



Six months outcome of rescue percutaneous coronary intervention compared to conservative treatment in patients with ST-segment elevation myocardial infarction with failed fibrinolytic therapy

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Abstract

Background: Fibrinolytic therapy restores patency of infarct related artery in about half of patients with STEMI. This study was designed to evaluate 6 months outcome after rescue PCI.

Methods: Sixty patients with STEMI were included in this controlled, prospective study. All patients had fibrinolytic therapy at baseline and had failed fibrinolysis detected by ECG and or persistence of chest pain. 50% of patients had rescue PCI and the others were treated conservatively. 30 days and 6 months major adverse cardiovascular events (MACE) were reported.

Results: After 30 days, angina required hospitalization was reported in 30% vs 7% in conservation and rescue groups ($P=0.01$). Target vessel revascularization was higher in conservative group (13%) than rescue group (0%), ($P=0.02$). The 6 months follow up showed no motility benefit. However, re-hospitalization due to ACS and target vessel revascularization were more in the conservative group than rescue group, 40% vs 13%, 30% vs 1% respectively ($P=0.02$). Heart failure and re-infarction showed no significant difference between both groups. The mean LVEF was higher in rescue PCI patients ($60\pm 7\%$ vs $45\pm 8\%$) ($P=0.001$).

Conclusion: Rescue PCI is safe, feasible and effective treatment option for patients with failed thrombolytic therapy.

Keywords: STEMI, fibrinolysis, rescue PCI, conservative treatment

Introduction

The benefits of an open infarct artery are well recognized, but despite proven advantage of primary percutaneous coronary intervention (PPCI), fibrinolysis remains the most common reperfusion strategy worldwide [1]. The future of patients with STEMI is dependent on the patency the culprit artery after reperfusion therapy [2]. Fibrinolysis is unable to restore normal coronary flow in 30-40% of treated patients [2]. The most appropriate treatment strategy for STEMI patients who have failed fibrinolytic therapy includes rescue PCI, repeat fibrinolysis, or conservative treatment. ACC/AHA guidelines for STEMI recommend rescue PCI as class IIa indication for patients who fail fibrinolytic therapy [1]. The lack of convincing data on how to treat STEMI patients who fail fibrinolytic therapy is reflected by the consistency in clinical practice where

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 and severe heart failure, when compared with repeat fibrinolytic therapy or conservative management [3]. However, this benefit was driven predominantly by a reduction in re-infarction, with no difference in survival between treatment strategies, moreover, this trial was terminated prematurely, before complete enrollment, raising concerns about the true estimate of benefits. 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 as-

sociated 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.

This study was designed to compare rescue PCI therapy versus conservative therapy in STEMI patients who have proven failed fibrinolysis to provide the best estimate of benefits and risks associated with these competing strategies.

Patients and methods

Study design

This prospective, controlled study included 60 patients with STEMI admitted to the coronary care unit (CCU) of cardiology department, Benha University Hospital, Benha, Egypt during the period from April 2009 to April 2011. We tested 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 and the study was approved by local ethics committee. Inclusion criteria were: Age: 30-80years, either sex, 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

- a. Full history and clinical examination.
- b. 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.
- c. Routine laboratory investigations including, random blood sugar and lipid profile, kidney function tests (BUN and creatinine), liver function tests (PT, SGOT and SGPT), cardiac markers (CK-MB and Troponin) on admission and 6 hours later, hemoglobin level.
2. All patients were given fibrinolytic therapy (streptokinase), (1.5million units over 60 minutes).
3. Failure of fibrinolysis was defined as less than 50% regression in the ST segment elevation in the leads with maximum ST elevation and/or persistence or worsening of chest pain, 90 minutes after the start of fibrinolytic therapy.
4. 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.
5. All patients received full anti-ischemic and anti-thrombotic drugs.

Rescue PCI procedure

The procedure was done according to the standard techniques of PCI. Femoral approach was the standard in all patients using 6 French sheaths. Diagnostic coronary angiography was done to detect the target vessel, X.B 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 TMI 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 point: 6 months adverse events including: All cause mortality, re-infarction, heart failure, target vessel revascularization (TVR).

Secondary end point: Left ventricular function at 6 months measured by echocardiography.

Statistical analysis

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

Study population

The mean age was 54±9 years (53±9.7 years Vs 55±9 years in rescue PCI group and conservative group respectively P=0.1). 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 67% of patients, 13% of patients had positive family history of 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 patients, 63% compared to 33%, p=0.02.

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 group 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 oedema was the main presenting symptom in 13% of patients (20%, 7%, in rescue PCI and conservative group respectively, P=0.2).

Time from symptom onset to admission

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.**

Table 1. Baseline characteristics of study population.

	Group I Rescue PCI n=30	Group II Conservative n=30	P-value
Age, years, mean±SD	53.2±9.7	54.8±9.1	0.1
Male gender, n (%)	23 (77%)	24 (80%)	0.2
Diabetes M	10 (33%)	19 (63%)	0.02
Hypertension	12 (40%)	11 (36%)	0.2
Smoking	18 (60%)	19 (63%)	0.3
Dyslipidemia	20 (67%)	20 (67%)	--
Family history of CAD	4 (13%)	4 (13%)	--
Prior PCI or CABG	0 (0%)	0 (0%)	--
Prior MI/CHF	0 (0%)	0 (0%)	--

CAD: Coronary artery disease; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass grafting; MI: Myocardial infarction; CHF: Congestive heart failure

Table 2. Time from symptom onset to admission.

	Group I	Group II	P-value
Within 3 hours, n(%)	19 (63%)	10 (33%)	0.01
Between 3 to 6 hours	10 (33%)	16 (53%)	0.02
>6 hours	1 (3%)	4 (13%)	0.03

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 & 125mmHg±29 in group II, while the mean heart rate was 85.7±14.5 in group I & 79.4±16 in group II, P=0.1). Killip II & III presentation was more in group I (47% & 20% versus 33% & 7%, P=0.2).

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=0.5). Anteroseptal infarction was evident in 3% of patients (0% Vs. 7% in group I and II respectively, P=0.4). Inferior infarction occurred in one patient only of the study (in 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**).

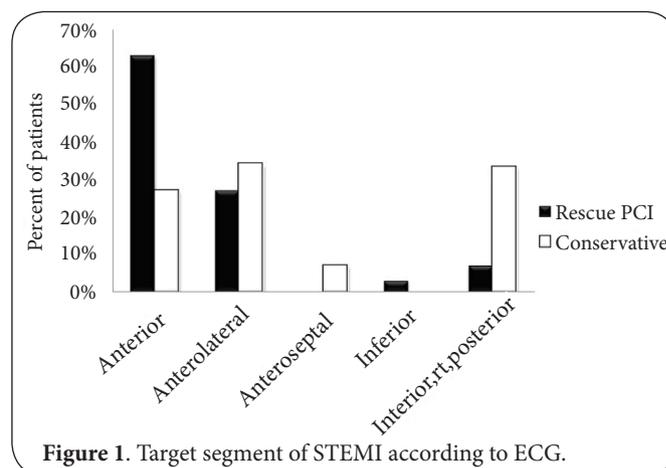


Figure 1. Target segment of STEMI according to ECG.

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, 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. Transfemoral approach was done in all patients. 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% cases had proximal occlusion. TIMI flow 0 was detected in 47% of patients, TIMI 1 in 47%, and TIMI II flow in 7% 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, 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±0.8 mm, 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. Distal embolization occurred in 13% of patients, No reflow in 13% of patients.

In hospital outcome

No mortality was reported in either group, also no reported cases of re-infarction, 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

Major adverse events were 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 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=0.3). 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=0.5).

Six months outcome

No reported cases of mortality. Re-hospitalization due to unstable angina was reported in 40% of patient in group II Vs 13% in group I. (P=0.02). Heart failure occurred in 20% Vs 10% in conservation Vs rescue group P=0.3. Target vessel revascularization was more in the conservative group than rescue group 20% Vs 1% respectively (P=0.001). The mean LVEF was significantly higher in group I than group II, 60±7% Vs 45±8% (P=0.001).

Discussion

Despite potential advantages of primary percutaneous coronary intervention (PPCI), fibrinolytic therapy remains the most common therapy for STEMI worldwide [5]. Practical guidelines for STEMI recommend rescue PCI as a class IIa indication in the treatment of patients with STEMI who had failed fibrinolytic therapy [6]. This controlled study evaluated the safety & efficacy of rescue PCI as an optional treatment in patients with STEMI who received fibrinolytic therapy but without evidence of successful reperfusion. We reported a better 6 months outcome with rescue PCI with lower re-hospitalization due to ACS, heart failure and better LVEF.

In our study the mean age was 54 years & the female patients represented 22% of the study population. In RESCUE trial the mean age was 59 years and female subjects represented 18% of the study population.

Most of patients in the present study (92%) had time from symptom onset within 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.

Time from symptom onset was shorter in rescue PCI patients. However this was not translated into better end points like mortality heart failure.

Anterior wall myocardial infarction was reported in (78%) of patients. In the REACT trial, anterior STEMI represented 43% of the study population. In another study which included 90 patients, anterior wall MI represented 56% of patients [7]. This difference may be related to small size and difference of the study population. The time from diagnosis of failure of fibrinolysis 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 h after failed fibrinolysis for patients with continuing or recurrent myocardial ischemia [9]. 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 [9]. 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 rescue group & 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 REAT trial it represented only 43% of patients. 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 Burjonroppa et al [10], 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 in our lab 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.

At 6 months, angina requiring hospitalization was reported in 13% in the rescue PCI group compared to 40% in the conservative group. In addition TVR was done in 20% of patients in the conservative group versus 3% in PCI group. These results are concordant 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 20% in the conservative therapy group compared to 10% in the rescue PCI group. The meta-analysis done by Wijeyesundera et al., [11] 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) of heart failure in the rescue PCI group after follow up period six months.

Study limitation

Small sample size.
Lack of randomization.

Conclusion

Rescue PCI improved clinical outcome compared to conservative approach in patients with STEMI who have failed fibrinolytic therapy.

List of abbreviations

STEMI: St Segment Elevation Myocardial Infarction
PCI: Percutaneous Coronary Intervention
MACE: Major Adverse Cardiovascular Events
CAD: Coronary Artery Disease

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	MS	MM	AR
Research concept and design	✓	✓	✓
Collection and/or assembly of data	✓	✓	✓
Data analysis and interpretation	✓	✓	✓
Writing the article	✓	✓	✓
Critical revision of the article	✓	✓	✓
Final approval of article	✓	✓	✓
Statistical analysis	✓	✓	✓

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