**ORIGINAL ARTICLE**

**Rescue PCI Versus a Conservative Approach for Failed Fibrinolysis in Patients with STEMI**

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<th>Appropriate treatment strategy for ST-Segment elevation myocardial infarction patients who have failed fibrinolytic therapy is uncertain.</th>
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<td>We tested the safety and efficacy of rescue PCI after failure of fibrinolysis.</td>
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<td>Sixty patients with acute ST-Segment elevation myocardial infarction were included in this controlled, prospective study. We aimed to evaluate the safety and efficacy of rescue PCI compared to conservative treatment in patients who initially received thrombolytic therapy but without clinical and or electrocardiographic evidence of successful reperfusion 90 minutes after start of fibrinolysis.</td>
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<td>Results</td>
<td>No mortality was reported in either group, no re-infarction, heart failure, stroke, recurrent ischemia, need for urgent intervention, arrhythmia, or major bleeding during the hospital stay. However, minor bleeding was 30%, 7% in rescue PCI and conservative group respectively (P= 0.01). After 30 days, angina requiring hospitalization occurred in 30% in the conservative group versus 7% in rescue PCI group (P= 0.01). Target vessel revascularization was higher in conservative group (13%) than rescue PCI group (0%), (P= 0.02). Development of heart failure occurred in 30% in conservative patients, compared to 20% in rescue PCI. Re-infarction occurred in one patient only of the study population (conservative group). No reported cases of mortality.</td>
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<td>Conclusions</td>
<td>Rescue PCI is a safe, feasible, and effective treatment option for patients who had failed fibrinolytic therapy.</td>
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<td>Keywords</td>
<td>Rescue PCI, Fibrinolysis, STEMI.</td>
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**INTRODUCTION**

ST-segment elevation myocardial infarction (STEMI) continues to be a major health problem in industrialized countries and is becoming increasingly common in developing countries. The benefits of an open infarct artery are well recognized, but despite proven advantages of primary percutaneous coronary intervention (PCI), fibrinolysis remains the most common reperfusion strategy worldwide (1). Clinical outcome of patients with STEMI are strongly dependent on the patency in the infarct–related artery after reperfusion therapy (2). Unfortunately fibrinolysis is unable to restore normal coronary flow in 30-40% of treated patients. Fibrinolytic therapy restores normal flow in only one half of STEMI patient, as assessed angiographically at 90min (2). The most appropriate treatment strategy for STEMI patients who fail fibrinolytic therapy is uncertain. Practice guidelines for STEMI recommend rescue PCI as a potential therapy; however, this recommendation is based primarily on expert opinions and consensus (1). Conservative therapy with no further reperfusion treatment, repeat fibrinolytic therapy, and rescue PCI are all being used commonly. The REACT (Rescue Angioplasty versus conservative treatment or repeat thrombolysis) trial demonstrated that rescue PCI is associated with an improvement in the composite end point of death, re-infarction, stroke or severe heart failure, when compared with repeat fibrinolytic therapy or conservative management (3). Repeated fibrinolysis did not improve outcome but increased the risk of bleeding when compared to conservative approach (3). A second contemporary study, the MERLIN (Middlesbrough Early Revascularization to Limit Infarction) trial did not show significant reduction of the primary end point of all-cause mortality associated
with rescue PCI when compared with conservative therapy (4). Furthermore, in both trials, patients treated with rescue PCI had increased bleeding, an important predictor of poor long-term outcome.

MATERIAL

Study Design
This controlled prospective study included 60 patients with STEMI who were admitted to the coronary care unit (CCU) of cardiology department, Benha University Hospital, Benha, Egypt during the period from April 2009 to April 2011. The study aimed to evaluate the safety and efficacy of rescue PCI compared to conservative treatment in patients who initially received fibrinolytic therapy but without clinical and or electrocardiographic evidence of successful reperfusion 90 minutes after start of fibrinolysis. All patients signed an informed consent. Inclusion Criteria were: Age: 30-80 years, either sexes were included; patients without absolute or relative contra-indications to fibrinolytic therapy, patients in whom fibrinolytic therapy failed to restore patency in infarct related artery clinically and or by ECG. While Exclusion Criteria were: inability to gain femoral access for intervention, life expectancy less than 6 months owing to non cardiac causes, cardiogenic shock, LBBB.

METHODS

Baseline Evaluation
Full history and clinical examination, 12 lead ECG on admission and at 90, 120 minutes after fibrinolysis and immediately after PCI in the rescue group and every 4 hours for 24 hours then once daily and whenever indicated. Routine laboratory investigations including, random blood sugar and lipid profile, kidney function tests (BUN and creatinine), liver function tests (PT, S GOT and SGPT), cardiac markers (CK-MB and Troponin) on admission and 6 hours later, hemoglobin level.

All Patients were given fibrinolytic therapy (streptokinase), (1.5 million units over 60 minutes). Failure of fibrinolysis was defined as at 90min after the beginning of fibrinolytic therapy, the ECG showed less than 50% decrease in the ST segment elevation in the leads with maximum ST elevation and/or persistence or worsening of chest pain.

Patients with fibrinolytic failure were subdivided into two groups:

Group I: Included 30 patients who underwent rescue PCI.

Group II: Included 30 patients who were treated conservatively.

All patients received full anti-ischemic and antithrombotic drugs (300mg aspirin, 300mg loading dose of clopidogrel, and unfractionated heparin).

Rescue PCI Procedure
The procedure was done according to the standard techniques of PCI. Femoral approach was the standard in all patients using 6-7 French sheaths. Diagnostic coronary angiography was done to detect the target vessel, XB or JL guiding catheters were used for left coronary lesions and JR guiding catheter for RCA lesions. Aspiration devices and glycoprotein inhibitors were used in patients with heavy thrombus burden and impaired TIMI flow grade after PCI. Bare-metal stents were used in all patients. The operator determined the size and length of the stent. Rescue PCI was done for the culprit lesion only. The sheath was removed 6 hours from the end of the procedure and compression was done manually. Follow up of all patients was done during the hospital stay.

Study End Points

• primary end points: 30 days combined end point of adverse events including: All cause mortality, re-infarction, heart failure, target vessel revascularization (TVR), major bleeding: defined according to the TIMI risk scale as intracranial, retroperitoneal, or intraocular clinically overt bleeding or any bleeding requiring blood transfusion or with hemoglobin decrease >5g/dl or (hematocrit decrease ≥15%), minor bleeding: defined as any other clinically overt bleeding not meeting the criteria for major bleeding.

• Secondary end points: left ventricular function after 30 days as detected by echocardiography.

Statistics
The collected data were tabulated and analyzed using SPSS version 17. Categorical variables were presented as number and percentages while continuous variables were expressed as mean±standard deviation. Chi square test (X2) "Z" test and student "t" tests were used. The accepted level of significance in this work was stated P <0.05.
RESULTS
The mean age was 54±9 years (53±9.7 years vs 55±9 years in rescue PCI group and conservative group respectively, (P >0.05). Seventy eight percent (78%) were males, 48% had diabetes mellitus, 38% were hypertensive. Smokers (either current or prior) were 62% of all patients, dyslipidemia was present in 76% of patients, 13% of patients had positive family history of ischemic heart disease (IHD). No prior history of PCI, CABG, myocardial infarction or heart failure. There were no statistically significant differences between either group in demographic criteria, risk factors or past medical history (Table 1). However diabetes mellitus was more common in conservative group, 63% compared to 33% in rescue PCI patients, P= 0.01.

Table 1: Baseline characteristics of study population:

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<tr>
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<th>Group I</th>
<th>Group II</th>
<th>P</th>
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<tr>
<td>Age,years, mean±SD</td>
<td>53.2±9.7</td>
<td>54.8±9.1</td>
<td>&gt;0.05</td>
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<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>23(77%)</td>
<td>24(80%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Female</td>
<td>7(23%)</td>
<td>6(20%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes M</td>
<td>10(33%)</td>
<td>19(63%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12(40%)</td>
<td>11(36%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Smoking</td>
<td>18(60%)</td>
<td>19(63%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>20(77%)</td>
<td>20(67%)</td>
<td></td>
</tr>
<tr>
<td>Family history of IHD</td>
<td>4(13%)</td>
<td>4(13%)</td>
<td></td>
</tr>
<tr>
<td>Prior PCI or CABG</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td></td>
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<tr>
<td>Prior MI/CHF</td>
<td>0(0%)</td>
<td>0(0%)</td>
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IHD= Ischemic Heart Disease; PCI= Percutaneous Coronary Intervention; CABG= Coronary Artery Bypass Grafting; CHF= Congestive Heart Failure.

Clinical Presentation on Admission
Chest pain was the main clinical presenting symptom among the study group (73%, 67%, 80%, in all patients, rescue PCI, conservative groups respectively, P >0.05), dyspnea was the main presenting symptom in 13% of patients (13%, 13%, in rescue PCI and conservative group respectively, P >0.05), pulmonary edema was the main presenting symptom in 13% of patients (20%, 7%, in rescue PCI and conservative group respectively, P >0.05).

Time From Symptom Onset to Admission to CCU
Most patients presented to CCU within 6 hours from symptom onset (92%), 63% of patients in rescue PCI Vs. 33% of those who were treated conservative presented within the first 3 hours (P= 0.01), while 33% Vs 53% were admitted between 3-6 hours in PCI group and conservative group respectively (P= 0.02), moreover 3% in PCI group Vs 13% in conservative group presented after 6 hours, P= 0.03 (Table 2).

Clinical Examination on Admission
There was no statistically significant difference between the study groups considering heart rate and systolic blood pressure at presentation (the mean systolic blood pressure was 136±25mmHg in group I and 125mmHg±29 in group II, while the mean heart rate was 85.7±14.5 in group 1 and 79.4±16 in group II, P >0.05) Killip II and III presentation was more in group I (47% and 20% versus 33% and 7%, P> 0.05)

Target Segment of STEMI According to ECG
Anterior MI was the most common type of infarction (45% of patients), 63% in group I Vs. 27% in group II (P= 0.01). Anterolateral infarction was present in 30% of patients, (27% in group I Vs. 34% in group II, P >0.05). Anteroseptal infarction was evident in 3% of patients (0% vs. 7% in group I and II respectively, P >0.05). Inferior infarction occurred in one patient only of the study (group I). While inferior and right ventricular and or posterior infarction was detected in 20% of all patients (7% and 33% in group I and II respectively, P= 0.01), (Figure 1).

Rescue PCI
The mean time from diagnosis of failed reperfusion till the start of sheath insertion in the cath-lab was 3.0±1.2 hours (range 1.5 to 6 hours), two patients (6.7%) had time of less than 2 hours, and 17 patients (57%) had time between 2-3 hours, while 11 patients (37%) had time between 3-6 hours. All patients received 10,000 U of UFH pre PCI. 6 Fr sheath was inserted in (87%) of patients, while 7 Fr in 13%. Transfemoral approach was done in all patients. Diagnostic coronary angiography was performed pre PCI. The target artery was LAD in 90% of cases, RCA in 10% of cases. Among the LAD patients, the occlusion was in proximal segment in 85%, in mid segment in 15%. In RCA patients 100% of cases had proximal occlusion.
TIMI flow 0 was detected in 47% of patients, TIMI I in 47%, and TIMI II flow in 6% of patients. XB guiding catheter was used in all patients who had LAD as the target artery. While JR catheter was used in those who had RCA as the target artery, floppy wire was used in 43% of cases, while coated wire was used in 57%. Predilatation was done in all cases either due to shortage of aspiration devices or presence of critical lesion after thrombus aspiration. Intracoronary glycoprotein inhibitors were injected in 43% of cases; this was followed by intravenous infusion for an average time 12 hours in 10% of patients, and manual aspiration devices were used in 9 patients (30%). Large thrombus burden or impaired TIMI flow were the main indications. Implantation of Bare-metal stent (BMS) was performed in 27 patients (90%). Twenty three patients had 1 stent while four patients had 2 stents. The mean stent diameter was 3.2±0.8mm; the mean stent length was 15±3.3mm. The mean implantation pressure was 13.5±1 ATM. Post dilatation was done in 17% of patients due to residual stenosis. TIMI flow at the end of rescue PCI was III in 90% of patients and II in 10% of patients (Figure 2). Of those who had TIMI 0 pre PCI, 13 patients (93%) had TIMI III and 1 patient (7%) had TIMI II. While those who had TIMI I pre PCI, 12 patients (86%) had TIMI III and 2 patients (14%) had TIMI II. Distal embolization occurred in 13% of patients, No reflow in 13% of patients, residual thrombus in 3% of patients and no cases of dissections, death, perforation, or arrhythmia were reported.

![Figure 2: TIMI flow grade post PCI](https://www.heartmirror.com)

### In hospital Outcome

No mortality was reported in either group, also no reported cases of reinfarction, heart failure, stroke, recurrent ischemia, need for urgent intervention, arrhythmia, or major bleeding during the hospital stay, but minor bleeding in 18% of patients, 30%, 7% in rescue PCI and conservative group respectively (P= 0.01)

### Thirty Days Outcome

Primary end point was reported in 50% of patients who were treated conservatively compared to 20% of patients treated with rescue PCI (p= 0.02). Angina requiring hospitalization was reported in 18% of patients, 30% in the conservative group compared to 7% in rescue PCI group (P= 0.01). Target vessel revascularization was performed in 13% of conservative group II Vs 0% in rescue PCI group I (P= 0.02). Development of heart failure occurred in 30% of conservative patients compared to 20% in rescue PCI patients (P >0.05). Re-infarction was reported in one patient (group II). No mortality, or major bleeding, but minor bleeding occurred in 30% and 7% in PCI and conservative group respectively (P= 0.01). There was a trend for positive correlation between time to cath lab and occurrence of heart failure and angina requiring re hospitalization with less frequency in those who had shorter time. Thirty days mean LVEF in group I was higher than group II, 50±8% Vs. 48%±9% but was not statistically significant (P >0.05).

### DISCUSSION

Despite potential advantages of primary percutaneous coronary intervention (PPCI), fibrinolytic therapy remains the most common therapy for STEMI worldwide (5). Appropriate treatment strategy for STEMI patients who fail fibrinolytic therapy is uncertain (6). This controlled study evaluated the safety and efficacy of rescue PCI as an optional treatment in patients with STEMI who received fibrinolytic therapy but without evidence of successful reperfusion. In the present study we found a better outcome with rescue PCI regarding recurrence of ischemia and need for TVR with a trend for better LVEF but with increased risk of minimal bleeding. In our study the mean age was 54 years (ranged from 30-75 years) and the female subjects represented 22% of the study population. In RESCUE trial the mean age was 59 years and female subjects represented 18% of the study population. In TAMI trial the mean age was 57 years and females represented 19% of the study population. In the present study, chest pain was the main presenting symptom, representing 73% of all patients. This was concordant with trials of rescue PCI as REACT, MERLIN and RESCUE trials in which chest pain was the main presenting symptom. Most of patients in the present study (92%) presented in the first 6 hours, 48% in the first 3 hours and another 44% of patients presented between 3-6 hours. Only 8% of patients presented after 6 hours. In REACT, MERLIN, and RESCUE trials the time from symptom onset to fibrinolytic therapy was 2, 3, 3 hours respectively. The difference between our results and these trials is related to the diagnosis, education of the patients, and long transport time. Anterior wall myocardial infarction occurred in (78%) of patients. The REACT trial which included 427 patients, the anterior wall MI represented 43% of the study group. In another study which included 90 patients, anterior wall MI represented 56% of the study group (7). This difference may be related to small sample size and difference of the study population.

In the present study, the time from diagnosis of failure of thrombolysis until the start of intervention was 3.1±1.2 hours. In MERLIN trial, the mean time from 60 minutes...
ECG (diagnosis of failure) to coronary angiography was 1.5±0.5 hour. While Ellis, et al. 1994 (8) reported that the mean time from presentation to angiography was 4.5±2 hours. In REACT trial the mean time from 90 minutes ECG to rescue PCI was 5±3 hours. Rescue PCI is defined as PCI within 12 hours after failed fibrinolysis for patients with continuing or recurrent myocardial ischaemia (4) A major limitation in adapting a strategy of rescue PCI is the difficulty in identifying patients for whom fibrinolytic therapy has not restored ante grade coronary flow (1). Unless unsuccessful fibrinolysis is recognized and treated quickly (within 3-6 hours of onset of symptoms), salvage of ischemic myocardium is unlikely. LAD was the main target vessel in the study group and represented 90%, while RCA was the target vessel in 10%. In the RESCUE trial all patients had LAD occlusion as target for infarction. However in the MERLIN trial it represented only 44%, in addition in REACT trial it represented only 43% of patients (1). Most of our patients (73%) had single vessel disease; to our knowledge this point in other trials is not known. Intra coronary glycoprotein inhibitors were used in 43% of rescue PCI patients. In MERLIN trial only 5 patients (3%) received glycoprotein inhibitors (4). In the study done by Burjonrappa et al. (9), 59% of patients received glycoprotein inhibitors and 43% of patients in the REACT trial received this medication. Aspiration devices were used in 9 patients (30%), mainly due to shortage of these devices. 90% of patients of the rescue group in our study had TIMI 3 flow post PCI. These results are in agreement with the results of the MERLIN trial (85%) of patients had TIMI 3 flow post PCI (4). In the present study there were no reported cases of major bleeding. In REACT trial, the incidence of major bleeding was 2.7% in the rescue PCI group and 3.6% in the conservative group. Angina requiring hospitalization occurred in 6.7% in the rescue PCI group compared to 30% in the conservative group. In addition TVR was done in 13% of patients in the conservative group versus 0% in PCI group. These results are accordant with the results of the MERLIN trial (4) in which 6.5% versus 20.1% had TVR in rescue PCI and conservative group respectively.

Congestive heart failure in the present study occurred in 30% in the conservative therapy group compared to 20% in the rescue PCI group. The meta-analysis done by wijeysundera et al. (10) which included six trials (including REACT, MERLIN and RESCUE trials) reported significant reduction in the relative risk (RR 0.73, 95% CI 0.54-10.00) in the rescue PCI group after follow up period from in hospital discharge to six months. Small sample size, difference in the study population, and shorter follow up time in our study may explain the difference in the results. There were no reported cases of mortality in the study group at 30 days follow up. This result was concordant with other studies (4, 10).

STUDY LIMITATIONS
Small sample size, lack of randomization, short follow up period.

CONCLUSION
Rescue PCI is a safe, feasible, and effective treatment option for patients who had failed fibrinolytic therapy after STEMI. In hospitals without PCI facilities, it may be recommended to transfer patients who have failed fibrinolysis to another hospital with PCI facilities to perform rescue PCI.

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REFERENCE