The Utility the Platelet-to-Lymphocyte Ratio in Predicting Angiographic Reflow After Primary Percutaneous Coronary Intervention in Patients with Acute ST-Segment Elevation Myocardial Infarction

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Abstract: Impaired coronary flow after primary percutaneous coronary intervention (PPCI) is associated with short and long-term morbidity and mortality in patients with acute ST-segment elevation myocardial infarction (STEMI). Recent studies have demonstrated that platelet-to-lymphocyte ratio (PLR) is associated with adverse cardiovascular outcomes. The aim of this study was to assess the relation between admission PLR and angiographic reflow following PPCI. A total of 72 patients with acute STEMI (age 55 ± 10 years; 91% men) occurring within 12 hours of the onset of symptoms who underwent PPCI were enrolled. The PLR and other laboratory parameters were measured before PPCI. The patients were divided into 2 groups based on the post-intervention Thrombolysis In Myocardial Infarction (TIMI) flow grade: normal reflow group (defined as post-intervention TIMI grade 3 flow) and none-reflow group (consisted of both patients with angiographic no-reflow defined as post-intervention TIMI grade 0-1 flow and slow flow defined as post-intervention TIMI grade 2 flow). There were 31 patients (22.5%) in none-reflow group (age 54 ± 10 and 93.5% male) and 41 patients in normal reflow group (age 55 ± 11 and 37% male). None-reflow group had significantly higher PLR compared to normal reflow group (196-262) versus (139-180), P=0.009). In logistic regression analysis, PLR (odds ratio (OR): 1.008, 95% confidence interval (CI):1.002-1.014, P<0.001) and were independent predictors of none-reflow after PPCI. [Safwat Ahmed Hagag Elhawary, Mamdouh Attia Mohamed Mahmoud, Ali Ali Ramzy, Mohamed Sarhan ELsayed and Ahmed Mahmoud Abdelaziz Ibrahim. The Utility the Platelet-to-Lymphocyte Ratio in Predicting Angiographic Reflow After Primary Percutaneous Coronary Intervention in Patients with Acute ST-Segment Elevation Myocardial Infarction. Nat Sci 2017;15(1):122-126]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 16. doi:10.7537/marsnsj150117.16.

Keywords: Platelet-to-lymphocyte ratio, post-intervention angiographic reflow, ST-segment elevation myocardial infarction.

1. Introduction

Early reperfusion after coronary occlusion in patients with ST-segment elevation myocardial infarction (STEMI) is associated with an improved prognosis (1).

Nevertheless impaired angiographic reflow is still a challenging major issue in the management of the patients with STEMI undergoing primary percutaneous coronary intervention (PPCI). It is well known that impaired coronary reflow is associated with larger infarct size, worse functional recovery higher incidence of complications, and short and long-term mortality in acute STEMI (2).

Several responsible mechanisms for impaired coronary reflow were identified in experimental models including extravascular compression, microvascular vasoconstriction, a platelet/leukocyte capillary plugging (3,4) Several studies have shown the relationship between non-reflow and increased inflammatory status.

The platelet-to-lymphocyte ratio (PLR) has recently been investigated as new predictor for major adverse cardiovascular outcomes. It has been found that higher PLR is associated with poor coronary collateral development in stable coronary artery disease and longterm mortality after non-STEMI (5,6).

2. Patients and Methods

In this study 72 patients with STEMI occurring within 12 hours of the onset of symptoms up to 18 hours if there was evidence of continuing ischemia or hemodynamic instability. From medical records, we obtained demographic information, cardiovascular history and risk factors for coronary artery disease (CAD), and treatment received during the in-hospital period. Patients who had been treated with antihypertensive drugs or those whose baseline blood pressure exceeded 140/90 mmHg are diagnosed with hypertension (HT). Diabetes mellitus (DM) is defined as fasting blood sugar level above 126 mg/dl or the use of anti-diabetic medications and undergoing PPCI in our institution are enrolled into the study.

STEMI was defined as: prolonged chest pain for >30 min with ST-segment elevation ≥1mm in ≥2
contiguous electrocardiogram leads, or with a new left bundle-branch block, and more than twofold increase in serum cardiocmarkers.

**Analysis of blood samples**

Complete blood counts and biochemical values were evaluated retrospectively from blood samples obtained by antecubital vein puncture upon admission to the emergency department. Total and differential leucocyte counts will be done. Other biochemical measurements and electrolyte levels were determined by standard laboratory method.

**Exclusion criteria included**

1. Cardiogenic shock on admission
2. Active infections
3. Systemic inflammatory disease history
4. Known malignancy
5. Hematologic disorders
6. Liver disease
7. Renal failure

The patients were divided into 2 groups based on the post-intervention Thrombolysis In Myocardial Infarction (TIMI) flow grade: normal-reflow group and none-reflow group. Normal-reflow was defined as post-intervention TIMI grade 3 flow. None-reflow group consisted of both patients with angiographic no-reflow (defined as post-intervention TIMI grade 0-1 flow) and slow flow (defined as post-intervention TIMI grade 2 flow).

**Patients were subjected to the following:**

1) **History:** Thorough history taking with particular stress on:
   - Age
   - Gender
   - Risk factors of coronary artery disease:
     I. Diabetes mellitus: defined in this study as history of Diabetes mellitus, use of anti diabetic drugs and newly diagnosed Diabetes mellitus.
     II. Hypertension: defined in this study as history of hypertension, use of anti hypertensive drugs and newly diagnosed hypertension.
     III. Smoking: defined in this study as
       - Current smoker
       - Ex-Smoker (defined as quit smoking in the past 6 months)
       - Full analysis of chest pain especially as regards duration (pain to first medical contact time, first medical contact to first balloon, inflation time and first medical contact to TIMI III flow) will be recorded.
     IV. Past history of myocardial infarction, coronary artery bypass graft (CABG), PCI, Thrombophilia and thrombocytopenia, Known hematological abnormalities.
     V. A positive Family history of premature CAD was defined in this study as history of CAD or sudden cardiac death in a first degree relative before the age of 55 year for men and 65 year for women.

2) **Clinical examination:**
   - I. General examination:
     - A. Arterial blood Pressure (ABP)
     - B. Heart rate
     - C. Weight, height and body mass index.
   - II. Local examination:
     - Presence of S3, mitral regurgitation.

3- **Twelve lead surface ECG:**

a) Number of anterior leads with anterior ST elevation.
   b) Maximum ST segment elevation.
   c) Presence of pathological Q waves.
   d) Presence of reciprocal depression.
   e) Degree of ST resolution 90 minutes post PCI (which will be classified to: less than 50%, 50-75%, >75%, total resolution), Presence of bundle branch block or any degree of heart block.

3- **Laboratory investigations:**

Complete blood counts and biochemical values were evaluated from blood samples obtained by antecubital vein puncture upon admission to the emergency department.

4- **Transthoracic echocardiography** was measured for all patients within 48 hours after PPCI (Vivid 3; GE Medical System, Horten, Norway). Left ventricular ejection fraction (LVEF) was measurement using the modified Simpson method.

5- **Coronary angiography and intervention procedural details (PPCI):**

- Femoral artery puncture was performed in all patients using seldingers technique.
- Each coronary was evaluated in at least 2 views.
- The non-culprit vessel was evaluated using a diagnostic catheter.
- The culprit vessel was immediately evaluated by a guiding catheter and site of occlusion identified.
- After assessment other coronaries the culprit vessel was treated by using the following techniques:
  1. Wiring of the culprit vessel.
  2. Thrombus aspiration in some patients.
  3. PTCA using undersized balloon in some patients.
  4. Stenting with BMS or DES.
  5. Post deployment PTCA in some patients.
  6. Deployed stent was assessed for proper deployment, absence of signs of dissection or perforation.

a) **Thrombolysis in myocardial infarction (TIMI) flow prior to and after procedure:**

- **Grade 0** (no perfusion): There is no antegrade flow beyond the point of occlusion.
Grade 1 (penetration without perfusion): The contrast material passes beyond the area of obstruction but "hangs up" and fails to opacify the entire coronary bed distal to the obstruction for the duration of the cineangiographic filming sequence.

Grade 2 (partial perfusion): The contrast material passes across the obstruction and opacifies the coronary bed distal to the obstruction. However, the rate of entry of contrast material into the vessel distal to the obstruction or its rate of clearance from comparable areas not perfused by the previously occluded vessel (e.g. the opposite coronary artery or the coronary bed proximal to the obstruction).

Grade 3 (complete perfusion): Antegrade flow into the bed distal to the obstruction occurs as promptly as antegrade flow into the bed from the involved bed and is as rapid as clearance from an uninvolved bed in the same vessel or the opposite artery

b) The TIMI thrombus scale.

Grade 0: no angiographic evidence of thrombus

Grade 1: angiographic features suggestive of thrombus
  - Decreased contrast density
  - Haziness of contrast
  - Irregular lesion contour
  - A smooth convex meniscus at the site of a total occlusion
  - Suggestive but not firmly diagnostic of thrombus.

Grade 2: definite thrombus present in multiple angiographic projections
  - Marked irregular lesion contour with a significant filling defect – the thrombus' greatest dimension is <1/2 vessel diameter

Grade 3: definite thrombus appears in multiple angiographic views
  - Greatest dimension from >1/2 to <2 vessel diameters

Grade 4: definite large size thrombus present
  - Greatest dimension >2 vessel diameters

Grade 5: definite complete thrombotic occlusion of a vessel
  - A convex margin that stains with contrast, persisting for several cardiac cycles

3. Results

In our study, we demonstrated that PLR on admission >187.86 predicted the angiographic none-reflow with 80.49% sensitivity and 58.06% specificity. A total of 72 patients with acute STEMI (age 55 ± 10 years; 91% men) occurring within 12 hours of the onset of symptoms who underwent PPCI were enrolled. The PLR and other laboratory parameters were measured before PPCI. The patients were divided into 2 groups based on the post-intervention Thrombolysis In Myocardial Infarction (TIMI) flow grade: normal reflow group (defined as post-intervention TIMI grade 3 flow) and none-reflow group (consisted of both patients with angiographic no-reflow defined as post-intervention TIMI grade 0-1 flow and slow flow defined as post-intervention TIMI grade 2 flow).

There were 31 patients (22.5%) in none-reflow group (age 54 ± 10 and 93.5% male) and 41 patients in normal reflow group (age 55 ± 11 and 37% male). None-reflow group had significantly higher PLR compared to normal reflow group (196-262) versus (139-180), P=0.009. In logistic regression analysis, PLR (odds ratio (OR): 1.008, 95% confidence interval (CI):1.002-1.014, P<0.001) and were independent predictors of none-reflow after PPCI.

There was a large number of diabetic patient in the none reflow group (no=20, 64.5% versus 13 patients (31%) in normal-reflow group p=0.006.

Ejection fraction was significantly lower in none-reflow group (mean 45.16±9.85 versus 52.49 ± 8.1 in reflow group, p<0.001).

Some of the possible interactions (age-PLR; gender-PLR; creatinine-PLR; and diabetes-PLR-hypertension –PLR, CK MB-PLR) were also assessed however they found to be non-significant

Table 1: Comparison between reflow group and non reflow group regarding age and sex

<table>
<thead>
<tr>
<th></th>
<th>Reflow</th>
<th>Non reflow</th>
<th>Independent t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.= 41</td>
<td>No.= 31</td>
<td>t/X²*</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>55.78 ± 10.92</td>
<td>54.87 ± 10.57</td>
<td>0.355</td>
</tr>
<tr>
<td>Range</td>
<td>35 – 87</td>
<td>32 – 80</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4 (9.8%)</td>
<td>2 (6.5%)</td>
<td>0.252*</td>
</tr>
<tr>
<td>Male</td>
<td>37 (90.2%)</td>
<td>29 (93.5%)</td>
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Table 2: Comparison between reflow group and non reflow group regarding risk factors

<table>
<thead>
<tr>
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<th>Reflow</th>
<th>Non reflow</th>
<th>Chi-square test</th>
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<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td>DM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>28</td>
<td>68.3%</td>
<td>11</td>
</tr>
<tr>
<td>Positive</td>
<td>13</td>
<td>31.7%</td>
<td>20</td>
</tr>
<tr>
<td>HTN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>23</td>
<td>56.1%</td>
<td>13</td>
</tr>
<tr>
<td>Positive</td>
<td>18</td>
<td>43.9%</td>
<td>18</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>20</td>
<td>48.8%</td>
<td>9</td>
</tr>
<tr>
<td>Positive</td>
<td>21</td>
<td>51.2%</td>
<td>22</td>
</tr>
<tr>
<td>Dyslipidemia</td>
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<td></td>
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</tr>
<tr>
<td>Negative</td>
<td>29</td>
<td>70.7%</td>
<td>18</td>
</tr>
<tr>
<td>Positive</td>
<td>12</td>
<td>29.3%</td>
<td>13</td>
</tr>
<tr>
<td>Family history</td>
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<tr>
<td>Negative</td>
<td>32</td>
<td>78.0%</td>
<td>20</td>
</tr>
<tr>
<td>Positive</td>
<td>9</td>
<td>22.0%</td>
<td>11</td>
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Table 2: Comparison between reflow group and non reflow group regarding laboratory data

<table>
<thead>
<tr>
<th></th>
<th>Reflow</th>
<th>Non reflow</th>
<th>Mann-Whitney test</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>No.= 41</td>
<td>No.= 31</td>
<td>Z/t*</td>
</tr>
<tr>
<td>CKMB</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Median (IQR) Range</td>
<td>81 (40 – 220)</td>
<td>146 (51 – 282)</td>
<td>-0.802</td>
</tr>
<tr>
<td></td>
<td>15 – 581</td>
<td>15 – 827</td>
<td></td>
</tr>
<tr>
<td>Creatinin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD Range</td>
<td>1.10 ± 0.32</td>
<td>1.20 ± 0.43</td>
<td>1.147*</td>
</tr>
<tr>
<td></td>
<td>0.5 – 2.0</td>
<td>0.7 – 2.9</td>
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</tr>
<tr>
<td>Platelet count</td>
<td></td>
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<tr>
<td>Mean ± SD Range</td>
<td>255.80 ± 75.25</td>
<td>275.87 ± 87.20</td>
<td>-1.046*</td>
</tr>
<tr>
<td></td>
<td>128 – 510</td>
<td>157 – 519</td>
<td></td>
</tr>
<tr>
<td>Lymphocytic count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD Range</td>
<td>1.97 ± 0.96</td>
<td>1.62 ± 0.80</td>
<td>1.649*</td>
</tr>
<tr>
<td></td>
<td>0.8 – 5.4</td>
<td>0.6 – 4</td>
<td></td>
</tr>
<tr>
<td>P/L</td>
<td></td>
<td></td>
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<tr>
<td>Median (IQR) Range</td>
<td>139.38 (105.71 – 180.63)</td>
<td>196.25 (130.00 – 262.73)</td>
<td>-2.604</td>
</tr>
<tr>
<td></td>
<td>51.20 – 425.00</td>
<td>41.50 – 442.50</td>
<td></td>
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<tr>
<td>HB</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean ± SD Range</td>
<td>13.26 ± 1.45</td>
<td>12.58 ± 1.83</td>
<td>1.725*</td>
</tr>
<tr>
<td></td>
<td>8.6 – 16</td>
<td>8 – 18</td>
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4. Discussion

Rapid restoration of infarct-related arterial flow is associated with improved ventricular performance and lower mortality in patients with STEMI. However, poor post-interventional reflow may limit the benefits of recanalization of the culprit vessel. Impaired angiographic reflow is strongly correlated with morbidity and mortality in acute STEMI. It is associated with larger infarct size, worse functional recovery, and higher incidence of complications. The pathophysiology of none-reflow has not been fully explained and its etiology appears to be multifactorial. These factors include ischemic endothelial damage, microvascular leukocytes and platelet plugging and complex interactions between leukocytes and platelets induced by the inflammatory process. Several studies have shown the relationship between none-reflow and increased inflammatory status.

This study was done to demonstrate that higher value of PLR was found in none-reflow group when compared to normal reflow group in patients with STEMI who underwent PPCI. This finding may contribute to explain the possible underlying mechanisms of poor post intervention flow.

This study demonstrated two major findings in patients with acute STEMI undergoing PPCI. First, the PLR on admission was significantly higher in post-intervention none-reflow group. Second, PLR can be considered as indicator of none-reflow following PPCI in patients with STEMI.

Increased platelet counts may reflect underlying inflammation as several inflammatory mediators stimulate megakaryocytic proliferation and produce relative thrombocytosis. Moreover, studies have shown that patients with coronary atherosclerosis have elevated levels of platelet monocyte aggregates in their bloodstream, which correlate with plaque stability. On the other side, lymphocytes represent a quiescent and controlling inflammatory pathway. In cancer patients, lymphocyte was responsible on the programmed cell death, apoptosis.

In our study, we showed that PLR was one of the factors for post-intervention none-reflow in acute STEMI. We speculate two factors that explain the superiority of PLR to either individual lymphocyte or platelet counts. First, the stability of PLR compared to the absolute platelet or lymphocyte counts, which
could be altered by many physiological and pathological conditions. Secondly and most importantly, the PLR represent two inversely related predictors and immune pathways.

Previous studies have demonstrated that higher platelet and lower lymphocyte counts were associated with adverse cardiovascular outcomes. The PLR has recently been investigated as a new predictor for adverse cardiovascular outcomes.

Reference