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RESEARCH

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Post-streptokinase PCI in STEMI patients exceeding the 24-h guidelines

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Abstract

Background: Due to delay in obtaining approval from insurance institution, performing PCI after successful reperfusion using streptokinase was postponed for >24 h-1 week. The study was conducted to investigate safety and efficacy of such delay in comparison to the ideal guidelines of PCI (≤24 h) in 129 STEMI patients received streptokinase followed by PCI. Patients were divided into two groups: (group 1 = 57; early PCI ≤ 24 h.) and (group 2 = 72; late PCI > 24 h.).

Results: Primary end point was death, congestive heart failure and reinfarction up to 30 days. Secondary end point was TIMI flow < G3, ischemic stroke, intracranial hemorrhage and non-intracranial bleeding. No statistical significant difference was found between both groups regarding LVEF, dimensions and myocardium wall preservation and incidence of complications and TIMI flow. No primary endpoints were detected. Five patients had secondary endpoints in early PCI and four in the late PCI. Suction device and IV Eptifibatide were used more in early PCI ($p = 0.003$).

Conclusions: The study suggests that relatively late PCI (> 24 h–1wk) after successful reperfusion using streptokinase in STEMI patients seems to be safe and effective in 30-day follow-up, provided that patients received DAPT and were subjected to close observation. The results seem safely applicable when we are forced to this choice; however lack of more investigations to this hypothesis is considered a limitation.

Keywords: Pharmaco-invasive (PI), ST-segment elevation myocardial infarction (STEMI), Streptokinase (SK), Coronary Angiography (CA), Percutaneous coronary intervention (PCI)

1 Background

While primary percutaneous coronary intervention (PPCI) is the first choice in managing patients with ST-segment elevation (STEMI)[1], Pharmaco-invasive approach is frequently used in many developing countries[2, 3]. When PPCI is not available, pharmaco-invasive approach is often a more suitable choice. Guidelines for managing STEMI patients illustrated ideal clinical practice of reperfusion by fibrinolytic followed by PCI within 24 h[4] [1]. Due to delay in obtaining approval from the insurance institution, performing PCI was postponed for more than 24 h and up to one week; however, most of the patients were kept in the hospital till receiving the financial approval. Therefore, this study was conducted to investigate the safety and the efficacy of such delay in performing PCI (> 24 h) in comparison to the ideal prescribed guidelines of earlier PCI (≤ 24 h) following successful reperfusion using streptokinase.

2 Methods

2.1 Study design

This is an observational cross-sectional study. It included 129 STEMI patients between October 2014 and August 2018. All the patients were presented with chest pain up to twelve hours from the onset of symptoms and were given one and a half million units of Streptokinase (SK). Successfully reperfused patients (129 patients) were divided into two groups according to the time between successful reperfusion and PCI performance: Group 1 = 57 patients had early PCI 3–24 h, whereas

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Group 2 = 72 patients had a delayed PCI > 24 h after Streptokinase.

2.2 Reperfusion by SK and its assessment

SK was administered (1.5 million units over 30–60 min.) and was combined with IV enoxaparin (30-mg) followed by subcutaneous injection of 1 mg /Kg of body weight. A loading dose of clopidogrel 300-mg was administrated followed by 150 mg for the first 2 weeks then 75 mg daily. In addition, a loading dose of aspirin was given: 300 mg; this was followed by 81 mg daily. Successful reperfusion was confirmed in all patients by resolutions of ST elevation > 50–70% at 60 to 90 min after SK therapy; chest pain relief; or occurrence of reperfusion arrhythmias.

2.3 Primary and secondary end points

Patients were followed up for 30 days, looking for primary end point (death, congestive heart failure or reinfarction) and secondary end point (TIMI flow grade less than 3, ischemic stroke, intracranial hemorrhage or non-intracranial bleeding).

2.4 Statistical analyses

Data were analyzed using the software, Statistical Package for Social Science (SPSS Inc. Released 2009, PASW Statistics for Windows, version 18.0: SPSS Inc., Chicago, Illinois, USA). Frequency distribution as percentage and descriptive statistics in the form of mean and standard deviation were calculated. Chi-square, t test, one-way ANOVA and correlations were done whenever needed. P values of less than 0.05 were considered significant.

3 Results

3.1 Baseline patients' characteristics

The mean age for all 129 pharmaco-invasive approach patients was (55.23 ± 10.62) year old with a minimum of 29 years and maximum 83 years (Table 1). There were 106 (82.2%) male patients and 23 (18.0%) female patients. Twenty-seven (20.9%) patients had a history of IHD and only 23 (17.8%) were on anti-ischemic drugs. Forty-two (33.6%) patients were diabetic, 52 (40.3%) were hypertensive and 76 (59.0%) were smokers. Successful reperfusion was confirmed by ST resolution, decrease/disappearance of chest pain or occurrence of reperfusion arrhythmia. Seventy patients had 50% ST resolution after 60–90 min, while 59 patients had 70% ST resolution. Reperfusion arrhythmias were detected in 28 (22%) patients only.

3.2 The procedure data

Radial access was used in 80 patients (62%) out of 129; 33 (41%) in group1 (≤ 24 h.) and 47 (59%) in (> 24 h.) group2. Suction devices were used in 6 patients (10.5%) in group 1 (≤ 24 h.), while it was used once (1.4%) in group 2 (> 24 h.); ($p = 0.030$). IV Eptifibatide administrated in 7 patients (12.3%) in group 1 (≤ 24 h.), while it was not used in (> 24 h.) group 2; ($p = 0.003$) (Fig. 1).

Table 1 Baseline patients' characteristics and ECG

Variable	Pharmaco-invasive n = 129 (%)
Demographic	
Age (mean ± SD) years	(55.23 ± 10.62)
Sex	
Male	106 (82.2)
Female	23 (18.0)
CV history	
HTN	52 (40.3)
DM	42 (33.6)
History of IHD	27 (20.9)
Adherence to anti-ischemic drugs^	23 (17.8)
Smoking	76 (59.0)
ECG: successful reperfusion	
ST resolution after SK	
50%	70 (54.2)
70%	59 (45.7)
Reperfusion arrhythmia	
Yes	28 (20.4)

PPCI: Primary Percutaneous coronary Intervention; HD: Ischemic heart disease, HTN: Hypertension,DM: Diabetes; ^ Anti-Ischemic medications: Aspirin, Clopidogrel, statins and Beta-Blockers, ± angiotensin-converting enzyme Inhibitors, ± Nitroglycerin

* $p \leq 0.05$

3.3 TIMI final results

There was no statistical difference between both groups regarding reaching TIMI flow results; ($p = 0.628$) (Fig. 1). TIMI flow G3 was achieved in 54 (94.7%) patients in group 1(≤ 24 h.) and 68 (94.4%) patients subsequently in group 2 (> 24 h.). TIMI flow G2 occurred in only 3 (5.3%) patients in group 1(≤ 24 h.) and in 4 (5.6%) patients in group2 (> 24 h.).

3.4 Echocardiographic data

No statistical significant difference was found between both groups regarding LVEF ($p = 0.571$), end-diastolic ($p = 0.267$) and end systolic dimensions ($p = 0.948$) (Fig. 2). In group 1(≤ 24 h.), akinetic segments detected in 21 patients (36.8%) and 20 (27.8%) patients; ($p = 0.108$) in group 2(> 24 h.).

Eighteen patients (31.6%) in group 1 showed hypokinetic segments versus 36 patients (50.0%) in group 2; ($p = 0.105$). Normal segment wall motion was detected in 18 patients (31.6%) in group 1(≤ 24 h.) versus 16 patients (22.2%) in group 2(> 24 h.); ($p = 0.983$).

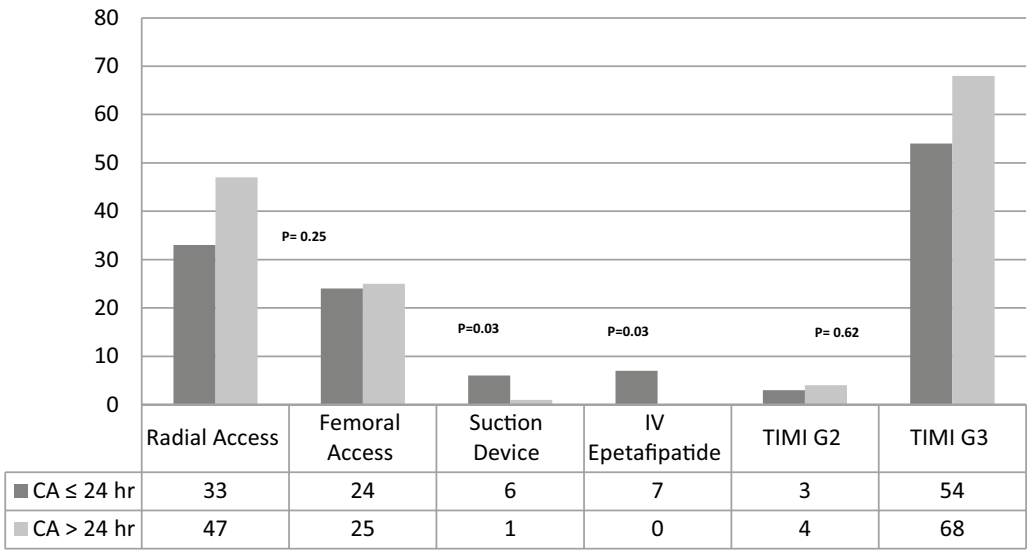

Fig. 1 Procedural data. This chart is representing number of patients who had Radial and femoral access, suction devices and IV Eptifibatide and TIMI flow final results in each group

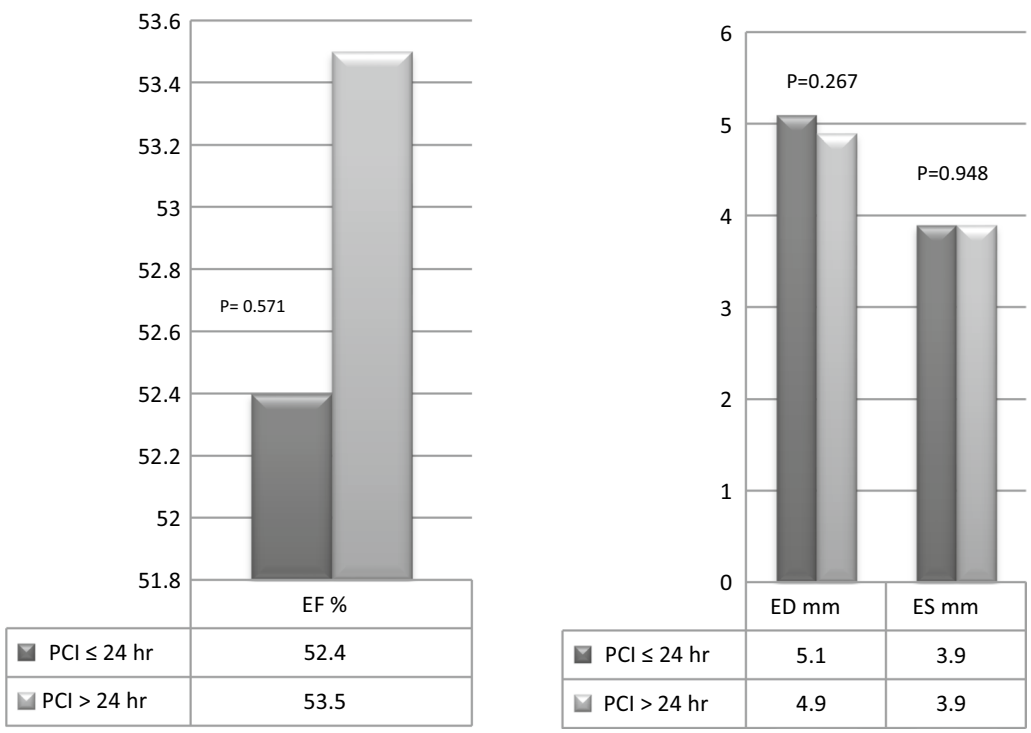

Fig. 2 Myocardial ejection fraction and dimensions. This chart is representing percentage of patients' myocardial ejection fraction and dimensions

Thinned walls were detected in 13 (22.8%) patients in the group1 (≤ 24 h.) against 12 (16.7%) patients in group 2 (> 24 h.).

3.5 Complications after 30 days follow-up

Primary end point (death, congestive heart failure or reinfarction) was not reported in both groups. Nine

patients had secondary end points all over the study. Three patients had TIMI flow G2 in group 1(≤24 h.) versus 4 patients in group 2(>24 h.). One patient had ischemic stroke and another had non-major bleeding in the early group 1(≤24 h.)

4 Discussion

Our study was an observational cross-sectional one, which investigates the safety and efficacy of performing PCI later than 24 h after successful fibrinolytic pharmaco-invasive approach reperfusion. The idea of the study was inspired by the unfortunate bureaucracy which delayed the financial approval on PCI from the insurance organization. Such delay was not consistent with all the guidelines [1, 5]; therefore, 80% of the patients were kept under observation in the hospital until PCI was done. The other patients (20%) were given strict instructions to rush to hospital on the occurrence of any chest pain and were daily followed up by phone. An assessment of such group of postponed PCI, contrary to the guidelines, was therefore worthwhile.

Most of the published trials had a window of 3–24 h after successful fibrinolysis [6–8]. In many trials, there was a wide variation of delay between successful thrombolysis to PCI. Median time of PCI in the CAPITAL-AMI trial [9] was 1.3 h, whereas in the GRACIA-1 trial it was 16.7 h [10]. A recent study by Salih Kilica, et al. [11]compared the outcomes of STEMI patients who received successful fibrinolytic treatment and performed PCI within 24—72 h (group 1) or ˃72 h (group 2). Coronary angiography was performed within 2.17 ± 0.38 days in group-1 and 2.9 ± 11.5 days in the Group-2. MACE rate was higher in Group-2 (21.3%) than Group-1(13.8%), but it was not statistically significant ($p = 0.661$), after 6 months follow-up. Long-term follow-up (median: 57 months) also revealed no statistical significant difference; 37.9% in Group-1 and 38.3% in Group-2 ($p = 0.974$). Their results showed no difference in MACE for both short- and long-term follow-up groups regarding overall cardiac mortality rate (7.9%), the re-infarction rate (19.7%) and heart failure (17.1%).

Suction device use and IV Eptifibatide administration rate were higher in the earlier PCI group (≤24 h.). In this group, suction device was used in 6 patients and IV Eptifibatide was administrated in 7 patients, while only one patient used suction device in the delayed PCI group (>24 h.) and no patients received IV Eptifibatide (Fig. 1).

Radial access was used more commonly (62.0%) than femoral access (38.0%) of all 129 patients (Fig. 1); 33 (41%) group 1 (≤24 h.) and 47 (59%) in group 2 (>24 h.). The Transradial approach (TRA) could lead to a decrease in incidence of overall bleeding complications [12, 13].

The unplanned delay in PCI timing after successful thrombolytic reperfusion (in second group ˃24 h.) allows for more dual antiplatelet administration. This could diminish the SK-induced platelet aggregation effect [14]. Although no significant difference regarding complication results in both groups; ($p = 0.189$), earlier PCI had 2 patients one with an ischemic stroke and another one with non-major bleeding. This result illustrates that delay in PCI, after successful SK reperfusion, did not add extra ischemic complications, provided that patients were subject to some restrictions in activity and strict intake of DAPT and were closely observed.

5 Limitations

Larger sample size and longer follow-up time would provide more definitive results to this work. However, pharmaco-invasive approach was a temporary solution for the limited availability of PPCI. However, addressing the problem of bureaucracy leading to delay in obtaining the approval from the insurance institution is necessary to help patients from rural areas with non-PCI capable hospitals. Lack of more investigations to this hypothesis is considered a limitation.

6 Future direction

In our hospitals, more efforts should be directed toward decreasing the elapsing period science reperfusion with thrombolytic therapy till performing CA/PCI in patients with STEMI.

7 Conclusions

This study suggests that relatively late PCI (>24 hours up to one week) after successful reperfusion using SK in STEMI patients seems to be safe and effective according to short-term follow-up, provided that patients received DAPT and were subjected to close observation. The results seem safely applicable when we are forced to this choice; however lack of more investigations to this hypothesis is considered a limitation.

Abbreviations

PPCI: Primary percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infraction; SK: Streptokinase; TIMI: The thrombolysis in myocardial infarction; IHD: Ischemic heart disease; LVEF: Left ventricular ejection fraction; TRA: Transradial approach.

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Authors' contributions

HBM was involved in methodology. ZME and HBM were involved in conceptualization. ZME was involved in investigation, data curation and writing—original draft preparation. KRA and HBM were involved in writing—review &

editing. KRA performed visualization. All authors have read and approved the manuscript.

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Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
The study protocol was approved by Research Ethical Committee of Beni-Suef University Faculty of Medicine (FM-BSU-REC). FM-BSU-REC is organized and operated according to guidelines of the Declaration of Helsinki, International Conference of Harmonization ICH, and United States Codes of Federal Regulations and resisted under the Federal Wide Assurance (FWA) for the protection of Human Subjects. (FWA#: FWA00015574 and Expires: 04/09/2023). All participating patients in the study signed an informed consent and their privacy rights were observed.

Consent for publication
All participating patients and authors verbally agreed to publish this work considering the patient's privacy rights.

Competing interests
We declare that we do not have competing interests.

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