Predictive Value and Impact of No-Reflow Phenomenon after Primary PCI

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Abstract

Background: Angiographic no-reflow after primary percutaneous coronary intervention (PCI) in patients with ST-elevation myocardial infarction (STEMI) may result in unfavorable outcome.

Objectives: The aim of the work was to study the outcome of STEMI patients with no-reflow phenomenon.

Patients and Methods: A total of 627 STEMI patients who underwent primary PCI within 24 hours of symptoms onset were divided into a normal flow group (thrombolysis in myocardial infarction [TIMI] flow grade 3) and a no-reflow group (TIMI flow grade <2), based on angiograms performed after PCI.

Results: A total of 78 patients (12.4%) developed no-reflow phenomenon. The in-hospital major adverse cardiac events (MACE) were significantly higher in the no-reflow group compared to the in the optimal flow group (30.7% vs. 6.1% respectively, p=0.001). The no-reflow group showed a significantly higher rate of six month MACE compared to the optimal flow group (26.5% vs. 11%, p=0.003). The rate of in-hospital mortality was 14.1% in the no reflow group compared to 2.9% in the optimal flow group (p=0.023).

Conclusion: Angiographic no-reflow predicts adverse outcome in terms of higher mortality and MACE rates.

Key Words: No-reflow – STEMI – MACE – Primary PCI – Impact.

Introduction

The aim of treatment for ST-Elevation Myocardial Infarction (STEMI) is to restore full antegrade blood flow into the Infarct-Related Artery (IRA) and minimize ischemic damage to the myocardium. Thrombolytic therapy is an option, but primary Percutaneous Coronary Intervention (PCI) is the treatment of choice, based on lower rates of recurrent ischemia or infarction and good success rates in restoring antegrade blood flow in the IRA [1,2].

No-reflow is a phenomenon in which myocardial ischemia and reduced antegrade flow occur despite the absence of proximal stenosis, spasm, dissection, or embolic cut off of major distal branches [3]. The beneficial effects of stents for patients with STEMI have been reported, but these effects have been reduced because of the development of no-reflow phenomenon after primary intervention [4,5]. Several studies have demonstrated that STEMI patients with angiographic no-reflow have worse functional recovery and more frequently manifest post-myo-cardial infarction complications and mortality rates in comparison to those with optimal flow [5-8].

Aim of the work:

The aim of the study was to determine the outcome of STEMI patients undergoing primary PCI and developing no-reflow phenomenon.

Patients and Methods

The current study was conducted on 627 patients admitted with STEMI and were subjected to primary percutaneous coronary interventions, and admitted to Cairo University Hospitals, Critical Care Department, starting from December 2004 to January 2013. Six months follow-up had been achieved in 472 patients.

We included patients presenting with STEMI and fulfilling the following criteria: Prolonged (>30 minutes) ischemic chest pain, ECG: ST segment elevation (>1mm) in 2 or more contiguous leads or new LBBB or ECG findings suggestive of posterior infarction and Presentation <24 hours from symptom onset.

We excluded patients with acute stent thrombosis following elective PCI resulted in STEMI and patients planned for primary PCI yet the
revascularization strategy was modified following diagnostic coronary angiography (transferred for coronary artery bypass grafting).

**Data collection:**

Data were collected through reviewing patients’ medical records, angiographic films and reports and follow-up records.

**Definition of no-reflow:**

No-reflow phenomenon was defined as TIMI flow grade < 2 post intervention that cannot be explained by severe dissection or abrupt closure of target lesion [9].

*Patients were divided into two groups:* No-reflow group (TIMI flow 0-2 post intervention) and the optimal flow group (TIMI flow 3 post intervention).

**Study outcome and endpoints:**

*The clinical end points were the combined rates of:*

- **MACE:** Defined as the composite of death, acute coronary syndromes: Unstable angina, ST elevation MI (STEMI) and non ST elevation MI (NSTEMI), target vessel revascularization (TVR): PCI or CABG for re-stenosis involving the target site, adjacent site and/or other new segments of the treated vessel, heart failure requiring hospitalization.

- **Mortality:** Either in hospital or within 6 month from discharge.

**Statistical analysis:**

Data were collected and coded prior to analysis using the professional statistical Package for Social Science (SPSS 17). All data were expressed as mean and standard deviation (SD). Frequency tables for all categorical data. Student t-test (unpaired) after checking normality was used for all continuous data. Mann Whitney test was used when the value of standard deviation was violated. Chisquare test was used for all categorical data to test for the presence of an association. *p*-value < 0.05 was considered significant.

**Results**

We conducted an observational single center study involving 627 patients admitted to critical care department, Cairo University with STEMI and were subjected to primary Percutaneous Coronary Interventions (PCI), in the period from December 2004 to January 2013. Four hundred seventy two patients out of 600 targeted patients (78.6%) could be followed-up for six months (the fate of 27 patients was in-hospital mortality on first admission). After the analysis of the post intervention data, patients were classified into two groups: The no reflow group (TIMI flow ≤ 2 post PCI) including 78 patients (12.4%) and the optimal (normal) flow group (TIMI flow=3 post PCI) including 549 patients (87.6%).

**A- In-hospital follow-up:**

**In-hospital major adverse cardiac events (MACE):**

During the in-hospital follow-up of patients with reported successful primary PCI, 58 patients (9.3%) had at least one MACE; including:

- Death in 27 patients (4.3%).
- Acute coronary syndrome (ACS) 43 patients (6.9%).
- Target vessel revascularization (TVR) 26 patients (4.1%) including; 19 patients had re-PCI (3%) and 7 patients (1.1%) were subjected to CABG.

The prevalence of in-hospital MACE was statistically significant higher in the no-reflow group compared to the optimal flow group (Table 1).

**In-hospital incidence of stroke:**

During the in-hospital follow-up, 5 patients (3.8%) had radiological and or clinical evidence of stroke, 3 patients (3.8%) in the no-reflow group and 2 patients in the optimal flow group (0.3%) (*p*-value 0.001) (Table 1).

**In-hospital mortality:**

During the in-hospital follow-up, 27 patients (4.3%) were reported as in hospital mortality. Eleven patients in the no-reflow group and 16 patients in the optimal flow group (*p*-value < 0.001) (Table 1).

**B- Six months follow-up:**

Four hundred seventy two patients (78.6%) had complete follow-up, while 128 patients were considered as lost follow-up cases and 27 cases of in hospital mortality were present (during the first admission).

**Six months Major Adverse Cardiac Events (MACE):**

Sixty eight patients (14.4%) had at least one MACE in the six months following discharge; including:

- Death in 12 patients (2.5%).
- Acute coronary syndrome in 19 patients (4%).
- Target vessel revascularization in 51 patients (10.8%) including; 39 patients had re-PCI (8.2%) and 12 patients (2.6%) were subjected to CABG.
The prevalence of six month MACE was significantly higher in the no-reflow group compared to the optimal flow group (Table 2).

Six month incidence of stroke:
During six months follow-up, 5 patients (1%) had radiological and or clinical evidence of stroke, 2 patients (3.1%) in the no-reflow group and 3 patients (0.9%) in the optimal flow group. (p-value 0.001).

Six month mortality:
During the six months follow-up, 12 patients (2.4%) were reported as mortality, 5 patients in the no-reflow group (7.8%) and 7 patients in the optimal flow group (1.7%). Six month Mortality was significantly higher in the no-reflow group compared to the optimal flow group (p-value 0.003) (Table 2).

Predictors of in-hospital MACE:
Multivariate regression analysis was done to determine predictors of in-hospital MACE. Cardiogenic shock and TIMI flow post intervention were independent predictors of in-hospital MACE.

No reflow phenomenon (TIMI flow grade <2 post intervention) increased odds of in-hospital MACE by 2.6, (CI 95%, 2.1-3.4, p-value <0.001).

Table (2): Six months MACE after primary PCI in both groups.

<table>
<thead>
<tr>
<th>MACE</th>
<th>No-reflow (64)</th>
<th>Optimal flow (408)</th>
<th>p.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>17 (26.5%)</td>
<td>49 (12%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Death</td>
<td>5 (7.8%)</td>
<td>7 (1.7%)</td>
<td>0.023</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>7 (10.9%)</td>
<td>12 (2.9%)</td>
<td>0.015</td>
</tr>
<tr>
<td>Target vessel revascularization</td>
<td>13 (20.3%)</td>
<td>36 (8.8%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Re-PCI</td>
<td>12 (18.7%)</td>
<td>27 (6.6%)</td>
<td>0.007</td>
</tr>
<tr>
<td>CABG</td>
<td>2 (3.1%)</td>
<td>10 (2.4%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CVS</td>
<td>2 (3.1%)</td>
<td>3 (0.9%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Fig. (2): Percentage of in-hospital total MACE and mortality in both groups.

Discussion
The post-interventional TIMI flow has an important prognostic value for in-hospital mortality and clinical outcome.

Our study showed that the no reflow group had a statistically significant higher rates of in-hospital mortality and MACE than the optimal flow group (In-hospital MACE was 30.7% in the no-reflow group vs. 6.1% in the optimal flow group p-value 0.001).

This was in concordant with Jibing Du et al., [10] who reported a statistically significant higher in-hospital mortality and MACE in the no-reflow group compared to the optimal flow group (in-hospital MACE was 6.7% vs. 1.8% group, p-0.04, while in-hospital MACE was 25% vs. 9.9%, p-0.002).

The primary outcomes of the PAMI studies, [11] reported that in-hospital MACE, occurred more frequently in patients with TIMI flow <2, the occurrence of in-hospital death was also significantly higher in the no-reflow group compared to the optimal flow group.

Kammler et al., [12] reported that in-hospital mortality was significantly higher in patients with
TIMI flow post intervention < 2 compared to those with optimal flow (TIMI 3) post intervention (32.9% vs. 6.4%, p < 0.0001).

Our study showed that the no-reflow group had a statistically significant higher rate of six month mortality and MACE compared to the optimal flow group (six month MACE was 26.5% in the no-reflow group vs. 11% in the optimal flow group p-value 0.003). This was in concordance with Ndrepepa et al., [13] who reported a statistically significant higher 1 year mortality and MACE rates in the no-reflow group compared to the optimal flow group.

Li Dong Bao et al., [14] also stated that the incidence of MACE during the 6-month follow-up period was significantly higher in the no-reflow group compared with the optimal flow group.

Jibing Du et al., [10] reported a statistically significant higher 1 year mortality prevalence in the no-reflow group compared to optimal flow group (11.7% vs. 3.7%, p = 0.014), he also stated that the incidence of MACE after one year was significantly higher in the no-reflow group (48.3% vs. 19.3%).

• The rates of in-hospital mortality and MACE are significantly higher in the no-reflow group compared with the optimal flow group.

• The no-reflow phenomenon is an independent predictor of in-hospital MACE.

• The rates of mortality and MACE during the 6-month follow-up period were significantly higher in the no-reflow group compared with the optimal flow group, warranting a more careful follow-up of this group of patients.

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References


الملخص العربي

العلاجية الطارئة كمثيل فعال لمضاعفات الجلطة لإعادة تروية عضلة القلب، ورغم من ذلك التقدم لم تزال النتائج السريرية غير مرضاية خاصة لهؤلاء الذين يعانون من ظاهرة عدم عودة سيريان الدم بعد أجزاء قسطرة الشرايين التاجية.


وكان الهدف من الدراسة هو تقييم الآثار المستقبلية المرتبطة على ظاهرة عدم عودة سيريان الدم بالشرايين التاجية بعد قسطرة القلب التاجية الطارئة.

وقد أظهرت النتائج ما يلي:

- تجنب تقدم الوضع بعد أجزاء القسطرة التاجية للعلاجية الطارئة إلى مجموعة未经 عودة سيريان الدم بالشرايين التاجية (السيران بميوزوم 162% وميوزوم 78% من المرضى) ومجموعة未经 عودة سيريان الدم (ميوزوم 78% من المرضى) (49 مريض).

- امتلأت الدراسة أن معدل حدوث المضاعفات القلبية المؤيدة في كان أعلى بصورة ملحوظة في مجموعة未经 عودة سيريان الدم كما كانت نسبة الوفاة أعلى في نفس المجموعة مقارنة بالمجموعة الأخرى.

- كما كشفت مضاعفات الوضع خلال الستة أشهر التالية للقسطرة أن معدلات الوفاة وحدوث المضاعفات القلبية المؤيدة كانت أعلى في مجموعة未经 عودة سيريان الدم مقارنة بمجموعة未经 عودة السريان العام.