2.801	0.019*	1.648	1.052-2.954	0.021*
Smoking	1.506	0.801-2.470	0.082			
Albumin	0.901	0.794-0.993	0.094			
Creatinine	0.995	0.903-1.104	0.036*	1.010	0.934-1.010	0.561
TC	0.864	0.657-1.094	0.140			
LDL-C	0.821	0.580-1.073	0.153			
Glucose	1.040	0.986-1.086	0.132			
Thrombus aspiration	0.605	0.323-0.962	0.072			
LVEF	0.289	0.039-0.526	0.210			
Trans-radial	0.933	0.803-1.190	0.580			

BMS, Body mass index; TC, Total cholesterol; LDL-C, Low-density lipoprotein cholesterol; LVEF, Left ventricular ejection fraction; Hb, Hemoglobin

Table 6: Univariable and Cox multivariable analyses for predictors of MACC at 1 year

Variables	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age (y)	1.065	1.010–1.154	0.042	1.098	1.001-1.170	0.025
Hb<11 g/dL	1.608	1.075-2.983	0.036	1.642	1.006-2.906	0.030
BMI (kg/m)	1.006	0.894-1.458	0.652			
Hypertension	1.570	1.460–2.905	0.026	1.630	1.730–3.102	0.032
Diabetes mellitus	1.610	0.875-2.641	0.021	1.573	1.041-2.738	0.045
Smoking	1.475	0.808-2.360	0.063			
Albumin	0.897	0.784-0.103	0.057			
Creatinine	1.001	0.967-1.110	0.187			
Uric acid	0.879	0.908-1.102	0.470			
TC	0.905	0.703-1.008	0.524			
LDL-C	0.884	0.682-1.045	0.246			
Glucose	1.010	0.975-1.0881	0.341			
Thrombus aspiration	0.665	0.333-0.966	0.075			
LVEF	1.209	0.546-8.646	0.278			
Trans-radial	0.883	0.644-1.283	0.643			

BMS, Body mass index; TC, Total cholesterol; LDL-C, Low-density lipoprotein cholesterol; LVEF, Left ventricular ejection fraction, Hb, Hemoglobin

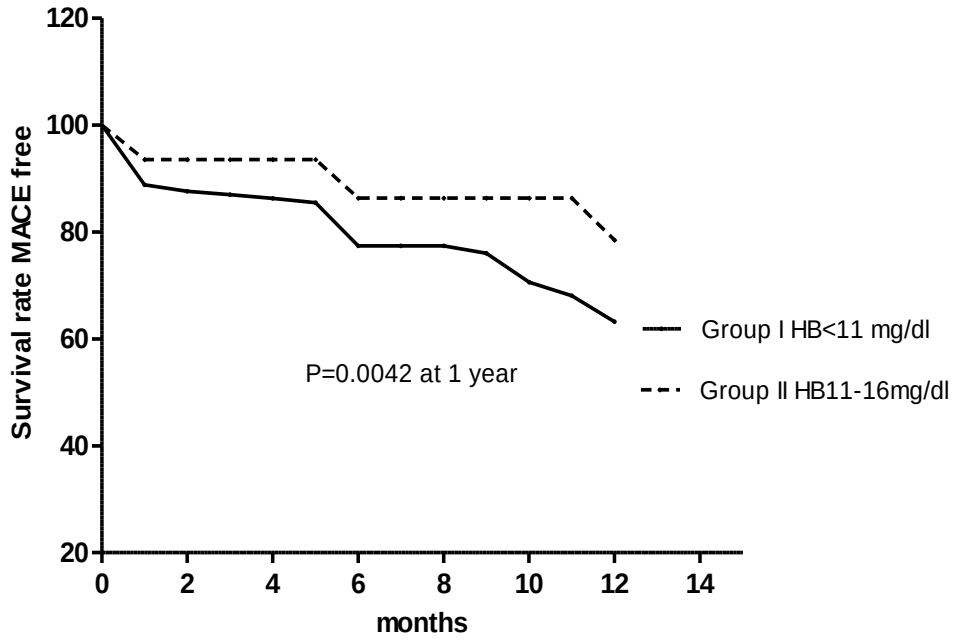

Figure 1: The image illustrates the MACCE-free survival follow-up curve for both groups.

HB, Hemoglobin

DISCUSSION

In our study, patients with lower Hb levels were older, had a lower BMI value, a higher incidence rate of diabetes, and a higher Killip class than the other group. These data chime in with a study by Moghaddam et al, [12] who investigated the association between anemia and outcomes in STEMI patients.

Our main finding was that patients presenting with STEMI and Hb levels below 11 g/dL after primary PCI had a higher incidence rate of MACCE. An Hb level of less than 11 g/dL was an independent predictor of MACCE at 30 days, 6 months, and 1 year after primary PCI. Moghaddam, et al [12] also showed that a low Hb level was associated with an increased rate of major adverse cardiac events (MACE) and with an increased rate of bleeding during the hospital stay. Nonetheless, they concluded that anemia was only an independent predictor of bleeding after adjustments for other risk factors. In contrast, Liu et al [13] showed that the risk of cardiogenic shock, heart failure, mortality, and bleeding was higher in patients with anemia.

Our findings at 30 days, 6 months, and 1 year after primary PCI are consistent with the findings of investigations by Greenberg et al [14] and Liu et al, [15] who reported that a low Hb level (<12 g/L) was associated with an increased incidence rate of MACCE during the follow-up period. Still, our findings are inconsistent with the HORIZON-AMI trial [16] and a study by Rathod et al, [17], reporting that anemia was not associated with 30-day and 1-year mortality. Therefore, the different associations between anemia and 30-day and 1-year mortality in different studies might be related to the different inclusion criteria of patients and the risk status of patient populations (eg, rates of Killip II to IV, diabetes, and anterior wall STEMI).

Anemia in STEMI patients exacerbates myocardial ischemia and directly increases the heart rate. It also not only causes poor oxygen delivery and tissue hypoxia but also activates the renin-angiotensin system. [18] Volume expansion accompanying anemia may lead to the development of chronic heart failure, [19] which may explain the findings of our study.

The results of the current investigation indicate that baseline Hb should be considered a predictor of the outcome in STEMI patients and that its role should be investigated in future studies. Nevertheless, the correction of anemia by erythropoietin in STEMI patients fails to improve mortality. [20, 21] The use of the trans-radial approach during primary PCI is encouraged to prevent bleeding complications and anemia. [22] STEMI patients with a high risk of gastrointestinal bleeding should be encouraged to take proton pump inhibitors as prophylaxis to avoid the occurrence of anemia.

CONCLUSIONS

Age, hypertension, and diabetes in STEMI patients with moderate-to-severe anemia were associated with an increased incidence rate of MACCE. Moderate-to-severe anemia at admission was an independent predictor of MACCE during hospitalization and on follow-ups at 30 days, 6 months, and 1 year following primary PCI.

Study Limitations

The results of the present study should be interpreted in light of the following limitations. Firstly, the number of patients included in this study was limited. Secondly, we only included Hb levels measured immediately after primary PCI and did not consider details regarding procedural complications, especially bleeding. Thirdly, the etiology of anemia in patients with a low baseline Hb concentration was unknown to us. However, we excluded patients with recent bleeding, known bleeding diathesis, or significant hematologic, oncological, or renal diseases. Fourthly, patients in Group I were older at baseline than those in Group II; consequently, the increased MACCE in Group I may have been affected by this factor, leading to increased MACCE in Group I.

Consent to Publish: Not applicable.

Availability of Data and Martial: The data sets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Conflict of Interest: None declared.

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Authors Contributions: MA participated in the follow-up of patients during hospitalization and the interpretation of coronary angiographic data. MA was also the major contributor to the writing of the manuscript. AA participated in the follow-up of patients during hospitalization and the interpretation of coronary angiographic data and prepared the collected clinical data for statistical analysis. TH analyzed and interpreted patient data. All the authors have read and approved the final manuscript.

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