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Original Article

Two-year follow-up data from the STEPP-AMI study: A prospective, observational, multicenter study comparing tenecteplase-facilitated PCI versus primary PCI in Indian patients with STEMI☆,☆☆

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ABSTRACT

Background: A pharmacoinvasive strategy may alleviate the logistical and geographical barriers in timely reperfusion of ST-segment elevation myocardial infarction (STEMI), especially in a developing country like India.

Aim: To assess the safety and efficacy of pharmacoinvasive strategy versus primary PCI in STEMI patients at 2 years.

Methods: Patients enrolled in STEPP-AMI, an observational, multicenter, prospective study of 200 patients presenting with STEMI, were followed up for 2 years. Group 'A' comprised of patients with pharmacoinvasive strategy ($n = 45$), and patients who underwent primary PCI ($n = 155$) formed group 'B'. Primary endpoint was composite of death, cardiogenic shock, reinfarction, repeat revascularization of the culprit artery, or congestive heart failure at 30 days, with follow-up till 2 years.

Results: The primary endpoint occurred in 11.1% and 17.8% in group A and in 3.9% and 13.6% in group B, at 30 days and 2 years, respectively ($p = 0.07$, RR = 2.87; 95% CI: 0.92–8.97 at 30 days and $p = 0.47$, RR = 1.31; 95% CI: 0.62–2.76). There was no difference in bleeding risk between groups, 2.2% in group A and 0.6% in group B ('p' = 0.4). The infarct-related artery patency varied at angiogram; it was 82.2% in arm A and 22.6% in arm B ('p' < 0.001). In group A, failed fibrinolysis occurred in 12.1%.

☆ The study was conducted by Madras Medical Mission, Chennai, India.
☆☆ Trial is registered with Clinical trial registry of India, CTRI number: REF/2011/07/002556.

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Conclusion: A pharmacoinvasive strategy resulted in outcomes that were comparable with primary PCI at 2 years, suggesting it might be a viable option in India. Larger studies are required to confirm these findings.

1. Introduction

ST-segment elevation myocardial infarction (STEMI) is a life threatening manifestation of coronary artery disease (CAD) requiring timely reperfusion. The incidence of STEMI is higher in the Indian population when compared to developed countries and results in significant mortality.[1] The current recommendations maintain primary percutaneous coronary intervention (PCI) as the treatment of choice in the management of STEMI, contingent upon rapid initiation of treatment at centers with a skilled PCI laboratory within suggested timelines.[2] However, unavailability of primary PCI capable hospitals across India and delays in transport have restricted the access to this life-saving modality to less than 10% of patients with STEMI.[3] Of those, patients who do reach the hospital early still have to deal with other issues, such as arranging for finances, as most Indian patients pay out-of pocket, even for the emergency services, such as primary PCI.[4]

On the other hand, introduction of fibrin-specific lytic agents like tenecteplase (TNK) has improved the infarct-related artery (IRA) patency rates significantly.[5] Rapid fibrinolytic treatment after STEMI improved the outcomes in patients treated within an hour of symptom onset, with tapering benefits after 3 h.[6] However, fibrinolysis is associated with high rates of reocclusion of IRA, hence a strategy of initial bolus lysis followed by early coronary angiogram within 3–24 h of fibrinolysis, with an appropriate PCI, now known as 'pharmacoinvasive strategy,'[7] has been considered as a good alternative in the treatment of STEMI, especially in a developing country such as India.[8]

2. Methods

This is prospective, observational, multicenter pilot study, which was conducted between August 2011 and May 2013. Study sites, which were capable of performing 24/7 primary PCI, were selected from Tamilnadu (3), Karnataka (1), and Kerala (1). All study centers were well equipped to handle cardiac emergencies. A total of 200 patients who fulfilled the inclusion/exclusion criteria with STEMI were enrolled in the study. Written informed consent was signed by all the patients and the study has been cleared by the ethics committees of the respective hospitals. As this is an observational study, the treatment options were chosen entirely by the patient and the attendants; hence, some patients who presented outside the recommended timelines for thrombolysis have received lytic therapy although all centers in the study were equipped with 24 × 7 primary PCI facilities. Thrombolysis was performed in the ICU of the hospital in all centers.

The aim of the study is to assess the safety, efficacy, and feasibility of a pharmacoinvasive strategy in comparison to primary PCI in patients with STEMI. The trial's inclusion and exclusion criteria and study protocol are described in the primary publication.[9] Definitions used in the study are given in the appendix.

3. Endpoints

Our primary endpoint was set at 30 days and is a composite of death, cardiogenic shock, reinfarction, repeat revascularization, and congestive heart failure, and extended to 2 years. Safety endpoints are bleeding endpoints assessed using the TIMI classification at 30 days.

4. Statistical analysis

The detailed description of statistical analysis is published previously.[9] As this was a pilot study, primarily conducted to assess feasibility of a pharmacoinvasive strategy in STEMI patients, a sample size of 200 patients was deemed sufficient for the study. Statistical analyses were performed using SAS software, version 9.2. Chi-square or Mantel-Haenszel test or Fischer's exact test were used for observed differences between groups. Relative risk estimates with 95% confidence intervals and Kaplan–Meier curves were used to compare differences in outcomes. A p-value of 0.05 was considered significant for all the statistical evaluations.

5. Results

The results of this trial, up to 1-year follow-up, have been published previously.[9] Out of the 200 total patients enrolled, the pharmacoinvasive arm (arm 'A') had 45 patients and PPCI arm (arm 'B') had 155 patients. Baseline characteristics were no different between both groups, except more patients in arm B were in killip's class I.[9] The salient points of procedural characteristics of patients are that 6.7% ($n = 3$) patients in arm A had insignificant disease; hence no intervention was performed for them, whereas 100% of patients in arm B required angioplasty and stent implantation. Patients in arm A also had better TIMI flow at CAG (TIMI 3 flow in 27.9%), higher radial procedures (76.7%), more IRA patency (82.2%), and less thrombus burden.[9] In arm 'A', 12.1% was the incidence of failed thrombolysis.

The timelines for the study are given in Table 1; median total ischemic times are similar for both groups (245 min vs. 260 min); average door-to-balloon time is 80 min and the door-to-needle